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Per la qualità clinica in Endocrinologia



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# **Chirurgia Conservativa per il Carcinoma Tiroideo. Perché? e Perché No? e, soprattutto, Quando? Orientamenti Attuali**

**Enrico Papini**

**Endocrinologia e Metabolismo, Regina Apostolorum**

# At the beginning we had 'The Laws'

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## CONSENSUS STATEMENT

**European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium**

Furio Pacini, Martin Schlumberger<sup>1</sup>, Henning Dralle<sup>2</sup>, Rossella Elisei<sup>3</sup>, Johannes W A Smit<sup>4</sup>, Wilmar Wiersinga<sup>5</sup> and the European Thyroid Cancer Taskforce

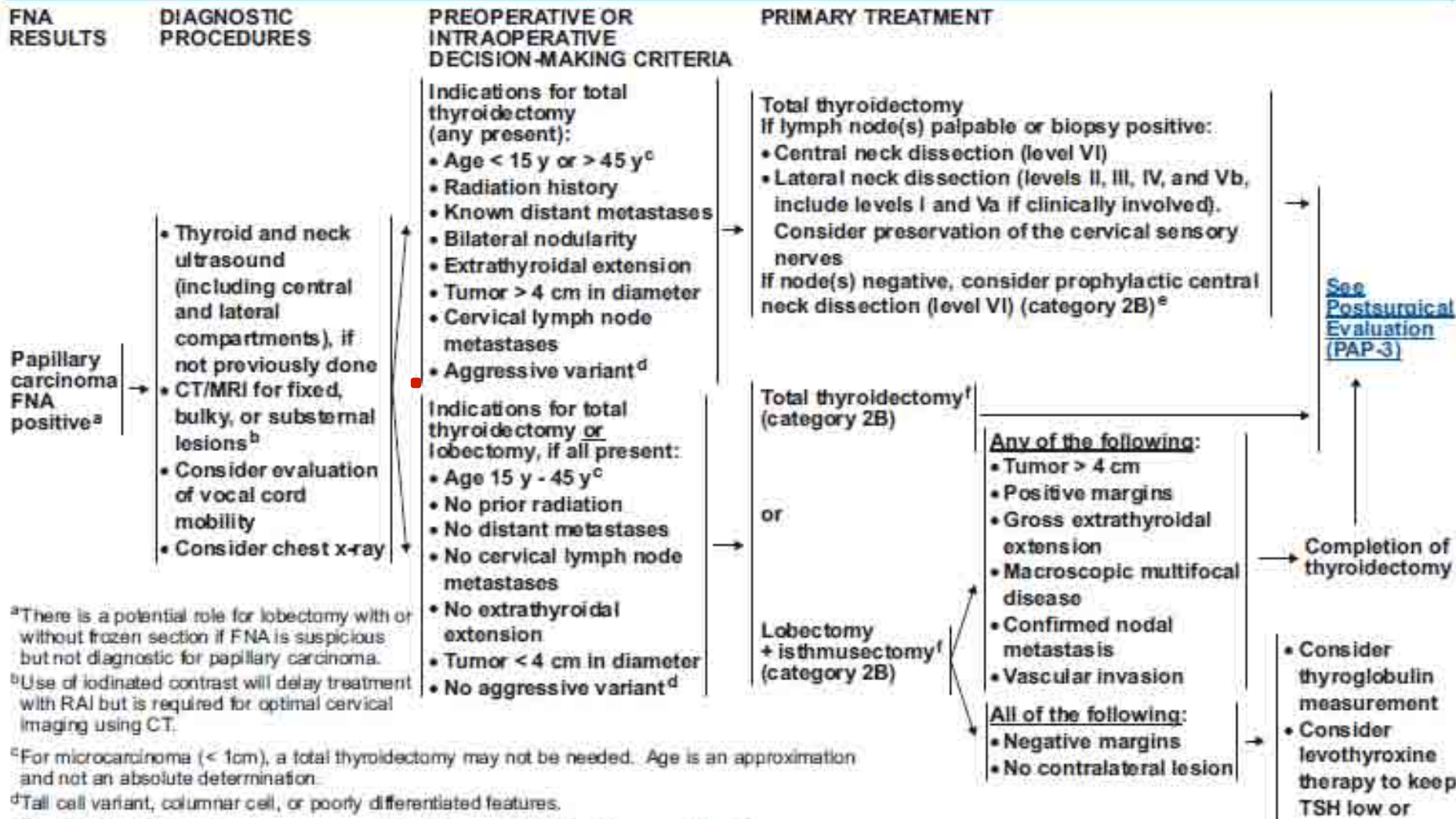
Apart from solitary well differentiated thyroid cancer less than 1 cm in diameter with no evidence for nodal or distant metastases, and no history of previous radiation exposure that may be operated on by less than total thyroidectomy, the standard surgical treatment is total (or near-total) thyroidectomy. This procedure decreases the risk of local recurrence and is performed with almost no morbidity under expert hands. Moreover, it facilitates postsurgical radioiodine ablation and adequate follow-up (16, 24–28). More limited thyroidectomy should not be performed, and if a patient is referred after less than near-total thyroidectomy, completion thyroidectomy should be proposed in the case of a

- **Standard surgery: total thyroidectomy**
- **Post-surgical radioiodine ablation**
- **Completion surgery in case of less than total thyroidectomy**

# Then came the doubts

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<sup>a</sup>There is a potential role for lobectomy with or without frozen section if FNA is suspicious but not diagnostic for papillary carcinoma.

