Coding Stage: Main Principles
Session 2

25th of May, 2021

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Overview

1. Introduction
   - Definition and importance of Stage
   - Staging systems in cancer registration over time
2. TNM classification
   - General rules of the TNM classification
   - Clinical and pathological Stage
   - T-, N- and M-category
3. Paediatric Cancer Stage
   - The Toronto Paediatric Cancer Stage Guidelines

3 essential factors in the management of cancer

Site

- Site of origin of the cancer
- E.g. breast, prostate, …

Characteristics

- Histologic/biologic characteristics
- E.g. Grade Group in prostate adenocarcinoma, HER2/neu positive breast adenocarcinoma

Extent

- Anatomical extent of the cancer or '**STAGE'**
- E.g. Stage (I, II, III, IV)

Stage: definition and importance

- **Stage**: Extent of the cancer at diagnosis
  - How much of it is there?
  - Common medical language to describe the extent of disease => estimate prognosis

- **'To stage'** versus **'the stage'**
  - The verb: To stage a patient, e.g. diagnostic workup before treatment

  - The noun: e.g. this is a stage III disease

- Important for the **Patient**
  - Treatment, Prognosis, Clinical Research

- Important for **Cancer Control** Activities
  - Public health &authorities: incidence, screening effectiveness, guideline adherence, resource planning
  - Oncology

Staging systems used over time in cancer registration

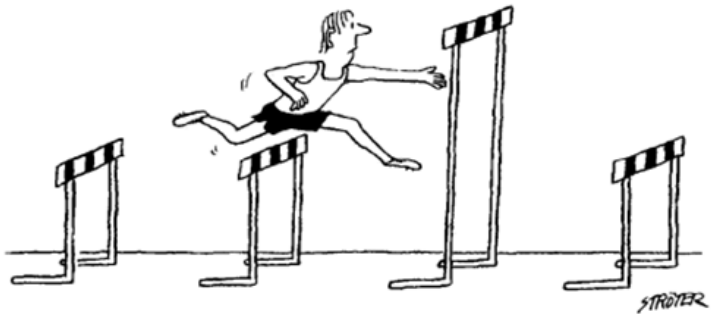
- **General**
  - Summary Stage
    - In situ, Local, Regional, Distant
  - Extent of Disease (eod) SEER
    - Several revisions: digits
  - TNM Classification UICC - AJCC
    - Tumour, Node, Metastasis
    - Essential TNM
    - ~~'Condensed TNM' (ENCR)~~
      - ~~Localized, local spread, regional spread, metastatic, unknown~~

- **Specific**
  - FIGO (gynaecologic tumours)
  - Clark / Breslow (melanoma)
  - Ann Arbor (lymphoma)
  - Dukes (colon and rectum)
  - Durie – Salmon (multiple myeloma)
  - ...

ENCR-JRC DATA call (2015): questionnaire

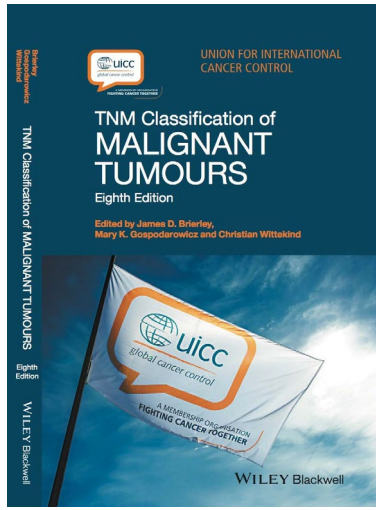
- Questionnaire ENCR-JRC DATA call 2015:
  - 72% of the Cancer Registries collect 'information about stage'
  - 46% of the Cancer Registries submitted data related to the extent of the disease - mostly TNM

- Information about stage
  - Relevance of stage information acknowledged
  - Availability of stage information limited
  - Heterogeneity in systems and definitions used
  - Comparability of data?



TNM classification

- The most extensive staging system that exists
- Used all over the world by clinicians and epidemiologists
- Comparability of data
- Changes over time to incorporate new evidence



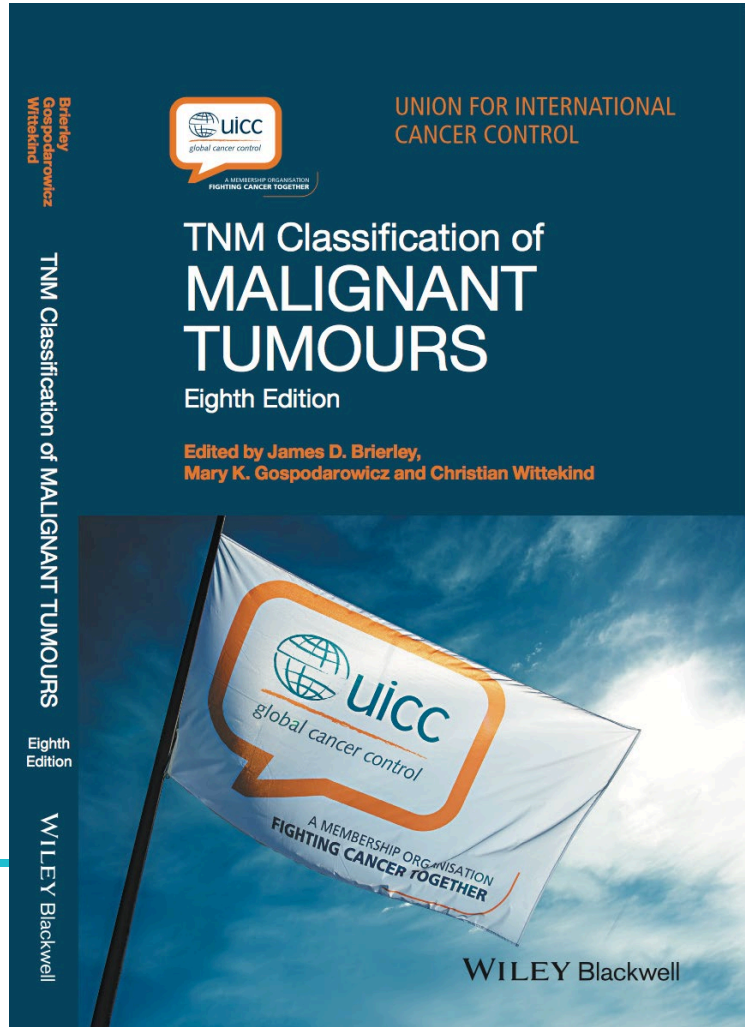
- Whose responsibility?
  - Managing physician who has the most complete information (clin/path.)

- Global harmonization of cancer staging classification through close collaboration with: WHO, IARC, IACR, IALSC, AJCC, FIGO, CDC, ICCR, NCI

"How much of it is there?" TNM classification

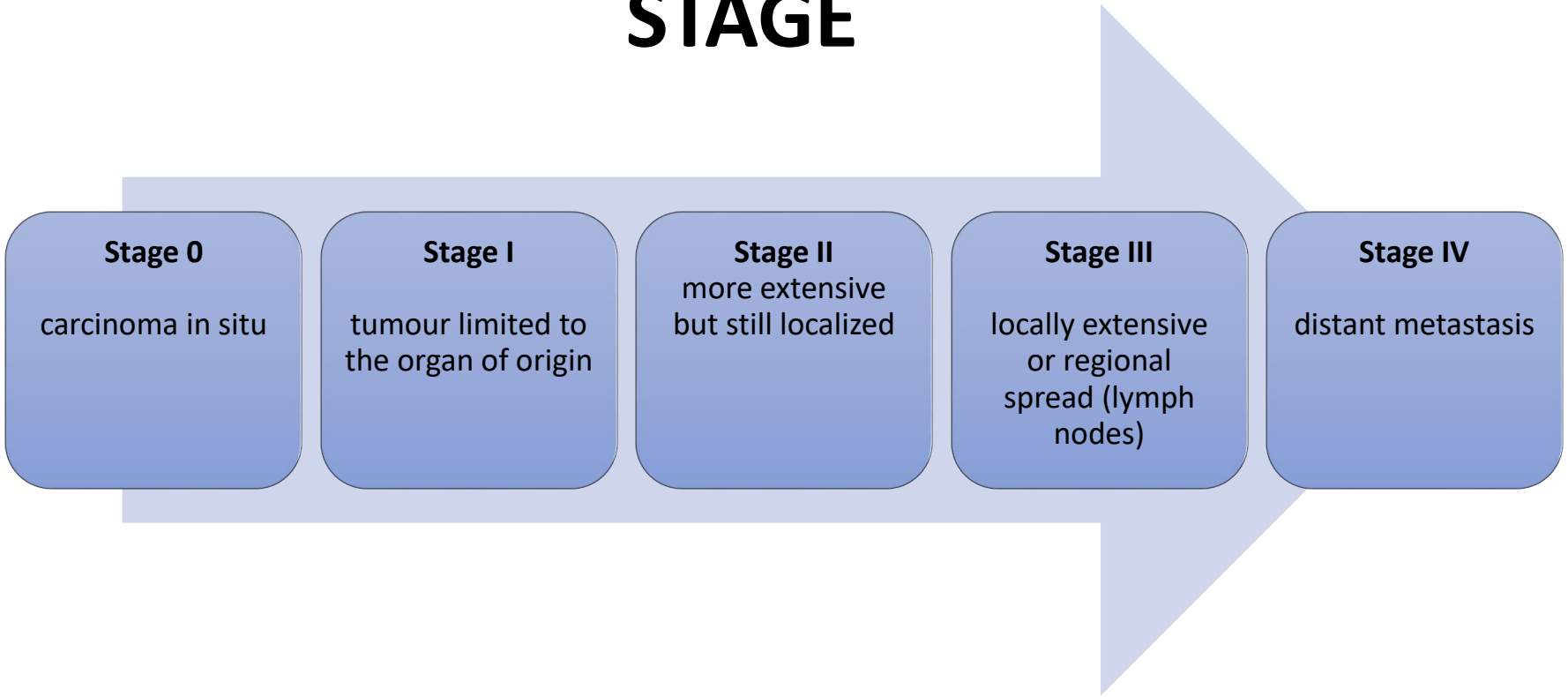
- Cancer stage is the **ANATOMIC EXTENT OF DISEASE**
- **Classification using T-, N- and M-categories**

- **Summarised as Stage (typically I, II, III, IV)**



The General Rules of the TNM system: Stages

STAGE



+ prognostic factors: 'PROGNOSTIC GROUP'

TNM: general principles (1)

T-category : **TUMOUR**
describes the extent of the primary tumour
Ta, Tis, T0, T1, T2, T3, T4, Tx

N-category : **NODE**
describes the absence or presence and extent of regional lymph node metastasis
N0, N1, N2, N3, Nx

M-category : Metastasis
describes the absence or presence of distant metastasis
M0, M1, ~~Mx~~

Summarised as 'STAGE' (typically, I, II, III, IV)

e.g., kidney cancer
cT1 N0 M0 = Stage I

TNM classification

- TNM classification depends on, and is specific for…
  - primary tumour localization (topography) **AND** histology (morphology)

    E.g. Specific TNM for Stomach cancer – carcinoma
    Specific TNM for GIST of the stomach
    Specific classification for Non-Hodgkin lymphoma of the stomach

- TNM not available for all tumours
  - For example no TNM for Brain tumours, no TNM for leukaemia

The General Rules of the TNM System: cTNM - pTNM

cTNM	pTNM	ypTNM
Clinical classification	Pathological classification	**Pathological** evaluation after neo-adjuvant therapy
Designated **BEFORE** treatment	Designated **AFTER** surgery	(Designated AFTER surgery)
To select and evaluate therapy	To guide adjuvant therapy, estimate prognosis and calculate end results	To guide adjuvant therapy, estimate prognosis and calculate end results

For Cancer Registries, it is recommended to register both cTNM and pTNM (or ypTNM)

The General rules of the TNM system: cTNM

- Clinical classification is based on any information gathered about the extent of cancer from the time of diagnosis until the initiation of primary treatment **or** decision not to treat

- Possible information that can be used:
  - clinical history and symptoms,
  - physical examination,
  - imaging,
  - endoscopy or surgical exploration without resection,
  - biopsy of primary site, biopsy of a single regional node, biopsy of a distant metastatic site

=> precision
=> must remain unchanged after establishment!

How to assign T, N, M? How to start…?

