

# 12th Congresso Nazionale AME & 6th Joint Meeting with AACE Bari, Italy, 7-10th November 2013



**Medical treatment of nodular goitre: still to be considered?  
"No, it is a doubtful bargain"**

**Laszlo Hegedüs, MD, DMSc  
Department of Endocrinology and Metabolism  
Odense University Hospital  
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**Medical treatment of nodular goitre: still to be considered?**  
**”No, it is a doubtful bargain”**

**My initial attempt at outlining the talk for this symposium**



**Is it possible to limit the talk to 20 min?**

**Do we really have to reopen this debate again?**

# **Medical (Levothyroxine, LT4?) therapy in benign nodular goitre**

## **Some issues covered**

- **Understanding phenotype variation and eligibility**
- **Theoretical basis for using L-T4 to shrink thyroid nodules**
- **Current guideline recommendations**
- **Efficacy of L-T4 in shrinking thyroid nodules**
- **Potential side-effects of L-T4 therapy**
- **Potential effect of L-T4 in decreasing risk of papillary thyroid cancer**
- **Focus on available alternatives**
- **Conclusions**
- **Need of additional studies/evidence?**
- **Need of revising current guidelines?**

**The revised  
ETA / AME / AACE  
Thyroid Nodule Guideline**

**Annual meeting of the  
European Thyroid Association**

**Lisbon  
September 5th – 9th 2009**

**Hossein Gharib, Enrico Papini, Ralf Paschke,  
Dan Duick, Roberto Valcavi, Laszlo Hegedüs, Paolo Vitti,  
and the AACE/AME/ETA Task Force on Thyroid Nodules**



R.P., L.H., P.V.



E.P., R.V.  
AMERICAN ASSOCIATION OF  
CLINICAL ENDOCRINOLOGISTS



H.G., D.D.  
ITALIAN ASSOCIATION OF  
CLINICAL ENDOCRINOLOGISTS



## 7.2.2. *Levothyroxine therapy for benign nodules*

- Routine levothyroxine therapy is **not recommended** (grade B; 1)
- Levothyroxine therapy or iodine supplementation may be considered in young patients with small nodular goiter and no evidence of functional autonomy (grade B; 1)
- .....



# Key Recommendations regarding levothyroxine therapy for thyroid nodules that are negative by Fine-Needle Aspiration

- **Use of LT4 therapy may be considered in the following (grade C):**
  - Patients from geographic areas with iodine deficiency
  - Young patients with small thyroid nodules
  - Nodular goiters with no evidence of functional autonomy
- **Use of LT4 therapy should be avoided in most cases and especially in the following (grade C):**
  - Large thyroid nodules and goiters, particularly in the presence of symptoms or signs of functional autonomy
  - Clinically suspicious lesions or lesions with an inadequate cytologic sample
  - Postmenopausal women and men older than 60 years
  - Patients with osteoporosis or systemic illnesses
  - Patients with cardiovascular disease
- **Facts to remember:**
  - LT4 treatment induces a clinically significant reduction of thyroid nodule volume in only a minority of patients (grade B)
  - Long-term TSH suppression may be associated with bone loss and arrhythmia in elderly patients and menopausal women (grade B)
  - LT4 treatment should never be fully suppressive (TSH <0.1 µIU/mL) (grade C)
  - Nodule regrowth is usually observed after cessation of LT4 therapy (grade C)
  - If nodule size decreases, LT4 therapy should be continued long term (grade D)
  - If thyroid nodule grows during LT4 treatment, reaspiration and possibly surgical treatment should be considered (grade D)

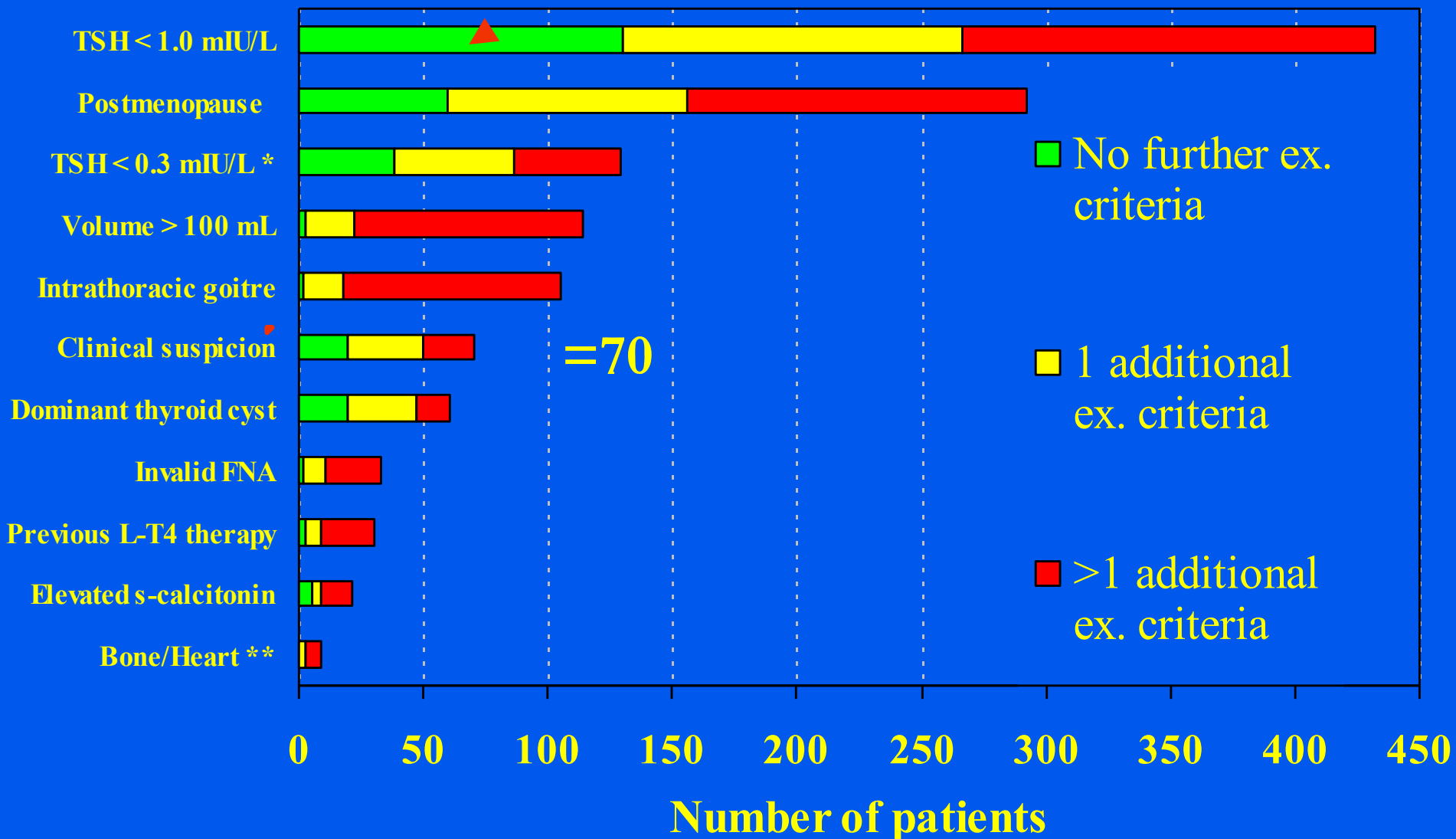
\*LT4 = levothyroxine; TSH = thyroid-stimulating hormone (thyrotropin).