<sup>b</sup>Use of iodinated contrast will delay treatment with RAI but is required for optimal cervical imaging using CT.

<sup>c</sup>For microcarcinoma (< 1cm), a total thyroidectomy may not be needed. Age is an approximation and not an absolute determination.

<sup>d</sup>Tall cell variant, columnar cell, or poorly differentiated features.

# And then ... summer 2014

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- ## Guidelines for the management of thyroid cancer

Third edition

Perros P, Colley S, Boelaert K, Evans C, Evans RM, Gerrard GE, Gilbert JA, Harrison B, Johnson SJ, Giles TE, Moss L, Lewington V, Newbold KL, Taylor J, Thakker RV, Watkinson J, Williams GR

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British Thyroid Association

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July 2014



# Differentiated Thyroid Cancer 2015

## What we believe to know “for sure”



**30% risk of recurrence**  
(Over estimate the risk of recurrence?)

**RAI ablation decreases recurrence by 50%**  
(Over estimate the impact of RAI on recurrence?)

**RAI ablation decreases the risk of death**  
(Over estimate the impact of RAI on survival?)

□ Furio Pacini, Personal Communication

# Last, possibly .... spring 2015

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## **2014 American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer**

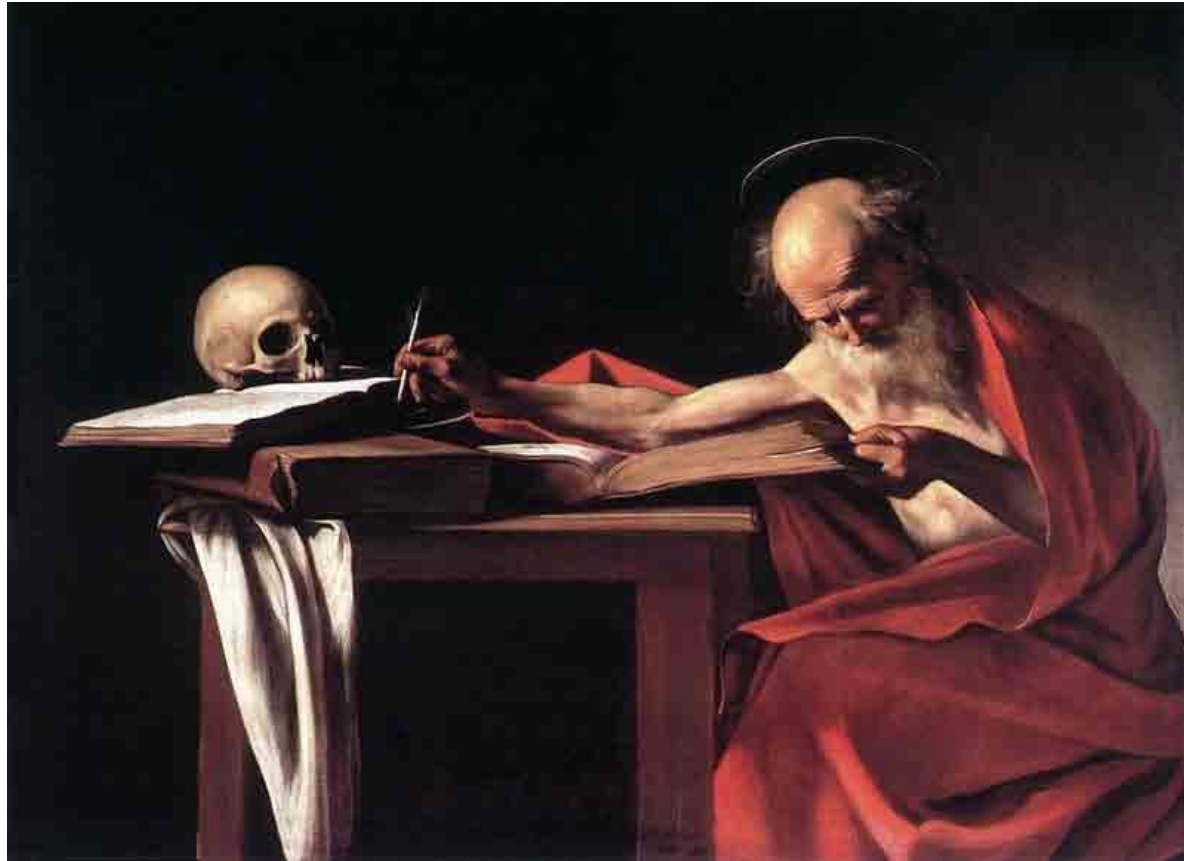
The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and  
Differentiated Thyroid Cancer

Bryan R. Haugen, M.D.<sup>1</sup> (Chair)\*, Erik K. Alexander, M.D.<sup>2</sup>, Keith C. Bible, M.D.,  
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Martin Schlumberger, M.D.<sup>10</sup>, Kathryn Schuff, M.D.<sup>11</sup>, Steven I. Sherman, M.D.<sup>12</sup>, Julie Ann  
Sosa, M.D.<sup>13</sup>, David L. Steward, M.D.,<sup>14</sup> R. Michael Tuttle, M.D.<sup>15</sup>, and Leonard Wartofsky,



# Can we put some order, again?

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# Basic Goals of Initial Therapy of DTC

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- Improve overall and disease-specific survival
- Decrease the risk of persistent or recurrent disease
- Permit disease staging and risk stratification.
- **Minimize treatment-related morbidity and worsening of the Quality of Life.**

Stavrakis AI et al. Surgery 2007

Gourin CG et al. Arch Otolaryngol Head Neck Surg 2010

# Goals of Initial Surgery

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- Remove the primary tumor
- Remove disease extended beyond thyroid capsule
- Facilitate post-surgery RAI treatment, if appropriate.

