Risk Stratification in the Management of Differentiated Thyroid Cancer

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DIPLOMATE OF THE AMERICAN BOARD OF INTERNAL MEDICINE; ENDOCRINOLOGY, DIABETES AND METABOLISM, AND THE AMERICAN BOARD OF CLINICAL LIPIDOLOGY

Disclosures

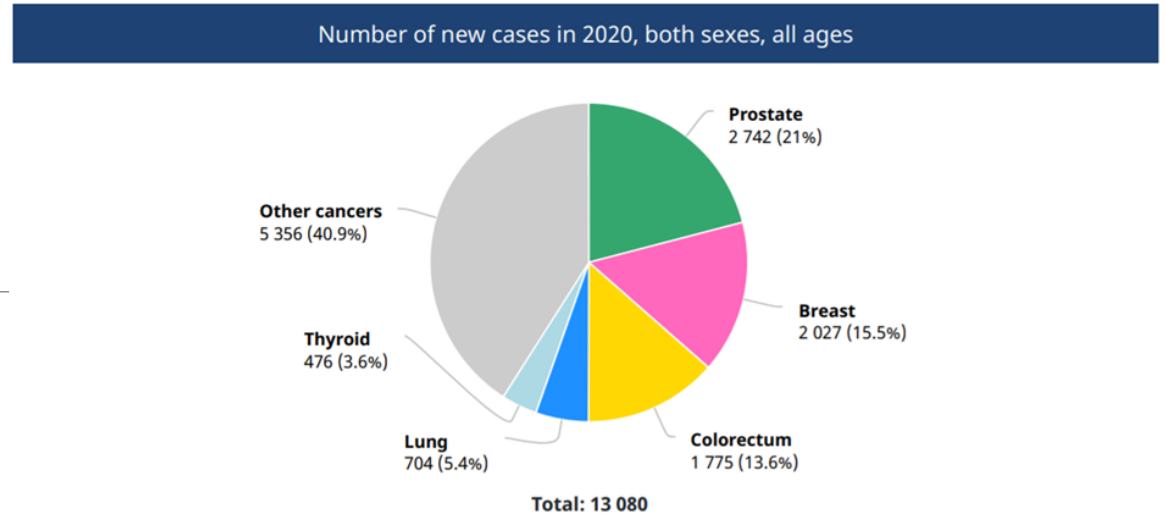
None

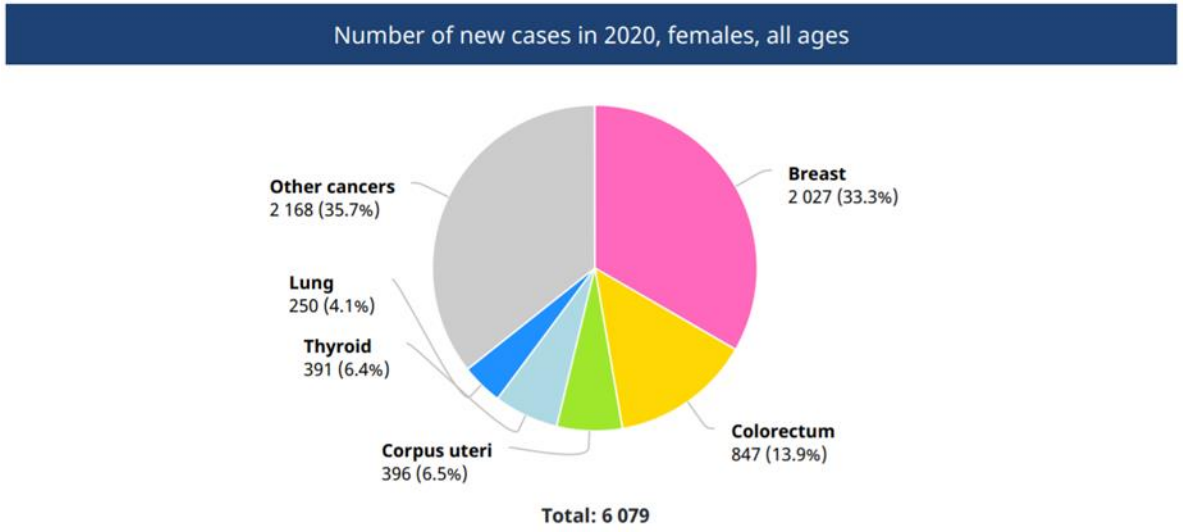
Learning Objectives

- Discuss the incidence and mortality of thyroid cancer in PR
- Discuss the concept of peri-diagnostic risk assessment in addition to intraoperative and post surgical stratification
- Evaluate the ideal candidates for a minimalistic approach
- Distinguish the differences in the AJCC 8th edition from 7th edition for disease mortality
- Discuss the ATA Risk stratification system for disease recurrence
- Discuss the dynamic risk assessment in the long-term follow-up
- Discuss the role of TSH suppression according to response to therapy categories
- Role of the molecular markers to the dynamic risk assessment

Thyroid Carcinoma 2020 PR Estimates

- 5-10% of thyroid nodules are malignant[1]
- Based on GLOBOCAN 2020[2], PR has the highest incidence rate of thyroid cancer in the Americas and the 4th highest rate worldwide.
- 3rd most common cancer in women.
- A rapid increase in the incidence has been observed during the last decade in both, men and women.



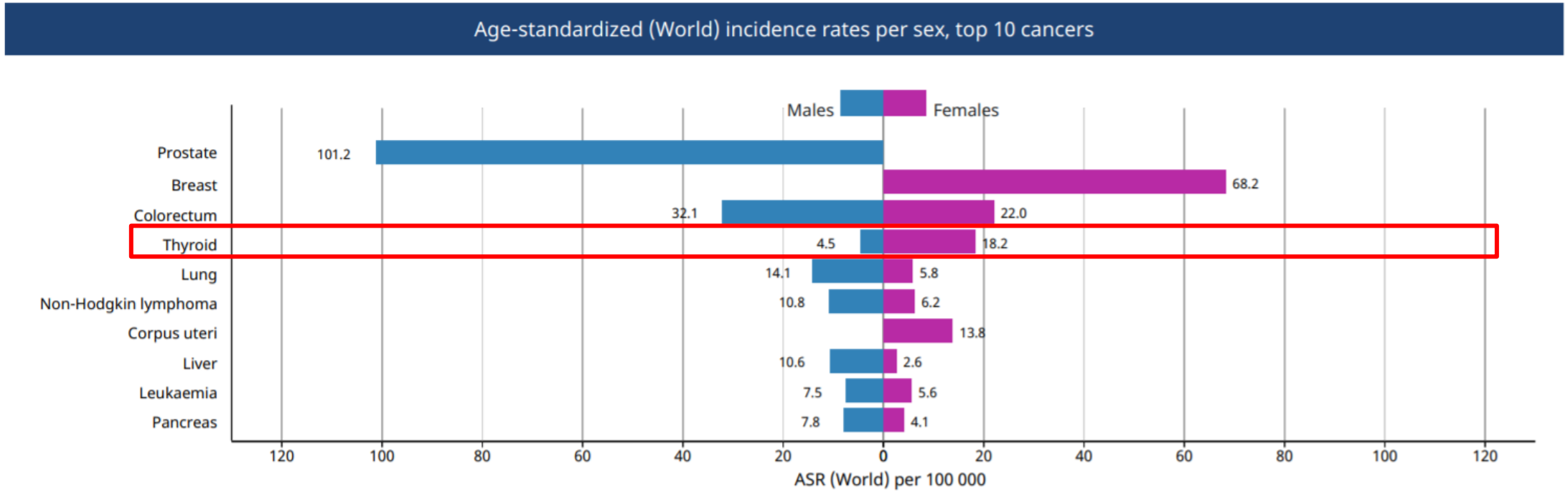


International Agency for Research on Cancer

World Health Organization

1. HEGEDUS, L. NEJM, 2004. 2. GLOBOCON, 2020

Incidence of Thyroid Cancer in PR



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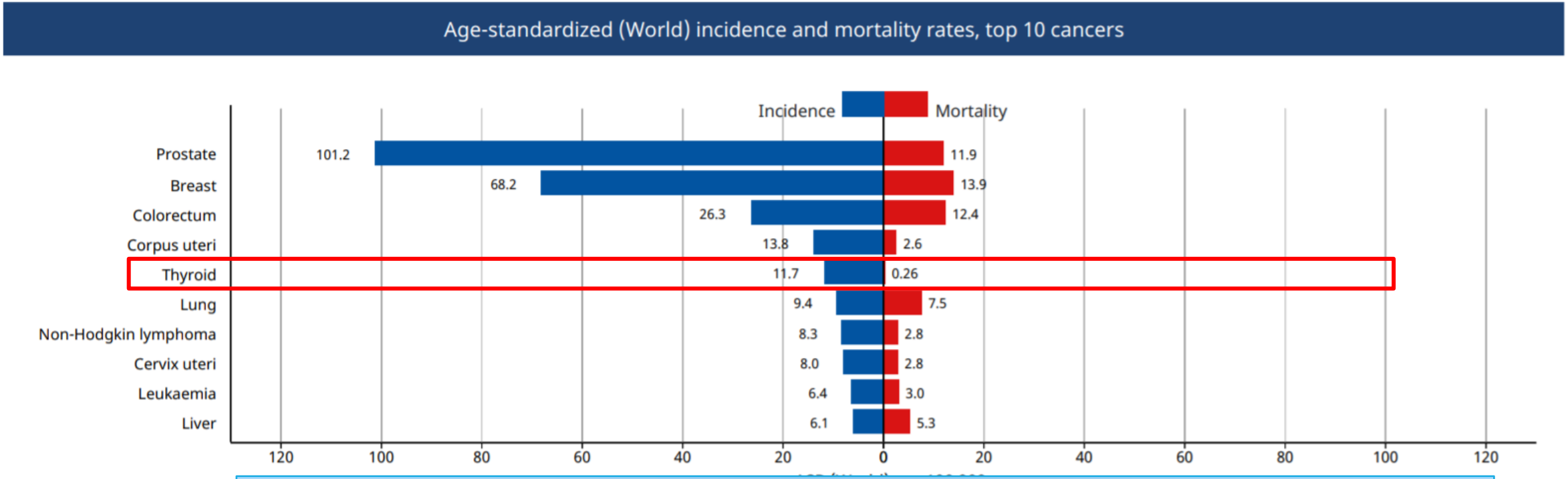
Mortality of Thyroid Cancer in PR



During the period 1987 to 2015 mortality rates from thyroid cancer declined 1.2% per year in women and 1.6% per year in men.

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Incidence of Thyroid Cancer in Puerto Rico and the US by racial/ethnic group, 2011–2015

