



Additional vitamin D supplementation does not affect muscle strength in the older women: A double-blind randomized controlled trial

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ABSTRACT

Background: The elderly, aged 60 and above, are expected to increase in number in the coming years. Aging brings about various changes, impacting both physical and mental health. Proper protein intake and exercise can boost muscle protein synthesis, while maintaining optimal vitamin D levels is crucial. Research is necessary to explore vitamin D's impact on elderly muscle mass.

Objective: This study aims to investigate the effect of adding vitamin d supplementation to protein and exercise on handgrip strength in healthy elderly.

Materials and Methods: 24 participants were randomized in a double-blinded, pilot study ages 60- 80 years Subjects were divided into two groups. Group 1 was given interventions of vitamin D supplementation 1000 UI/day combining soy + oats milk as a protein and exercise. The second group was given intervention of soy+ oats milk protein, and exercise. The intervention program was administered for 8 weeks. Data comparison within and between groups were analyzed by Independent T-test, Mann-Whitney, and Paired T-test

Results: Data from all participants was analyzed, before and after interventions of handgrip was increased in both of groups from a mean of 17.18kg to 18.06kg for the right hand and 15.17kg to 18.26kg for the left hand in Group 1, 13.80kg to 16.86kg for the right hand and 15.45kg to 17.32kg for the left hand in Group 2. Results of the difference test analysis between the two groups (ANOVA $t = 0.548$, $P = 0.172$) showed no difference between group 1 and group 2.

Conclusion: In this study, there was no effect of adding vitamin D supplementation on handgrip at healthy elderly participants.

Keywords: Vitamin D; Protein; Exercise; Healthy elderly

BACKGROUND

By 2050, it is anticipated that 22% of the global population will be over 60, with roughly 5% over 80.¹ As the global population ages, physical weakness, disability, and chronic diseases associated with poor skeletal muscle and bone health become more common.² Muscle strength is a key measure of elderly health since it is linked to undesirable outcomes such as sarcopenia, coronary heart disease, neurodegenerative disease, chronic renal disease, COPD, sepsis, and immunological diseases, as well as impaired mobility, disability, and even mortality.^{2,3} Hormones, inflammation, insulin resistance, and biological factors such as gender and physical endurance, such as the ability to resist infection or other stressors, all may influence muscle mass loss in the elderly, increasing the risk of decreased skeletal muscle performance. Nutritional status and physical exercise are two additional factors that contribute to impaired skeletal muscle performance in the elderly.¹

Geriatric anorexia is characterized by an impairment in appetite and food intake as an inevitable consequence of the aging process.^{1,4} Anorexia, insufficient food intake, sarcopenia, cachexia, and/or a combination of these variables may lead to malnutrition and accidental weight loss. Geriatric anorexia, in particular, is a cause of unintended weight loss that damages skeletal muscle tissue. Furthermore, energy intake reduces rapidly than energy expenditure, causing abnormalities in appetite regulation, homeostasis, and body weight.⁵ Disease-related malnutrition induces rapid withering of skeletal muscle, whereas geriatric malnutrition causes a gradual but cumulative decrease of muscle mass.⁶

Elderly people have a higher protein need than adults (1.0-1.2 g/kg body weight), and a sufficient protein diet is critical to prevent malnutrition and sarcopenia.^{7,8} Protein intake recommendations primarily depend on the concept of anabolic resistance, which describes the decreased ability of muscles to respond to anabolic stimuli as individuals age. Protein consumption in the elderly is frequently significantly below the recommended intake^{9,10}, raising the risk of malnutrition. In addition to fulfilling protein needs that rise with age, some studies have indicated that physical activity can balance and even improve muscle function in the elderly.¹¹

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Exercise can help prevent age-related denervation. The existence of angular and atrophic muscle fibers, which are not present in lifelong trained muscles, indicates selective denervation of elderly muscles. A previous study has discovered that long-term vigorous exercise increases muscle fiber reinnervation, resulting in good impacts on muscle structure and function, eventually leading to a delay in diminished mobility.¹² Chair-based exercise (CBE), practiced while sitting, is utilized as an alternative and provides an acceptable and accessible method of exercise for elderly people with physical limitations who are possibly unable to participate in other exercise programs. Chair-based exercise may assist the elderly to maintain their independence, mobility, and balance.¹³ The handgrip dynamometer (HGD) is an essential instrument for assessing muscular strength in this context because it provides a simple, rapid, dependable, and consistent measurement of total muscle strength. Furthermore, handgrip strength (HGS) is regarded as a critical indicator for dysentery diagnosis since low HGS is a good predictor of reduced muscle mass and a clinical marker of inadequate physical performance.¹⁴

