Epidemiology and aetiology of Hepatobiliary-Pancreatic tumors: Insight into the Indian context

Dr Shikha Goyal

Assistant Professor

Department of Radiotherapy

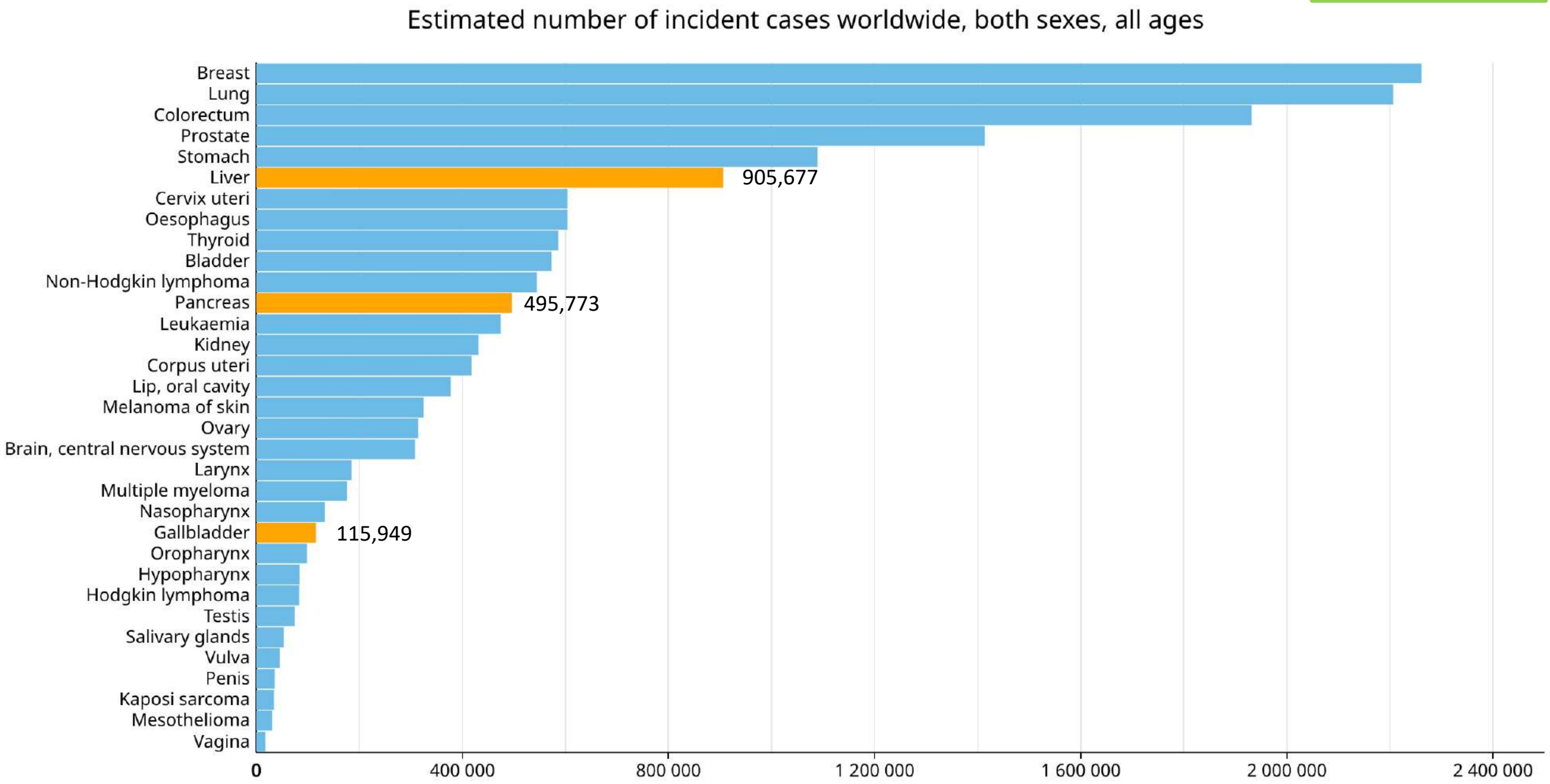