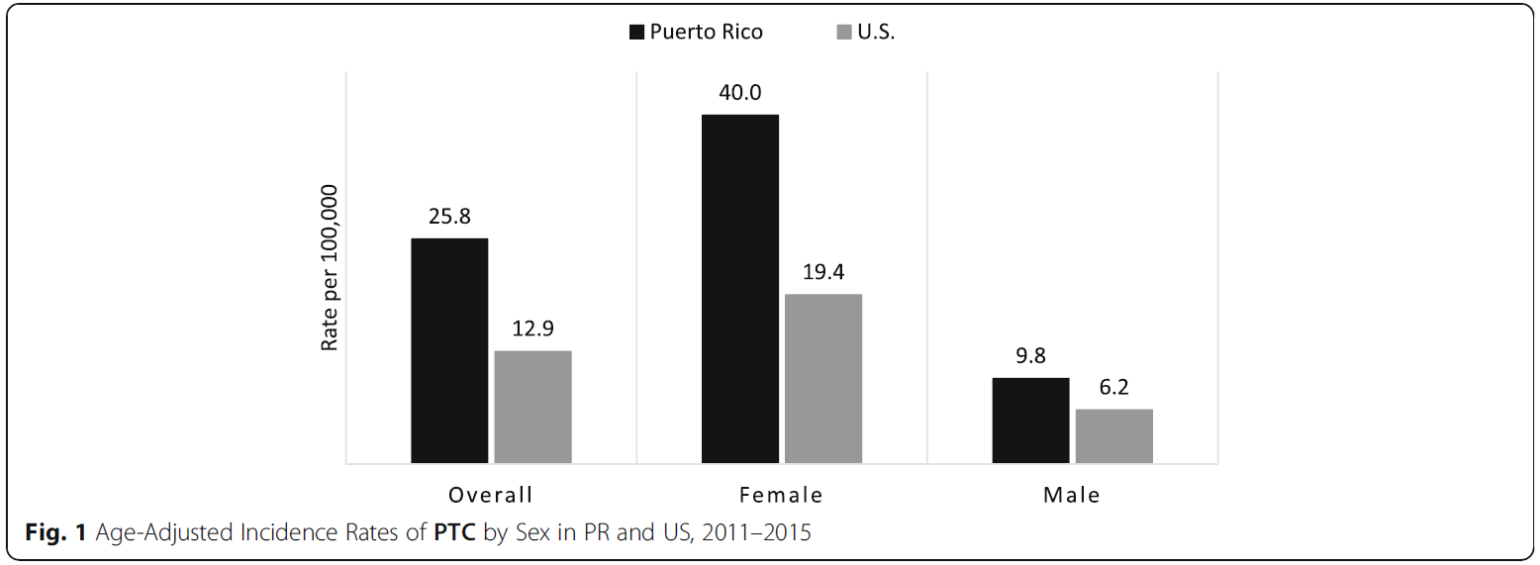


Fig. 1 Age-Adjusted Incidence Rates of **PTC** by Sex in PR and US, 2011–2015

Incidence Rates by Age-Groups and Sex in PR and US, 2011-2015

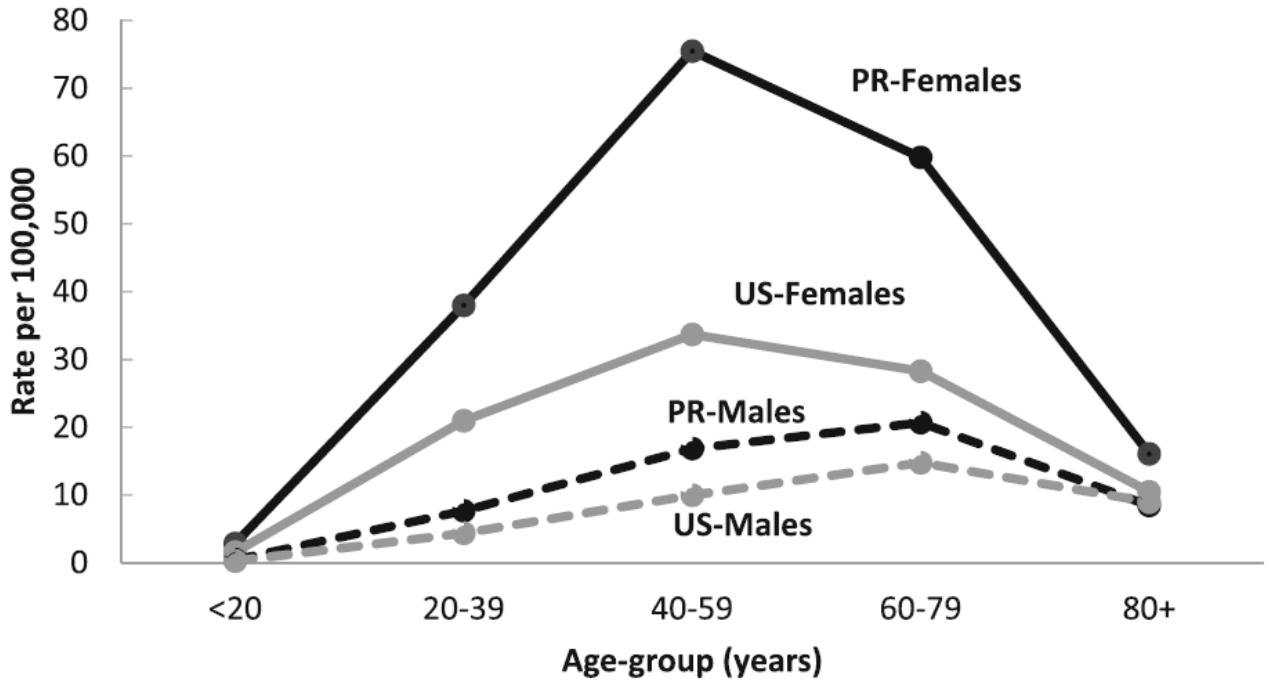
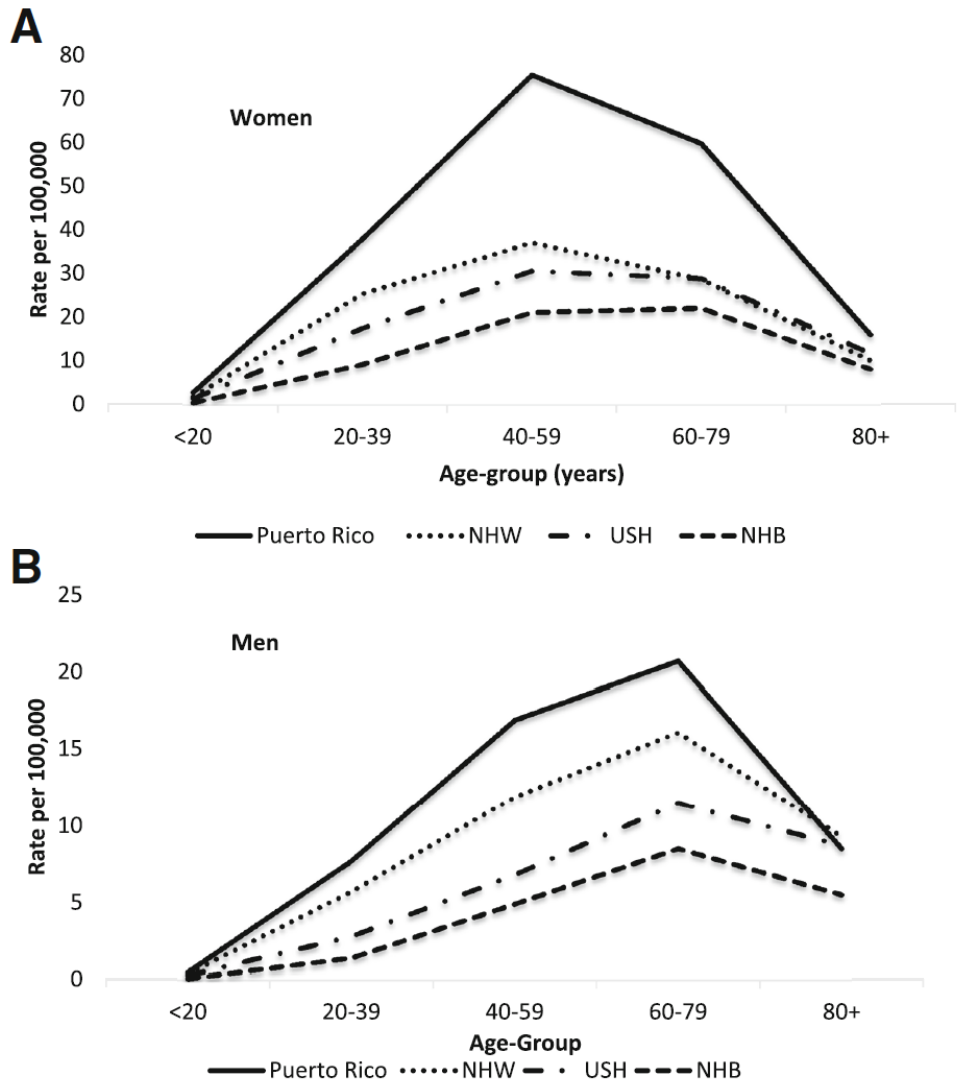


Fig. 2 Age-Adjusted Incidence Rates of **PTC** by Age-Groups and Sex in PR and US, 2011–2015

Incidence Rates by Age-Groups, Sex and Race/Ethnicity in PR and US, 2011-2015



e-Adjusted Incidence Rates of **PTC** by Sex and Race/Ethnicity in PR and US, 2011–2015. Women (**a**), Men (**b**)

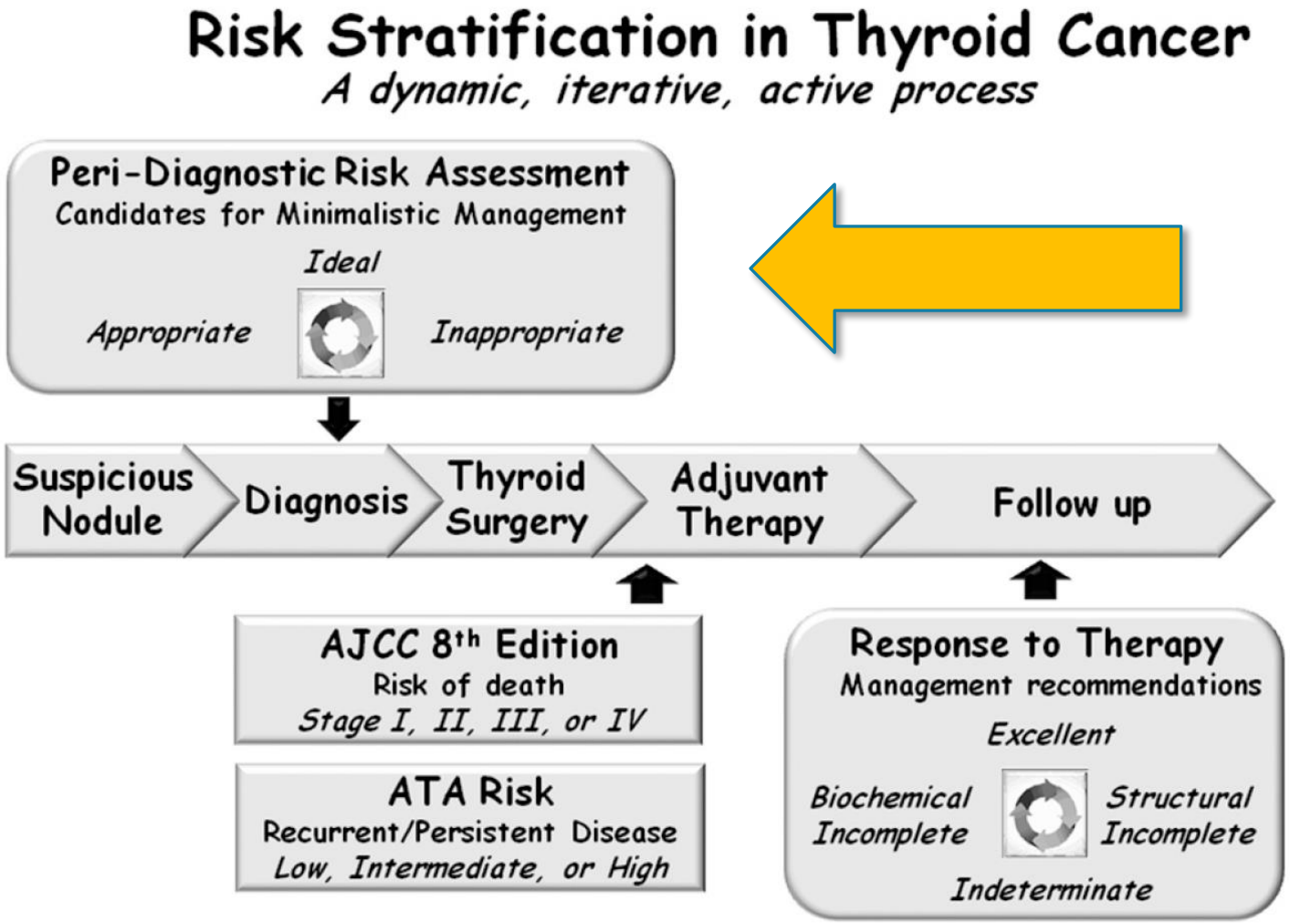
TORTOLERO-LUNA ET AL. BMC CANCER (2019) 19:637

Reasons that explain the increase in TC incidence and population differences.

- Multifactorial
- Overdiagnosis of small lesions
  - Increase use of new diagnostic modalities[1]
  - increase medical surveillance
  - Increase access to healthcare services[2]
- Radiation exposure from CT scans
- Nutritional, Obesity, Insulin Resistance[3]
- Physical Inactivity[4]
- High Socioeconomic Status[5]

1. HALL SF, ET AL. CANCER MED. 2014;3(1):154–161. 2. GUAY B, ET AL. THYROID. 2014;24(3):552–5. 3. KITAHARA CM, ET AL. EPIDEMIOLOGY AND PREVENTION. 4THED. NEW YORK: OXFORD UNIVERSITY PRESS; 2018. 839–860 P. 4. CASH SW, ET AL. CANCER EPIDEMIOL. 2013; 37(1):46–53. 5. HARARI A, ET AL. JCEM. 2014;99(1):133–41.

Since the vast majority of these subclinical thyroid cancer foci progress either slowly or not at all, it is critical to reevaluate the traditional management approach.



