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Upper GI Cancers

Presentation plan

1. Introduction
2. Epidemiology
3. Gastric cancer and pancreatic cancer
 - a. Risk factors
 - b. Symptoms
 - c. Location
 - d. Diagnosis
 - e. Histopathology
 - f. Staging
 - g. Treatment of early/localised disease
 - h. Treatment of metastatic disease
4. Oesophageal cancer

Upper GI Tract Cancers

Division according to localisation of the primary tumor:

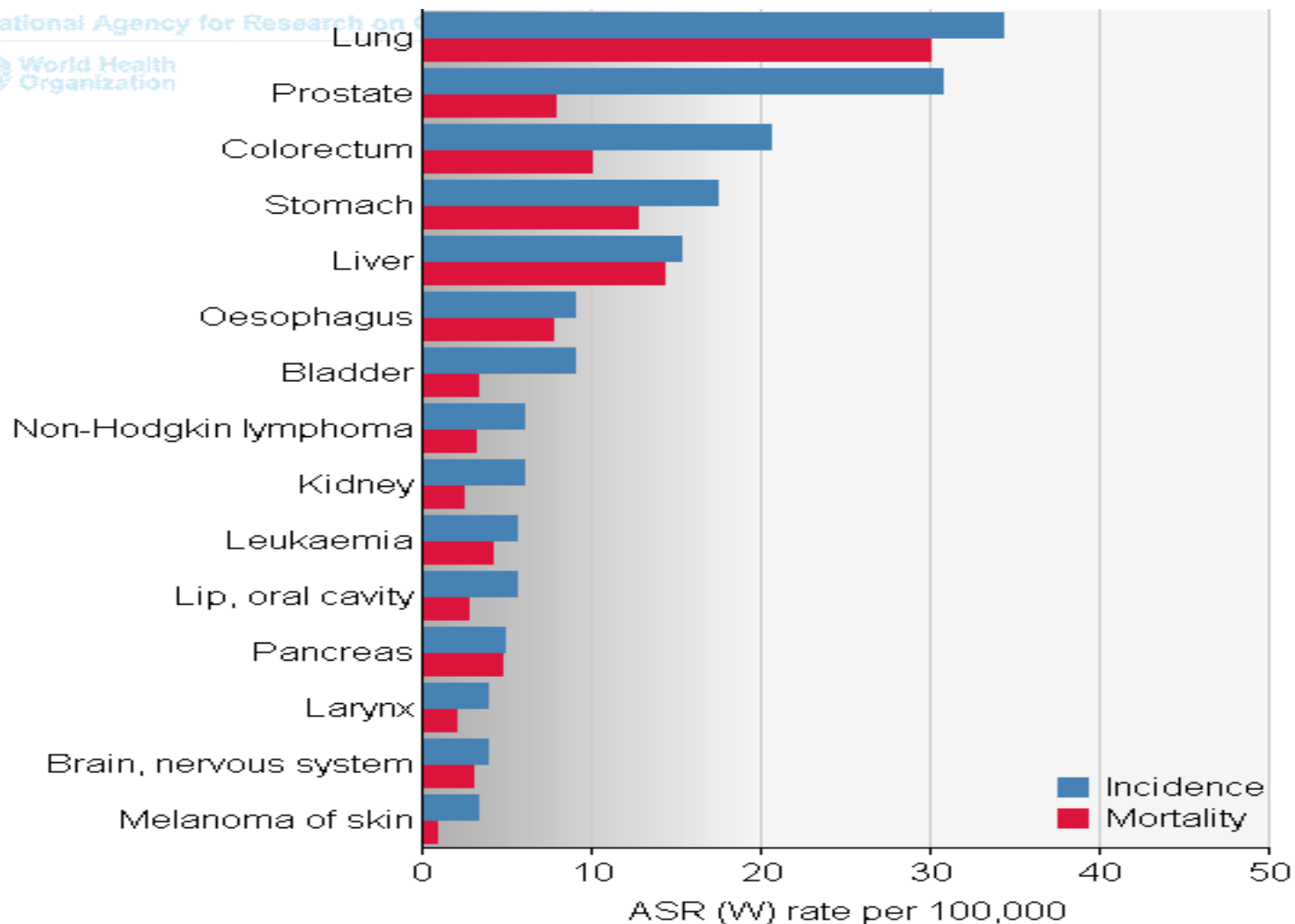
- **Gastric Cancer**
- **Pancreatic Cancer**
- **Oesophageal Cancer**
 - Biliary Cancer*
 - HCC*

Epidemiology

International Agency for Research on Cancer



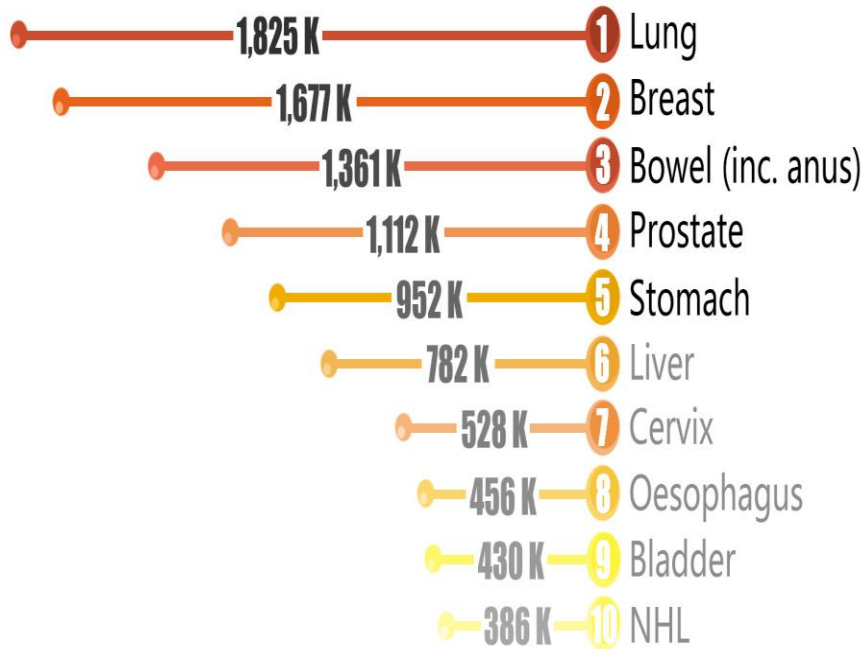
World Health Organization



Most Common Cancers Worldwide

[Cases per year]

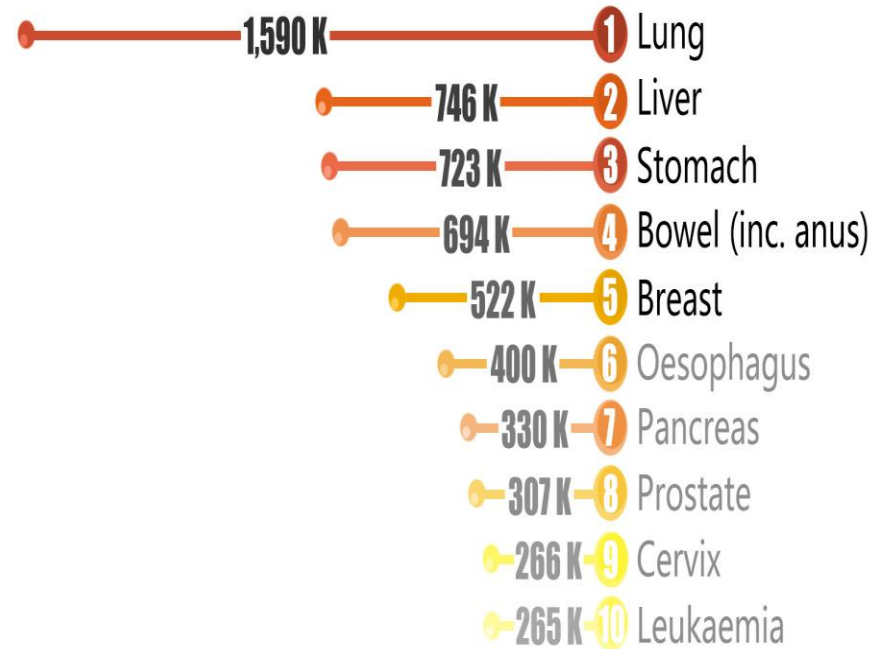
Total: **14.1** million



Most Common Causes of Cancer Death

[Deaths per year]

Total: **8.2** million



STOMACH/PANCREAS

GASTRIC CANCER

- **Decline in incidence**
(Western Europe, North America) ↓
- 5-year survival rate ≈ 15%
- The **most common** upper GI cancer
- Inherited genetic predisposition 1-3%

PANCREATIC CANCER

- **Incidence is rising** ↑
- Mean age at onset - ca. **70 years**
- 5-year SR when surgically resected ≈ **20%**
- 5-year SR ≈ **5%** in metastatic setting
- One of most fatal cancers for both sexes
- Only <10% due to inherited germline mutations

Risk factors

GASTRIC CANCER

- **Helicobacter pylori** infection
- **Tobacco use**
- Alcohol use
- High salt diet
- Processed meat
- **Nitrozoamines**
- Male gender
- Low fruit and vegetable intake