A recent study has highlighted the impact of vitamin D insufficiency on muscle health, specifically the implications on muscle mass and function in the elderly and patients with chronic conditions. Vitamin D is primarily responsible for improving calcium absorption in the intestine for bone mineralization and regulating calcium levels in the circulatory system. Vitamin D has recently been demonstrated to have extra-skeletal effects. An observational meta-analysis study and comprehensive review found that blood vitamin D insufficiency increases the likelihood of muscular mass and strength loss in the elderly.¹⁵ Nonetheless, there is insufficient evidence of a definite link between vitamin D status and muscle hypertrophy or strength in the literature. Based on this description, it is obvious that adequate protein consumption and physical exercise, as well as optimal serum vitamin D levels, could serve as triggers for protein synthesis in the muscles of the elderly. The primary objective of this study is to assess the effect of combining vitamin D supplementation with protein and physical activity on hand grip strength in relatively healthy elderly individuals.

MATERIALS AND METHODS

This study implemented a double-blind randomized control trial design with a randomized allocation procedure in the form of cards. The subjects were divided into two groups: intervention and placebo. Data was recorded for 7 months, from June to December 2021. The target group of the study was all elderly individuals aged 60-80 in the West Semarang sub-district of Semarang City. The required minimum number of samples was estimated using a method for paired numerical analytic research. A total number of 24 persons who satisfied the requirements were then randomly assigned to one of two groups (intervention or placebo).

Respondents or prospective research subjects had to complete health screenings such as interviews and blood tests such as vitamin D serum, random blood sugar levels, creatinine, and comprehensive blood checks to determine the health state of the elderly. Participants who fulfilled the following clinical and physical health criteria were eligible: 1) capable to walk and stand independently; 2) Had mild physical activity; 3) had never received or were currently receiving long-term corticosteroid therapy; and 4) had no histories of chronic diseases such as diabetes with complications, kidney failure, NAFLD, liver disease, digestive disorders, or thyroid gland dysfunction.

Supplementation of protein and vitamin D and exercise, were the independent variables in this study, whereas hand grip strength and serum vitamin D levels in the blood were the dependent variables. Subjects who fulfilled the criteria signed informed consent and were re-screened by research assistants and researchers for anthropometric measurements such as initial handgrip measurements, body weight, height, BMI, muac, and BIA using digital scales. Local cadres were trained to execute the assignment in 8 weeks. The intervention group received chair-based exercise, protein, and vitamin D, while the placebo group received chair-based exercise, protein, and a vitamin B placebo. The chair exercise was completed in 2 stages. The first week, one session lasted 20 minutes, and the next week, it was raised to 30 or 40 minutes.

Data for primary measures baseline of participant were analyzed by descriptive and comparative statistical analyses. For comparison within and between groups were analyzed by Independent T-test, Mann-Whitney, and Paired T-test. The study has been approved by the ethics committee of the Medicine Faculty of Diponegoro University (No. 282/EC/KEPK/FK-UNDIP/XII/2020).

RESULTS

Table 1. Subject Characteristics

| | Intervention group (n = 12) Mean ± SD | Placebo group (n = 12) Mean ± SD | p-value |
|--------------------------|--|---|----------------|
| Age (y) | 62.67 ± 2.67 | 63.08 ± 2.6 | 0,616b |
| Height (cm) | 154 ± 6.55 | 153.91 ± 3.11 | 0,969a |
| Weight (kg) | 64.40 ± 7.87 | 63.83 ± 8.64 | 0,869a |
| BMI (kg/m ²) | 27.15 ± 2.76 | 26.94 ± 3.5 | 0,873a |
| Muscle mass (kg) | 36.85 ± 3.83 | 36.65 ± 5.71 | 0,924a |
| Visceral fat | 8.33 ± 1.98 | 8.66 ± 2.82 | 0,741a |
| Lean body mass (kg) | 40.78 ± 4.50 | 40.58 ± 2.91 | 0,902a |
| Body fat percentage (%) | 36.63 ± 3.85 | 35.34 ± 5.8 | 0,528a |
| Protein (%) | 10.54 ± 2.25 | 10.02 ± 2.83 | 0,626a |

