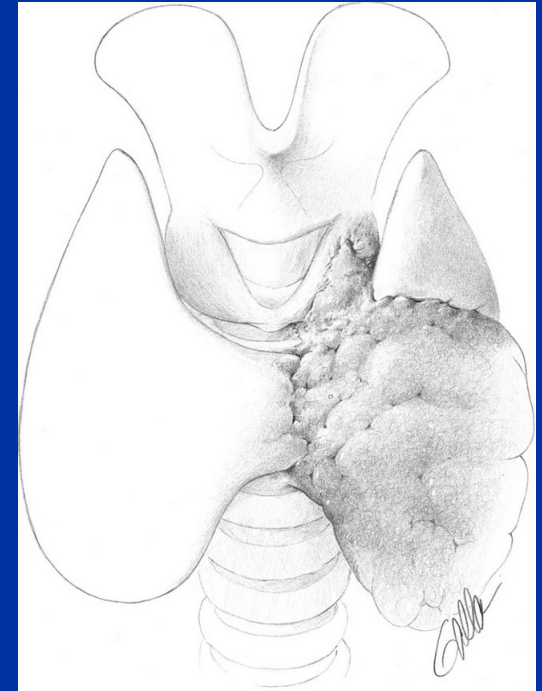


Thyroid Malignancy: Staging and Treatment

Presented for the
**Kentucky Cancer Registry's 36th
Annual Advanced Cancer Registrar's
Workshop**



Drawing Randolph's Surgery of the
Thyroid and Parathyroid Glands

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Only One Disclosure.

They pay me to do the greatest job in the world, ENT-Head and Neck Surgeon!





Objectives of the Talk

- Understand the pathologic and prognostic differences in the three large groupings of thyroid cancer: *Well Differentiated Thyroid Cancer, Medullary Thyroid Cancer and Anaplastic Thyroid Cancer*
- Understand basic principles of management of the three major thyroid cancer: initial work-up, therapy and follow-up evaluations.
- Understand the fundamentals of AJCC clinical staging of thyroid cancer
- Thyroid lymphoma (not discussed today)



Thyroid cancer: US epidemiology

- 3% of all cancers
 - 43,800 new US cases
 - Male 11,860. Female 31,940
 - 2,230 Deaths: Men 1,070, Women 1,160
 - Younger age of diagnosis 49 women, 54 men
 - Frequency of types
 - Differentiated Thyroid Cancer:
 - Papillary thyroid cancer 80-94%
 - Follicular thyroid cancer 9-15%.
 - Medullary thyroid cancer 1-2%
 - Anaplastic thyroid cancer 1-3%
- North American Association of central cancer registries, 2021
- National Center for Health Statistics, CDCP 2021



Risk Factors

- Family History
- Radiation exposure
 - Especially under 5
 - Low dose exposure
 - Chernobyl, Nuclear test sites
- Iodine deficiency
- Obesity
- Estrogen
- Dietary nitrites
- Autoimmune thyroiditis



Pathology of Thyroid Cancer

- Three major types: Well differentiated, Medullary & Anaplastic
 - (Thyroid lymphoma not covered: coded as lymphoma)
- WDTC:
 - Well differentiated has important subtypes
- Can be discovered outside of the thyroid
 - Incidentally discovered in cervical nodes
 - Thyroglossal duct cysts
 - Mediastinal disease separate from thyroid
 - Malignant Struma Ovarii



Well Differentiated Thyroid Cancer: Pathology

- Papillary Carcinoma
 - More nodal metastases.
 - Subtypes
 - Micro PTC majority
 - Tall cell PTC, Insular variant
 - Poorly differentiated PTC
- NIFTP (NonInvasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features)
 - Survival excellent used to be PTC
- Follicular cell carcinoma
 - Most micro invasive
 - Distant metastases
- Hurthle Cell Carcinoma
 - more aggressive? More regional mets, less Iodine symporter



WHO Classification of Tumors

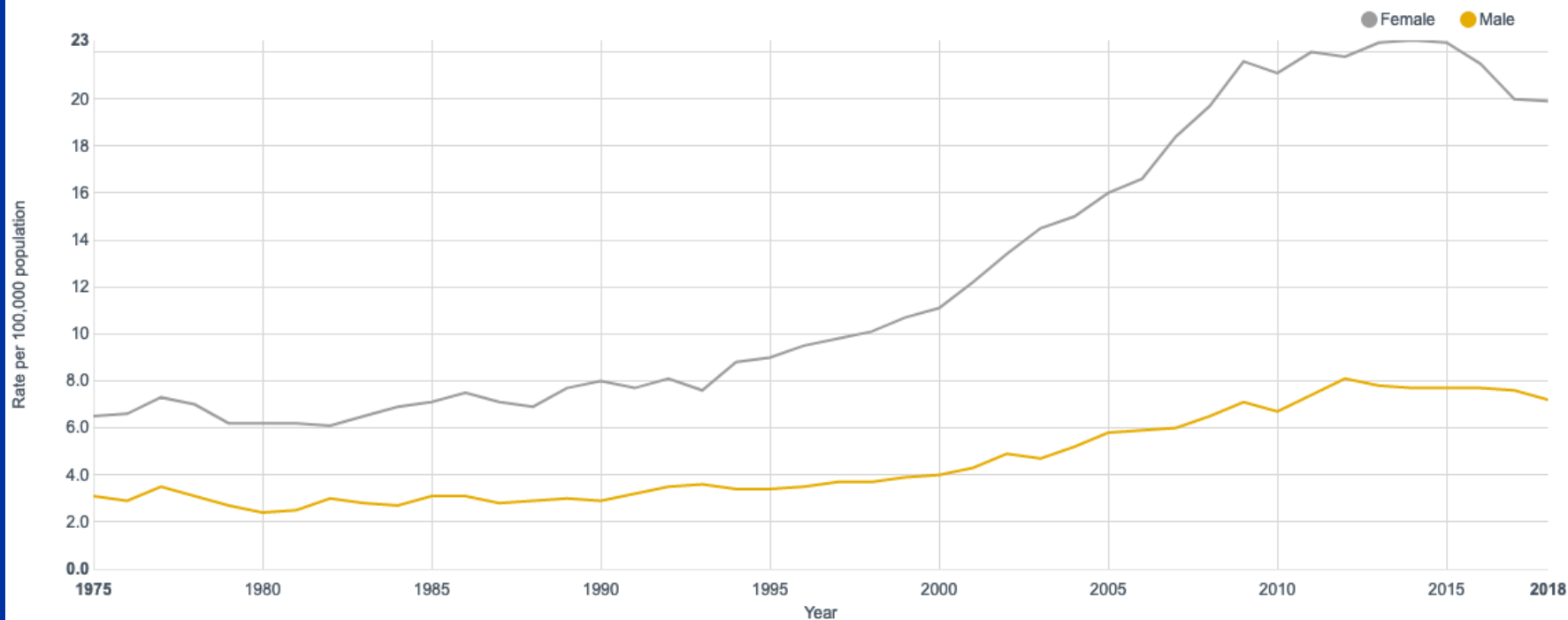
Code	Description
8050	Papillary carcinoma
8341	Papillary microcarcinoma
8340	Follicular variant
8230	Solid variant
8290	Hurthle cell variant
8330	Follicular carcinoma
8331	Encapsulated noninvasive
8335	Minimally invasive
8350	Widely invasive
8290	Hurthle cell carcinoma
8337	Poorly differentiated carcinoma (used for insular carcinoma as a subtype of poorly differentiated)
8021	Anaplastic carcinoma



Incidence trends in thyroid cancer

Trends in incidence rates, 1975-2018

Thyroid, by sex



Per 100,000, age adjusted to the 2000 US standard population.

