First a Little History

“TNM classification is a means of recording facts observed by the clinician whereas staging implies interpretation of these facts regarding prognosis.”

UICC: *TNM Classification of Malignant Tumors*. Geneva; 1968.
Fundamentals of Stage Grouping

Survival is

**Monotonically** decreasing

**Distinctive** between groups

**Homogeneous** within groups
Main Analytic Goal of the 8th Edition

Determine if TNM classifications can be shared?
8th Edition Staging
Esophagus and Esophagogastric Junction
Category Changes

T peritoneum = T4a

N and M: unchanged

Grade: no G4

Location: 2 cm rule!

awaits genomic confirmation
Location

Location – Esophagogastric Junction

epicenter of cancer ≤ 2 cm into cardia = Esophagus

epicenter of cancer > 2 cm into cardia = Stomach
Regional Lymph Nodes

Regional lymph node

Simplified

Specific

Stations
## WECC Centers

| Center              | N   |
|---------------------|-----|
| Africa              | 38  |
| South America       | 498 |
| Australia           | 1,936|
| Asia                | 4,448|
| Europe              | 5,849|
| North America       | 9,885|
| **Total**           | 22,654|
Stage Grouping Analysis

Machine learning analysis using Random Forest techniques

Risk-adjusted for 39 variables

Outcome: All cause mortality, hard end-point that is superior to soft end-point of cancer recurrence or disease specific mortality once multiple non-cancer-related risk factors for mortality are taken into account.
Analytic Strategy

3-step step Random Forest Analyses

1) From individual patient risk-adjusted survival curves, create clusters of survival curves separated by 5%

2) Label curves with specific TNM and non-anatomical categories and coalesce around those curves

3) Confirm homogeneity within the groups by lack of important variables associated with mortality
pTNM
Squamous Cell Carcinoma - pTNM

![Graph showing risk-adjusted survival over years for different pTNM stages.]
What’s New – pTNM Squamous Cell Ca

Stage 0

**Consensus vs Data-driven**

Stage I

T1 sub-category analysis – IA-IB

Stage IB, IIA, IIB

pT2N0M0 (G1 - IB, IIA)

pT3N0M0 (IIA, IIB - G2-3 U/M)

Stage III

regrouping and redistribution – no IIIC

Stage IV

sub-grouping Consensus vs **Data-driven**
# pTNM Squamous Cell Carcinoma

## Tis
- Tis: O

## T1a
- T1a: G1
  - G2-3

## T1b
- T1b: G1
  - G2-3

## T2
- T2: G1
  - G2-3

## T3
- T3: G1
  - G2-3

## T4a
- T4a: IIa
  - IIb

## T4b
- T4b: IVA

|      | L | U/M | N0 | N1 | N2 | N3 | M1 |
|------|---|-----|----|----|----|----|----|
| Tis  |   |     | O  |    |    |    |    |
| T1a  | IA| IA  | IIB| IIIA| IVA| IVB|
|      | IB| IB  | IIB| IIIA| IVA| IVB|
| T1b  | IB| IB  | IIB| IIIA| IVA| IVB|
| T2   | IB| IB  | IIIA| IIIB| IVA| IVB|
|      | IIa| IIa | IIIA| IIIB| IVA| IVB|
| T3   | IIa| IIa | IIIB| IIIB| IVA| IVB|
|      | IIa| IIa | IIIB| IIIB| IVA| IVB|
| T4a  | IIIB| IIIB| IVA| IVA| IVA| IVB|
| T4b  | IVA| IVA| IVA| IVA| IVA| IVB|

- T1b L: L1
- T1b N0: N0
- T1b U/M: U/M
- T1b N1: N1
- T2 N0: N0
- T2 U/M: U/M
- T2 N1: N1
- T2 N2: N2
- T2 N3: N3
- T2 M1: M1
- T3 N0: N0
- T3 U/M: U/M
- T3 N1: N1
- T3 N2: N2
- T3 N3: N3
- T3 M1: M1
- T4a N0: N0
- T4a U/M: U/M
- T4a N1: N1
- T4a N2: N2
- T4a N3: N3
- T4a M1: M1
- T4b N0: N0
- T4b U/M: U/M
- T4b N1: N1
- T4b N2: N2
- T4b N3: N3
- T4b M1: M1