PANCREATIC CANCER

- **Cigarette smoking**
- **Obesity**
- Chronic pancreatitis
- Alcohol consumption
- Red meat, saturated fat
- Processed food
- Helicobacter pylori, HBV
- **High fruit&folate intake reduces the risk**

STOMACH/PANCREAS

GASTRIC CANCER

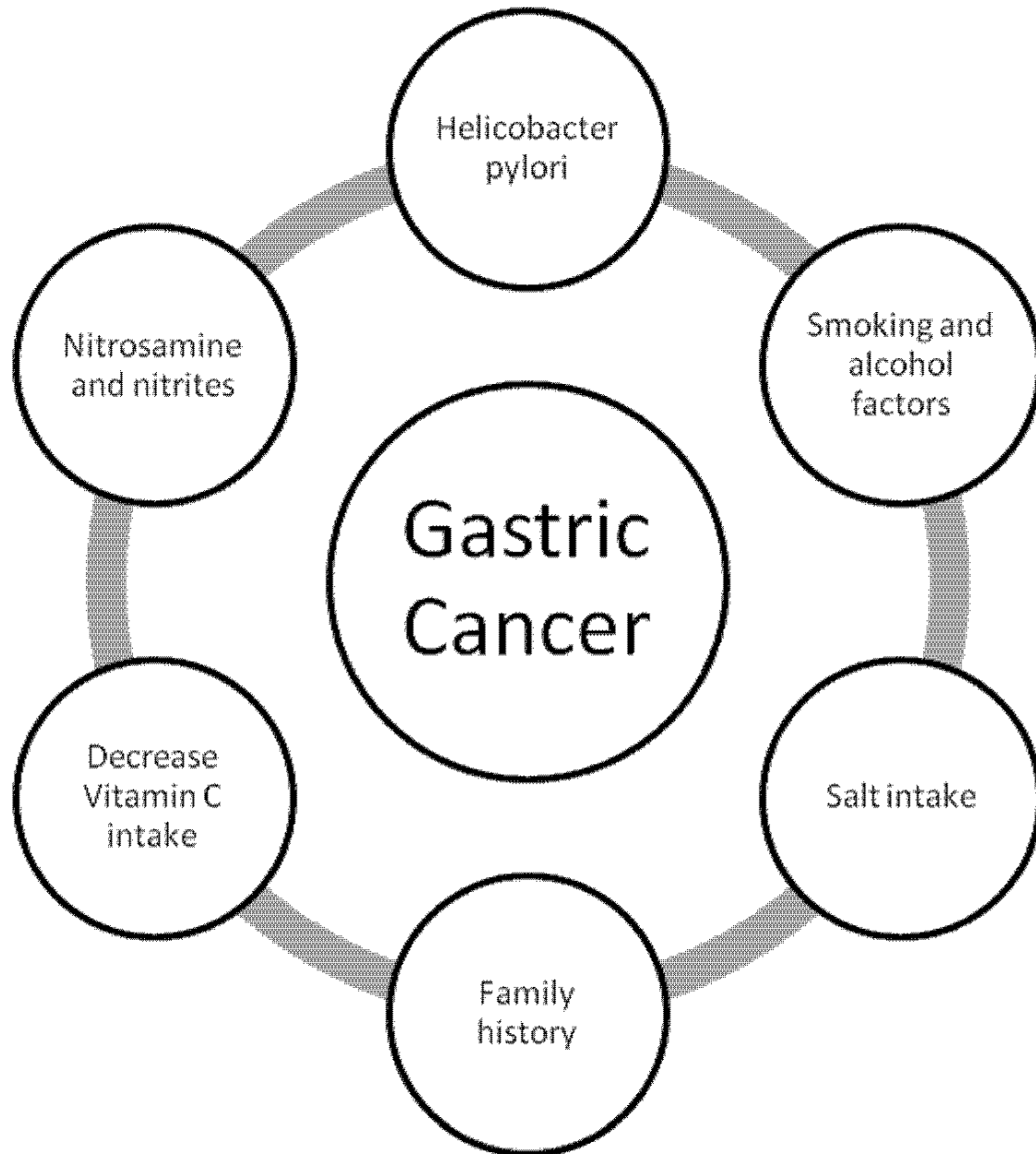
Syndromes predisposing:

- HDGC (hereditary diffuse gastric cancer)
 - HNPCC
 - FAP
- Peutz Jegher's syndrome

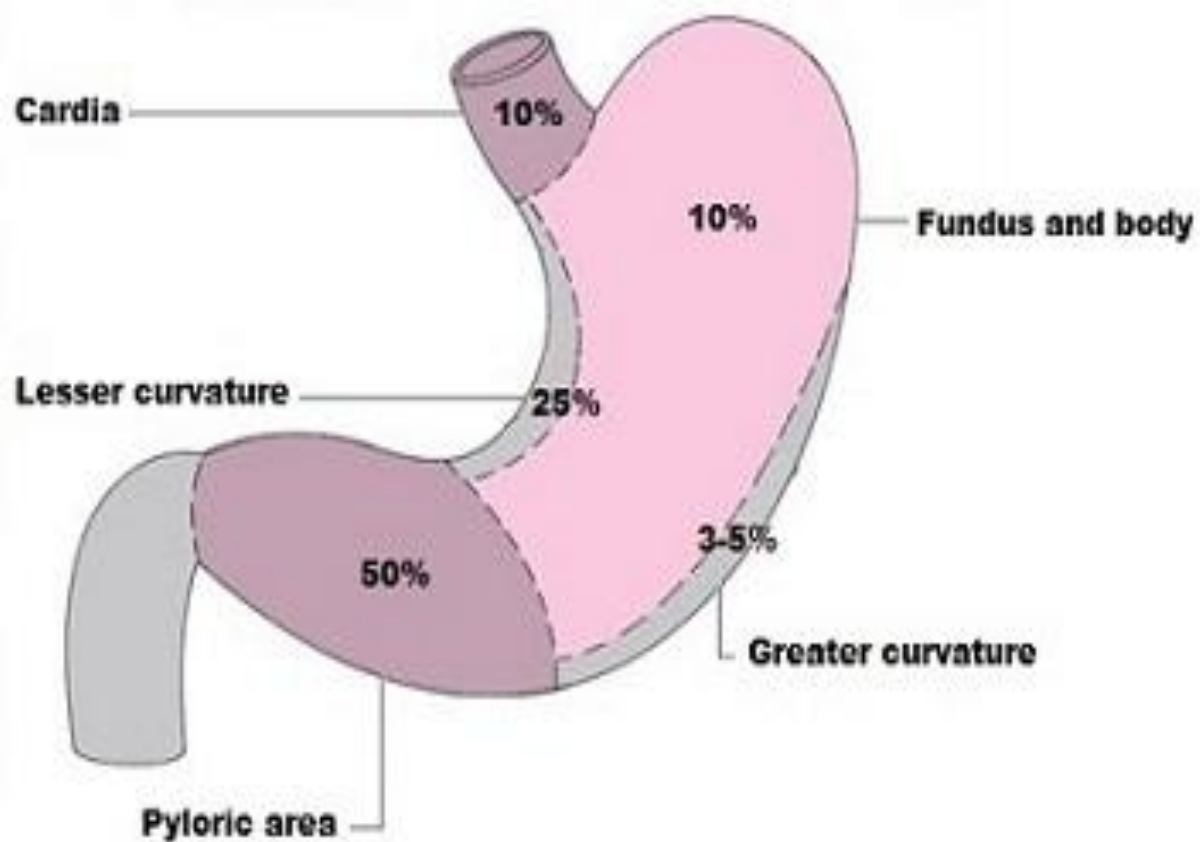
PANCREATIC CANCER

Syndromes predisposing:

- Li-Fraumeni syndrome
 - HNPCC
 - BRCA2 mutation !
- Peutz-Jegher's syndrome



Locations of Stomach Cancer by Percentage





SYMPTOMS OF GASTRIC CA.

