



Associazione Medici Endocrinologi

16° Congresso Nazionale AME
Joint Meeting with AACE Italian Chapter

Update in Endocrinologia Clinica

Roma, 9 - 12 novembre 2017



ITALIAN CHAPTER

Ipotiroidismo nell'anziano.
Processo alla terapia sostitutiva

Enrico Papini

Endocrinologia & Metabolismo

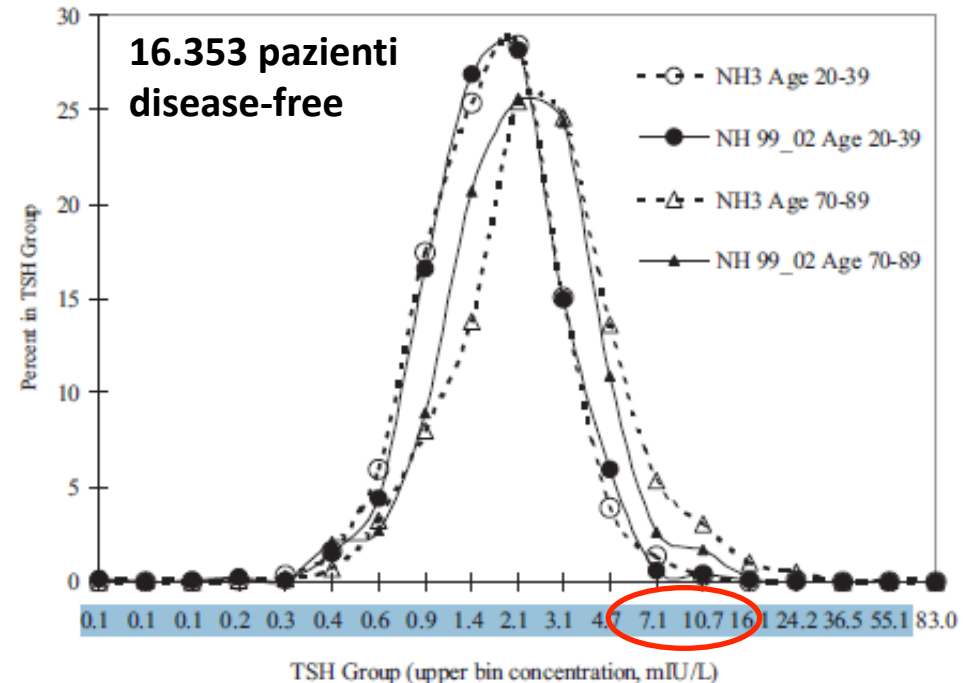
Ospedale Regina Apostolorum

Ipotiroidismo Subclinico: Quasi una epidemia nell'anziano

Prevalenza riportata nella popolazione adulta-anziana: 4.0-20.0%

- Sesso femminile
- Razza Caucasica
- Aree iodo-sufficienti
- BMI
- Tireopatia autoimmune

Stato fisiopatologico
o
reale patologia?



Subclinical thyroid disease

Scientific review and guidelines for diagnosis and management

Table 1. Quality of Evidence on the Strength of Association and Risks/Benefits of Treatment of Subclinical Hypothyroidism

Clinical Condition	Strength of Association		Benefits of Treatment	
	Serum TSH 4.5-10 mIU/L	Serum TSH >10 mIU/L	Serum TSH 4.5-10 mIU/L	Serum TSH >10 mIU/L
Progression to overt hypothyroidism	Good	Good	*	*
Adverse cardiac end points	Insufficient	Insufficient	No evidence	No evidence
Elevations in serum total and LDL cholesterol	Insufficient	Fair	Insufficient	Insufficient
Cardiac dysfunction	†	Insufficient	Insufficient	Insufficient
Systemic hypothyroid symptoms	None	Insufficient	Insufficient	Insufficient
Neuropsychiatric symptoms	None	Insufficient	Insufficient	Insufficient