- Determine *primary site* and *histology*
- Look up site *chapter*
- Is the *histology included* in this chapter? Yes => Continue
- Review the *list of regional lymph nodes*
- Was surgery the first treatment? If yes: Determine Clinical TNM *and* Pathologic TNM
- Was surgery preceded by radio-and/or systemic treatment? If yes: Determine clinical (cTNM) and ypTNM

- Determine T, N, M with the medical information

- Find 'Stage' information in the tables
- (Assign clinical, pathological or ypTNM **stage** by summarizing the T-, N- and M- categories)

T-category

The General Rules of the TNM System: cT category

- **cT1-T4** Invasive tumours
  Increasing size and/or depth/local extent of the primary tumour

- **cTX** Primary tumour cannot be assessed =>to be avoided
- **cT0** No evidence of primary tumour
  - E.g. occult breast carcinoma
- **cTis** Carcinoma in situ - epithelial tumours
- **cTa** Non-invasive papillary carcinoma
  Bladder, renal pelvis, ureter, urethra, Penis

T-category: different criteria for different cancers

T1-T4

- Subcategories T1a, T1b, etc. are often used
- Exceptions: ovary, vulva: only T1-T3

BASED on

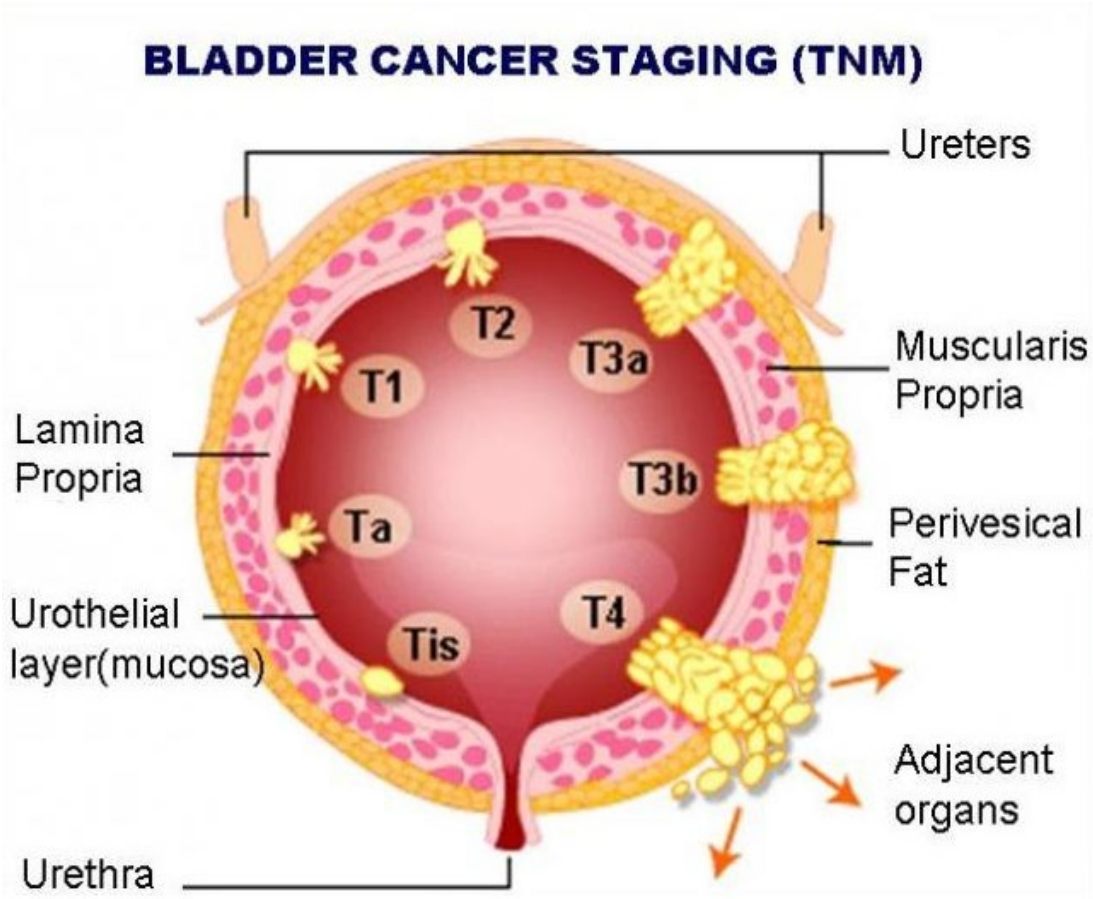
- Tumour **size**
  - Breast, parotid gland, oral cavity
- **Depth** of invasion through wall of organ
  - Colon, bladder, melanoma
- Location and **extension**
  - Lung, larynx, pancreas
- **Other** factors
  - Tumour multiplicity (liver)
  - Combination

Example T-category based on size only

- Example: **Gastrointestinal Stromal Tumour (GIST)**
  - **T1** ≤ 2 cm
  - **T2** >2 cm, ≤ 5 cm
  - **T3** >5 cm, ≤ 10 cm
  - **T4** >10 cm

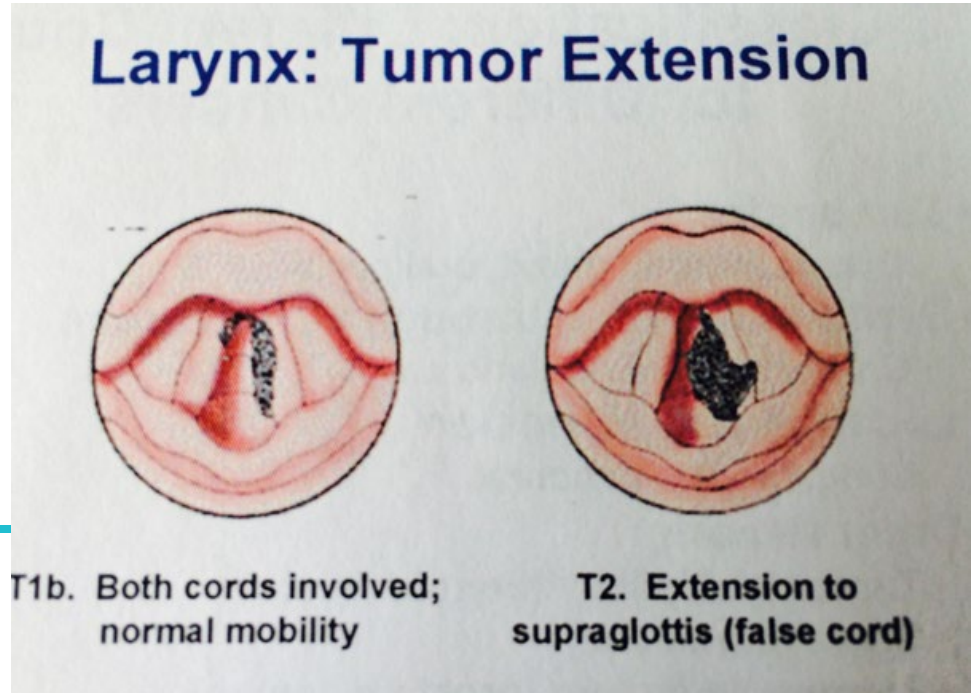
Example T-category based on depth of invasion

- Example: **Bladder**
  - **T1** subepithelial connective tissue
  - **T2** muscularis propria
  - **T3** perivesical tissue
  - **T4** beyond bladder

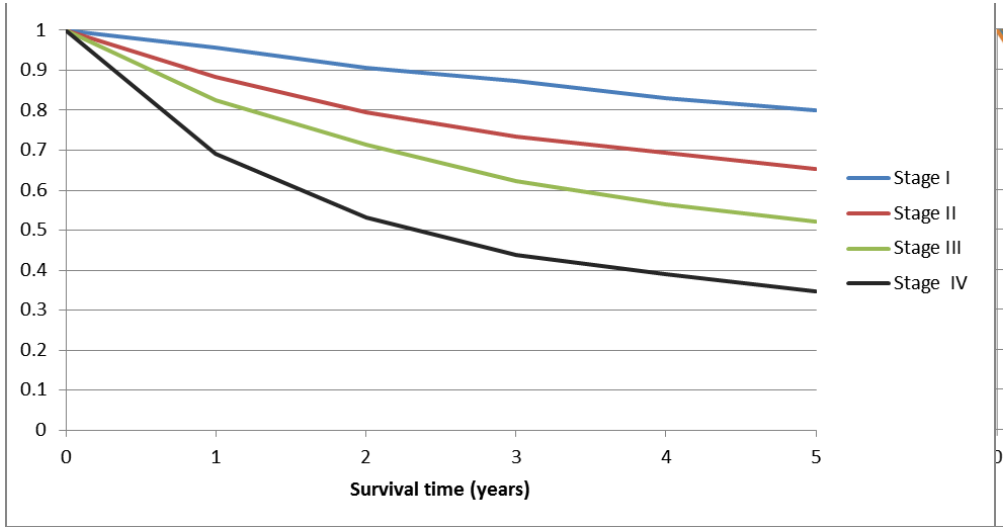


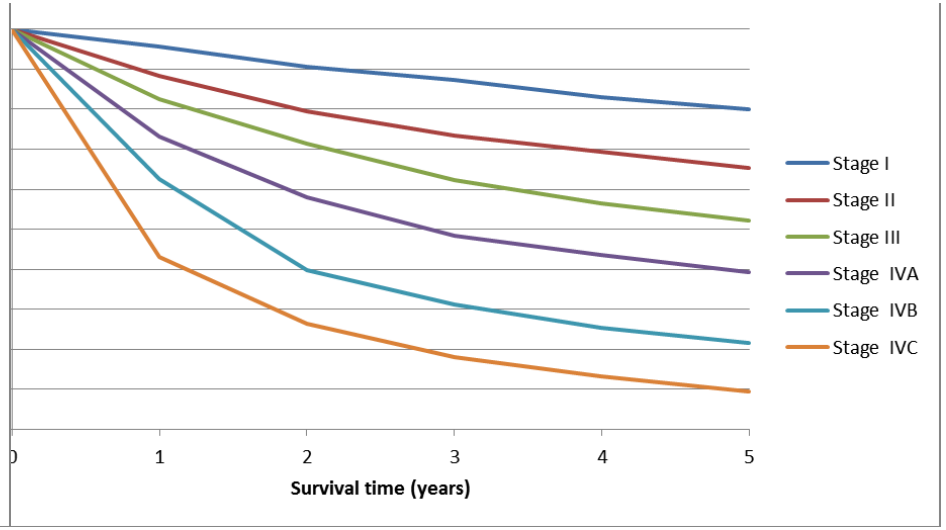
Example T-category based on extension

- Example: **Larynx (glottis)**
  - **T1** One T1a/both vocal cords T1b, normal mobility
  - **T2** Extension to supraglottis/subglottis, impaired cord mobility
  - **T3** Confined to larynx with vocal cord fixation
  - **T4a** Moderately advanced local disease
  - **T4b** Very advanced local disease



Head and Neck Cancer 2009-2013, 5 year rel survival, Belgium



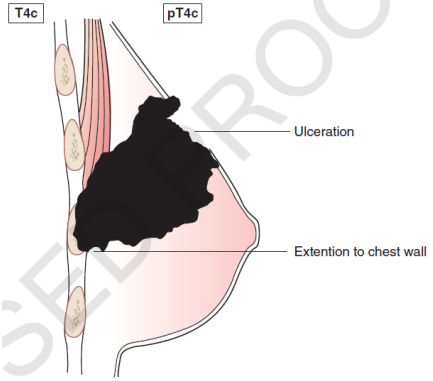


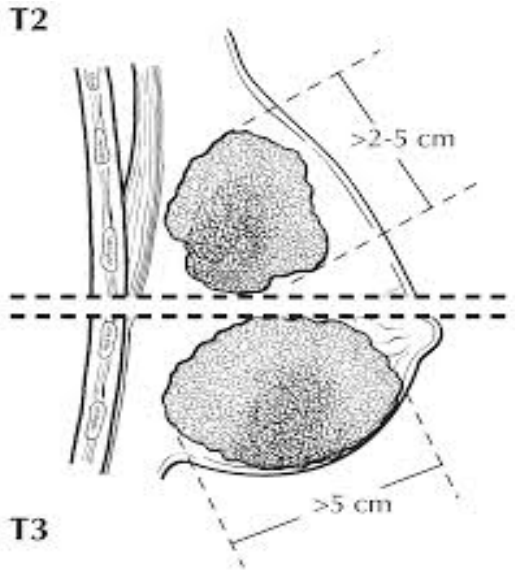
	T	N	M
Stage IV A	1,2,3	2	0
Stage IV A	4a	0,1,2	0
Stage IV B	4b	Any	0
Stage IV B	Any	3	0
Stage IV C	Any T	Any N	1

TNM, 7th edition

Example T-category based on size and extension

- Example: **Breast**
  - **T1** ≤ 2 cm
  - **T2** >2 cm, ≤ 5 cm
  - **T3** >5 cm
  - T4 involving chest wall and/or skin





