



Roma, 9-12 novembre 2017



ITALIAN CHAPTER



TRUST Study «la difesa»

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Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism



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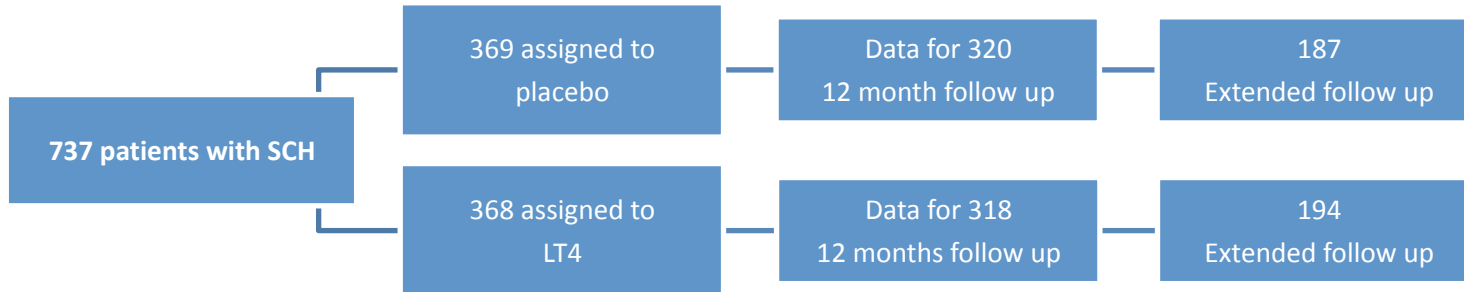
- «...treatment with levothyroxine in older persons with subclinical hypothyroidism provided no symptomatic benefits»



Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism



- Disegno dello studio: trial multicentrico, doppio-cieco, randomizzato, placebo-controllo, gruppi paralleli





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- Questionario ThyPRO: validato*

*

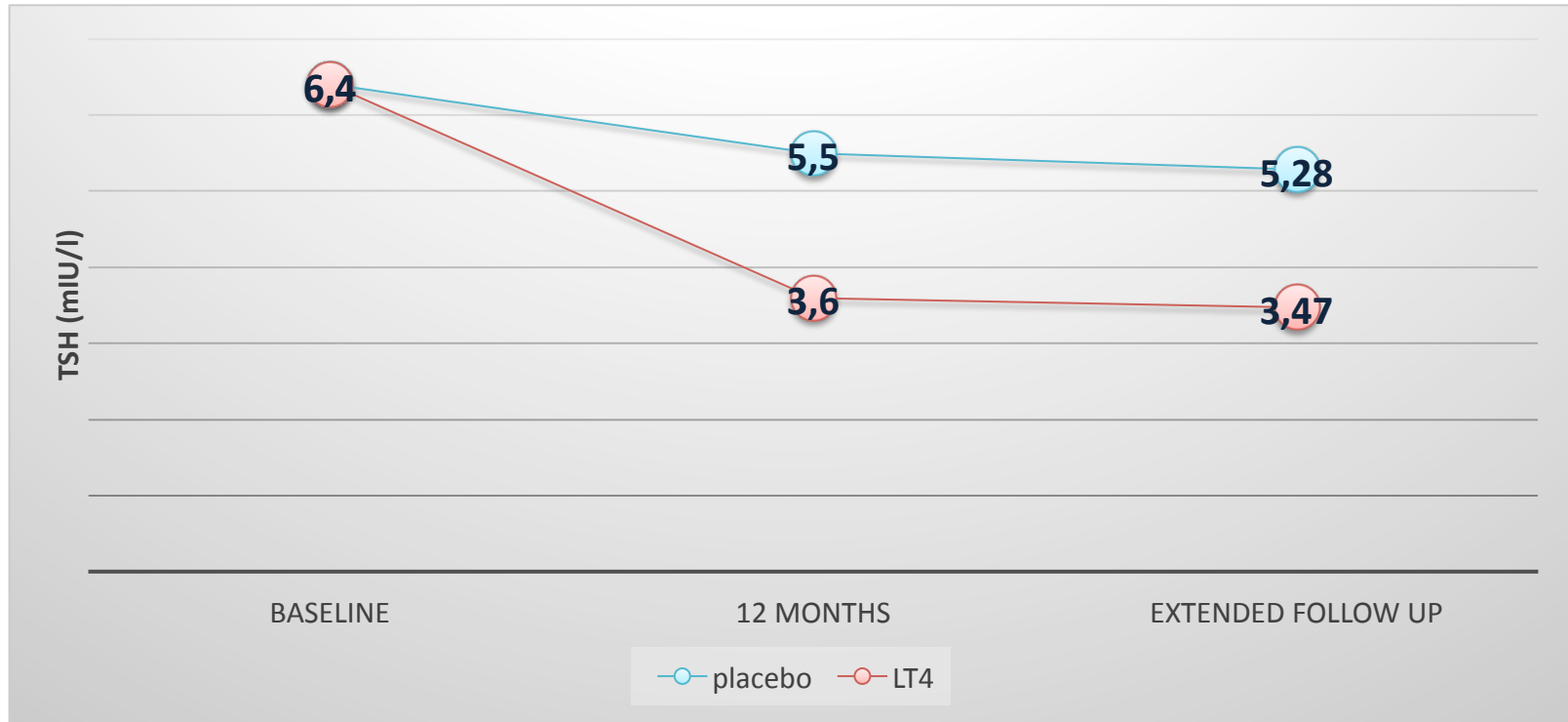
1. Rasmussen SL: Eur Thyroid J 2016
2. Wong CK: J Clin Epidemiol 2016
3. Watt T: Health Qual Life Outcomes 2014
4. Watt T: Qual Life Res 2014
5. Watt T: J Clin Endocrinol Metab: 2014
6. Watt T: Eur J Endocrinol 2010
7. Watt T: Qual Life Res: 2009)



Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism



- Differenza TSH: persistente (1.9mIU/L)





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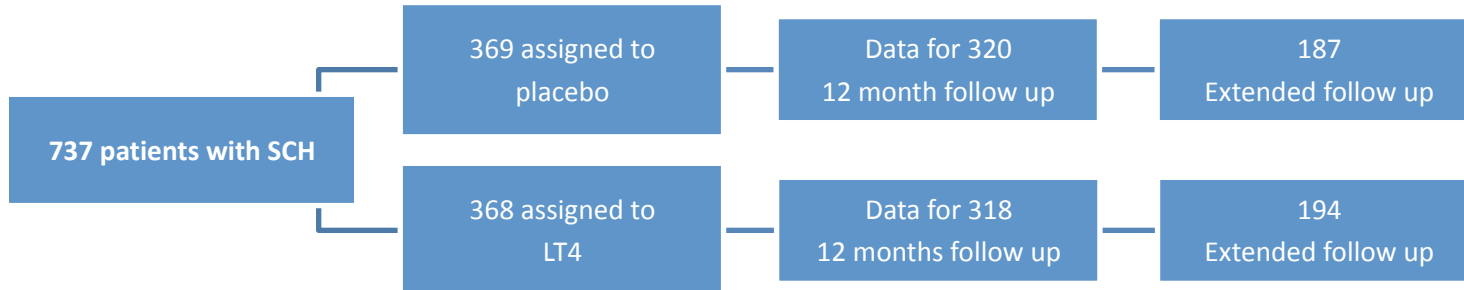
- The two primary outcomes were changes in two domains (**hypothyroid symptoms** and **tiredness score**) on the thyroid-related quality of life questionnaire (ThyPRO) at one year
- Secondary outcomes include general **health-related quality of life** (EuroQol)



Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism



- Per l'outcome primario: il numero richiesto considerato statisticamente significativo era **750** pazienti considerando una variazione del 3.0% "Hypothyroid Symptoms", e del 4.1% "Tiredness score"; **540** pazienti considerando una variazione del 3.5% per "Hypothyroid Symptoms" e del 4.9% per "Tiredness score".
- Inoltre, per "compensare" i drop-out sono state utilizzate correzioni statistiche ("modified intention-to-treat analysis" e "multiple imputations for missing data")



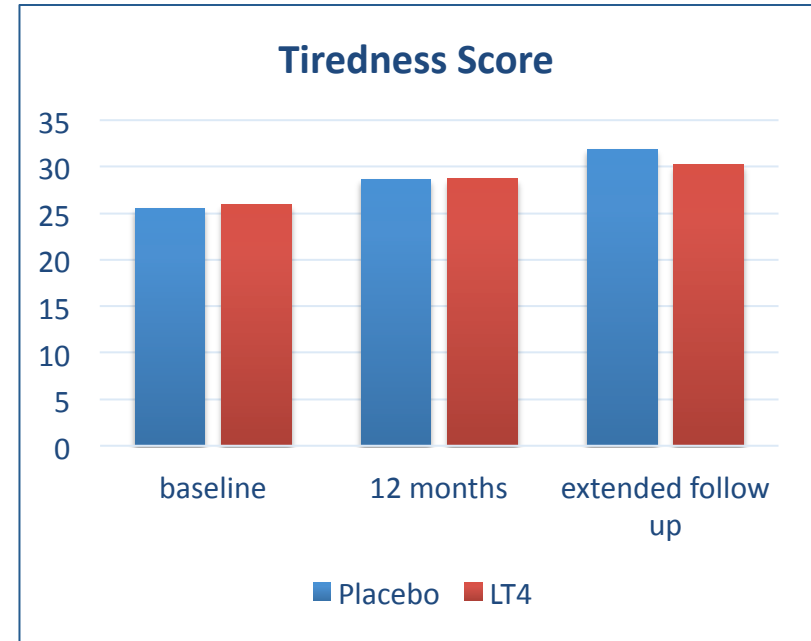
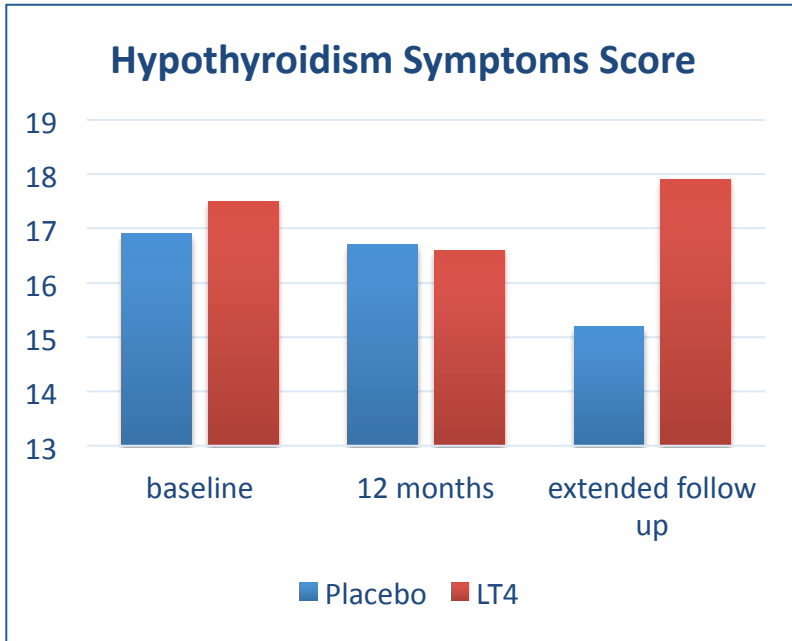