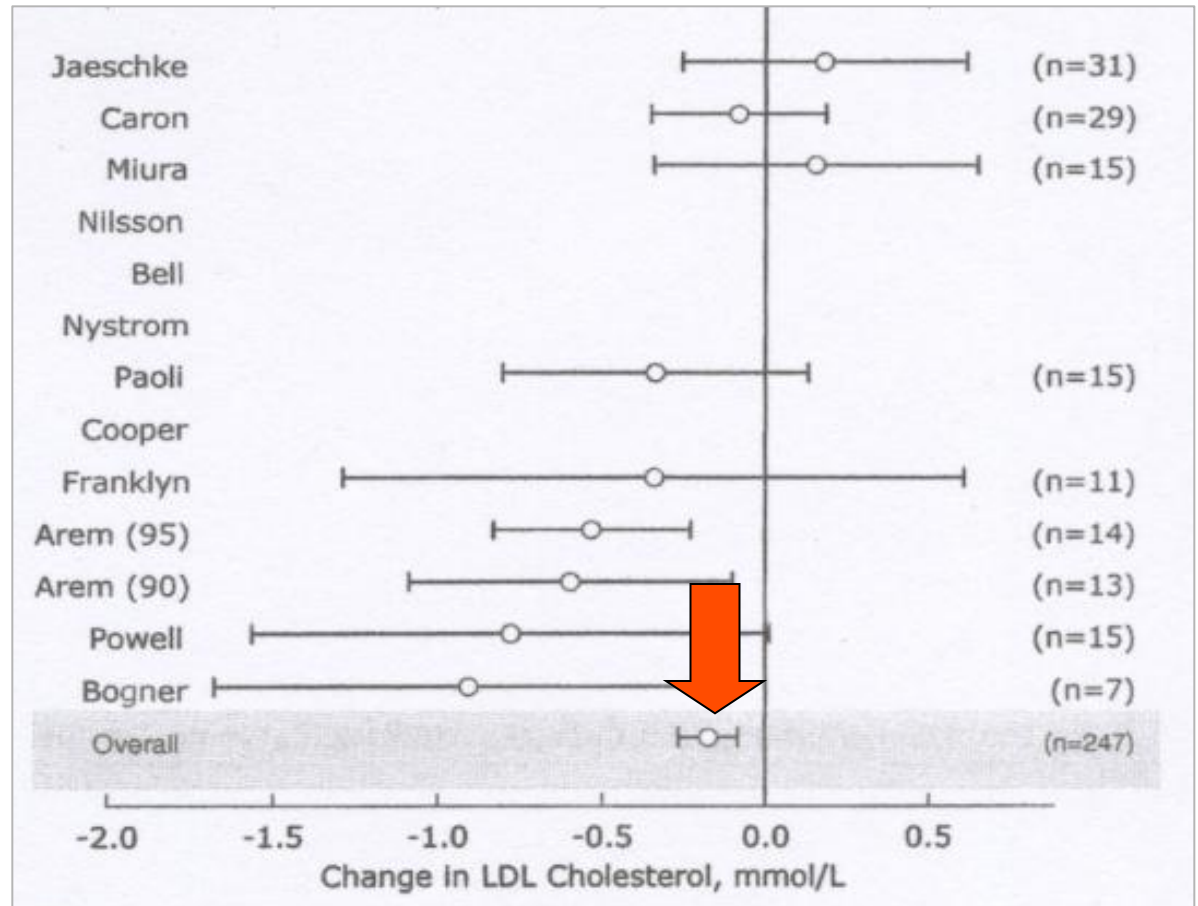
Abbreviations: LDL, low-density lipoprotein; TSH, thyroid-stimulating hormone.

*Thyroid hormone therapy normalizes serum TSH at any TSH concentration. Overt hypothyroidism occurs earlier in untreated patients with serum TSH >10 mIU/L than in those with serum TSH between 4.5 and 10 mIU/L.

†Data did not distinguish between serum TSH concentrations between 4.5 and 10 mIU/L and >10 mIU/L.