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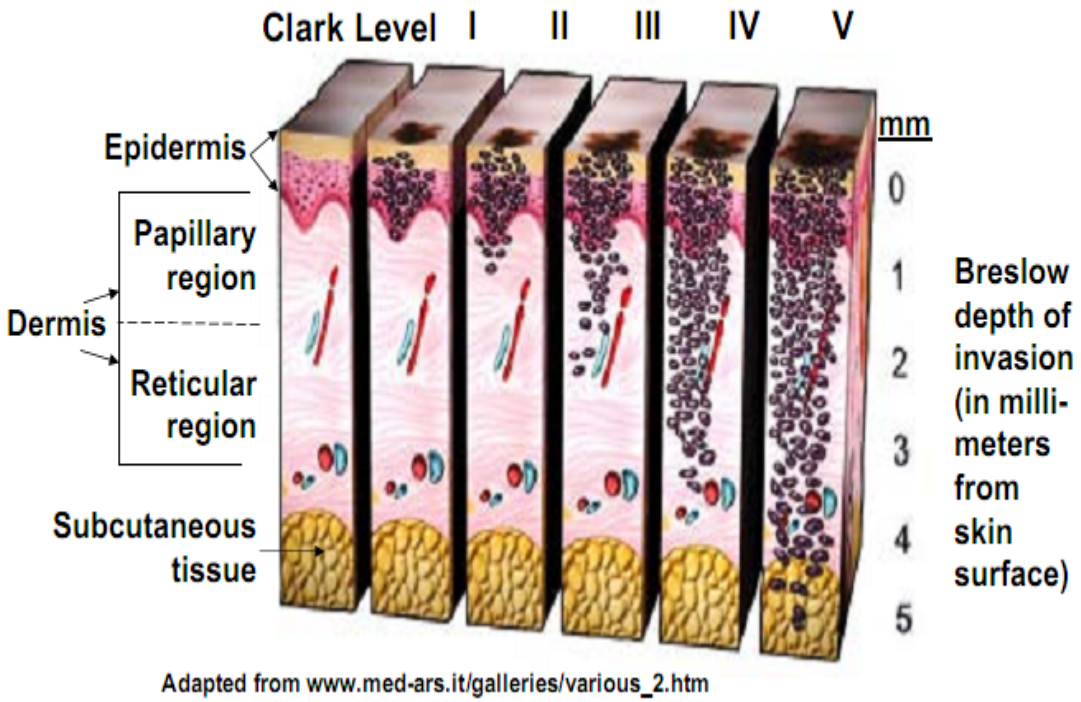
T-category values: cT and pT

- pT categories (mostly) correspond to the cT categories

- Special cases or exceptions:
  - Melanoma: no cT category but only pT categories: extent of tumour after excision
  - Testis: pT after orchiectomy (except pTis and pT4), there are no cT categories
  - Oropharynx: different T-categories p16+/HPV+ versus p16-/HPV- or no result
  - Prostate: no pT1 category – no pT2 **sub**categories

Example Melanoma thickness: only pT possible!

- **Clark Level and Breslow Depth of Invasion**



Adapted from www.med-ars.it/galleries/various_2.htm

pTX: primary tumour cannot be assessed
pT0: no evidence of primary tumour
pTis: melanoma in situ
pT1: tumour 1.0 mm or less in thickness
pT2: tumour >1 mm but not more than 2 mm in thickness
pT3: tumour > 2mm but not more than 4 mm in thickness
pT4: tumour > 4 mm in thickness

With or without ulceration:
pT1a less than 0.8mm in thickness without ulceration
pT1b less than 0.8 mm in thickness with ulceration or 0.8 mm or more but no more than 1 mm in thickness, w/o ulceration

pT2a without ulceration
pT2b with ulceration
Etc.…

No cT categories for skin melanoma!

Example Prostate cancer: cT and pT categories

T – Primary Tumour

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour

T1 Clinically inapparent tumour that is not palpable
- T1a Tumour incidental histological finding in 5% or less of tissue resected
- T1b Tumour incidental histological finding in more than 5% of tissue resected
- T1c Tumour identified by needle biopsy (e.g., because of elevated PSA)

T2 Tumour that is palpable and confined within prostate
- T2a Tumour involves one half of one lobe or less
- T2b Tumour involves more than half of one lobe, but not both lobes

T3 Tumour extends through the prostatic capsule*
- T3a Extraprostatic extension (unilateral or bilateral) including microscopic bladder neck involvement
- T3b Tumour invades seminal vesicle(s)

T4 Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall

pT

- **No pT1** because insufficient tissue to assess the highest pT category
- No subcategories for pT2

The General Rules of the TNM System: T-category and additional descriptor 'm'

The suffix **m** is used to indicate the presence of multiple primary tumours at a single site. This can also be indicated by the number of primary tumours

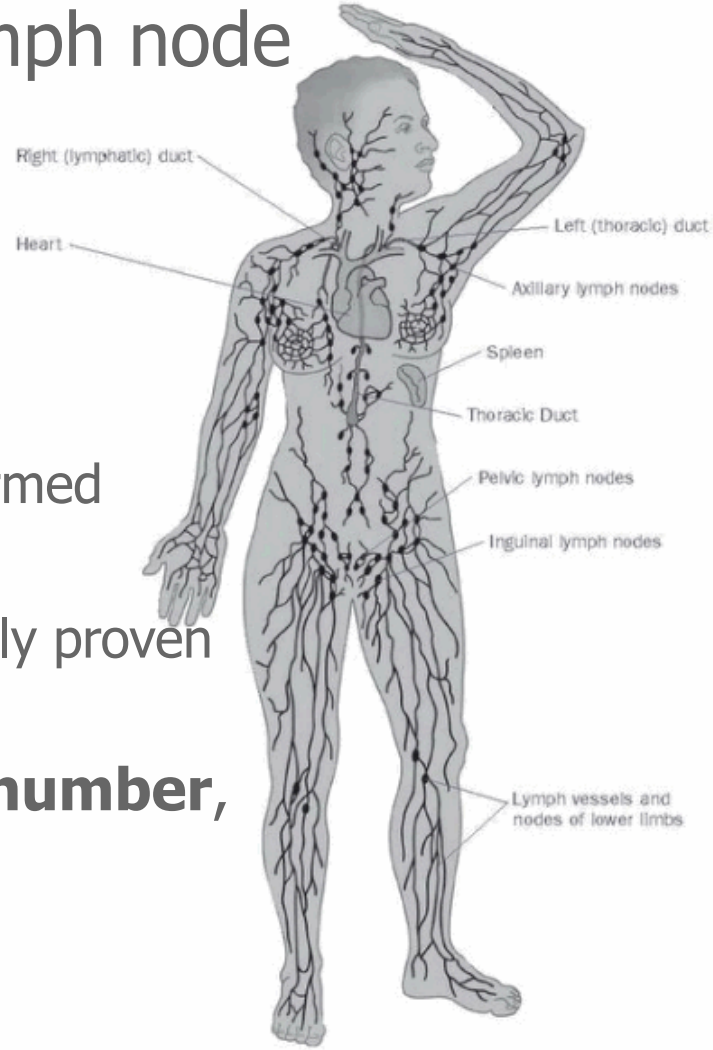
Example:

- Thyroid: T2(m)
- Breast: T1c(m) or T1c (3)
  - What if invasive and in situ component? Only take the dimension of the invasive component

N-category

N: Regional lymph nodes - Lymph node involvement

- Absence or presence of metastases in primary lymph node drainage area of a cancer



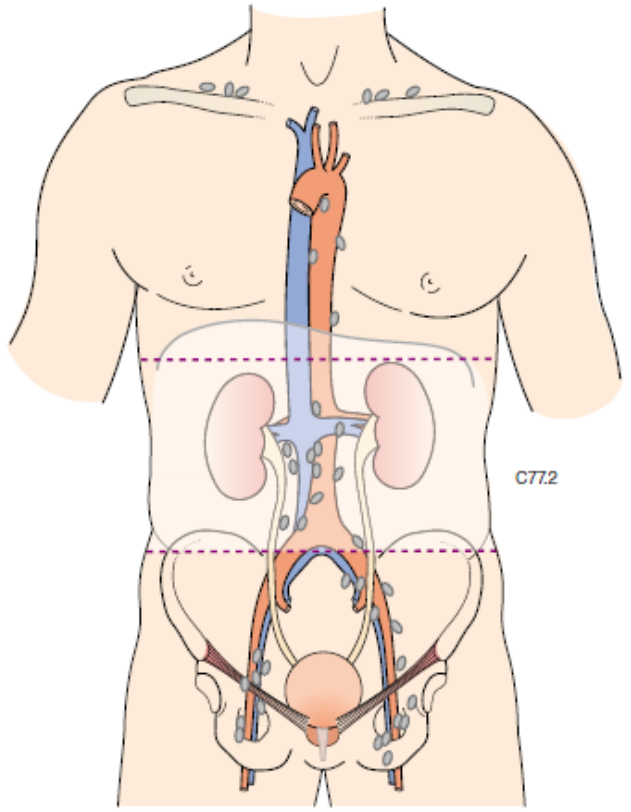
N-category

- **NX** Regional lymph nodes cannot be assessed
  No clinical or pathological investigations have been performed
- **N0** No regional lymph node metastasis
  Regional lymph nodes have been clinically or pathologically proven to be **free of metastatic disease**
- **N1=>N3** Increasing involvement of regional lymph nodes by **number**, **location** or **size**

Example N-category values: presence or absence (only)

- Example: **Kidney**
  - **N0** no regional lymph nodes
  - **N1** metastasis in regional lymph node(s)

The regional lymph nodes are the hilar, abdominal para-aortic, and paracaval nodes. Laterality does not affect the N categories.



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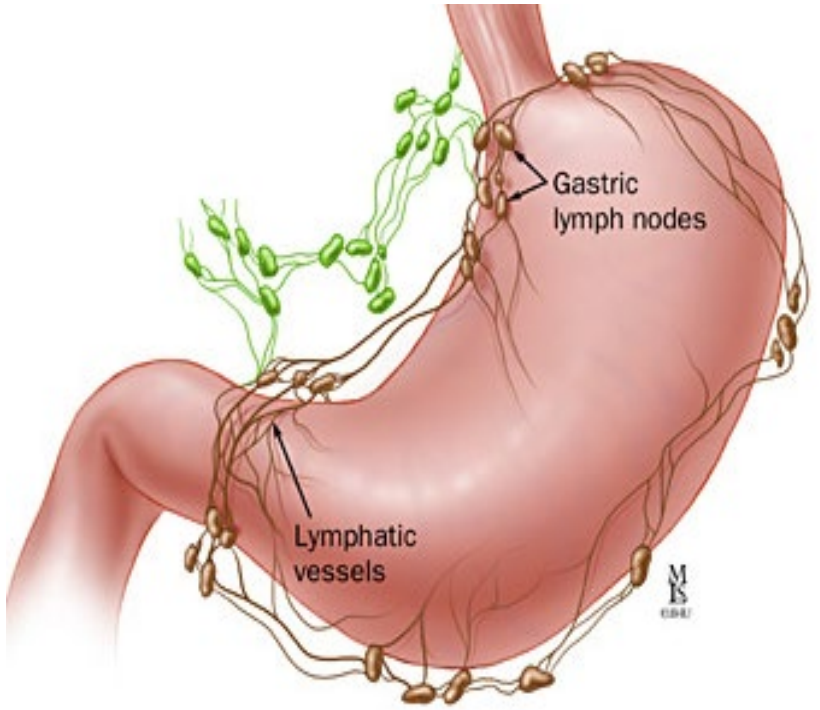
Example N- category based on number

- Example: **Stomach**
  - **N1** 1-2 regional nodes involved
  - **N2** 3-6 regional nodes involved
  - **N3** 7 or more node involved



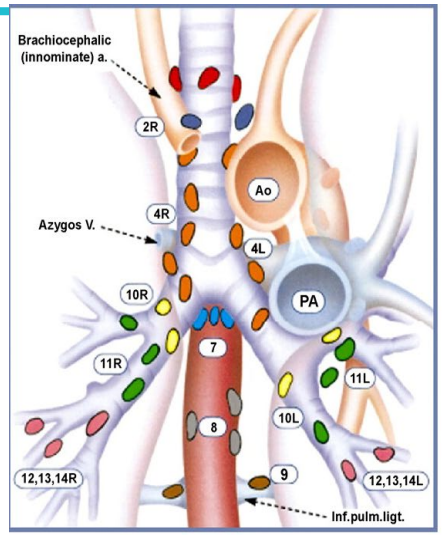
Example N-category based on Location

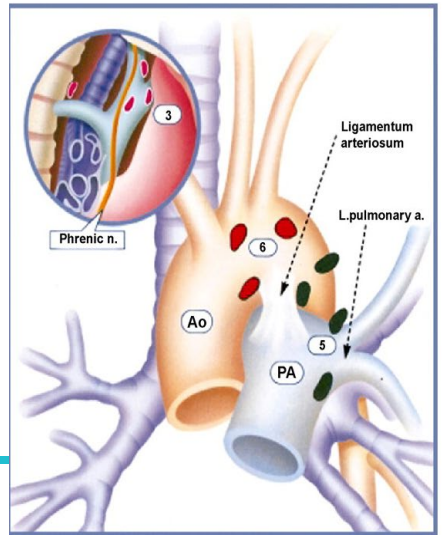
- Example: **Lung**

N1 ipsilateral peribronchial and/or hilar and intrapulmonary nodes

N2 ipsilateral mediastinal and/or subcarinal nodes

N3 contralateral mediastinal, hilar, scalene or supraclavicular nodes





Superior Mediastinal Nodes

- 1 Highest Mediastinal
- 2 Upper Paratracheal
- 3 Pre-vascular and Retrotracheal
- 4 Lower Paratracheal (including Azygos Nodes)