PGIMER, Chandigarh

July 23, 2022

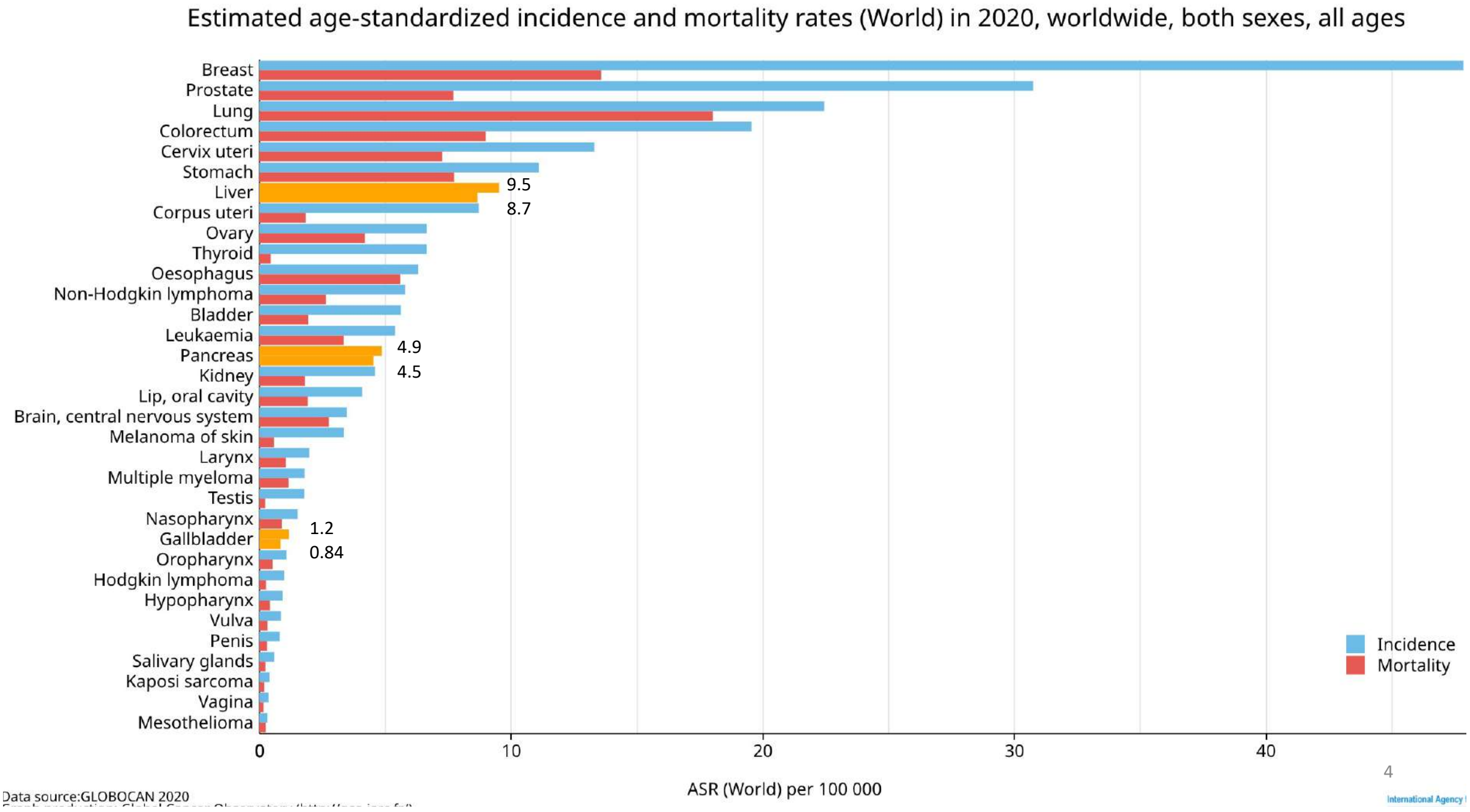
Hepatobiliary malignancies of interest

- Carcinoma gall bladder
- Hepatocellular carcinoma
- Carcinoma pancreas
- Cholangiocarcinoma

