

# INPLASY PROTOCOL

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The authors declare that there  
is no conflict of interest  
regarding this meta-analysis.

## Association of Thyroid Hormone Therapy with Mortality in Adults with Subclinical Hypothyroidism: A systematic review and meta-analysis

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**Review question / Objective:** **P:** Adults diagnosed with subclinical hypothyroidism; **I:** Thyroid hormone therapy; **C:** No treatment; **O:** Improving all-cause and cardiovascular mortality.

**Condition being studied:** Conflicting results of the association between subclinical hypothyroidism and mortality were published from several large-scale meta-analyses. Both American Thyroid Association and European Thyroid Association do not recommend treatment of subclinical hypothyroidism if TSH is 10 mIU/L or less unless the patient is symptomatic. There is no meta-analysis studying the impact of thyroid hormone therapy for subclinical hypothyroidism on mortality.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 June 2020 and was last updated on 23 June 2020 (registration number INPLASY202060086).

### INTRODUCTION

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symptomatic. There is no meta-analysis studying the impact of thyroid hormone therapy for subclinical hypothyroidism on mortality.

## METHODS

**Search strategy:** Terms: subclinical hypothyroidism, thyroxine treatment, mortality. Databases: Pubmed, Embase, Scopus, Web of Science, Clinicaltrials.gov.

**Participant or population:** Adults with subclinical hypothyroidism.

**Intervention:** Levothyroxine.

**Comparator:** Untreated group or placebo.

**Study designs to be included:** Observational studies and randomized controlled trials.

**Eligibility criteria:** 1. participants are adults with diagnosis of subclinical hypothyroidism; 2. outcomes included all-cause mortality and/or cardiovascular-related mortality of both thyroid hormone-treated and untreated groups; 3. original articles.

**Information sources:** For RCTs: original articles and trial registers. For observational studies: original articles and contact with authors.

**Main outcome(s):** All-cause mortality.

**Additional outcome(s):** Cardiovascular mortality.

**Quality assessment / Risk of bias analysis:** We will use the Newcastle–Ottawa Scale for cohort/case-control studies and Cochrane Risk of Bias Tool for randomized controlled trials.

**Strategy of data synthesis:** We will synthesize the RRs that were obtained from both RCTs and observational studies to calculate the pooled RRs in our meta-analysis. We will calculate the pooled RRs and their 95% confidence intervals (CIs)

using the DerSimonian and Laird random effects model.

**Subgroup analysis:** The subgroups-to-analysis will be study design, sample size, mean age, and baseline risks of cardiovascular diseases.

**Sensitivity analysis:** A sensitivity analysis will be conducted by omitting each study individually to evaluate the influence of each study on the overall pooled estimate.

**Language:** English.

**Country(ies) involved:** Taiwan and the U.S.

**Keywords:** Subclinical hypothyroidism, Thyroid hormone therapy, Mortality.

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