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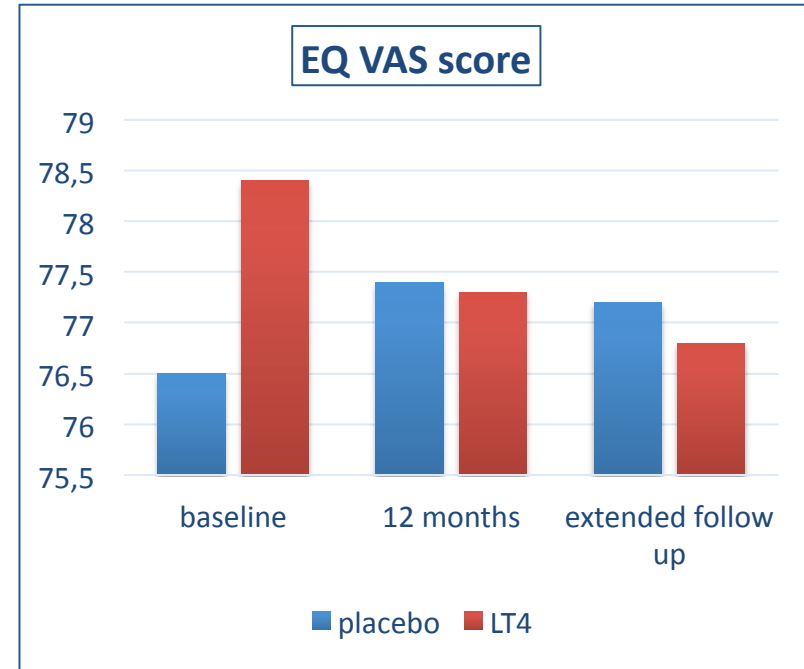
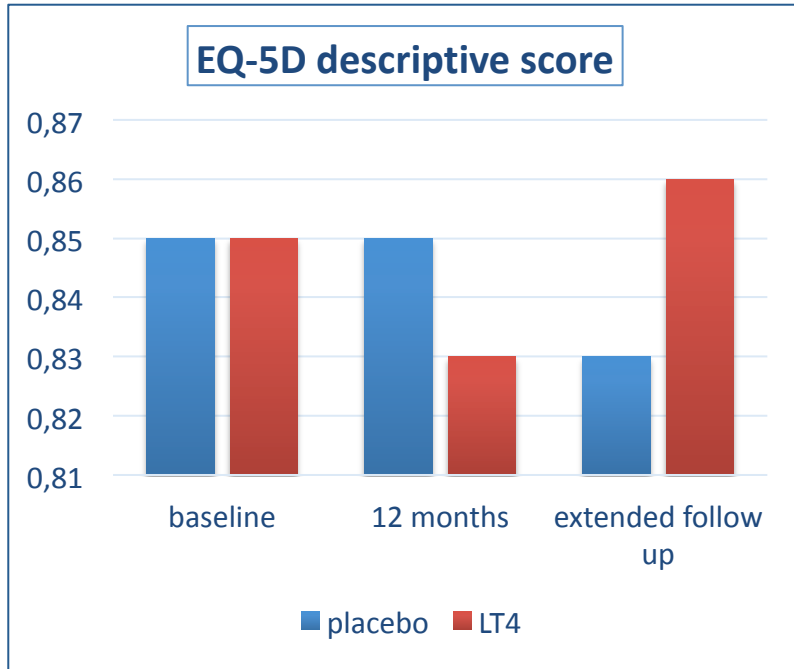
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Health Related Quality of Life