N_2=single digit, ipsilateral
N_3=single digit, contralateral or supraclavicular

Aortic Nodes

- 5 Subaortic (A-P window)
- 6 Para-aortic (ascending aorta or phrenic

Inferior Mediastinal Nodes

- 7 Subcarinal
- 8 Paraesophageal (below carina)
- 9 Pulmonary Ligament

N_1 Nodes

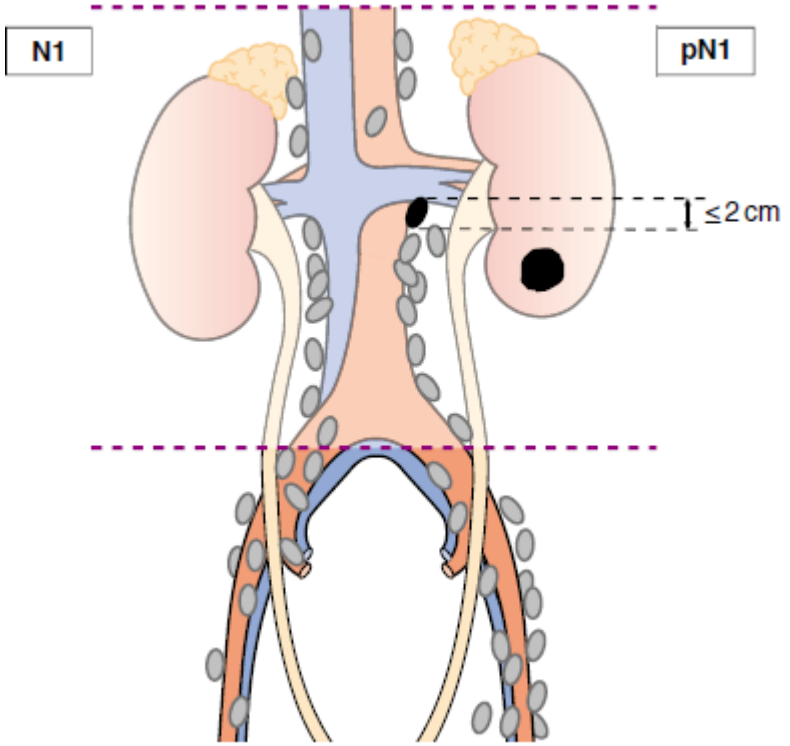
- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Example N-category based on size and number

- Example: **Renal pelvis and ureter**

  N1 single node, 2 cm or less

  N2 single node >2 cm or multiple nodes



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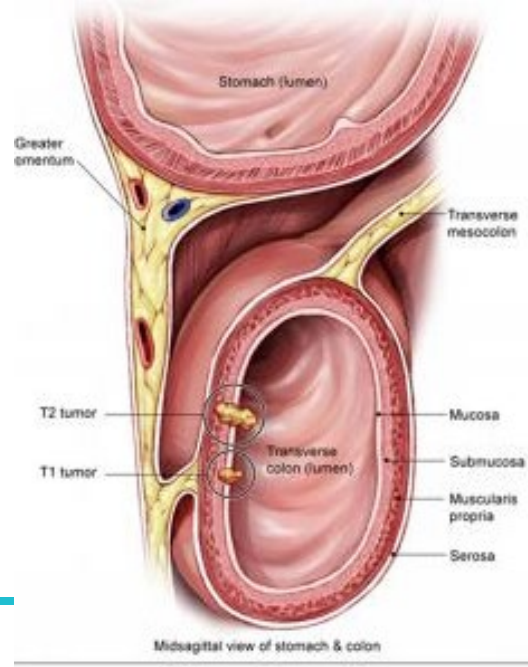
The General Rules of the TNM system: pN

- Pathological assessment of lymph nodes ideally requires -but is not limited to- the resection of a minimum number of nodes
  - Is specific for every tumour site, e.g. breast: 6 or more, colorectal 12 or more etc.
  - If less than the expected number resected, the N category is still assigned by the same criteria as if the expected number of nodes were assessed
- Examination of a single node without pathological examination of the primary is considered a biopsy and should be classified as 'clinical'=>cN
- It is *not* necessary to pathologically confirm the status of the highest N category to assign the pN (TNM 8th edition rule)

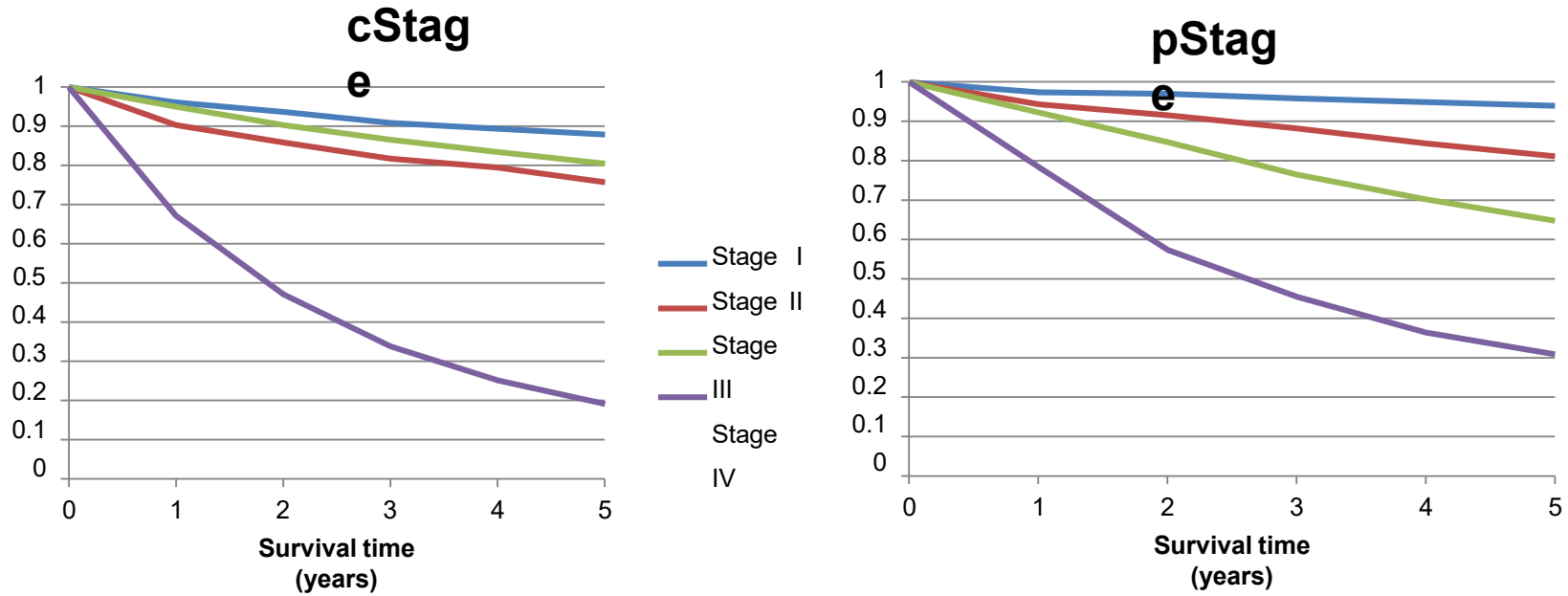
Example pN

- A 49 year old man undergoes a sigmoid colectomy for a cancer
- The tumour invades into the muscularis propria (T2)
- None out of 9 identified lymph nodes contain metastases
  - 12 is the number of nodes ordinarily to be included
    - pT2 pN0 (not NX although only 9 nodes resected)
    - Best annotation: pT2 pN0 (0/9)



Primary Tumor (*T*)
T1 or T2

Rectal cancer: c Stage and p Stage



Example: c- and p-Stage for Rectal cancer
5-year relative survival, 2009-2013, Belgium

N-category: cN and pN

- Most pN categories correspond to the cN categories
  - Exceptions (= different cN and pN categories)
    - Head and neck tumours
    - Skin carcinoma of the head and neck
    - Breast cancer
    - Merkel cell carcinoma
    - Penis
    - Testis

N-category: oral cavity cN and pN definitions

N – Regional Lymph Nodes

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
- N2 Metastasis described as:
  - N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
  - N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
  - N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
- N3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
- N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

Notes

* The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extranodal extension.

Midline nodes are considered ipsilateral nodes.

pN – Regional Lymph Nodes

- pNX Regional lymph nodes cannot be assessed
- pN0 No regional lymph node metastasis
- pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
- pN2 Metastasis described as:
  - pN2a Metastasis in a single ipsilateral lymph node, less than 3 cm in greatest dimension with extranodal extension or, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
  - pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
  - pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
- pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
- pN3b Metastasis in a lymph node more than 3 cm in greatest dimension with extranodal extension or, multiple ipsilateral, or any contralateral or bilateral node(s) with extranodal extension

Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

The General Rules of the TNM System: sentinel node

- The sentinel lymph node is the first lymph node to receive lymphatic drainage from a primary tumour.
  - it can be detected by a variety of techniques
  - can be biopsied

- If it contains metastatic tumour => other lymph nodes may contain tumour and a node dissection may be warranted.

- If it does not contain metastatic tumour => other lymph nodes not likely to contain tumour, then a lymph node dissection is not necessary.

The General Rules of the TNM System

Sentinel node

NX (sn)	Sentinel lymph node could not be assessed
N0 (sn)	No sentinel lymph node metastasis
N1 (sn)	Sentinel lymph node metastasis

Excisional biopsy of a sentinel node, in the absence of assignment of a pT, is classified as a clinical N,

e. g. cN1(sn)

pN is used for sentinel node biopsy only in conjunction with a pathological T assignment

M-category

The General Rules of the TNM system: cM category

- **cM0** No distant metastasis
- **cM1** Distant metastasis

  M1 subcategories are rare

  - example: prostate
    - M1a non-regional lymph nodes
    - M1b bone(s)
    - M1c other site(s)

    In case of multiple metastatic sites: most advanced category is used. Highest value: M1c

- **Note**
  - the **cMX category is considered to be inappropriate** as clinical assessment of metastasis can be based on physical examination alone.
  - General examination is enough: *assume cM0* unless there is definite evidence of metastatic disease

The General Rules of the TNM system: pM category

- **pM1** Distant metastasis microscopically confirmed
- Note: pM0 and pMX are NOT valid categories.

The General Rules of the TNM system: Use of X

X

is used only when either the T category or the N category can not be assessed

example:
a thyroid cancer when there are no nodes identified in a thyroidectomy specimen: pNX is appropriate

The General Rules of the TNM System: Use of X

X

- Should be used as little as possible
  - Because frequently no assignment of a stage group will be possible…
  - Except when distant metastases (c/pM1) are present

- Do not use X when in doubt about T or N or M: chose the lower, i.e. less advanced category

TNM

https://www.uicc.org/resources/tnm

TNM Classification of Malignant Tumours

- TNM Project Structure
- Publications and Resources
- E-learning
- Helpdesk
- Essential TNM

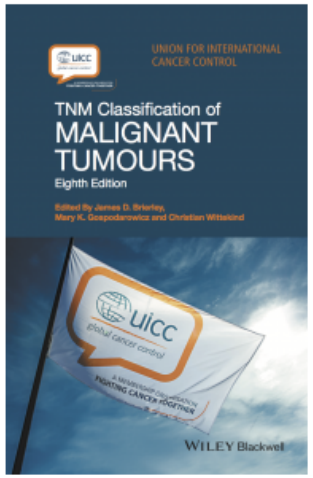
Cancer Atlas

UICC Journals

IARC Cancer Today

Cancer and COVID-19 resources

What is the TNM cancer staging system?



The *TNM Classification* of Malignant Tumors (TNM) is a globally recognised standard for classifying the extent of spread of cancer.