^aIndependent T-test, ^bMann-Whitney

A total of 24 subjects who fulfilled the requirements were divided into two groups, each group consisted of 12 subjects: the intervention group and the placebo group. The intervention group averaged 64.4 kg, while group 2 averaged 63.83 kg. The outcomes of bioelectrical impedance analysis (BIA) measurements revealed that the average level of protein in the body of individuals in the Intervention Group and in the Placebo Group was 10.54% and 10.02% respectively. In the Placebo Group, the average body fat percentage, muscle mass, and visceral fat were 35.35%, 36.65 kg, and 8.66, respectively. Meanwhile in the Intervention Group, the average body fat percentage, muscle mass, and visceral fat were 36.63%, 36.85 kg, and 8.33, respectively.

Table 2. Mean Value of Hand Grip Strength Before and After Treatment

| | Intervention Group (mean ± SD) | Placebo Group (mean ± SD) | p-value |
|------------|---|--|----------------|
| Before | 16.17 ± 4.31 | 15.21 ± 4.61 | 0.608a |
| After | 18.52 ± 4.87 | 17.07 ± 5.41 | 0.499a |
| p-value | 0.021c | 0.010c | |
| Change (Δ) | 2.35 ± 2.59 | 1.86 ± 2.8 | 0.954b |

^aIndependent T-test, ^bMann-Whitney, ^cPaired T-test

The average value of hand grip strength before the intervention was determined using the handgrip dynamometer test in the intervention group, which revealed that both groups were increased and there were differences between the two groups before and after treatment in hand grip strength. The results of the intervention both groups were classified as being typical for elderly people aged 60 to 80 years¹³. In the elderly, normal hand grip strength is used to assess nutritional condition and frequent mobility in activities¹⁴.

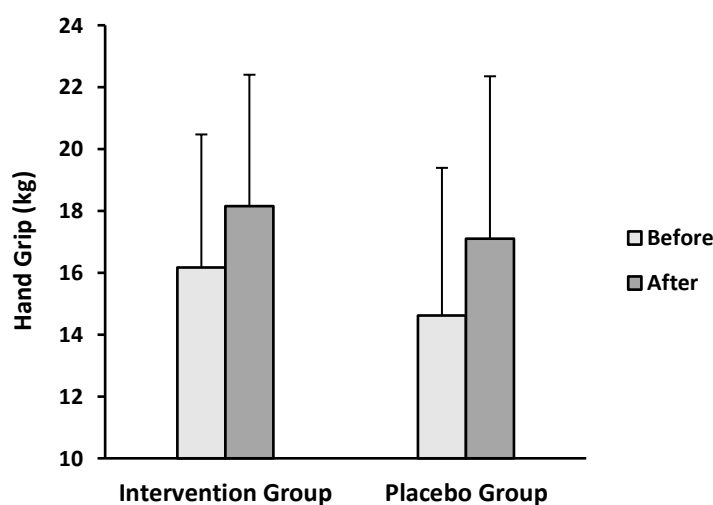


Figure 1. Changes in hand grip between the intervention and placebo groups

The average findings of hand grip strength following intervention for the intervention group were 18.06 kg for the right hand and 18.26 kg for the left hand. The right hand averaged 16.89 kg, while the left hand averaged 17.32 kg. The intervention resulted were no difference in hand grip strength between the intervention group and the placebo group (Mann-Whitney p-value: 0.954). The increase in hand grip strength before and after the intervention did not indicate a different test difference between the two groups. It is expected that the results of the several tests are not different because prior studies with the same strategy achieved positive benefits on hand grip strength in the elderly by providing more protein, exercise, and vitamin D supplementation. Another option for this study is the small number of subjects.