6-Month Treatment with LT4

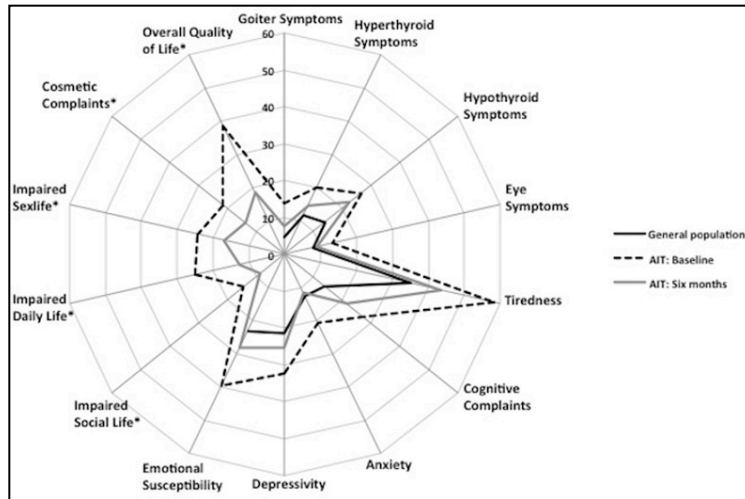


63 patients

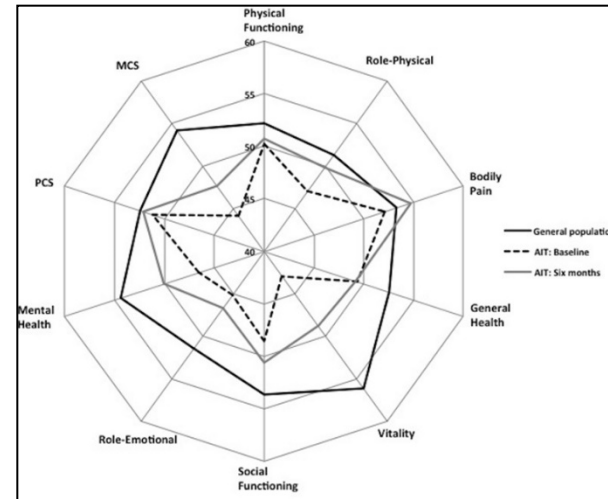
Age: 47 y (median)

TSH: 8.1 mIU/L (median)

ThyPRO radar plot



SF-36 Radar plot





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Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism



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Secondary outcomes

- *Hand-grip strength (dynamometer)*
- *Executive cognitive functions (letter-digit coding test)*
- *Blood pressure*
- *Weight*
- *BMI*
- *Waist circumference*
- *Activities of daily living (Barthel Index)*
- *Instrumental activities of daily living score*
- *Fatal and non-fatal cardiovascular events*





Hypothyroid Symptoms Fail to Predict Thyroid Insufficiency in Old People: A Population-Based Case-Control Study

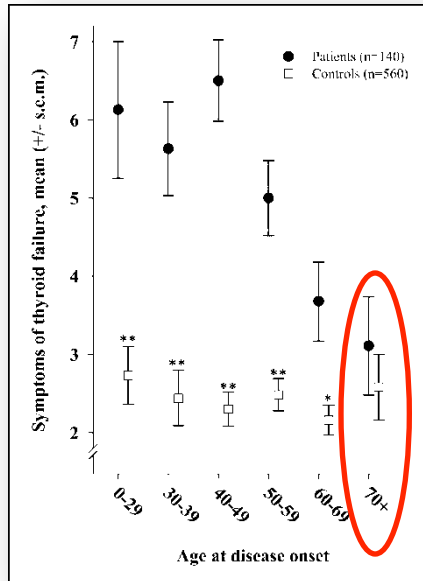
538,734 citizens; 140 overt hypo; median TSH: 54.5 mIU/l



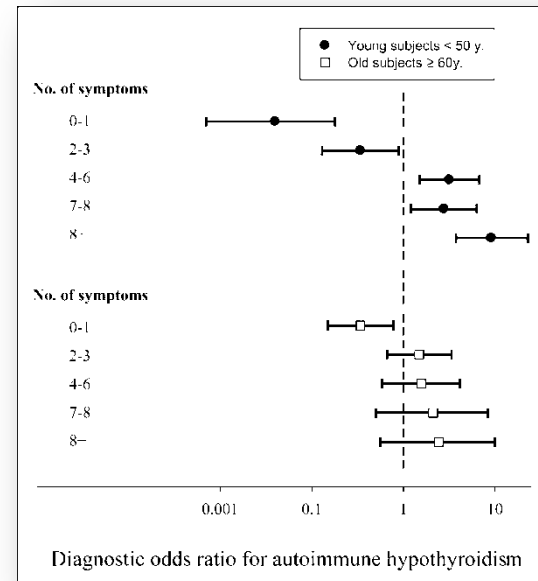
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Mean number of symptoms present at disease onset in autoimmune overt hypothyroidism



ORs for autoimmune overt hypothyroidism in the presence of different number of symptoms