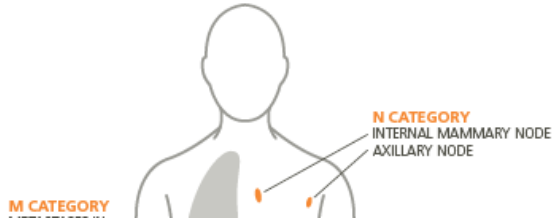
The classification of cancer by anatomic disease extent, i.e. stage, is the major determinant of appropriate treatment and prognosis. Stage is an increasingly important component of cancer surveillance and cancer control and an endpoint for the evaluation of the population-based screening and early detection efforts.

The UICC has published the UICC TNM classification of malignant tumors for over 50 years. **The UICC TNM classification is the internationally accepted standard for cancer staging.**

The UICC TNM Classification is an anatomically based system that records the primary and regional nodal extent of the tumor and the absence or presence of metastases.

What does TNM stand for?

Each individual aspect of TNM is termed as a category:



TNM Classification of Malignant Tumours

- Global Advisory Group
- Groups and panel
- Publications and Resources
- E-learning
- Helpdesk

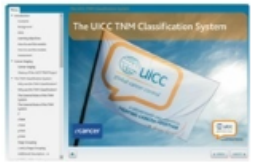
Cancer Atlas

UICC Journals

IARC Cancer Today

E-learning

UICC TNM E-Learning Modules



eCancer and UICC jointly produced a set of 7 modules on TNM staging for the purpose of educating and informing the global cancer community on the globally accepted classification of malignant tumours.

The following modules are now available to download:

- Module 1: Introduction to the UICC TNM Classification System
- Module 2: UICC TNM Breast Cancer Classification
- Module 3: UICC TNM Prostate Cancer Classification
- Module 4: UICC TNM Colorectal Cancer Classification
- Module 5: UICC TNM Cervix Cancer Classification
- Module 6: UICC TNM Lip and Oral Cavity Cancer Classification
- Module 7: UICC TNM Lung Cancer Classification

In French: TNM e-Modules en français

- Module: l'introduction à la classification TNM
- Module: Le système de classification TNM de l'UICC

Each module takes approximately 30 minutes to complete and includes a voice-over and interactive quiz.

By the end of each module, users should:

- know the general principles of the UICC TNM Classification of Malignant Tumours,
- understand the structure of the UICC TNM Classification 8th edition and
- be able to apply the UICC TNM Classification to different cancer sites

Learn more about eCancer.

Short educational videos: Cancer Staging Series

Watch this short video series produced in collaboration with Princess Margaret Cancer Centre to learn what cancer staging is, its importance for patients, research and cancer control, and the terminology used in

1. Importance of Cancer Staging
2. What is Cancer Stage
3. General Rules for Cancer Staging
4. Cancer Staging Examples
5. Staging Terminology
6. Importance of Common Stage Language
7. Why stage language changes and how this affects usage
8. Essential TNM

TNM Help desk

TNM Classification of Malignant Tumours
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Cancer Atlas

UICC Journals

IARC Cancer Today

Please download the FAQ's page for answers to your questions on cancer staging. If you do not find the answer to your question, complete the form and send it to the TNM help desk. Please fill in all fields.

I am a *
– Select –

Title *
Dr

First name *

Last name *

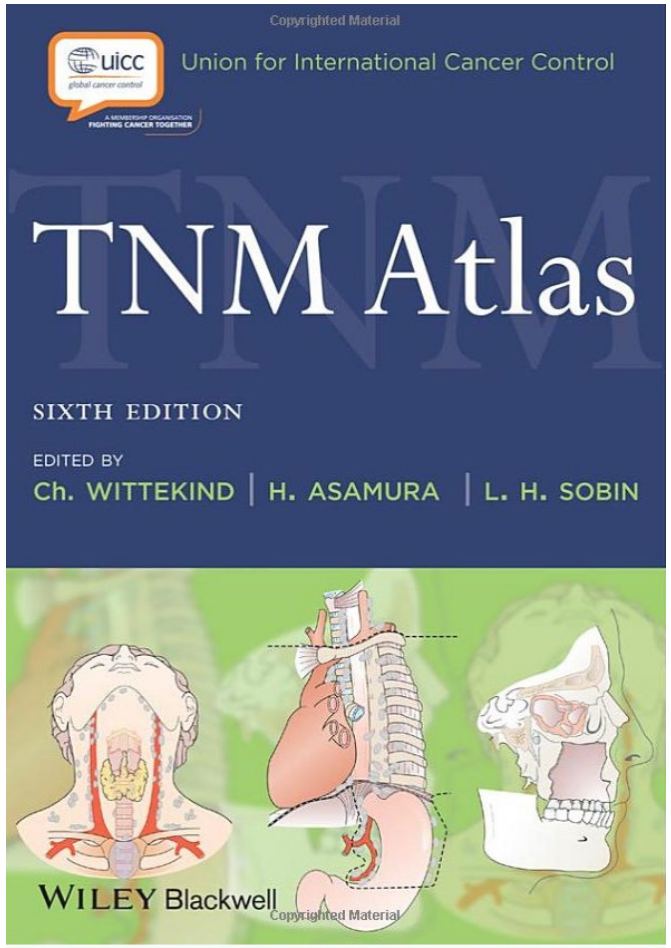
Organization *

Country *
- Select -

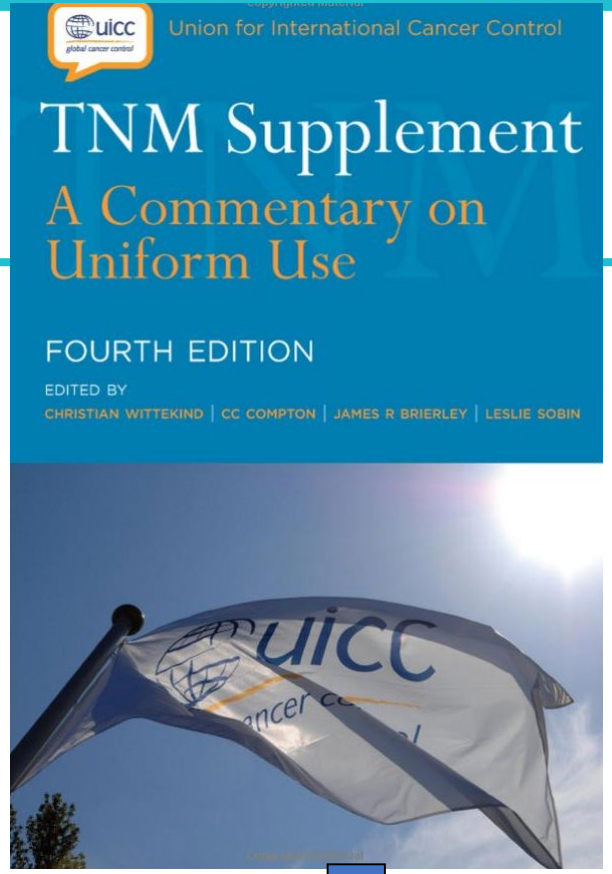
Email *

My TNM question *

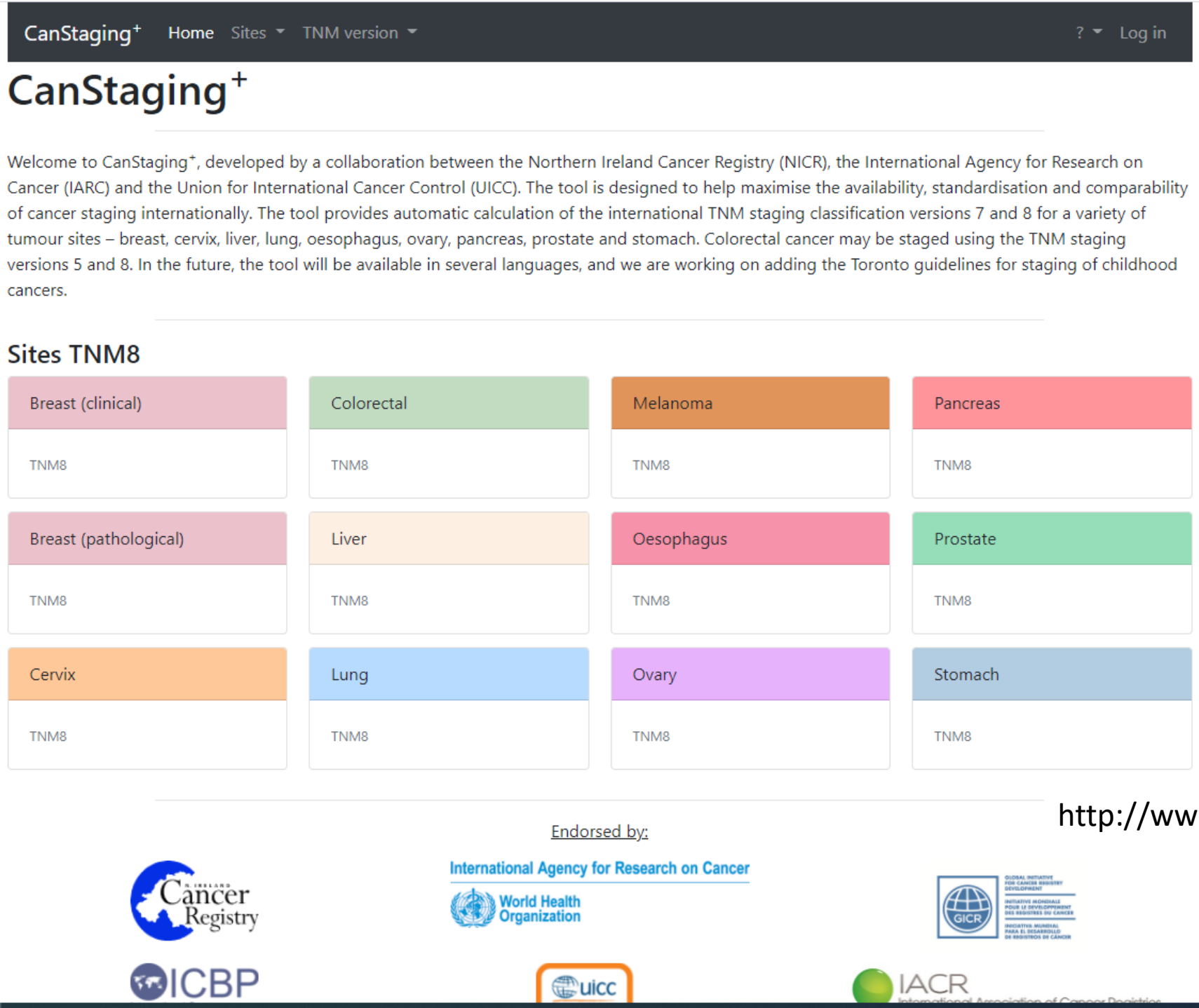
Acceptance of use of data and our privacy policy



Upcoming new edition related to the 8th edition TNM classification, **Summer 2021**



TNM Supplement, 5th edition related to the 8th edition TNM classification, 2019



http://www.canstaging.org/tool

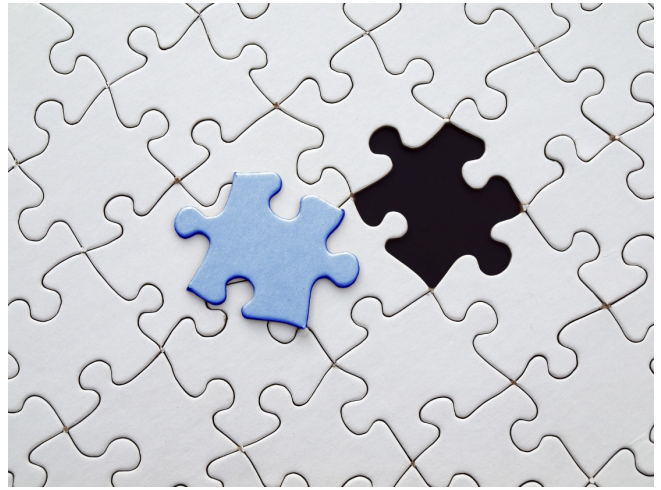
Europe
of Canc

Take home messages for Cancer Registries

1. Stage is a very important **prognostic factor** and should be included in population based cancer registration
2. Use the existing international **TNM classification** and **Paediatric Cancer Stage**
3. Apply the **general rules** of the TNM classification and the Toronto Paediatric Cancer Stage Guidelines
4. Whenever possible, **register cTNM and (y)pTNM**
   - Training is needed for data managers according to the registration method: from understanding TNM to active applying TNM
   - CanStaging+ Tool could be a useful tool to facilitate TNM registration
   - Close collaboration with clinicians is recommended
   - Validation and consistency checks needed, avoid 'X' (and missing stages) as much as possible
5. If resources are very limited in cancer registration, use the 'Essential TNM'