Modificazioni del metabolismo lipidico dopo terapia sostitutiva con levotiroxina: LDL-Colesterolo

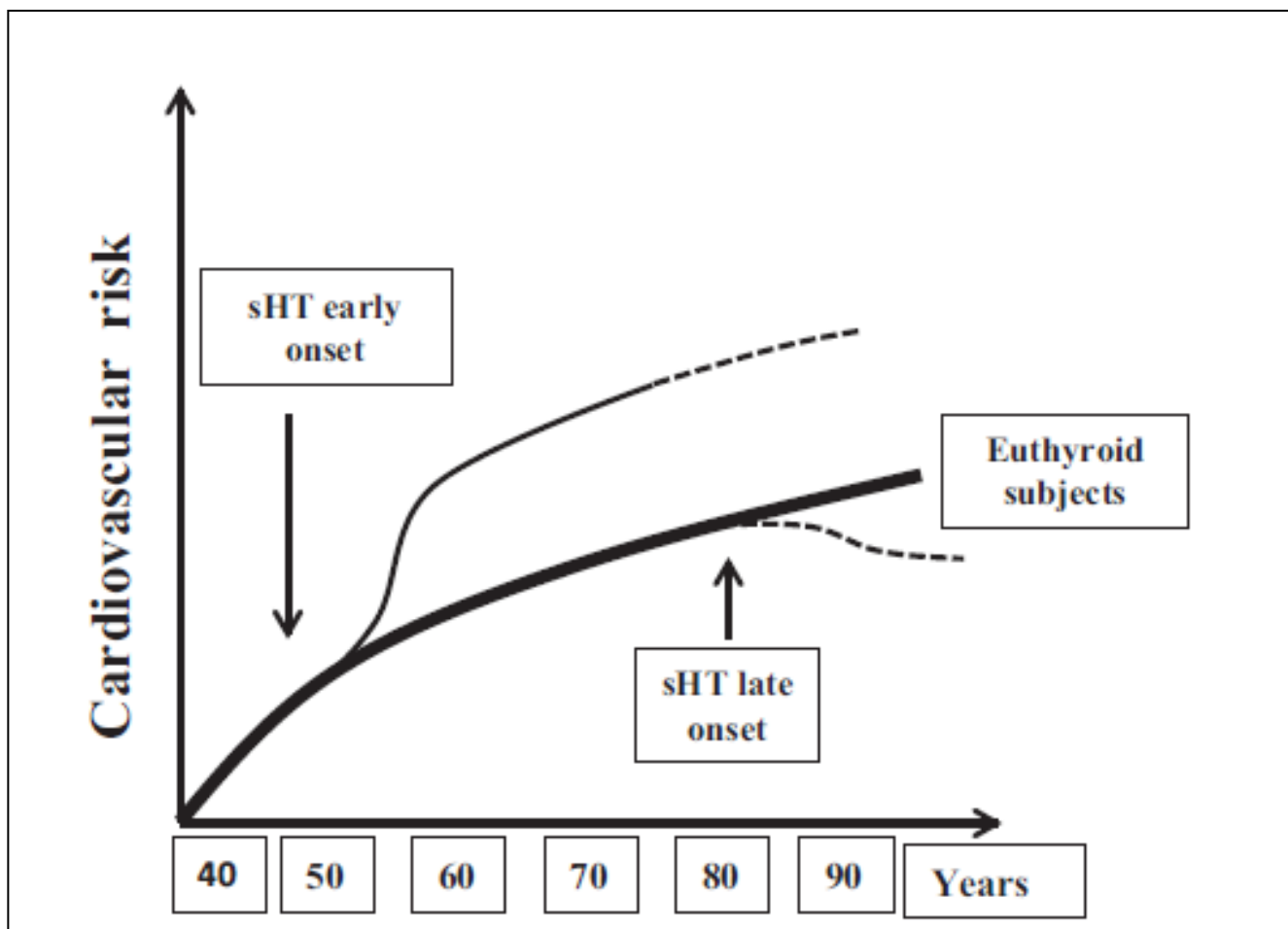
- 1786 articoli pubblicati
letteratura
- 13 studi di intervento con
gruppo di controllo
- 247 pazienti valutati
- riduzione media del
colesterolo LDL dopo
LT4 = -10 mg / dl (95% CI,
da - 4.0 a - 16)



Danese MD et al. Effects of Thyroxine Therapy on Serum Lipoproteins in Patients with Mild Thyroid Failure: A Quantitative Review of the Literature. J Clin Endocrinol Metab 2000; 85: 2993 - 3001