From Detection to Final Follow-Up

TUTTLE, M AND ALZAHRANI, AS. J CLIN ENDOCRINOL METAB 104: 4087–4100, 2019

Differentiating “Detectable Findings” from “Actionable Findings”

Risk Stratification Decision-Making Framework

Detectable Findings

Key Factors

Tumor size (Volume)

Tumor location

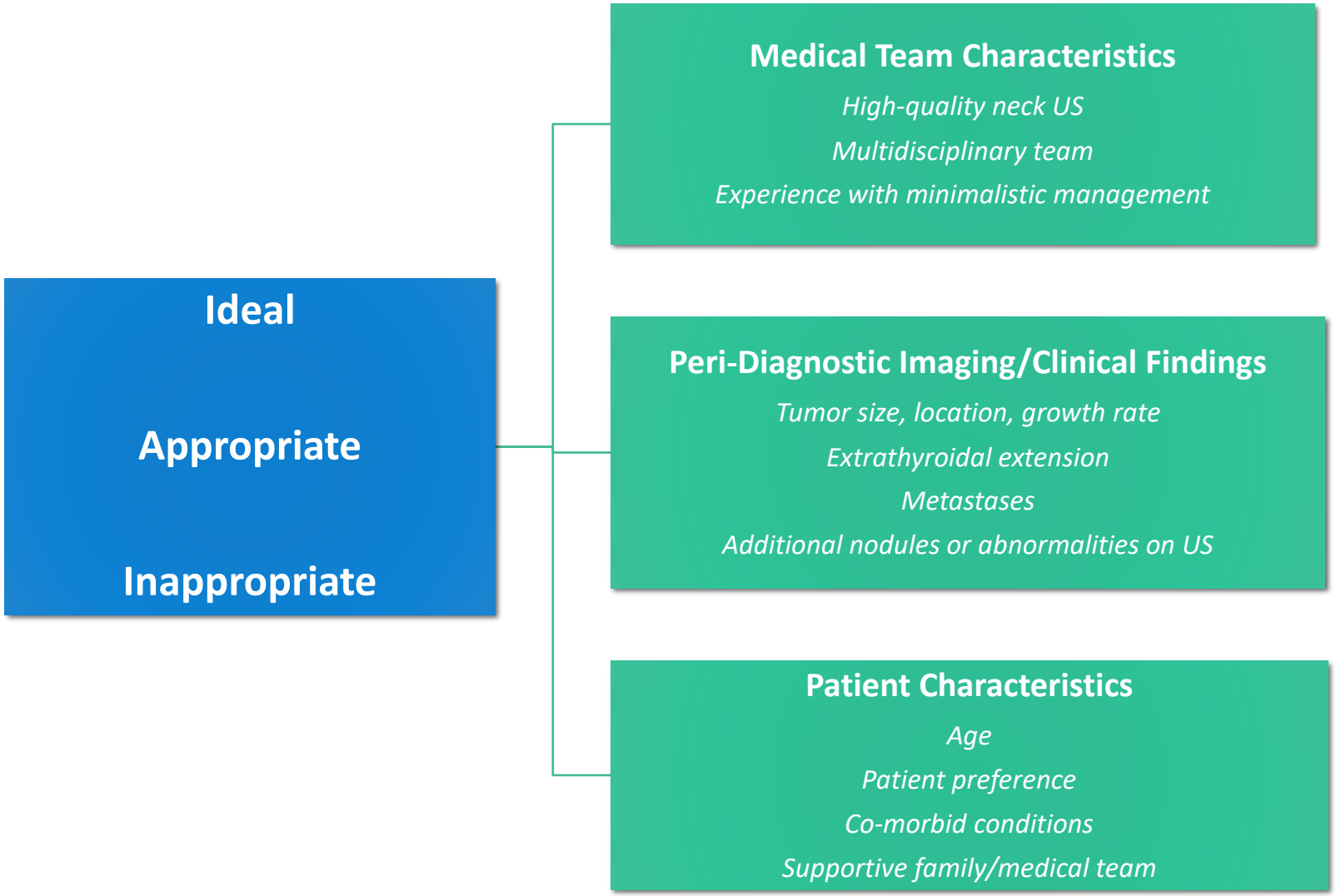
Tumor Growth Rate (doubling time)

Symptoms

Patient Preference

Peri-Diagnostic Risk Stratification

Selecting Candidates for Minimalistic Initial Management Options



TUTTLE, M AND ALZAHRANI, AS. J CLIN ENDOCRINOL METAB 104: 4087–4100, 2019

A risk-Stratified Approach to Decision Making in Probable or Proven Papillary Microcarcinoma

Ideal Candidate for Active Surveillance

Tumor/Neck US Characteristics

- Solitary thyroid nodule
- Well-defined margins
- Surrounded by ≥2 mm normal thyroid parenchyma
- Previous US w/ stability
- cN0
- cM0

Patient Characteristics

- Older patients (>60 y/o)
- Willing to accept active surveillance
- Understands that sx intervention may be necessary in the future
- Expected to be compliant with follow-up plans
- Supportive significant others
- Life-threatening comorbidities

Medical Team Characteristics

- Experienced multidisciplinary management team
- High-quality neck US
- Prospective data collection
- Tracking/reminder program to ensure proper follow-up

BRITO ET AL. THYROID. 2016;26(1):144-149

American Association of Endocrine Surgeons

Estimation of the lifetime probability of disease progression of papillary microcarcinoma of the thyroid during active surveillance

Akira Miyauchi, MD, PhD [a,*], Takumi Kudo, MD, PhD [b], Yasuhiro Ito, MD, PhD [a], Hitomi Oda, MD [a], Hisanori Sasai, MD, PhD [c], Takuya Higashiyama, MD, PhD [a], Mitsuhiro Fukushima, MD, PhD [a], Hiroo Masuoka, MD, PhD [a], Minoru Kihara, MD, PhD [a], and Akihiro Miya, MD, PhD [a]

[a] *Department of Surgery, Kuma Hospital, Kobe, Japan*
[b] *Department of Internal Medicine, Kuma Hospital, Kobe, Japan*
[c] *Department Head and Neck Surgery, Kuma Hospital, Kobe, Japan*

Table II.
Observed rates of tumor enlargement, novel nodal metastasis and disease progression at 10-year active surveillance and estimated lifetime probability of these events according to the age group at the presentation

Age at presentation	Observed events at 10-year surveillance (%)			Estimated lifetime probability (%) calculated according to Hypothesis A		
	Tumor enlargement	Novel nodal metastasis	Disease progression	Tumor enlargement	Novel nodal metastasis	Disease progression
20s	22.0	16.5	36.9	46.0	26.9	60.3
30s	8.4	6.1	13.5	30.7	12.5	37.1
40s	11.2	3.7	14.5	24.3	6.8	27.3
50s	6.5	2.4	5.6	14.8	3.3	14.9
60s	6.3	0.3	6.6	8.9	0.9	9.9
70s	2.8	0.6	3.5	2.8	0.6	3.5

Tumor enlargement is defined as increase in tumor size by ≥3 mm. Disease progression is defined as ≥3 mm tumor enlargement and/or appearance of novel nodal metastasis.

- From 1993–2013 at Kuma Hospital
- 1,211 low-risk papillary microcarcinoma patients aged 20–79 years underwent active surveillance
- No increase in disease-specific mortality in patients with disease progression

AKIRA MIYAUCHI, ET AL. SURGERY. 2017

Appropriate Candidate for Active Surveillance

Tumor/Neck US Characteristics

- MPMC
- Subcapsular location (not RLN, w/o evidence of ETE)
- Ill-defined margins
- Background US findings that will make follow-up difficult (thyroiditis, nonspecific lymphadenopathy, multiple other benign-appearing thyroid nodules)
- FDG-avid PMC

Patient Characteristics

- Middle-aged patients (18-59 years)
- Strong family hx of PTC
- Child-bearing potential

Medical Team Characteristics

- Experienced endocrinologist or thyroid surgeon
- Neck US routinely available

THYROID
Volume 26, Number 1, 2016
Mary Ann Liebert, Inc.
DOI: 10.1089/thy.2015.0313

Incidences of Unfavorable Events in the Management of Low-Risk Papillary Microcarcinoma of the Thyroid by Active Surveillance Versus Immediate Surgery

Hitomi Oda,[1] Akira Miyauchi,[1] Yasuhiro Ito,[1,2] Kana Yoshioka,[3] Ayako Nakayama,[3] Hisanori Sasai,[3] Hiroo Masuoka,[1] Tomonori Yabuta,[1] Mitsuhiro Fukushima,[1] Takuya Higashiyama,[1] Minoru Kihara,[1] Kaoru Kobayashi,[1] and Akihiro Miya[1]

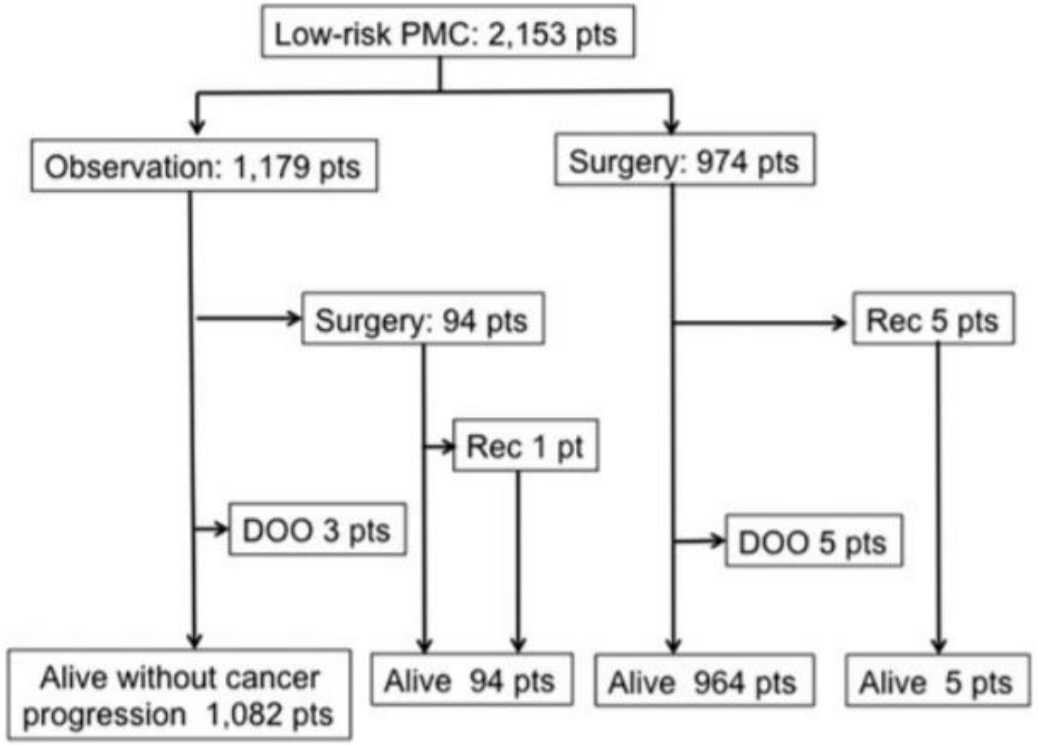


FIG. 1. Flow of the management and oncological outcomes of 2153 patients with low-risk papillary microcarcinoma (PMC). Of the observation group, 94 patients underwent surgery for various reasons. Rec: recurrence; DOO, died of other causes unrelated to thyroid cancer.

- 2005-2013 at Kuma Hospital
- Low risk Papillary Microcarcinoma
- Similar characteristics as the ideal and appropriate candidate

ODA H, ET AL. THYROID. 2016. 26(1): 150-155

TABLE 2. UNFAVORABLE EVENTS FOLLOWING ACTIVE SURVEILLANCE AND IMMEDIATE SURGERY

Unfavorable events	*Intended management*		p-*Value*
	Active surveillance, 1179 pts	*Immediate surgery, 974 pts*	
Later surgery (pts)	94	0	<0.0001
Temporary VCP (%)	7 (0.6%)	40 (4.1%)	<0.0001
Permanent VCP (%)	0 (0%)	2 (0.2%)	n.s.
Temporary Hypo-PT (%)	33 (2.8%)	163 (16.7%)	<0.0001
Permanent Hypo-PT (%)	1 (0.08%)	16 (1.6%)	<0.0001
On L-thyroxine (%)	244 (20.7%)	644 (66.1%)	<0.0001
Postsurgical hematoma (%)	0 (0%)	5 (0.5%)	<0.05
Postsurgical abscess (%)	0 (0%)	0 (0%)	n.s.
Surgical scar (%)	94 (8.0%)	974 (100%)	<0.0001
Recurrence in neck (pts)	1	5	n.s.
Death (%)	3 (0.3%)	5 (0.5%)	n.s.

VCP and Hypo-PT in the active surveillance group occurred in patients who converted to surgery later for various reasons, except for one patient who developed idiopathic Hypo-PT and another who developed transient idiopathic VCP contralateral to the microcarcinoma. All deaths in the present series were due to causes unrelated to thyroid cancer.

VCP, vocal cord paralysis; Hypo-PT, hypoparathyroidism.

Inappropriate Candidate for Active Surveillance

Tumor/Neck US Characteristics

- Evidence of aggressive cytology on FNA
- Subcapsular location adjacent to RLN
- Evidence of ETE
- Clinical evidence of invasion to RLN or trachea
- N1 disease (initial or follow-up)
- M1 disease
- Increase in size ≥3mm in a confirmed PTC

Patient Characteristics

- Young patients (<18 years)
- Unlikely to be compliant with follow-up plans
- Not willing to accept an observation approach