- Exercises general principles

https://create.kahoot.it/share/general-exercises/e1e462ac-009e-4865-ab53-af44c198468c



Coding stage: Session 2

Toronto Paediatric Cancer Stage Guidelines

Liesbet Van Eycken

Paediatric cancer and Stage information

- Adult cancers
  - Main method of staging = TNM classification (UICC/AJCC)

- Childhood cancers
  - Heterogeneous, rare, biologically different to adult cancers
  - TNM not applicable or not existing for most paediatric cancers
  - Mostly staged by disease-specific staging systems
    - Different systems for the same disease
    - Differences between countries

- Need for consistency in collection of staging data
  → Facilitate international comparisons and studies

Toronto Consensus Meeting

- October 2014 in Toronto, Canada
- 26 international experts (from 17 countries, 6 continents)
  - Variety in expert fields, geography, resource settings
- Tiered staging system with adaptations for low-income countries (fewer resources, limited/no advanced imaging)
  - Tier 1: for registries with limited resources
  - Tier 2: for well-resourced cancer registries
  - Tier 3: optional additional prognostic factors
- Recommendations for staging systems to be used by cancer registries for 18 major childhood malignancies

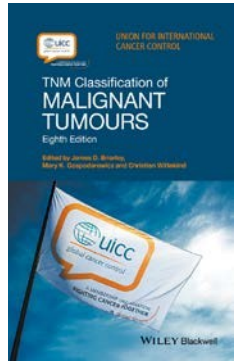
Toronto Paediatric Cancer Stage Guidelines

- Published in: Lancet Oncol 2016;17: 163–72

Paediatric cancer stage in population-based cancer registries: the Toronto consensus principles and guidelines

Sumit Gupta, Joanne F Aitken, Ute Bartels, James Brierley, Mae Dolendo, Paola Friedrich, Soad Fuentes-Alabi, Claudia P Garrido, Gemma Gatta, Mary Gospodarowicz, Thomas Gross, Scott C Howard, Elizabeth Molyneux, Florencia Moreno, Jason D Pole, Kathy Pritchard-Jones, Oscar Ramirez, Lynn A G Ries, Carlos Rodriguez-Galindo, Hee Young Shin, Eva Steliarova-Foucher, Lillian Sung, Eddy Supriyadi, Rajaraman Swaminathan, Julie Torode, Tushar Vora, Tezer Kutluk, A Lindsay Frazier

- Endorsed by the UICC and included in the TNM 8th edition
- Endorsed by ENCR, IACR



- 2nd Consensus meeting, Lyon, 21st of October 2019

Publication Lancet Oncol 2020; 21:e444-51 Gupta S et al

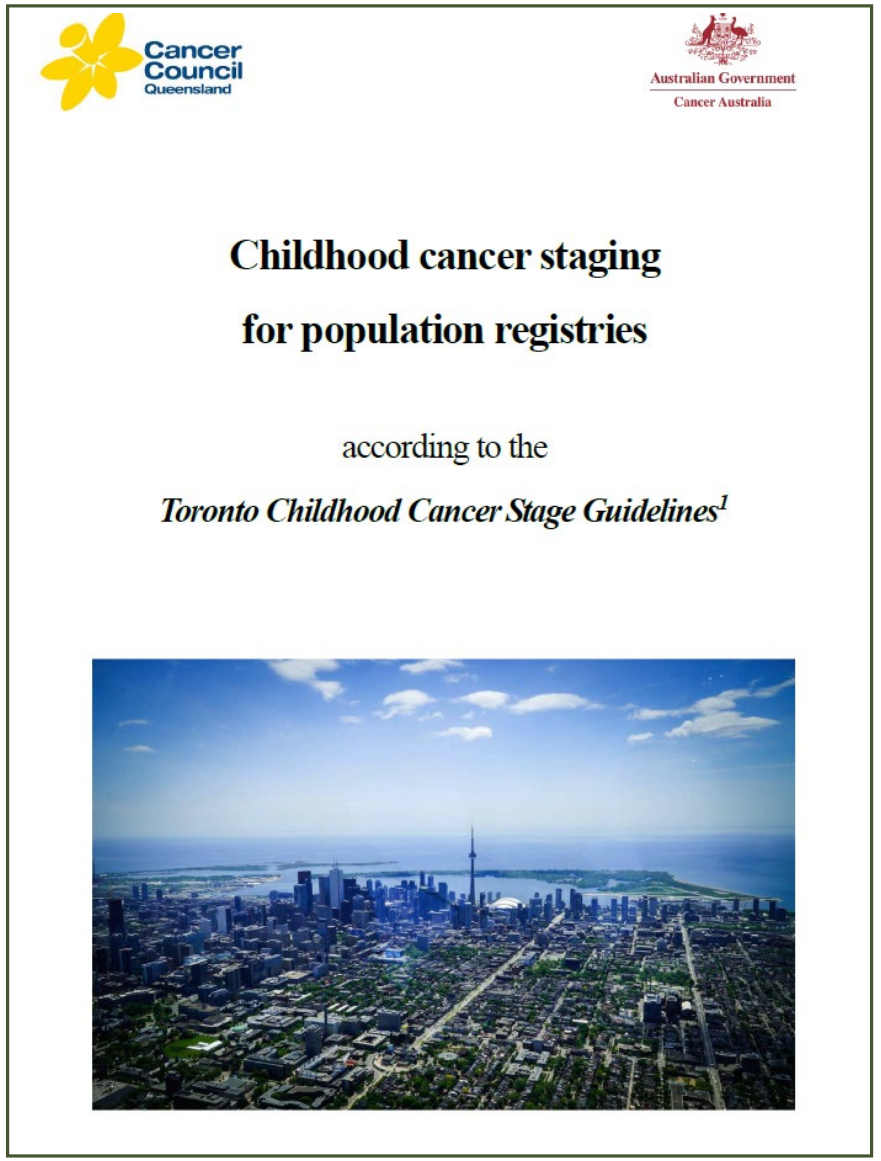
Development of paediatric non-stage prognosticator guidelines for population- based cancer registries and updates to the 2014 Toronto Paediatric Cancer Stage Guidelines

Staging systems recommended for 16 childhood malignancies	
Acute lymphoid leukaemia	Osteosarcoma
Acute myeloid leukaemia	Ewings sarcoma
Hodgkin lymphoma	Retinoblastoma
Non-Hodgkin lymphoma	Hepatoblastoma
Neuroblastoma	Testicular germ cell tumours
Wilms tumour	Ovarian germ cell tumours
Rhabdomyosarcoma	Medulloblastoma
Non-rhabdomyosarcoma soft tissue sarcoma	Ependymoma

The Toronto Paediatric Cancer Stage Guidelines have been expanded into clear staging rules for registries

- available on International Association of Cancer Registries website.

All population cancer registries can use these rules to assign childhood cancer stage in the same way.



Content Paediatric Tumours (TNM 8th edition UICC)

- Gastro-intestinal Tumours
  - Hepatoblastoma: Tier 1 and 2
- Bone and Soft Tissue Tumours
  - Osteosarcoma Tier 1 and 2
  - Ewing Sarcoma Tier 1 and 2
  - Rhabdomyosarcoma Tier 1 and Tier 2 (modified TNM)
  - Soft Tissue Sarcoma other than Rhabdomyosarcoma: Tier 1 and 2 (TNM)
- Gynaecologic Tumours: Ovary Tier 1 and Tier 2 (TNM-FIGO)
- Urological Tumours
  - Wilms Tumour Tier 1 and Tier 2 (2 Tier 2 systems: 1 after surgical resection prior to chemo, SIOP if preop chemo)
- Ophtalmic Tumours
  - Retinoblastoma Tier 1 and Tier 2 (determined after enucleation = pathologic classification)/ IRSS (Internat. Class for Intraocular RB)
- Malignant Lymphoma
  - Hodgkin Lymphoma
  - Non Hodgkin Lymphoma Tier 1 and Tier 2 St Jude/Murphy system
- Central Nervous System
  - Medulloblastoma and Ependymoma Tier 1 and Tier 2
  - Neuroblastoma Tier 1 and Tier 2 (International Neuroblastoma Risk Group Staging System (INRGSS)

General rules of Paediatric Cancer Stage

- Stage reflects extent of disease at diagnosis (except for Wilms tumour)
- Metastases are assessed at diagnosis for all cancers
- If the medical record is complete, but there is no mention of a data item in the record, it is assumed to be negative/absent
- For malignancies where the TNM staging system is recommended, refer to the TNM general rules

Paediatric tumours: Hepatoblastoma

- **Tier 1 and 2**
  - Metastatic: distant metastasis present
  - Localised: Tumour confined to the liver including regional lymph nodes

  - Paediatric Oncology: 'Pretext classification'
    - Will become tier 2

Paediatric cancer: Rhabdomyosarcoma

Tier 1

Metastatic	Distant metastases present
Localized	Tumour confined to the area of origin including regional lymph nodes

Prognostic Grouping

The prognostic grouping for rhabdomyosarcoma includes favourable anatomic sites and unfavourable anatomic sites.

Favourable anatomic sites: Orbit, head and neck(excluding parameningeal tumours) and genitourinary sites (excluding bladder and prostate tumours)

Unfavourable anatomic sites: Bladder, prostate, extremity, cranial, parameningeal, trunk, retroperitoneum and all other sites not noted as favourable

Stage I	Any T	Any N	M0	Favourable Site
Stage II	T1a, T2a	N0	M0	Unfavourable Site
Stage III	T1a, T2a	N1	M0	Unfavourable Site
	T1b, T2b	Any N	M0	Unfavourable Site
Stage IV	Any T	Any N	M1	Any Site

Tier 2

A modified TNM Clinical Classification with the addition of favourable or non-favourable tumour site.

T – Primary Tumour*

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Confined to a single anatomic site
T1a	Tumour 5 cm or less in greatest dimension
T1b	Tumour more than 5 cm in greatest dimension
T2	Extension beyond anatomic site
T2a	Tumour 5 cm or less in greatest dimension
T2b	Tumour more than 5 cm in greatest dimension

N – Regional Lymph Nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

	Tier 1 staging system	Tier 2 staging system
ALL	CNS neg/ pos	CNS 1/ 2/ 3
AML	CNS neg/ pos	CNS neg/ pos
CML	(none)	(none)
Hodgkin's lymphoma	Ann Arbor stage I/ II/ III/ IV A/ B	Ann Arbor stage I/ II/ III/ IV A/ B
Non-Hodgkin lymphoma	Limited/Advanced	St Jude/Murphy stage I/ II/ III/ IV
Neuroblastoma	Localised/ Locoregional/ Metastatic/ INRGSS - MS disease	INRGSS - Localised L1/ Locoregional L2/ Metastatic M/ MS disease
Wilms' tumour	Localised/ Metastatic	NWTSG or SIOP stage I/ II/ III/ IV
Rhabdomyosarcoma	Localised/ Metastatic	TNM stage I/ II/ III/ IV
Non-rhabdomyosarcoma soft-tissue sarcomas	Localised/ Metastatic	TNM stage I/ II/ III/ IV
Osteosarcoma	Localised/ Metastatic	Localised/ Metastatic
Ewing's sarcoma	Localised/ Metastatic	Localised/ Metastatic
Retinoblastoma	Localised (intraocular) / Regional (orbital or regional lymph nodes) / Distant (extra-orbital)	IRSS stage 0/ I/ II/ III/ IV
Hepatoblastoma	Localised/ Metastatic	Localised/ Metastatic
Testicular	Localised/ Regional/ Metastatic	TNM stage I/ II/ III
Ovarian	Localised/ Regional/ Metastatic	FIGO stage I/ II/ III/ IV
Astrocytomas	(none)	(none)
Medulloblastoma and other CNS embryonal tumours	M0 or localised/ M+ or metastatic	M0/ 1/ 2/ 3/ 4
Ependymoma	M0/ M+	M0/ 1/ 2/ 3/ 4

TNM 8th edition and Paediatric Tumours

- ALL and AML: Stage not published in the TNM booklet

- Neuroblastoma Tier 2 is not specified in the TNM booklet
- INRGSS: International Neuroblastoma Risk Group Staging System

  Stage L1: Locoregional tumor without Imaging derived risk factors (IDRFs)