Brierley JD et al. Cancer 1997  
Hay ID et al. W J Surg 2002

# Rationale for a Complete Surgical Approach

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- Completeness of surgery is the most important treatment variable for the prognosis
- RAI and TSH suppression play only adjunctive roles in most patients
- Staging is the basis for risk stratification and disease management.

*Cooper DS et al. Thyroid 1998*

*Mazzaferri EL. Endocr Pract 2000*

# Rationale for a Complete Surgical Approach

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- PTC involves cervical lymph nodes in up to 50% of patients at histology
- Preoperative US identifies only half of affected lymph nodes due to the presence of the thyroid and to technical limits
- US may reliably rule out only gross extracapsular extension.

**So, the more is the better?**

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# Why a Less Invasive Approach Could Be Preferred?

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- Data on improved survival and recurrence rate after total thyroidectomy may be obsolete
- They were based on less effective preoperative staging and follow-up
- The frequency of cancer histotypes and advanced tumors was different.

# Surgical Approach to High-Risk DTC

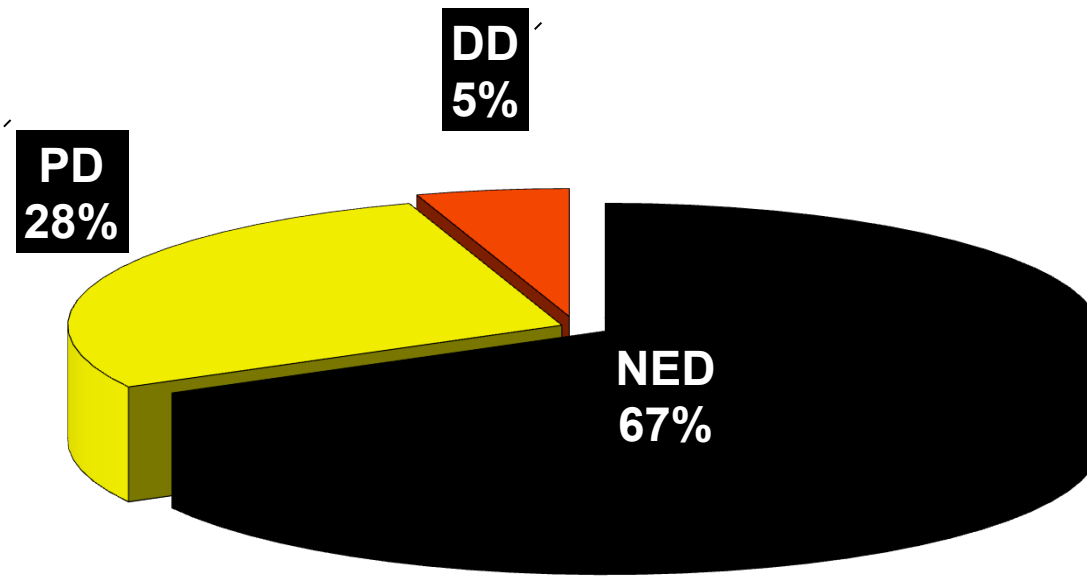
- Patients with “high-risk disease” require an aggressive approach and a personalized strategy.
- Complete control of local disease is mandatory
- **But they are frequent in oncologic centers only.**





# Sloan-Kettering Cancer Center Cohort Status at Final Follow-up (588 patients)

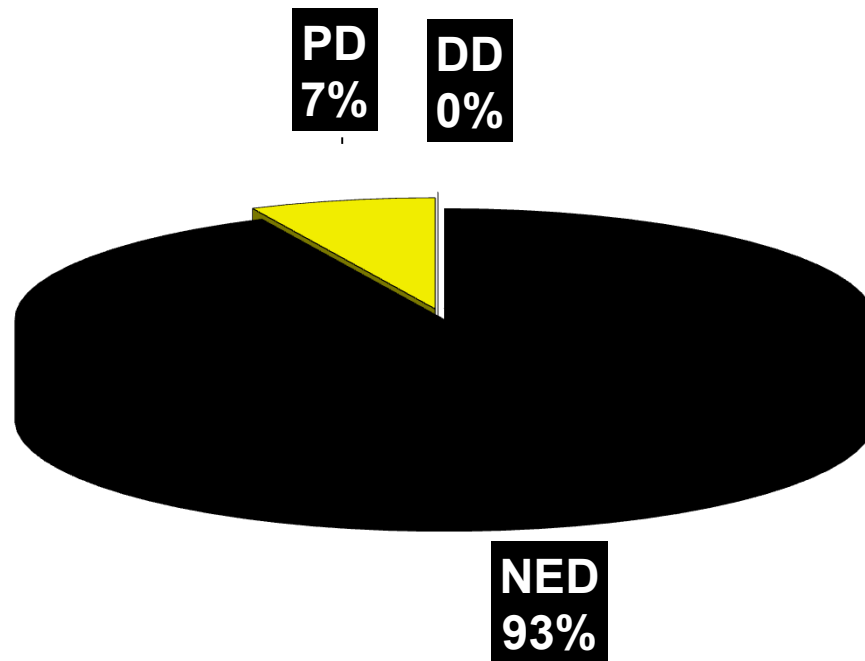
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ND: no evidence of disease; PD: persistent disease; DD: death of disease