Data sources: Surveillance, Epidemiology, and End Results (SEER) 9 registries, National Cancer Institute, 2021

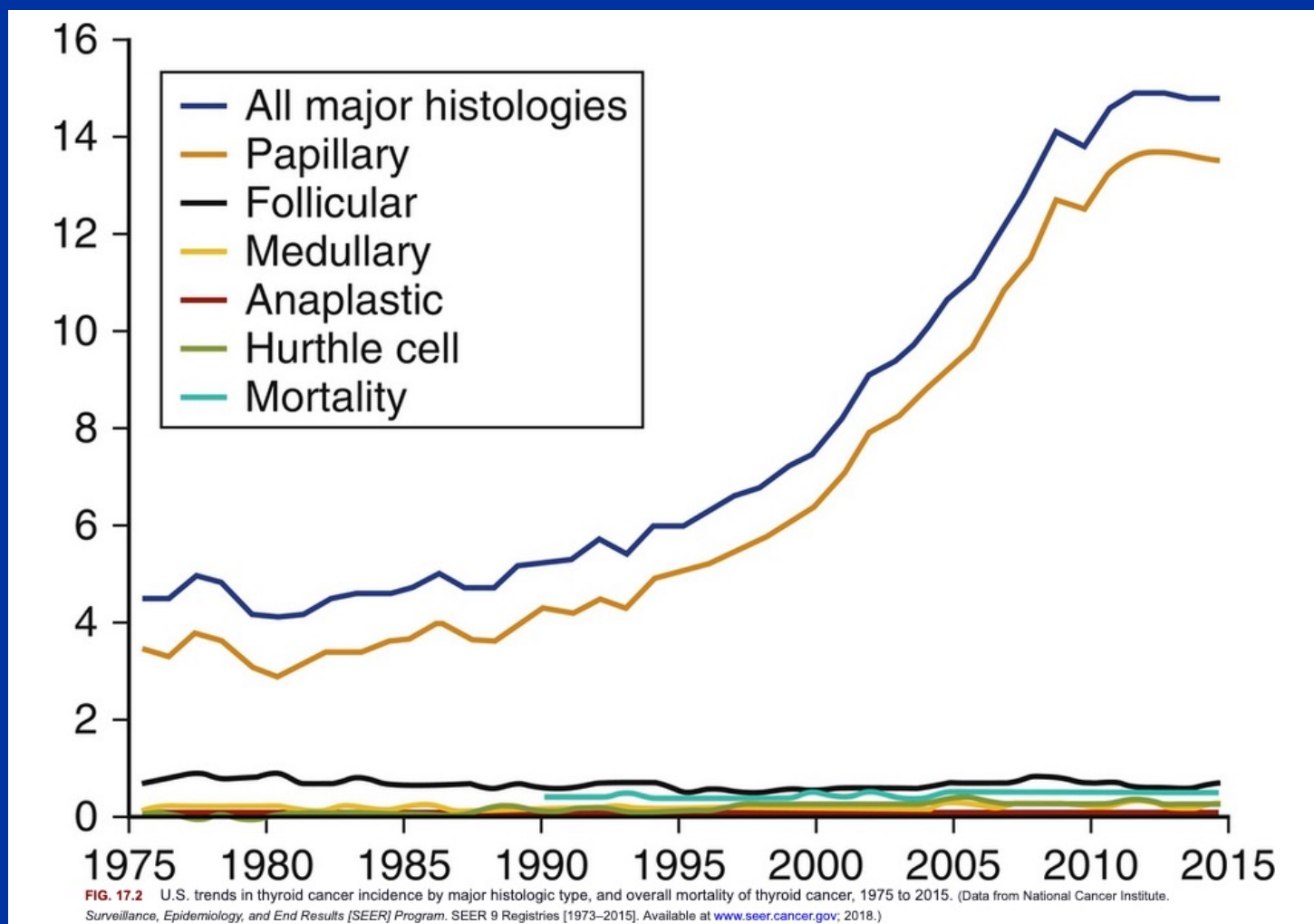


Early Diagnosis: Not always better!

- 4-15 fold increase in diagnosis over past 30 years depending upon the country
- Worse in Asia
- Almost entirely Papillary thyroid cancer
 - South Korea '99-08 PTC 87% to 97% of cases
- Average tumor diameter is decreasing
 - South Korea '99-08 18mm to 8 mm
- 70-90% of women Dx with asx Cancer
- Are we overtreating?