# Eligibility for L-T4 therapy in nontoxic goitre

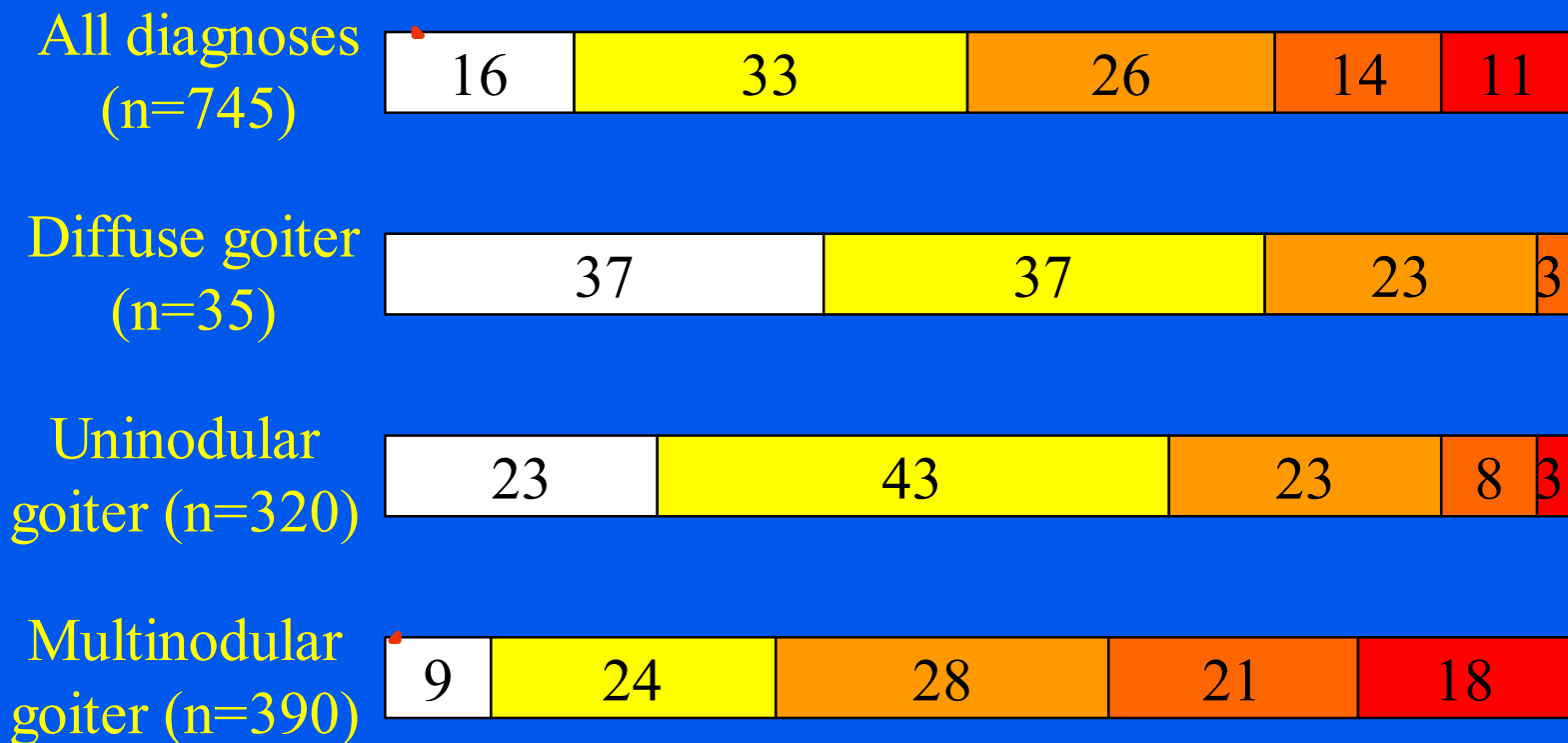
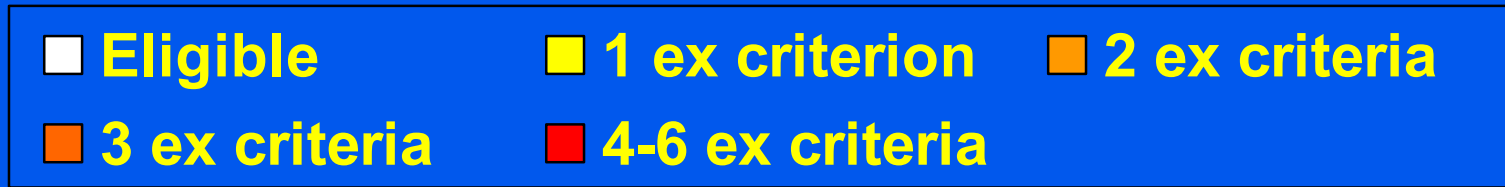
Prevalence of exclusion criteria, according to guidelines, in 745 consecutive patients