# Papillary Thyroid Cancer Study Group Clinical Findings at First Postoperative Follow-Up (1020 patients)

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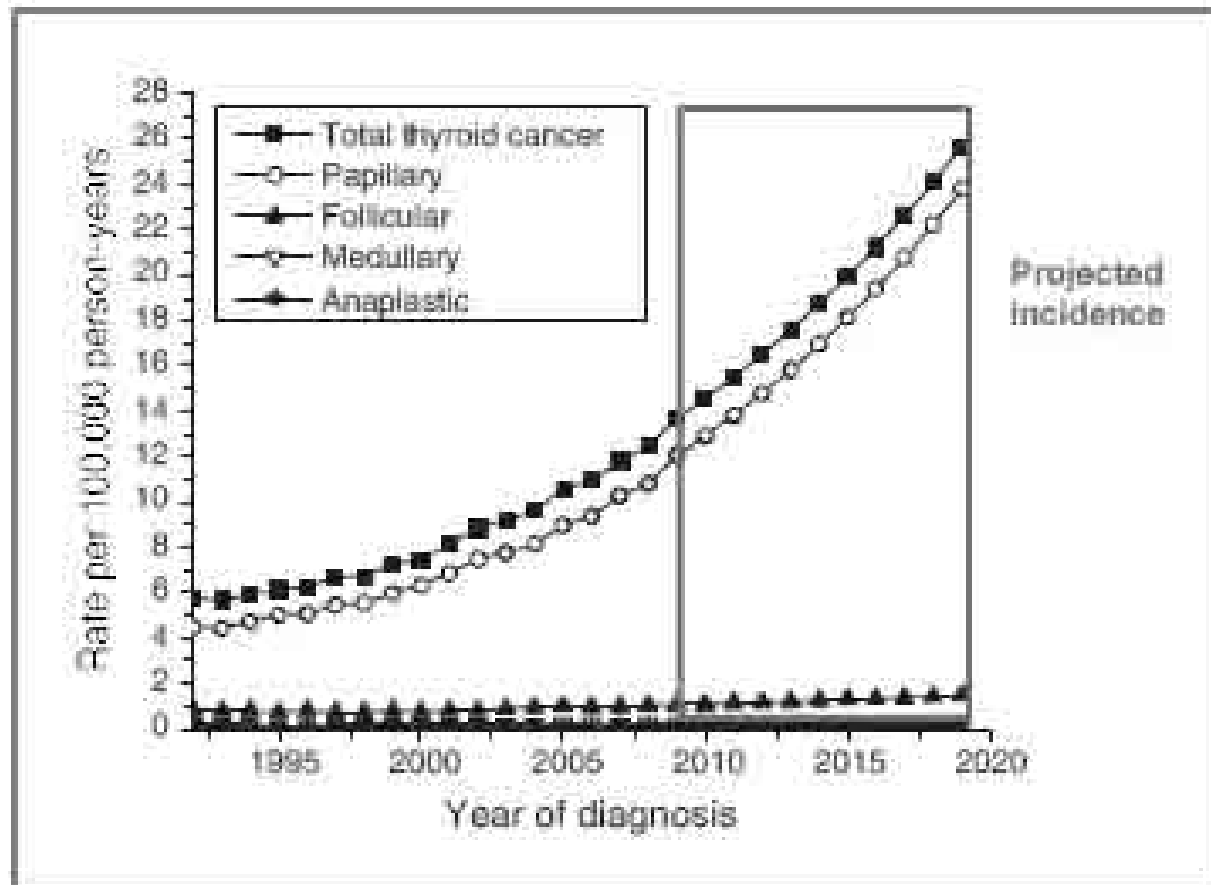
ND: no evidence of disease; PD: persistent disease; DD: death of disease

# Cancer Epidemiology, Biomarkers & Prevention

## The Clinical and Economic Burden of a Sustained Increase in Thyroid Cancer Incidence

Briseis Aschebrook-Kilfoy, Rebecca B. Schechter, Ya-Chen Tina Shih, et al.

*Cancer Epidemiol Biomarkers Prev* Published OnlineFirst May 15, 2013.



