Pancreatic cancer

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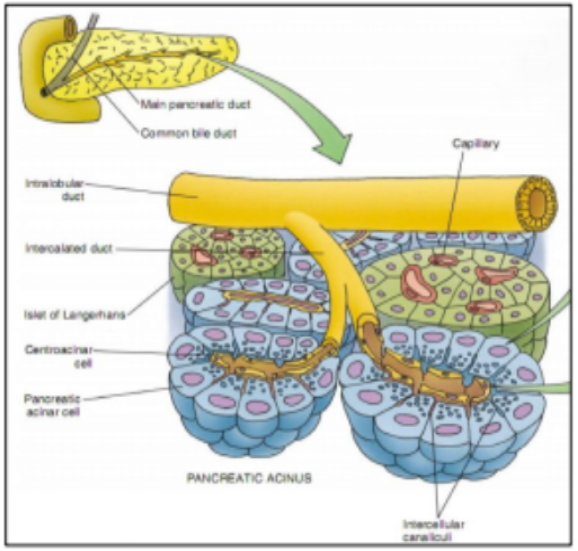
DDRI

PANCREAS

Stroma

capsule, septa & reticular fibers.



Parenchyma

Pancreas is a **mixed** gland:

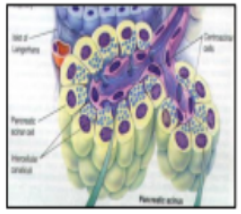
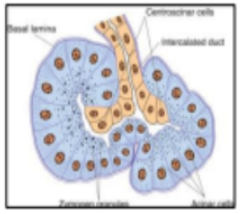
- **Exocrine part (acini & ducts):** produces digestive pancreatic enzymes.
- **Endocrine part (islets of Langerhans):** produces hormones.

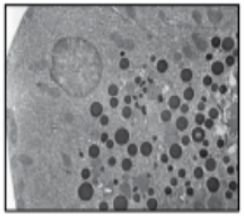
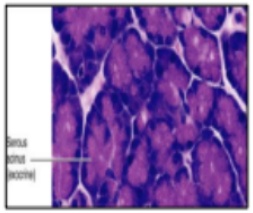
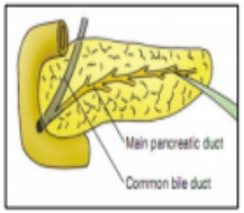
Histology of Pancreas

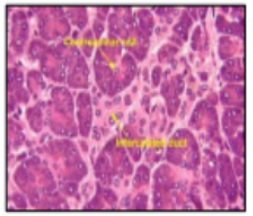
- Acinar cells (80%)
- Ductal cell (10-15%)
- Endocrine/islet cell(1-2%)

➢ Exocrine Pancreas

Pancreatic Acini	Pancreatic Acinar Cells	Duct System
○ They are serous acini: secreting a thin fluid rich in digestive pancreatic enzymes. ○ Centroacinar cells: Their nuclei appear in the center of the acini. They represent the beginning of the ducts. ○ No myoepithelial cells around the acini.	○ Pyramidal in shape. ○ Nuclei are basal. ○ Cytoplasm: • Basal part Basophilic (due to abundant rER). • Apical part Acidophilic (due to secretory granules).	○ Centroacinar cells. ○ Intercalated ducts (low cuboidal). ○ Intralobular ducts (NOT prominent). in parotid gland Intralobular ducts is prominent ○ Interlobular ducts. ○ Main pancreatic duct.

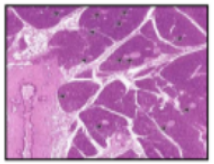




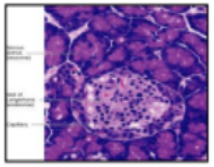


➢ Endocrine Pancreas

Islets of Langerhans:

- Pale-staining spherical collections of endocrine cells, scattered among the acini.
- Richly vascularized by fenestrated capillaries.
- Each islet is surrounded and supported by reticular fibers.
- 1 million islets in human pancreas.
- Most numerous in the tail of pancreas.





Cells of the Islets:

5 types of cells in each islet

Cannot be differentiated from one another by routine stains. We can differentiated Between 5 cell by immune stain

Β (B) cells	α (A) cells	δ (D) cells	G cells	PP cells
• Constitute 70% of islet cells. • Concentrated in islet center. • Function: secrete insulin which ↓ blood sugar.	• Constitute 15-20%. • Concentrated in islet periphery. • Granules are much more numerous, more tightly packed, smaller, and denser than those of Β cells. • Function: secrete glucagon which ↑ blood sugar.	• Constitute 5-10% • Scattered throughout the islet. • Granules are less dense than those of Β and α cells. • Function: secrete somatostatin which ↓ release of hormones from endocrine pancreas and enzymes from exocrine pancreas.	• Constitute 1% of islet cells. • Scattered throughout the islet. • Function: secrete gastrin which ↑ production of HCl by parietal cells of the stomach.	• Constitute 1% of islet cells. • Scattered throughout the islet. • Function: secrete pancreatic polypeptide which ↓ exocrine secretions of pancreas.

