

# INPLASY PROTOCOL

To cite: Wang et al.  
Association between  
gastroesophageal reflux  
disease and depression  
disorder: a protocol for  
systematic review and meta  
analysis. Inplasy protocol  
202090026. doi:  
10.37766/inplasy2020.9.0026

Received: 06 September 2020

Published: 06 September 2020

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**Support:** Government - funded  
(No.36102).

**Review Stage at time of this  
submission:** The review has  
not yet started.

**Conflicts of interest:**  
None.

## Association between gastroesophageal reflux disease and depression disorder: a protocol for systematic review and meta analysis

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**Review question / Objective:** Is there an association between gastroesophageal reflux disease and depression disorder?

**Condition being studied:** Gastroesophageal reflux disease (GERD) is defined as a condition in which gastric contents reflux to the esophagus, causing troublesome symptoms such as heartburn and acid regurgitation. GERD is one of the most prevalent gastrointestinal disorders globally, showing an increasing prevalence in several developing countries. This disorder runs a chronic course, leads to a considerable deterioration in the quality of life of patients, and is associated with a high economic burden worldwide. Many studies have investigated the relationship between functional gastrointestinal disorder and psychological factors. A close relationship has been established between the brain and the gastrointestinal tract. For example, stress and emotions can affect gastrointestinal function, as well as the occurrence of gastrointestinal symptoms and disease. Likewise, the state of the gastrointestinal organs may affect a person's emotional status. Psychological factors may influence the severity of a functional gastrointestinal disorder by affecting the perception of pain through an action on the gut-brain axis—a concept that is also applicable to patients with GERD. To date, a few studies describing GERD have shown that psychological factors, particularly anxiety and depression, play an important role in patients with GERD. However, a comprehensive explication of this association had not yet been given.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 September 2020 and was last updated on 06 September 2020 (registration number INPLASY202090026).

### INTRODUCTION

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condition in which gastric contents reflux to the esophagus, causing troublesome symptoms such as heartburn and acid regurgitation. GERD is one of the most prevalent gastrointestinal disorders globally, showing an increasing prevalence in several developing countries. This disorder runs a chronic course, leads to a

considerable deterioration in the quality of life of patients, and is associated with a high economic burden worldwide. Many studies have investigated the relationship between functional gastrointestinal disorder and psychological factors. A close relationship has been established between the brain and the gastrointestinal tract. For example, stress and emotions can affect gastrointestinal function, as well as the occurrence of gastrointestinal symptoms and disease. Likewise, the state of the gastrointestinal organs may affect a person's emotional status. Psychological factors may influence the severity of a functional gastrointestinal disorder by affecting the perception of pain through an action on the gut-brain axis—a concept that is also applicable to patients with GERD. To date, a few studies describing GERD have shown that psychological factors, particularly anxiety and depression, play an important role in patients with GERD. However, a comprehensive explication of this association had not yet been given.

## METHODS

**Search strategy:** Two authors will screen the titles and abstracts of the all records retrieved in above electronic databases independently to find potentially eligible reviews. According to the inclusion and exclusion criteria outlined above, the full texts of them will be retrieved for further identification. Any disagreement will be resolved by discussion or by consultation with a third author. The search strategy for PubMed is presented in Table 1 and the strategy will be modified upon the requirement of other databases.

**Participant or population:** The patients with clinically diagnosed GERD, regardless of race, gender, and age.

**Intervention:** There is no intervention. Exposure will be depression.

**Comparator:** Controls will include healthy individuals, general population or patients with any respiratory disorder other than GERD.

**Study designs to be included:** All potential case-controlled studies will be included, which identified the association between GERD and DD, regardless language and publication status limitations.

**Eligibility criteria:** Children and adults (all gender, cultures, sociodemographics and age) with signs and symptoms of GERD and/or Depression. Diagnostic criteria of GERD: classic symptoms (at least mild heartburn and/or regurgitation occurring 2 or more days per week), pH monitoring, endoscopic records, and other tests. Diagnostic criteria of depression: WHO released the classification of international disease and health problems, the 10th edition (ICD - 10) diagnostic criteria; the American psychiatric association's diagnostic statistical manual of mental disorders, fourth edition (DSM - IV) diagnostic standards and the Chinese classification and diagnostic criteria for mental disorders, third edition (CCMD - 3) diagnostic standards. And including other recognized diagnostic criteria.

**Information sources:** We will search the following electronic bibliographic databases: PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, the Chinese BioMedical Literature Database, China National Knowledge Infrastructure (CNKI), the China Science and Technology Journal database (VIP) and Wanfang Data. In addition, ongoing trials will be retrieved from the WHO ICTRP Search Portal, the Chinese Clinical Trial Register and The Clinical Trials Register. Articles related to gastroesophageal reflux disease and depression will be searched. And language and time will be unlimited.

**Main outcome(s):** An established association between GERD and depression.

**Additional outcome(s):** An established cause and effect relationship between GERD and depression.

**Data management:** Two authors will screen the titles and abstracts of the all records retrieved in above electronic databases

independently to find potentially eligible reviews. According to the inclusion and exclusion criteria outlined above, the full texts of them will be retrieved for further identification. Any disagreement will be resolved by discussion or by consultation with a third author. Data will be extracted by two reviewers independently using a pre-designed data extraction form. A third reviewer will validate data. The following data will be extracted: General information, Trial characteristics, Intervention(s) and control(s), Participants, Study methodology, Outcomes, Results, etc.

#### **Quality assessment / Risk of bias analysis:**

The methodological quality of eligible studies will be assessed by two review authors independently according to the the Cochrane Handbook for Systematic Reviews of Interventions. The following characteristics will be assessed: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), other bias. Based on the assessments of the studies against these seven domains, they will be classified as being of “low risk”, “high risk” or “unclear risk” of bias. Any disagreements will be resolved by discussion or discussed with another reviewer if necessary.

**Strategy of data synthesis:** We will generate a narrative synthesis summarizing findings from the included studies. Data of interest will be collected from the included articles and arranged in the following table fields: author and year of publication, population, intervention, comparison characteristics and outcomes (PICO).

**Subgroup analysis:** If results of the meta-analysis are significantly heterogeneous, subgroup analyses of the control groups might be performed.

**Sensibility analysis:** If sufficient trials are identified, we plan to conduct a sensitivity analysis comparing the results using all trials with high methodological quality:

studies classified as having a ‘low risk of bias’ versus those identified as having a ‘high risk of bias’.

**Country(ies) involved:** China.

**Keywords:** Gastroesophageal Reflux; Human; Depression; Depression Disorder.

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

Author 1 - Yangang Wang - Conceptualization.

Author 2 - Shixiong Zhang - Formal analysis.

Author 3 - Yu Liu - Data curation.

Author 4 - Panpan Zhou - Methodology.

Author 5 - Huiqing Wu - Supervision.