Authors' objectives
To review information on the benefits of screening with a thyroid-stimulating hormone (TSH) test for thyroid dysfunction in asymptomatic patients seeking primary care for other reasons. A subsidiary aim was to evaluate the efficacy of treatment for subclinical thyroid dysfunction.

Searching
The authors reviewed the original literature from 1989 to 1996 to identify articles that were not included in the original College background paper (Helfand & Crapo, 1990; see Other Publications of Related Interest). In a MEDLINE search, the MeSH terms "thyroid function tests" and "thyroid diseases" were combined with the term "mass screening" and the textwords "screening" or "case finding". A separate MEDLINE search (1970 to 1996) was conducted for controlled studies of the effect of thyroid-directed treatments on potential complications of subclinical thyroid disease. Periodic handsearching of endocrinologic and major medical journals, review of the reference lists of retrieved articles, and retrieval of articles reviewed in the Helfand & Crapo (1990) paper supplemented the MEDLINE searches. [A: Experts and interested parties who peer-reviewed the study were invited to bring unpublished material to the attention of the authors]

Study selection
Study designs of evaluations included in the review
Screening studies and controlled studies of treatment for subclinical thyroid dysfunction.

Specific interventions included in the review
A test of serum thyroid-stimulating hormone (TSH) or thyroxine for thyroid dysfunction.

L-thyroxine treatment for subclinical thyroid dysfunction.

Reference standard test against which the new test was compared
The review did not include any diagnostic accuracy studies that compared the performance of the index test with a reference standard of diagnosis.

Participants included in the review
Asymptomatic patients seeking primary care. Patients receiving treatment for subclinical hypothyroidism or subclinical hyperthyroidism were also included, regardless of whether the studies involved patients identified by screening. Patients were from the general adult population, a demographic segment of the adult population, or among patients seen in the general office setting. Studies of screening in inpatients, institutionalised patients, and patients known to have diabetes, depression, obesity, or other conditions were excluded.

Outcomes assessed in the review
The prevalence of overt and subclinical thyroid dysfunction, the evidence for the efficacy of treatment, and the incidence of complications in defined age and sex groups were extracted from each study.

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

Assessment of study quality
The authors do not state that they assessed validity. [A: The validity of the included studies was not assessed using a scoring system. However, the methodological characteristics of the 3 randomised trials were reported in the text and...
Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

To assess effectiveness, the authors reviewed randomised trials and other comparison studies that contained information about the effect of treatment on each complication. For each controlled trial, the difference between the probability of a response in the treatment and control groups for each complication studied was recorded (the inverse of this is the number needed to treat).

Methods of synthesis
How were the studies combined?
Information from population-based and office-based studies of screening were pooled to estimate the prevalence of each type of thyroid dysfunction.

For each complication, estimates of the prevalence and effectiveness of treatment were used to calculate the number needed to treat (NNT) and the number needed to screen to benefit one patient.

How were differences between studies investigated?
The authors did not report a test for heterogeneity.

The results were divided into three sections:

1. Benefits of detecting overt hyperthyroidism and overt hypothyroidism.
2. Benefits of detecting subclinical hyperthyroidism.
3. Benefits of detecting subclinical hypothyroidism.

Results of the review
There were 33 screening studies and 23 controlled studies of treatment for subclinical hypothyroidism or subclinical hyperthyroidism. The total number of participants was not stated.

Screening can detect symptomatic but unsuspected overt thyroid dysfunction. The yield is highest for women older than 50 years of age. Among all women older than 60 years of age, office-based screening detected 14 cases of overt hypothyroidism or hyperthyroidism per 1000 women, or 1 case per 71 women (95% CI: 59 women, 111 women) screened.

Treating subclinical hyperthyroidism: Because no randomised trials of antithyroid treatment in asymptomatic persons have been done, the effect of early treatment in preventing atrial fibrillation or bone fracture in the future is not known. Given the sparse data that are available, it is not clear that monitoring these persons with thyroid function tests would:

1. Prevent the spontaneous development of overt hyperthyroidism or atrial fibrillation.
2. Reduce the time spent in these states.

Treating subclinical hypothyroidism: Results of three small trials on symptom relief are inconsistent and data are insufficient to determine whether treatment is beneficial in patients with a mildly elevated TSH level. Early treatment is most likely to be effective in patients who have a markedly elevated TSH level (greater than or equal to 10 mU/L). On the basis of randomised trials, 1 in 8.3 of these women (1 in 519 screened) may benefit from L-thyroxine therapy given to relieve symptoms. By 5 years, treatment would prevent overt hypothyroidism in 1 of 2 patients, or in 1 of 112 patients screened. There are no data from randomised trials about the benefit of treatment to prevent hypothyroidism.
Treatment may reduce the cholesterol level by an average of 8% in patients who have a TSH level of 10 mU/L or more and an elevated serum cholesterol level. One in every 250 patients screened may benefit. If therapy were effective in every patient (NNT=1), 1 case of coronary artery disease could be prevented for every 95 to 200 patients treated by 5 years. However, the probability of cholesterol reduction and the prevalence of other cardiac risk factors in women found by screening to have a TSH level greater than or equal to 10 mU/L are not known, so the actual benefit is uncertain.

Authors' conclusions
Office-based screening to detect overt thyroid dysfunction may be indicated in woman older than 50 years of age. Evidence of the efficacy of treatment for subclinical thyroid disorder is inconclusive.

CRD commentary
The authors present a clear review question. Inclusion and exclusion criteria were appropriate.

The search could have been extended to include other databases such as EMBASE. Handsearching of journals was performed only "periodically" and the specific journals searched were not stated. The validity of the included studies was not formally assessed. Sufficient study detail was only presented for recent screening studies and three randomised trials of treatment for subclinical hypothyroidism. No details on other studies were reported. Tests for heterogeneity were not performed before the studies were combined.

The conclusions follow from the results, but both should be interpreted with the limitations above in mind.

Implications of the review for practice and research
Practice: The authors state the following.

1. Primary care office-based screening with a sensitive TSH test in women older than 50 years of age may be indicated.

2. A free thyroxine test should be done in women older than 50 years of age when the TSH level is undetectable or is 10 mU/L or greater.

3. Screening in women younger than 50 years of age and in men is not warranted because the prevalence of unsuspected overt thyroid dysfunction is low.

4. Patients who are found to have relatively specific symptoms and signs (such as goiter, nodule, eye findings of Graves disease or tremor) should be referred to an endocrinologist for consideration of treatment, but the management of patients with none of these findings is not clear.

5. The available evidence is not sufficient to recommend for or against treatment for subclinical hypothyroidism.

Research: The authors make the following suggestions for future research.

1. Large randomised trials are needed to determine the likelihood that treatment will improve quality of life in otherwise healthy patients who have mildly elevated TSH levels.

2. Larger, well-designed randomised trials are needed to determine whether treatment would be effective in office based screening of otherwise healthy primary care patients.

3. Future prospective, concurrent comparison studies should examine the effects of screening on health outcomes. These studies should be large enough to determine the likelihood that specific subgroups of patients will benefit from treatment in relation to their age, sex, clinical findings, quality of life, and TSH level.

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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.