GLOBOCAN 2020



GLOBOCAN 2020



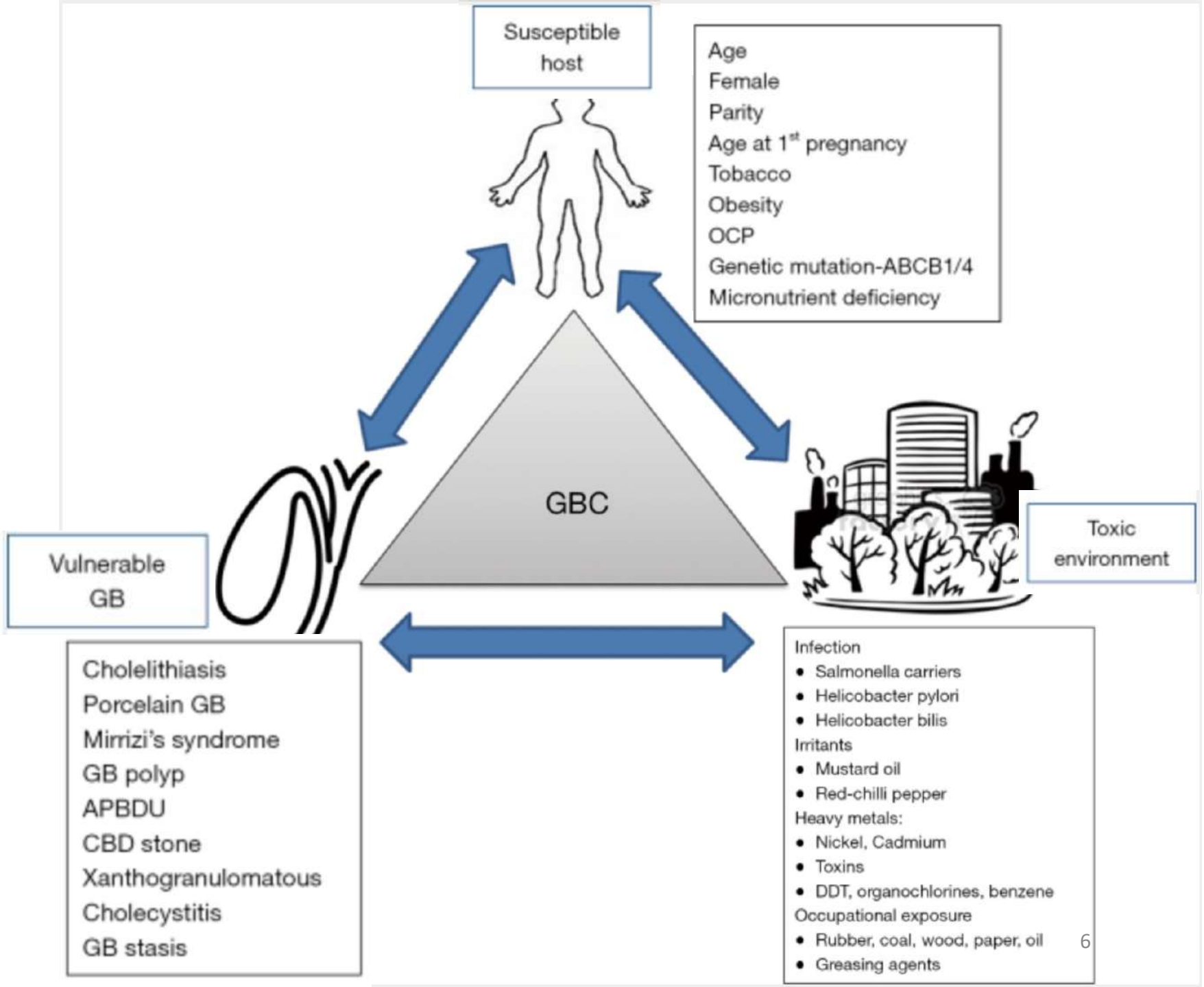
Data source:GLOBOCAN 2020

International Agency

Carcinoma gall bladder

- Globally, the burden of gallbladder / other biliary tract cancers has risen over last 30 years
- Traditionally believed to be a disease of low socioeconomic groups

Risk Factors Ca GB



GB demographics

Age	Incidence (AAR /100,000)	Mortality (AAR /100,000)
20-49 y	0.16	0.08
50-64 y	1.47	0.77
65-74 y	4.91	2.68
>75 y	8.69	5.05

Age

- Incidence increases with age
- US data: median age 67 years

Gender

- Women are affected two to six times more often than men
- Association with high parity and number of pregnancies – possible relation with female sex hormones
- Increased co-expression of ER/PR in women with Ca GB: potential target for intervention