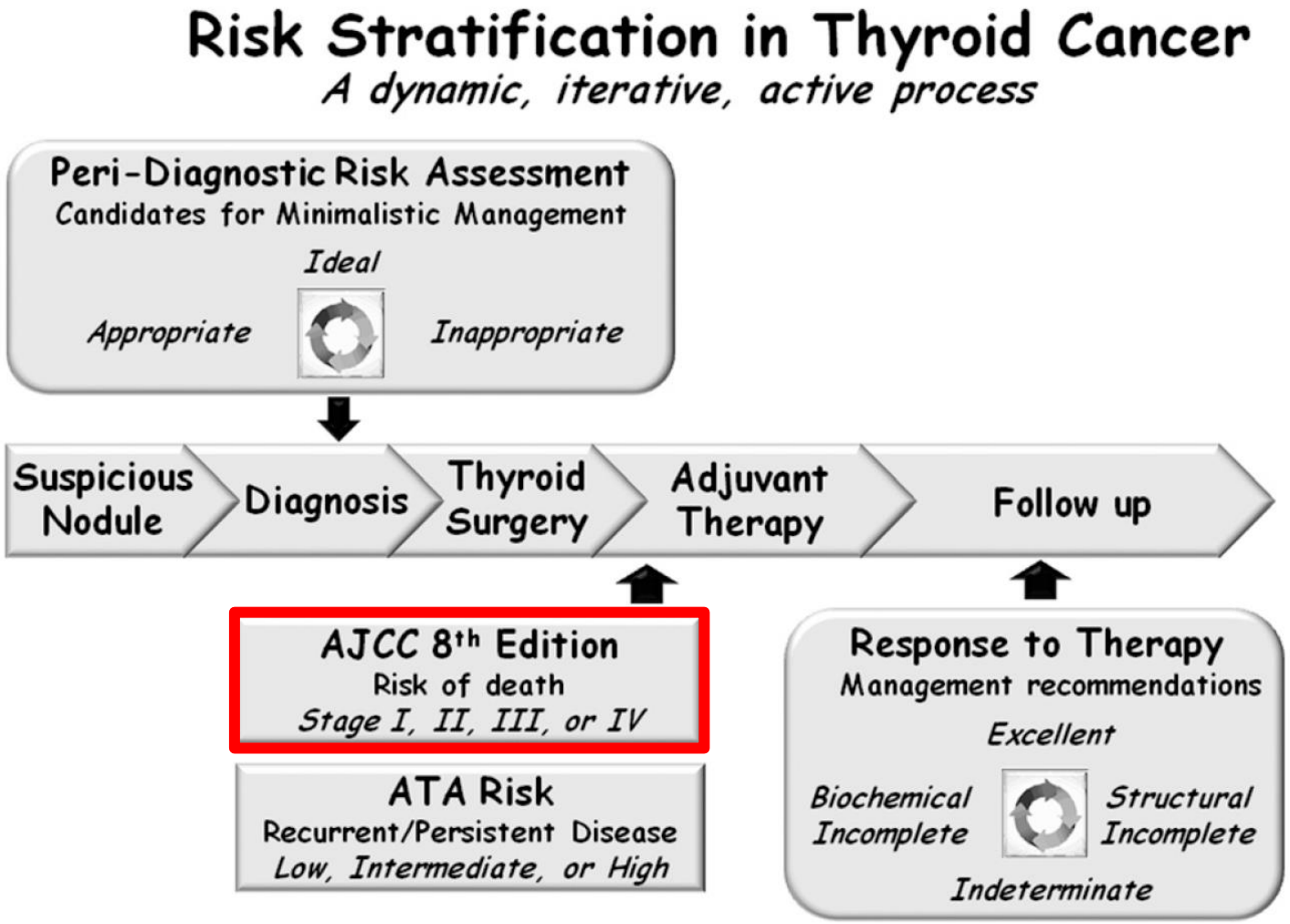
Medical Team Characteristics

- Reliable neck US not available
- Little experience with thyroid cancer management

THYROID
Volume 31, Number 2, 2021
Mary Ann Liebert, Inc.
DOI: 10.1089/thy.2020.0330

Indications and Strategy for Active Surveillance of Adult Low-Risk Papillary Thyroid Microcarcinoma: Consensus Statements from the Japan Association of Endocrine Surgery Task Force on Management for Papillary Thyroid Microcarcinoma

Iwao Sugitani,[1] Yasuhiro Ito,[2] Dai Takeuchi,[3] Hirotaka Nakayama,[4] Chie Masaki,[5] Hisakazu Shindo,[6] Masanori Teshima,[7] Kazuhiko Horiguchi,[8] Yusaku Yoshida,[9] Toshiharu Kanai,[10] Mitsuyoshi Hirokawa,[11] Kiyomi Y. Hames,[5] Isao Tabei,[12] and Akira Miyauchi[2]



Assessing Mortality Risk

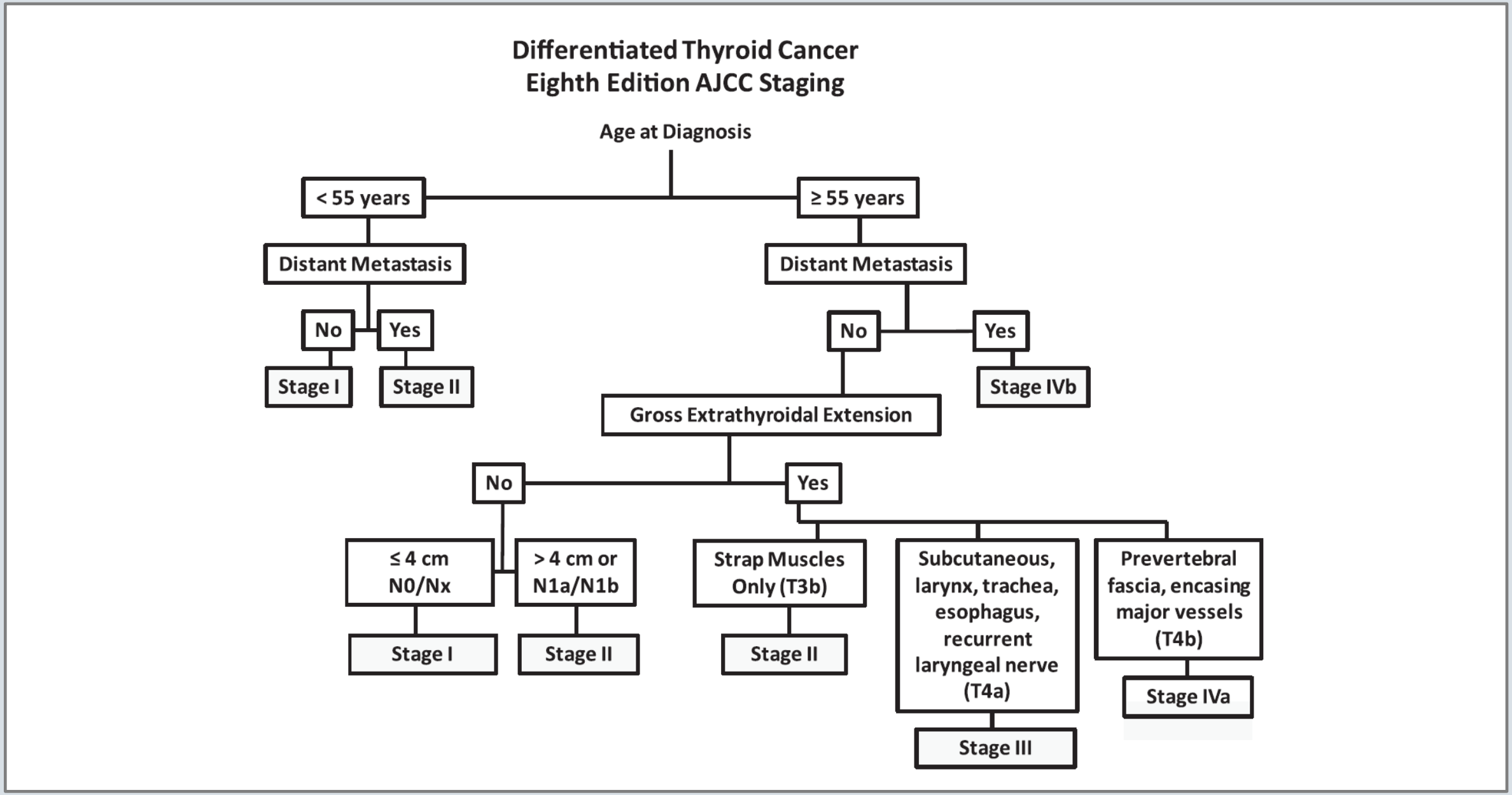
Predictive Models for Disease Specific Mortality

TABLE 1
Comparing Different Factors Used in Ten Different Stage Classifications

Classification	EORTC	UICC/AJCC	AGES	AMES	MACIS	Clinical Class	Ohio	SAG	Noguchi	MSK
Histologies	All	All	Papillary	Differentiated	Papillary	Differentiated	Differentiated	Papillary	Papillary	Differentiated
Grade	No	No	Yes	No	No	No	No	Yes	No	No
Age (yrs)	Continuous	<45	Continuous	<41 male <51 female	Continuous	<45	No	<70	Variable	<45
Gender (better prognosis)	Yes (female)	No	No	Yes (female)	No	No	No	Yes (female)	Yes (male)	No
Size (in cm)	No	≤1 1–4 >4	Continuous	<5 ≥5	Continuous	≤1 1–4 >4	≤1.5 1.5–4.4 ≥4.5	No	<3 cm	≤1 1–4 >4
Extrathyroid invasion	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Residual disease	No	No	No	No	Yes	No	No	No	No	No
Lymph nodes	No	Yes	No	No	No	Yes	Yes	No	Yes	No
Multifocal	No	No	No	No	No	No	Yes	No	No	No
Metastases	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Validation	Yes	Unknown	Yes	Unknown	Yes	Unknown	Unknown	Unknown	Unknown	Unknown

EORTC: European Organization for Research and Treatment of Cancer; UICC: International Union Against Cancer; AJCC: American Joint Committee on Cancer; AGES: Age, Grade, Extrathyroid extent and Size; AMES: Age, Metastases, Extrathyroid extension, and Size; MACIS: Metastases, Age, Completeness of resection, Invasion, and Size; SAG: Sex, Age, and Grade; MSK: Memorial Sloan-Kettering Cancer Center.

BRIERLEY JD, ET AL. CANCER 1997; 79:2414 –23.



TUTTLE, M AND ALZAHRANI, AS. J CLIN ENDOCRINOL METAB. 2019;104: 4087–4100

Major Changes in the AJCC/TNM 8th Edition

Age point cut-off 55 years of age

- 8th edition -- 10-year DSS rates for stage I-IV 99.5%, 94.7%, 94.1%, and 67.6%
- 7th edition – 10-year DSS rates for stage I-IV 99.7%, 97.3%, 96.6% and 76.3%[1]
- >55 y/o had 103 differently expressed genes related to pathways associated to aggressive TC.[2]

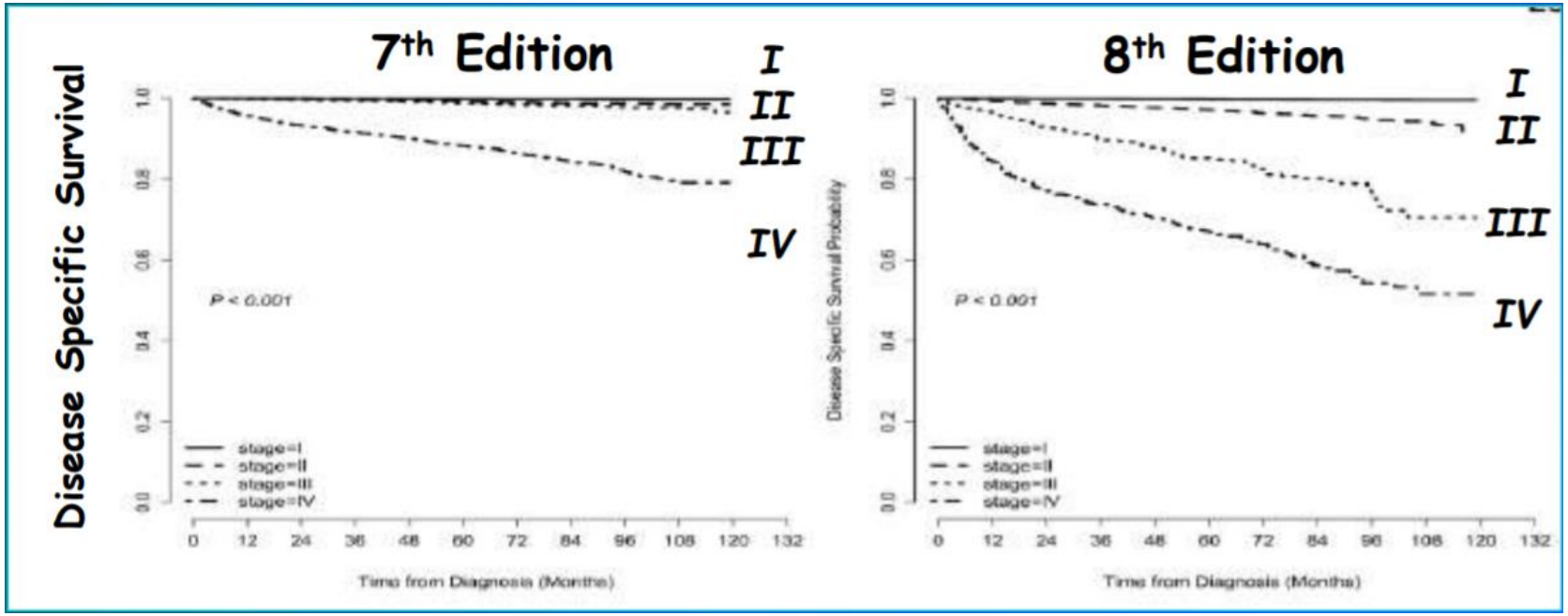
mETE

- Eliminated from 8th edition
- Does not influence disease-free survival, locoregional failure, and distant metastases failure.
- No longer assignment of stage III to older patients with mETE or LN mets.