  Stage L2: Locoregional tumor with one or more IDRFs

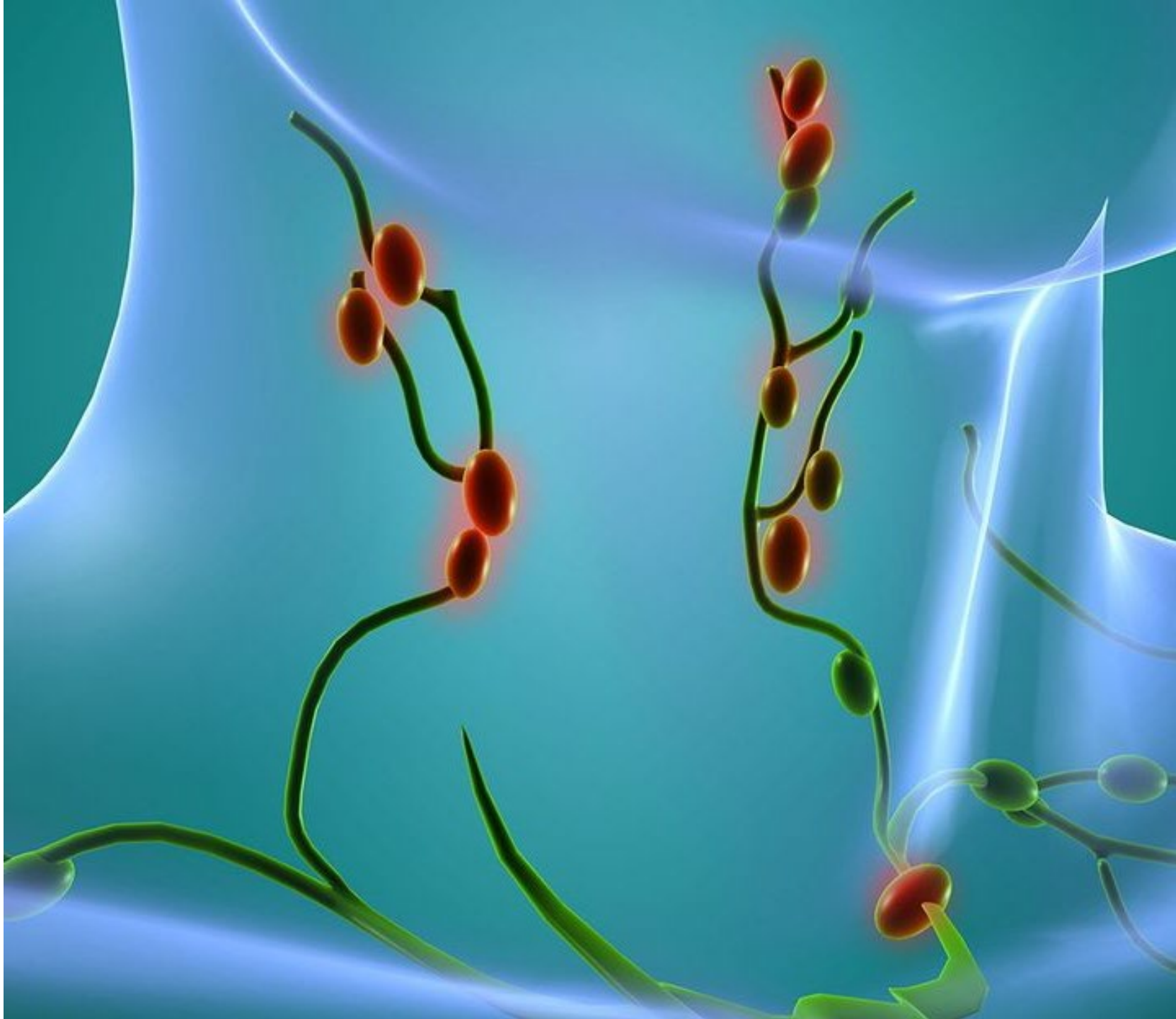
  Stage M: Distant metastatic disease (except Ms)

  Stage Ms: INRG Stage L1 or L2 tumor with metastatic disease confined to skin and/or liver and/or bone marrow

Hodgkin lymphoma

Staging requires assessment of:

- Number of nodal regions involved
- Number of extra-lymphatic organs or sites involved
- Anatomic location (above or below diaphragm)



Lymphatic regions above the diaphragm

1. Waldeyer's Ring
- Oropharynx (palatine tonsil)
- Nasopharynx (palatine tonsil)
- Adenoids
- Base of tongue (lingual tonsil)

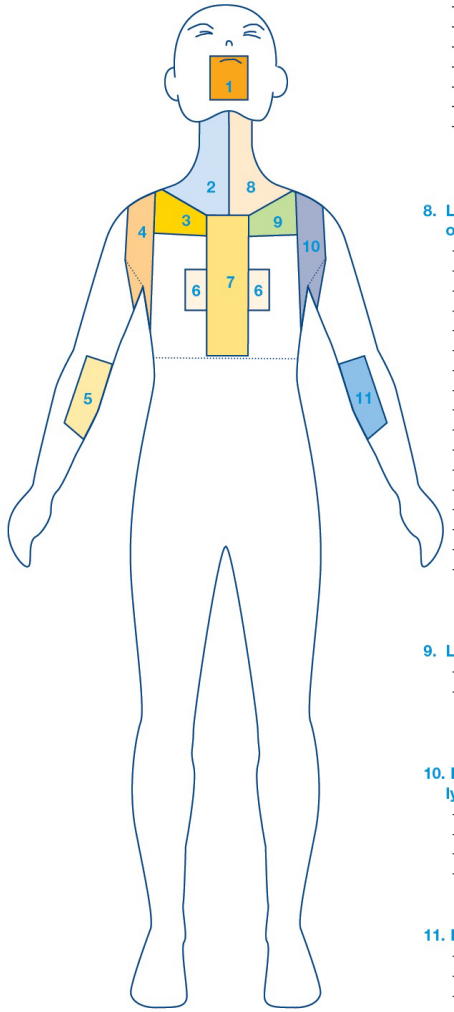
2. Right cervical, supraclavicular, occipital and pre-auricualar
- R Auricular lymph node
- R Cervical lymph node
- R Facial lymph node
- R Jugular lymph node
- R Mandibular lymph node
- R Occipital lymph node
- R Parotid lymph node
- R Preauricular lymph node
- R Prelaryngeal lymph node
- R Pretracheal lymph node
- R Retropharyngeal lymph node
- R Scalene lymph node
- R Sublingual lymph node
- R Submandibular lymph node
- R Submaxillary lymph node
- R Submental lymph node
- R Supraclavicular lymph node

3. Right infraclavicular
- R Infraclavicular lymph node
- R Subclavicular lymph node

4. Right axillary and pectoral lymph nodes
- R Axillary lymph node
- R Pectoral lymph node
- R Subscapular lymph node
- R Internal mammary

5. Right epitrochlear and brachial
- R Brachial lymph node
- R Cubital lymph node
- R Epitrochlear lymph node

6. Hilar
- Bronchial lymph node
- Bronchopulmonary lymph node
- Hilar lymph node
- Pulmonary hilar lymph node



7. Mediastinal
- Diaphragmatic lymph node
- Esophageal lymph node
- Innominate lymph node
- Intercostal lymph node
- Mediastinal lymph node
- Parasternal lymph node
- Paratrachael lymph node
- Peritrachael lymph node
- Pulmonary lymph node, NOS
- Thoracic lymph node
- Tracheal lymph node
- Tracheobronchial lymph node
- Subaortic lymph node (para-aortic)

8. Left cervical, supraclavicular, occipital and pre-auricualar
- L Auricular lymph node
- L Cervical lymph node
- L Facial lymph node
- L Jugular lymph node
- L Mandibular lymph node
- L Occipital lymph node
- L Parotid lymph node
- L Preauricular lymph node
- L Prelaryngeal lymph node
- L Pretracheal lymph node
- L Retropharyngeal lymph node
- L Scalene lymph node
- L Sublingual lymph node
- L Submandibular lymph node
- L Submaxillary lymph node
- L Submental lymph node
- L Supraclavicular lymph node

9. Left infraclavicular
- L Infraclavicular lymph node
- L Subclavicular lymph node

10. Left axillary and pectoral lymph nodes
- L Axillary lymph node
- L Pectoral lymph node
- L Subscapular lymph node
- L Internal mammary

11. Left epitrochlear and brachial
- L Brachial lymph node
- L Cubital lymph node
- L Epitrochlear lymph node

Lymphatic regions below the diaphragm

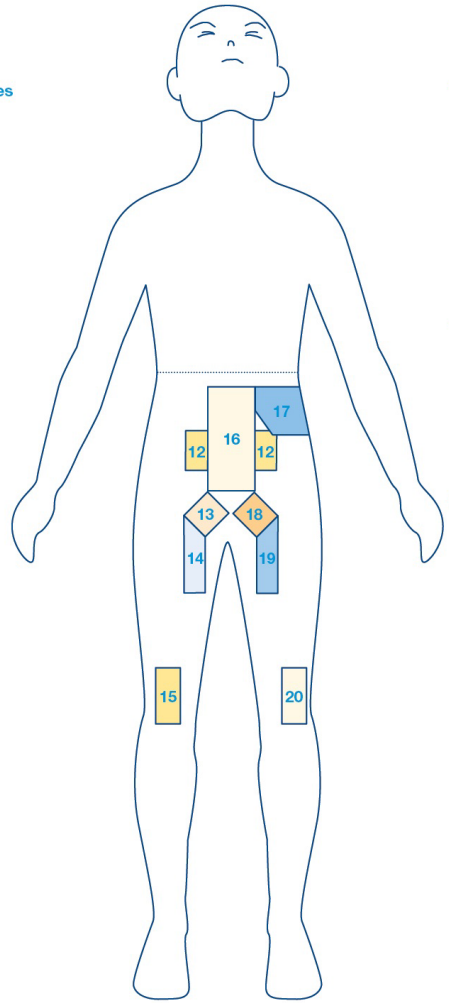
12. Mesenteric
- Abdominal lymph node
- Colic lymph node
- Gastric lymph node
- Ileocolic lymph node
- Inferior mesenteric lymph node
- Intestinal lymph node
- Mesenteric lymph node
- Midcolic lymph node
- Superior mesenteric lymph node

13. Right pelvic and iliac lymph nodes
- R Hypogastric lymph node
- R Internal iliac
- R Inferior epigastric lymph node (External iliac)
- R Intrapelvic lymph node
- R Obturator lymph node
- R Paracervical lymph node
- R Parametrial lymph node
- R Presymphysial lymph node
- R Sacral lymph node

14. Right inguinal and femoral
- R Femoral lymph node
- R Inguinal lymph node
- R Lymph node of Cloquet
- R Lymph node of groin
- R Lymph node of lower limb
- R Lymph node of Rosenmuller
- R Subinguinal lymph node

15. Right popliteal
- R Popliteal lymph node
- R Tibial lymph node

16. Paraaortic
- Aortic lymph node
- Celiac lymph node
- Lumbar lymph node
- Pancreatic lymph node
- Para-aortic lymph node
- Peri-aortic lymph node
- Peripancreatic lymph node
- Pyloric lymph node
- Retroperitoneal lymph node
- Common duct lymph node
- Hepatic lymph node
- Porta hepatic lymph node
- Portal lymph node



17. Splenic and splenic hilar
- Spleen
- Splenic lymph node, NOS
- Splenic hilar lymph node

18. Left pelvic and iliac lymph nodes
- L Hypogastric lymph node
- L Internal iliac
- L Inferior epigastric lymph node (External iliac)
- L Intrapelvic lymph node
- L Obturator lymph node
- L Paracervical lymph node
- L Parametrial lymph node
- L Presymphysial lymph node
- L Sacral lymph node

19. Left inguinal and femoral
- L Femoral lymph node
- L Inguinal lymph node
- L Lymph node of Cloquet
- L Lymph node of groin
- L Lymph node of lower limb
- L Lymph node of Rosenmuller
- L Subinguinal lymph node