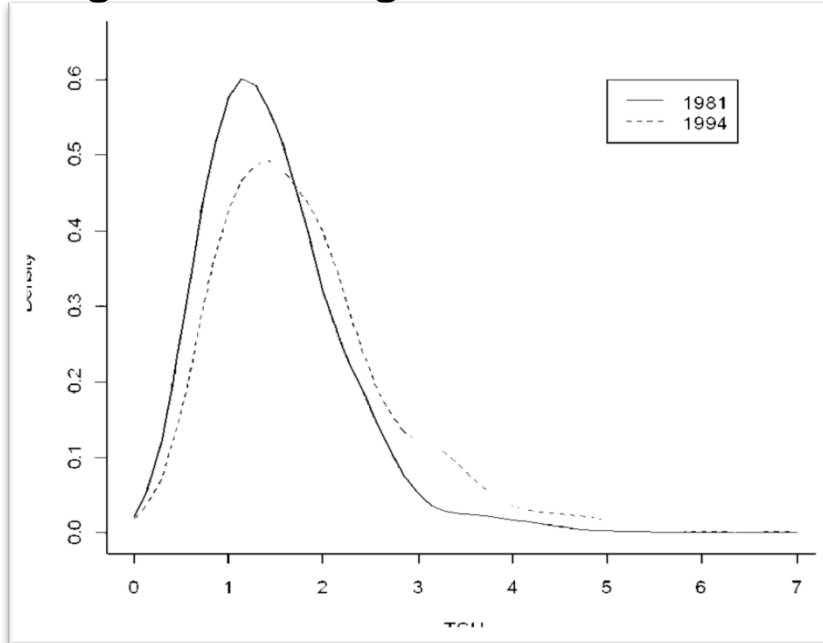
TSH change across ages



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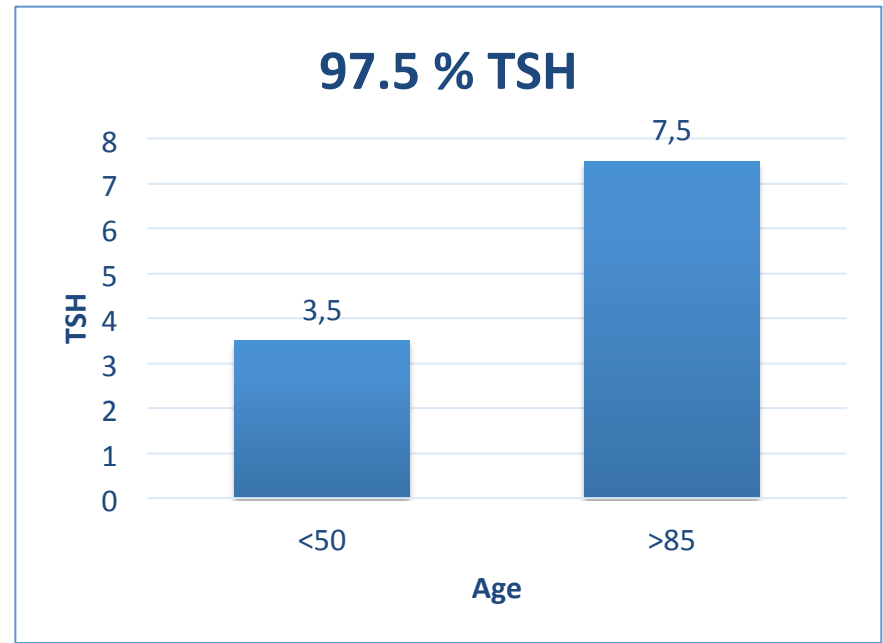
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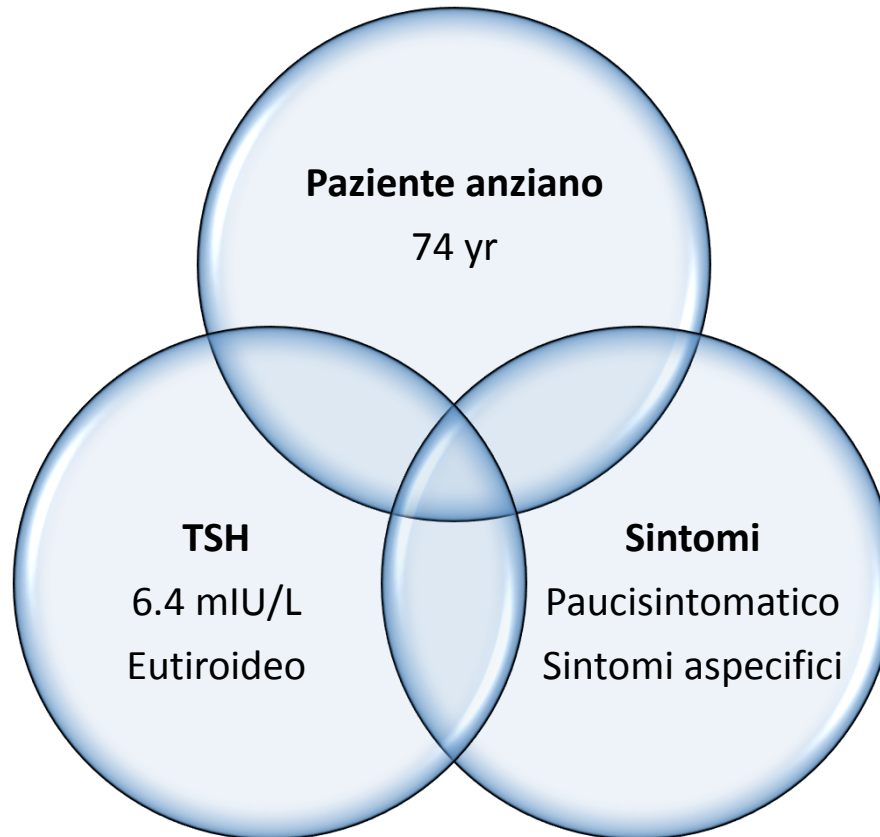
Longitudinal Change in TSH



- 908 patients
- 13 yr follow up
- TPOAb, TgAb, Drugs: excluded

NHANES III







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Cognitive Function in the Elderly



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- 599 participants were followed up from age **85** y through age **89** y
- TSH and FT4 were not associated with disability in daily life, depressive symptoms, and cognitive impairment at baseline or during follow-up
- *Increasing levels of TSH were associated with a lower mortality rate*

Gusseklou J et al. JAMA 2004

- RCT: effect of LT4 in Subclinical Hypothyroidism in 97 patients >65y
- Mini-Mental State; Examination Middlesex Elderly Assessment of Mental State (covering orientation, learning, memory, numeracy, perception, attention, and language skills); Trail-Making A and B
- No significant changes in any of the measures of cognitive function over time and no between-group difference in cognitive scores at 6 and 12 months.