GB demographics

Geography/ethnicity

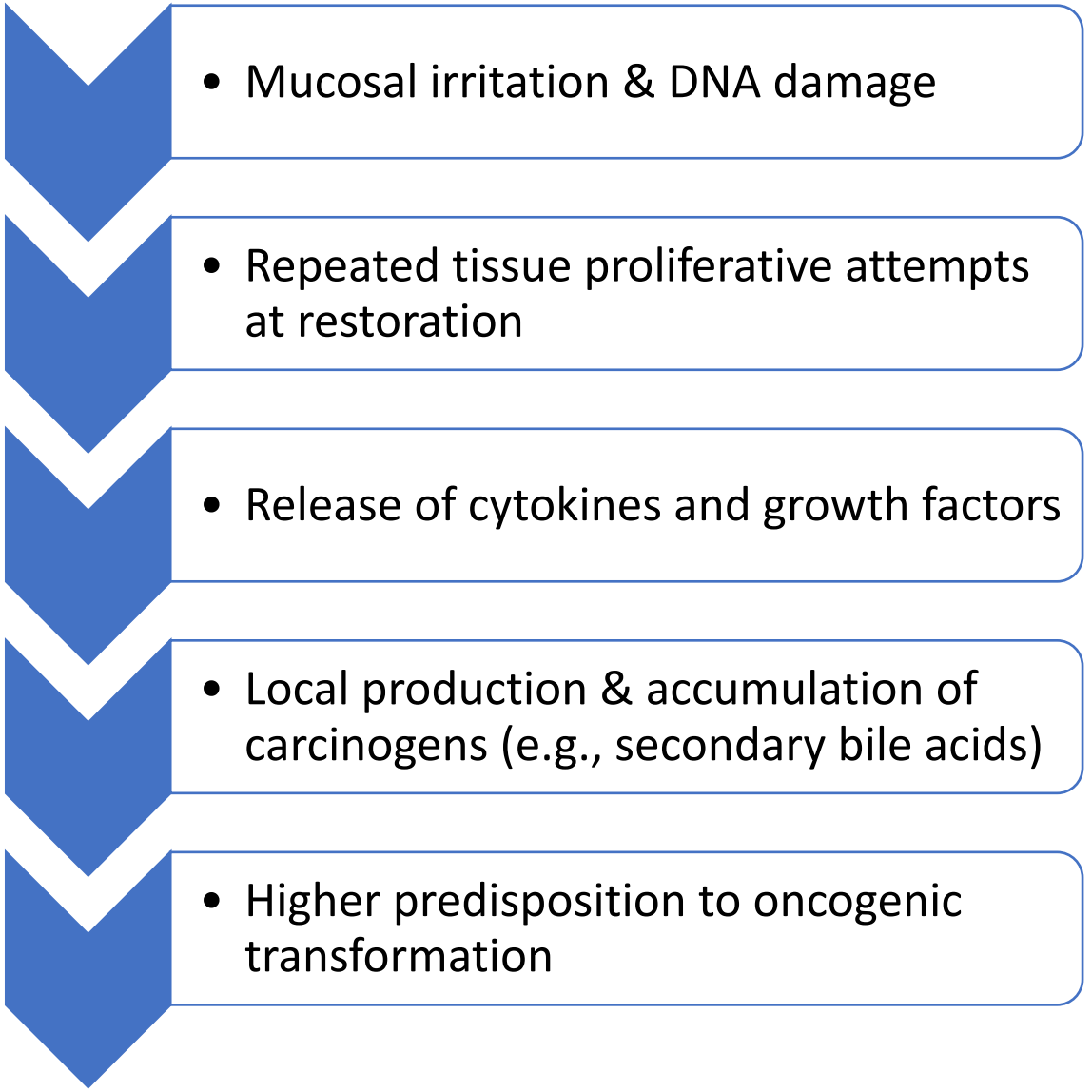
- Widely variable geographic pattern
- Incidence
  - High: Latin America and Asia >> Eastern and central Europe (Hungary, Germany, Poland)
  - Within Asia - northern Indian females, Pakistani females, Korean males
    - Korean men: Highest in Asia (AAR 8.1) – risk remains even in Koreans in US
  - Low incidence: United States, western Europe (UK, France, Norway), Mediterranean European countries
    - More common in White compared with Black people
- Mortality:
  - Native American Indians: mortality exceeds that from breast, cervix, pancreas, ovary

GB risk factors

1. Chronic GB inflammation

Major factor in carcinogenesis

- **Gallstone disease**
- **Porcelain gallbladder**
- **Gallbladder polyps**
- **Primary sclerosing cholangitis**



