



## IPOTIROIDISMO: TARGET DI TERAPIA NELL'ANZIANO

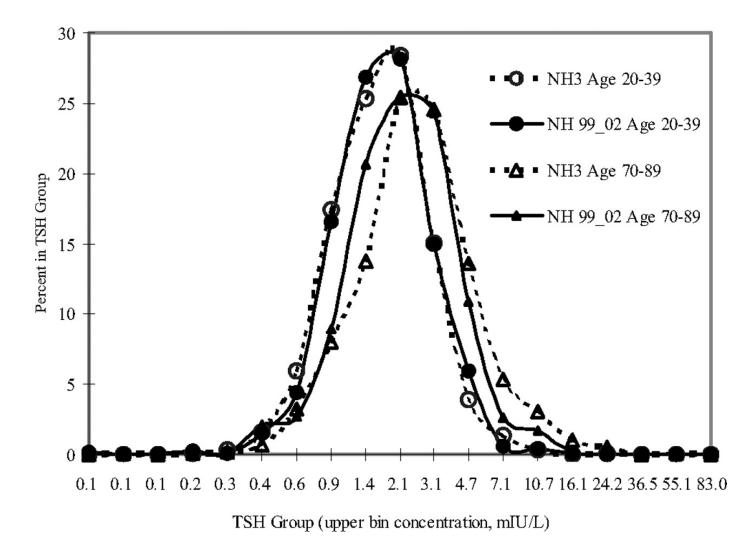
Fabio Vescini

## Invecchiamento e funzione tiroidea

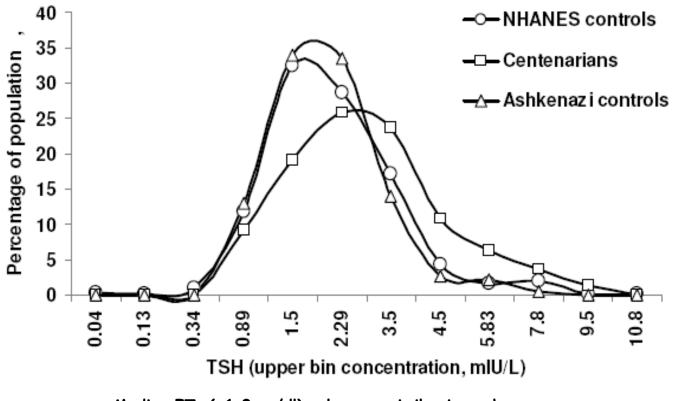


### **TSH** distribution

Comparison of U.S. disease-free populations by age groups NHANES III (1988-1994) and NHANES 1999-2002



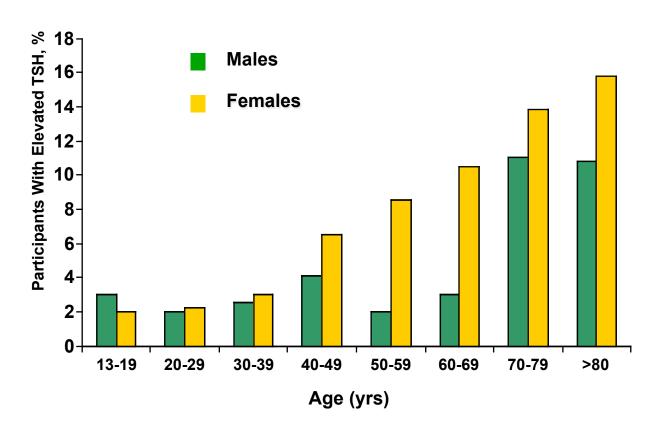
## Extreme Longevity and Increased Serum TSH Value



Median  $FT_4$  ( $\approx 1.0$  ng/dl) value was similar in each group

236 Ashkenazi Jewish centenarians living independently, median age: 97.7 yrs 188 younger unrelated Ashkenazi Jews (controls), median age: 71.0 yrs 605 NHANES controls, age range 60-79 yrs