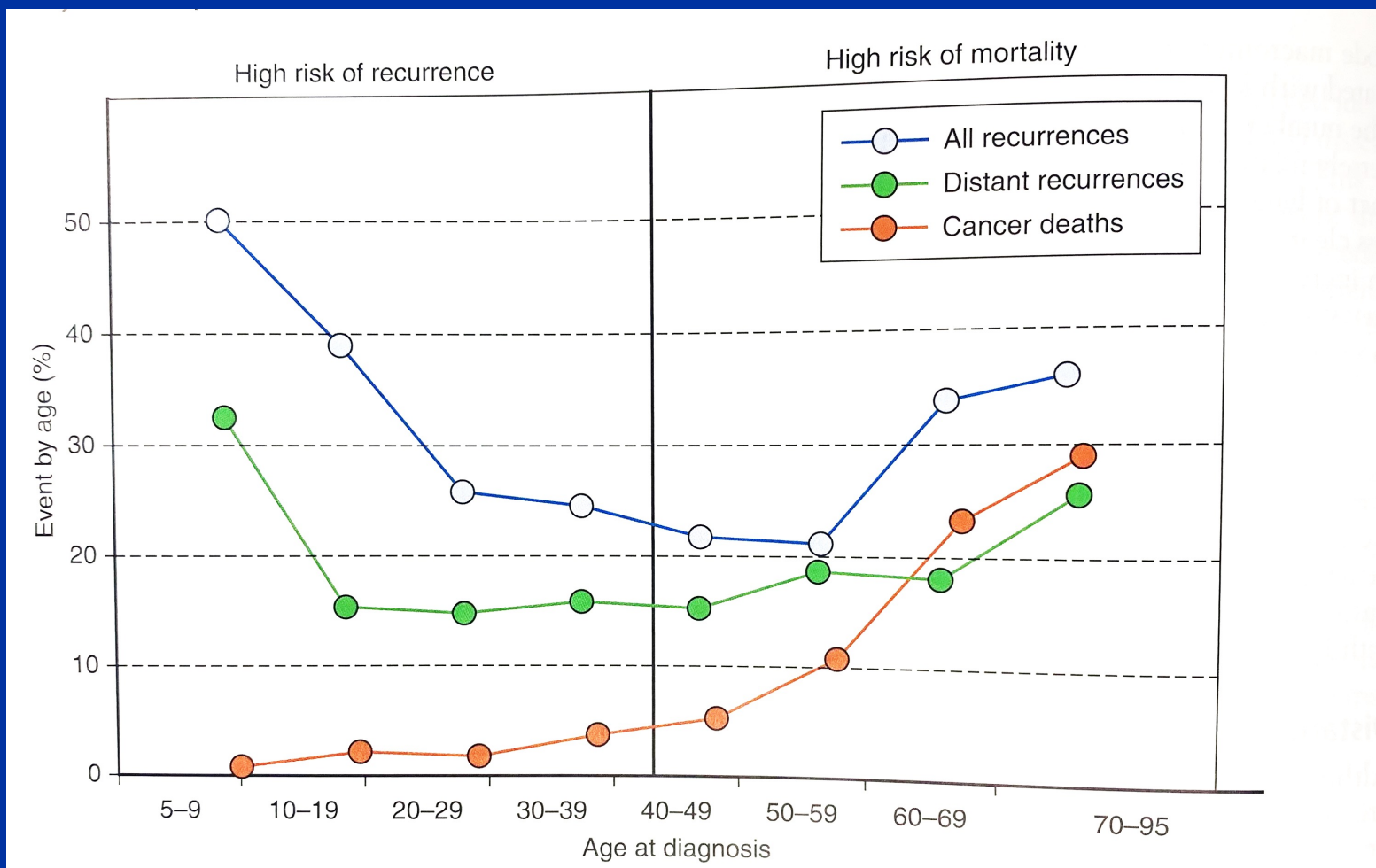


Incidence rates by cancer type





Morbidity of DTC by Age

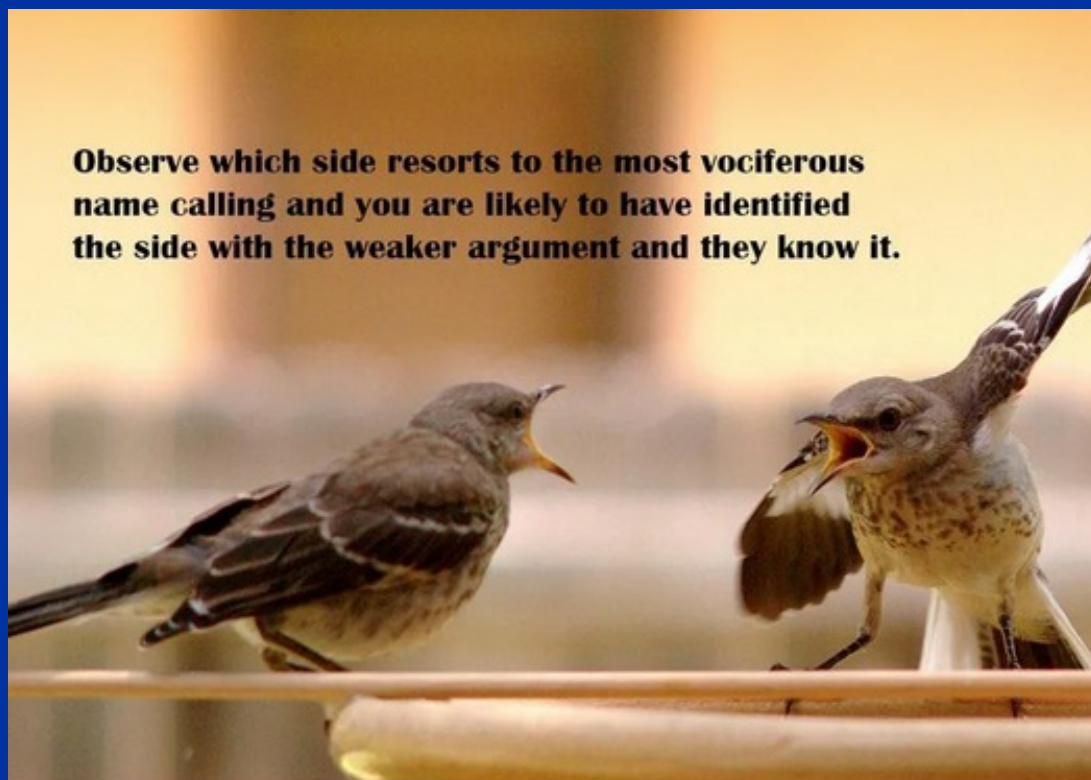


Mazzaferri, EL, Jhiang, SM. Am J Med 97:4189 1994



Treatment of DTC: Piles of Controversy

- DTC does well and we may be overtreating
- Treatment options evolving
 - Observation
 - Ablation
 - Surgery
 - Radioactive iodine
 - External Beam Radiotherapy
- Follow up
 - Maintain mild suppression of TSH
 - Thyroglobulin
 - Ultrasound
 - I131 scanning
 - If Rising TG neg I131: FGD CT-PET





Medullary Thyroid Cancer

- C-cells
- Secretes Calcitonin, CEA
- Two subtypes
 - Hereditary forms 25%
 - MEN 2a and 2b, Familial MTC
 - RET proto Oncogene 10q11
 - Point mutations exon location correlate with outcome
 - Sporadic Form 75% More aggressive
 - Up to 10% with mutation
 - Screen family members if hereditary!



Medullary treatment and follow-up

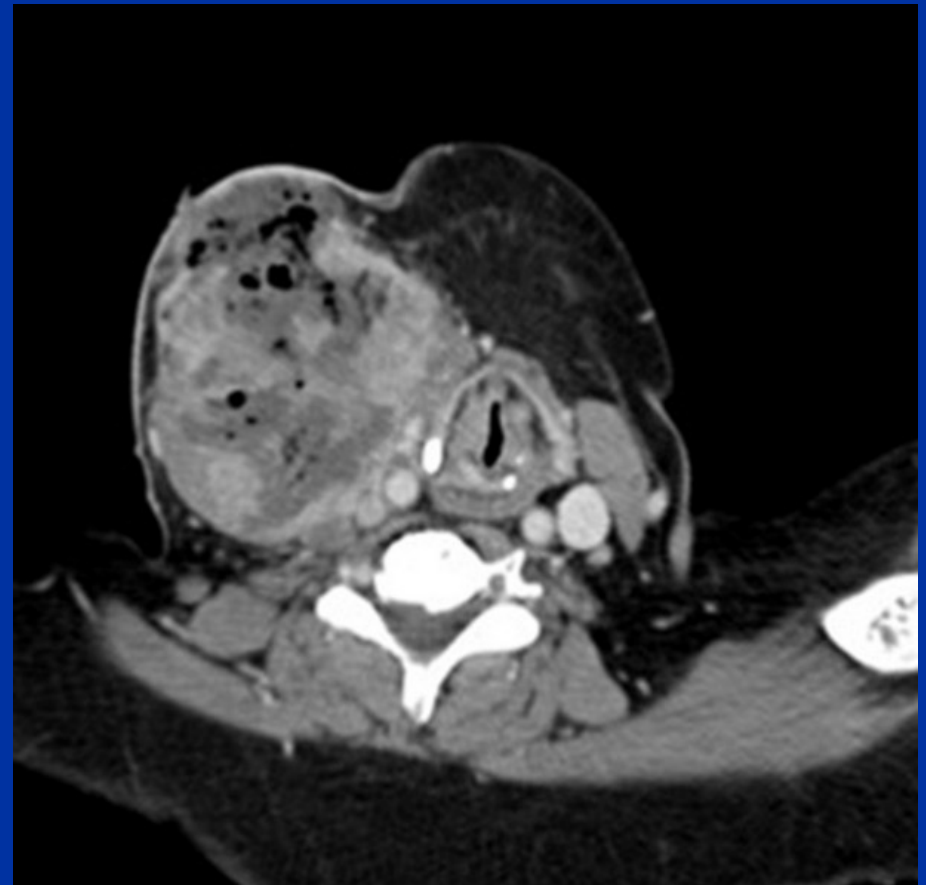
- Treatment
 - Surgery: Aggressive
 - EBRT: Radiation therapy
 - Targeted therapy (Tyrosine Kinase inhibitors)
- Slow moving
 - 70-90% 10 year survival
 - Many with distant mets live for many years
- Follow with Calcitonin, CEA
 - If elevated CT neck, chest. Abd
 - CT PET vs Dotatate PET