The majority have exclusion criteria



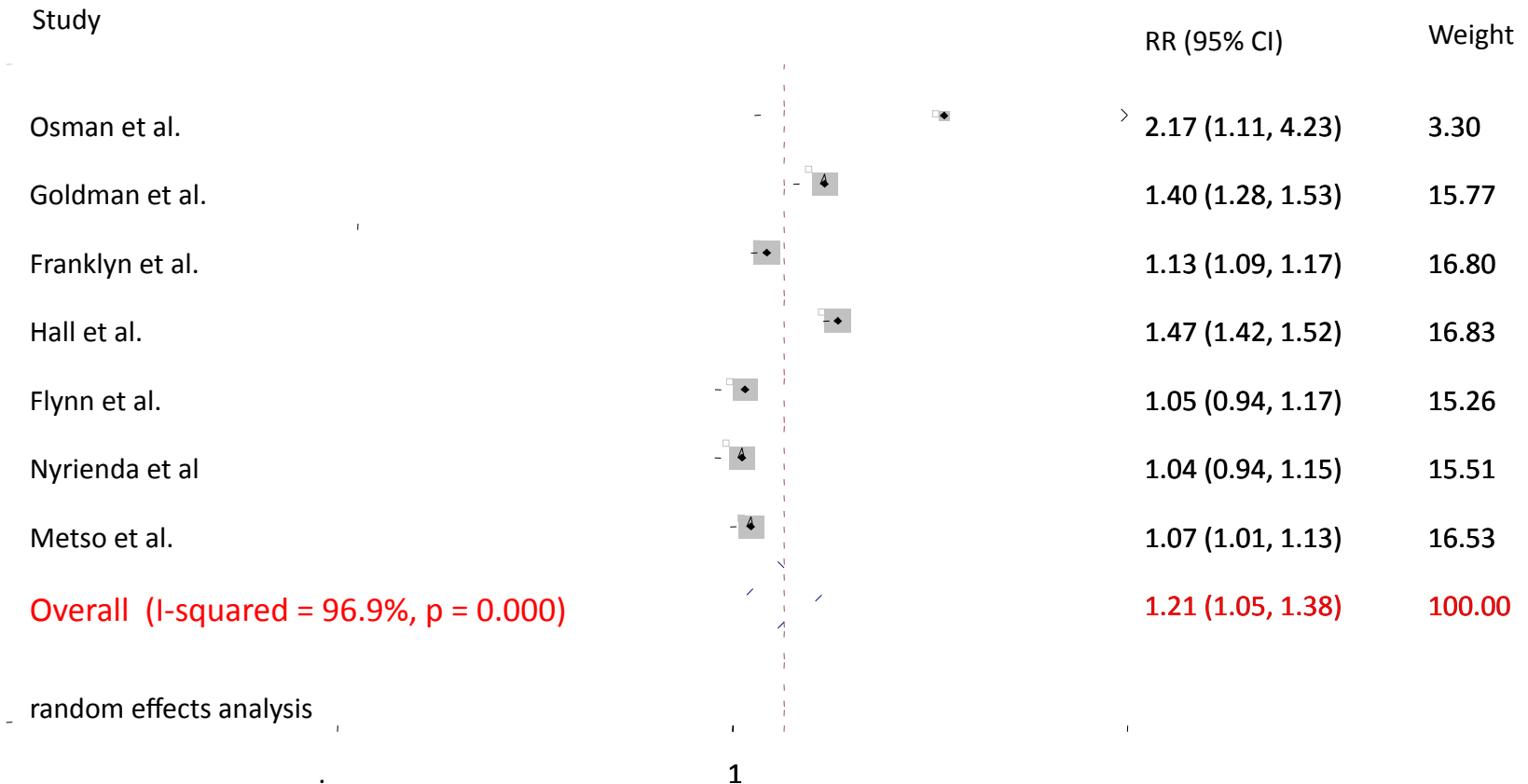
# Eligibility for L-T4 therapy according to diagnoses in percent

## Few percent are eligible!



# L-T4 therapy is associated with overt or subclinical hyperthyroidism in many, which leads to increased morbidity and mortality.