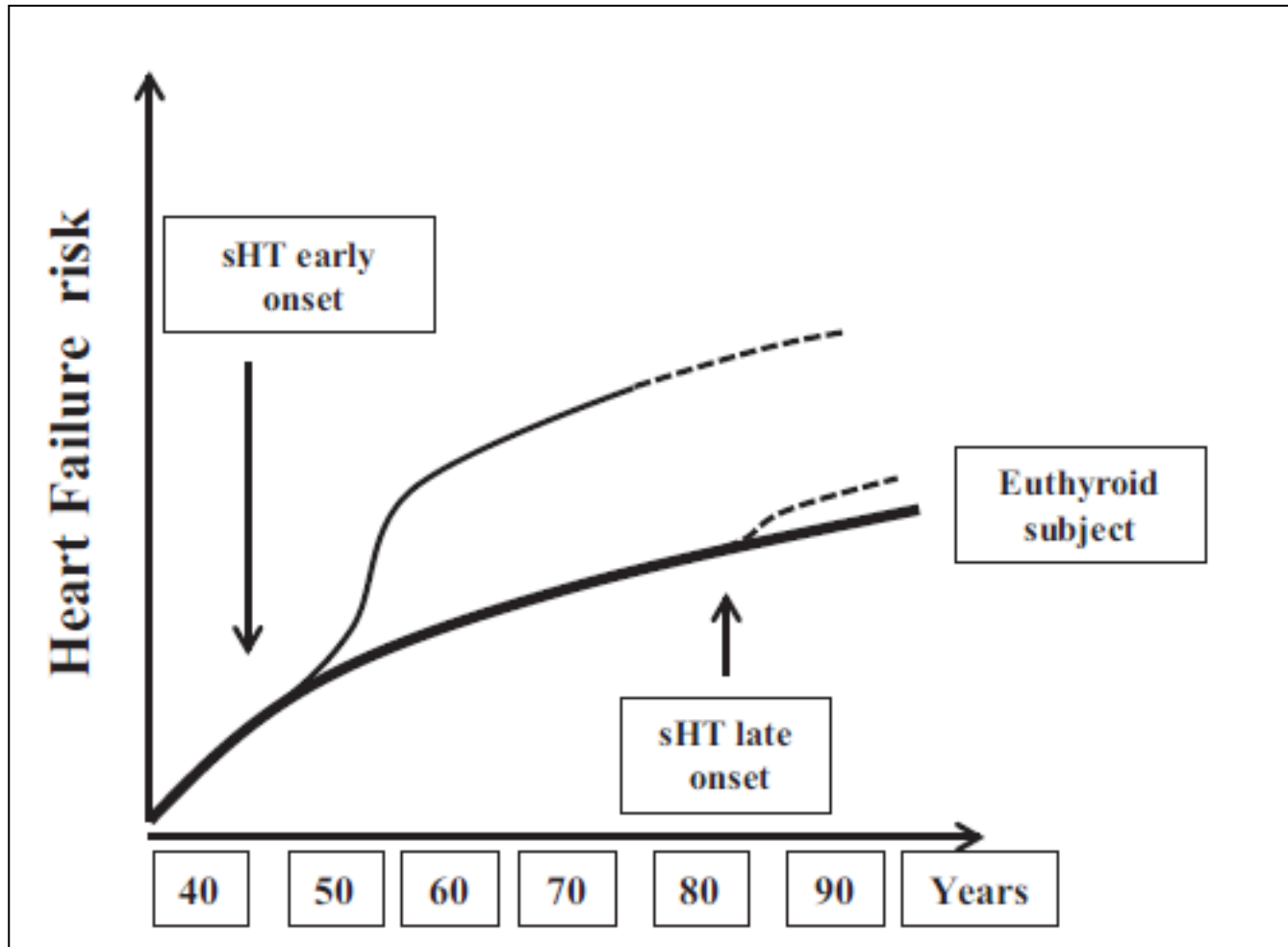
Is Subclinical Hypothyroidism a Cardiovascular Risk Factor in the Elderly?

Giuseppe Pasqualetti, Sara Tognini, Antonio Polini, Nadia Caraccio & Fabio Monzani



Is Subclinical Hypothyroidism a Cardiovascular Risk Factor in the Elderly?

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Subclinical Hypothyroidism

To treat or treat not?