Pearle J et al. J Clin Endocrinol Metab 2010

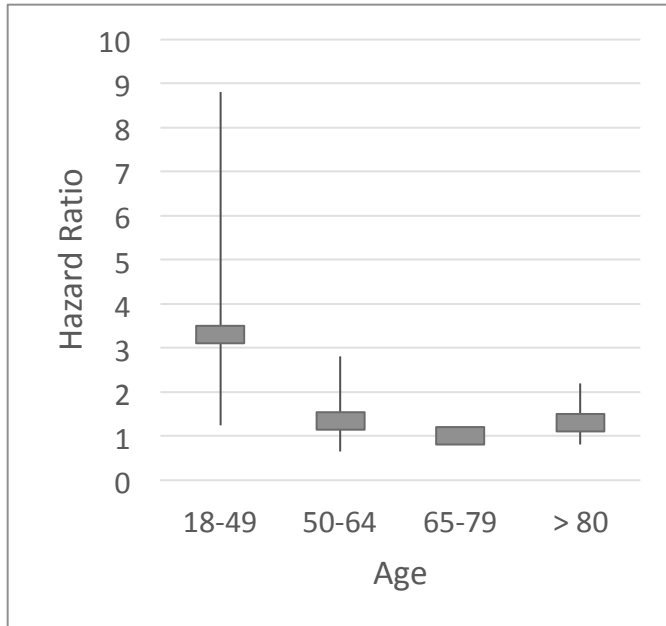


Subclinical Thyroid Dysfunction and the Risk of Stroke and Fatal Stroke

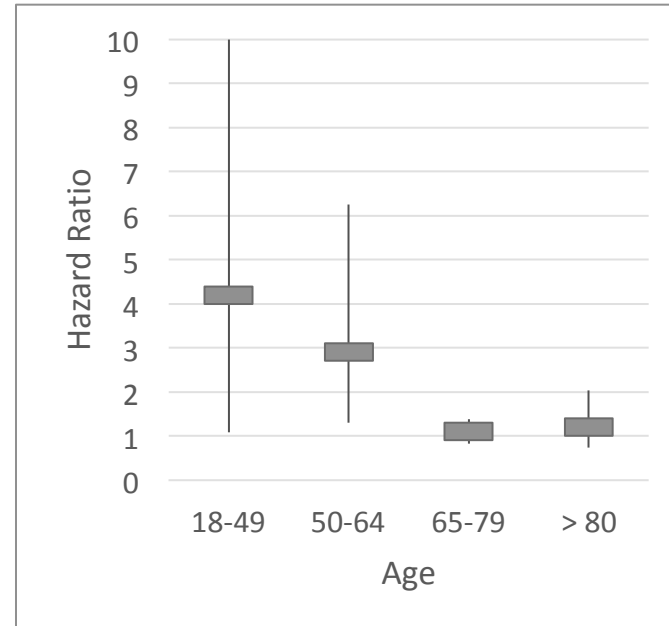


45 573 subjects (3451 subclinical hypo)
from 17 cohorts and followed up from 1972-2014

Stroke events by age



Fatal stroke by age





The Influence of Age on the Relationship between Subclinical Hypothyroidism and Ischemic Heart Disease: A Metaanalysis



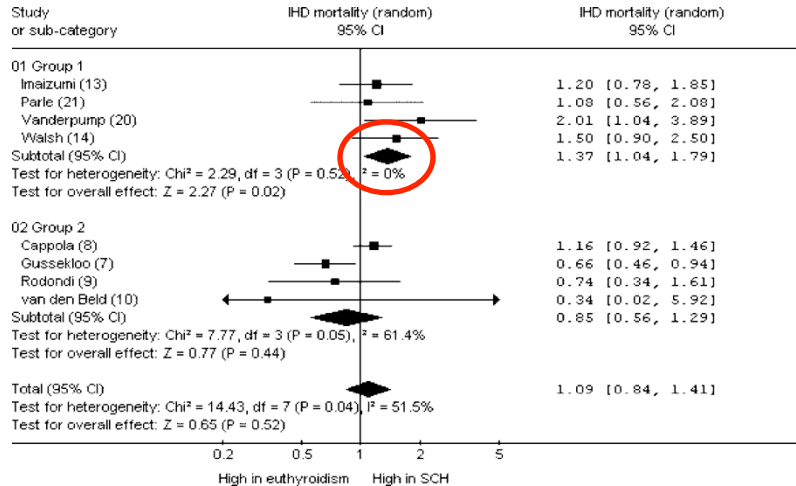
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Cardiovascular mortality in longitudinal studies

< 65 yr

> 65 yr



- **Objective:** to investigate whether age and gender influence IHD prevalence, incidence, and mortality in people with SCH.
- **Data Synthesis:** There were 15 studies included for analysis with 2,531 SCH participants and 26,491 euthyroid individuals.



The Influence of Age on the Relationship between Subclinical Hypothyroidism and Ischemic Heart Disease: A Metaanalysis

