Screening for thyroid disease

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CRD summary
This review aimed to evaluate the usefulness of thyroid function tests. The authors concluded that large randomised trials are needed to investigate effects on quality of life in healthy people with abnormal thyroid-stimulating hormone levels and normal thyroxine levels. The poor search, small number of trials identified, small sample sizes and lack of methodological details, make the reliability of the results uncertain. A more thorough review might have provided more answers.

Authors' objectives
To determine whether it is useful to order a thyroid function test in patients who have no history of thyroid disease and who have few or no signs or symptoms of thyroid dysfunction.

Searching
MEDLINE (1966 to February 2002), EMBASE (1966 to February 2002), PREMEDLINE (March 2002) and the Cochrane Library (Issue 2, 2002) were searched; the search terms were reported. Reference lists of reviews, personal collections of full-text articles of the authors, and endocrinologic and medical journals were handsearched for additional and earlier articles.

Study selection
Study designs of evaluations included in the review
Controlled trials of the treatment of thyroid dysfunction and observational studies of the long-term adverse effects of therapy were eligible for inclusion.

Specific interventions included in the review
Studies of levothyroxine therapy were eligible for inclusion. The studies had to include at least some patients that were taking replacement doses of thyroxine to be eligible for inclusion. Studies of suppressive doses of thyroxine were excluded. The dose of levothyroxine used in the included studies ranged from 25 microg (titred up) to 150 microg.

Participants included in the review
Studies that used elevated thyrotropin (TSH) as a criterion for entry, in any population, were included. The participants in the included studies were predominantly women, with at least 3 studies restricted to women. The mean age, where reported, ranged from 49 to 68 years. The studies were generally carried out in out-patient clinics; one study was a population screening-based study.

Outcomes assessed in the review
The studies had to report at least one health outcome (symptoms, cognitive function, or quality of life) or lipid levels to be eligible for inclusion.

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

Assessment of study quality
The internal validity of the included randomised trials was assessed using criteria from the U.S. Preventive Services Task Force. Such criteria related to: randomisation; allocation concealment; similarity of the control and treatment groups at baseline; specification of eligibility criteria; blinding of the patients, assessors and carers; use of an intention-to-treat analysis; and attrition. The studies were scored as good, fair or poor. The author did not state how validity was assessed, or how many reviewers performed the validity assessment.
Data extraction
The author did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The author extracted pre- and post-treatment signs and symptoms, TSH levels or low-density lipoprotein (LDL) cholesterol levels for each study and, where reported, the number of participants experiencing adverse events.

Methods of synthesis
How were the studies combined?
The studies were discussed in a narrative synthesis.

How were differences between studies investigated?
Differences between the studies were discussed in the text.

Results of the review
Eight randomised controlled trials (RCTs) investigating hypothyroidism (n>291, one study did not state sample size) were included in the review. The duration of follow-up ranged from 6 to 12 months.

Of the 8 RCTs, five were rated as poor quality, two as fair and one as good.

Efficacy of treatment for subclinical hypothyroidism (8 studies).

One study reported a statistically significant improvement in symptoms in those with Graves' disease, measured using the Cooper Questionnaire, with levothyroxine compared with placebo (P=0.037). This was deemed the highest quality trial. Another, lower quality, study reported no significant difference in symptoms between the levothyroxine and placebo group in this subgroup of patients.

Two studies, one of people with Graves' disease and one of people with Hashimoto's thyroiditis, reported a statistically significant pre-post reduction in lipids in those treated with levothyroxine, with no reduction in the placebo group. However, when the treatment and placebo groups were compared directly, there was no statistically significant difference in lipids in either trial.

Three trials of people (primarily women) with subclinical hypothyroidism who were not previously treated for Graves' disease reported no effect of levothyroxine on symptoms or lipids, one reported small improvements in cognitive measures, and one a 0.9 mmol/L reduction in LDL cholesterol. Two of these studies were deemed to have poor internal validity.

Adverse events (3 studies).

One study reported a drop-out rate of 10% (2 people) due to nervousness and palpitations, another 11% (2 people) due to unspecified complications, while the third reported increased anxiety scores in the levothyroxine group.

Authors' conclusions
Large randomised trials are needed to determine whether treatment will improve quality of life in healthy patients who have abnormal TSH levels and normal thyroxine levels.

CRD commentary
The review question was clear in terms of the participants, interventions, outcomes and study design. The author searched several relevant sources, but it was unclear whether any language restrictions were applied and publication bias was not investigated. There were no details of the methods used for the study selection, validity assessment and data extraction stages, therefore it was not possible to determine whether any efforts were made to reduce the introduction of error and bias during the review process. The decision to combine the studies in a narrative seemed appropriate. Considering the small number of trials, with small sample sizes, and the lack of methodological details, the results of...
the review should be treated with caution; it may be that a more thorough review could have shed further light on the question.

**Implications of the review for practice and research**

**Practice:** The author did not state any implications for practice.

**Research:** The author stated that large randomised trials of treatment are needed to determine the likelihood that treatment will improve quality of life in otherwise healthy patients who have abnormal TSH levels and normal thyroxine levels.

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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.