Anaplastic thyroid Cancer

- Frequently from DTC, Squamous differentiation common
- Difficult to diagnose on FNA
- Presentation Rapidly enlarging neck mass
- Most aggressive frequently unresectable at presentation
- Regional and distant disease the rule
- 1 year Survival > 10% (that is much improved)
- Presents like thyroid lymphoma



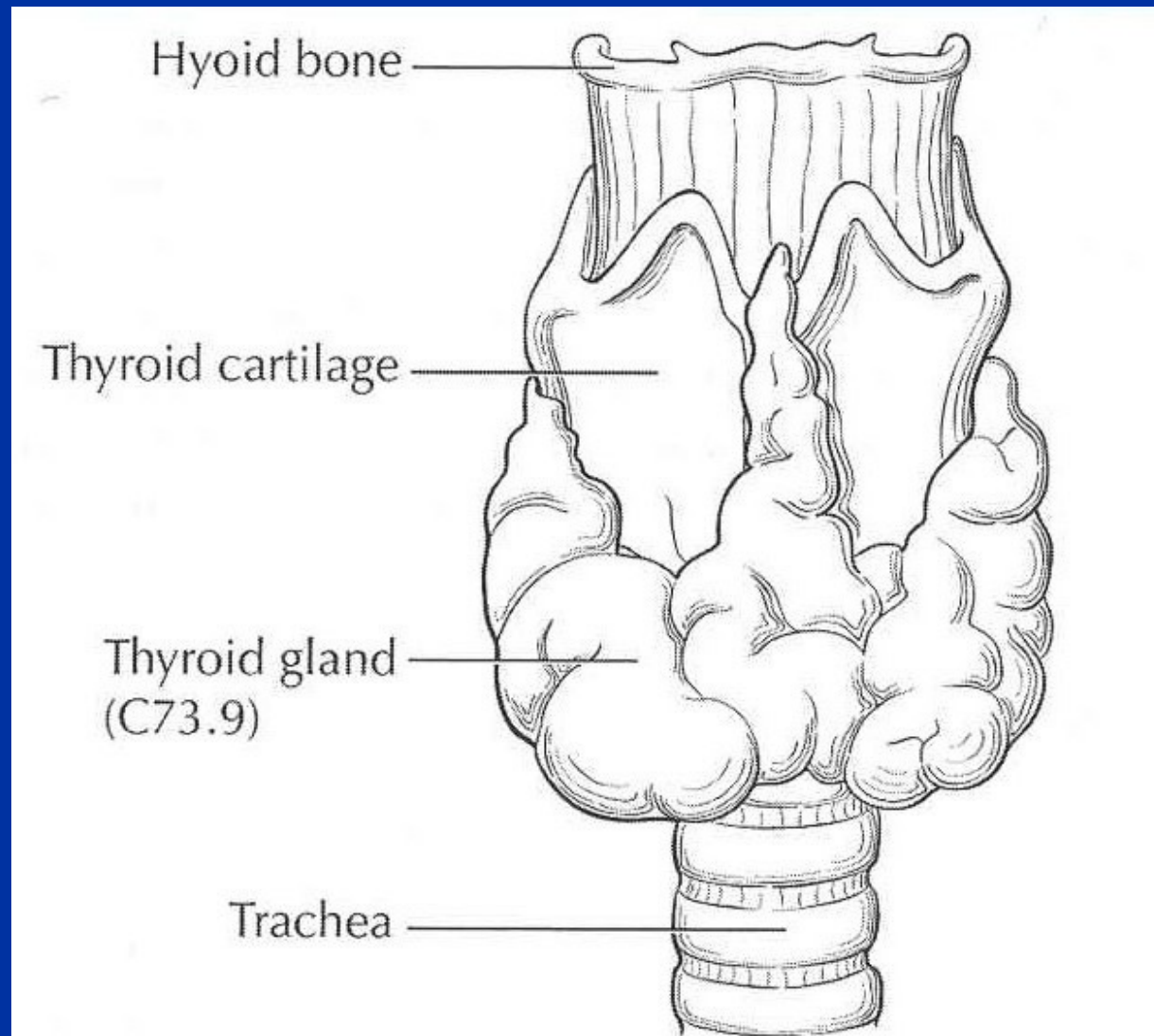


Anaplastic Treatment and Followup

- Aggressive early therapy to central compartment disease
- Surgery best hope of cure if R1 resection possible
- XRT with taxane
- CARIS or Foundation 1 mandatory
 - New targeted therapy offers some hope
 - Debrafenib/trametinib if BRAFV600E mutated