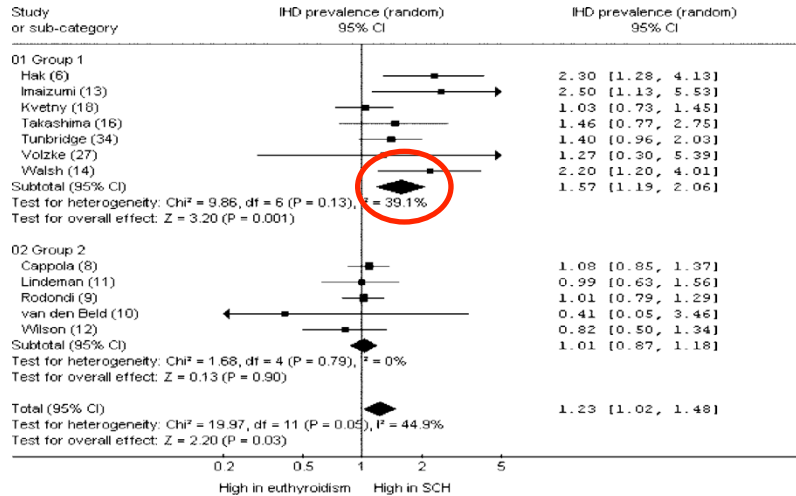


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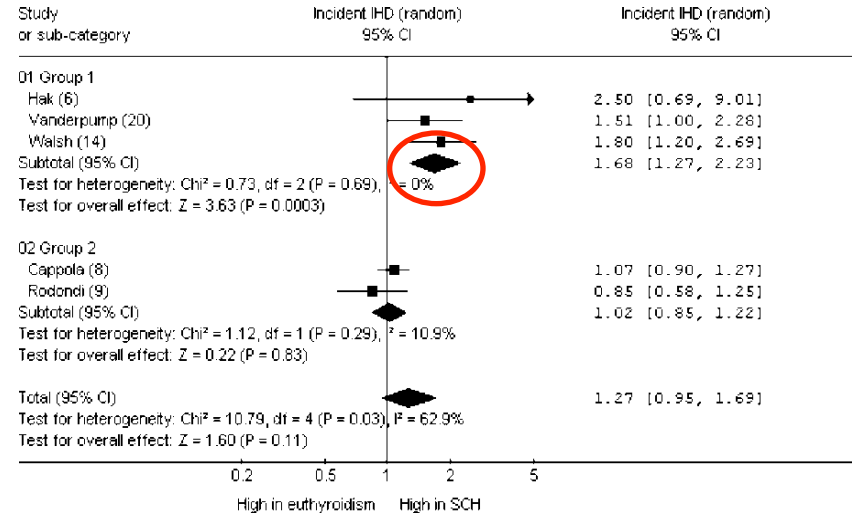
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IHD prevalence in cross-sectional studies

< 65 yr

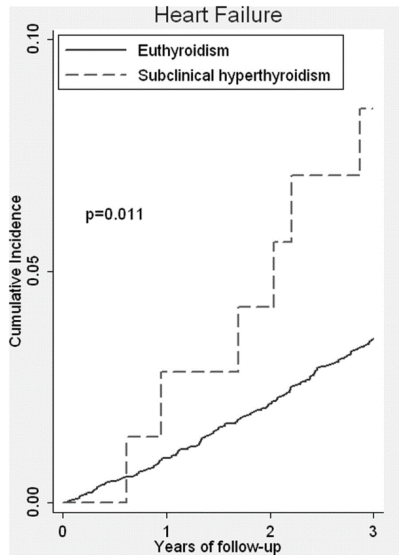


IHD incidence in longitudinal studies





Cumulative incidence of heart failure hospitalization



- The Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) is a prospective cohort study
- Patients included men and women aged 70–82 yr (n = 5316) with **known cardiovascular risk factors or previous cardiovascular disease**.
- 3.2-yr follow-up period

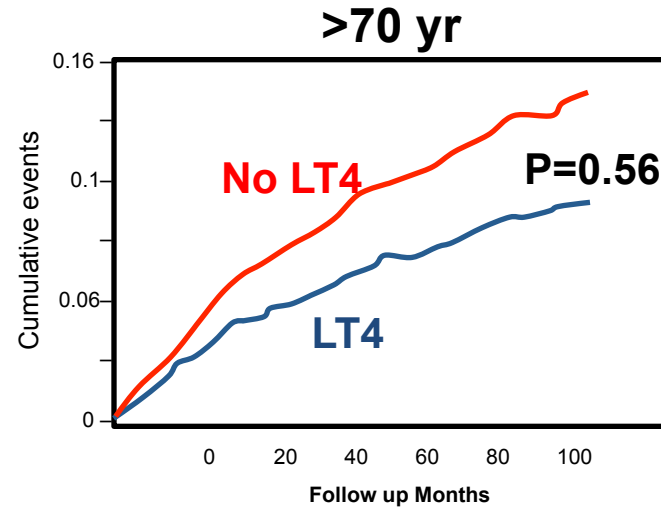
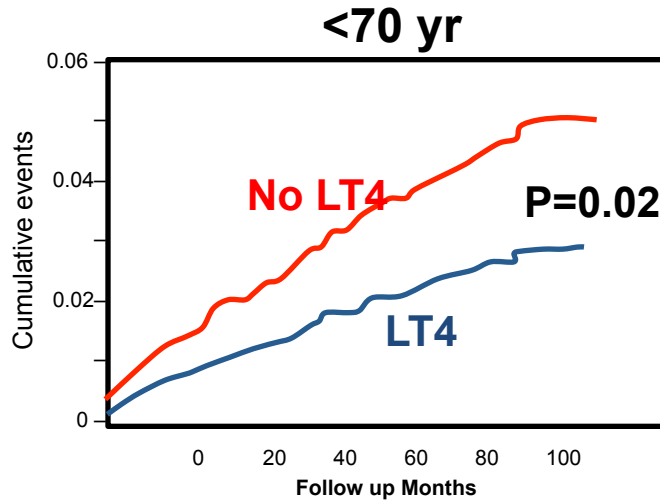


Levothyroxine Treatment of Subclinical Hypothyroidism, Fatal and Nonfatal Cardiovascular Events, and Mortality