## Prevalence of Elevated Serum TSH by Decade of Age and Gender



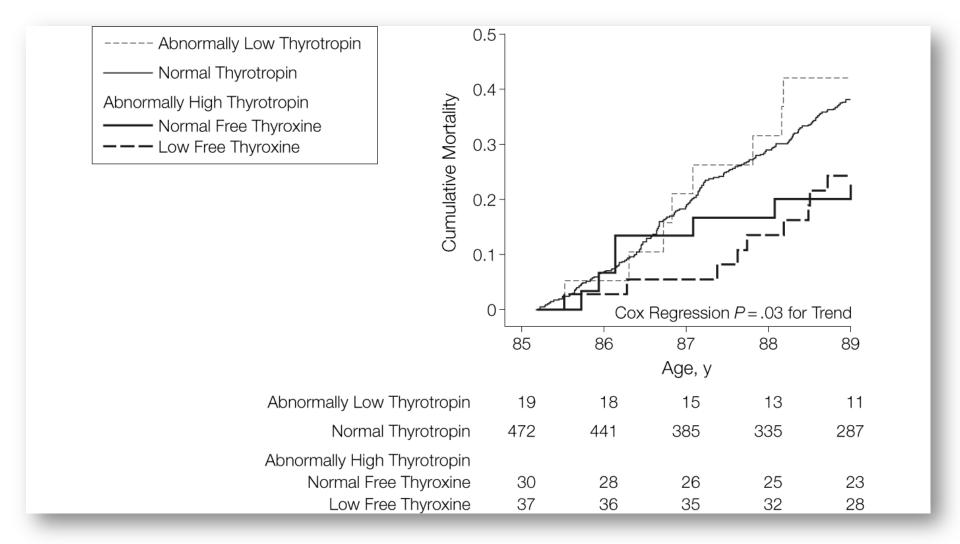
- Up to 40 years of age, prevalence is relatively low and similar between males and females
- Between 40 and 70 years of age, a higher percentage of female patients have elevated TSH levels
- At >70 years of age, prevalence is high and similar between males and females



#### Thyroid Status, Disability and Cognitive Function, and Survival in Old Age

Gussekloo J, et al.

JAMA. 2004;292(21):2591-2599

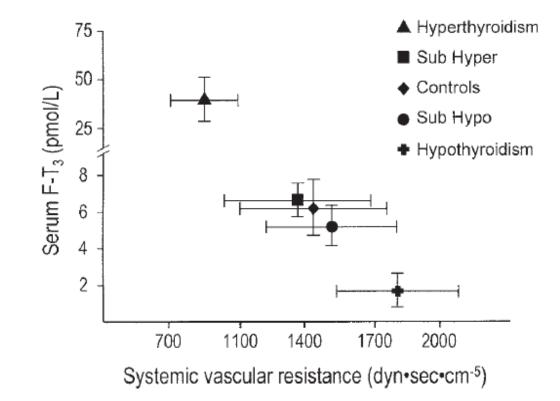


## Effetti dell'ipotiroidismo



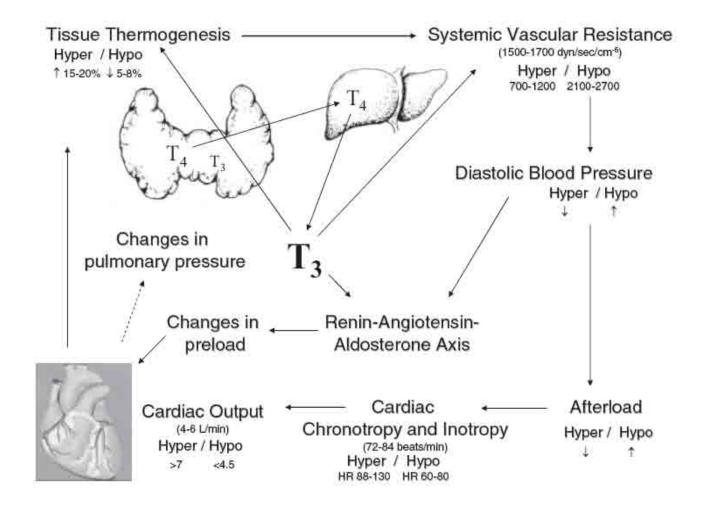
# Serum FT3 levels and systemic vascular resistance