1. NIXON IJ, ET AL. THYROID. 2016; 26(3):373-380. 2. KIM K, ET AL. WORLD J SURG. 2018.

Projecting Survival in Papillary Thyroid Cancer: A Comparison of the 7th and 8th Editions of the AJCC/UICC Staging Systems in Two Contemporary National Patients Cohorts

SEER
64,342 patients



Major Changes in the AJCC/TNM 8th Edition

Mediastinal lymph nodes mets

- 7th edition – level VII considered N1b
- 8th edition – level VII considered N1a
- Reclassifies patients from stage IVa to stage II

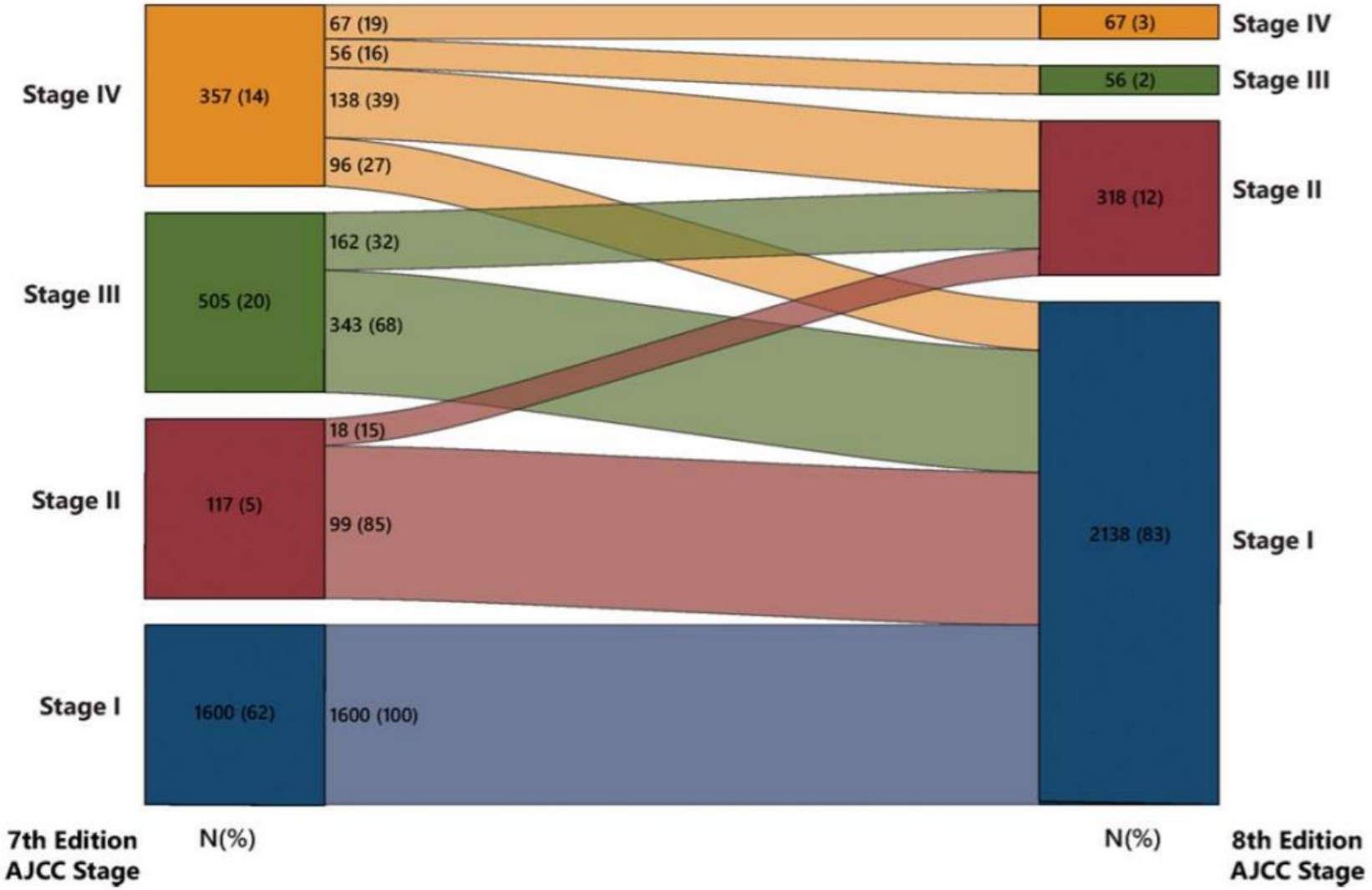
N1 disease

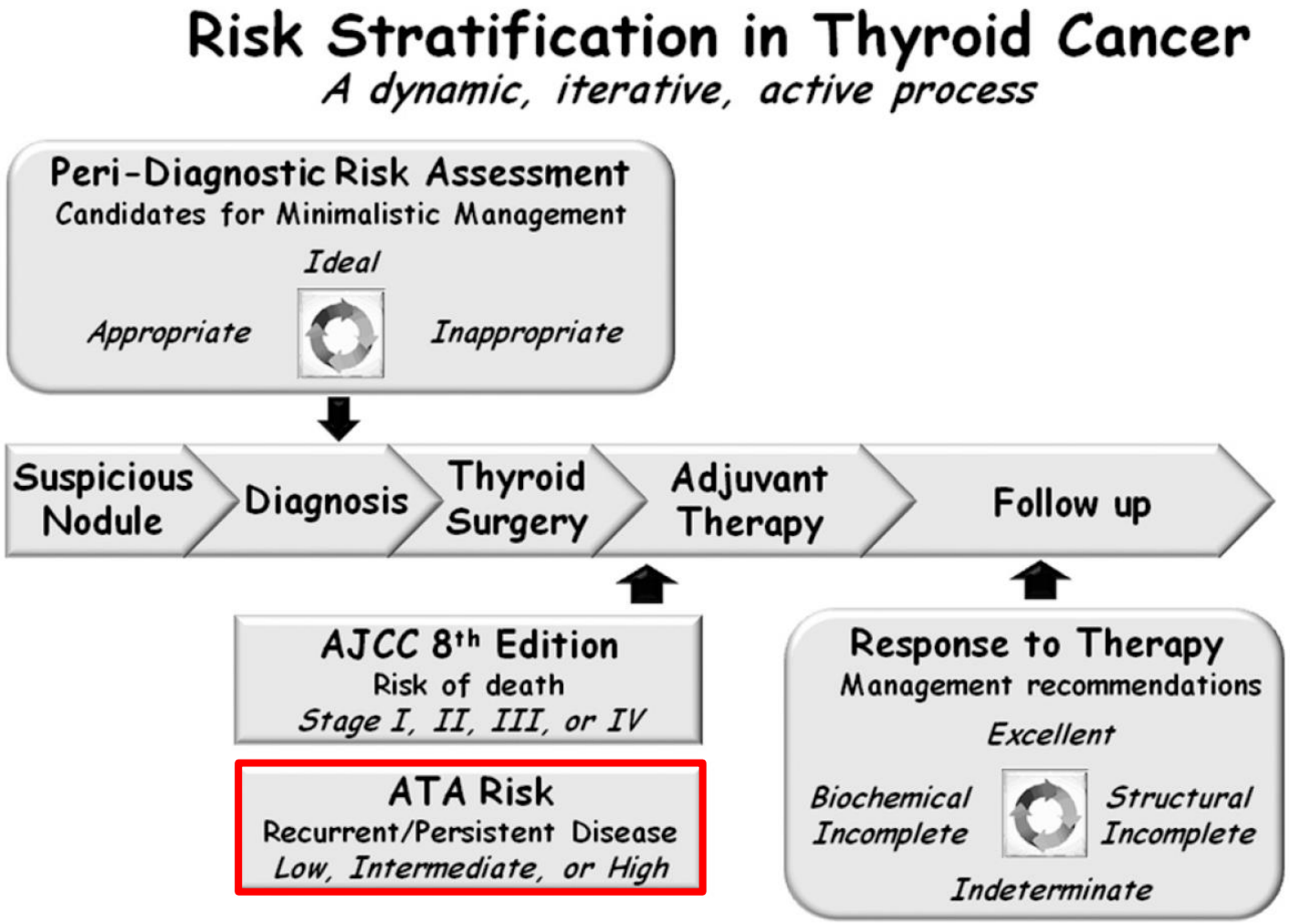
- No longer upstages older patients to stage III or IV[1]
- <55 years – stage I
- >55 years stage II

1. TUTTLE RM, ET AL. THYROID. 2017; 27(6): 751-756.

Transition from the 7th Edition to the 8th edition

MD Anderson Cancer Center

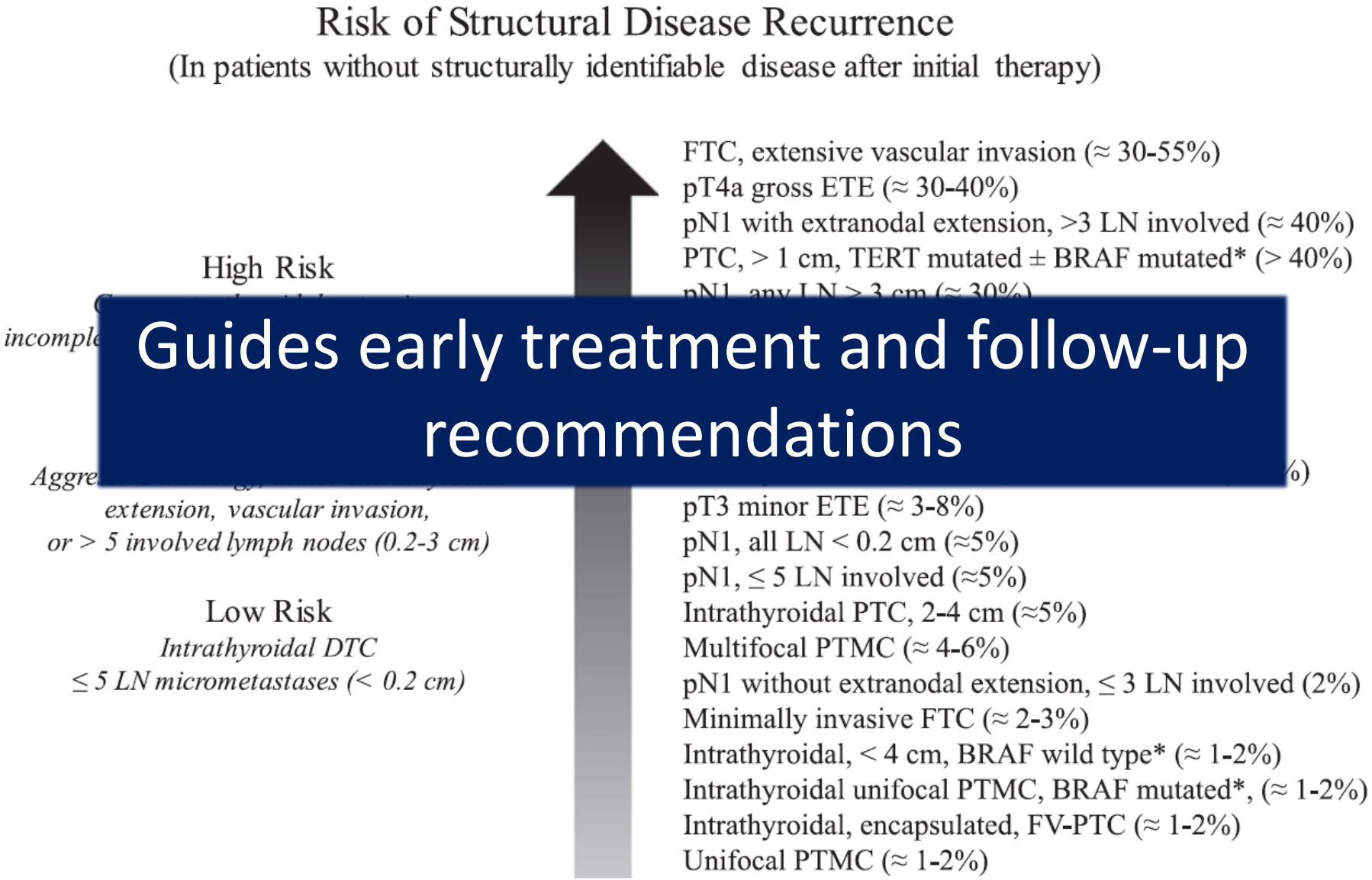




Determining Risk of Recurrence

Low (all of these)	Intermediate	High
Any size and intrathyroidal; Complete resection	Microscopic invasion into perithyroidal soft tissues	Gross ETE; incomplete tumor resection
N0 ***or ≤5 LN <0.2cm***; M0	Clinical N1 ***or >5 LN (all <3cm)***	***N1 (any LN ≥3cm)***; M1
No aggressive histology¶ or ***Intrathyroidal PTC,FV Intrathyroidal FTC (no-min vascular invasion < 4 foci) Intrathyroidal PTC BRAF^{V600E}***	Aggressive histology¶ or ***Multifocal, microPTC with ETE & BRAF^{V600E}***	***FTC with extensive vascular invasion (> 4 foci)***
No vascular invasion	Vascular invasion	
No uptake outside thyroid bed, if RAI given	Uptake outside thyroid bed, if RAI given	Inappropriate postop Tg suggestive of M1

Initial Static Risk Stratification of Recurrence + 2015 ATA Updates



HAUGEN BR, ET AL. THYROID. 2016;26(1):1-133

Retrospective Studies Validate ATA Initial Risk Stratification System

ATA risk	*Study*	*NED, %*	*Biochemical incomplete, %*[b]	*Structural incomplete, %*[c]
Low	Tuttle *et al.* (538)	86	11	3
	Castagna *et al.* (542)	91	ND[a]	ND[a]
	Vaisman *et al.* (539)	88	10	2
	Pitoia *et al.* (543)	78	15	7
Intermediate[a]	Tuttle *et al.* (538)	57	22	21
	Vaisman *et al.* (539)	63	16	21
	Pitoia *et al.* (543)	52	14	34
High	Tuttle *et al.* (538)	14	14	72
	Vaisman *et al.* (539)	16	12	72
	Pitoia *et al.* (543)	31	13	56

- **NED**: stimulated Tg < 1ng/mL with no disease radiologically or clinically
- **Biochemical incomplete**: suppressed Tg>1ng/mL, stimulated Tg>10ng/mL, or rising Tg antibody in absence of structural disease
- **Structural incomplete**: structural disease that is bx-proven or highly suspicious for disease +/- abnormal Tg