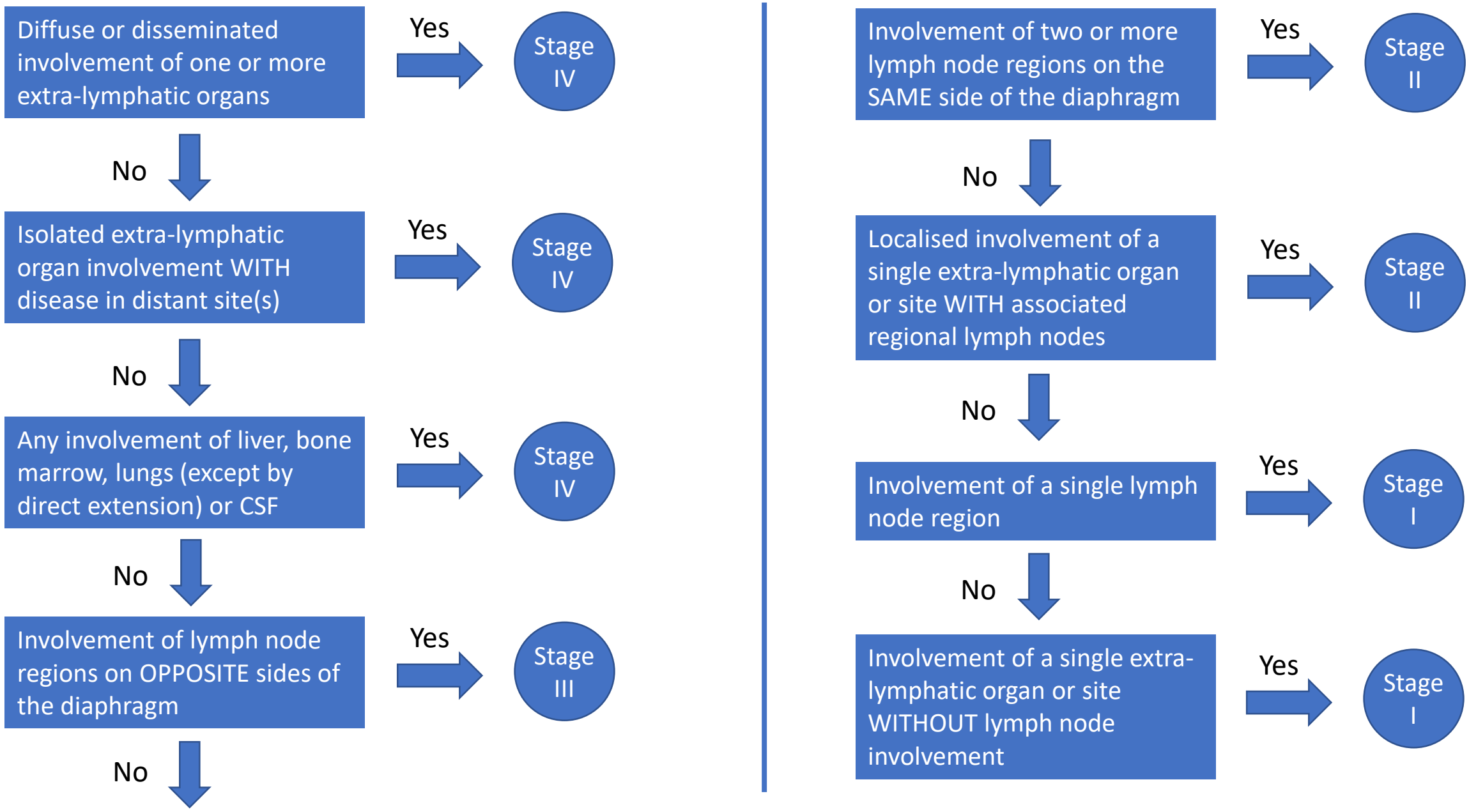
20. Left popliteal
- L Popliteal lymph node
- L Tibial lymph node

Hodgkin lymphoma

Constitutional symptoms

- Suffix A = no constitutional symptoms
- Suffix B = constitutional symptom recorded
- Constitutional symptoms include:
  - Fevers (>38C/100.4F)
  - Drenching night sweats
  - Unexplained weight loss (>10%)

Hodgkin lymphoma



Hodgkin lymphoma

Example

Pathology report

Site	Involvement
Cervical lymph nodes, left	Involvement +
Site	Involvement
Cervical lymph nodes, right	Involvement +
Site	Involvement
Mediastinal lymph nodes	Involvement +

Doctors' notes

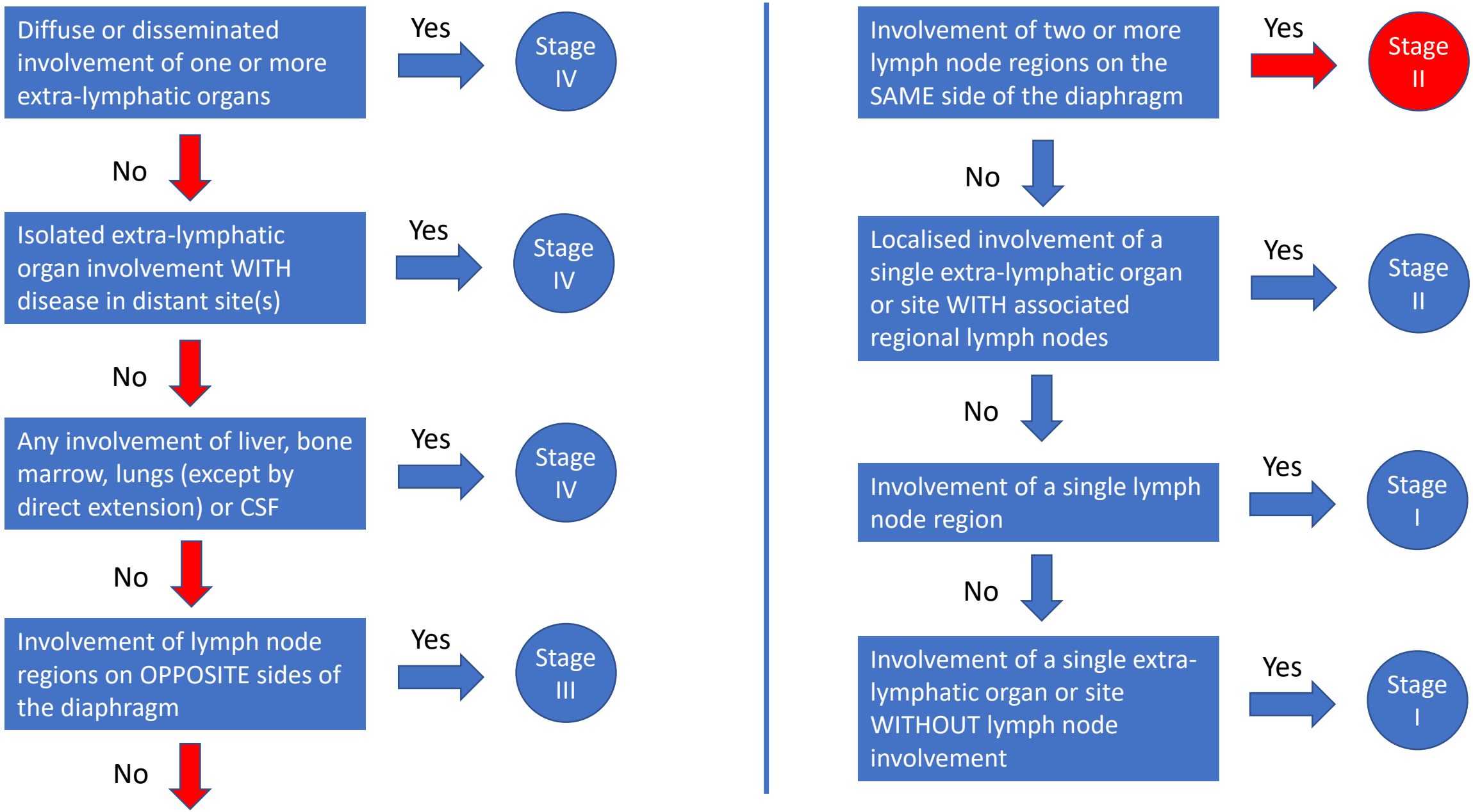
Involvement of liver, bone marrow, lung or CSF

None

Constitutional symptoms

· Absent

Hodgkin lymphoma



Conclusions

- Recording stage in a cancer registry
  - Offers specific information for Public Health/ surveillance and oncology objectives
  - Needs validation and consistency checks
  - Invites to work on ‘comparability’
  - But also has to tackle difficulties… complexity, missing data, diagnostic precision differences, versions and updates…

Supplementary slides

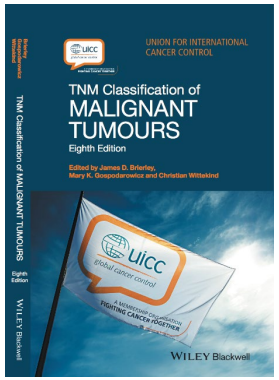
- Objectives and History TNM
- General rules TNM
  - ycTNM – ypTNM
  - LVI: lymphovascular invasion
  - ITC: isolated tumour cells
- Other staging systems

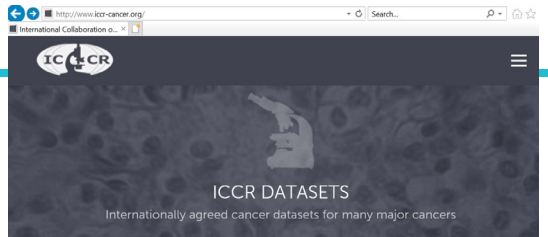
The Objectives of Staging

- To aid in the planning of treatment
- To give some indication of prognosis
- To assist in evaluation of the results of treatment
- To facilitate the exchange of information and aid research
- To contribute to research
- **To support cancer control activities**

History TNM

- **1943-1952 TNM** developed by Pierre Denoix (France)
- 1968 International Union Against Cancer (UICC): TNM classification of Malignant Tumours
- 1969 UICC TNM General rules
- **1974 UICC TNM Classification of Malignant Tumours, 2nd edition**
- **1978 UICC TNM Classification of Malignant Tumours, 3rd edition**
- 1982 UICC TNM Classification of Malignant Tumours, revised 3rd edition
- **1987 UICC TNM Classification of Malignant Tumours, 4th edition**
- 1992 UICC TNM Classification of Malignant Tumours, revised 4th edition
- **1997 UICC TNM Classification of Malignant Tumours, 5th edition**
- **2002 UICC TNM Classification of Malignant Tumours, 6th edition**
- **2009 UICC TNM Classification of Malignant Tumours, 7th edition**
- *2016 UICC TNM Classification of Malignant Tumours, 8th edition* ***(effective as from 2017)***
  - ***Some registries as from 2018 (e.g. US)***





Additional descriptor: prefix ‘y’

In those cases in which classification is performed during or following neo-adjuvant, the cTNM or pTNM category is identified by a **y** prefix.

The **y**cTNM or **y**pTNM categorizes the extent of tumour actually present at the time of that examination.

Example:

ycTNM: **clinical** evaluation after neo-adjuvant chemoradiotherapy for rectal cancer

ypTNM: **pathological** evaluation after neo-adjuvant chemoradiotherapy for rectal cancer

The General Rules of the TNM System: ycTNM - ypTNM

y Symbol - Classifying Treated Tumours

The ypTNM classification deals with the pathological evaluation of the extent of cancer after neoadjuvant therapy. Therefore, the ypTNM should consider only viable tumour cells and not signs of regressed tumour tissue such as necrotic cell, mucin, debris, scars, etc.

The General Rules of the TNM System: optional descriptors

Additional descriptors

V venous invasion

L lymphatic invasion

Pn perineural invasion

- L – Lymphatic invasion
  - LX: lymphatic invasion cannot be assessed
  - L0: no lymphatic invasion
  - L1: lymphatic invasion
- V – Venous invasion
  - VX: venous invasion cannot be assessed
  - V0: no venous invasion
  - V1: venous invasion
- Pn – Perineural invasion
  - PX: perineural invasion cannot be assessed
  - P0: no perineural invasion
  - P1: perineural invasion

The General Rules of the TNM System: ITC

Isolated tumour cell - ITC

ITC may be found in lymph nodes or in metastatic sites including the bone marrow and non regional nodes

- Single tumor cell or Small clusters of cells not more than 0.2mm in size
- Small clusters of cells comprising fewer than 20 cells in a single cross section (Can be up to 200 in breast)

If found by immunohistochemical techniques or morphological techniques in all tumour sites (except Melanoma and Merkel cell ca) the **N-category 0 is applied**

The General Rules of the TNM System: cTNM

- The accuracy of the cTNM depends on…
  - the use/availability/sensitivity/extent of staging procedures used
- It is not necessary to assess the whole body by imaging before you can assign a cM
- General examination is enough: *assume cM0* unless there is definite evidence of metastatic disease

Other staging systems

- Extent of disease
- Dukes stage (obsolete)
- FIGO stage (almost equivalent to TNM)

- **Five main categories**
  - **In situ**
  - **Localized**
  - **Regional**
    - **to lymph nodes**
    - **by direct extension**
    - **to lymph nodes and direct extension**
  - **Distant**
  - **Unknown**

- Ann Arbor stage (lymphoma) => Modified: The Lugano Classification
- International Prognostic Scoring System (haematological malignancies)
- Condensed TNM (obsolete)

Condensed TNM - ENCR

- When T, and/or N, and/or M have not been explicitly recorded in the clinical/pathological records, the cancer registry should attempt to score extent of disease according to the **scheme**:
- **T**: L (localized) A (advanced) X (unspecified)
- **N**: 0 + X
- **M**: 0 + X

- Extent of disease:
  - Localized: TLN0M0
  - Local spread: TAN0M0
  - Regional spread: anyT/N+/M0
  - Metastatic: anyT/anyN/M+

- Use and utility?
- PLEASE: DO NOT USE THIS SYSTEM TO REGISTER THE STAGE OF THE TUMOUR !