

# INPLASY PROTOCOL

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**Support:** None.

**Review Stage at time of this submission:** Preliminary searches.

**Conflicts of interest:**  
None declared.

## INTRODUCTION

**Review question / Objective:** What's the association between the gut microbial homeostasis and the autoimmune thyroid disease? What's the potential mechanisms of the gut microbiota in AITD? If the altered

## Association Between Gut Microbiota and Autoimmune Thyroid Disease: A Systematic Review and Meta-Analysis

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**Review question / Objective:** What's the association between the gut microbial homeostasis and the autoimmune thyroid disease? What's the potential mechanisms of the gut microbiota in AITD? If the altered gut microbiota accelerates or prevents disease progression?

**Condition being studied:** Hashimoto's thyroiditis (HT) and Graves' disease (GD) are the most prevalent forms of autoimmune thyroid disease (AITD), which are the risk factors for hypothyroidism, cardiovascular diseases and adverse pregnancy outcomes. We have already known that the gut microbiota is relevant to human body's natural immune system. Besides, several studies proved that the inflammasome plays a key role in the pathogenesis of Hashimoto's thyroiditis, which can be regulated by the gut microbiota. Thus, there might be a possible relevance between the gut microbiota and AITD. We aim to elucidate the changes of gut microbiome in patients with AITD and try to figure out what's role that the altered microbiota plays in the pathogenesis of AITD.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 April 2021 and was last updated on 26 April 2021 (registration number INPLASY202140135).

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## METHODS

**Search strategy:** We will search the following databases without restriction of language or publication period to find relevant publications: PubMed (MEDLINE), Web of Science, Embase and Cochrane. We may use the following terms: "(Thyroid disease OR Thyroiditis OR Hashimoto Disease OR Graves Disease) AND (Microbiota OR Gastrointestinal Microbiome OR Gut Microbiota). At least three independent reviewers will participate in the searches and all the relevant literatures will be screened manually by reading the title/abstract as well as full text. We will eliminate irrelevant studies based on the clear inclusion and exclusion criteria. All the searches will be finished before the final analyses.

**Participant or population:** Inclusion criteria: 1) Adults (above 18 years old) who are diagnosed Autoimmune Thyroid Disease concluding Hashimoto's thyroiditis and Graves' Disease by measuring the clinical parameters such as thyroid peroxidase antibodies (anti-TPO) and anti-TSH receptor antibody (TRAb) level. 2) Including information about sample and prevalence of specific bacteria assessed. Exclusion criteria: 1) People with other immune disease, history of thyroid surgeries, or pregnancy. 2) patients who used antibiotics in the last week before collection of fecal samples.

**Intervention:** 16SrRNA sequence technique is performed to test the taxonomy of bacteria between the AITD group and healthy controls.

**Comparator:** Healthy subjects with matched age, sex, BMI, and dietary habits.

**Study designs to be included:** 1) case-control studies or cohort studies.

**Eligibility criteria:** 1) investigating gut bacteria on adults diagnosed with AITD. 2) including information about sample and prevalence of the specific bacteria assessed. 3) written in English.

**Information sources:** PubMed (MEDLINE), Web of Science, Embase and Cochrane.

**Main outcome(s):** The main outcome is the association between AITD and the gut microbiota, which includes the percentage or relevant abundance of the altered bacteria at phylum to species levels. Besides the bacterial diversity between the AITD and the healthy controls will represent the gut microbiota community has changed in the process of the AITD disease.

**Quality assessment / Risk of bias analysis:** We will use The Newcastle Ottawa Scale (NOS) to evaluate all the included essays, including the trial group selection, comparability, exposure and outcome. The total score ranges from five to nine (with nine is the highest) and a higher score indicating higher quality.

**Strategy of data synthesis:** A fixed-effect model and a random-effects model will be used to report the results. Statistical heterogeneity will be assessed by the I<sup>2</sup> value, which represents the total variation across different studies. We may choose a random-effects model if the I<sup>2</sup> index > 50%, otherwise, a fixed-effects model will be used. Before the data synthesis, we will calculate the ratio of the bacterial percentage of AITD patients and assess the relative abundance value in patients with AITD compared to controls. If possible, we also plan to analyze the influence of bias

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control and evidence of publication bias by using funnel plots and regression analysis.

**Subgroup analysis:** None.

**Sensitivity analysis:** The sensitivity analysis was done by the STATA version 12.0 through deleting one essay.

**Language:** English.

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

**Keywords:** Gut microbiota; autoimmune thyroid disease; Hashimoto's thyroiditis.

**Contributions of each author:**

**Author 1 - Boshen Gong -** The author searched the electronic data base and extracted the data included.

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**Author 2 - Fanrui Meng -** The author searched the data base and did statistical synthesis.

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**Author 3 - Yang Yang -** The author made the inclusion and exclusion criteria.

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