A value less than 24 was considered to indicate cognitive impairment. Other information on demographics, smoking, and the use of medication were collected using standardized questionnaires. Weight, body-mass index (BMI), and the level of physical activity and exercise, nutrition and disease were also evaluated by standardized questionnaires. Participants were classified according to TSH and FT$_4$ and FT$_3$ concentrations into five categories: (1) overt hypothyroidism (TSH >4.68 µIU/ml, FT$_4$ <0.78 ng/dl); (2) subclinical hypothyroidism (TSH >4.68 µIU/ml, FT$_4$ = 0.77 to 2.19 ng/dl); (3) euthyroidism (TSH = 0.46 to 4.68 µIU/ml), (4) subclinical hyperthyroidism (TSH <0.46 µIU/ml, FT$_4$ = 0.77 to 2.19 ng/dl, FT$_3$ = 2.77 to 5.27 pg/ml); and (5) overt hyperthyroidism (TSH <0.46 µIU/ml, FT$_4$ >2.19 ng/dl, FT$_3$ >.27 pg/ml). Four patients with low T$_3$ syndrome with normal FT$_3$ and TSH levels were excluded from the analysis.

**RESULTS**

Subclinical hypothyroidism was more prevalent in older than in younger participants (3.5% vs. 0.4%, P<0.03), as was subclinical hyperthyroidism (7.8% vs. 1.9%, P<0.002). Serum TSH and FT$_4$ declined with age in euthyroid participants, while FT$_3$ increased. Older participants (≥65 years) with subclinical hyperthyroidism had lower mean (±SD) MMSE scores than did euthyroid subjects (22.61±6.88 vs. 24.72±4.52, P<0.03). Participants with subclinical hyperthyroidism were, in an adjusted analysis, significantly more likely to have cognitive dysfunction (hazard rate [HR], 2.26; *P = 0.003). Data are from Tables 1 and 2 in Ceresini et al.
Conclusions
Subclinical hyperthyroidism is the most prevalent thyroid dysfunction in older Italian persons and is associated with cognitive impairment.

Commentary
The prevalence of overt and subclinical hypothyroidism in elderly populations is high as 20% (1). With aging, the prevalence increases 1% or 2% in iodine-deficient geographic areas and up to 7% or 8% in iodine-sufficient areas (1). However, inconsistent findings have been found in epidemiologic studies investigating the relationship between subclinical hypothyroidism and cognitive dysfunction (2). In the present study, the odds of having poorer cognitive function were greater for subclinical hypothyroidism than for stroke, diabetes mellitus, and Parkinson’s disease. Thus, in this large population-based study, the overall prevalence of thyroid dysfunction tended to be higher in older than in younger persons, with subclinical hypothyroidism being the most highly prevalent condition associated with cognitive deterioration. A study from the Netherlands found that subclinical hypothyroidism in the elderly increased the risk of dementia and Alzheimer’s disease. A recent study by Samuels et al. (3) found mild decrements in health status and mood in when subclinical hypothyroidism was induced in a blinded, randomized fashion. More importantly, there were independent decrements in working memory, which suggested to the authors that subclinical hypothyroidism specifically impacts brain areas responsible for working memory. Whether treating the subclinical hyperthyroidism—or for that matter, subclinical hypothyroidism—would ameliorate cognitive dysfunction is unknown, but some studies suggest this might not be the case (4). However, other cross-sectional or longitudinal observations have failed to demonstrate an association between thyroid dysfunction and cognition (2, 5). Still, there is a high prevalence of autoimmune thyroid disorders in patients with Alzheimer’s disease (6), and other studies have found an association between autoimmune-associated subclinical hyperthyroidism and dementia (7). This intriguing observation by Ceresini et al. will certainly spark further investigation.

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References