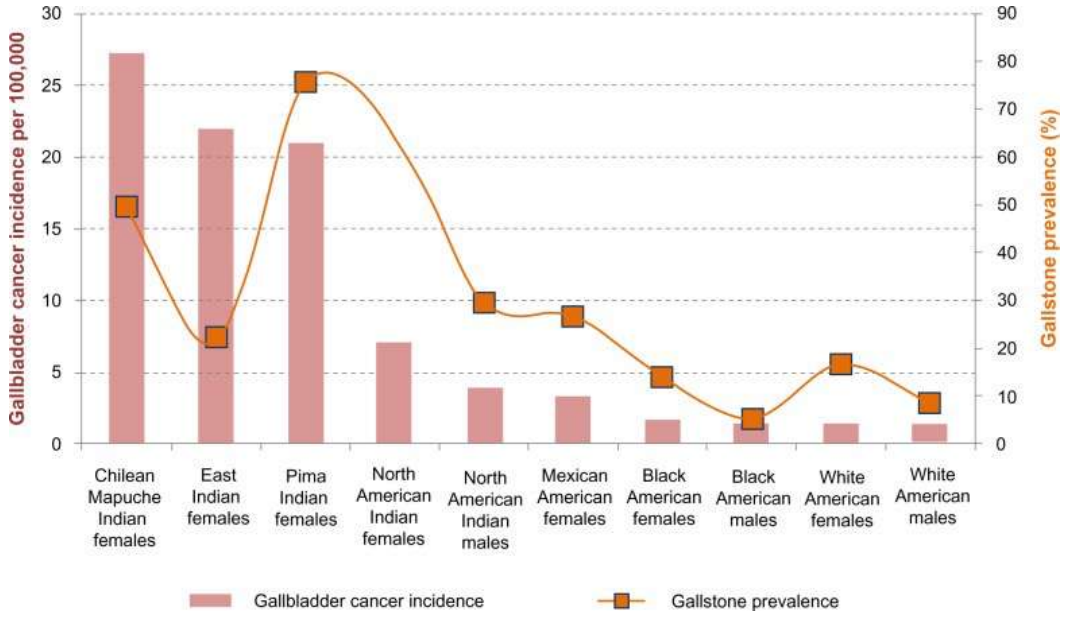
Inflammation—metaplasia — dysplasia — carcinoma sequence

GB risk factors

Gallstone disease

- ~85% patients with Ca GB have gallstones
- Only 0.5-3% pts with gallstones have Ca GB
- Compared to healthy individuals, patients with symptomatic GB disease (gallstones or self-reported cholecystitis) 34-fold more likely to develop Ca GB

- **Gallstone characteristics** influence risk
  - Stone size: 10-fold increase for stones >3 cm
  - Stone type - Cholesterol gallstones
  - Longer duration of stones (6-12 fold for >20y)



Cholecystectomy for gallstones: inverse correlated with Ca GB rates

- Poor socioeconomic status → limited access
- In the West, decline in incidence as well as mortality

GB risk factors

Porcelain gallbladder

- Calcium deposition in GB wall (<1%, women in 50s)
- ~25% risk of Ca GB
- Risk of malignancy: Stippled calcification > transmural calcification

→ Prophylactic removal of GB with partial calcification, stippled, or multiple punctate calcifications

Gallbladder polyps

- Most are non-malignant
- Risk of malignancy: large polyps (>10 mm – 25% are malignant), solitary or sessile mass, associated gallstones, Age >50 y, rapid growth
- EUS may help distinguish b/w benign and malignant polyp, follow up every 6-12m if not resected

Primary sclerosing cholangitis

6% may have GB masses, of which half may be Ca GB

Annual screening USG is recommended; Cholecystectomy if lesions >0.8 cm)

GB risk factors

2. Chronic Infections

- Chronic bacterial cholangitis
  - *Salmonella* (eg, *S. typhi and S. paratyphi*) and *Helicobacter* (eg, *H. bilis*)
  - Ca GB risk increases 12-fold in typhoid carriers

Degradation of bile constituents (ie, bacterial hydrolysis of primary bile acids forming carcinogens and/or the action of β-glucuronides) --> malignant transformation

Contributors: chronic inflammation, alterations of tumor suppressor genes (*p53*) or proto-oncogenes (*K-ras*)

- Chronic parasitic infestations
  - Clonorchis and Opisthorchis
  - Contributors: chronic inflammation, increased biliary stone formation

GB risk factors

3. Anatomic changes

- **Congenital biliary cysts** (intra- or extrahepatic)
  - more often linked to cholangiocarcinomas (risk increases with age)
  - more often in patients with an anomalous pancreaticobiliary duct junction
- **Anomalous pancreaticobiliary duct junction**
  - Congenital anomaly (picked on ERCP/MRCP/EUS)
  - More common in Asians (Japanese), young women
  - 10% of GB cancer
  - Lesser risk of invasion and metastases
  - Higher reflux of pancreatic juice into the biliary tree → increased amylase levels in bile, intraductal activation of proteolytic enzymes, alterations in bile composition → inflammatory and malignant change
  - Prophylactic cholecystectomy is recommended