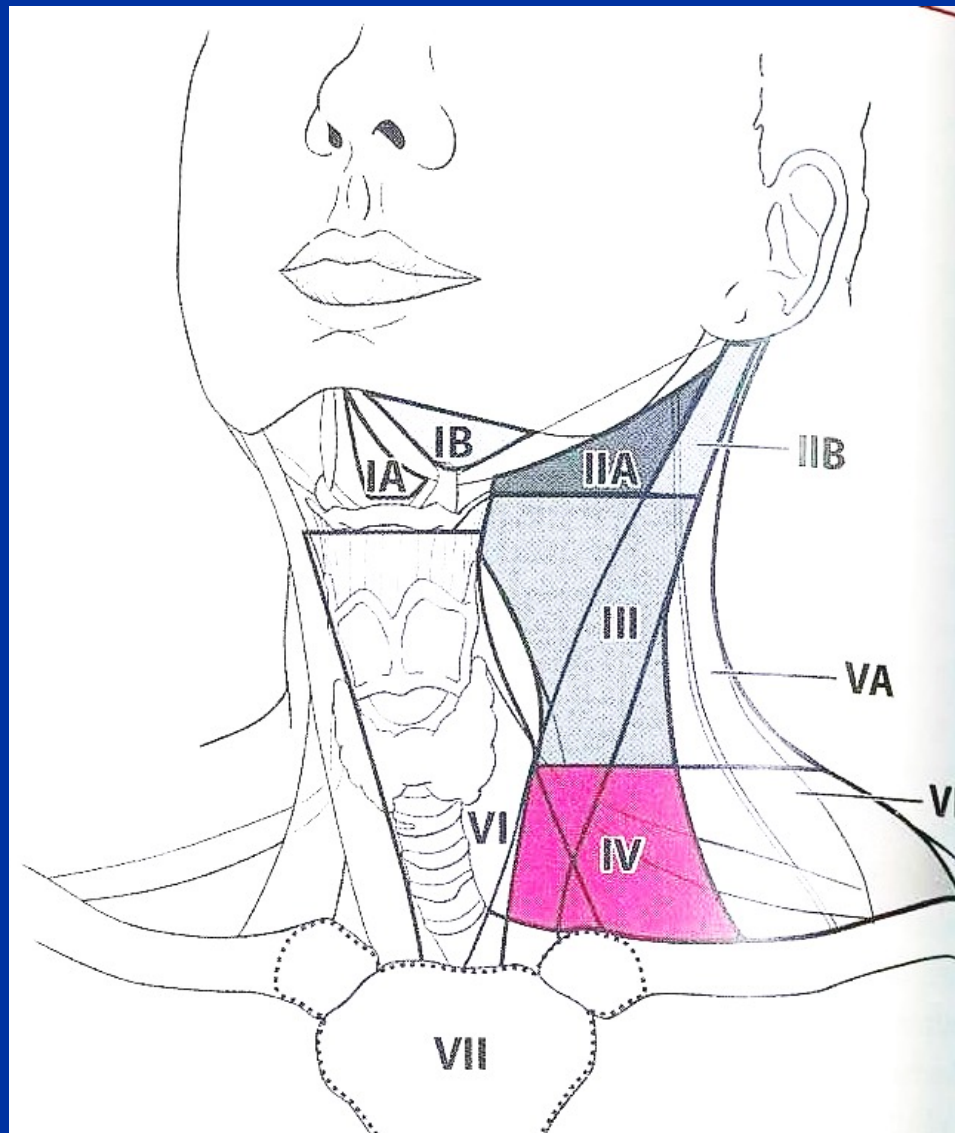


Thyroid Anatomy





Location of Lymph Nodes





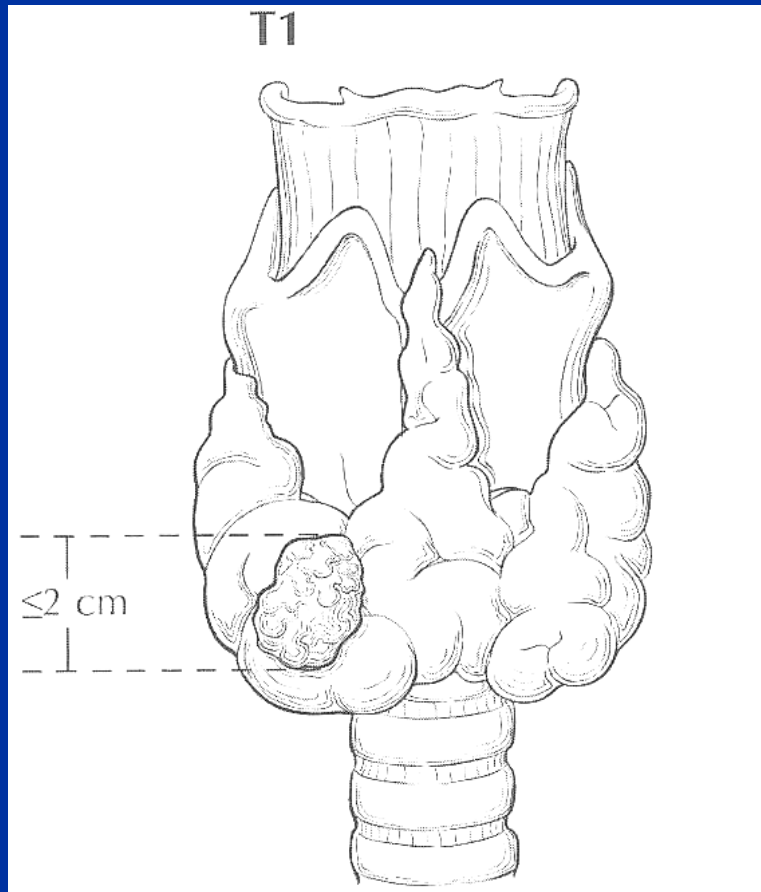
Nodal Staging

Definition of Regional Lymph Node (N)

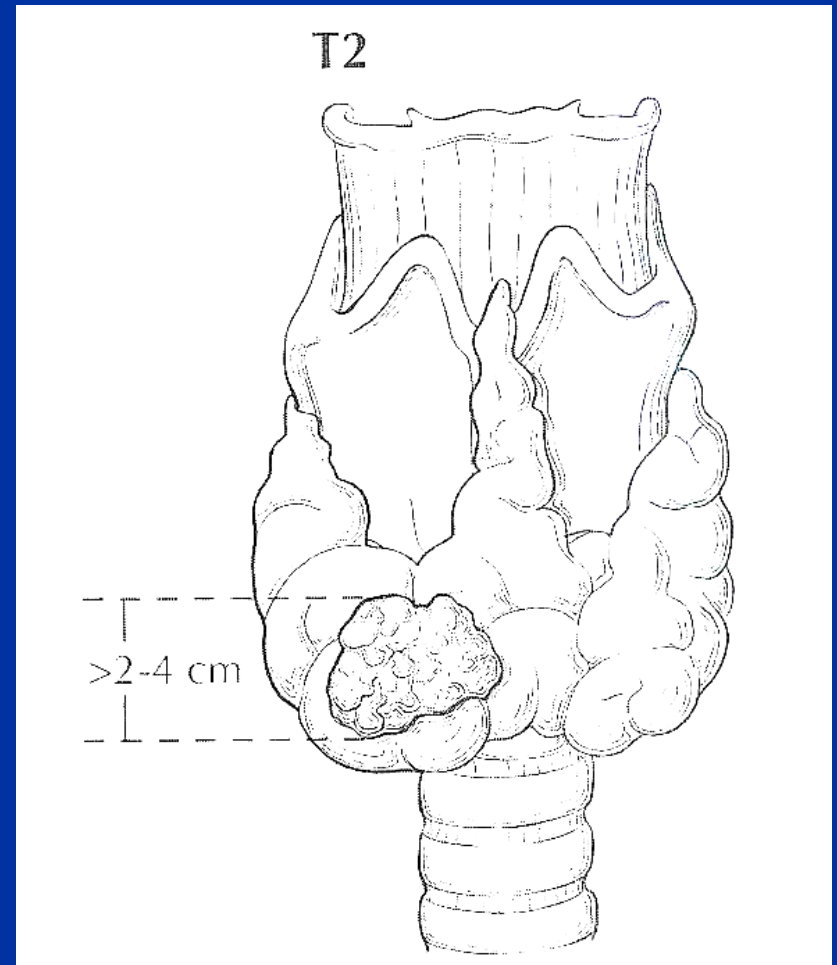
N Category	N Criteria
NX	Regional lymph nodes cannot be assessed
N0	No evidence of locoregional lymph node metastasis
N0a	One or more cytologically or histologically confirmed benign lymph nodes
N0b	No radiologic or clinical evidence of locoregional lymph node metastasis
N1	Metastasis to regional nodes
N1a	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian, or upper mediastinal) lymph nodes. This can be unilateral or bilateral disease.
N1b	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (levels I, II, III, IV, or V) or retropharyngeal lymph nodes



