Effects of thyroid hormone suppression therapy on adverse clinical outcomes in thyroid cancer

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Authors' objectives
To evaluate the effect of thyroid hormone suppression therapy (THST) on the clinical outcomes of papillary and/or follicular well-differentiated thyroid cancer (ThyrCa).

Searching
MEDLINE and EMBASE were searched using the search terms listed in the report. Manual searches of literature (1937 to 2000) were also performed. There were no language restrictions, but only published studies were eligible for inclusion.

Study selection
Study designs of evaluations included in the review
The review did not state a priori inclusion criteria for study design. The included studies were described as case series, registry, retrospective chart review, retrospective analysis, prospective cohort, natural history study and short-term intervention. The follow-up ranged from 12 to 18 weeks to up to 39 years. The studies had to have a comparator group to be included in the meta-analysis.

Specific interventions included in the review
The inclusion criteria specified THST as a component of the treatment for ThyrCa. The comparators were not stated a priori and those included were not stated in the report. The most frequently used treatment was levothyroxine. Desiccated thyroid was also used and many studies did not specify which form of THST was used.

Participants included in the review
The inclusion criteria specified patients with well-differentiated papillary and follicular ThyrCa.

Outcomes assessed in the review
The outcomes of interest were disease progression, disease recurrence and mortality.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not use a formal method to assess validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. For each study included in the meta-analysis, an incidence risk ratio and 95% confidence intervals (CIs) were calculated for the adverse clinical outcome reported, i.e. disease progression (1 study), disease recurrence (2 studies) and death (7 studies).

Methods of synthesis
How were the studies combined?
A meta-analysis was used to calculate the combined relative risk (RR) of an adverse clinical outcome with 95% CIs using the Mantel-Haenszel method. This involved pooling mortality, disease progression and recurrence from separate
trials into one outcome measure. The authors also performed an overall analysis of causal inference using modified
Hill criteria (see Other Publications of Related Interest) in which they included all 28 studies identified.

How were differences between studies investigated?
The Breslow-Day chi-squared test was used to assess statistical heterogeneity between the studies in the meta-analysis.

Results of the review
Twenty-eight studies were identified but only 10 were included in the meta-analysis. These included case series,
retrospective chart review, retrospective analysis, prospective cohort, and registry studies that the authors described
collectively as longitudinal cohort studies. The number of participants was 4,174.

The meta-analysis showed that THST decreased the risk of adverse clinical outcomes (RR 0.73, 95% CI: 0.60, 0.88,
P<0.05). There was significant heterogeneity between the studies (P=0.001) with the results of 3 studies being in
favour of the comparator.

The Hill criteria analysis found that a ‘probable’ association exists between THST and the reduction of major adverse
clinical events.

Authors' conclusions
The authors stated that THST appears justified in patients with papillary or follicular ThyCa.

CRD commentary
The inclusion criteria were not reported clearly and no details were given about the conduct of the review. Hence, the
potential for bias cannot be ruled out. Since only published studies were eligible for inclusion there is also the
possibility of publication bias in the review. The quality of the design and conduct of the included studies was not
assessed. Important details of the included studies (e.g. participant characteristics and comparators) were missing from
the report, making it difficult to interpret the findings. The authors' pooling of data from disparate study designs in the
presence of significant statistical heterogeneity raises serious doubts about the reliability of the pooled estimate of the
treatment effect. The authors' conclusions are probably too strong given the weak strength of the evidence reviewed
and the apparent shortcomings in the methodology of the review.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that larger-scale, better designed studies, either prospective or derived from ongoing
cancer registries, are needed to better define the effect of THST on major adverse clinical events in this malignancy.

Bibliographic details
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Other publications of related interest
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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.