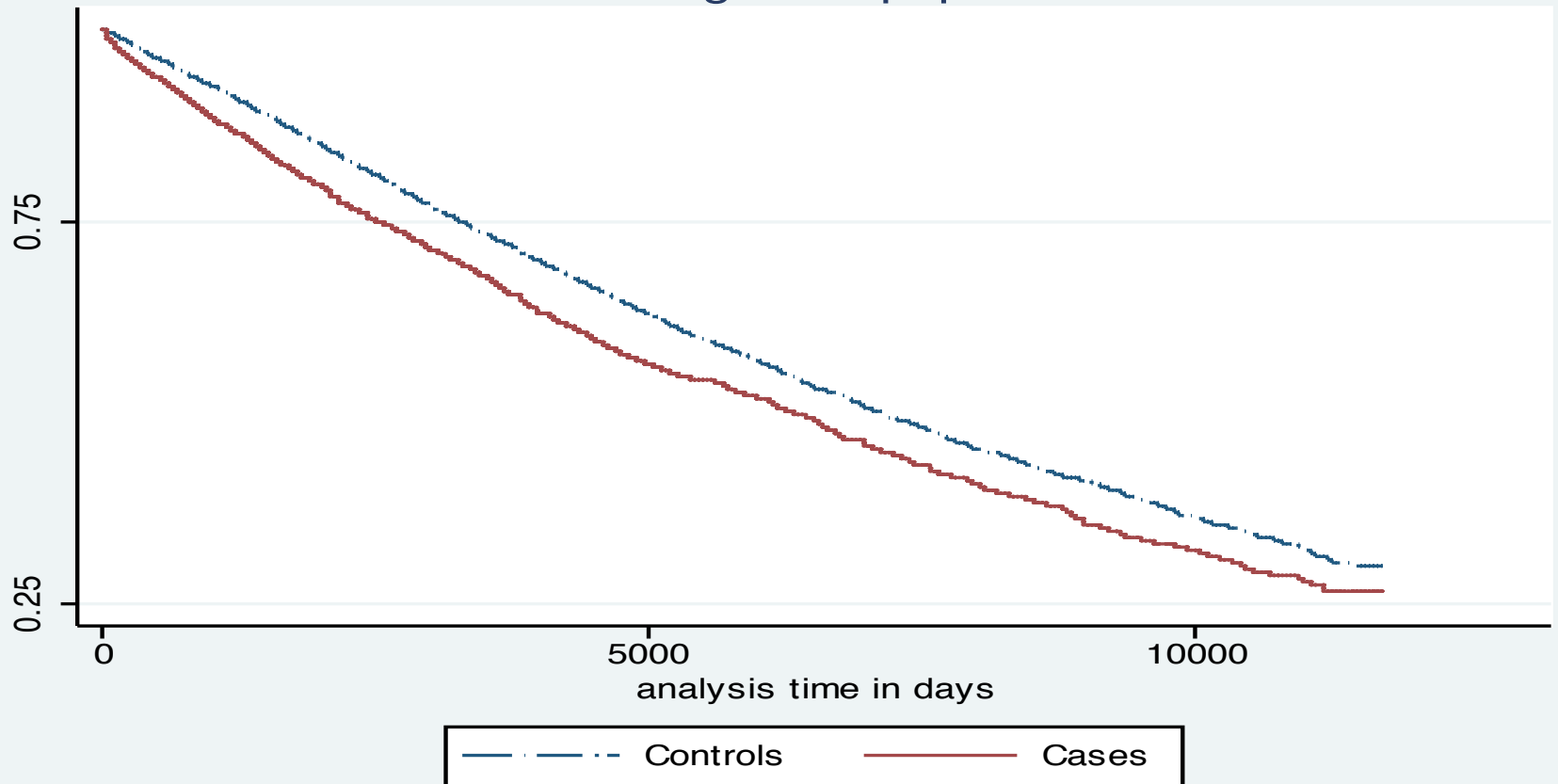
## Hyperthyroidism is associated with excess mortality; a meta-analysis



# Hyperthyroidism and excess mortality, also when treated. Population-based Danish register-study

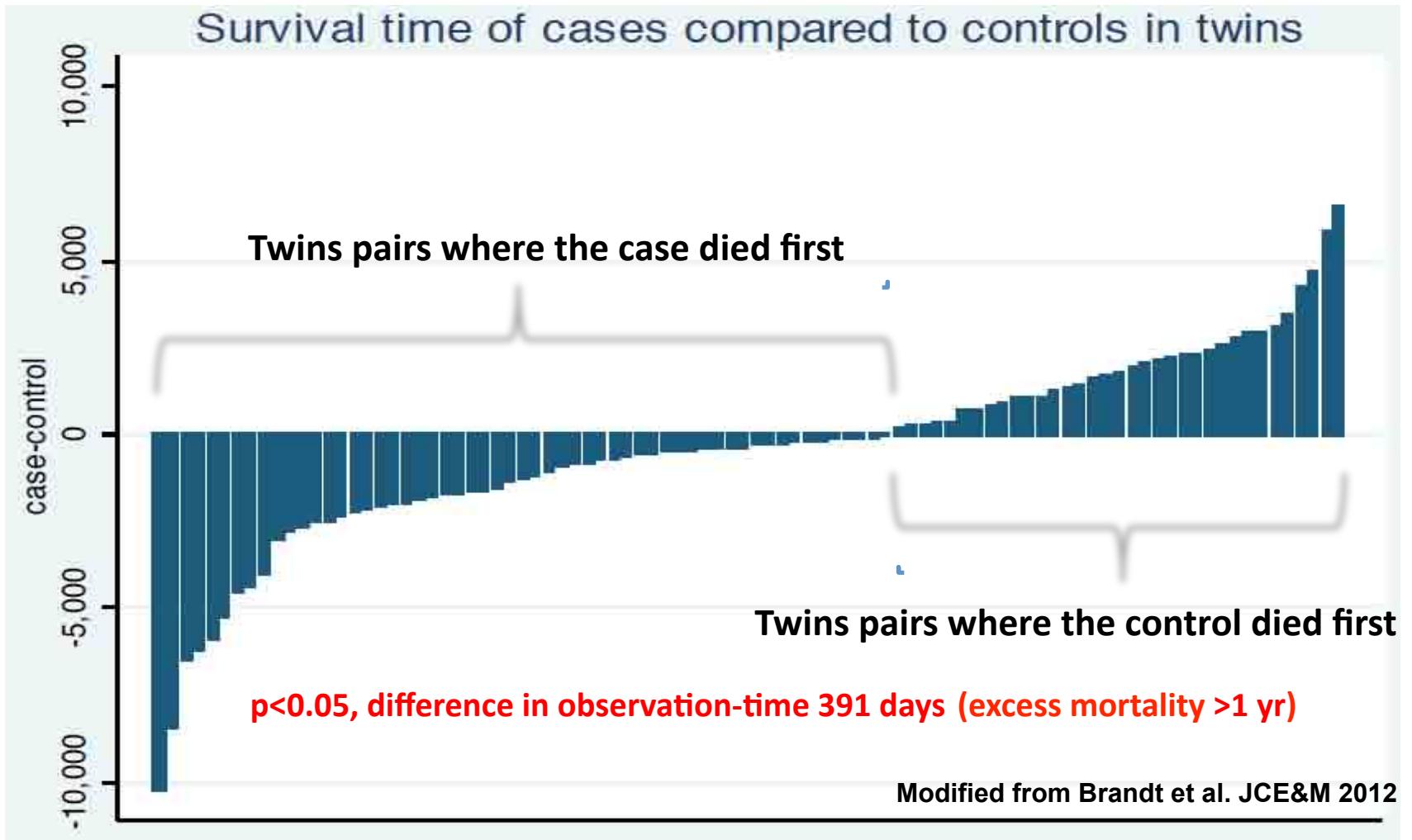
Kaplain-Meier survival curve in singletons