Symptoms



Discomfort
or pain in the
stomach area



Nausea
and vomiting



Difficulty
swallowing



Weightloss



Vomiting blood or
having blood in the stool



Feeling full
or bloated after
a small meal



10 Warning Signs of PANCREATIC CANCER



that you must know



1

Jaundice



2

Diabetes



3

Abdominal &
Lower Back Pain



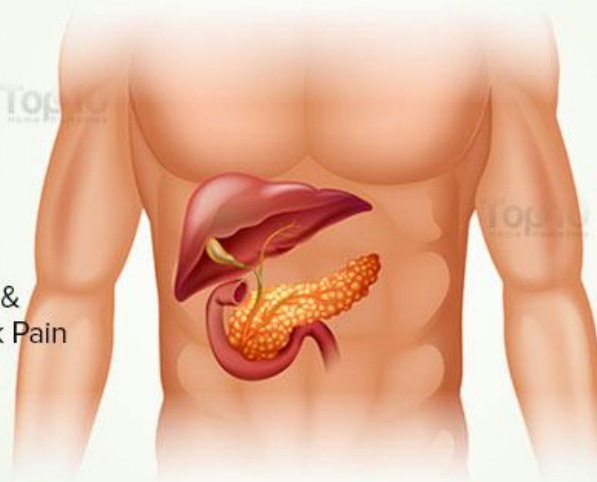
4

Weight
Loss



5

Nausea
& Vomiting



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Home Remedies

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6

Greasy or Light
Colored Stool



7

Lack of
Appetite



8

Changes in
Urine Color



9

Fatigue &
Weakness



10

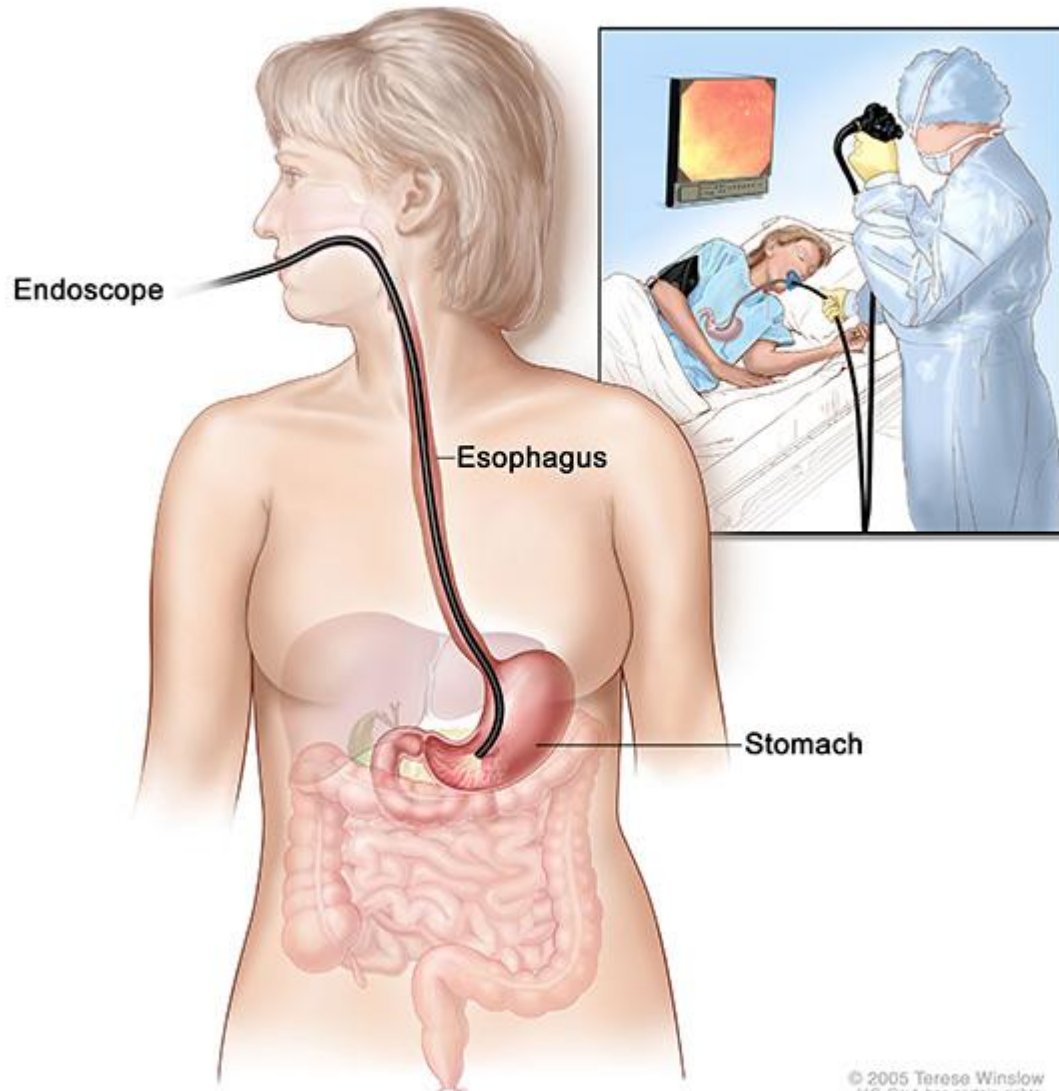
Bloating

DIAGNOSIS/STAGING

- Histopathological examination by means of **biopsy** (primary tumor or metastases?)
- Stomach – **gastroscopy**
- Pancreas – depending on the staging (no biopsy -> resection/EUS-guided biopsy/biopsy of metastases)
- Both types of cancer – **CT scan for staging**
- **EUS** – additional method (**different indication** in gastric & pancreatic cancer)*

*remember both cancers are commonly diagnosed at already advanced stage (!)

Upper Endoscopy



STAGING

- Do we need EUS in advanced gastric or pancreatic cancer? Why/why not?
- If you have had a primary tumor located in pancreas and metastases in the liver, which one would you decide to take biopsy from? Or maybe both?
- Do we routinely use PET for staging of pancreatic or gastric cancer?

STAGING

- Is MRI a better diagnostic method in gastric cancer?
- Is MRI a better diagnostic method in pancreatic cancer?
- Why do we perform EUS in gastric cancer (metastases excluded)?
- Why do we perform EUS in pancreatic cancer (metastases excluded)?

EUS

IN GASTRIC CANCER

- Assessment of the **T** and **N stage**
- Determine proximal and distal extent of the tumor
- Decision regarding **endoscopic resection** (endoscopic mucosal resection (EMR) or submucosal dissection (ESD))

IN PANCREATIC CANCER

- Assessment of **vascular invasion**
- **Prediction of resectability**
- But limited value in detection of metastatic lymph nodes

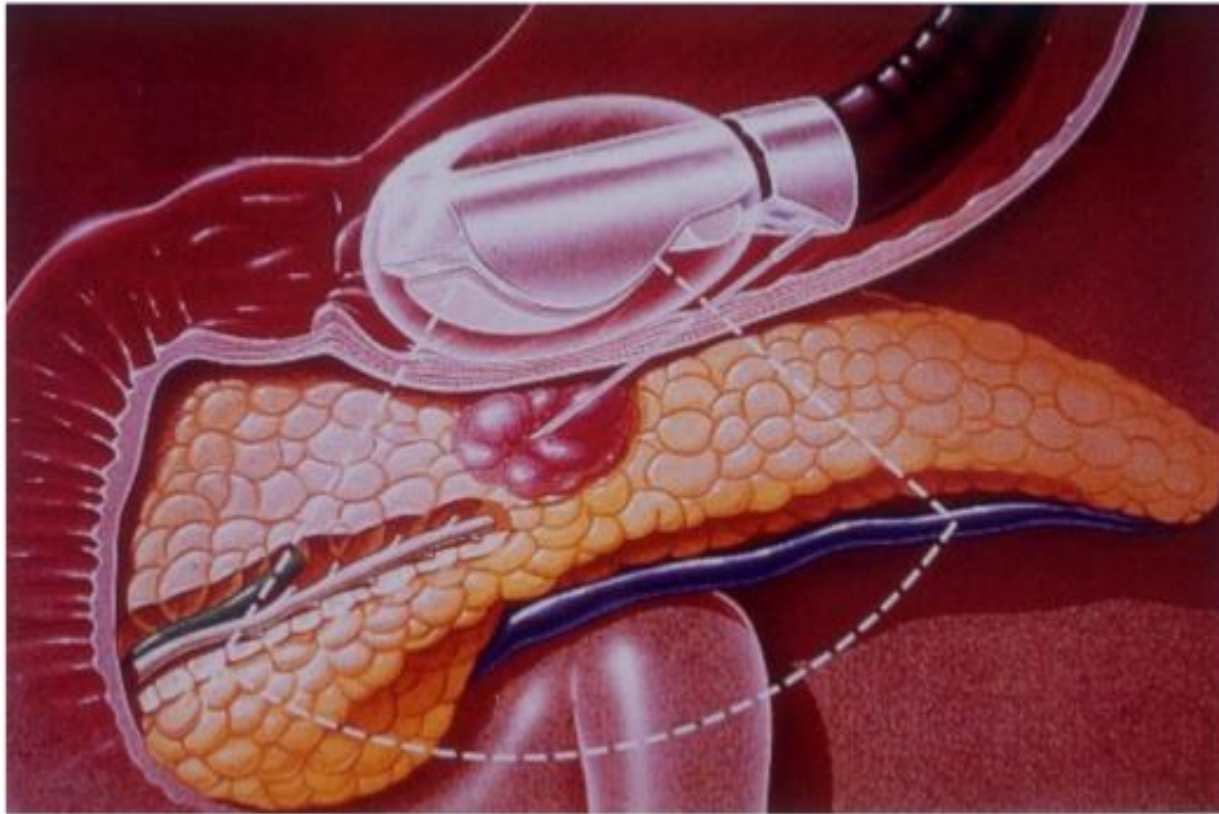
Endoscopic ultrasound (EUS)