# Present DTC patients are similar to those in the past?

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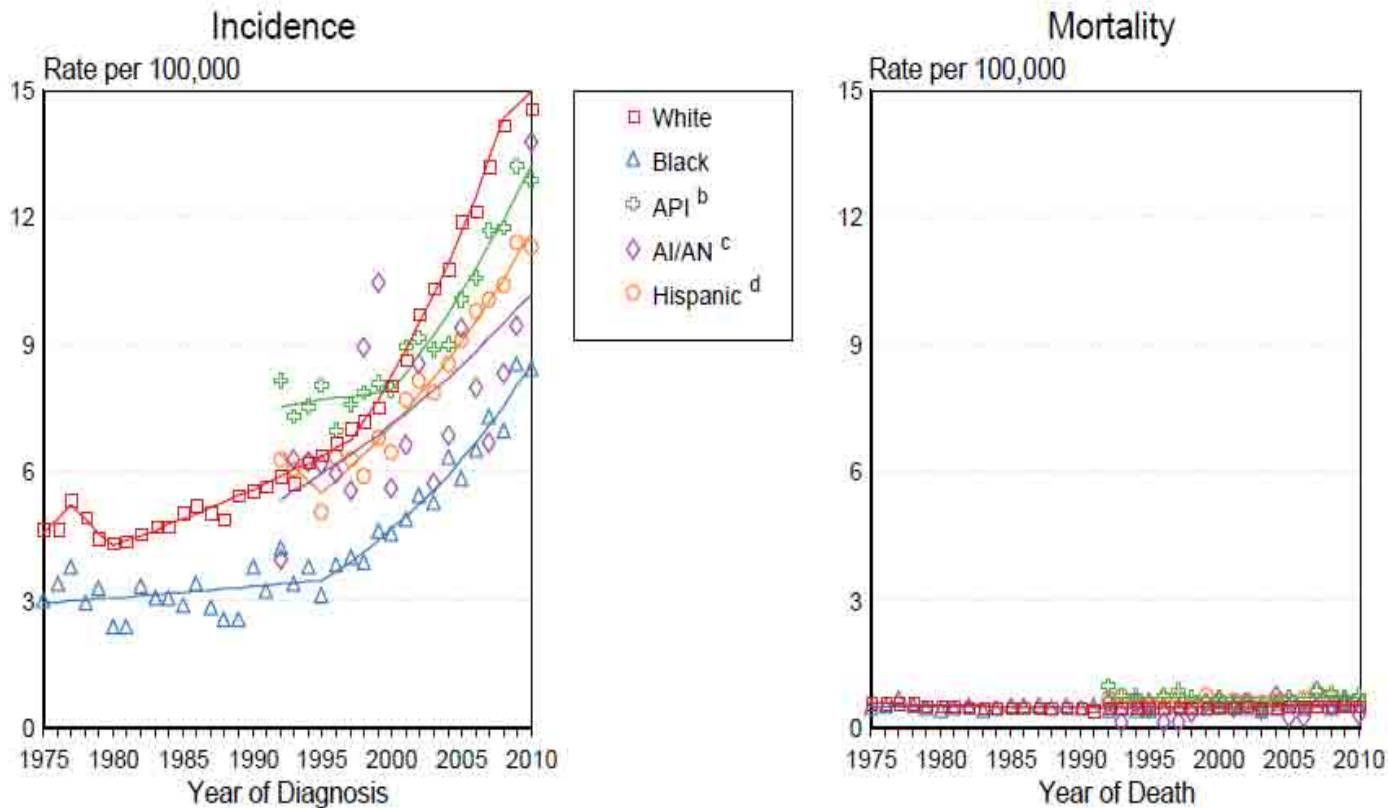
- Presently, the great majority of DTC are papillary
- Most are < 20 mm in diameter (pT1)
- Only a minority show gross extrathyroid extension (pT4).

# What is the present outcome of DTC?

## SEER Incidence and US Death Rates<sup>a</sup> Cancer of the Thyroid, Both Sexes

Joinpoint Analyses for Whites and Blacks from 1975-2010

and for Asian/Pacific Islanders, American Indians/Alaska Natives and Hispanics from 1992-2010



# What is the role of lymph node metastases?

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- Clinical implication of micrometastases is less relevant than macroscopic involvement
- Preoperative US may identify suspicious cervical adenopathy in 20% of DTC patients, properly changing surgical approach
- Cytology and FNA-Tg reliably confirm the presence of nodal metastases.

