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## Is thyroid status a common denominator of age-related disease?

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# CHAPTER 8

Correspondence: Thyroid Hormone Therapy for  
Older Adults with Subclinical Hypothyroidism

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**To the editor:**

On the basis of previous observational findings,<sup>1</sup> the TRUST trial was initiated to provide evidence as to whether subclinical hypothyroidism is causally linked to disease in old age. Despite being the largest trial to date with 737 participants, it was underpowered to address the association between hypothyroidism and cardiovascular disease, as highlighted in the Discussion section.

We conducted a two-sample mendelian randomization study with 20 genetic variants for circulating levels of thyrotropin and 3 genetic variants for circulating levels of free thyroxine<sup>2</sup> on summary data of a genomewide association study consisting of 60,801 case patients with coronary artery disease and 123,504 controls from the CARDIoGRAMplusC4D Consortium.<sup>3</sup> On the basis of statistical analyses that have been described previously,<sup>4</sup> we found no evidence for a causal relationship between circulating levels of thyrotropin or free thyroxine and the risk of coronary artery disease (odds ratio of 0.99 per standard deviation of increase in thyrotropin,  $P=0.83$ ; and odds ratio of 1.02 per standard deviation of increase in free thyroxine,  $P=0.74$ ). Thus, even if the TRUST trial had been considerably larger and had longer follow-up, it is likely that the investigators would have found no beneficial effect of levothyroxine treatment on the incidence of coronary artery disease, similar to their findings with respect to other outcomes.

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