Table 3. Mean Value of Vitamin D Serum Before and After Treatment

| | Intervention Group (mean ± SD) | Placebo Group (mean ± SD) | p-value |
|------------|-----------------------------------|------------------------------|---------|
| Before | 17.89 ± 5.05 | 15.73 ± 4.69 | 0.290a |
| After | 20.13 ± 6.72 | 19.11 ± 3.64 | 0.650a |
| p-value | 0.010c | 0.004c | |
| Change (Δ) | 2.24 ± 2.5 | 3.38 ± 3.24 | 0.312b |

^aIndependent T-test, ^bMann-Whitney, ^cPaired T-test

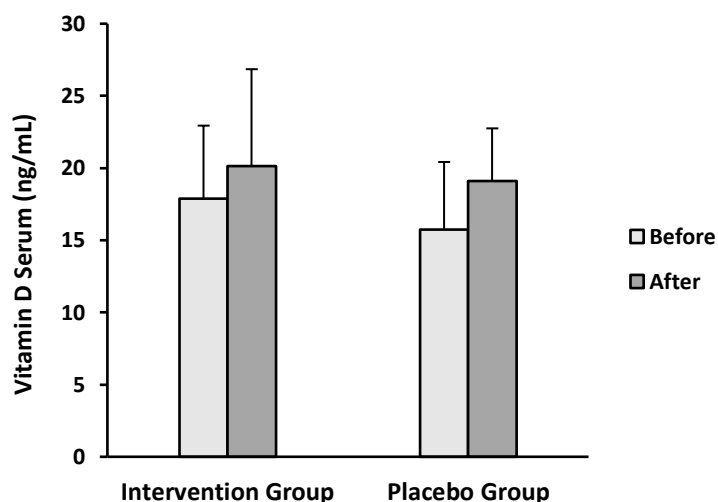


Figure 2. Changes in vitamin D serum between the intervention and placebo groups

The average vitamin D serum levels following intervention in both groups were increase in both groups 20.13 ng/mL and 19.11 ng/mL, respectively. The intervention resulted were no difference in vitamin D serum between the intervention group and the placebo group (Mann-Whitney p-value: 0.312).

DISCUSSION

Vitamin D intervention combined with protein and exercise for 8 weeks resulted in an increase in hand grip strength and serum vitamin D levels in both the intervention and placebo groups. This outcome is in line with previous studies conducted on 380 sarcopenic primarily independent-living elderly with a low skeletal muscle mass index. The use of a vitamin D and leucine-enriched whey protein oral nutritional supplement for 13 weeks improved muscle mass and lower-extremity function in sarcopenic older individuals. Both groups improved in handgrip strength with no significant between-group differences.¹⁶ In addition, the outcomes of this study are consistent with research who found that exercise and vitamin D supplementation may improve muscle strength in the elderly, and that combining the two can increase muscle strength significantly.¹⁷

A meta-analysis study BY Liao et al¹⁷ found that protein supplementation paired with resistance exercise training has a general beneficial impact on body composition in elderly persons, including muscle volume, muscle strength, and physical mobility.¹⁷ The effect of vitamin D supplementation on increasing muscle strength in elderly individuals in good health is consistent with research published in 2016 discovered

that protein, vitamin D supplementation, and aerobic exercise can result in increased muscle strength, physical function, and quality of life.¹⁸ The average age of the subjects in the intervention group and in the placebo group was 62 ± 2.67 years and 63 ± 2.67 years respectively. Age is regarded as the strongest factor influencing hand grip strength in healthy subjects, as it declines with increasing age.^{19,20}

Protein consumption before or after resistance exercise has been shown to promote muscle protein synthesis more than protein consumption at other times.²¹ The amount of EAA (essential amino acids) in a protein diet could be inadequate to support protein synthesis in the skeletal muscle of elderly individuals. Higher doses (10-15 g) appear to be required to boost muscle protein synthesis to levels that are comparable to those seen in young persons. Most protein sources, whether in the form of animal or plant-based, have 5-8 g of EAAs per 20 g of protein. Participants in the current study consumed 30 g of oat immediately following exercise, which may have been sufficient to generate gains in lean body mass or strength.²¹