Primary Tumors of Exocrine Pancreas(W.H.O)

I-Benign

-serous cystadenoma

-mucinous cystadenoma

-intraductal papillary mucinous adenoma

-mature cystic teratoma

II-Borderline

mucinous T + moderate dysplasia ,solid-seudopapillary T

III-Malignant

Ductal adenocarcinoma, giant cell T, serous & mucinous carcinoma, acinar cell carcinoma ,pancreatoblastoma, miscellanous

Exocrine Pancreatic Cancer(PC)

- %85-90 are adenocarcinomas arising from the ductal epithelium.

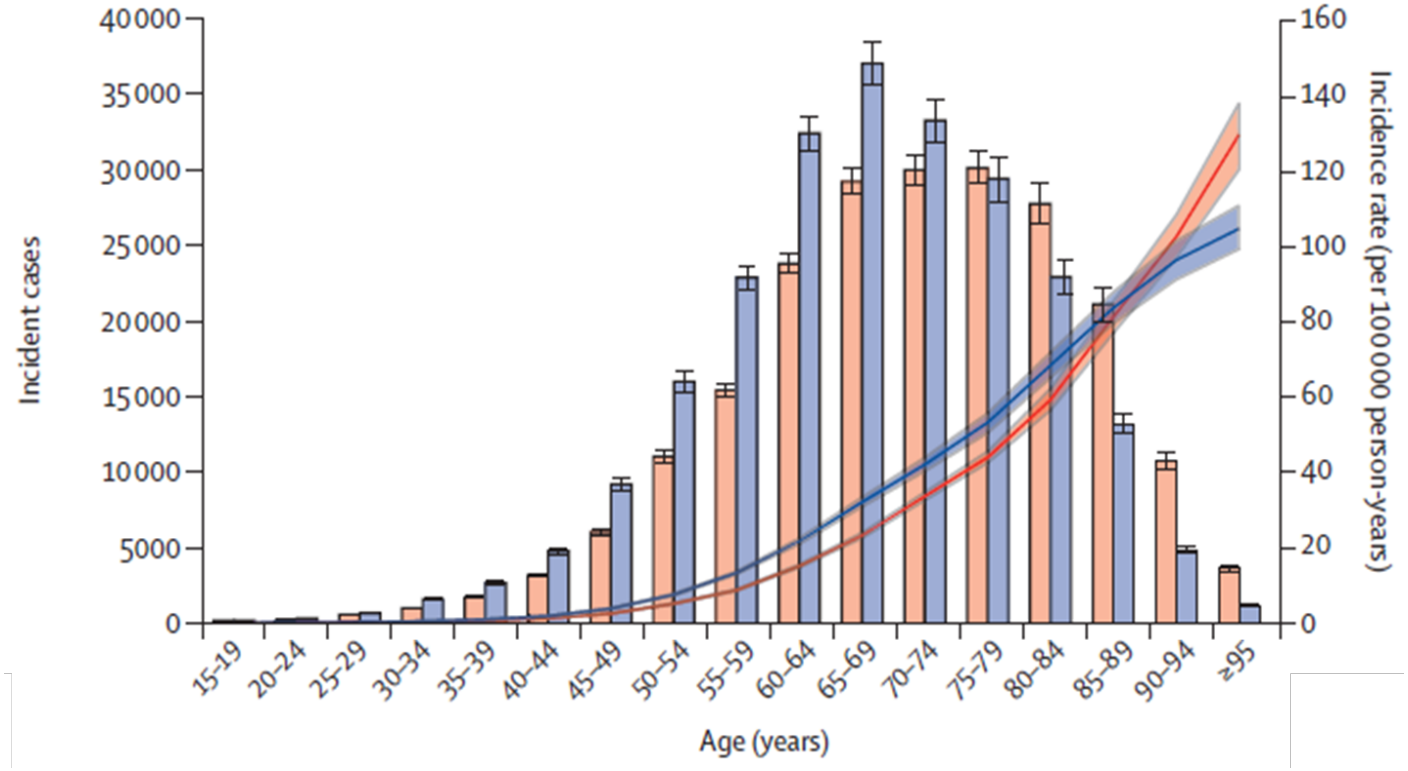
- PC, once considered a rare cancer, is a growing cause of cancer mortality worldwide.

- the worldwide annual incidence increased by 2·3 times from 1990 to 2017, from 196 000 (95% CI ;193 000–200 000) cases in 1990 to 441 000 (433 000–449 000) cases in 2017.

- Much of this increase is due to population ageing.
- Age is the strongest risk factor for pancreatic cancer