Echoendoscope

Ultrasound transducer



Fine Needle Aspiration



STOMACH/PANCREAS

GASTRIC CANCER

- 90% adenocarcinoma
- Other: **GIST, NET, lymphomas, MANEC**

PANCREATIC CANCER

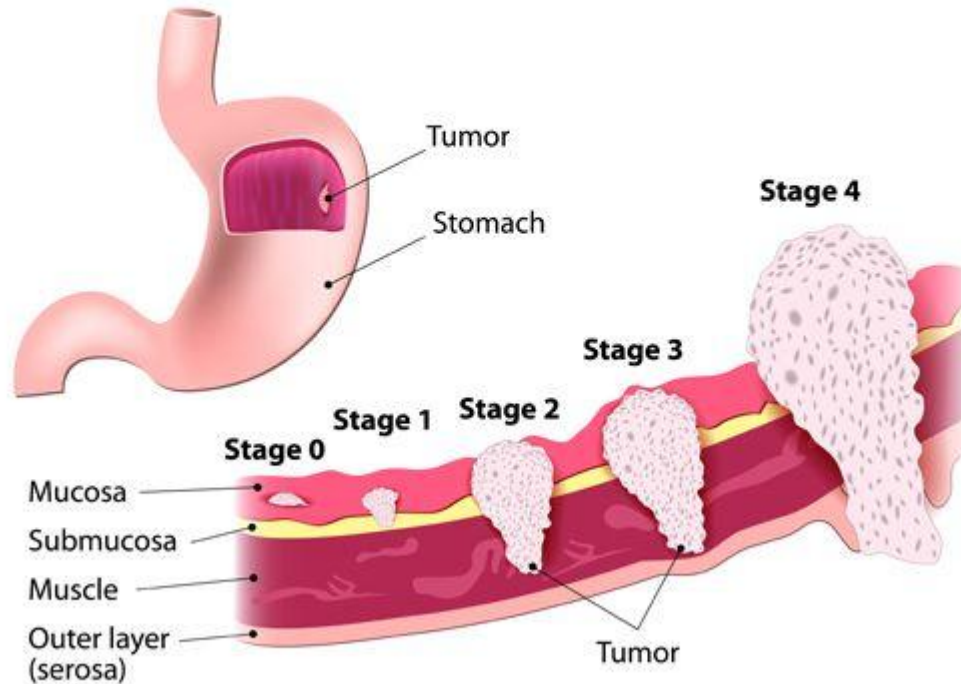
- 95% adenocarcinoma (80-85% PDAC – pancreatic ductal adenocarcinoma)
- Other acinar cell pc (better prognosis), undifferentiated/adenosquamous carcinomas (worse)
- **NET**

GASTRIC CANCER

Staging & Treatment



Stages of Stomach Cancer



The digestive system

Mouth (oral cavity)

Throat

Oesophagus

Liver

Stomach

Pancreas

Large
bowel

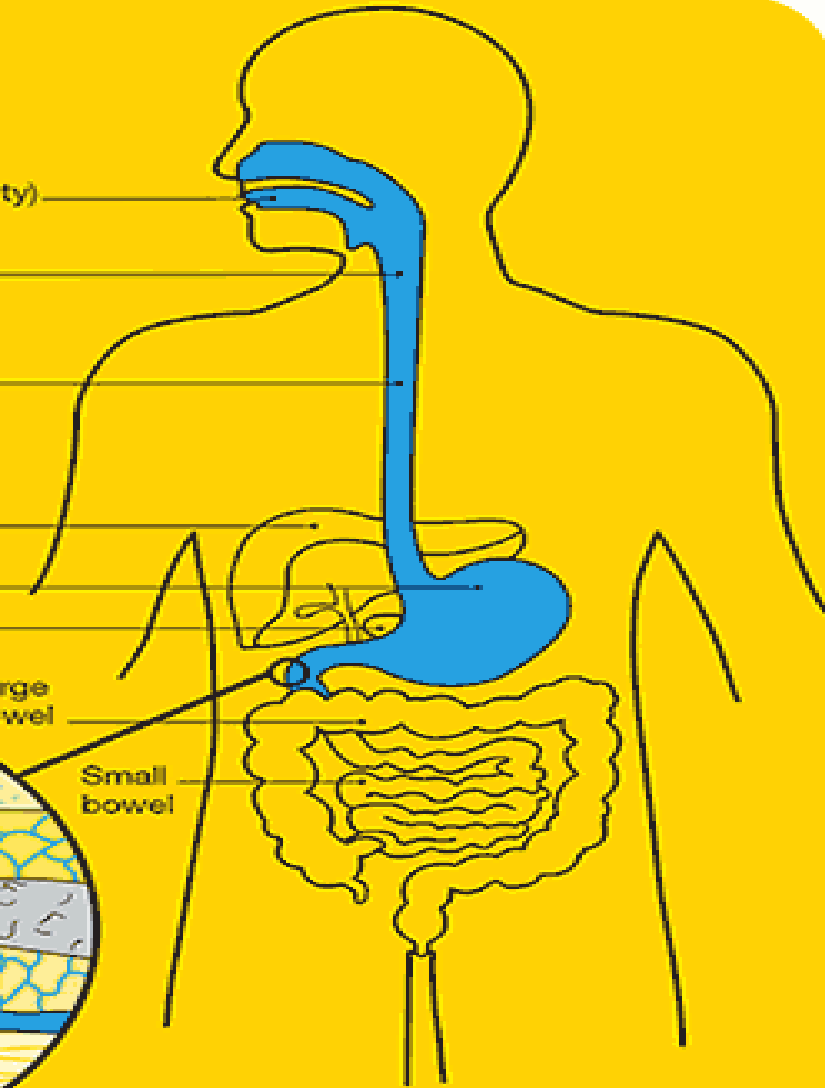
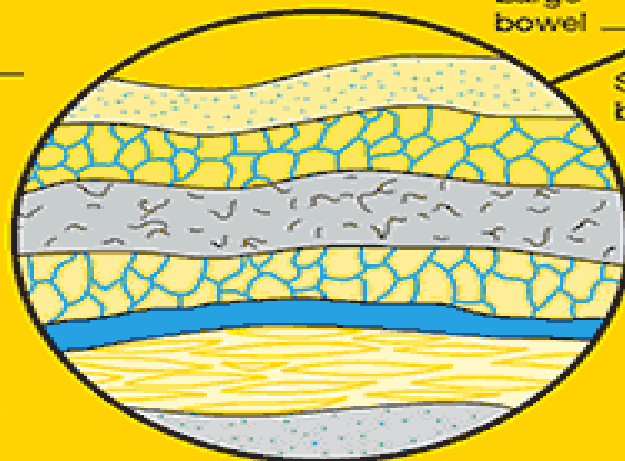
Small
bowel

Mucosa

Submucosa

Muscle layer

Outer layer



Staging determines the treatment

- **IA -> T1aNo** (confined to the mucosa, non-ulcerated, <2cm, well-diferentiated): **ESD**
- IA -> T1No (not for local treatment): **sugery** (gastrectomy + perigastric lymph nodes, D1+)
- **IB-III (>=T2No): perioperative chemotherapy + surgery** (gastrectomy+ D2 lymphadenectomy) or surgery + adjuvant chemoradiotherapy
- IV: metastases -> pallaitive treatment: BSC or **systemic chemotherapy (cth)**
- Inoperable cases with no metastases – **cth** or BSC

What is important in gastric cancer staging according to multimodality treatment?

- **T stage!** – decision about neoadjuvant treatment (-> back to EUS)
- **M stage** – decision systemic chth, no surgery (-> back to CT : commonly liver, lymph nodes (not regional lymph nodes!), adjacent structures)
- **CT** -> low sensitivity to detect peritoneal spread (very common in gastric cancer) -> consider **laparoscopy** in T_{3/4} stage

Metastatic gastric cancer

- Systemic treatment -> **chemotherapy**
- **Doublet or triplet chemotherapy** > better than monotherapy
- Mainly **fluoropyrimidines/platinum agents/anthracyclines**
- Palliation of symptoms -> radiotherapy (primary tumor, bone metastases)

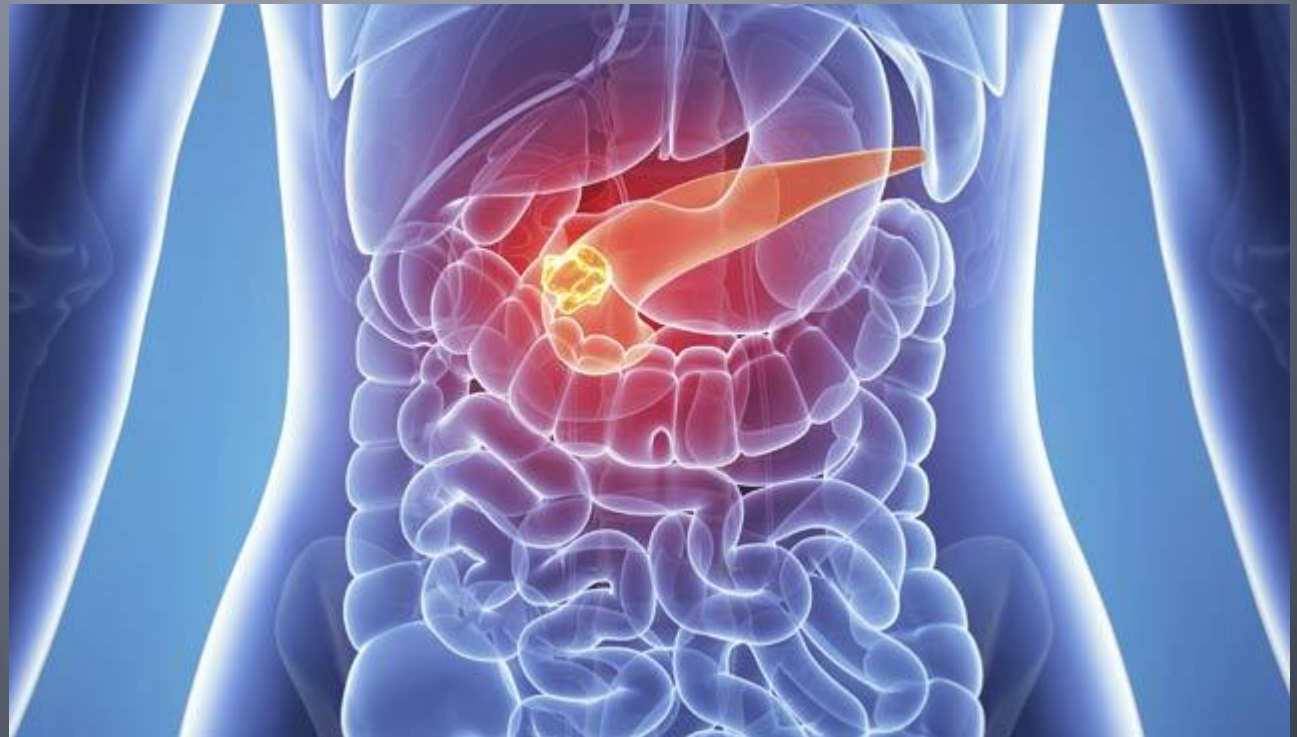
- ! Remember to assess HER2 overexpression!
- When **HER2 positive gastric cancer** -> **add trastuzumab to chemotherapy** (TRA+CX)

