



**Universiteit  
Leiden**  
The Netherlands

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

Vliet, N.A. van

### **Citation**

Vliet, N. A. van. (2023, January 25). *Is thyroid status a common denominator of age-related disease?*. Retrieved from <https://hdl.handle.net/1887/3512954>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3512954>

**Note:** To cite this publication please use the final published version (if applicable).



# CHAPTER 8

Correspondence: Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism

**Nicolien A van Vliet, Raymond Noordam, Diana van Heemst**

*N Engl J Med* 2017 Oct 5;377(14):e20. doi: 10.1056/NEJMc1709989.

**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.

**Acknowledgments**

No potential conflict of interest relevant to this letter was reported.

## REFERENCES

1. Rodondi N, den Elzen WP, Bauer DC, et al. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. *Jama*. Sep 22 2010;304(12):1365-74. doi:10.1001/jama.2010.1361
2. Porcu E, Medici M, Pistis G, et al. A meta-analysis of thyroid-related traits reveals novel loci and gender-specific differences in the regulation of thyroid function. *PLoS genetics*. 2013;9(2):e1003266. doi:10.1371/journal.pgen.1003266
3. Nikpay M, Goel A, Won HH, et al. A comprehensive 1,000 Genomes-based genome-wide association meta-analysis of coronary artery disease. *Nature genetics*. Oct 2015;47(10):1121-30. doi:10.1038/ng.3396
4. Bos MM, Smit RA, Trompet S, van Heemst D, Noordam R. Thyroid signaling, insulin resistance and type 2 diabetes mellitus: a Mendelian randomization study. *The Journal of clinical endocrinology and metabolism*. Mar 09 2017;doi:10.1210/jc.2016-2816