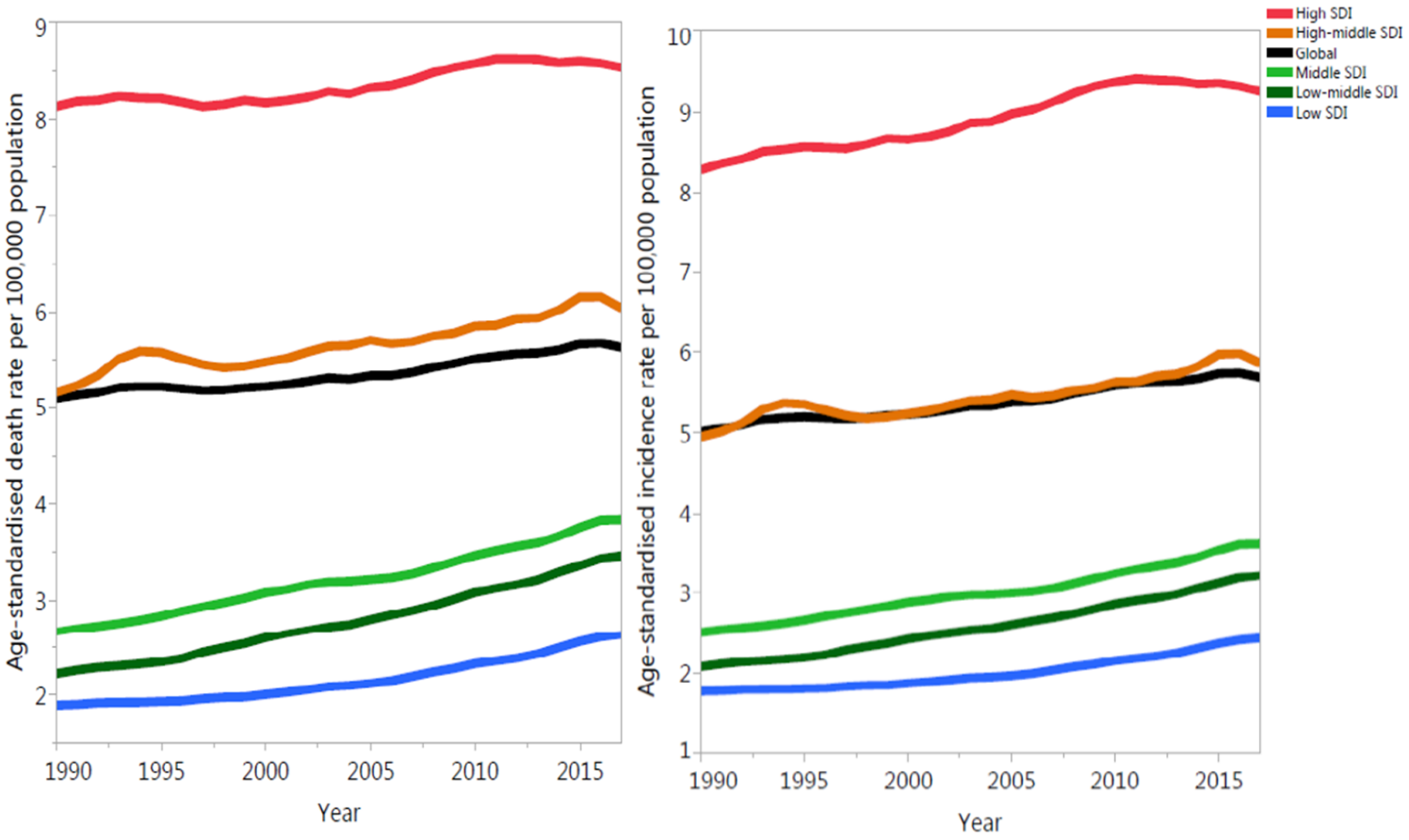
- <5/ 100 000 person-years in the 4 th decade of life to > 60/100 000 person-years at the start of the 8 th decade.

Global number of incident cases and incidence rate of PC per 100 000 person-years by age and sex, 2017