Frasoldati A et al. Cancer 2003

Leboullex S et al. J Clin Endocrinol Metab 2007

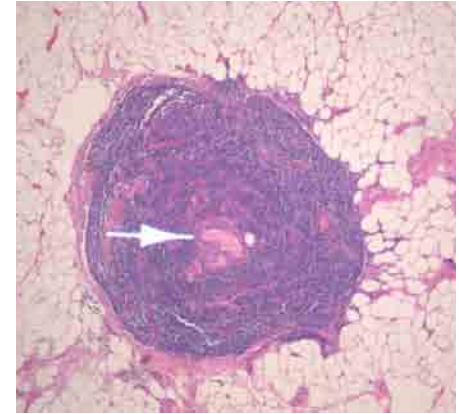
Matsuzu K et al. World J Surg 2014

Nixon IJ et al. Surgery 2012

# What is the clinical impact of micrometastases?

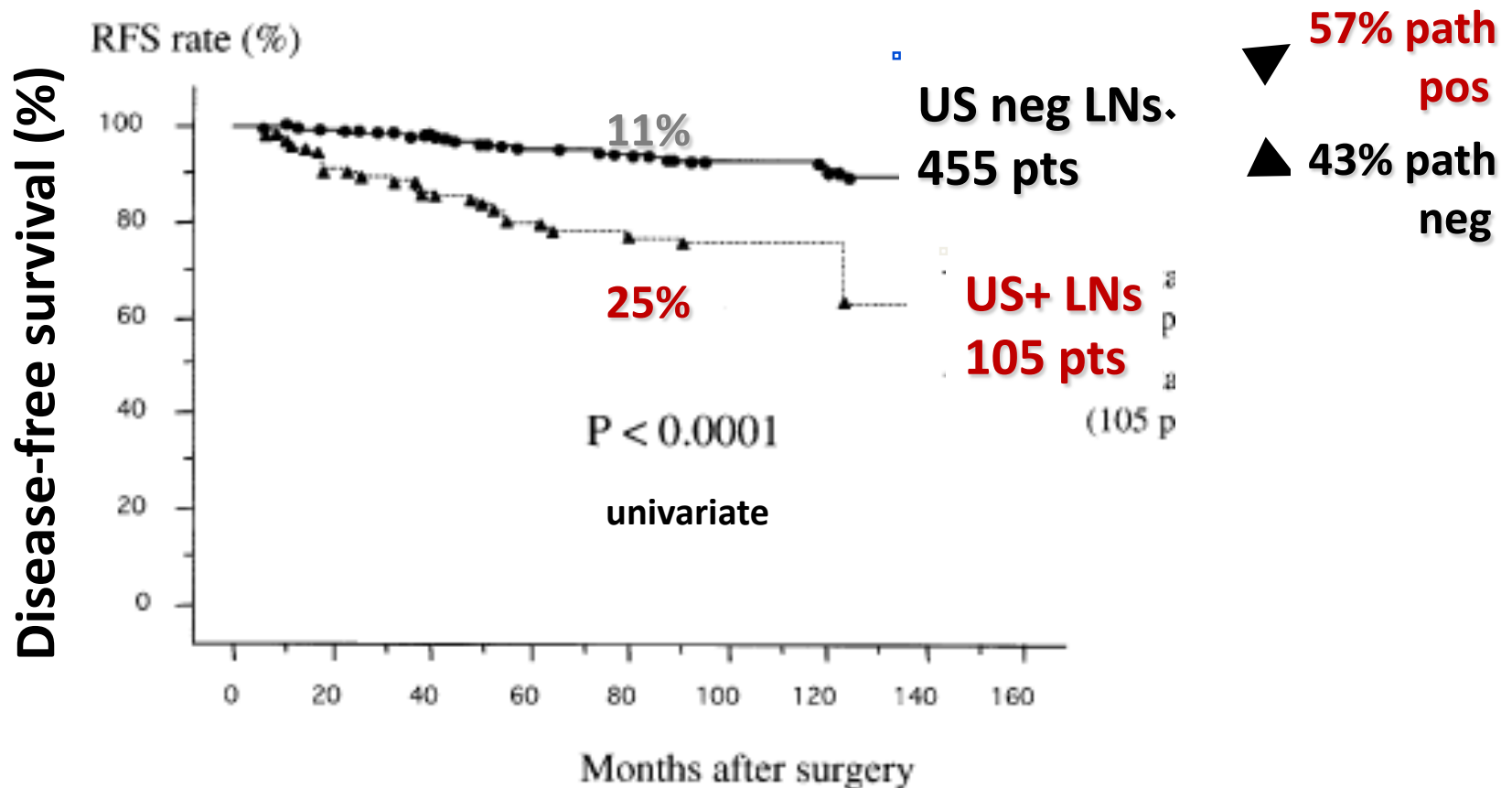
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- On routine neck dissection, small size metastatic LNs are present:
  - Up to 80-90% central neck
  - 30-60% lateral neck
- If not performed, this does NOT increase clinical recurrence (incidence: 2-4%)
- LNs with pathologically detected micrometastases do not impact recurrence.



