Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Screening for subclinical hypothyroidism in the elderly, using thyroid-stimulating hormone (TSH), triiodothyronine (T3) and thyroxine (T4) serum level measurements, was studied.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised men and women aged 60 years who attended clinics periodically for health examinations.

Setting
The setting was primary care. The economic analysis was carried out in Milan, Italy.

Dates to which data relate
The dates to which the data related, were not reported. The price year was 1996.

Source of effectiveness data
The effectiveness data were derived from a decision-analytical model published in 1996.

Modelling
A Markov model was developed where a hypothetical cohort of elderly patients made transitions between health states at annual intervals for 15 years. The health states were well, euthyroid state, subhypothyroidism, overt hypothyroidism, myxoedema, coronary heart disease (CHD) and death. Serum TSH measurements were added every 5 years and, if abnormal, serum T3 and T4 levels were also measured. Patients diagnosed with subclinical hypothyroidism were also tested for the presence of anti-thyroid antibodies.

Outcomes assessed in the review
The outcomes assessed in the review and used as model inputs were the prevalence and incidence of subclinical hypothyroidism, and the probabilities of transition from one state to another.
Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Three primary studies were included in the review. One was an unpublished Italian survey on the prevalence of subclinical hypothyroidism. The second was a published decision-analytical model, which was used to derive the incidence of subclinical hypothyroidism and the probabilities of transition from one state to another (Danese et al., see Other Publications of Related Interest). The remaining study was a published meta-analysis of data on the reduction in total cholesterol level with thyroxine (Tanis et al., see Other Publications of Related Interest).

Methods of combining primary studies
A narrative method was used to report the outcome estimates.

Investigation of differences between primary studies
Not reported.

Results of the review
The prevalence of subclinical hypothyroidism was estimated to be 11% in the elderly female population and 5% in the elderly male population.

The incidence of subclinical hypothyroidism was estimated to be 2.8% in the elderly female population and 0.14% in the elderly male population.

The average relative reduction in total cholesterol levels achievable with thyroxine was approximately 6%.

Methods used to derive estimates of effectiveness
The authors made assumptions to derive the estimates of prevalence of hypercholesterolaemia and the sensitivity of early hypothyroidism screening. The annual probabilities of developing CHD were calculated using a formula derived from the Framingham prediction model (Anderson et al., see Other Publications of Related Interest).

Estimates of effectiveness and key assumptions
The prevalence of hypercholesterolaemia was 25%.

The sensitivity of early hypothyroidism screening was 100%.

The annual probability of developing CHD was not reported.
Measure of benefits used in the economic analysis
The health benefits were measured in terms of the quality-adjusted life-years (QALYs) gained. A published decision-analytical model was used to estimate the utility adjustment for life assigned to each health state. The average numbers of QALYs for each strategy were reported. The QALYs were discounted at an annual rate of 5%.

Direct costs
The perspective adopted was that of the NHS in Italy. The costs reflected 1996 values. The direct costs included those of screening (cholesterol, TSH, T3 and T4 measurements, and anti-thyroid antibody determination), the cost of myxoedema, the average annual cost of CHD, annual treatment with thyroxine for overt hypothyroidism and for subclinical hypothyroidism (average daily dose of 100 to 125 microg), average annual cost of pharmacological treatment for hypercholesterolaemia, and specialist consultations. The cost of myxoedema was estimated from the current charges of hospital admission and treatment fees. Clinical examinations by general practitioners were not included. Official fees for the screening tests, as obtained from the Ministry of Health, were used as a proxy of their actual costs to the NHS. The costs and the quantities were not reported separately. The costs were discounted at an annual rate of 5%.

Statistical analysis of costs
No statistical analysis of the costs was performed.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
Italian lira (L).

Sensitivity analysis
One-way sensitivity analyses were performed on the probabilities and utilities.

Estimated benefits used in the economic analysis
Over 15 years, the additional benefits of annual testing for subclinical hypothyroidism were 0.64 QALY gained in a female population and 0.28 QALY gained in a male population.

If testing were performed every 15 years, the additional benefits of testing were 0.06 QALY gained in a female population and 0.11 QALY gained in a male population.

Cost results
Over 15 years, the incremental costs of annual testing for subclinical hypothyroidism were L608,142 in a female population and L220,934 in a male population.

If testing were performed every 15 years, the incremental costs of testing were L223,230 in a female population and L157,452 in a male population.

Synthesis of costs and benefits
Over 15 years, the cost-effectiveness ratio of annual testing for subclinical hypothyroidism was L950,843 per QALY gained in a female population and L789,386 per QALY gained in a male population.

If testing were performed every 15 years, the cost-effectiveness ratio of testing was L3,424,183 per QALY gained in a
female population and £1,484,324 per QALY gained in a male population.

In a female population, the best cost-effectiveness ratio was observed when the patients were tested for subclinical hypothyroidism every 3 years (£589,195 per QALY gained). Increasing the frequency to every 4 to 5 years gave less favourable results, with decreasing marginal benefits and a lower cost-effectiveness ratio.

In a male population, the best cost-effectiveness ratio was observed when patients were screened every 2 to 3 years (£671,377 and £672,123 per QALY gained, respectively), with the cost per QALY gained increasing thereafter due to the very limited marginal benefit achieved.

The results were sensitive to variations in the prevalence of subclinical hypothyroidism and in the effectiveness of thyroxine in reducing cholesterol serum levels. Better cost-effectiveness profiles were obtained for populations with a higher disease prevalence and a higher relative cholesterol reduction.

**Authors’ conclusions**
A screening policy for subclinical hypothyroidism in the elderly population in a primary-care setting could be worthwhile, with a relatively low additional cost per quality-adjusted life-year (QALY) gained, especially in the female population.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator, no intervention, was clear. It represented current practice in the authors’ setting. You should decide if it represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The principal input parameters for the model were derived from published studies. However, it was unclear whether the review was conducted in a systematic way to identify relevant research and minimise biases. The authors did not report in detail the method used to derive the estimates of effectiveness. It was difficult to judge the internal validity due to the limited reporting on how the estimates of effectiveness were derived. When the effectiveness estimates were derived from the authors’ assumption about the sensitivity of early hypothyroidism screening, the authors did not justify their assumption. The probability estimates were investigated using a sensitivity analysis. The ranges used appear to have been appropriate, although they were not explicitly justified.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. The decision analysis model used to derive a measure of health benefit was appropriate. The quality of life estimates were derived from a published study. However, the authors did not report whether these estimates reflected the aggregated preferences of the patients for different health outcomes.

**Validity of estimate of costs**
The authors reported that the costs were estimated from the NHS perspective and, as such, the indirect costs were not included in the analysis. It would appear that all the costs relevant to the perspective have been included, with the exception of clinical examinations by general practitioners. This exclusion was justified. The costs and the quantities were not reported separately and no sensitivity analysis of the costs was conducted. These factors will limit the generalisability of the results obtained. Discounting was undertaken since all the costs occurred during 14 years. A sensitivity analysis on the discount rate was performed. The price year was reported, which will aid any future reflation exercise.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. The limitation of generalisability of the results to other settings or countries was addressed. The authors do not appear to have presented
their results selectively. The authors reported further limitations to their study, which have been addressed already.

**Implications of the study**
The authors suggested that, as the costs could be significant when applied at the population level, the screening policy deserves further assessment through well-designed primary research.

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**Bibliographic details**

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

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