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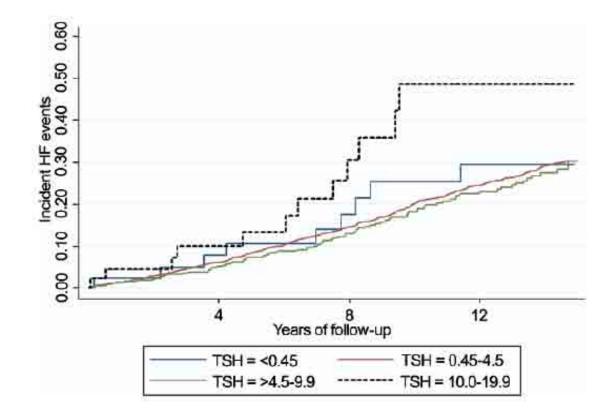


# Effects of thyroid hormone on cardiovascular system

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### **TSH and Incident Heart Failure Events**



#### The Cardiovascular Health Study: 3044 adults >65 yrs of age

Participants with TSH 10.0-19.9 mU/l who were untreated by LT4 replacement had a greater incidence of HF events compared with euthyroid participants (41.7 vs. 22.9 × 1,000 person/year, p=0.01)

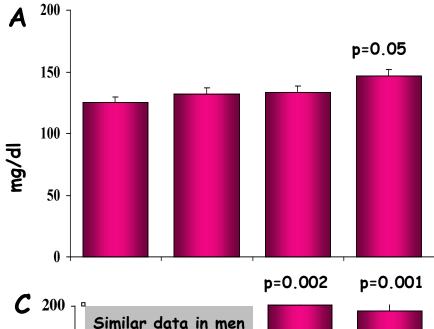
Rodondi et al. JACC 2008

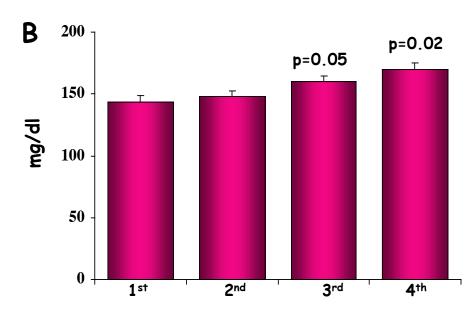
#### TSH quartiles and LDLc value according to women's age

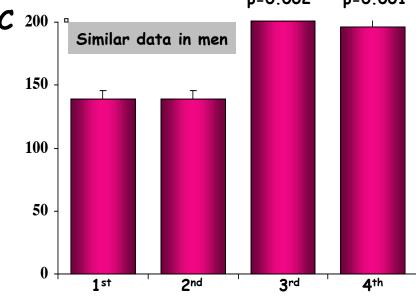
Age Groups A: 30-49 years B: 50-64 years C: >65 years

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1<sup>st</sup> quartile: TSH <0.36 mUI/L 2<sup>nd</sup> quartile: TSH >0.36 <3.60 mUI/L 3<sup>rd</sup> quartile: TSH >3.60 <10 mUI/L 4<sup>th</sup> quartile: TSH >10 mUI/L









Review article: Current opinion | Published 23 December 2014, doi:10.4414/smw.2014.14058 Cite this as: Swiss Med Wkly. 2014;144:w14058

## Subclinical hypothyroidism: summary of evidence in 2014

Christine Baumgartner<sup>a</sup>, Manuel R. Blum<sup>a</sup>, Nicolas Rodondi<sup>a</sup>

Table 2: Risk for Coronary Heart Disease (CHD) mortality and events and heart failure events according to thyroid-stimulating hormone levels.