HAUGEN BR, ET AL. THYROID. 2016;26(1):1-133

Effect of Age on Response to Therapy and Mortality in Patients With Thyroid Cancer at High Risk of Recurrence

Sona Shah[1] and Laura Boucai[1]

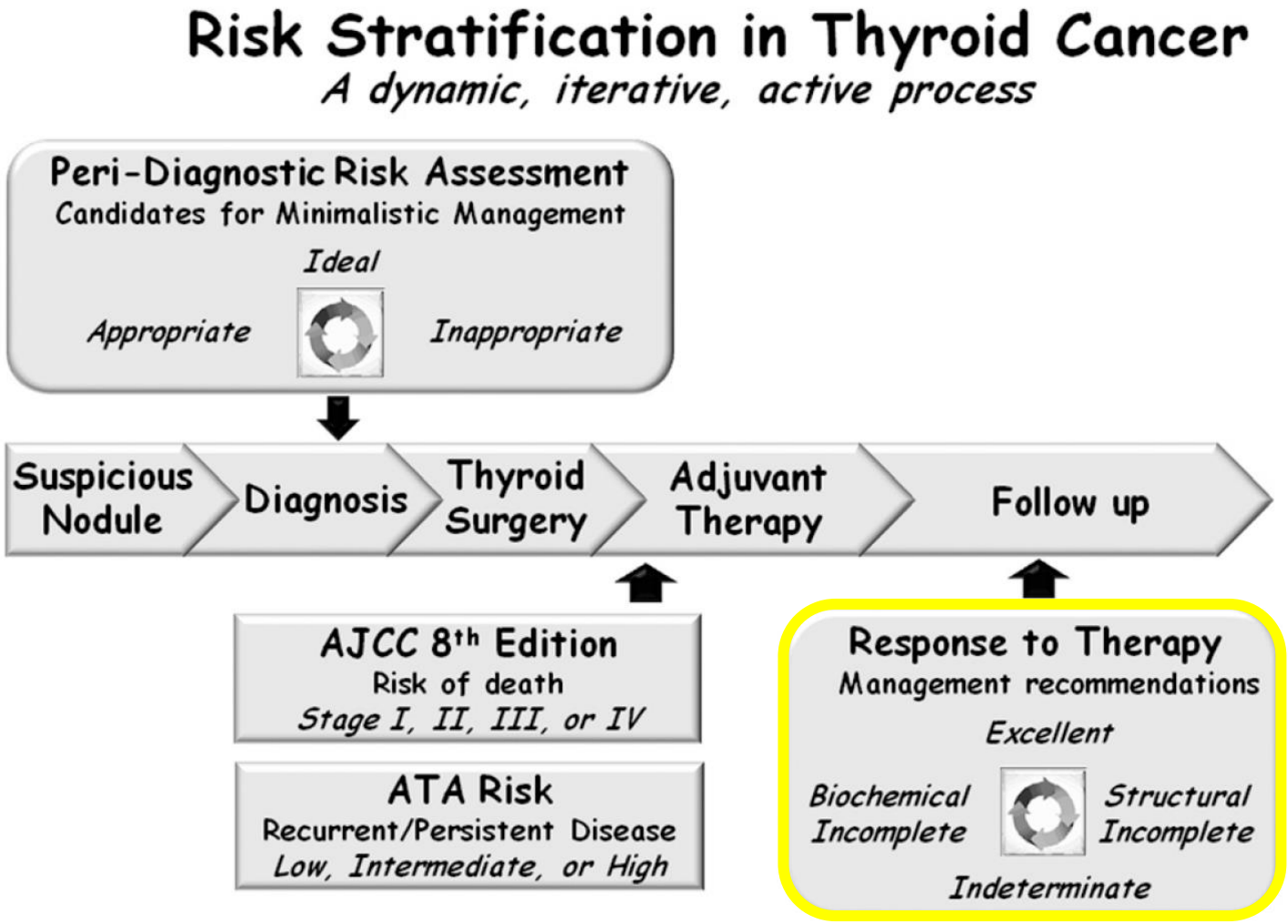
[1]Department of Medicine, Division of Endocrinology, Memorial Sloan-Kettering Cancer Center, New York, New York 10065

- Retrospective cohort study of 320 patients
- Median age 49.3 years
- Follicular cell-derived thyroid carcinoma classified at ATA high risk
- Followed for a median of 7 years

Table 2. Response to Therapy at Final Follow-Up Stratified by Age

	Age <55	Age ≥55	Total
Excellent	79 (40.3%)	34 (27.5%)	113 (35.3%)
Biochemical incomplete	10 (5%)	8 (6.5%)	18 (5.6%)
Indeterminate	43 (22%)	16 (13%)	59 (18.5%)
Structural incomplete	64 (32.7%)	66 (53%)	130 (40.6%)
Total	196	124	320

χ^2 $P = 0.002$.



Dynamic Risk Assessment

Results that modify risk

- Results of RAI scanning post-treatment
- Change in serum thyroglobulin (Tg) over time
- Change in serum Tg antibodies over time
- Physical exam or symptoms
- Findings on ultrasound at follow-up visits
- Stimulated Tg levels
- Other cross-sectional imaging findings
- FDG-PET imaging results

Response to Therapy Definitions

- No clinical, biochemical, or structural evidence of disease
- Persistent abnormal thyroglobulin values in the absence of localizable disease
- Persistent or newly identified loco-regional or distant metastases
- Non-specific biochemical or structural findings which cannot be confidently classified as either benign or malignant

HAUGEN, THYROID 2015. TUTTLE, THYROID 2010 .VAISMAN, CLIN ENDO 2012 . MOMESSO END MET NA 2014

Response to Therapy Definitions

Tg cut points based on initial therapy

	Total Thyroidectomy & RAI ablation	Total Thyroidectomy	Lobectomy
Excellent	Tg <0.2	Tg <0.2	Tg <30
Indeterminate	Tg 0.2-1.0	Tg 0.2-5.0	-
Biochemical Incomplete	Tg >1.0	Tg >5.0	Tg >30

Summary of studies analyzing dynamic risk assessment in patients with differentiated thyroid cancer treated with total thyroidectomy and radioiodine remnant ablation.

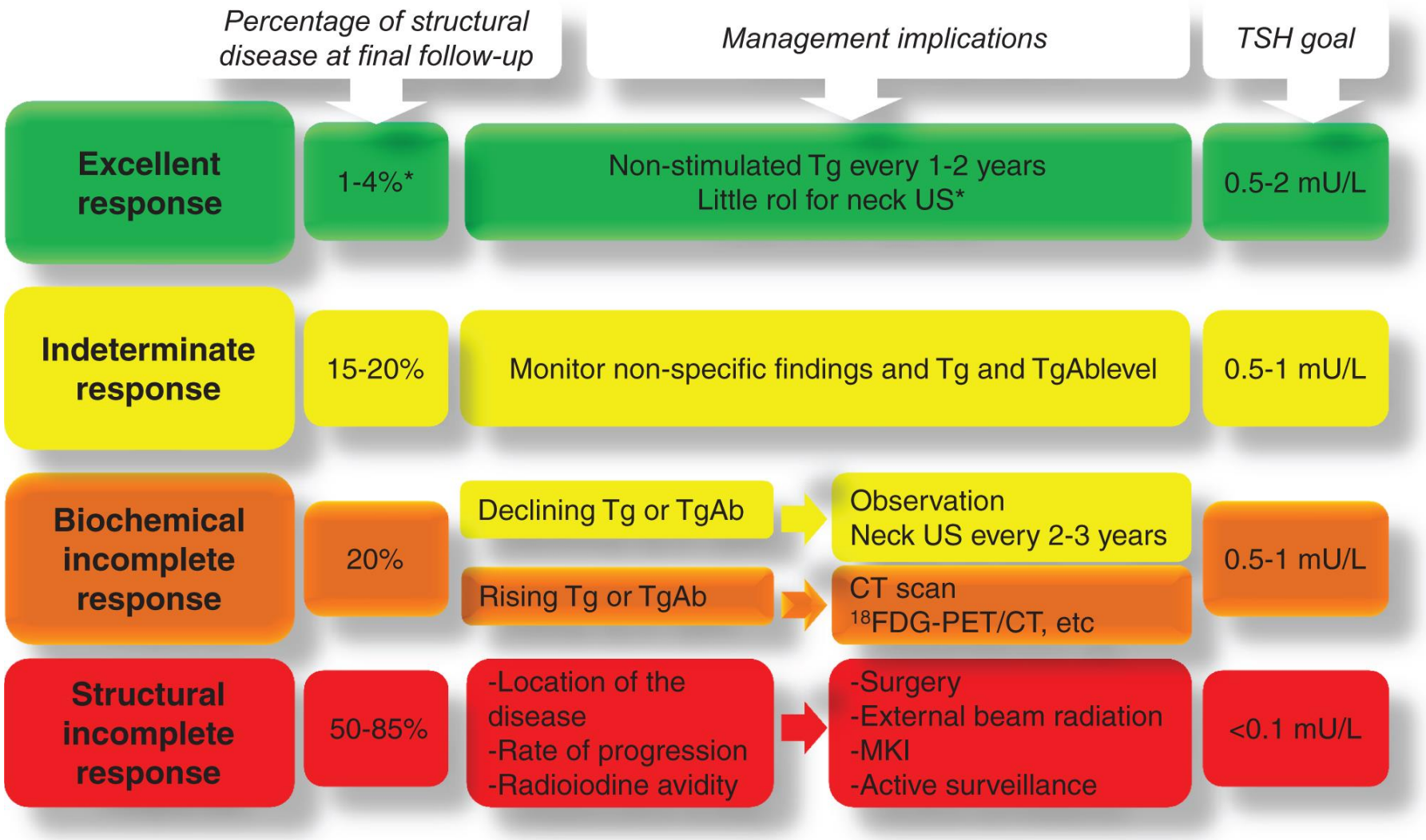
	No. of patients	Patients included	Median follow-up (months)	Persistent/recurrent disease based on each response-to-therapy category
Tuttle *et al.* 2010	588	All-risk patients	84	Exc 4% IR 0% BIR/SIR 57%
Castagna *et al.* 2011	512	All-risk patients	81.6	Exc 3.4% BIR/SIR 66%
Hong *et al.* 2014	398	All-risk patients	128	Exc 1.3% SIR 75.9%
Pitoia *et al.* 2015	149	Low- and intermediate-risk patients	72	Exc 1.6% BIR/SIR 31.8%
Kowalska *et al.* 2016	916	All-risk patients	84	Exc 1.2% IR/BIR/SIR 16.2%
Trimboli *et al.* 2017	201	Low- and intermediate-risk patients	29	onT4-Tg <0.28 ng/mL[a]: 0% onT4-Tg >0.28 ng/mL[a]: 52% Exc 0.5% IR 37.5% BIR 50% SIR 85.7%
Jeon *et al.* 2018	1359	Patients with excellent response	104.4	Exc 1%
Lee *et al.* 2018	667	PTC 1-4 cm	124	Exc 4.1 IR 17.6% BIR 53.4% SIR 81.5%
Schlumberger *et al.* 2018[b]	726	Low-risk patients	64.8	Exc 0.16% All initial responses 0.5%
Dehbi *et al.* 2019[b]	434	T1-T3 N0/N1/Nx M0 (TNM 6th ed.)	78.4	Exc 0%; all initial responses 4.8%
van Velsen *et al.* 2019	236	High-risk patients	72	Exc 14%
Tian *et al.* 2019	767	High-risk patients	67.2	Pre-ablation s-Tg <1 ng/mL and negative anti-Tg: 2.9%

Summary of studies analyzing dynamic risk assessment in differentiated thyroid cancer patients treated without radioiodine ablation

	No. of patients	Patients included	Median follow-up (months)	Persistent/recurrent disease based on each response-to-therapy category
Momesso *et al.* 2016	TT: 320 L: 187	Low risk: 433 Intermediate risk: 74	100.5	Exc 0% IR 1.3% BIR 31.6% SIR 100%
Park *et al.* 2017	TT: 64 L: 293	Low risk: 187 Intermediate risk: 170	103.2	Exc 0.78 IR1.5% BIR 16.7% SIR 100%
Abelleira *et al.* 2017	TT: 88	Low risk: 78 Intermediate risk: 10	28	Exc 0% IR 5.6%
Lee *et al.* 2018	TT: 26 L: 69	Low and intermediate risk	124	Exc 7.4% IR 0% BIR 0% SIR 100%
Cho *et al.* 2018	L: 619	Low risk: 340 Intermediate risk: 279	103	Exc 1.6% IR 3.8% BIR 2.9% SIR 100%