Vitamin D may have an effect on skeletal muscle cells due to the existence of the vitamin D receptor, and it may also be required for proper muscle function and protein synthesis.²² The current identification of the vitamin D receptor (VDR) in human skeletal muscle raises the possibility that vitamin D could play an important role in the prevention of muscular deterioration during aging.²³ However, epidemiological studies on blood 25-hydroxyvitamin D [25(OH)D] and muscle strength in older people have produced inconsistent results.^{24,25} The effect of vitamin D can be explained by two mechanisms: long-term and short-term reactions in skeletal muscle including both genetics and non-genomics. In the first pathway, secosteroid hormone stimulates the proliferation and differentiation of muscle cells via nuclear VDR-mediated gene transcription in myoblasts, resulting in the development of skeletal muscle fibers.^{26,27} Vitamin D may be implicated in the rapid control of calcium messenger systems and growth-related signal transduction in non-genomic pathways, altering skeleton muscle contraction.²⁶

In this study, there was no difference in the effectiveness of vitamin D supplementation between the two groups. These outcomes may develop as a result of a variety of strengths and limitations. The fact that none of the respondents who passed the inclusion criteria quit the study and had a good overall adherence to the treatment were two of our study's strengths. The primary limitation of this study is that the results of the level vitamin D serum are typically less than 20 ng/mL or are classed as serum vitamin D deficiency. Previous research revealed that aged men and women with serum vitamin D in their blood were in the low range and the muscle strength increased following 4 months of 2500 ug/day vitamin D supplementation.²⁸ Study similarly found no change in muscle mass strength between the elderly who were given Vitamin D and a placebo for three months and as high as 2800 IU/day.²⁹

The second limitation of this study is that the intervention only conducted on women. In a recent study published in 2019, found that serum vitamin D concentrations were substantially related with hand grip strength in males over 50 years old, but not in men under 50 years old or women over and under 50 years old.³⁰

CONCLUSIONS

This study revealed no difference in hand grip strength or vitamin D serum between groups that received or did not receive vitamin D in healthy elderly people who exercised and were given protein as 8-week intervention.

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REFERENCES

1. Tieland M, Trouwborst I, Clark BC. Skeletal muscle performance and ageing. *J Cachexia Sarcopenia Muscle* 2018; 9: 3–19.
2. Landi F, Camprubi-Robles M, Bear DE, et al. Muscle loss: The new malnutrition challenge in clinical practice. *Clinical Nutrition* 2019; 38: 2113–2120.
3. Mehmet H, Yang AWH, Robinson SR. Measurement of hand grip strength in the elderly: A scoping review with recommendations. *J Body Mov Ther* 2020; 24: 235–243.
4. Morley JE. Anorexia of aging: A true geriatric syndrome. *J Nutr Health Aging* 2012; 16: 422–425.
5. Arosio B, Cesari M. Nutrition and Muscle Health. *Nutrients* 2021; 13: 797.