TSH level	HRs for CHD mortality (95% CI)	HRs for CHD events (95% CI)	HRs for heart failure events (95% CI)
TSH 10.0–19.9 mIU/I	1.58 (1.10–2.27)	1.89 (1.28–2.80)	1.86 (1.27–2.72)
TSH 7.0–9.9 mIU/I	1.42 (1.03–1.95)	1.17 (0.96–1.43)	1.65 (0.84–3.23)
TSH 4.5–6.9 mIU/I	1.09 (0.91–1.30)	1.00 (0.86–1.18)	1.01 (0.81–1.26)
TSH 0.45–4.49 mIU/l*	1.00 (reference)	1.00 (reference)	1.00 (reference)
TSH 0.10–0.44 mIU/I	1.24 (0.96–1.61)	1.27 (1.03–1.58)	1.31 (0.88–1.95)
TSH <0.10 mIU/I	1.84 (1.12–3.00)	1.08 (0.69–1.69)	1.94 (1.01–3.72)

Adapted according to [10, 11, 27]. CHD = coronary heart disease; CI = confidence interval; HR = hazard ratio (age and gender-adjusted); TSH = thyroid-stimulating hormone.

\* TSH 0.5-4.49 mIU/I for association between subclinical hypothyroidism and CHD mortality and CHD events.



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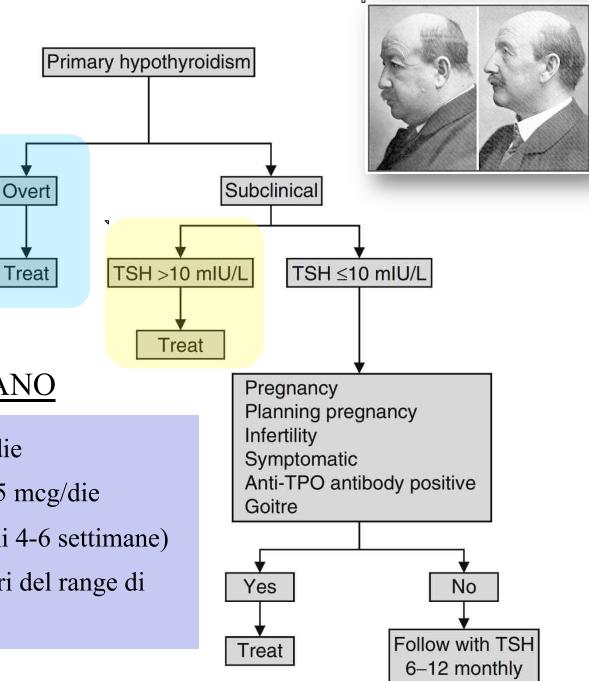
## Subclinical hypothyroidism: summary of evidence in 2014

Christine Baumgartner<sup>a</sup>, Manuel R. Blum<sup>a</sup>, Nicolas Rodondi<sup>a</sup>

#### Table 1: Level of evidence in 2014 on the risks of treatment and the benefits of subclinical hypothyroidism.

Clinical condition	Strength of association	
	TSH 4.5–9.9 mIU/I	TSH ≥10 mIU/I
Progression to overt hypothyroidism		Stronger
Elevation in serum total cholesterol and LDL		Stronger
Risk of coronary heart disease		Stronger
Risk of congestive heart failure	9	Stronger
Cardiac dysfunction		Insufficient
Systemic symptoms of hypothyroidism		Insufficient
Neuropsychiatric symptoms (e.g., depression, cognitive dysfunction)		Insufficient
Muscle strength		Insufficient
Fatigue		Insufficient





