

INPLASY PROTOCOL

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None declared.

Association of subclinical thyroid dysfunction with the risk of vertebral fracture: A systematic review and meta-analysis

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Review question / Objective: To investigate the relation between subclinical thyroid dysfunction and the risk of vertebral fracture.

Eligibility criteria: Study was included if they met: (1) Participants: general population free of vertebral fracture; (2) Exposure: SCH or SH; (3) Control: TSH within normal range; (4) Outcome: the effect estimate (risk ratio [RR], hazard ratio [HR], or odds ratio [OR]) with 95% confidence intervals (CIs) for comparisons of SCH or SH and euthyroidism; and (5) Study design: the study had to have prospective cohort design.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 May 2023 and was last updated on 24 May 2023 (registration number INPLASY202350093).

INTRODUCTION

Review question / Objective: To investigate the relation between subclinical thyroid dysfunction and the risk of vertebral fracture

Condition being studied: Subclinical thyroid dysfunction have demonstrated associated with an elevated risk of nonvertebral fractures, whereas the association of

subclinical thyroid dysfunction with the risk of vertebral fracture remained controversial.

METHODS

Search strategy: ("hypothyroidism" OR "subclinical hypothyroidism" OR "hyperthyroidism" OR "subclinical hyperthyroidism" OR "thyroid diseases" OR "thyroid function" OR "thyroid status") AND

("fracture" OR "fractures") AND ("vertebral" OR "spine").

Participant or population: General population free of vertebral fracture.

Intervention: SCH or SH.

Comparator: TSH within normal range.

Study designs to be included: The study had to have prospective cohort design.

Eligibility criteria: Study was included if they met: (1) Participants: general population free of vertebral fracture; (2) Exposure: SCH or SH; (3) Control: TSH within normal range; (4) Outcome: the effect estimate (risk ratio [RR], hazard ratio [HR], or odds ratio [OR]) with 95% confidence intervals (CIs) for comparisons of SCH or SH and euthyroidism; and (5) Study design: the study had to have prospective cohort design.

Information sources: We systematically searched PubMed, EmBase, and the Cochrane library to identify potential included studies throughout May 2023.

Main outcome(s): The effect estimate (risk ratio [RR], hazard ratio [HR], or odds ratio [OR]) with 95% confidence intervals (CIs) for comparisons of SCH or SH and euthyroidism.

Quality assessment / Risk of bias analysis: The methodological quality of included studies were assessed using the Newcastle-Ottawa Scale (NOS), which have already partially validated for assessing the quality of observational studies in meta-analysis.

Strategy of data synthesis: The associations of subclinical thyroid dysfunction with the risk of vertebral fracture were examined based on the effect estimate and 95%CI in individual study, and the random-effects model was applied to calculate the pooled RR and 95%CI, which considering the underlying varies among included studies. I² and Cochren Q statistic were applied to assess the

heterogeneity across included studies, and the significant heterogeneity was defined as I² > 50.0% or P < 0.10.

Subgroup analysis: Subgroup analyses for the associations of subclinical thyroid dysfunction with the risk of vertebral fracture were performed based on sample size, median age, male proportion, follow-up duration, adjusted level, and study quality, while the difference between subgroups was compared using interaction P test.

Sensitivity analysis: The robustness of pooled conclusion was assessed using a sensitivity analysis through sequential removing single study.

Language restriction: No restriction were placed on published language.

Country(ies) involved: China.

Keywords: subclinical thyroid dysfunction; vertebral fracture; systematic review; meta-analysis.

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