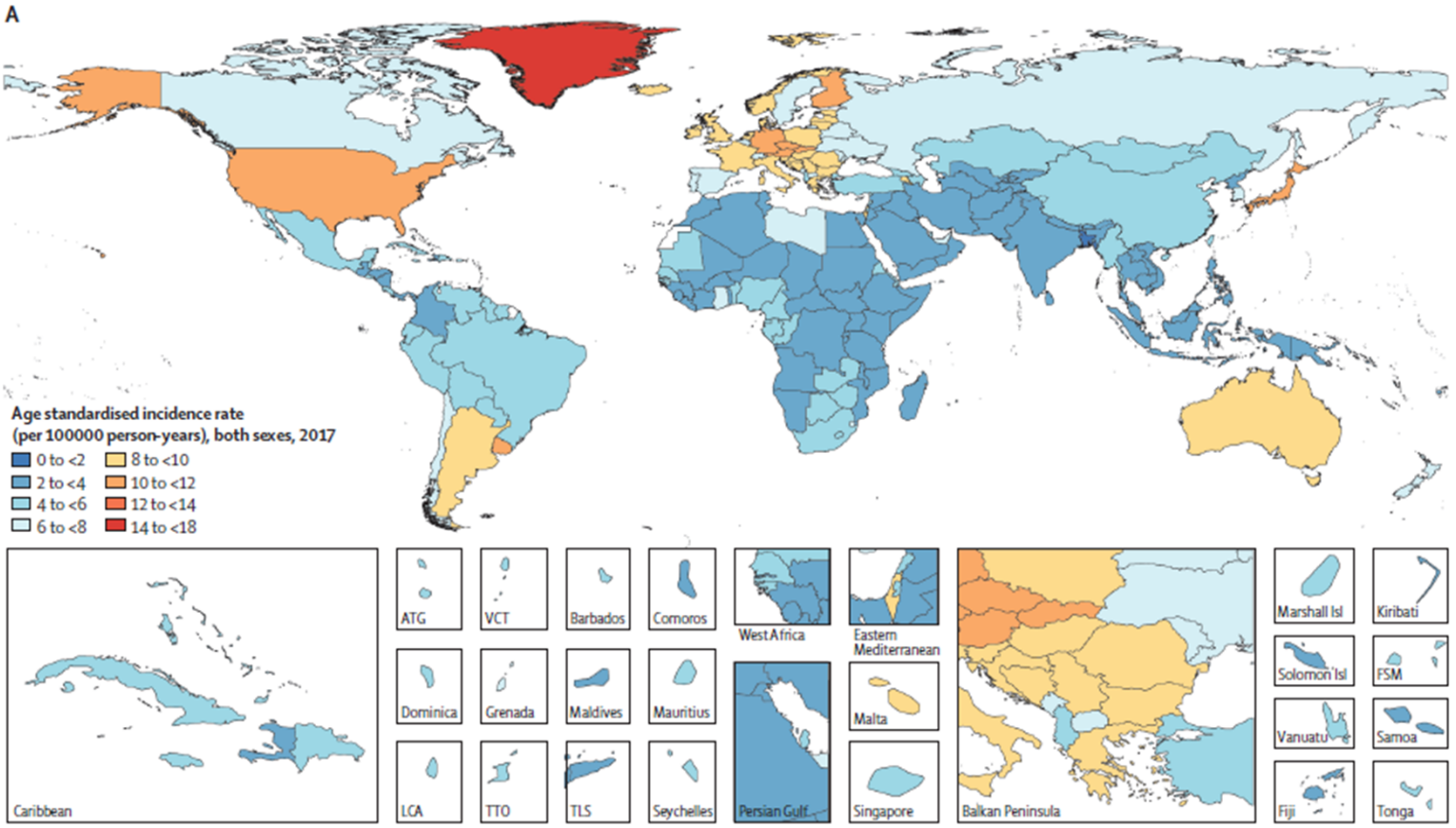


- In 2012, 8% of the global population was older than age 65 years.
- Just 3 years later, this proportion increased to 8·5%, and by 2050 it is expected to be 16·7%.

Trend of age-standardized rate of incidence and death due to PC by SDI categories



Age-standardised incidence rate of PC per 100 000 person-years by country, 2017



- Although the large changes in population demographics and improvements in diagnosis are important drivers of the increased burden of PC observed over the past 25 years, changes in modifiable risk factors also play a part.

- 20–30% of PC risk is due to inherited genetic factors
- cigarette smoking, alcohol consumption, obesity and DM have important roles in PC

Risk Factors

Genetic

-hereditary pancreatitis(trypsin G Ab,AD) ,40% Pca at age 70(50-80 x)