A: Background population



# Hyperthyroidism (treated) and mortality

Waterfall plot showing the difference in survival time between cases and controls in disease discordant and death concordant twin pairs



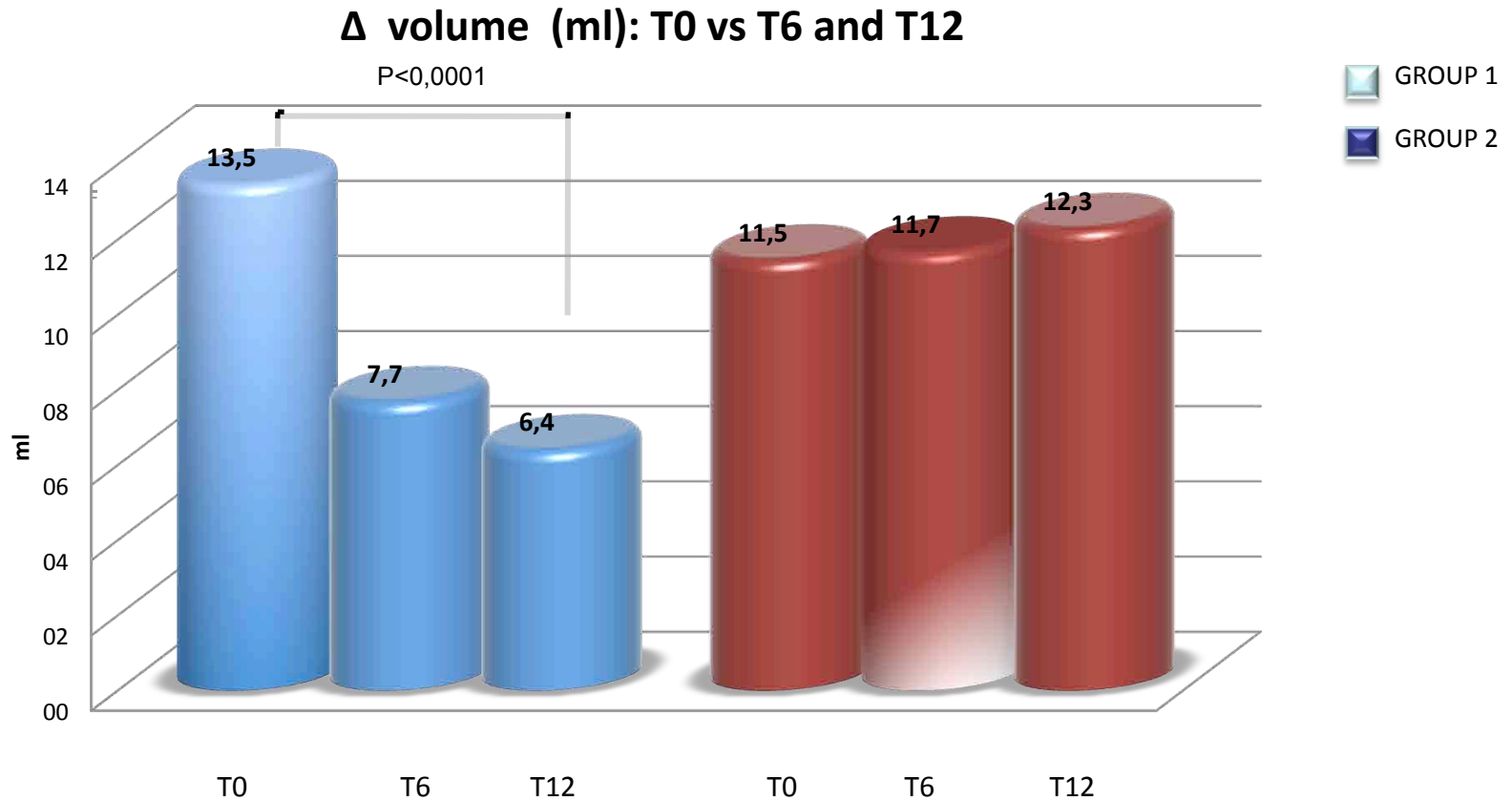
## **Judging the value of L-T4 therapy for benign nodular goitre lies in the eye of the beholder**