Early T stage



T1a < 1cm T1b 1-2 cm within Thyroid



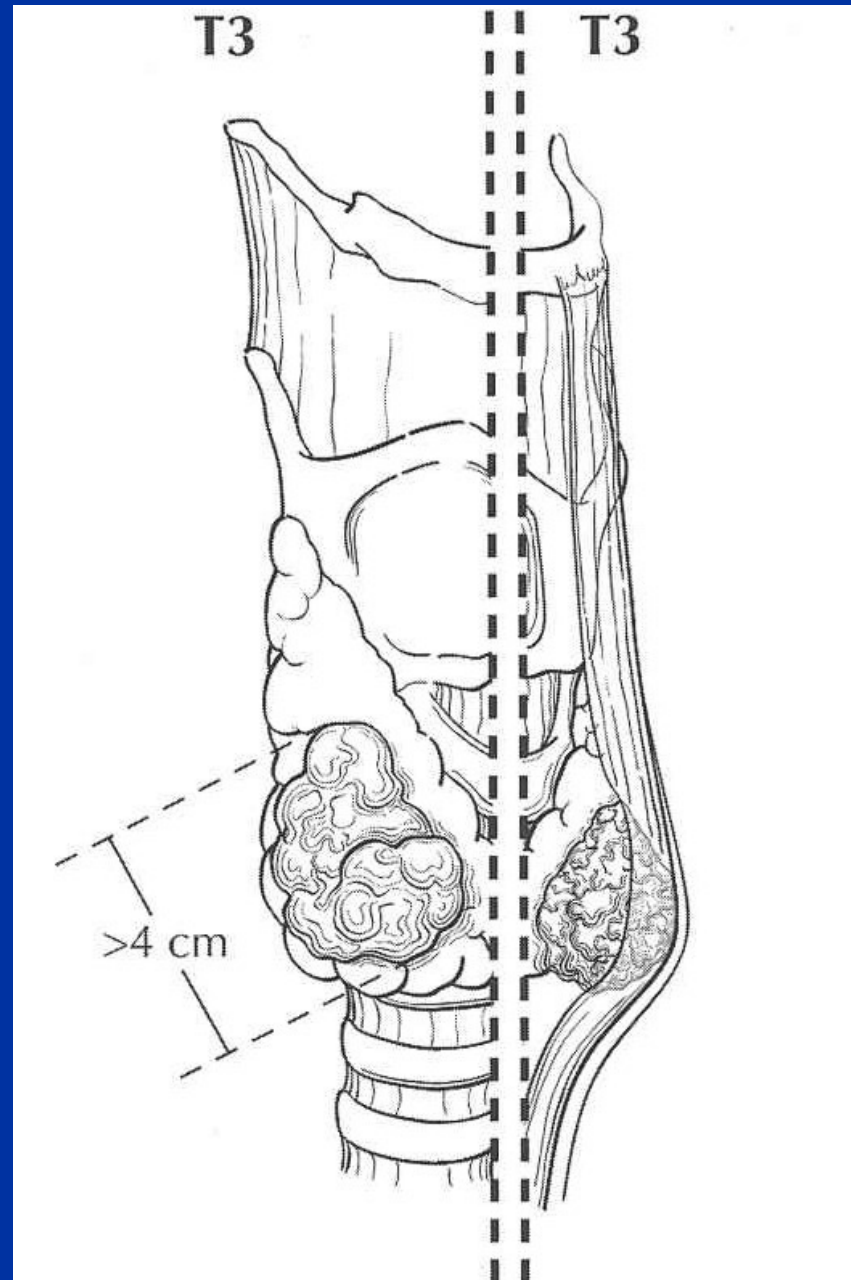


Early Primary Staging

T Category	T Criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤ 1 cm in greatest dimension limited to the thyroid
T1b	Tumor > 1 cm but ≤ 2 cm in greatest dimension limited to the thyroid
T2	Tumor > 2 cm but ≤ 4 cm in greatest dimension limited to the thyroid



