***Should we treat subclinical hypothyroidism?***

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Subclinical hypothyroidism is a laboratory definition: a raised concentration of thyroid stimulating hormone (TSH) yet a normal concentration of free thyroid hormone, without specific symptoms of thyroid dysfunction. Patients with subclinical hypothyroidism have an increased risk of progressing to overt hypothyroidism. Yet uncertainty exists as to the benefits of treating such patients.

**What is the evidence of the uncertainty?**

Recent systematic reviews of cohort studies have shown a significant increase in coronary heart disease and cardiovascular related mortality in people with subclinical hypothyroidism and a TSH concentration >10 mU/l, but no difference in overall mortality.[1](http://www.bmj.com/content/337/bmj.a834#ref-1) [2](http://www.bmj.com/content/337/bmj.a834#ref-2) The benefits of treating subclinical hypothyroidism are also uncertain: although two systematic reviews have suggested that treatment may decrease total cholesterol and low density lipoprotein cholesterol levels, particularly in people with TSH concentrations of >10 mU/l,[3](http://www.bmj.com/content/337/bmj.a834#ref-3) [4](http://www.bmj.com/content/337/bmj.a834#ref-4) no research has shown a decrease in coronary heart disease or mortality with treatment.

The *Clinical Evidence* review reports mixed results from small randomised controlled trials on the effect of treatment on symptoms.[5](http://www.bmj.com/content/337/bmj.a834#ref-5) One trial found a significant increase in anxiety scores but no difference in quality of life with treatment.[6](http://www.bmj.com/content/337/bmj.a834#ref-6) A second small randomised controlled trial found limited evidence of symptom improvement.[7](http://www.bmj.com/content/337/bmj.a834#ref-7) Patients report that fatigue may improve with treatment, but quality of life measures do not change.[8](http://www.bmj.com/content/337/bmj.a834#ref-8) Neuropsychological testing shows no difference between subclinical hypothyroid and euthyroid males.[9](http://www.bmj.com/content/337/bmj.a834#ref-9)

Two to four per cent of patients with subclinical hypothyroidism will develop overt hypothyroidism each year.[10](http://www.bmj.com/content/337/bmj.a834#ref-10) No research has been conducted to show whether early treatment decreases this progression.

There are risks associated with treatment: about a fifth of patients diagnosed with subclinical hypothyroidism will receive treatment that results in hyperthyroidism.[11](http://www.bmj.com/content/337/bmj.a834#ref-11) Bone mineral density may be reduced with treatment, though no research has shown an increased fracture risk.[12](http://www.bmj.com/content/337/bmj.a834#ref-12) A low TSH concentration following treatment may be associated with an increased risk of atrial fibrillation.[13](http://www.bmj.com/content/337/bmj.a834#ref-13)

Several organisations have made recommendations on the screening and treatment of subclinical hypothyroidism. The British Thyroid Association recommends treatment if TSH concentration is higher than 10 mU/l or if it is lower but the patient has goitre or is trying to become pregnant.[14](http://www.bmj.com/content/337/bmj.a834#ref-14) The United States Preventive Services Task Force found insufficient evidence for or against screening for subclinical hypothyroidism because of poor evidence that screening leads to improvement in clinically important outcomes.[15](http://www.bmj.com/content/337/bmj.a834#ref-15)

In 2004 a consensus conference published an evidence based review concluding that general screening for and treatment of subclinical hypothyroidism should not be done.[16](http://www.bmj.com/content/337/bmj.a834#ref-16) However, illustrative of the uncertainty surrounding this topic, a consensus statement from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society emerged from the same conference to recommend routine screening in adults, pregnant women, and those contemplating pregnancy and treatment of most patients with raised TSH concentrations of 4.5-10 mU/l.[17](http://www.bmj.com/content/337/bmj.a834#ref-17)

**Is ongoing research likely to provide relevant evidence?**

Research registries at the Medical Research Council, NHS Trusts Clinical Trials Register, the UK Clinical Trials Gateway, and the US National Institutes of Health do not list current ongoing research on subclinical hypothyroidism ([www.controlled-trials.com/mrct/](http://www.controlled-trials.com/mrct/)). A Cochrane protocol (for a systematic review) is under way to evaluate the effectiveness of thyroid hormone therapy for subclinical hypothyroidism ([www.cochrane.org/reviews/en/info\_327301022023450202.html](http://www.cochrane.org/reviews/en/info_327301022023450202.html)).

**What should we do in the light of the uncertainty?**

In general, patients should not be routinely screened for or treated for subclinical hypothyroidism, as the end point of treatment is not certain, no evidence exists of long term benefit, and treatment may not be risk-free. However, mildly raised TSH concentrations accompanied by vague symptoms such as fatigue or depressive mood may justify a short trial of treatment as long as therapeutic goals are clearly outlined with the patient. If no demonstrable improvement in these outcomes occurs, the drug should be discontinued. Although no guidelines exist on how long to observe these patients for, a trial of three to six months would allow time to normalise the patient’s TSH level and assess for any improvement in symptoms. Patients who are discovered to have mildly raised TSH concentrations should be monitored yearly for development of overt hypothyroidism.

**Notes**

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