- Patients whose serum TSH exceed 10 mIU/L are at increased risk for heart failure and cardiovascular mortality, and should be considered for treatment with LT4
- Treatment for patients with TSH between the upper limit and 10 mIU/L should be considered particularly in case of:
 - symptoms suggestive of hypothyroidism
 - positive TPOAb
 - atherosclerotic cardiovascular disease
 - heart failure or associated risk factors.

Grade B, BEL

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Il motivo del dibattito

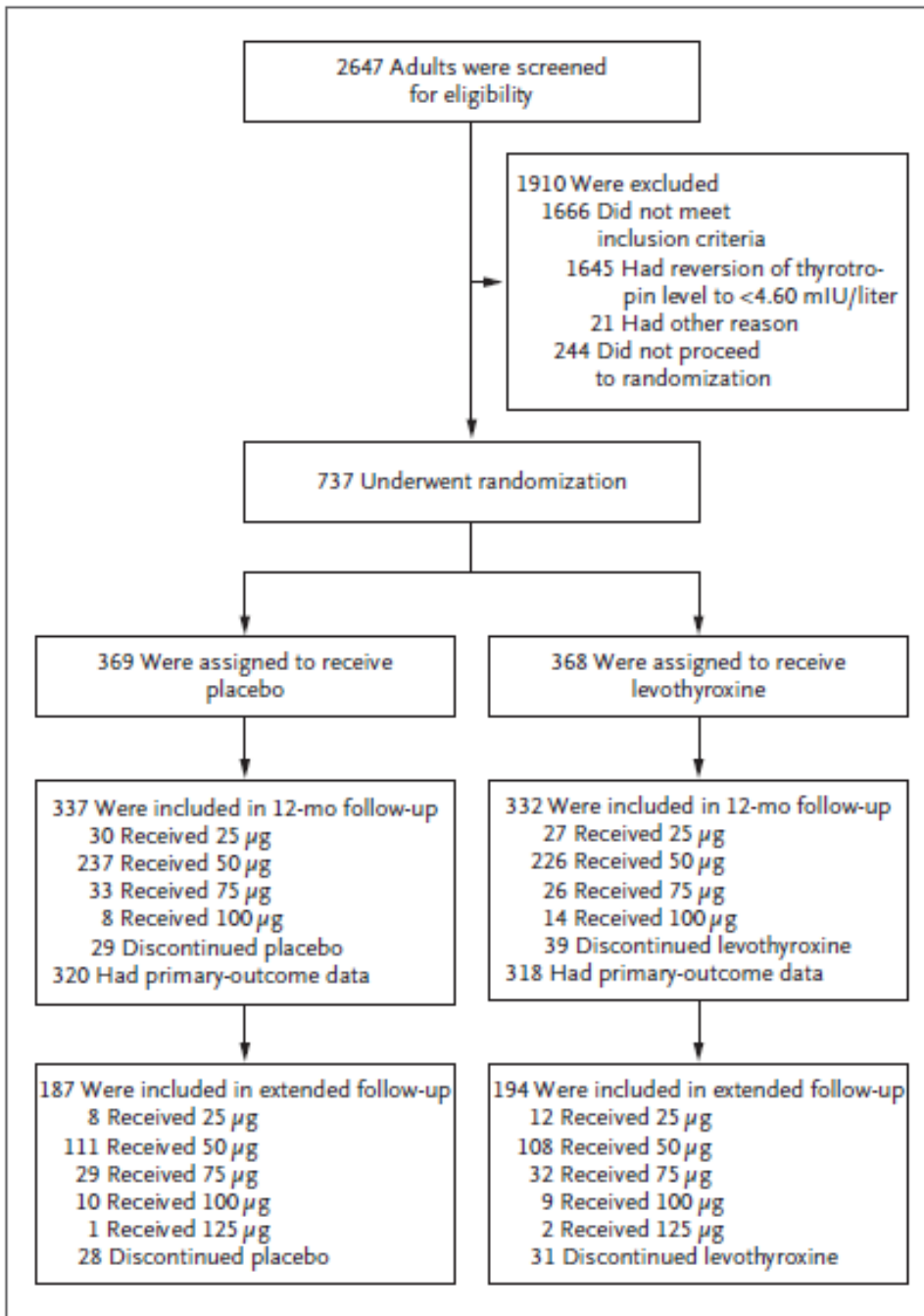
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism

D.J. Stott, N. Rodondi, P.M. Kearney, I. Ford, R.G.J. Westendorp, S.P. Mooijaart, N. Sattar, C.E. Aubert, D. Aujesky, D.C. Bauer, C. Baumgartner, M.R. Blum, J.P. Browne, S. Byrne, T.-H. Collet, O.M. Dekkers, W.P.J. den Elzen, R.S. Du Puy, G. Ellis, M. Feller, C. Floriani, K. Hendry, C. Hurley, J.W. Jukema, S. Kean, M. Kelly, D. Krebs, P. Langhorne, G. McCarthy, V. McCarthy, A. McConnachie, M. McDade, M. Messow, A. O'Flynn, D. O'Riordan, R.K.E. Poortvliet, T.J. Quinn, A. Russell, C. Sinnott, J.W.A. Smit, H.A. Van Dorland, K.A. Walsh, E.K. Walsh, T. Watt, R. Wilson, and J. Gussekloo, for the TRUST Study Group*

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Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism

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- Popolazione anziana con ipotiroidismo subclinico (età media: 65 anni)
- TSH (media): 6.4 mIU/L
- Studio prospettico randomizzato
- Disegno accurato del trial
- Ampio campione di pazienti (737)
- Questionari validati
- Follow-up di 12 mesi
- Rivista di elevato prestigio

Table 1. Characteristics of the Participants at Baseline.*

Characteristic	Placebo Group (N = 369)	Levothyroxine Group (N = 368)
Age — yr		
Mean	74.8±6.8	74.0±5.8
Range	65.1–93.4	65.2–93.0
Female sex — no. (%)	198 (53.7)	198 (53.8)
White race — no. (%)†	362 (98.1)	362 (98.4)
Standard housing — no. (%)‡	356 (96.5)	358 (97.3)
Previous medical conditions and clinical descriptors — no./total no. (%)		
Ischemic heart disease§	50/369 (13.6)	50/368 (13.6)
Atrial fibrillation	44/368 (12.0)	45/364 (12.4)
Hypertension	183/366 (50.0)	192/368 (52.2)
Diabetes mellitus	54/368 (14.7)	63/368 (17.1)
Osteoporosis	47/367 (12.8)	41/364 (11.3)
Current smoking	33/369 (8.9)	29/368 (7.9)
Median no. of concomitant medicines (IQR)	4 (2–6)	4 (2–6)
Median Mini-Mental State Examination score (IQR)¶	29 (28–30)	29 (27–30)
Weight <50 kg — no. (%)	5 (1.4)	5 (1.4)
Laboratory results		
Thyrotropin — mIU/liter	6.38±2.01	6.41±2.01
Median (IQR)	5.76 (5.10–6.94)	5.73 (5.12–6.83)
Range	4.60–17.60	4.60–17.60
Free thyroxine — pmol/liter	13.3±1.9	13.4±2.1
Outcome measures**		
Hypothyroid Symptoms score	16.9±17.9	17.5±18.8
Tiredness score	25.5±20.3	25.9±20.6
EQ-5D descriptive index	0.847±0.171	0.846±0.187
EQ visual-analogue scale score	76.5±16.3	78.4±15.3
Hand-grip strength — kg	27.5±11.3	28.0±10.2
Letter–digit coding test score	25.2±8.3	24.9±7.4
Blood pressure — mm Hg		
Systolic	140.4±18.9	141.2±18.7
Diastolic	74.8±11.7	74.1±11.6
Body-mass index	27.7±4.6	28.1±5.3