GB risk factors

4. Genetics

- Family history (25% risk)
- Interaction between innate genetic predisposition and exposure to environmental risk factors
- Multistep sequence involving cumulative genetic and epigenetic alterations

5. Obesity

- Higher risk with BMI > 30 kg/m^2 (OR 1.8-2.1)
- RR increased by 1.59 for women and 1.09 for men for each 5-point increase in BMI
- Diabetes – increases risk of GSD, higher risk of Ca GB even without gallstones

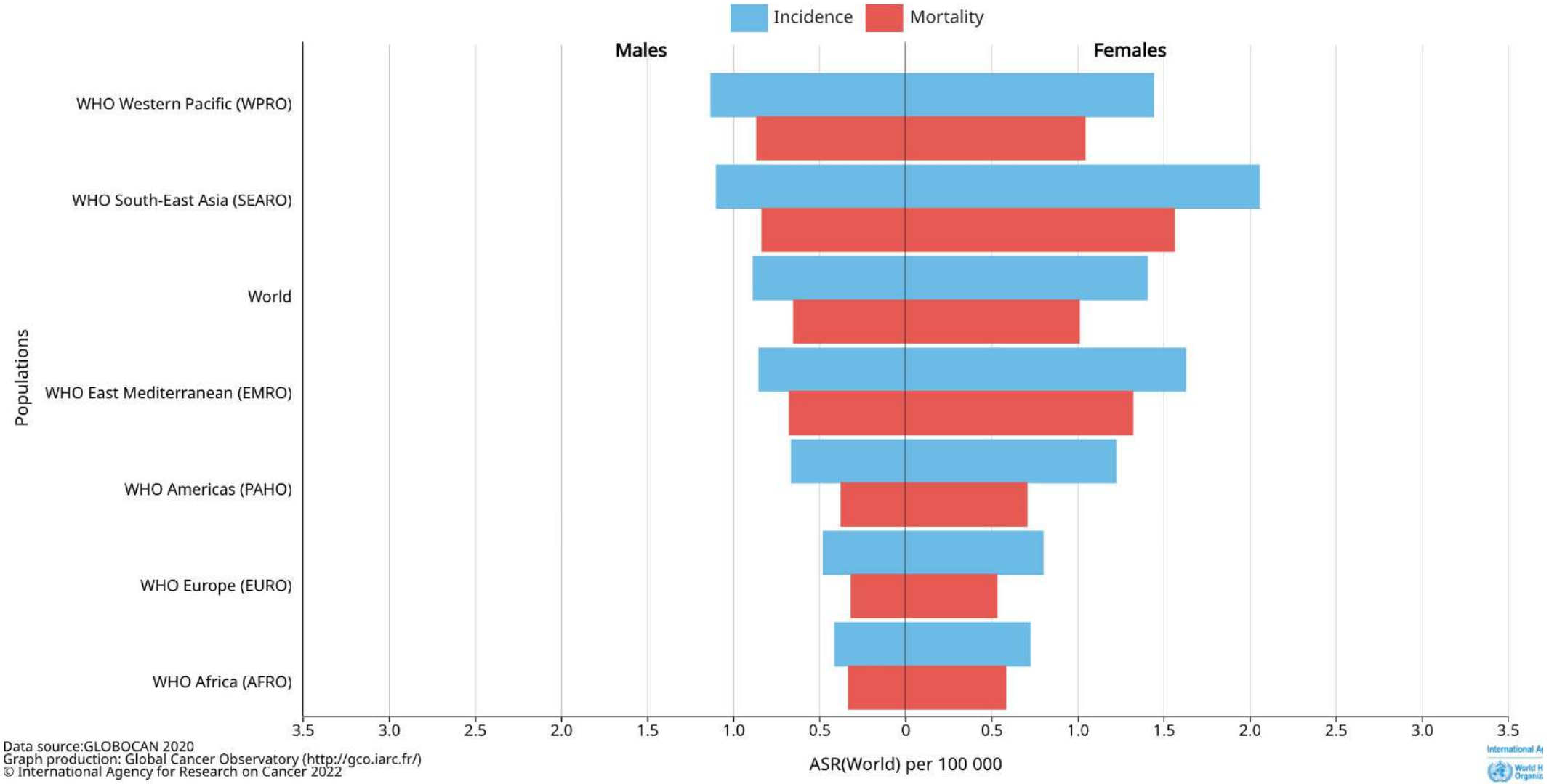
GB risk factors

6. Exposures

- Heavy metals, like nickel and cadmium, have been implicated
- Workers in the oil, paper, chemical, shoe, textile, and cellulose acetate fiber manufacturing industries
- Miners exposed to radon (inhaled)
- Tobacco consumption
- Drugs: methyldopa, isoniazid, ?OCP/HRT
- Exposure to aflatoxin, a mycotoxin that commonly contaminates corn, soybeans, and peanuts