6. Norman K, Haß U, Pirlich M. Malnutrition in Older Adults—Recent Advances and Remaining Challenges. *Nutrients* 2021; 13: 2764.
7. Deutz NEP, Bauer JM, Barazzoni R, et al. Protein intake and exercise for optimal muscle function with aging: Recommendations from the ESPEN Expert Group. *Clinical Nutrition* 2014; 33: 929–936.
8. Bauer J, Biolo G, Cederholm T, et al. Evidence-Based Recommendations for Optimal Dietary Protein Intake in Older People: A Position Paper From the PROT-AGE Study Group. *J Am Med Dir Assoc* 2013; 14: 542–559.
9. Hengeveld LM, Boer JMA, Gaudreau P, et al. Prevalence of protein intake below recommended in community-dwelling older adults: a meta-analysis across cohorts from the PROMISS consortium. *J Cachexia Sarcopenia Muscle* 2020; 11: 1212–1222.
10. Hengeveld LM, Wijnhoven HA, Olthof MR, et al. Prospective associations of poor diet quality with long-term incidence of protein-energy malnutrition in community-dwelling older adults: the Health, Aging, and Body Composition (Health ABC) Study. *Am J Clin Nutr* 2018; 107: 155–164.
11. Backx EMP, Tieland M, Borgonjen-van den Berg KJ, et al. Protein intake and lean body mass preservation during energy intake restriction in overweight older adults. *Int J Obes* 2016; 40: 299–304.
12. Mosole S, Carraro U, Kern H, et al. Long-Term High-Level Exercise Promotes Muscle Reinnervation With Age. *J Neuropathol Exp Neurol* 2014; 73: 284–294.
13. Cordes T, Schoene D, Kemmler W, et al. Chair-Based Exercise Interventions for Nursing Home Residents: A Systematic Review. *J Am Med Dir Assoc* 2021; 22: 733–740.
14. Lima TRL, Almeida VP, Ferreira AS, et al. Handgrip Strength and Pulmonary Disease in the Elderly: What is the Link? *Aging Dis* 2019; 10: 1109.
15. Samefors Maria. *Aspects of Vitamin D Deficiency in Elderly People in Nursing Homes and in Patients with Type 2 Diabetes with Emphasis on Mortality, Cardiovascular Morbidity and Mental Health*. Linköping University Electronic Press, 2020.
16. Bauer JM, Verlaan S, Bautmans I, et al. Effects of a Vitamin D and Leucine-Enriched Whey Protein Nutritional Supplement on Measures of Sarcopenia in Older Adults, the PROVIDE Study: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Am Med Dir Assoc* 2015; 16: 740–747.
17. Liao C-D, Tsao J-Y, Wu Y-T, et al. Effects of protein supplementation combined with resistance exercise on body composition and physical function in older adults: a systematic review and meta-analysis. *Am J Clin Nutr* 2017; 106: 1078–1091.
18. Rondanelli M, Klersy C, Terracol G, et al. Whey protein, amino acids, and vitamin D supplementation with physical activity increases fat-free mass and strength, functionality, and quality of life and decreases inflammation in sarcopenic elderly. *Am J Clin Nutr* 2016; 103: 830–40.
19. Abe T, Thiebaut RS, Loenneke JP. Age-related change in handgrip strength in men and women: is muscle quality a contributing factor? *Age (Dordr)* 2016; 38: 28.
20. Kim B-J, Kwak MK, Lee SH, et al. Lack of Association Between Vitamin D and Hand Grip Strength in Asians: A Nationwide Population-Based Study. *Calcif Tissue Int* 2019; 104: 152–159.
21. Arnarson A, Gudny Geirsdottir O, Ramel A, et al. Effects of whey proteins and carbohydrates on the efficacy of resistance training in elderly people: double blind, randomised controlled trial. *Eur J Clin Nutr* 2013; 67: 821–826.
22. Dzik KP, Kaczor JJ. Mechanisms of vitamin D on skeletal muscle function: oxidative stress, energy metabolism and anabolic state. *Eur J Appl Physiol* 2019; 119: 825–839.
23. Olsson K, Saini A, Strömberg A, et al. Evidence for Vitamin D Receptor Expression and Direct Effects of 1 α ,25(OH)2D3 in Human Skeletal Muscle Precursor Cells. *Endocrinology* 2016; 157: 98–111.
24. Orces CH. Prevalence of clinically relevant muscle weakness and its association with vitamin D status among older adults in Ecuador. *Aging Clin Exp Res* 2017; 29: 943–949.
25. Iolascon G, de Sire A, Calafiore D, et al. Hypovitaminosis D is associated with a reduction in upper and lower limb muscle strength and physical performance in post-menopausal women: a retrospective study. *Aging Clin Exp Res* 2015; 27: 23–30.
26. Christakos S, Hewison M, Gardner DG, et al. Vitamin D: beyond bone. *Ann N Y Acad Sci* 2013; 1287: 45–58.
27. Sanders KM, Scott D, Ebeling PR. Vitamin D Deficiency and its Role in Muscle-Bone Interactions in the Elderly. *Curr Osteoporos Rep* 2014; 12: 74–81.

28. Grimnes G, Kubiak J, Jorde R. Four months vitamin D supplementation to vitamin D insufficient individuals does not improve muscular strength: A randomized controlled trial. *PLoS One* 2019; 14: e0225600.
29. Bislev LS, Langagergaard Rødbro L, Rolighed L, et al. Effects of Vitamin D3 Supplementation on Muscle Strength, Mass, and Physical Performance in Women with Vitamin D Insufficiency: A Randomized Placebo-Controlled Trial. *Calcif Tissue Int* 2018; 103: 483–493.
30. Wang J, Wang X, Gu Y, et al. Vitamin D is related to handgrip strength in adult men aged 50 years and over: A population study from the TCLSIH cohort study. *Clin Endocrinol (Oxf)* 2019; 90: 753–765.