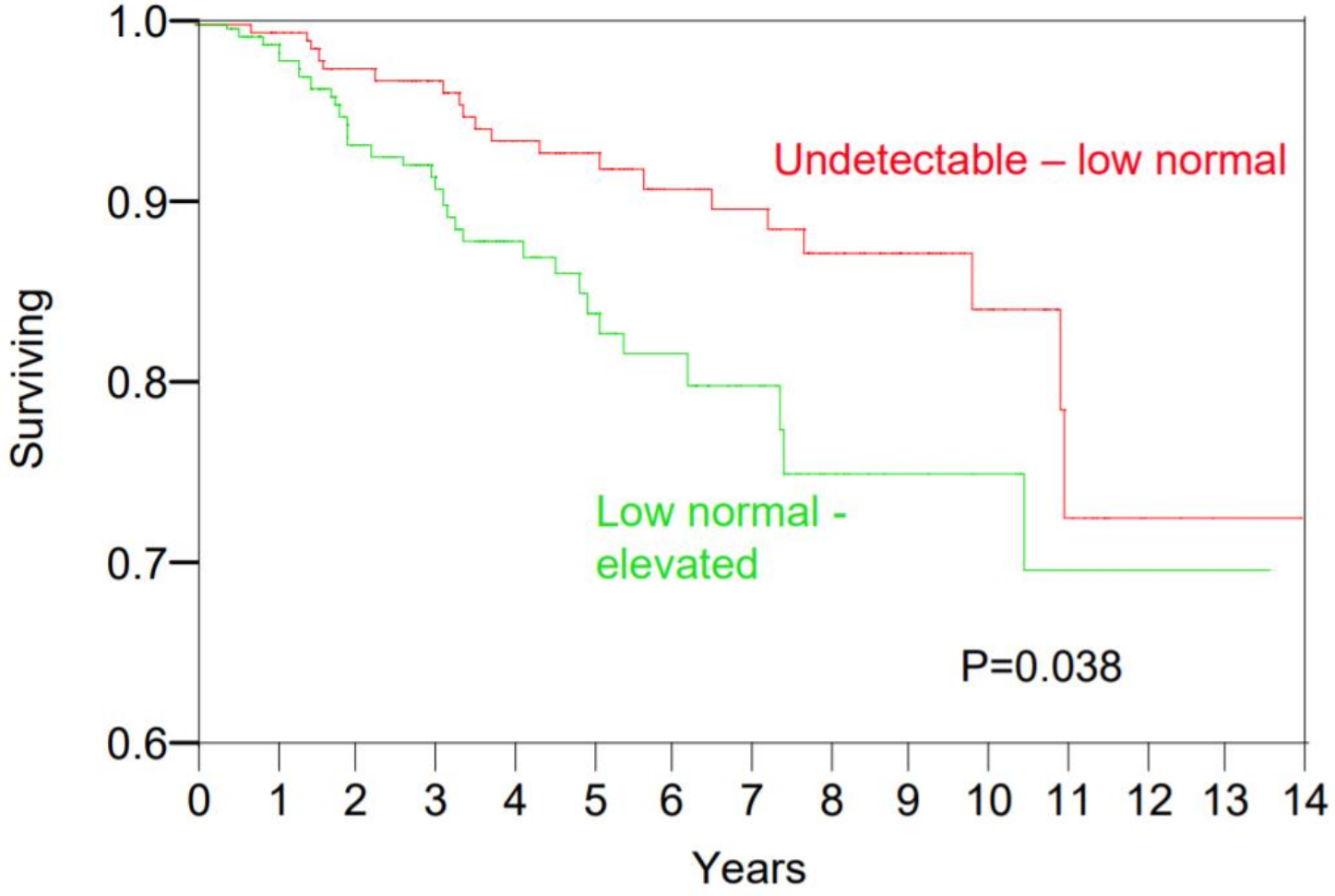
1. HEGEDUS, L. NEJM, 2004.

Risk of structural disease at the end of follow-up and management recommendations for each response-to-therapy category



F PITOIA AND F JERKOVICH. ENDOCRINE-RELATED CANCER. (2019) 26, R553–R566

Overall survival improved with TSH suppression – Stages III & IV DTC



Prospective, multi-institutional registry

Outcome measures – overall survival, DSS and DFS

TH suppression therapy (TSH <0.1) improved survival in high risk (Stage III and IV)

Moderate TH suppression therapy (TSH 0.1-0.5) improved survival in Stage II
No benefit with TSH <0.03

No benefit in Stage I

JONKLAAS J. THYROID. 2006 DEC;16(12):1229-42.

VOLUME 31 · NUMBER 32 · NOVEMBER 10 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Long-Term Cardiovascular Mortality in Patients With Differentiated Thyroid Carcinoma: An Observational Study

Esther N. Klein Hesselink, Mariëlle S. Klein Hesselink, Geertruida H. de Bock, Ron T. Gansevoort, Stephan J.L. Bakker, Eline J. Vredeveld, Anouk N.A. van der Horst-Schrivers, Iwan C.C. van der Horst, Pieter W. Kamphuisen, John T.M. Plukker, Thera P. Links, and Joop D. Lefrandt

Retrospective Study of 2 cohorts
524 patients with DTC
1,572 sex- and age-matched controls
Mean age 49 years
Median follow-up was 8.5 years

Primary aim – CV mortality
Secondary aim – Relation between TSH level and CV mortality/All-cause mortality

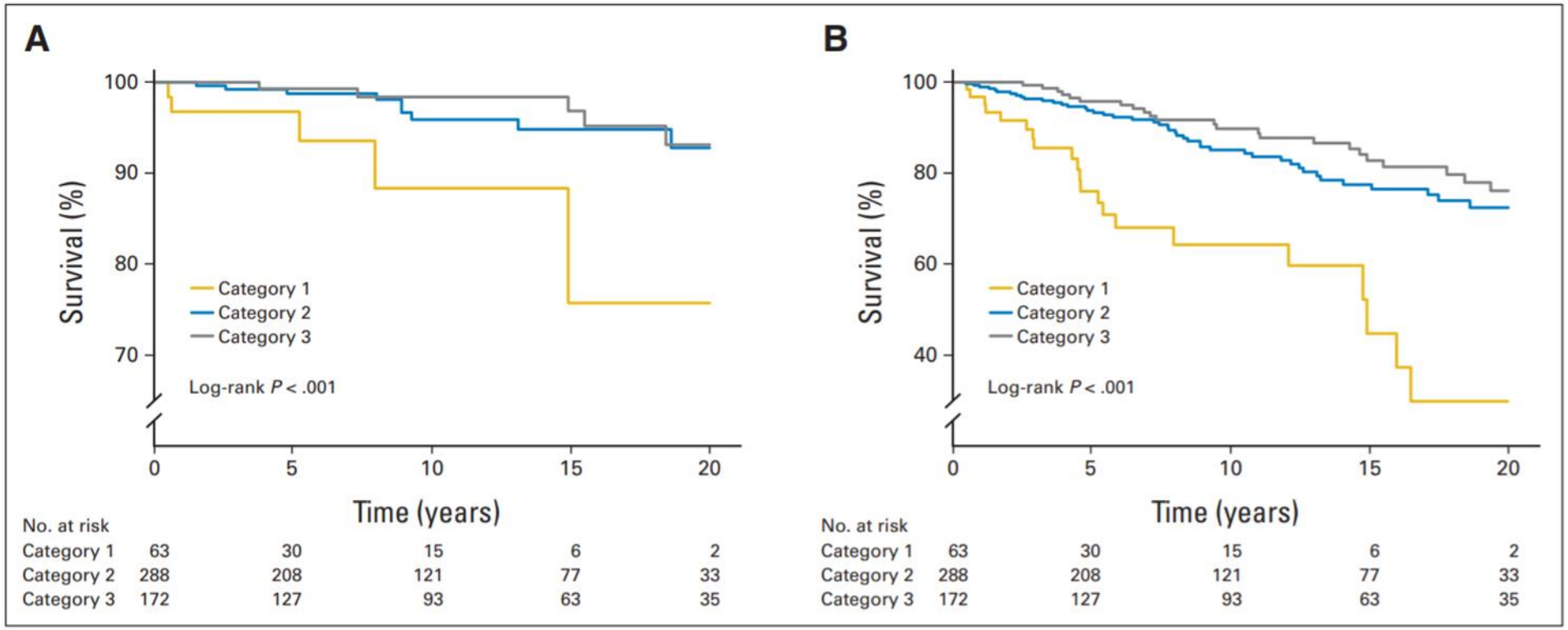


Fig 3. Kaplan-Meier survival curves for (A) cardiovascular mortality and (B) all-cause mortality for patients with differentiated thyroid carcinoma, by thyroid-stimulating hormone (TSH; also known as thyrotropin) category. TSH category 1, geometric mean TSH < 0.02 mU/L; category 2, geometric mean TSH 0.02 to 0.2 mU/L; and category 3, geometric mean TSH > 0.2 mU/L.

EnM
ENDOCRINOLOGY AND METABOLISM

Original Article

Endocrinol Metab 2019;34:150-157
https://doi.org/10.3803/EnM.2019.34.2.150
pISSN 2093-596X · eISSN 2093-5978

Postoperative Thyroid-Stimulating Hormone Levels Did Not Affect Recurrence after Thyroid Lobectomy in Patients with Papillary Thyroid Cancer

Myung-Chul Lee[1], Min Joo Kim[2,3], Hoon Sung Choi[4], Sun Wook Cho[2], Guk Haeng Lee[1], Young Joo Park[2], Do Joon Park[2]

ATA Guidelines 2015 Recommendation 59

(Weak recommendation, Low-quality evidence)

(E) For low-risk patients who have undergone lobectomy, TSH may be maintained in the mid to lower reference range (0.5–2 mU/L) while surveillance for recurrence is continued. Thyroid hormone therapy may not be needed if patients can maintain their serum TSH in this target range.

(Weak recommendation, Low-quality evidence)