Metastatic gastric cancer

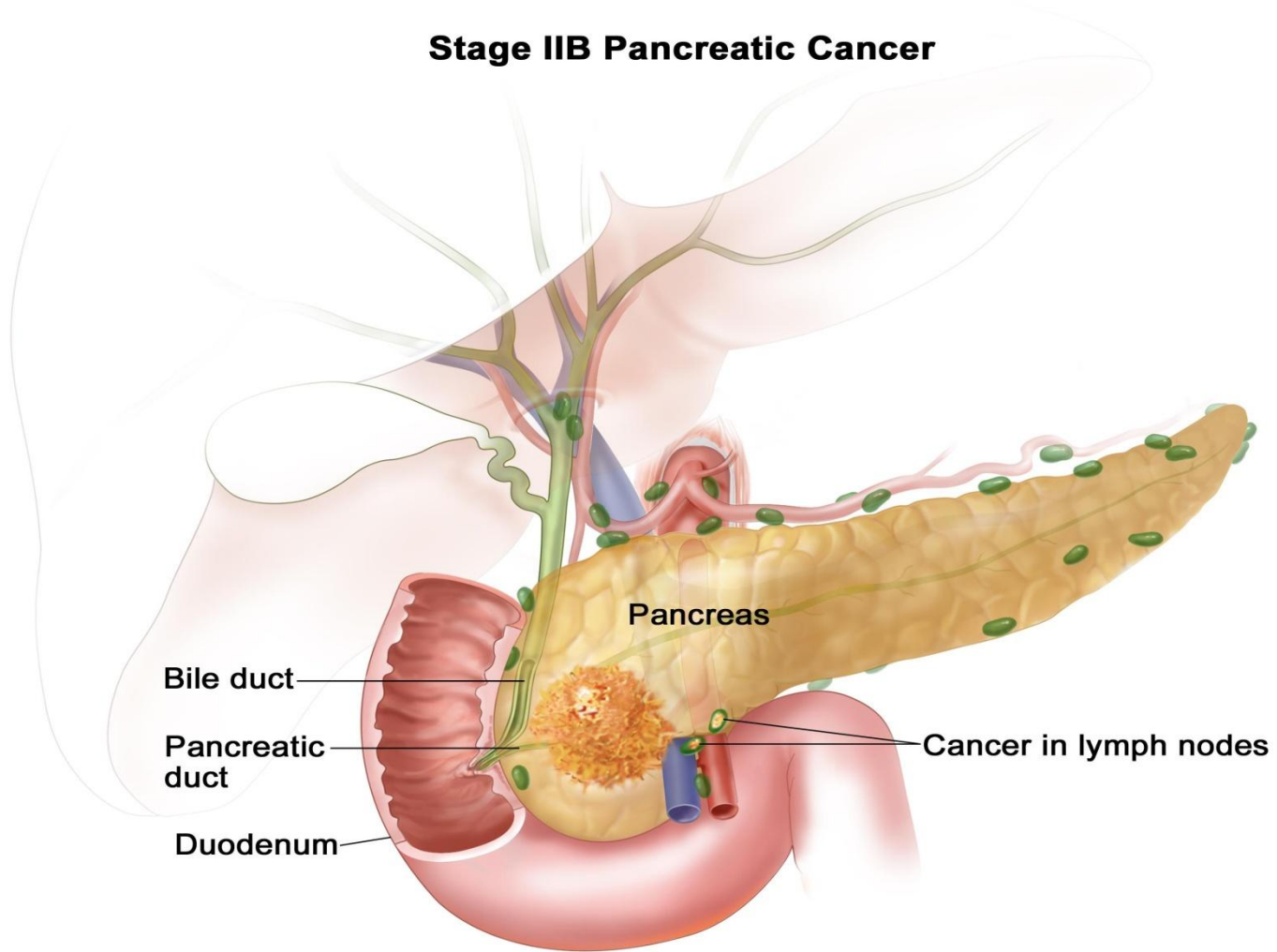
- Do we resect the primary tumor when metastases are already present?
- Does it influence overall survival?

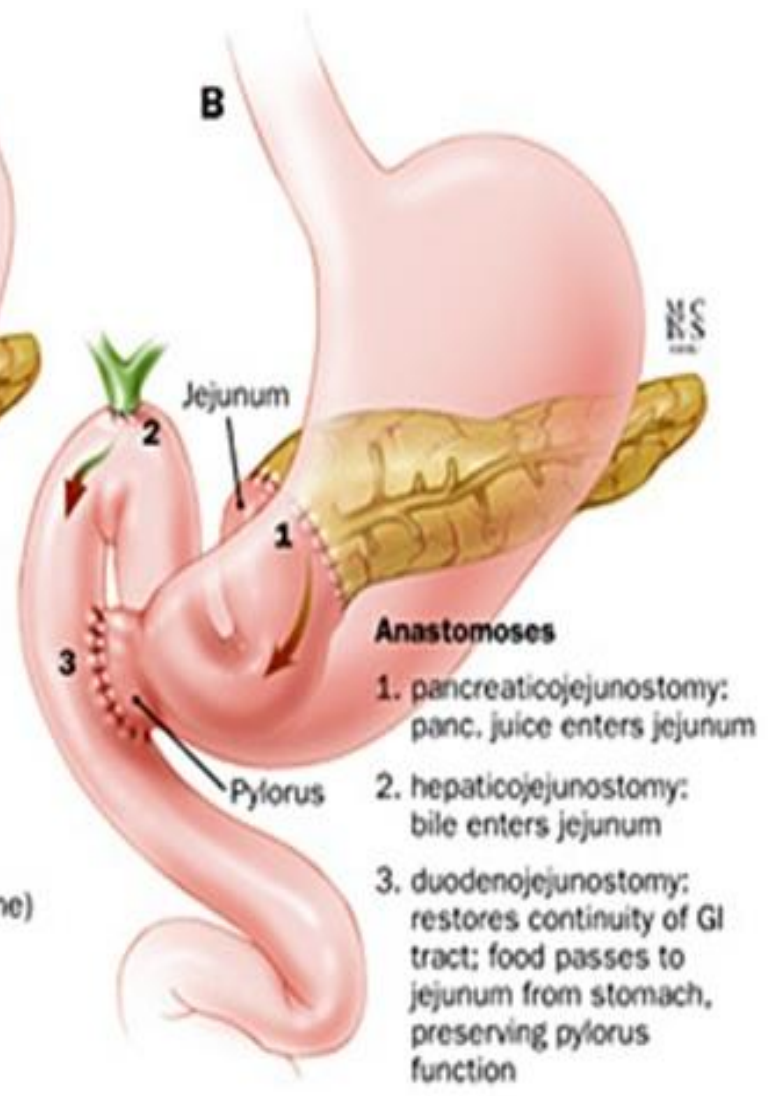
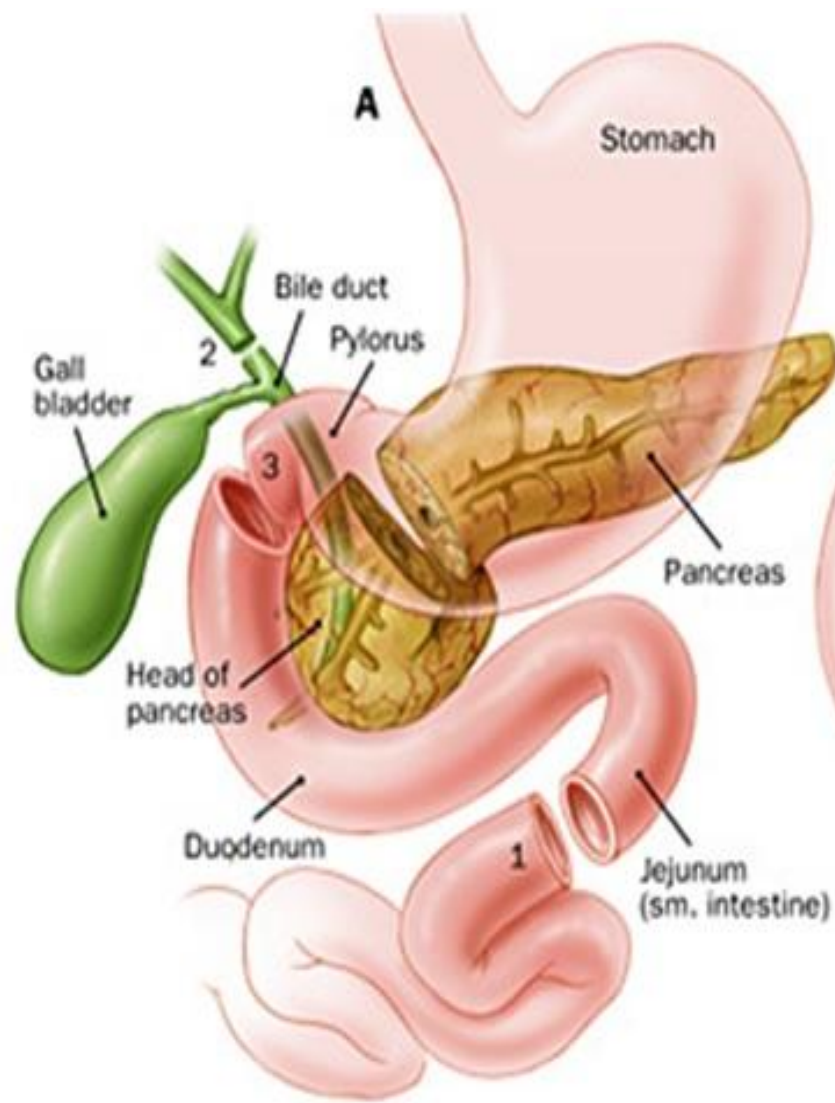
Pancreatic Cancer