T3





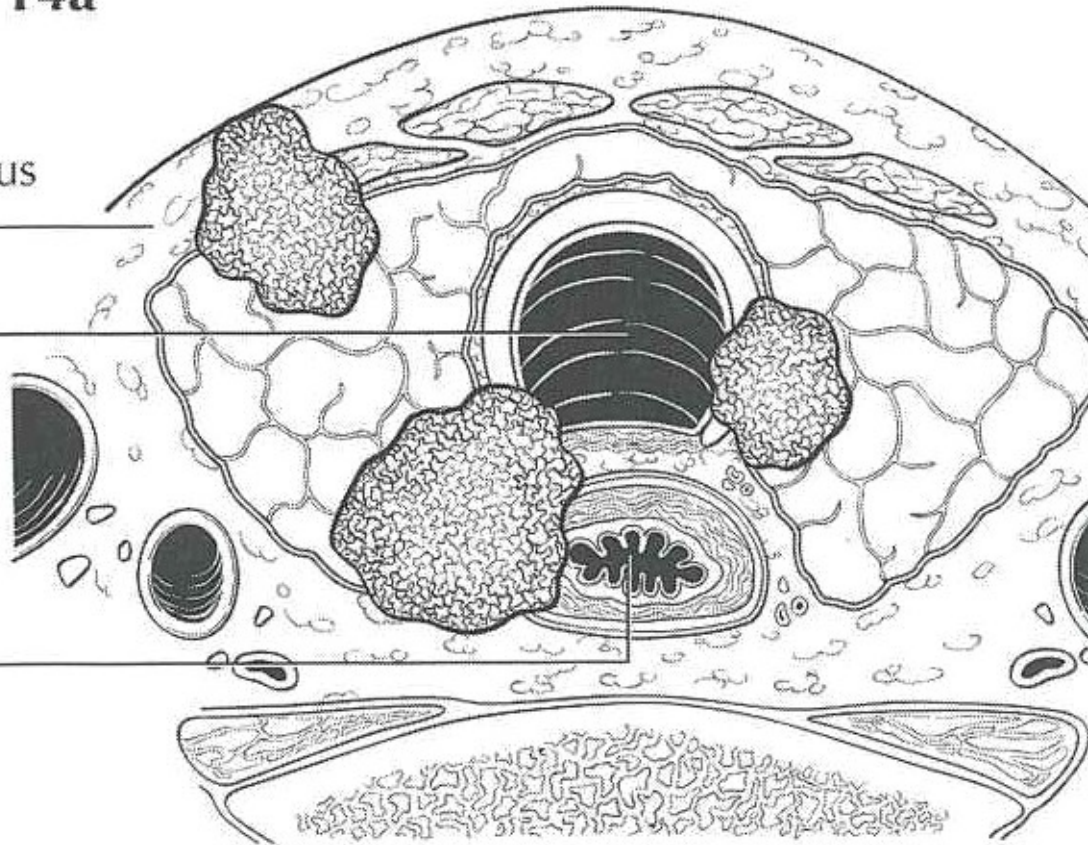
T4 a: Resectable with Morbidity

T4a

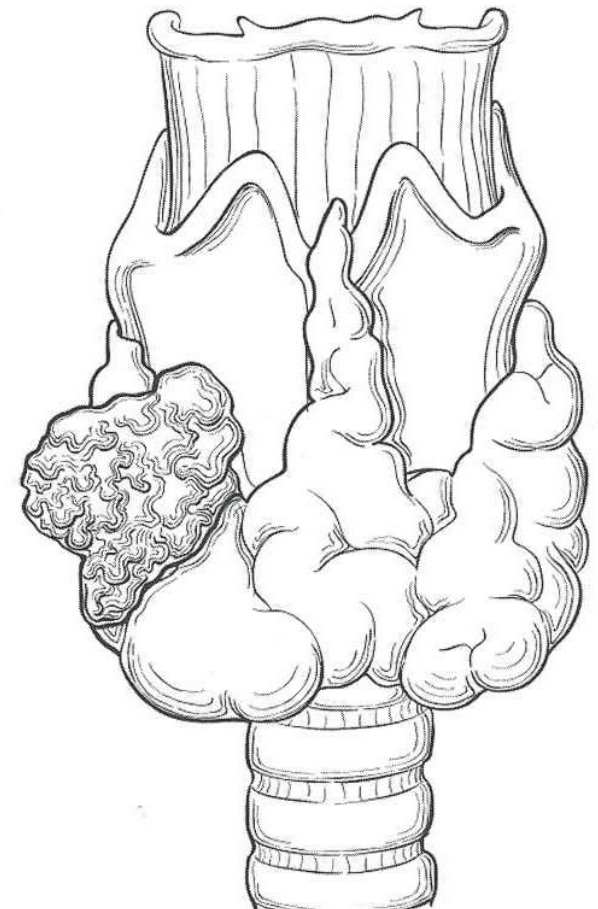
Subcutaneous
soft tissue

Trachea

Esophagus

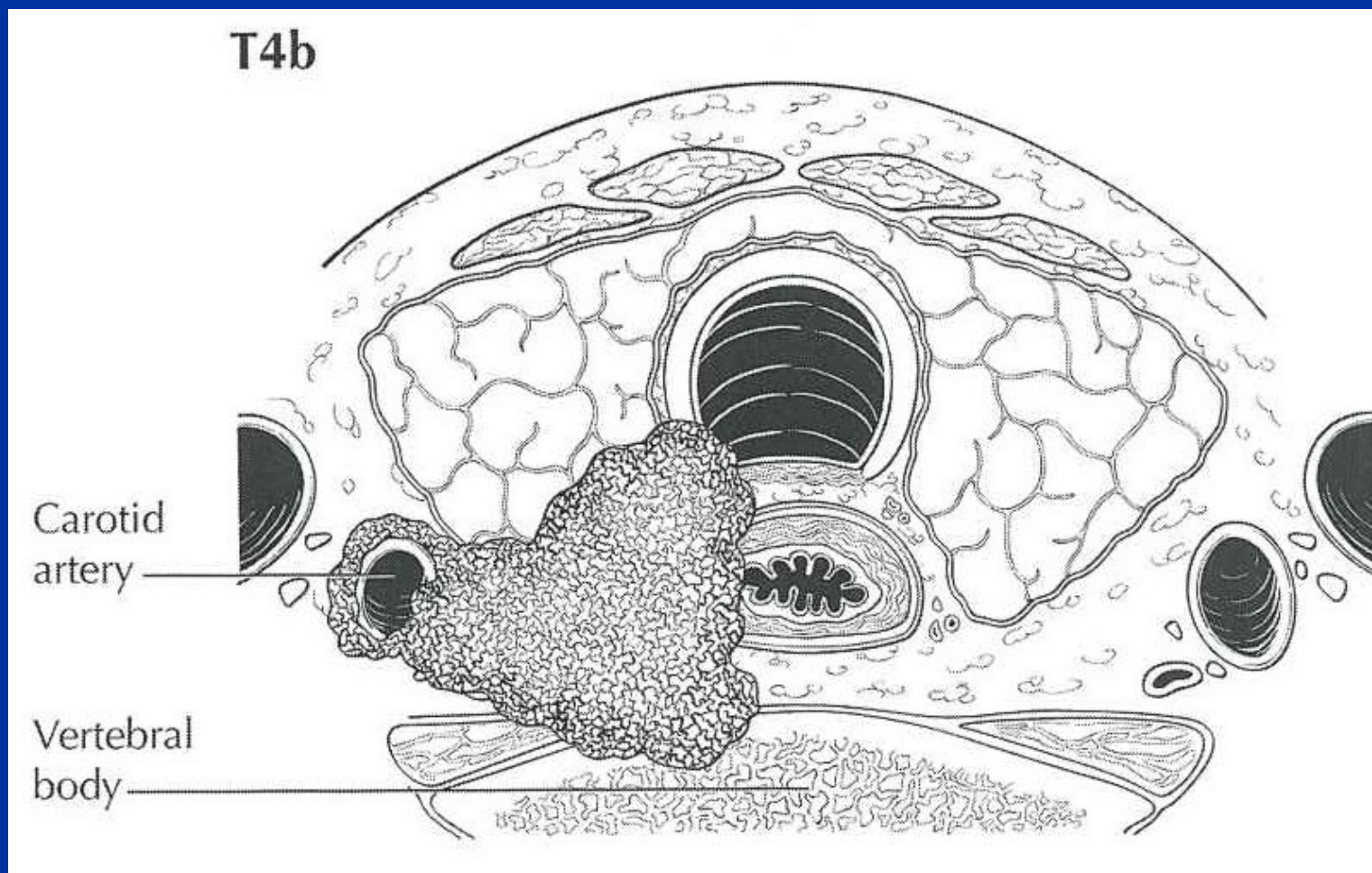


T4a





T4b: Unresectable



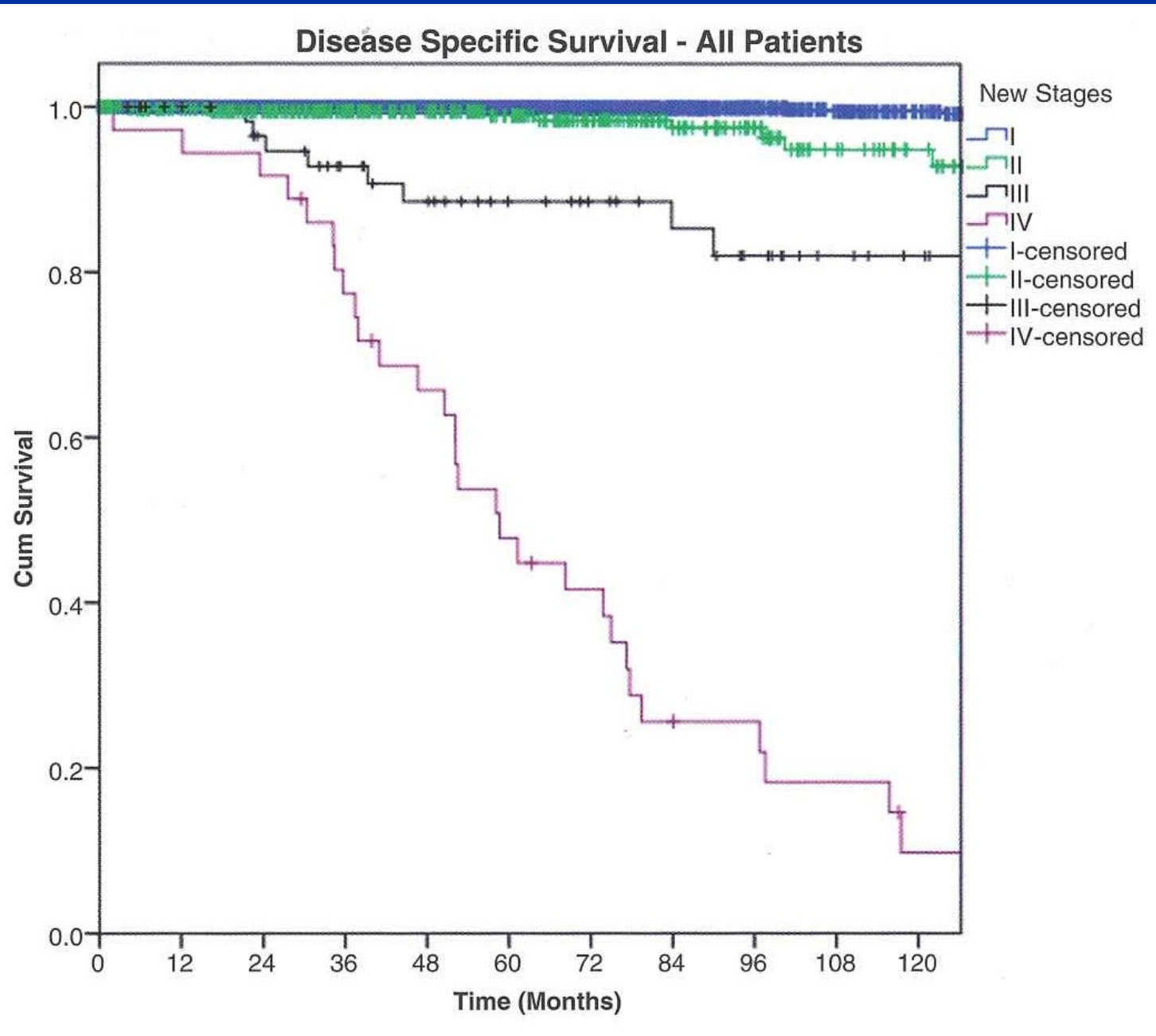


Late Primary Staging

T3	Tumor >4 cm limited to the thyroid, or gross extrathyroidal extension invading only strap muscles
T3a	Tumor >4 cm limited to the thyroid
T3b	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing the carotid artery or mediastinal vessels from a tumor of any size