- **Poor efficacy of LT4-therapy**
- **Potential side-effects of LT4-therapy**
- **No consensus of prophylactic LT4-therapy as anti-neoplastic therapy**
- **If efficacious, only in relatively small solid nodules in euthyroid patients**
- **These are generally asymptomatic**
- **Ample alternatives with better efficacy in this situation**
  - **Percutaneous ethanol injection therapy**
  - **Laser ablation**
  - **Radiofrequency ablation**
- **If multinodular, better efficacy with radioiodine**



Italian multicenter study (**Laser** versus **observation**) in around 200 benign solid solitary nodules

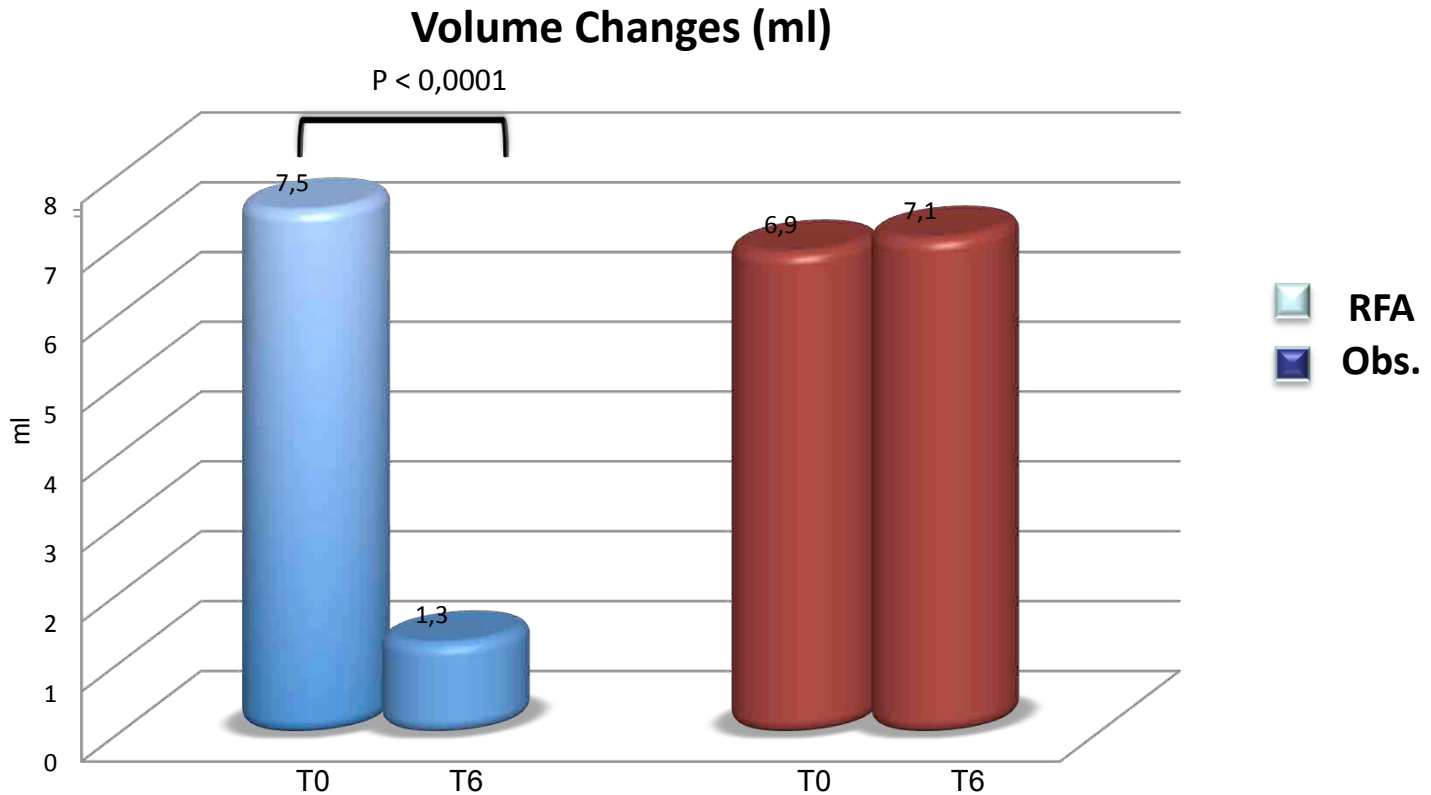
# Volume changes (ml) at 12 months



Borrowed, with kind appreciation, from E. Papini et al.