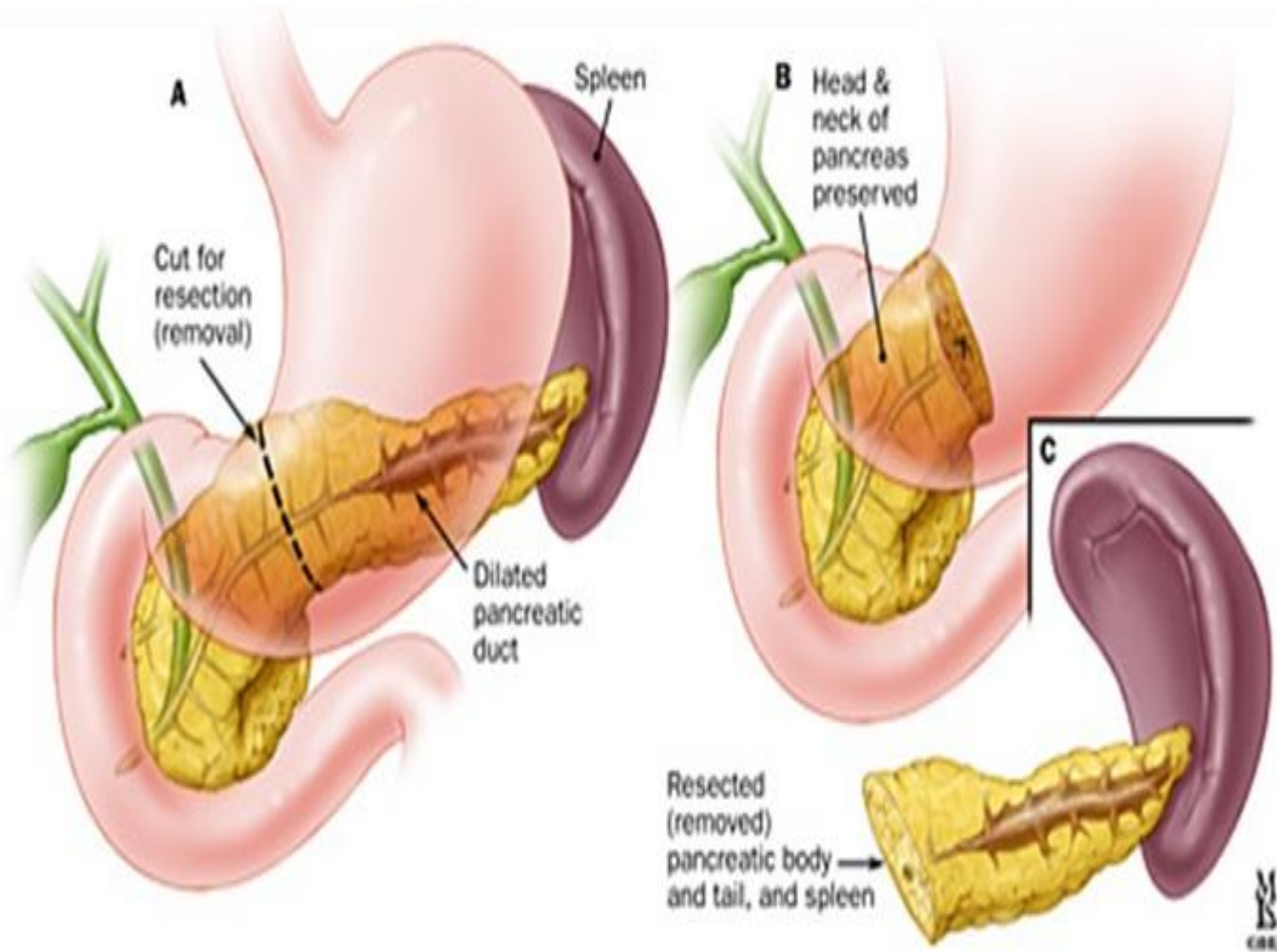
Staging & Treatment



Stage IIB Pancreatic Cancer







Pancreatic cancer surgery

- What's the standard of care for pancreatic cancer?
 - a. Open surgery
 - b. Laparoscopy
 - c. Both

Pancreatic cancer surgery

- What determines the type of surgery in pancreatic cancer?

Pancreatic cancer surgery

- Pancreatic cancer surgery involves lymphadenectomy
- Standard lymphadenectomy include removal of 15 or more lymphnodes
- ...but AJCC recommended 10 LN, 8th edition of TNM says 12 lymph nodes

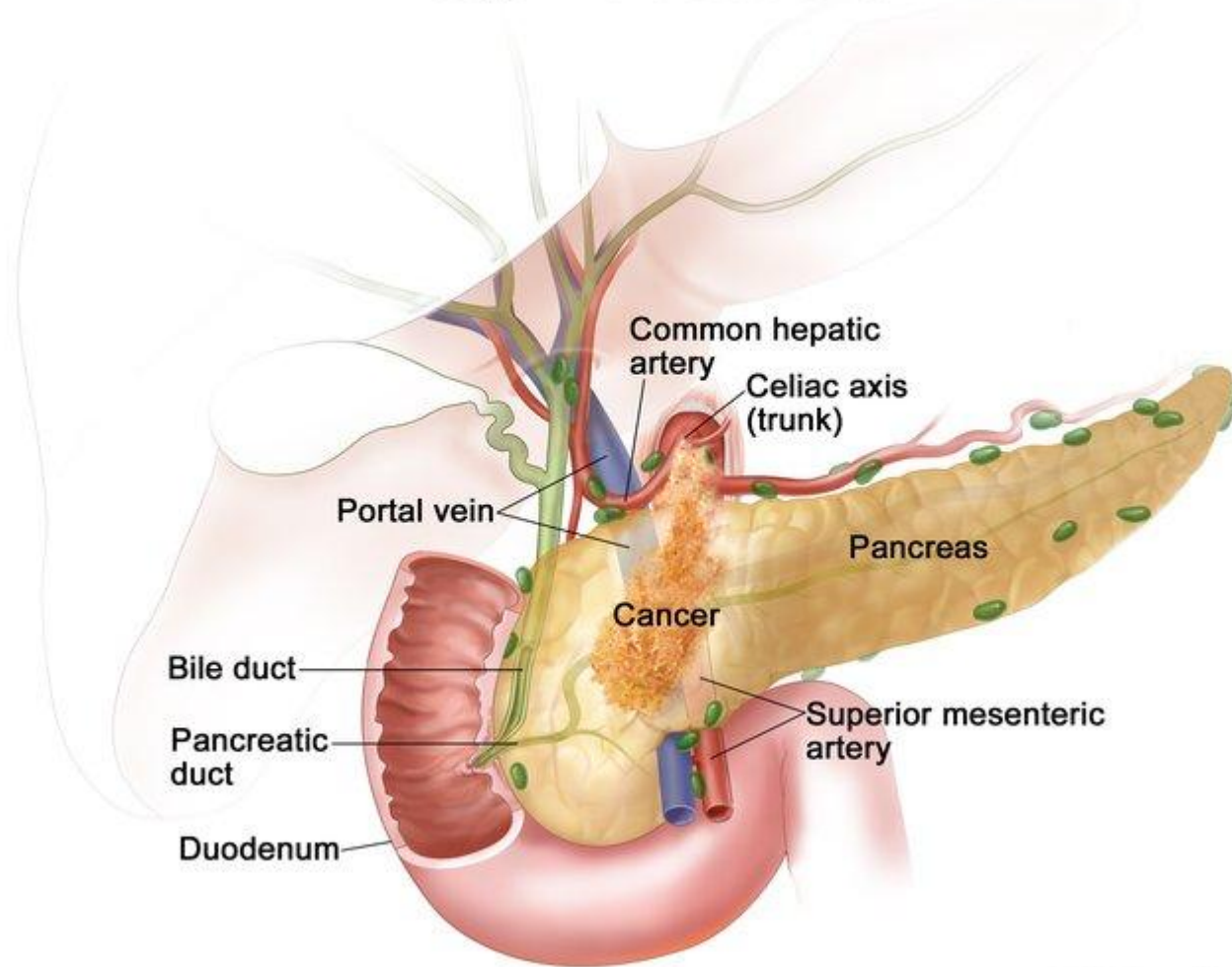
Adjuvant chemotherapy

- CONKO-001 gemcytabine better than observation
- Improves DFS (Δ 6 mth) and OS (Δ 2,5 mth)