- pTNM: pT1a N0 M0 U/M
- Squamous Cell Carcinoma

- Tis: Tis
- T1a: T1a
- T1b: T1b
- T2: T2
- T3: T3
- T4a: T4a
- T4b: T4b

- G1: G1
- G2-3: G2-3

- L: L
- U/M: U/M
- N0: N0
- N1: N1
- N2: N2
- N3: N3
- M1: M1

- Coefficients: T1a, T1b, T2, T3, T4a, T4b
- Stages: Tis, T1a, T1b, T2, T3, T4a, T4b
Squamous Cell Carcinoma - pTNM
Adenocarcinoma - pTNM
What’s New – pTNM Adenocarcinoma

Stage 0

**Consensus vs Data-driven**

Stage I

T1 sub-category analysis – IA-IC

Stage II

pG3T2N0M0 - IIA

pT1N1M0 meets pT3N0M0 – IIB

Stage III

regrouping and redistribution – no IIIC

Stage IV

sub-grouping Consensus vs Data-driven
# pTNM Adenocarcinoma

|   | N0 | N1 | N2 | N3 | M1 |
|---|----|----|----|----|----|
| **Tis** | O |    |    |    |    |
| **T1a** |   | IA | IIB | IIIA | IVA | IVB |
|        | G1 | IB | IIB | IIIA | IVA | IVB |
|        | G2 | IC |     |      |     |     |
|        | G3 |    |     |      |     |     |
| **T1b** |   | IB | IIB | IIIA | IVA | IVB |
|        | G1 | IC | IIB | IIIA | IVA | IVB |
|        | G2 |    | IIIA | IVA | IVB |    |
|        | G3 | IC | IIB | IVA | IVB |    |
| **T2** |   | IC | IIIA | IIIB | IVA | IVB |
|        | G1 | IIA |     |      |     |     |
|        | G2 |    |     |      |     |     |
|        | G3 |    |     |      |     |     |
| **T3** |   | IIB | IIIB | IIIB | IVA | IVB |
|        |      |  |     |      |     |     |
| **T4a** |   | IIIB | IIIB | IVA | IVA | IVB |
|        |      |  |     |      |     |     |
| **T4b** |   | IVA | IVA | IVA | IVA | IVB |
Squamous Cell Carcinoma - pTNM

The graph illustrates the risk-adjusted survival rates over different years for various stages of squamous cell carcinoma, denoted as p0 to pIVB. The survival rates decrease as the years progress, with each stage showing a distinct pattern.
Squamous Cell Carcinoma - ypTNM

![Graph showing risk-adjusted survival over years for different ypTNM stages.](image-url)
Adenocarcinoma - pTNM
Adenocarcinoma - ypTNM

The graph shows the risk-adjusted survival rates over years for different stages of adenocarcinoma. The stages are ordered from ypI to ypIVA, with each stage represented by a different colored line. The survival rates decrease as the years progress, indicating the impact of each stage on survival outcomes.
What is New – ypTNM

Can ypTNM share pTNM staging?
1) Unique categories (ypTisN1-3M0 and ypT0N0-3M0)
2) Dissimilar stage group compositions
3) Markedly different survival profiles
   Require separate ypStage groupings

Identical for Adenocarcinoma and Squamous Cell Carcinoma
What is New – ypTNM

ypT0-2N0-3M0

Stage II  ypT3N0M0

Stage IVB  ypM1
| Stage   | ypTNM Description |
|---------|-------------------|
| Stage I | ypT0-2N0M0        |
| Stage II| ypT3N0M0          |
| Stage IIIA| ypT0-2N1M0    |
| Stage IIIB| ypT0-2N2M0   |
|          | + ypT3N1-2M0 and ypT4aN0M0 |
| Stage IVA| ypT0-2N3        |
|          | + yp T3N3M0, ypT4aN1-3M0, and ypT4bN0-3M0 |
| Stage IVB| ypM1            |
| ypTNM | N0 | N1 | N2 | N3 | M1 |
|-------|----|----|----|----|----|
| T0    | I  | IIIA | IIIB | IVA | IVB |
| Tis   | I  | IIIA | IIIB | IVA | IVB |
| T1    | I  | IIIA | IIIB | IVA | IVB |
| T2    | I  | IIIA | IIIB | IVA | IVB |
| T3    | II | IIIB | IIIB | IVA | IVB |
| T4a   | IIIB | IVA | IVA | IVA | IVB |
| T4b   | IVA | IVA | IVA | IVA | IVB |
cTNM
Squamous Cell Carcinoma - pTNM