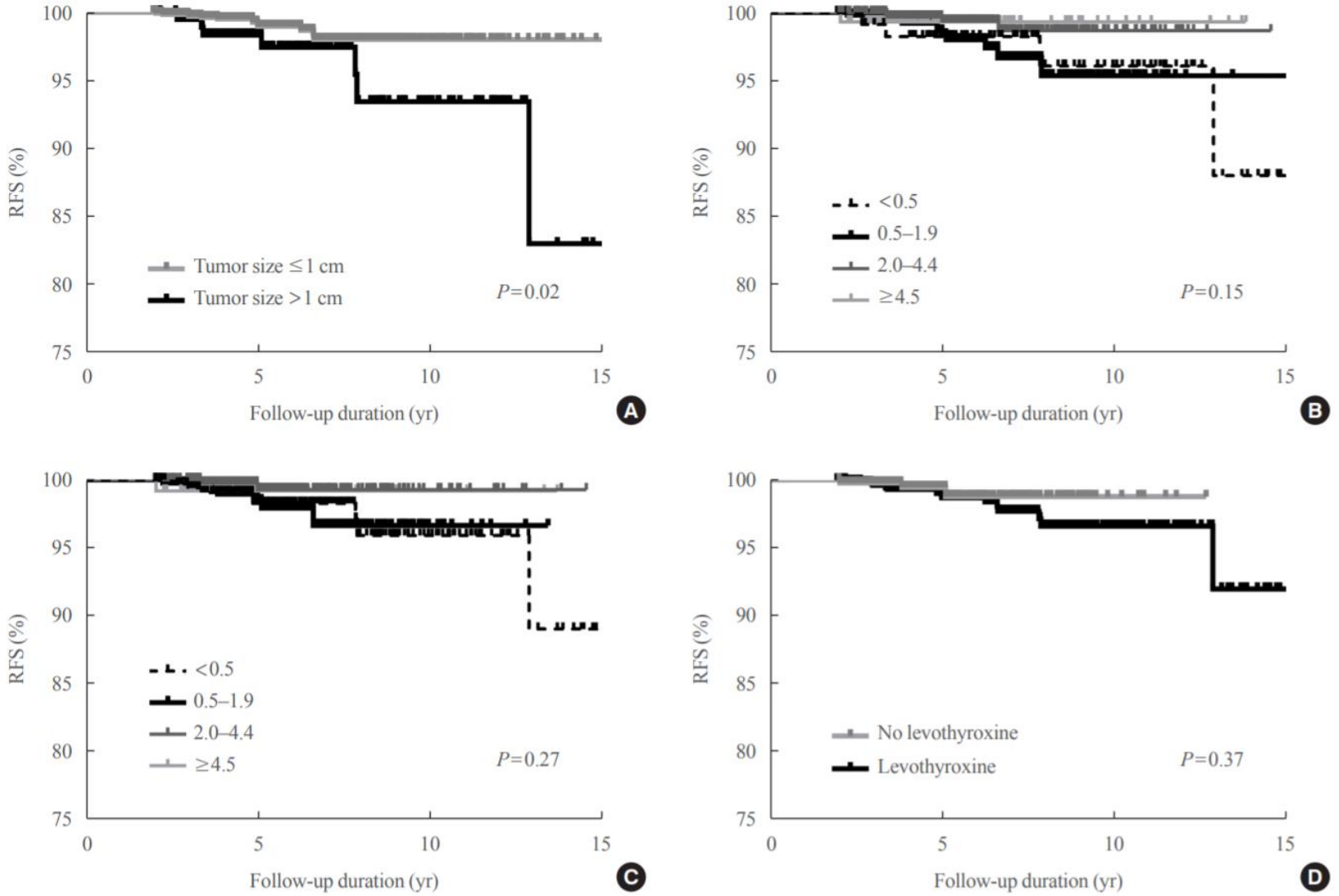
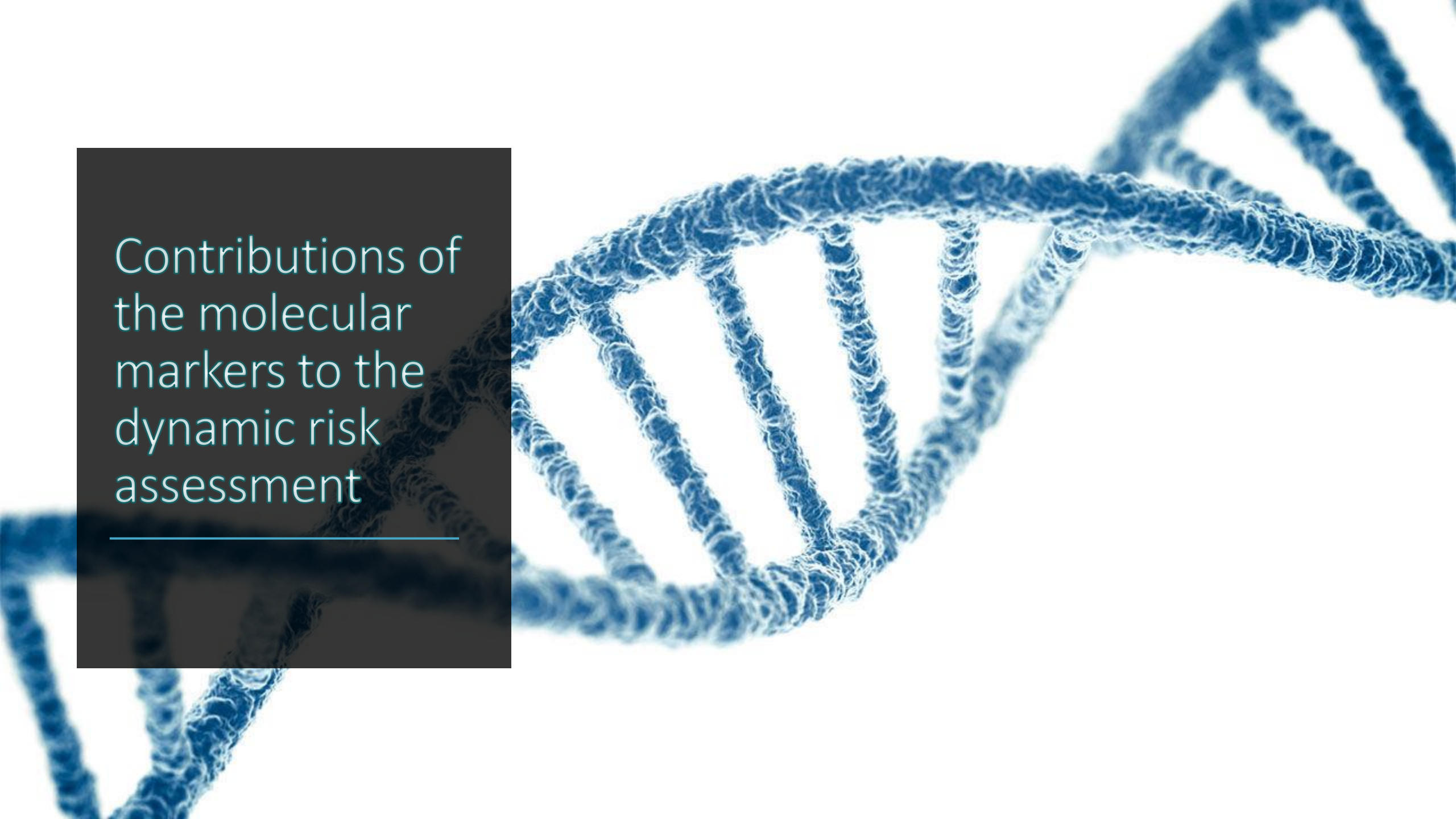
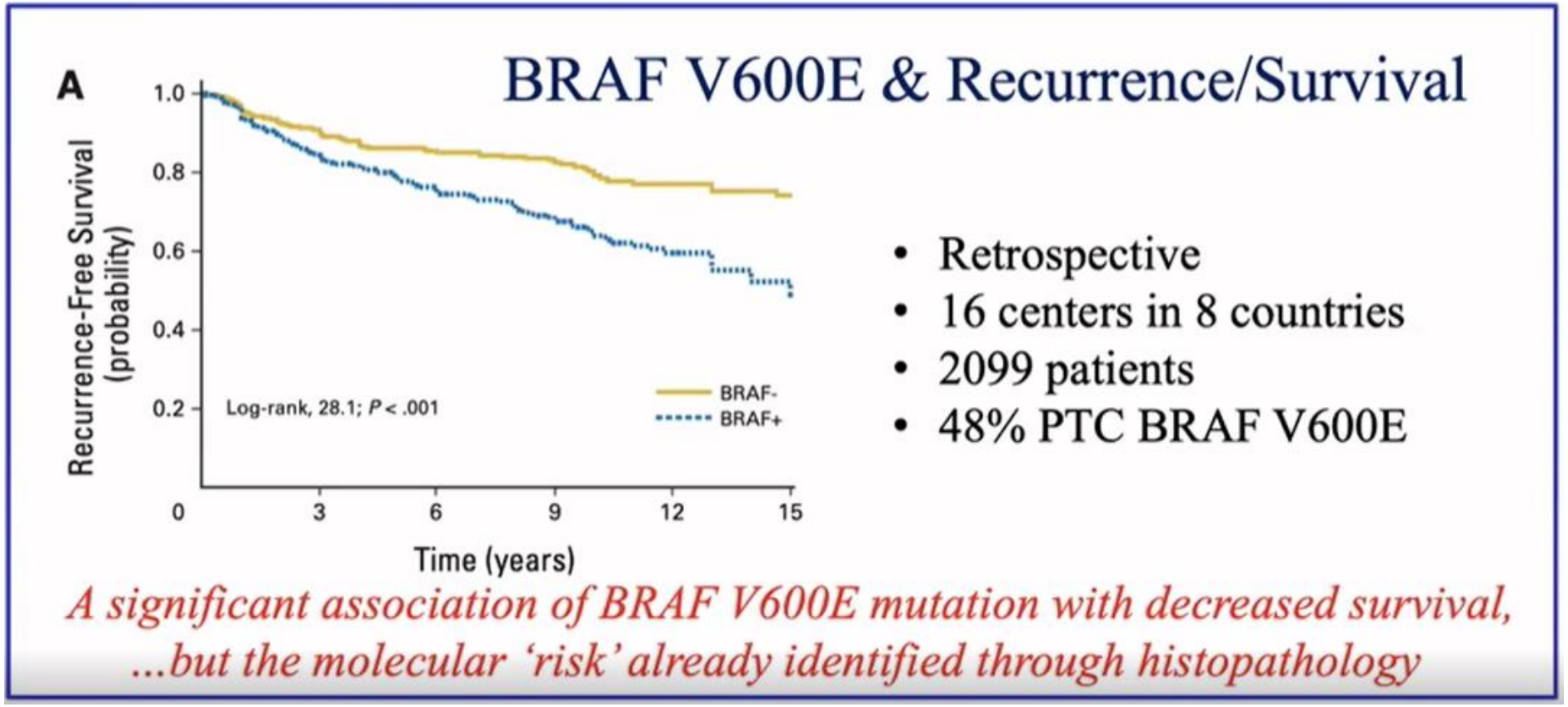


Fig. 1. Kaplan-Meier curves of recurrence-free survival (RFS). (A) Tumor size. (B) Mean thyroid-stimulating hormone levels for 5 years after surgery (TSH_{5yrs}) values. (C) Dominant TSH_{5yrs} values. (D) Levothyroxine use.

Contributions of the molecular markers to the dynamic risk assessment



What about BRAF?



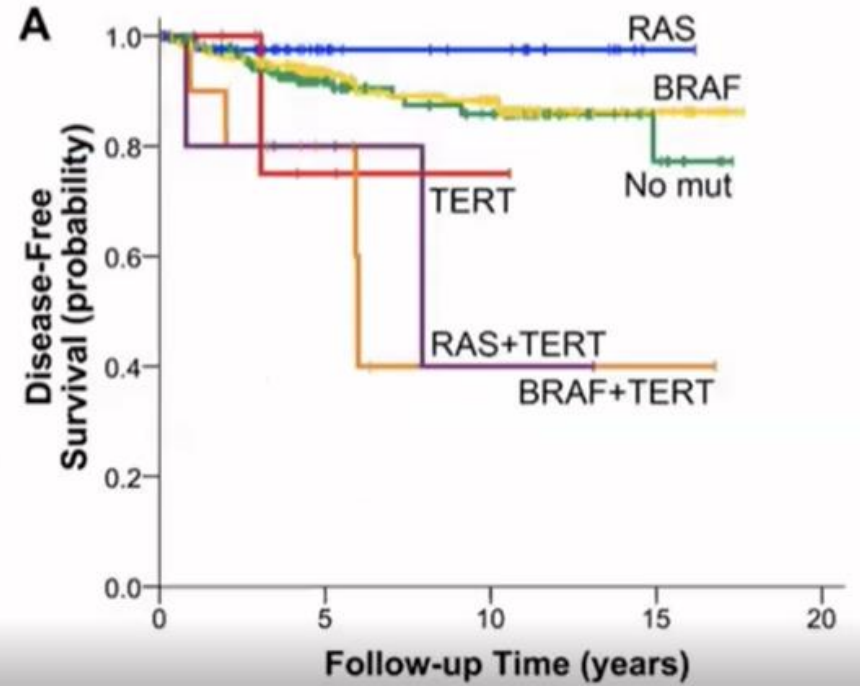
XING ET AL. JCO. 2014

Identifying multiple genomic alterations more powerful than one

…but mostly for very advanced cancer

BRAF, *TERT* & *RAS* - Recurrence Free Survival

Incremental & synergistic effects of the coexisting *three* mutations.



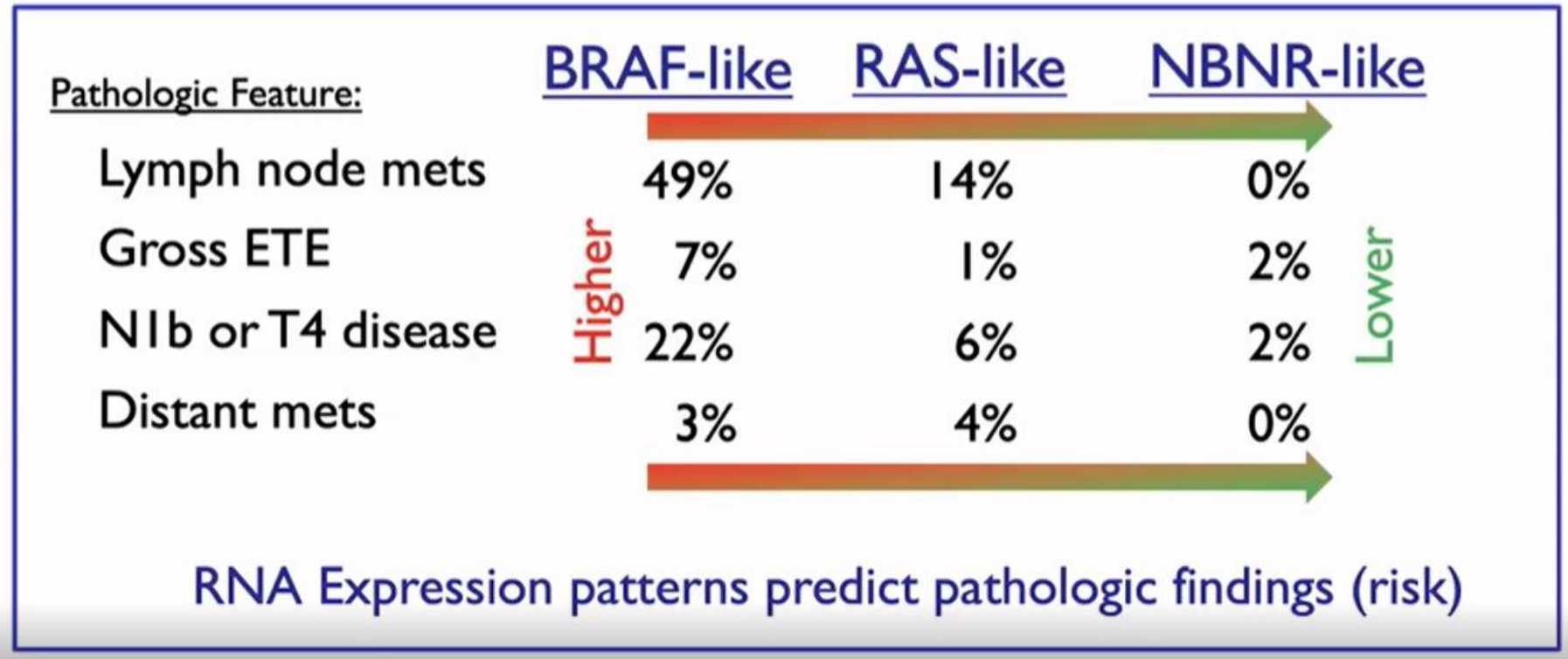
SONG ET AL. CANCER. 2015

Three Prognostic Categories

Braf-like vs. Ras-like vs. NBNR

Tang et al:

- RNA expression / Histopathologic correlation from two databases (TCGA)
- Analysis of 571 (from 676) thyroid cancer cases into BRAF-like, RAS-like, Non-BRAF/Non-RAS-like. *(?about 15% into another category)*



Three Prognostic Categories

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Association of specific genomic alterations with RNA expression classes:

BRAF V600-like	BRAF V600-like/RAS-like overlap	RAS-like	Non-BRAF-Non-RAS
BRAF V600E *BRAF* fusions *RET* fusions	*NTRK1-3* fusions *ALK* fusions *FGFR2* fusions	*H/K/NRAS* *BRAF* K601E *TSHR*	*DICER1* *EIF1AX* *EZH1* *SOS1* *PAX8/GLIS3* fusion *PAX8/PPARG* fusion *PTEN* *SPOP* *THADA* fusions

Higher → Lower

RNA Expression groupings (more so than DNA mutations) inform us which genomic findings are independently predictive

Risk Stratification in Thyroid Cancer

A dynamic, iterative, active process