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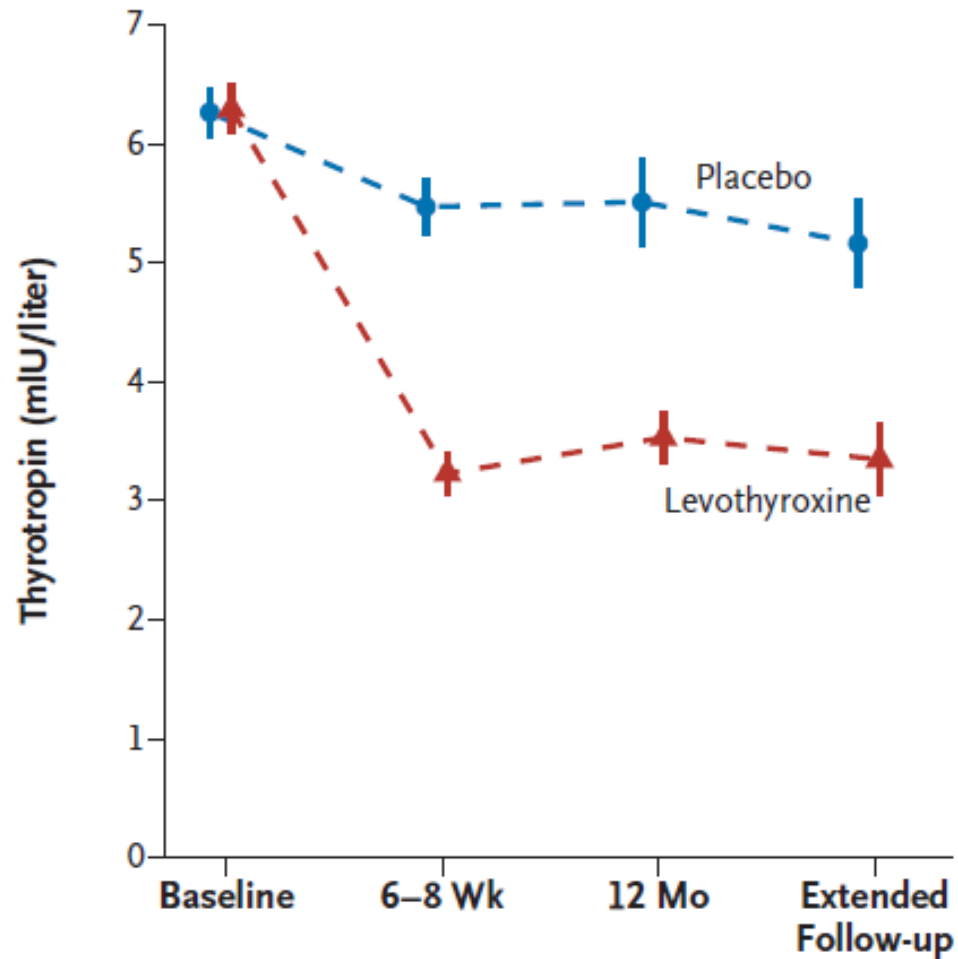


Figure 2. Thyrotropin Levels in the Placebo Group and Levothyroxine Group.

Dopo 6 settimane, differenza statisticamente significativa dei valori del TSH nel gruppo in trattamento attivo vs:

- gruppo di controllo
- livelli basali.

Variabili cliniche ed eventi avversi

Variable	All Patients (N=737)	Placebo Group (N=369)	Levothyroxine Group (N=368)	Hazard Ratio (95% CI)
Clinical outcome				
Fatal or nonfatal cardiovascular event — no. (%)	38 (5.2)	20 (5.4)	18 (4.9)	0.89 (0.47–1.69)
Cardiovascular death — no. (%)	3 (0.4)	1 (0.3)	2 (0.5)	—
Death from any cause — no. (%)	15 (2.0)	5 (1.4)	10 (2.7)	1.91 (0.65–5.60)
Serious adverse event				
No. of patients with ≥1 serious adverse event	181 (24.6)	103 (27.9)	78 (21.2)	0.94 (0.88–1.00)†
No. of events	343	201	142	—
Adverse event of special interest				
New-onset atrial fibrillation — no. (%)	24 (3.3)	13 (3.5)	11 (3.0)	0.80 (0.35–1.80)
Heart failure — no. (%)	9 (1.2)	6 (1.6)	3 (0.8)	—
Fracture — no. (%)	17 (2.3)	8 (2.2)	9 (2.4)	1.06 (0.41–2.76)
New diagnosis of osteoporosis — no. (%)	7 (0.9)	4 (1.1)	3 (0.8)	—
Withdrawal				
Permanent discontinuation of trial regimen — no. (%)	160 (21.7)	79 (21.4)	81 (22.0)	1.06 (0.78–1.44)
Withdrawal from follow-up — no. (%)	41 (5.6)	22 (6.0)	19 (5.2)	0.84 (0.46–1.56)