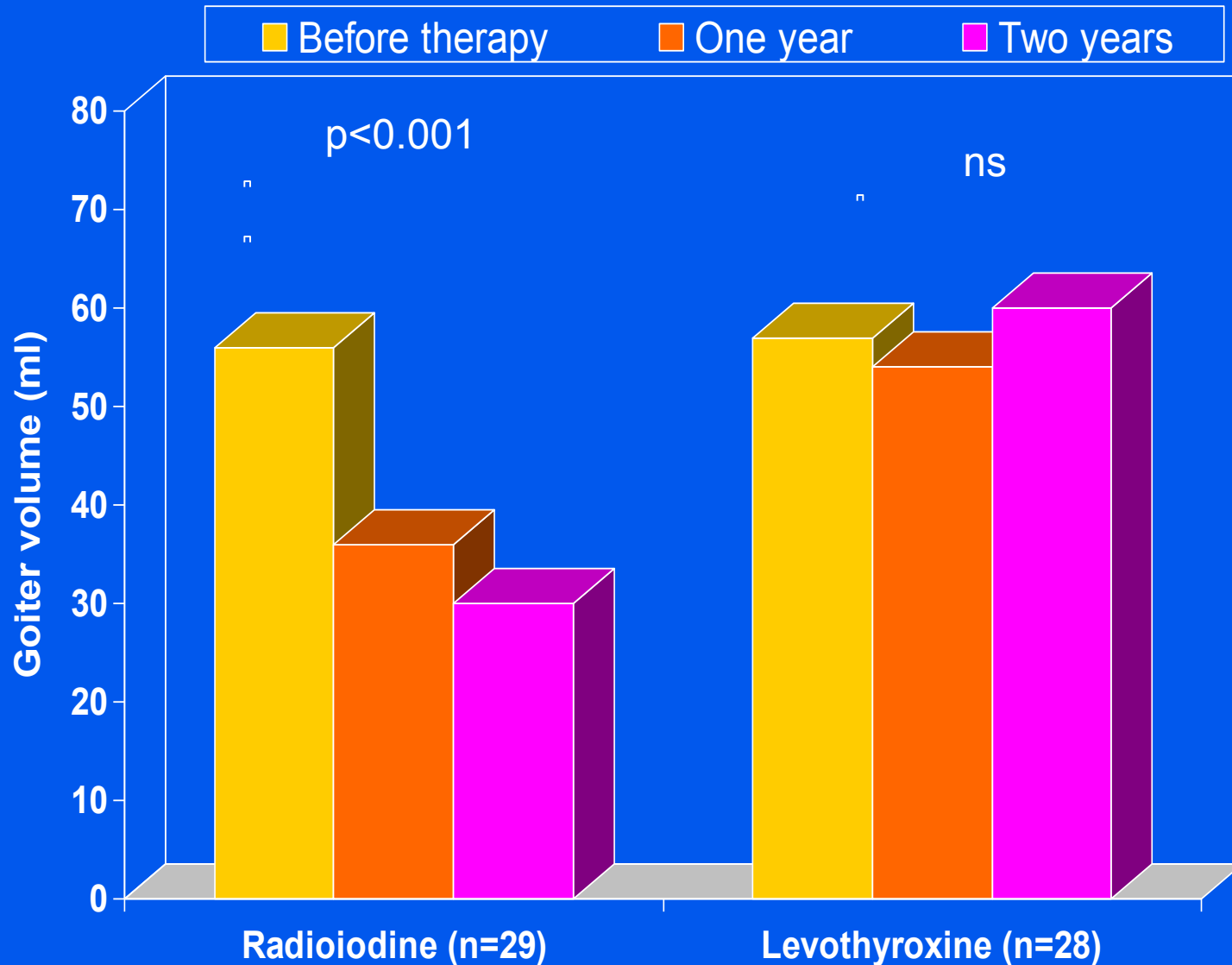
Jung Hwan Baek<sup>1,2</sup>  
Yoon Suk Kim<sup>1</sup>  
Ducky Lee<sup>2</sup>  
Jung Yin Huh<sup>4</sup>  
Jeong Hyun Lee<sup>1</sup>

# Benign Predominantly Solid Thyroid Nodules: Prospective Study of Efficacy of Sonographically Guided Radiofrequency Ablation Versus Control Condition



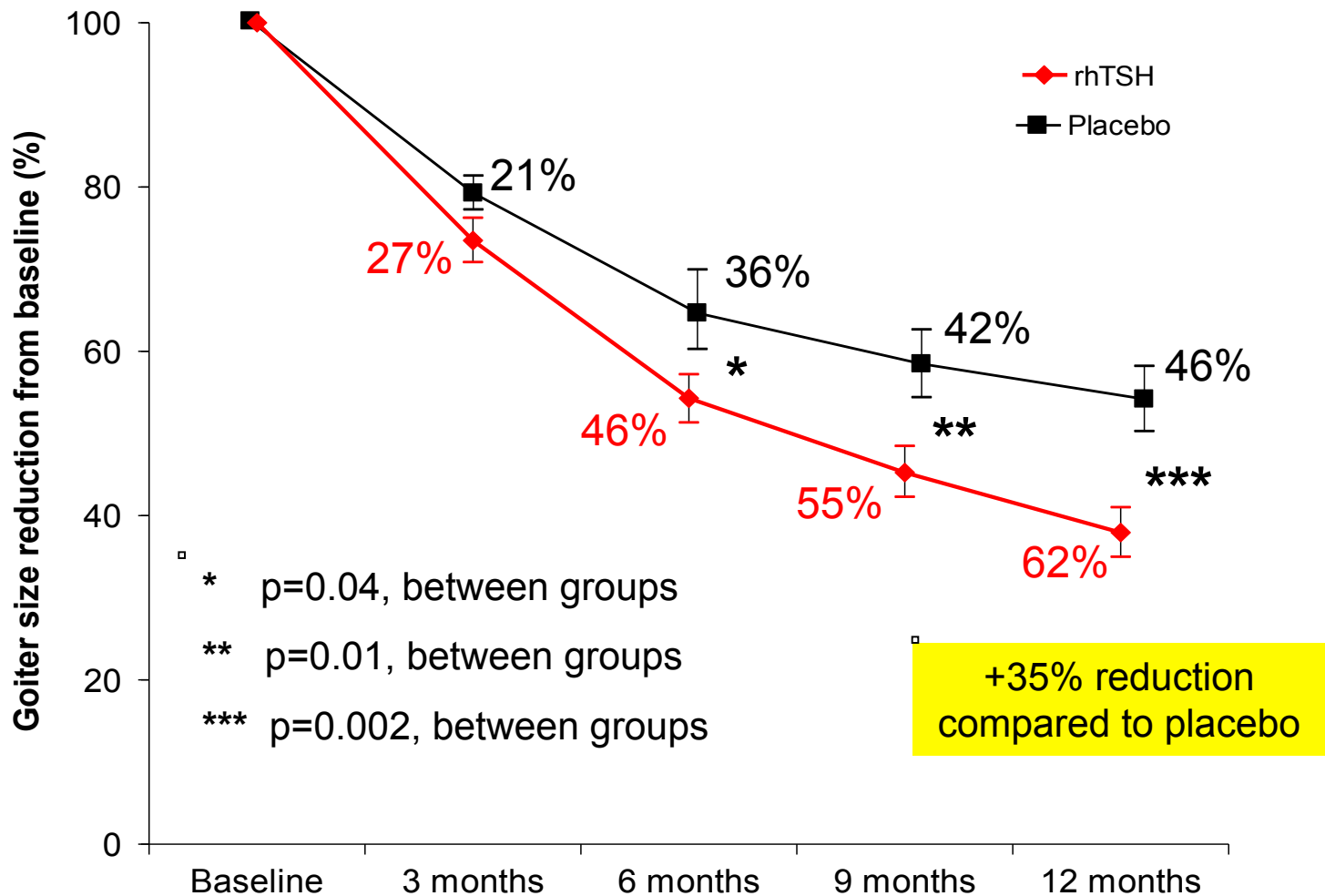
# Multinodular nontoxic goiter reduction: radioiodine versus L-T4