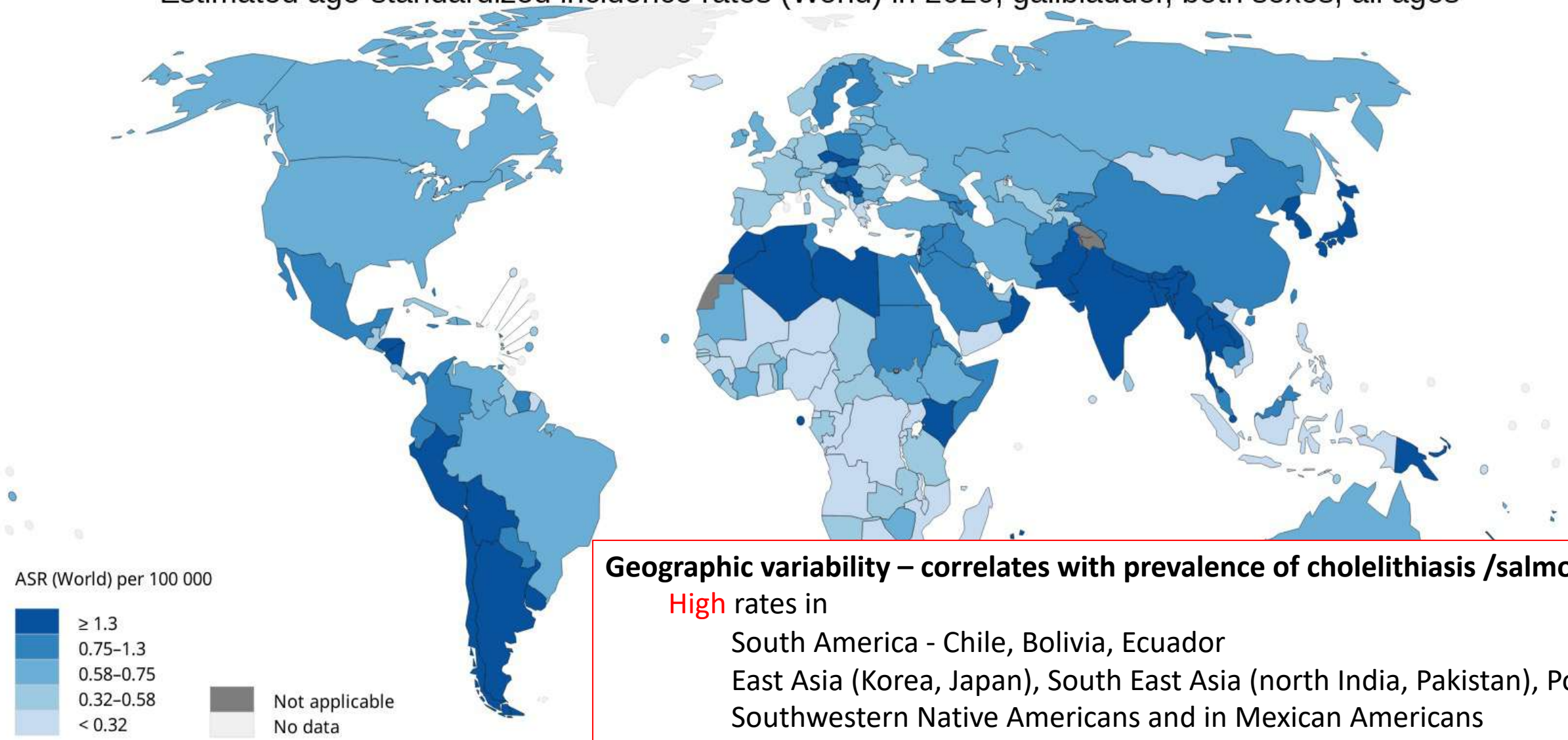
GLOBOCAN 2020

Estimated age-standardized incidence and mortality rates (World) in 2020, gallbladder, all ages (excl. NMSC)