# Most US-positive lateral neck LNS does impact recurrence rate

Pre-op US on 460 pts → thyroidectomy with neck dissection



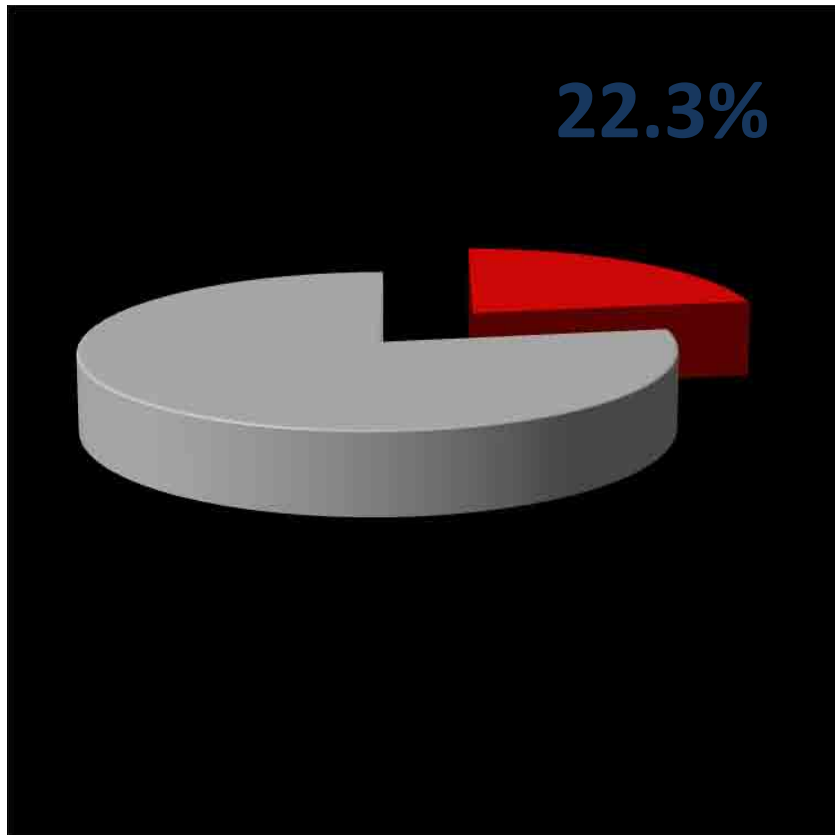


# Risk of persistent/recurrent disease has changed

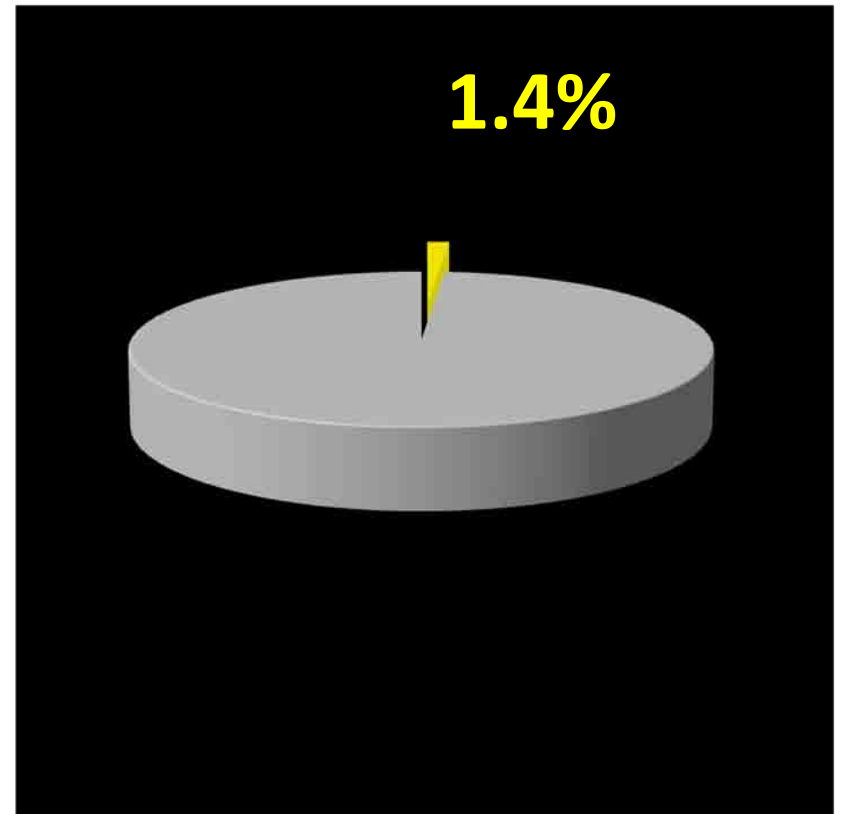
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Mazzaferri A , Am J Med, 1994

Durante et al., JCE&M, 2013



241/1077 pts



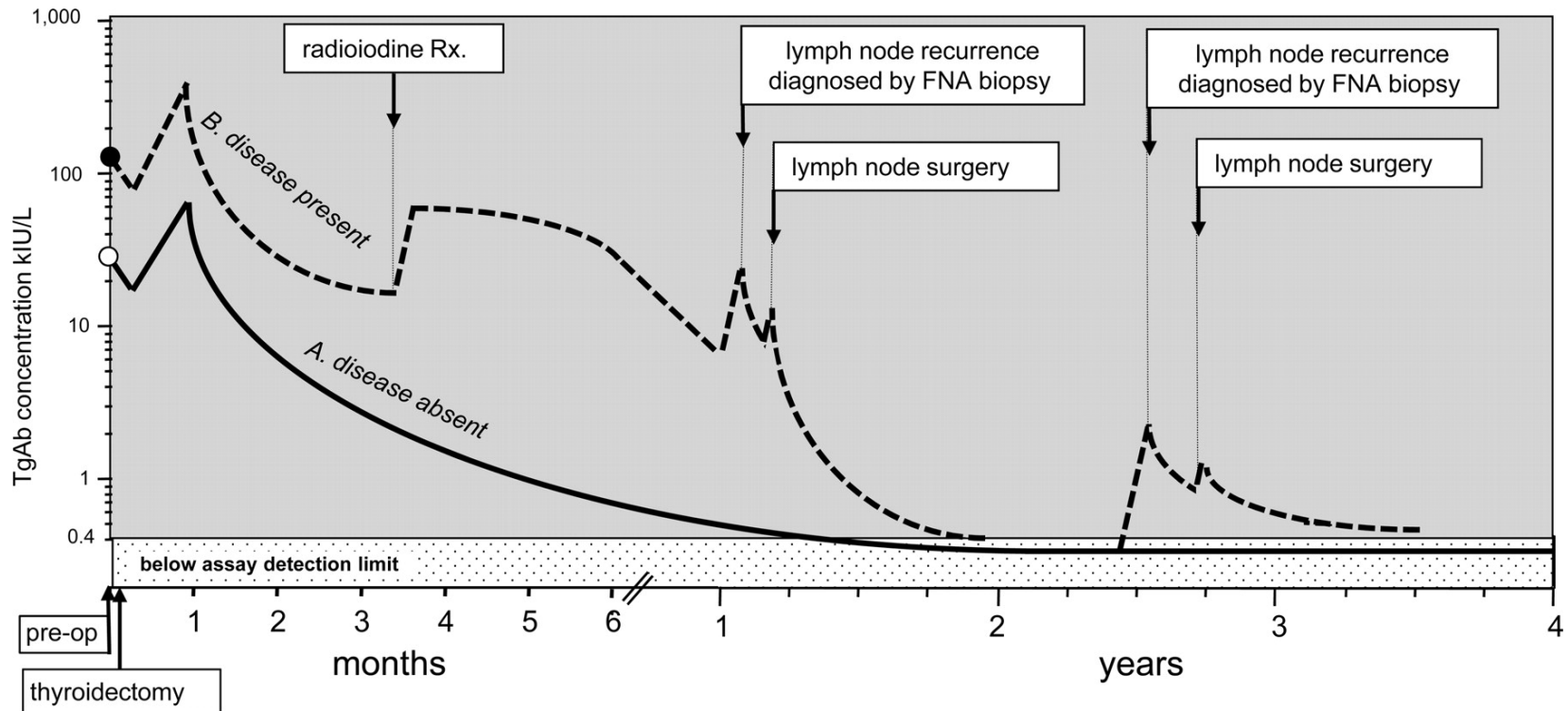
13/1020 pts

# What is the role of RAI Ablation?

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- RAI was one of the major reasons in support of total thyroidectomy
- Currently, no evidence of improved survival in low- and intermediate-risk PTC after RAI
- Improvement of risk of local recurrences appears moderate
- Follow-up is mostly based on Tg determination and neck US.