- ESPAC-3 trial -> GEM vs fluorouracil
- No difference in OS
- FU more toxic, mainly mucositis

- ESPAC-4 trial -> GEM+cabecitabine > GEM
- 5 yr OS 29% vs 16% LANCET 2017 mOS Δ 2,5 mth

Stage III Pancreatic Cancer



Metastatic pancreatic cancer

- **CT scan** for localisation of metastases
 - Patient general condition
- Performance status, nutritional status
 - & comorbidities
 - **Biopsy** to confirm diagnosis (histopathology!)
 - Systemic chemotherapy
- **FOLFIRINOX** or **GEM/Nab-PTX** PS 0-1
- **Gemcytabine alone** – PS2, bilirubin 1.5xUNL

Metastatic pancreatic cancer

- What will be the best choice for patient with metastatic pancreatic cancer with performance status 3?

Oesophageal cancer

SCC

- Risk factors: **smoking & alcohol consumption**
- Incidence increases with age, peak \approx 70 yo
- Men \approx Women
- Incidence is stable
- Mortality declined
- Localisation: more often proximal or middle

ADENOCARCINOMA

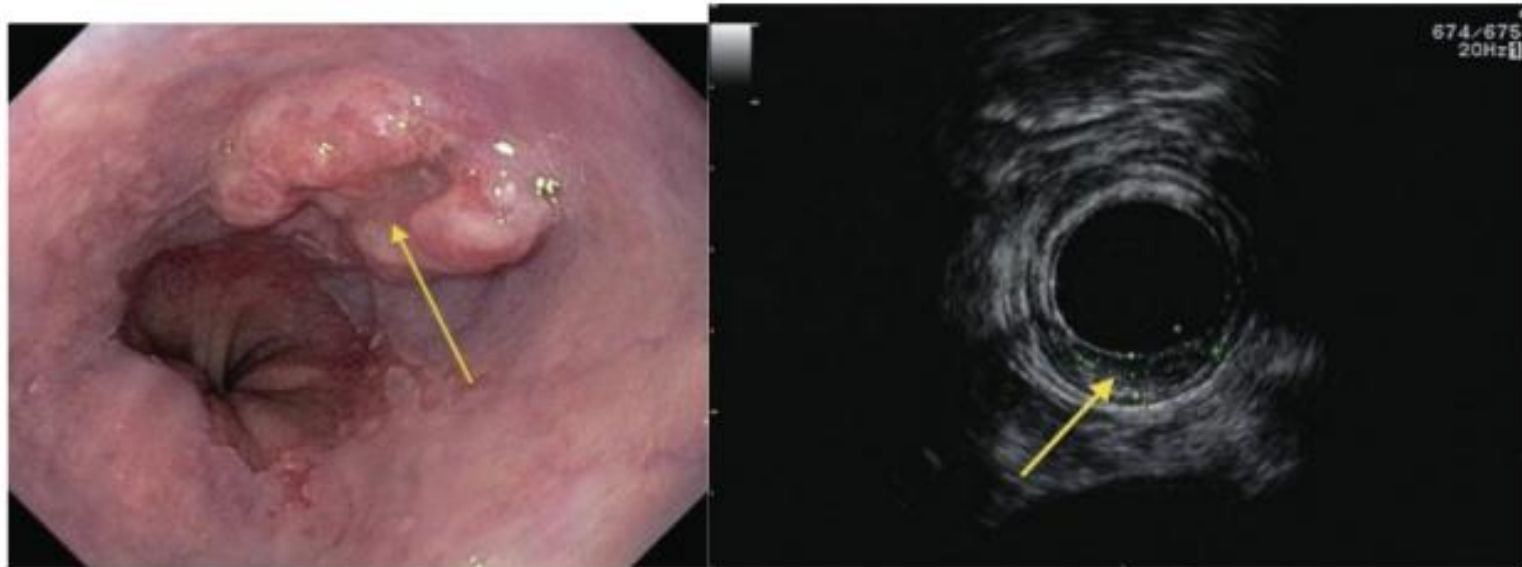
- Risk factors: **obesity & gastro-oesophageal reflux**
- Age (increases with age)
- **Men (4x) > Women**
- Incidence is rising \uparrow
- Mortality rates are rising
- Localisation: more often distal

SYMPTOMS

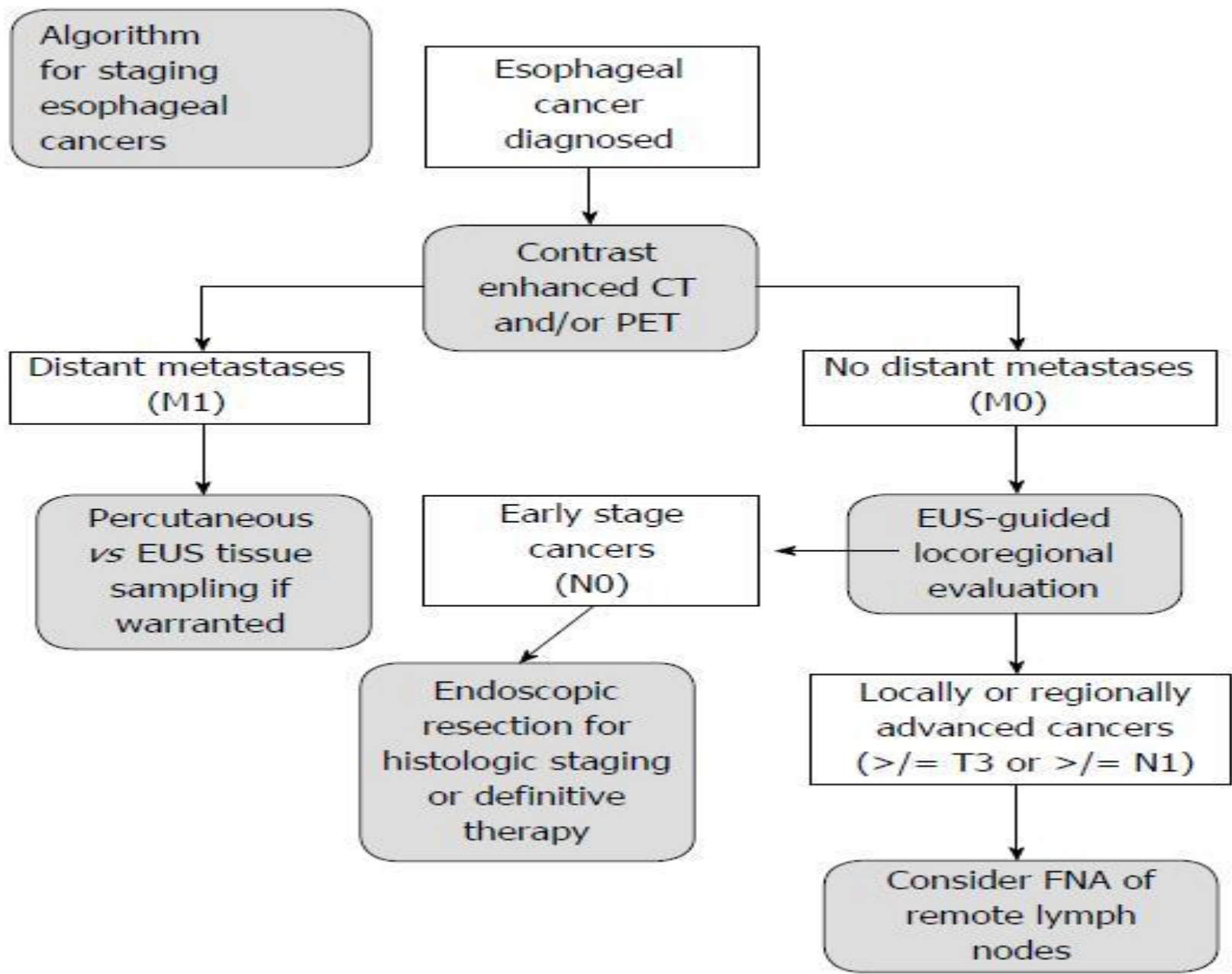
- Dysphagia, Odynophagia !
- Especially associated with WEIGHT LOSS
 - Emesis
 - GI bleeding
 - Recurrent Aspiration

DIAGNOSIS & STAGING

- **Endoscopy** of upper GI
Biopsy -> DIAGNOSIS
- Clinical examination
- **CT neck, chest, abdomen**
-> STAGING
- **EUS** -> endoscopic ultrasound
(very high sensitivity and specificity for T feature)
- -> **T&N** evaluation
= **determination of resectability**
- **PET/CT: candidates for oesophagectomy**, to find undetected metastases



- T lesion, adenocarcinoma in lower thoracic esophagus with central depression shown by yellow arrow (a); endoscopic ultrasound (EUS)
- image showing **submucosal invasion** but no involvement of muscularis propria (MP) shown by yellow arrow (b).