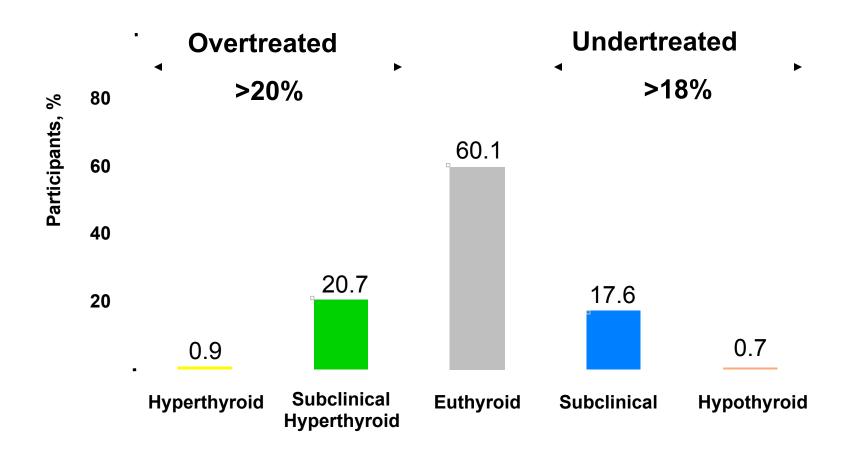
#### TERAPIA NELL'ANZIANO

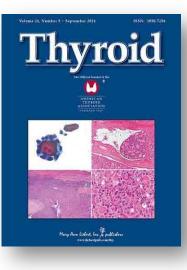
- Levo-tiroxina: 1 mcg/Kg/die
- Dosi scalari partendo da 25 mcg/die (incremento posologia ogni 4-6 settimane)
- Target TSH: limiti superiori del range di norma

Khandelwal and Tandon. Drugs 2012; 72 (1): 17-33.

#### **Thyroid Status of Treated Patients**

Colorado Thyroid Disease Prevalence Study (1525 pts.)





THYROID Volume 24, Number 12, 2014 © American Thyroid Association DOI: 10.1089/thy.2014.0028

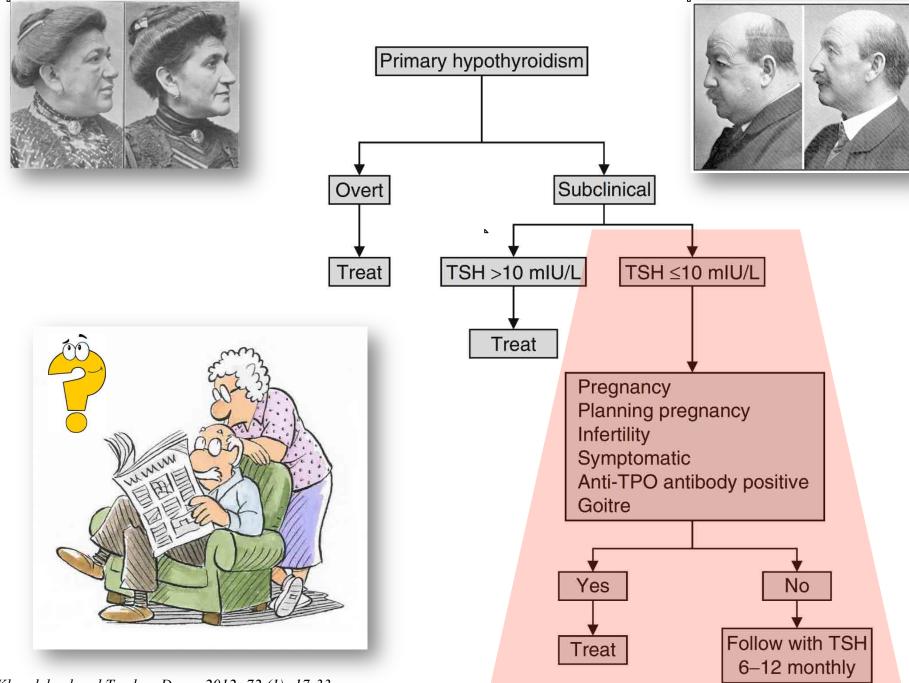
#### SPECIAL ARTICLE

#### Guidelines for the Treatment of Hypothyroidism

Prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement

Jacqueline Jonklaas,<sup>1\*†</sup> Antonio C. Bianco,<sup>2\*‡</sup> Andrew J. Bauer,<sup>3†</sup> Kenneth D. Burman,<sup>4†</sup> Anne R. Cappola,<sup>5†</sup> Francesco S. Celi,<sup>6‡</sup> David S. Cooper,<sup>7†</sup> Brian W. Kim,<sup>2‡</sup> Robin P. Peeters,<sup>8‡</sup> M. Sara Rosenthal,<sup>9†</sup> and Anna M. Sawka<sup>10†</sup>

- The deleterious health effects of <u>iatrogenic</u> <u>thyrotoxicosis</u> include atrial fibrillation and osteoporosis.
- We recommend avoiding thyroid hormone excess and subnormal serum TSH values, particularly TSH values below 0.1 mIU/L, especially in <u>older persons</u> and postmenopausal women.