## Lack of efficacy of L-T4



# Augmenting the effect of 131-I in multinodular goitre.

## Effect of 0.3 mg rhTSH on mean goitre volume reduction in benign nontoxic multinodular goitre. Double-blind randomized study



# Medical (Levothyroxine, LT4?) therapy in benign nodular goitre

## Some issues covered

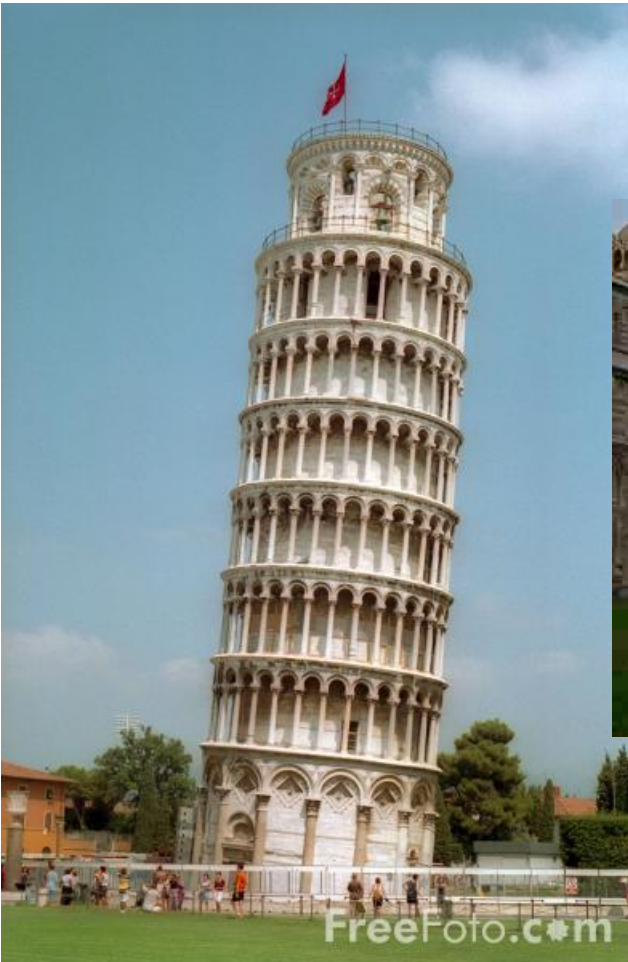
- Understanding phenotype variation and eligibility **(Covered. Few eligible)**
- Theoretical basis for using L-T4 to shrink thyroid nodules **(Covered)**
- Current guideline recommendations **(Covered. Discouraged)**
- Efficacy of L-T4 in shrinking thyroid nodules **(Covered. Efficacy poor)**
- Potential side-effects of L-T4 therapy **(Covered. Considerable)**
- Potential effect of L-T4 in decreasing risk of papillary thyroid cancer **(Hypothesis?)**
- Much better treatment options available
- Conclusions
- Need of additional studies/evidence? **(To be debated)**
- Need of revising current guidelines? **(Already decided)**

# **Judging the value of L-T4 therapy for benign nodular goitre lies in the eye of the beholder**

## **Further conclusions**

- **If efficacious, only in relatively small solid nodules in euthyroid patients**
- **These are generally asymptomatic**
- **Ample alternatives with better efficacy in this situation**
  - **Percutaneous ethanol injection therapy**
  - **Laser ablation**
  - **Radiofrequency ablation**

# Judging the value of L-T4 therapy for benign nodular goitre lies in the eye of the beholder



Without L-T4 therapy?



With L-T4 therapy?



Or, mirage in Pisa (Fata Morgana)?

**Medical treatment of nodular goitre: still to be considered?  
"No, it is a doubtful bargain"**



**In my view, balancing efficacy versus side-effects of LT4-therapy in nodular nontoxic goitre makes this a poor bargain**