Overall Staging Predicts Survival





Differentiated Thyroid Staging

AJCC PROGNOSTIC STAGE GROUPS

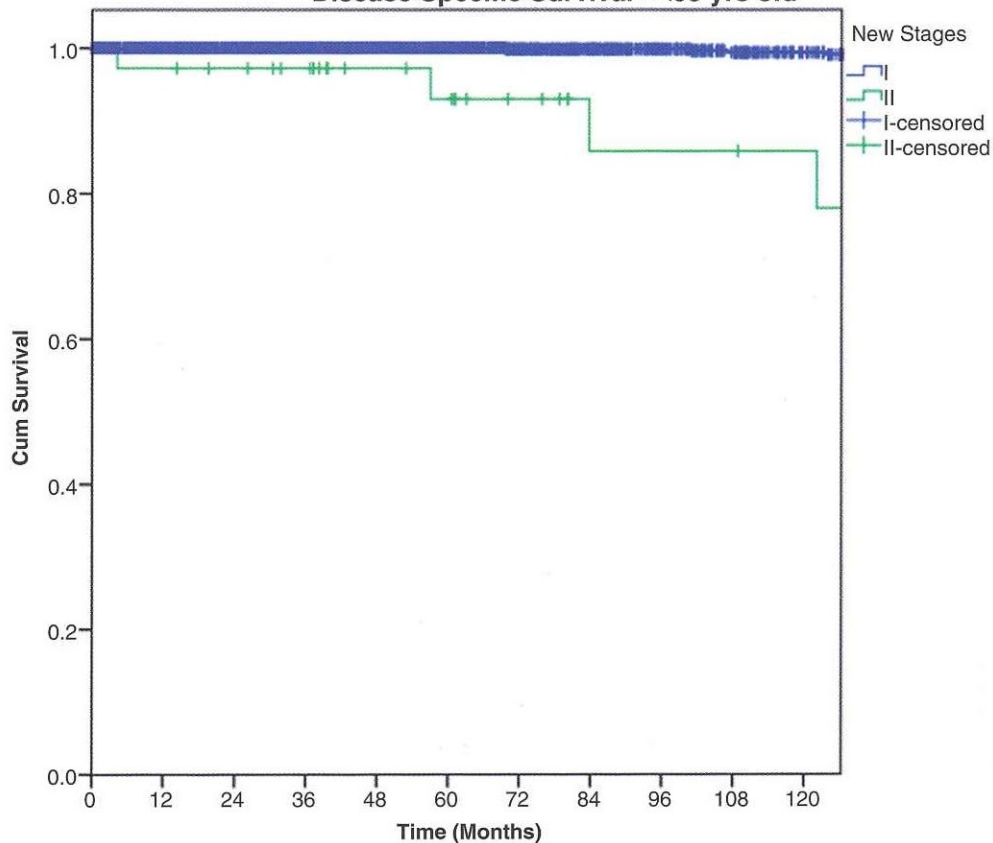
Differentiated

When age at diagnosis is...	And T is...	And N is...	And M is...	Then the stage group is...
<55 years	Any T	Any N	M0	I
<55 years	Any T	Any N	M1	II
≥55 years	T1	N0/NX	M0	I
≥55 years	T1	N1	M0	II
≥55 years	T2	N0/NX	M0	I
≥55 years	T2	N1	M0	II
≥55 years	T3a/T3b	Any N	M0	II
≥55 years	T4a	Any N	M0	III
≥55 years	T4b	Any N	M0	IVA
≥55 years	Any T	Any N	M1	IVB

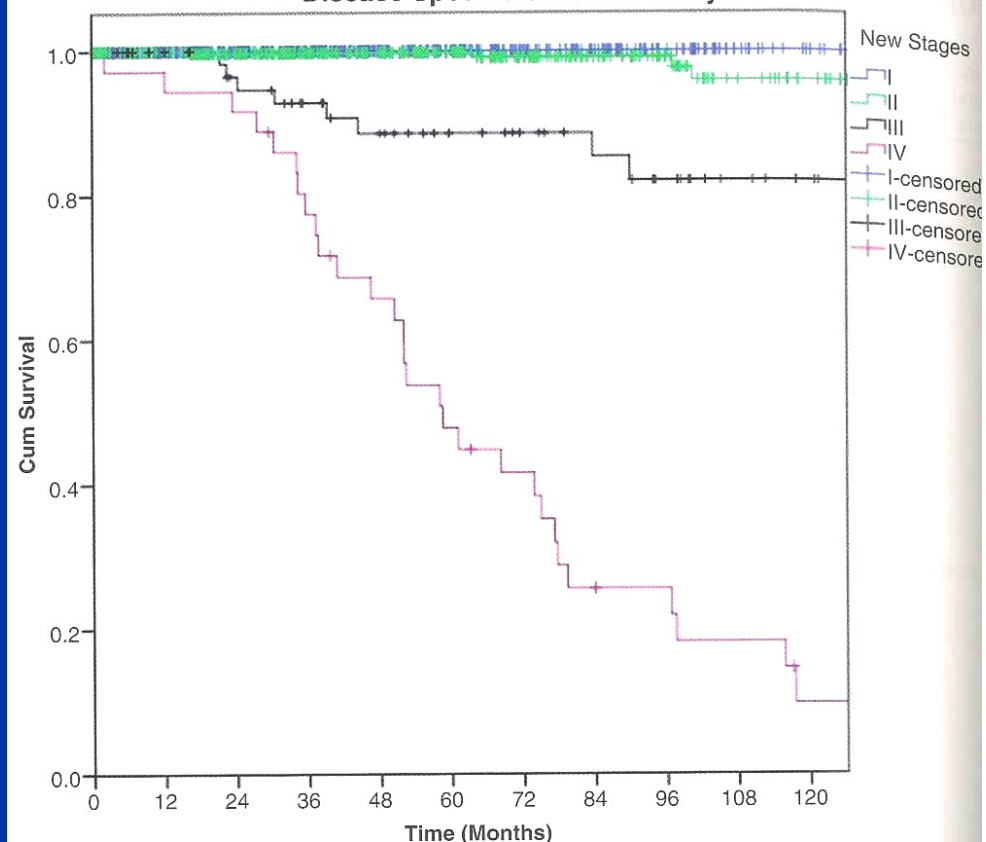


DTC: Age & sex Predict Survival

Disease Specific Survival - <55 yrs old



Disease Specific Survival - >55 yrs





Medullary Thyroid Cancer Staging

When T is...	And N is...	And M is...	Then the stage group is...
T1	N0	M0	I
T2	N0	M0	II
T3	N0	M0	II
T1-3	N1a	M0	III
T4a	Any N	M0	IVA
T1-3	N1b	M0	IVA
T4b	Any N	M0	IVB
Any T	Any N	M1	IVC



Anaplastic Thyroid Staging

Anaplastic

When T is...	And N is...	And M is...	Then the stage group is...
T1–T3a	N0/NX	M0	IVA
T1–T3a	N1	M0	IVB
T3b	Any N	M0	IVB
T4	Any N	M0	IVB
Any T	Any N	M1	IVC



Registry Data Collection

REGISTRY DATA COLLECTION VARIABLES

1. Histology
2. Age at diagnosis
3. Number of involved lymph nodes
4. Maximum diameter of involved lymph nodes
5. Size of largest metastatic foci within an involved lymph node



Any Questions?