-Non hereditary Pancreatitis : 2% /10y

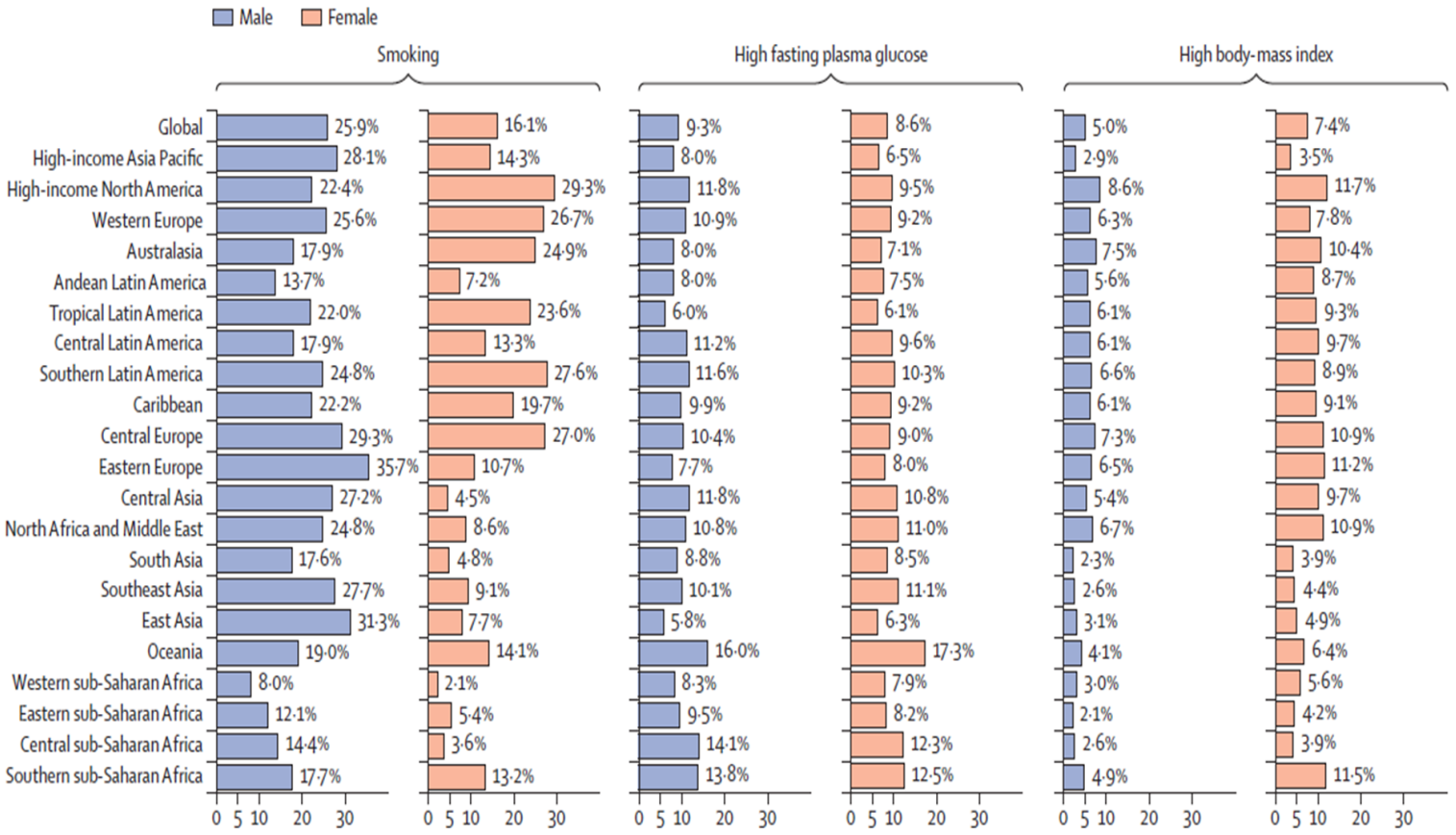
-Familial Peutz-Jeghers Syndrome:132x

-FAMMM syndrome(P16 Germline mutation),20-43x

-BCRA2 ,3.5-10x

-First Degree(one →2.3x, two →6x, 3≤ →32x)

Attributable risk factors for PC in 2017.



- Lifetime risk: 1.2% in U.S.A, M/F=1.3
- Incidence: increasing in developed countries ,increasing in Iran & developing countries!
- 4th leading cause of cancer –related death in U.S.A, Iran?
- Median age :72 y in U.S.A ,Mean age in Iran; 65± 4.2 y.
- In U.S.A rarely diagnosed 50Y>, in Iran 6% are 45 Y> .

Attributable risk factors for PC in Iran.

Risk factors	Total	Male	Female
Smoking	4.6%	16%	2%
Opium use	5.9%	11%	0%
Diabetes mellitus	8.2%	6%	12%
Family history of cancer	10.9%	11%	10%

Pancreatic Cancer UK

Do you know the symptoms of pancreatic cancer?

Tummy pain or back pain

Unexplained weight loss or loss of appetite

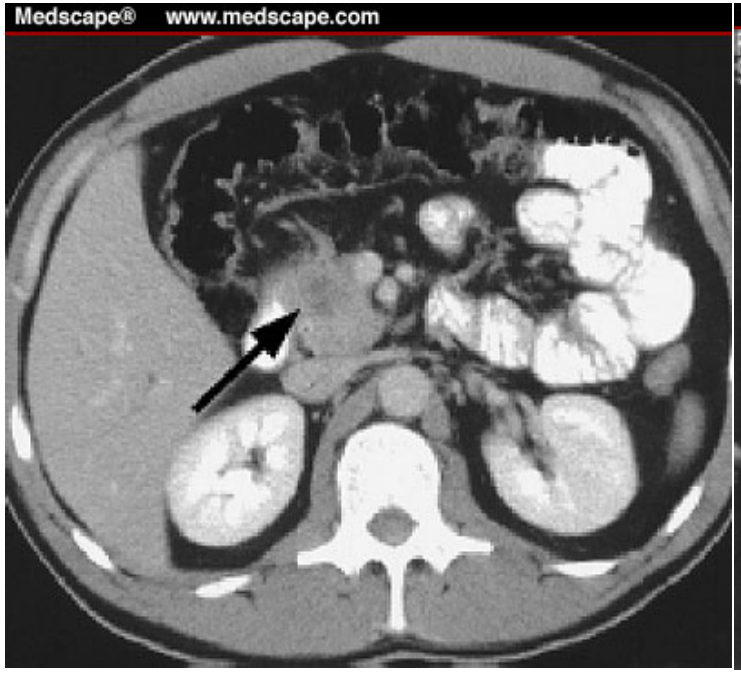
Jaundice (yellow skin or eyes and itchy skin)