Clinical Outcomes

Table 2. Outcomes at 12 Months and Extended Follow-up*

Variable	Baseline		At 12 Mo				At Extended Follow-up Visit†			
	Placebo (N=166)	Levothyroxine (N=168)	Placebo (N=120)	Levothyroxine (N=118)	Difference (95% CI)	P Value	Placebo (N=187)	Levothyroxine (N=194)	Difference (95% CI)	P Value
Thyrotropic — mIU/liter	6.38±2.01	6.41±2.01	5.48±2.68	5.63±2.11	-1.92 (-2.24 to -1.59)	<0.001	5.28±2.50	5.47±2.08	-1.88 (-2.32 to -1.45)	<0.001
Median (IQR)	5.76 (5.10 to 6.94)	5.70 (5.12 to 6.83)	4.90 (3.91 to 6.46)	3.16 (2.45 to 4.22)	—	—	4.94 (3.78 to 6.26)	3.00 (2.26 to 4.16)	—	—
Primary outcomes ‡										
Hypothyroid Symptoms score	16.9±17.9	17.5±18.8	16.7±17.5	16.6±16.9	0.0 (-2.0 to 2.1)	0.99	15.2±15.9	17.9±19.1	1.0 (-1.9 to 3.9)	0.50
Tiredness score	25.5±20.3	25.9±20.6	28.6±19.5	28.7±20.2	0.4 (-2.1 to 2.9)	0.77	31.9±22.1	30.2±20.5	-3.5 (-7.0 to 0.0)	0.05
Secondary outcomes										
EQ-5D descriptive score	0.847±0.171	0.846±0.187	0.853±0.201	0.853±0.212	-0.025 (-0.050 to 0.000)	0.05	0.829±0.209	0.844±0.188	0.040 (0.005 to 0.075)	0.03
EQVAS score	76.5±16.3	78.4±15.3	77.4±13.7	77.3±15.6	-1.3 (-3.2 to 0.6)	0.18	77.2±13.5	76.8±14.2	-0.8 (-3.2 to 1.7)	0.56
Hand-grip strength — kg	27.5±11.3	28.0±10.2	27.1±11.2	27.5±10.5	-0.1 (-0.9 to 0.7)	0.84	24.9±10.6	24.4±10.1	-0.6 (-1.7 to 0.6)	0.34
Blood pressure — mm Hg										
Systolic	140.4±18.9	141.2±18.7	138.4±17.8	138.5±18.7	0.1 (-2.1 to 2.4)	0.90	137.5±19.2	136.8±17.6	1.1 (-4.1 to 2.1)	0.51
Diastolic	74.8±11.7	74.1±11.6	73.5±11.1	72.8±11.4	-0.1 (-1.5 to 1.3)	0.93	72.3±11.4	72.0±11.5	0.3 (-1.4 to 2.4)	0.59
Body mass index	27.7±4.6	28.1±5.3	27.7±4.6	27.9±5.1	0.0 (-0.2 to 0.2)	0.89	27.2±4.5	27.9±4.9	0.2 (-0.1 to 0.5)	0.30
Waist circumference — cm	97.5±12.8	98.5±13.6	96.8±13.1	98.0±13.2	0.4 (-0.4 to 1.3)	0.34	96.0±13.8	97.6±13.4	0.3 (-0.9 to 1.5)	0.66
Adverse symptom assessment										
Hyperthyroid Symptoms score‡	30.5±11.2	30.5±11.2	30.3±11.3	30.5±10.8	0.6 (-0.7 to 1.9)	0.35	9.8±11.0	11.1±11.7	0.7 (-1.2 to 2.5)	0.46

- No significant change in the two groups for:
 - hypothyroid symptom score
 - tiredness score

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In conclusion, this trial indicated that treatment with levothyroxine in older persons with subclinical hypothyroidism provided no symptomatic benefits.



La terapia dell'ipotiroidismo subclinico nell'anziano è inutile (se non dannosa)?

La parola alle parti