# Changes in TgAb trends in patients rendered disease-free by surgery vs patients with persistent/recurrent disease



# What is the Outcome of Surgery?

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# The National Cancer Data Base 1985 - 1998

Total thyroidectomy 43227 vs Lobectomy 8946

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- **10-yr Survival**

Thyroidectomy **98.4%** vs Lobectomy **97.1%** ( $p < 0.05$ )

- **10-yr Recurrence**

Thyroidectomy **7.7%** vs Lobectomy **9.8%** ( $p = 0.05$ )\*

*\*Significant differences ONLY for size > 1 cm*

## **SEER Data Base 1983-2002**

Total Thyroidectomy 12598 vs Lobectomy 3266

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- **10-yr Overall Survival**

Thyroidectomy **90.4%** vs Lobectomy **90.8%** (NS)

- **10-yr Specific Survival**

No difference at multivariate analysis



**35% reduction in loco-regional recurrence.**

# Surgical Complications

The Health Care Utilization Project Nationwide Inpatient Sample

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- High-volume centers (>100 cases/yr) **7.5%**
- Intermediate centers (> 10 cases/yr) **13.4%**
- Low-volume centers (< 10 cases/yr) **18.9%**

**Thyroid resections in high-volume centers < 20%**

# Complications Rate (HCUP-NIS) Total Thyroidectomy vs Lobectomy

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- **High-volume centers**

Total Thyroidectomy **14.5%** vs Lobectomy **7.6%**

- **Low-volume centers**

Total Thyroidectomy **24.1%** vs Lobectomy **11.8%**



## So, which are the Recommendations?

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2014 American Thyroid Association Management Guidelines for Patients with  
Thyroid Nodules and Differentiated Thyroid Cancer

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- Thyroid cancer > 4 cm or with gross extrathyroid extension (cT4) or metastatic disease to nodes (cN1) or distant sites (M1):
  - ***Total thyroidectomy and gross removal of all primary tumor, unless contraindications.***

2014 American Thyroid Association Management Guidelines for Patients with  
Thyroid Nodules and Differentiated Thyroid Cancer

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- Thyroid cancer > 1 cm and <4 cm (cT2) without extrathyroid extension or lymph node metastases (cN0):
  - **Either total thyroidectomy or lobectomy.**

2014 American Thyroid Association Management Guidelines for Patients with  
Thyroid Nodules and Differentiated Thyroid Cancer

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- Prophylactic central-compartment dissection in PTC cN0 patients ONLY in case of:
  - ***advanced primary tumors (cT3 or cT4)***
  - ***clinically involved lateral neck nodes (cN1b).***

2014 American Thyroid Association Management Guidelines for Patients with  
Thyroid Nodules and Differentiated Thyroid Cancer

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- Thyroid cancer < 1 cm unifocal and without extrathyroid extension (cT1a) or lymph node metastases (cN0):
  - **If surgery is chosen, lobectomy.**

▪  
**2014 American Thyroid Association Management Guidelines for Patients with  
Thyroid Nodules and Differentiated Thyroid Cancer**

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- BRAF mutational status appears to add little incremental prognostic value to clinico-pathologic staging:
- ***BRAF testing is NOT routinely recommended.***

▫ **British Thyroid Association Guidelines for the Management of  
Thyroid Cancer**

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- Thyroid lobectomy is recommended for patients with unifocal microPTC and no other risk factors.

*Key recommendation*

## British Thyroid Association Guidelines for the Management of Thyroid Cancer

Table 8.1. Risk factors for future recurrence and/or lymph node metastases in patients with thyroid microPTC (excluding patients who present with local or distant metastases)

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### Clinical and/or radiological features

Non-incidenta<sup>1,2,3,4,6,44,47,50–54</sup>

PET-positive<sup>37</sup>

### Histological features

Larger size (6–10 mm)<sup>3,11,21,24,28,35,35,37,49,50–51</sup>

Multifocal and/or bilateral<sup>1,11,23,27,32,33,37,44,47,49,50,57,59,63–64</sup>

Extra-thyroidal extension<sup>11,12,25,27,31,32,37,41,44,50,51,54,55,57,65–67</sup>

Poorly differentiated component<sup>28,38</sup>

Desmoplastic fibrosis and/or infiltrative growth pattern<sup>30</sup>

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## British Thyroid Association Guidelines for the Management of Thyroid Cancer

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- Personalised Decision Making** involves clinicians and patients working together to find a solution, that best suits the circumstances of the individual patient. This process consists of:
- a Discussion in the multi-disciplinary team (MDT) meeting, where the evidence for and against an intervention is weighted and potential benefits and detrimental effects considered
  - b Consideration of risk factors for tumour-specific mortality and recurrence that apply to the intervention. Within this group of patients there is a spectrum of risk defined by clinical and histopathological parameters. Generally the greater the number of risk factors the stronger is the case in favour of the intervention
  - c Consideration of the patient's comorbidities, personal circumstances and values

**So, we have just to think, discuss and make  
the best choice all together!**