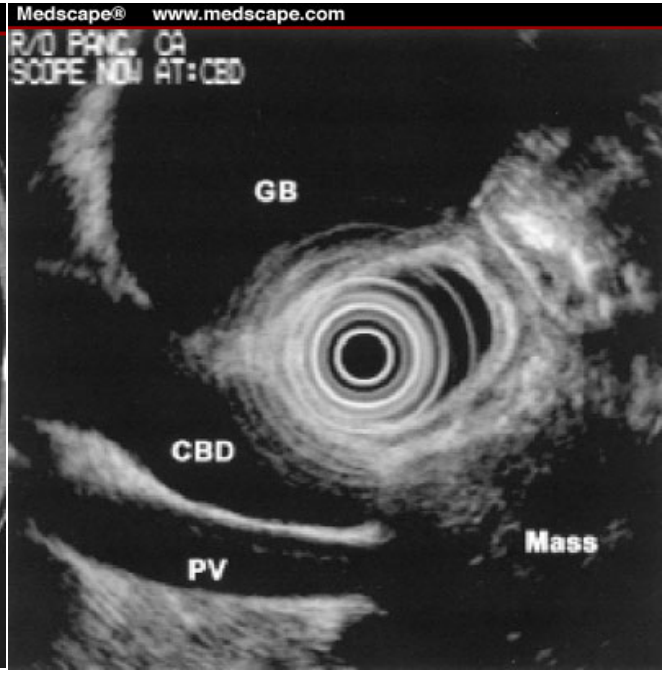
Change in bowel habits

Indigestion

If you have jaundice, go to your GP or A&E without delay. If you have any of the other symptoms for four weeks or more, and you don't know why you have them, go to your GP. Remember that these symptoms could have more common causes.

Diagnosis , staging , and prognosis





Staging

AJCC staging

TX :Primary tumor cannot be assessed

T0: No evidence of primary tumor

Tis :Carcinoma in situ

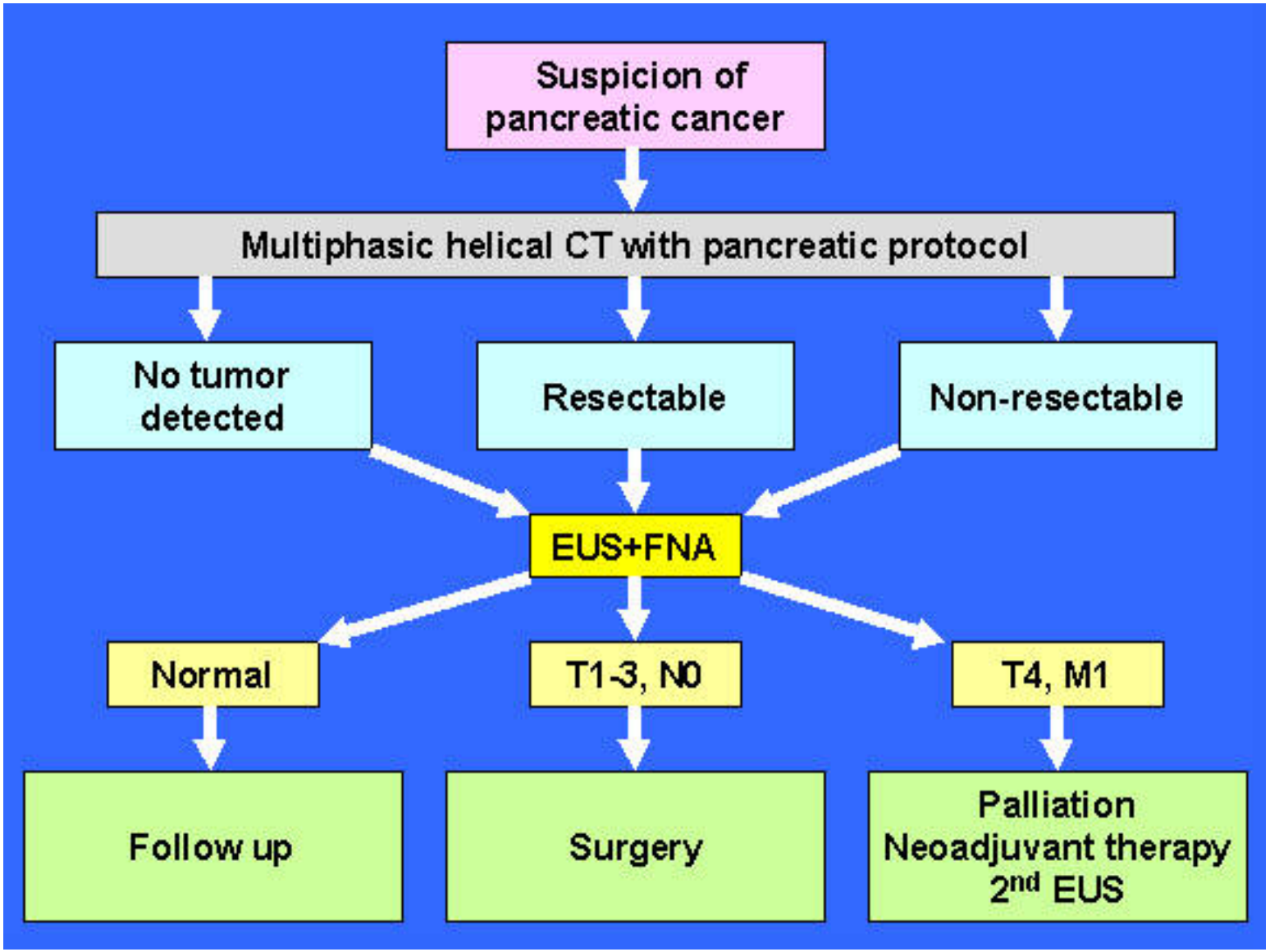
T1 :Tumor limited to P, ≤ 2cm

T2: Tumor limited to P, > 2cm

T3: : T beyond P , No celiac or SMA involvement

T4: Celiac or SMA involvemet

Stage 0	**Tis**	**N0**	**M0**
Sage I	T1, T2	N0	M0
Stage II	T1-T3	N0-N1	M0
Stage III	T4	N1	M0
Stage IV	Any T	Any N	M1