The graph shows the risk-adjusted survival rates over years for different stages of squamous cell carcinoma (pT0, pT1A, pT1B, pT2A, pT2B, pT3A, pT3B, pT4A, pT4B). The survival rates decrease as the stage increases, indicating a higher risk of death for more advanced stages.
Squamous Cell Carcinoma - cTNM
What is New – cTNM
Squamous Cell Carcinoma

cT1-T2  not distinctive by cN0-1

cT3  distinctive by cN0-1

cT4  cancers are not subcategorized
### cTNM Squamous Cell Carcinoma

|          | N0 | N1 | N2 | N3 | M1 |
|----------|----|----|----|----|----|
| Tis      | O  |    |    |    |    |
| T1       |    | I  | I  | III| IVA| IVB|
| T2       |    | II | II | III| IVA| IVB|
| T3       |    | II | III| III| IVA| IVB|
| T4a      |    | IVA| IVA| IVA| IVA| IVB|
| T4b      |    | IVA| IVA| IVA| IVA| IVB|

**Cancer Staging**

- **Tis** (Tis): Carcinoma in situ
- **T1**, **T2**, **T3**, **T4a**, **T4b**: Local invasion
- **N0**, **N1**, **N2** - Regional lymph node involvement
- **N3**: Distant lymph node involvement
- **M1**: Metastasis

**TNM Staging**

- **T**: Tumor size
- **N**: Lymph node involvement
- **M**: Metastasis
### What is New – cTNM

**Squamous Cell Carcinoma**

| Stage   | Description |
|---------|-------------|
| Stage 0 | cTis        |
| Stage I | cT1N0-1M0   |
| Stage II| cT2N0-1M0 plus cT3N0M0  
cT1-2N1M0 and cT3N0M0 are cStage III adenocarcinomas |
| Stage III| cT3N1M0 and cT1-3N2, mirroring pStage IIIA-B squamous cell carcinoma |
| Stage IVA| Most advanced cancers are subgroupped |
| Stage IVB| cM1 |
Squamous Cell Carcinoma - cTNM
What is New – cTNM Adenocarcinoma

cT1-2 distinctive by cN0-1

cT3-4 not distinctive by cN0-1

cT4 subcategorization
## cTNM Adenocarcinoma

|       | N0 | N1 | N2 | N3 | M1 |
|-------|----|----|----|----|----|
| Tis   | O  |    |    |    |    |
| T1    | I  | IIA| IVA| IVA| IVB|
| T2    | IIB| III| IVA| IVA| IVB|
| T3    | III| III| IVA| IVA| IVB|
| T4a   | III| III| IVA| IVA| IVB|
| T4b   | IVA| IVA| IVA| IVA| IVB|
What is New – cTNM Adenocarcinoma

Stage 0  cTis
Stage I  cT1N0M0
Stage II subgrouped IIA cT1N1M0 and IIB cT2N0M0
Stage III cT2N1M0 and cT3-4aN0M0 unlike cStage SCCa but mirroring pStage III adenocarcinoma
Stage IVA merging of cN2-3
AJCC Cancer Staging Manual

Eighth Edition

Springer
UICC 8th Edition - CAUTION

Borrowed (Incompletely) from AJCC 8th Edition

- **cTNM** Identical to AJCC
- **pTNM**
  1) Pathologic Stage Groups*
  2) Prognostic Pathologic Stage Groups*
- **ypTNM** not presented*

* Problematic
What’s Next

9th Edition

Heightened collaboration?

cTNM improved staging and documentation

pTNM genetic signature (cTNM / ypTNM)

ypTNM precision cancer care
