

INPLASY

Association between Proton Pump Inhibitor and Risk of Dementia: Evidence from Eighteen Studies

INPLASY2025120003

doi: 10.37766/inplasy2025.12.0003

Received: 1 December 2025

Published: 2 December 2025

Wang, YC; Yeh, HC; Kung, YY; Islam, MM; Kung, WM.

Corresponding author:

Woon-Man Kung

nskungwm@yahoo.com.tw

Author Affiliation:

Taipei Medical University.

ADMINISTRATIVE INFORMATION

Support - No financial support.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2025120003

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 December 2025 and was last updated on 2 December 2025.

INTRODUCTION

Review question / Objective We aimed to conduct a comprehensive systematic review with meta-analysis to quantify risk of dementia among proton pump inhibitor users.

Condition being studied Association between Proton Pump Inhibitor and Risk of Dementia.

METHODS

Participant or population This article analyzed de-identified individual participant data from previously published studies. No new data involving human participants or animals were collected by any of the authors.

Intervention The concept of “intervention” is not directly applicable to this type of study.

Comparator The concept of “comparator” is not directly applicable to this type of study.

Study designs to be included This meta-analysis was conducted with the suggestions from Cochrane Systematic Reviews, and the study results are disclosed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Eligibility criteria Our study included observational researches and randomized controlled trials that assessed dementia risks with proton pump inhibitor usage. To be included, studies needed to provide appropriate information regarding selection of patients with dementia, identification of proton pump inhibitor users, and the effect size with 95% confidence intervals.

Information sources Our study systematically searched the most popular electronic databases such as PubMed, Embase, Scopus, and Web of Science for researches reported from January 1, 2000 to June 1, 2022. From the 1,723 studies of the initial search, 18 studies consisting of

1,070,835 patients with participants, were eligible for this meta-analysis. Of the 18 studies, 12 were cohort, 4 were case-control, 1 was cross-sectional, and 1 was a randomized controlled trial.

Main outcome(s) With this most recent pooled analysis of 18 studies, we found no relationship between proton pump inhibitor usage and dementia risk.

Quality assessment / Risk of bias analysis We used a modified Newcastle-Ottawa scale to assess the risk of bias from the selected enclosed case-control and cohort studies. We used the Joanna Briggs Institute critical appraisal checklist for randomized controlled trial and cross-sectional study.

Strategy of data synthesis We analyzed the pooled risk ratios with 95% confidence intervals to assess the magnitude of proton pump inhibitor usage outcomes on risk of dementia.

Subgroup analysis The subgroup analysis showed that there was no relationship between proton pump inhibitor usage and dementia risk among the subgroups.

Sensitivity analysis The pooled analysis demonstrated high heterogeneity in the studies. A sensitivity analysis was conducted to calculate the overall effect in each study of the primary findings.

Country(ies) involved Taiwan and United States.

Keywords Proton Pump Inhibitor; Dementia; Alzheimer's Disease; Meta-Analysis.

Contributions of each author

Author 1 - Yao-Chin Wang - Conceptualization, Methodology, Project Administration, Writing-Original Draft.

Email: vkwang8888@yahoo.com.tw

Author 2 - Hsien Chang Yeh - Data Curation, Validation, Visualization.

Email: b101111124@tmu.edu.tw

Author 3 - Yen Yun Kung - Investigation, Resources.

Email: kathyvivikung@gmail.com

Author 4 - Md. Mohaimenul Islam - Formal Analysis, Software.

Email: 2010rubel@gmail.com

Author 5 - Woon-Man Kung - Supervision, Validation, Writing- Reviewing and Editing.

Email: nskungwm@yahoo.com.tw