Suspicion of pancreatic cancer
Multiphasic helical CT with pancreatic protocol
No tumor detected
Resectable
Non-resectable
EUS+FNA
Normal
T1-3, N0
T4, M1
Follow up
Surgery
Palliation
Neoadjuvant therapy
2nd EUS

Treatment

- Surgery

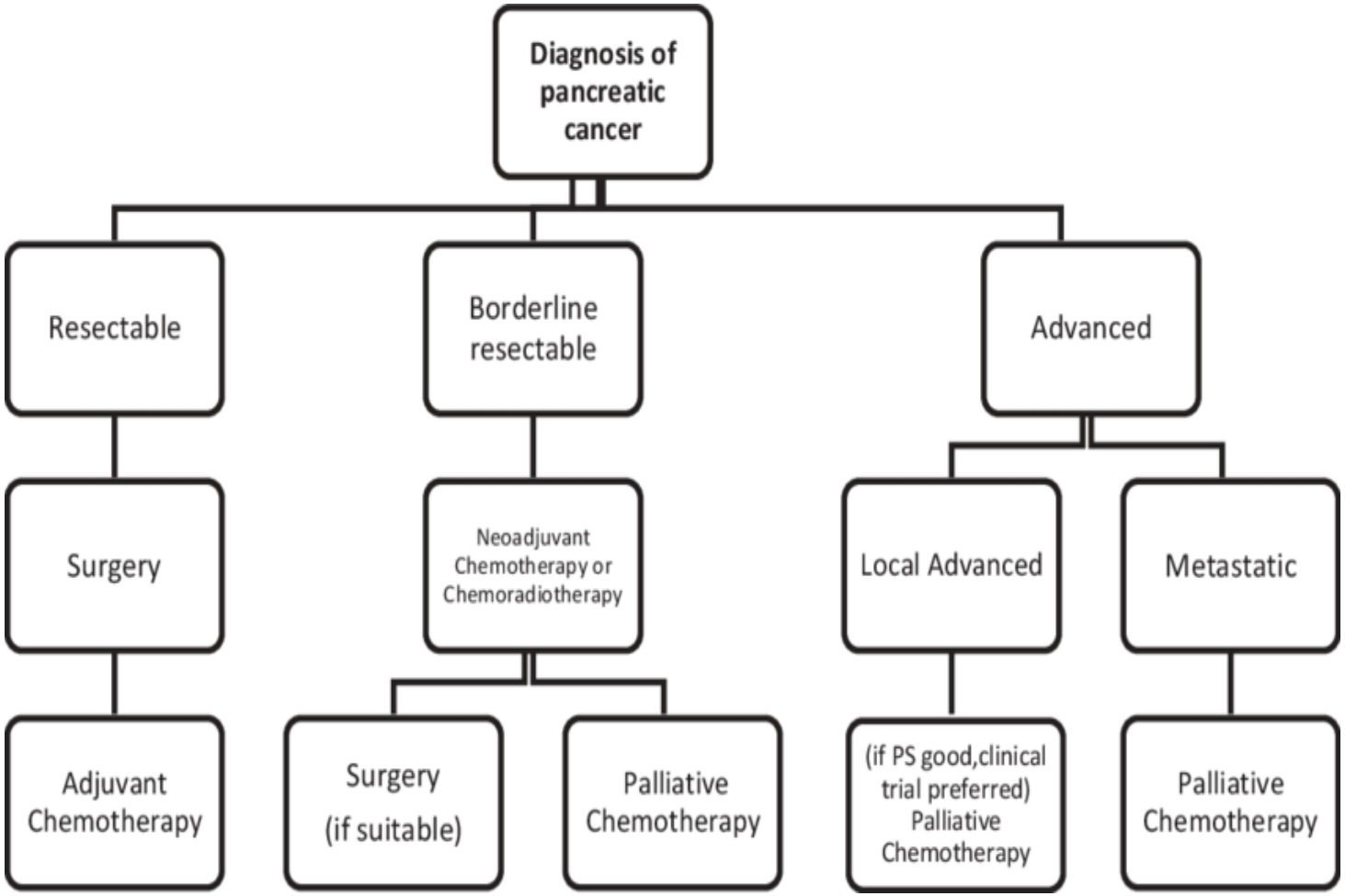
  No for metastatic patient , no extension to celiac axis, SMA ,Aorta , HA, no encasement or occlusion of SMV, or PV.