Khandelwal and Tandon. Drugs 2012; 72 (1): 17-33.



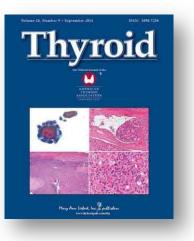
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## Subclinical hypothyroidism: summary of evidence in 2014

Christine Baumgartner<sup>a</sup>, Manuel R. Blum<sup>a</sup>, Nicolas Rodondi<sup>a</sup>

#### Table 1: Level of evidence in 2014 on the risks of treatment and the benefits of subclinical hypothyroidism.

Clinical condition	Strength of association	
	TSH 4.5–9.9 mIU/I	TSH ≥10 mIU/I
Progression to overt hypothyroidism	Good	Stronger
Elevation in serum total cholesterol and LDL	Fair	Stronger
Risk of coronary heart disease	Insufficient	Stronger
Risk of congestive heart failure	Insufficient	Stronger
Cardiac dysfunction	Insufficient	Insufficient
Systemic symptoms of hypothyroidism	Insufficient	Insufficient
Neuropsychiatric symptoms (e.g., depression, cognitive dysfunction)	Insufficient	Insufficient
Muscle strength	Insufficient	Insufficient
Fatigue	Insufficient	Insufficient



THYROID Volume 24, Number 12, 2014 © American Thyroid Association DOI: 10.1089/thy.2014.0028

#### Guidelines for the Treatment of Hypothyroidism

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#### **Should elderly patients be considered for treatment?**

- Routine treatment is not recommended for elderly (> 65 yrs) and very-elderly (> 80 yrs) patients with subclinical hypothyroidism at TSH levels < 10 mUI/L (Grade A).</li>
- Also treatment is not recommended for SH if the aim is to improve cognitive function in elderly people (Grade A).
- However in > 65 years old, treatment can be considered on an individual basis (Grade D).

### Hypothyroidism in the Elderly: Pathophysiology, Diagnosis and Treatment

Peter Laurberg, Stig Andersen, Inge Bülow Pedersen and Allan Carlé

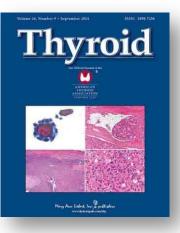


Drugs Aging 2005; 22 (1): 23-38

The clinical symptoms and signs of hypothyroid may be very confounding in elderly patients.

- Fatigue
- slow cerebration
- cold intolerance
- dry skin
- constipation
- weight abnormalities
- arthralgia and myalgia
- depression
- alterations of hair
- dyspnoea and oedema

If caused by hypothyroidism respond well to thyroid hormone replacement therapy, whereas thyroid hormones have no effect, apart from placebo, on such abnormalities in euthyroid individuals



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#### Guidelines for the Treatment of Hypothyroidism

