The Reply

Dr. Modarressi suggests in his letter that our interpretation of the TRUST study¹ needs caution because patients who had a thyroid-stimulating hormone (TSH) level between 4.6 and 6.9 mIU/L could be physiologically euthyroid. We disagree and provide 3 specific points in response.

When we designed the TRUST trial, we chose to set a TSH target of 0.40-4.59 mIU/L with levothyroxine treatment, which was the range used to define euthyroidism in the Thyroid Studies Collaboration² and contemporary guidelines,³ despite the current discussion of using an age-specific reference.⁴

We enrolled only participants who had persistent elevated TSH levels (4.60-19.99 mIU/L).^{1,5} The TSH value was required to be within the eligibility window on at least 2 occasions that were 3 months to 3 years apart. In the TRUST trial, among the 2647 older adults screened for eligibility, 1645 did meet inclusion criteria because of a reversion of TSH level.⁵ The TSH levels among participants randomized in the placebo group remained elevated over the study period (5.29 mIU/L in average).¹ Therefore, we can assume that participants who were truly euthyroid were not studied in the TRUST trial.

The proportion of older participants with TSH \geq 7 mIU/L in our study (23.8%) was representative, as the prevalence of such abnormality at this age category accounts for about 10% of the elderly population.⁴ In our study, prespecified stratification according to baseline TSH levels (4.6-6.9, 7.0-9.9, \geq 10 mIU/L) yielded similar results without statistical interactions.¹ These findings were replicated in another trial of patients with subclinical hypothyroidism where levothyroxine compared with placebo had no impact on cardiac function.⁶ Because the vast majority of patients treated for subclinical hypothyroidism in practice have a TSH value between 4.6 and 6.9 mIU/L,⁴ the inclusion of those participants enabled us to evaluate the treatment effect of levothyroxine in this key subgroup.

Although we agree that age-specific reference for the diagnosis of subclinical hypothyroidism in the elderly needs to be rediscussed,⁴ current findings found no benefits of levothyroxine on cardiac function among older adults with subclinical hypothyroidism, including among those with TSH \geq 7 mIU/L.^{1,6}

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