- Chemotherapy (adjuvant ,neo-adjuvant)
- "targeted therapies"

  I-Growth factor inhibitors[erlotinib (Tarceva)

  II-Anti-angiogenesis factors

- Immune therapy (vaccine, monoclonal antibodies)


Diagnosis of pancreatic cancer
Resectable
Borderline resectable
Advanced
Surgery
Neoadjuvant Chemotherapy or Chemoradiotherapy
Local Advanced
Metastatic
Adjuvant Chemotherapy
Surgery (if suitable)
Palliative Chemotherapy
(if PS good,clinical trial preferred) Palliative Chemotherapy
Palliative Chemotherapy

- Tumor location

  70% in head ,15% in body, 15% in tail

- IHC markers

- Molecular pathology

  Combination of P16 & k-ras mutation is uncommon in other human tumors & may be a molecular “signature for pancreatic adenocarcinoma

- Tumor markers

Prognosis :

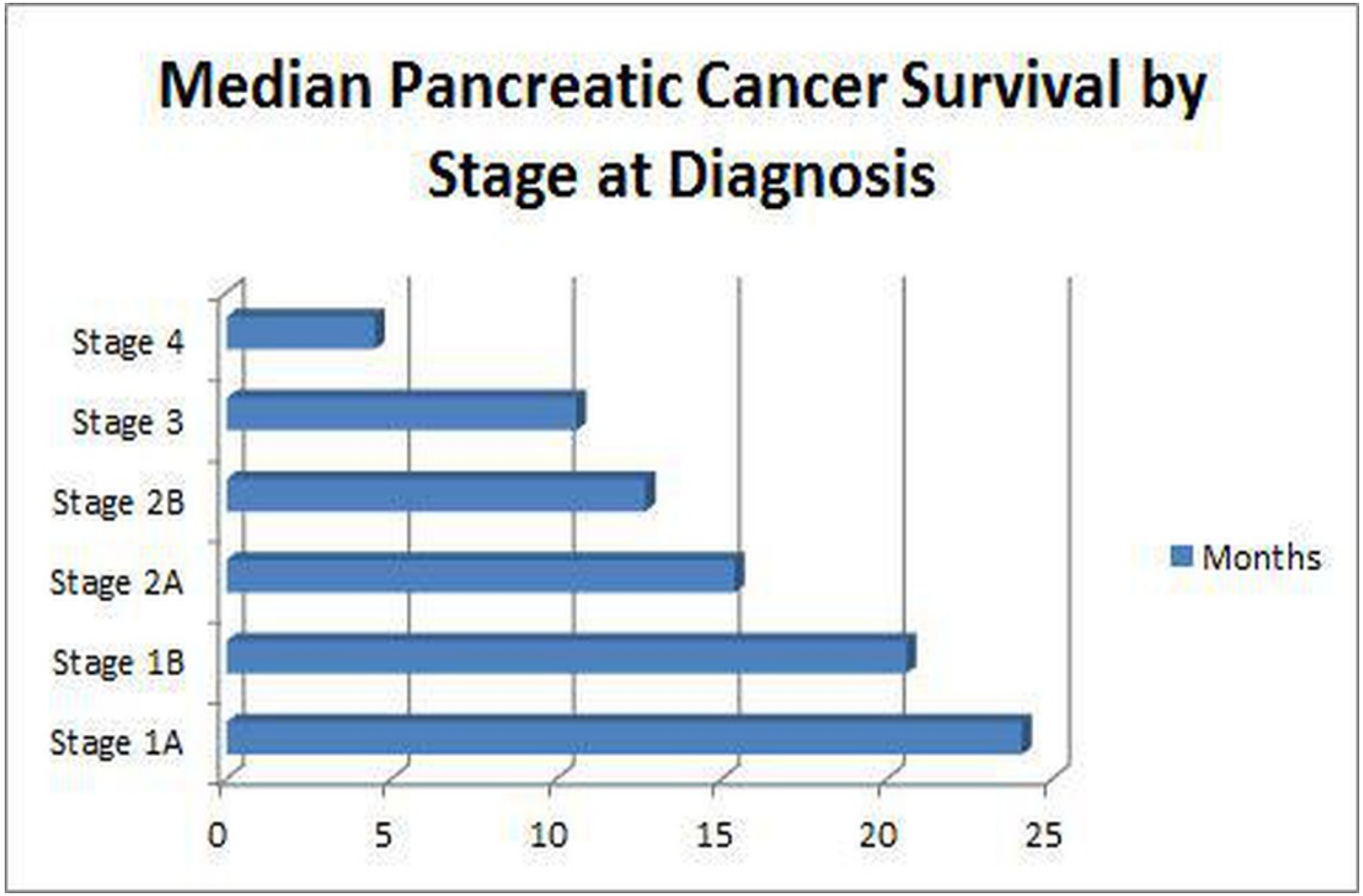
%15 - 20 have resectable disease!

%30 – 40%;locally advanced un-resectable ,8-12 m median survival.

%40 ;metastatic disease .

5 v survival: <5%

Prognosis


Median Pancreatic Cancer Survival by Stage at Diagnosis
Stage 4
Stage 3
Stage 2B
Stage 2A
Stage 1B
Stage 1A
0
5
10
15
20
25
Months

Prognosis of PC In Iran

https://doi.org/10.1371/journal.pone.0243511

Median survival time was 6.5 months, and 1-, and 5-year survival rates were 26.2%, and 1.5%.

Patients who were older ($p<0.001$), illiterate ($p = 0.004$), unmarried ($p = 0.003$), rural inhabitant ($p = 0.013$), and opium user ($p = 0.039$), had lower overall survival.

Only 10.4% of patients underwent surgery


Thank
You