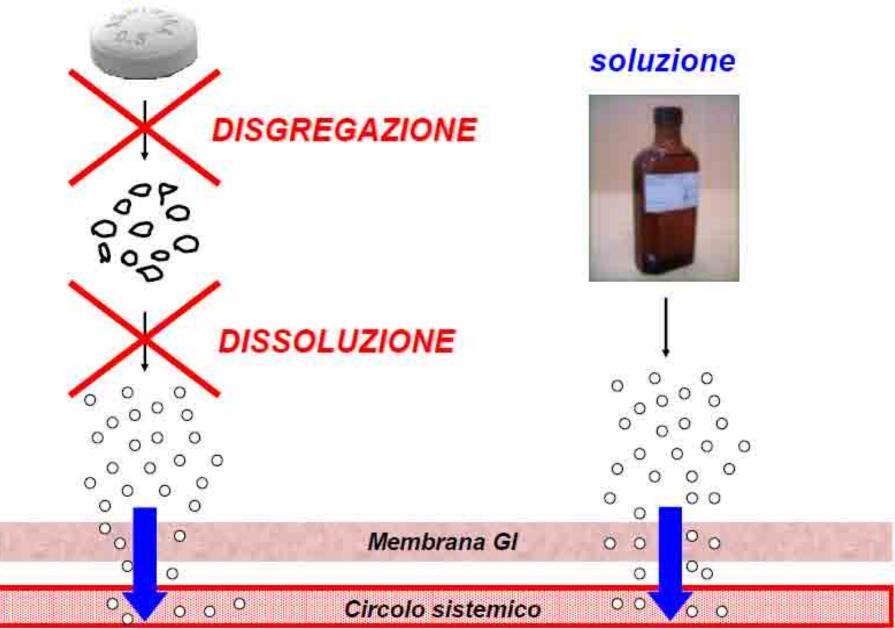
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Jacqueline Jonklaas,<sup>1\*†</sup> Antonio C. Bianco,<sup>2\*‡</sup> Andrew J. Bauer,<sup>3†</sup> Kenneth D. Burman,<sup>4†</sup> Anne R. Cappola,<sup>5†</sup> Francesco S. Celi,<sup>6‡</sup> David S. Cooper,<sup>7†</sup> Brian W. Kim,<sup>2‡</sup> Robin P. Peeters,<sup>8‡</sup> M. Sara Rosenthal,<sup>9†</sup> and Anna M. Sawka<sup>10†</sup>

### How to initiate and adjust doses in elderly and in patients with cardiopathy?

- In patients older than 60 yrs with SH and also in those with ischemic cardiac disease or heart failure, start levothyroxine therapy at lower doses (12.5 25 mcg/day) (Grade B).
- LT4 dose should be increased slowly, while monitoring for the development of angina or other cardiac symptoms such as tachyarrhythmias (Grade D).







### Il dilemma del medico:

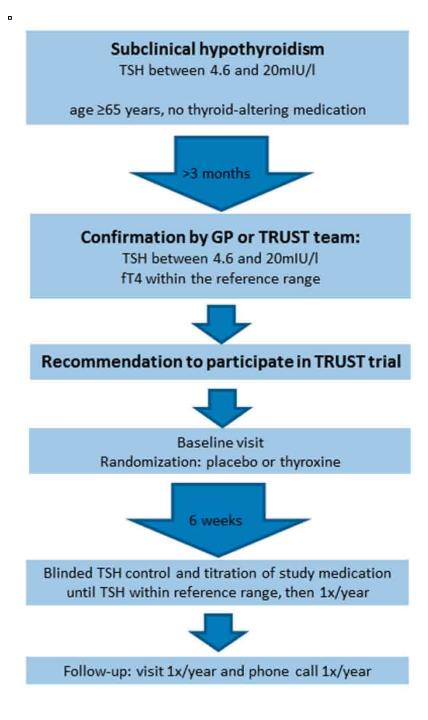
Trattare o non trattare l'ipotiroidismo subclinico dell'anziano?

#### **PRO**:

- Prevenire la progressione verso l'ipotiroidismo clinico (specie in caso di Ab+)
- Alleviare i sintomi
- Migliorare la dislipidemia
- Probabilmente ridurre il rischio di scompenso cardiaco

#### **CONTRO:**

- Un numero significativo di soggetti con forma subclinica non progredirà verso l'ipotiroidismo franco
- Spesso i sintomi "da ipotiroidismo" non sono dovuti ad esso
- Rischio di sovradosaggio della LT4 (tachiaritmie)
- L'ipo subclinico potrebbe avere "effetti protettivi" nei pazienti molto anziani



## **The TRUST Study**

(Thyroid hormone Replacement for Untreated older adults with Subclinical hypothyroidism: a randomised placebo-controlled Trial)

• European multicentre study

• Examines thyroid hormone replacement

therapy versus placebo in elderly individuals

with persisting subclinical hypothyroidism

• A total of 3,000 participants will be enrolled



Rodondi N, Bauer DC. Subclinical hypothyroidism and cardiovascular risk: how to end the controversy. J Clin Endocrinol Metab. 2013;98(6):2267–9