UK General Practitioner Research Database (2001-2009)

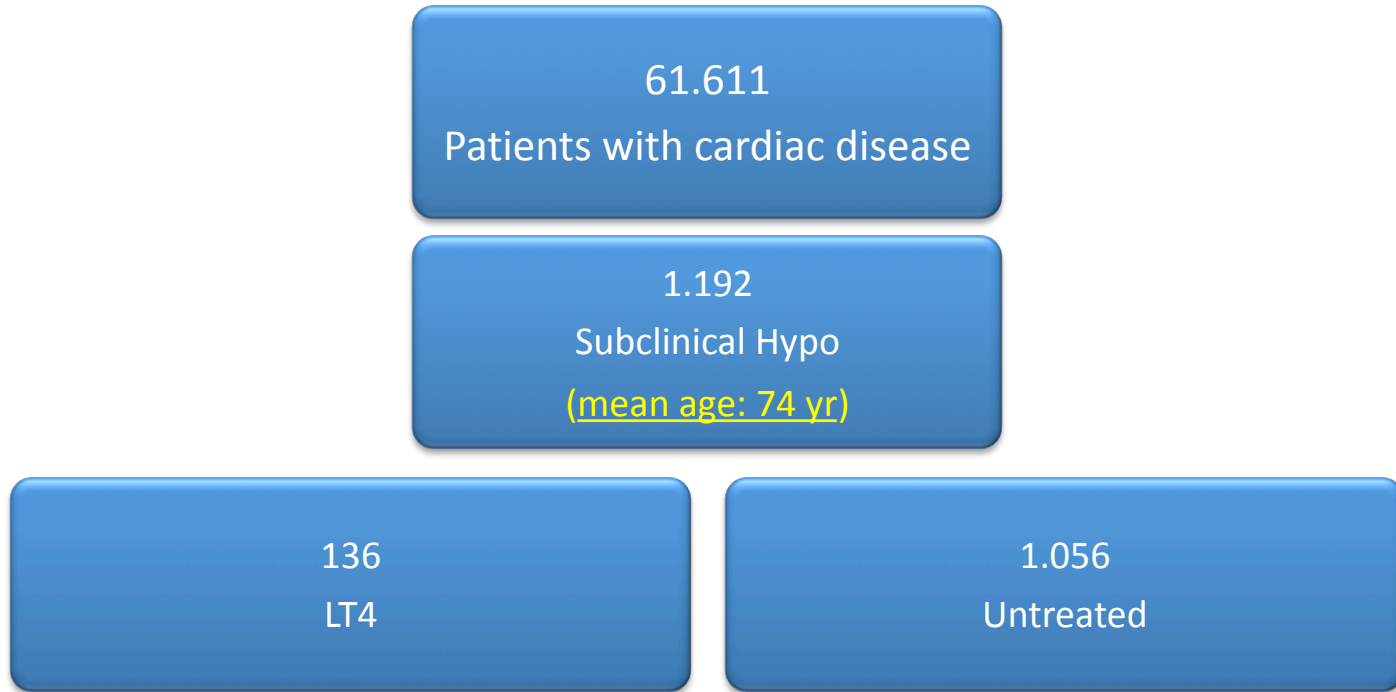


IHD events (fatal and nonfatal)



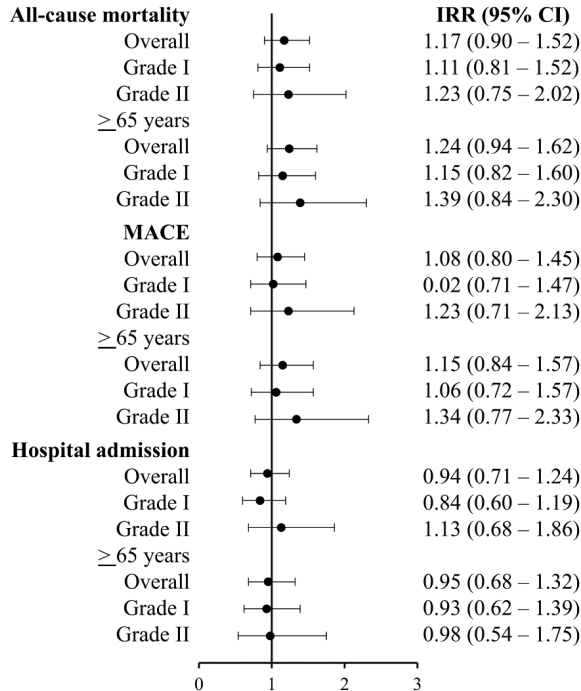


Long-Term Outcome in Levothyroxine Treated Patients With Subclinical Hypothyroidism and Concomitant Heart Disease





Long-Term Outcome in Levothyroxine Treated Patients With Subclinical Hypothyroidism and Concomitant Heart Disease



Follow-up time of 5.6 y
694 (58.2%) patients died

Patients treated with LT4: no significant increased risk of all-cause mortality, MACE, or hospital admission

LT4 treatment in patients with SCH and heart disease was not associated with a significant benefit nor risk



Conclusioni



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- Lo studio è RCT, metodologicamente corretto
- Potenza statistica adeguata per l'outcome primario
- Ha confermato l'assenza di efficacia della terapia sostitutiva nell'anziano con Ipo Subclinico (assenza di «malattia»?)
- Ha confermato precedenti studi sulla inutilità della L-T4 nell'anziano
- Ha indirettamente confermato la necessità di range di riferimento età-specifici