Thyroid function and the risk of fibrosis of the liver, heart and lung in humans: Protocol for a systematic review and meta-analysis

**Review question**
What is the association of thyroid function with the risk of fibrosis of the liver, heart and lung in humans?

**Searches**
An expert medical librarian will perform the search through Pubmed, Web-of-Science, Embase Ovid and Medline Ovid. There will be no language nor date restrictions.

**Types of study to be included**

*Inclusion criteria*
(i) Observational studies that investigated the association of thyroid function with fibrosis of the liver, heart, or lung, in humans;  
(ii) Studies reporting effect estimates with 95% confidence intervals (CIs), or mean differences with standard deviations (p-values), or prevalence differences (p-values).  
(iii) No restrictions on publication year or language.

*Exclusion criteria*
(i) Case-reports, letters to the editor, proceedings, reviews, systematic reviews, meta-analyses, conference abstracts, and animal studies.  
(ii) Studies that focused exclusively on the role of thyroid function altering medications on fibrotic diseases.

**Condition or domain being studied**
Thyroid function, fibrosis.

**Participants/population**
Population with data available on thyroid function and fibrotic diseases of the liver, lung, and heart.

**Intervention(s), exposure(s)**
Thyroid hormones, thyroid status
Main outcome(s)
Fibrotic diseases of the liver, heart and lung, evaluated via noninvasive or invasive measures.

Data extraction (selection and coding)
This systematic review will be conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines for transparent reporting. Four electronic databases, including Pubmed Publisher, Web-of-Science, Embase and Medline Ovid, will be searched with the help of expert librarians. Two independent reviewers will screen the titles and abstracts. The full text articles of potentially relevant articles will be obtained and independently evaluated. Any disagreement regarding inclusion will be resolved through consensus. A third independent reviewer will be assigned in case of persisting disagreement. Full texts and reference lists of the selected articles will be hand searched in order to identify additional studies. A predesigned data collection form will be used to extract relevant information from the selected studies, including article source, sample size, demographics of study participants, methods of assessing thyroid function and fibrosis, study results and conclusions.

Risk of bias (quality) assessment
The quality of the included studies will be assessed separately by two reviewers using the Newcastle–Ottawa Scale (NOS) for non-randomized studies in meta-analyses. The NOS scale evaluates the study quality based on 3 domains, namely selection of participants, comparability of study groups, and ascertainment of the outcomes of interest. Each study could have a maximum of 9 stars.

Strategy for data synthesis
We will provide a narrative synthesis of the findings of eligible studies. The effect estimates with 95% confidence intervals (CIs), or mean differences with standard deviations (p-values), or prevalence differences (p-values), will be reported in a summary table. If a meta-analysis is possible, the effect estimates will be pooled, and forest plots will be constructed. Heterogeneity will be assessed by using the $I^2$ statistic, with $I^2 \leq 25\%$ considered as low, $I^2$ between 25% and 75% as moderate, and $I^2 \geq 75\%$ as high. Statistical analyses will be performed in Stata version 15.1 (StataCorp LLC, Texas, USA).

Analysis of subgroups or subsets
The following sensitivity analyses will be performed, if applicable: (1) We will use random-effects models in order to test for heterogeneity; (2) We will exclude the studies that provide unadjusted estimates.
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Type and method of review
Systematic review, Meta-analysis
Funding sources/sponsors
Arjola Bano was supported by an exchange fellowship from the European Thyroid Association. The funding source had no role in the selection, critical appraisal, or synthesis of evidence

Conflicts of interest
None

Language
English

Country
Switzerland

Stage of review
Review Ongoing

Subject index terms
Thyroid function; fibrosis of the liver, lung and heart; humans

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