Special aspects about staging

- Tracheobronchoscopy
- To rule out invasion of respiratory tract
- Tumors at or above tracheal bifurcation
- Laparoscopy
- To exclude peritoneal involvement
- OGJ, T₃/T₄
- Exploration for synchronous cancer
- SCC -> due to the shared risk factors with other cancers
- Mainly: HNC (ENT specialist), lung cancer (bronchoscopy)

Patient general condition as a factor limiting the treatment

Remember about nutritional status assessment and nutritional support from the very beginning and for the whole period of treatment

STAGING according to TNM

ESOPHAGUS STAGING FORM		
CLINICAL <i>Extent of disease before any treatment</i>	STAGE CATEGORY DEFINITIONS	PATHOLOGIC <i>Extent of disease through completion of definitive surgery</i>
<input type="checkbox"/> y clinical – staging completed after neoadjuvant therapy but before subsequent surgery	TUMOR SIZE: _____	LATERALITY: <input type="checkbox"/> left <input type="checkbox"/> right <input type="checkbox"/> bilateral
<input type="checkbox"/> TX <input type="checkbox"/> T0 <input type="checkbox"/> Tis <input type="checkbox"/> T1 <input type="checkbox"/> T1a <input type="checkbox"/> T1b <input type="checkbox"/> T2 <input type="checkbox"/> T3 <input type="checkbox"/> T4 <input type="checkbox"/> T4a <input type="checkbox"/> T4b	<p style="text-align: center;">PRIMARY TUMOR (T)</p> Primary tumor cannot be assessed No evidence of primary tumor High-grade dysplasia * Tumor invades lamina propria, muscularis mucosae, or submucosa Tumor invades lamina propria or muscularis mucosae Tumor invades submucosa Tumor invades muscularis propria Tumor invades adventitia Tumor invades adjacent structures Resectable tumor invading pleura, pericardium, or diaphragm Unresectable tumor invading other adjacent structures, such as aorta, vertebral body, trachea, etc. *High-grade dysplasia includes all non-invasive neoplastic epithelium that was formerly called carcinoma <i>in situ</i> , a diagnosis that is no longer used for columnar mucosae anywhere in the gastrointestinal tract.	<input type="checkbox"/> TX <input type="checkbox"/> T0 <input type="checkbox"/> Tis <input type="checkbox"/> T1 <input type="checkbox"/> T1a <input type="checkbox"/> T1b <input type="checkbox"/> T2 <input type="checkbox"/> T3 <input type="checkbox"/> T4 <input type="checkbox"/> T4a <input type="checkbox"/> T4b
<input type="checkbox"/> NX <input type="checkbox"/> N0 <input type="checkbox"/> N1 <input type="checkbox"/> N2 <input type="checkbox"/> N3	<p style="text-align: center;">REGIONAL LYMPH NODES (N)</p> Regional lymph nodes cannot be assessed No regional lymph node metastasis Regional lymph node metastases involving 1 to 2 nodes Regional lymph node metastases involving 3 to 6 nodes Regional lymph node metastases involving 7 or more nodes	<input type="checkbox"/> NX <input type="checkbox"/> N0 <input type="checkbox"/> N1 <input type="checkbox"/> N2 <input type="checkbox"/> N3
<input type="checkbox"/> M0 <input type="checkbox"/> M1	<p style="text-align: center;">DISTANT METASTASIS (M)</p> No distant metastasis (no pathologic M0; use clinical M to complete stage group) Distant metastasis	<input type="checkbox"/> M1

Region of esophagus	Extent	Draining nodes
Upper third	Cricopharyngeus to aortic arch	Internal jugular, cervical, supra-clavicular
Middle third	Aortic arch to inferior pulmonary veins	Paratracheal, hilar, subcarinal, pericardial, paraesophageal
Distal third	Inferior pulmonary veins to gastro-esophageal junction	Lesser curve stomach, left gastric, celiac

Treatment of early stages

- **Endoscopic methods for T_{1a} adenocarcinoma**
 - a) Endoscopic mucosal resection (EMR)
 - b) Endoscopic submucosal dissection (ESR)
- **For limited disease (T₁-T₂N₀) -> SURGERY:**
 - a) Transthoracic oesophagectomy (Ivor-Lewis procedure)
 - b) Or hybrid minimally invasive oesophagectomy (IL proc.+laproscopic gastric mobilisation&open right thoracotomy) -> lower complication rate

Locally advanced disease

SCC

ADENOCARCINOMA

Preoperative treatment for both -> higher rate of Ro resection, better local control&survival

Either

A. **Preoperative CRT + surgery**

Or

B. **Definitive CRT** (salvage surgery an option)

CRT without surgery is recommended for cervically localised tumors

Either

A. **Preoperative CRT+ surgery**

Or

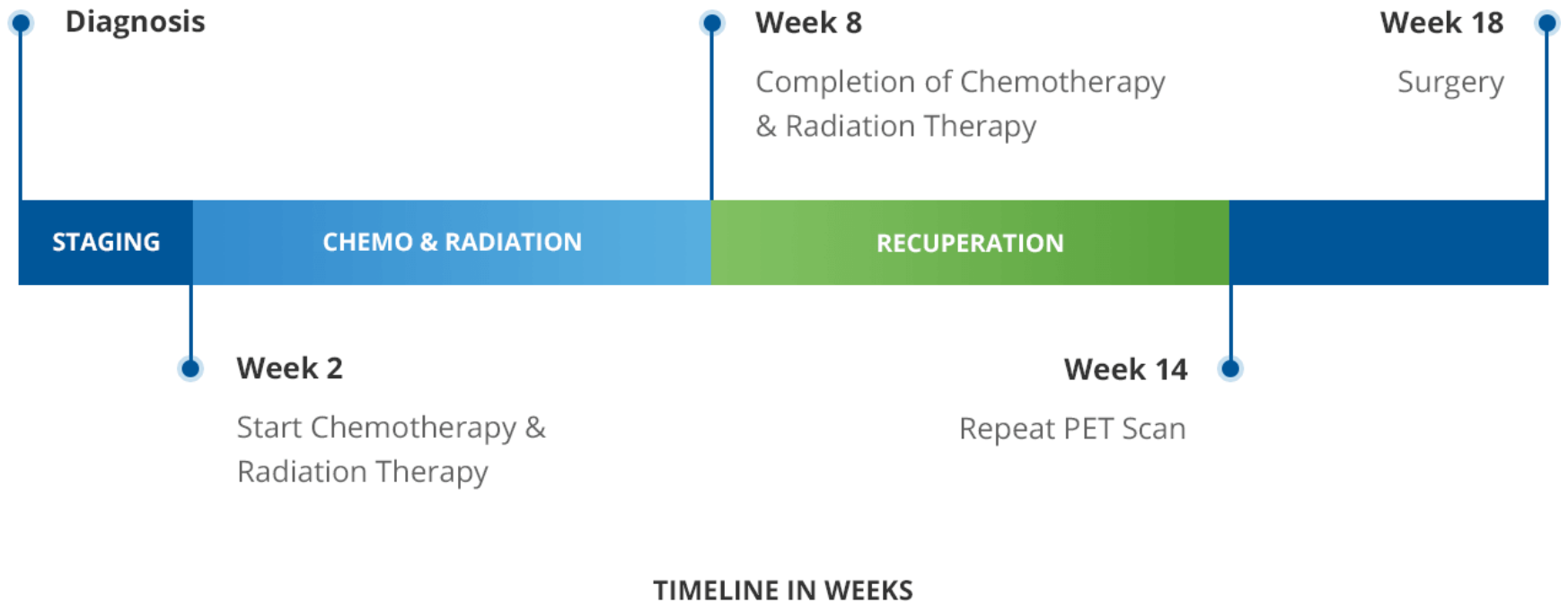
B. **Perioperative chemotherapy** (platinum/fluoropyrimidine) **+surgery**

Always surgery!

Chemoradiotherapy

- Cisplatin/5-FU + RTH 41.1-50.4 Gy (1.8-2 Gy/fr)
- Carboplatin AUC₂ + paclitaxel 50 mg/m², weekly, for 5 weeks + RTH 41.4 Gy/23fractions
- -> CROSS trial (T₁N₁, T₂-T₃No-1 included)

Esophageal Cancer Treatment Timeline



Questions

- Why do we go for PET after crth in radical treatment of oesophageal cancer?
 - Why this diagnostic procedure?
- What if we observe CR after neoadjuvant treatment in radiological examinations?
 - Is PET relevant for identification of CR?

Metastatic setting

- Symptoms palliation:
 - Ex. Brachytherapy for relief of dysphagia
 - Metal stent placement

 - Additional: HER2 testing in metastatic AC of oesophagus (esp. lower/OGJ)
- Systemic treatment:
 - AC: treatment according to gastric cancer guidelines (no strong evidence)
 - SCC: cth value uncertain, cisplatin/5FU, cisplatin doubles – RR↑, no OS benefit; results worse than for AC

**Comments and discussion
welcome!**