Data source:GLOBOCAN 2020
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)

GLOBOCAN 2020



Geographic variability – correlates with prevalence of cholelithiasis /salmonella

High rates in

South America - Chile, Bolivia, Ecuador

East Asia (Korea, Japan), South East Asia (north India, Pakistan), Poland

Southwestern Native Americans and in Mexican Americans

Low rates in

North America

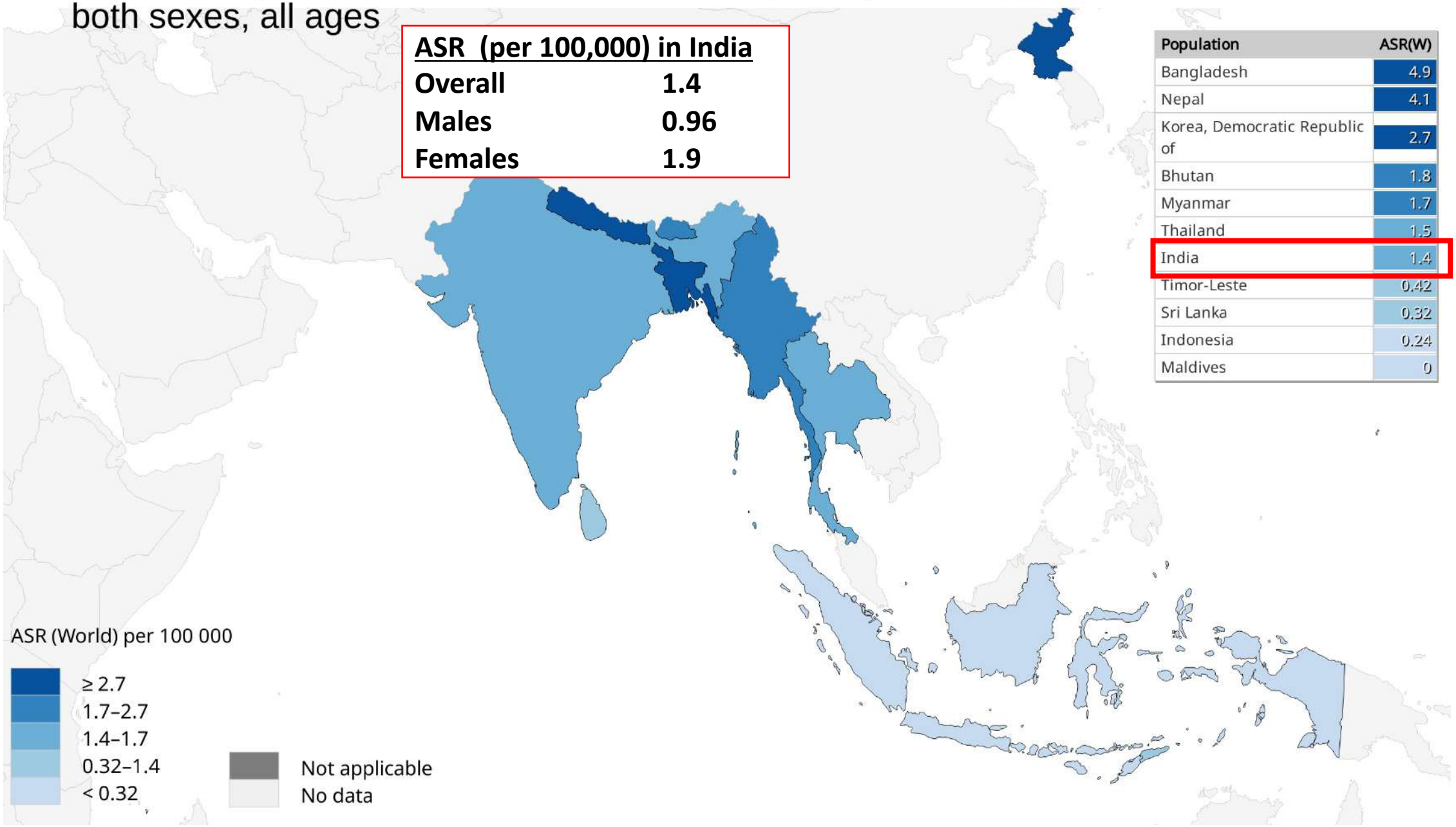
GLOBOCAN 2020

Estimated age-standardized incidence rates (World) in 2020, gallbladder, both sexes, all ages

ASR (per 100,000) in India

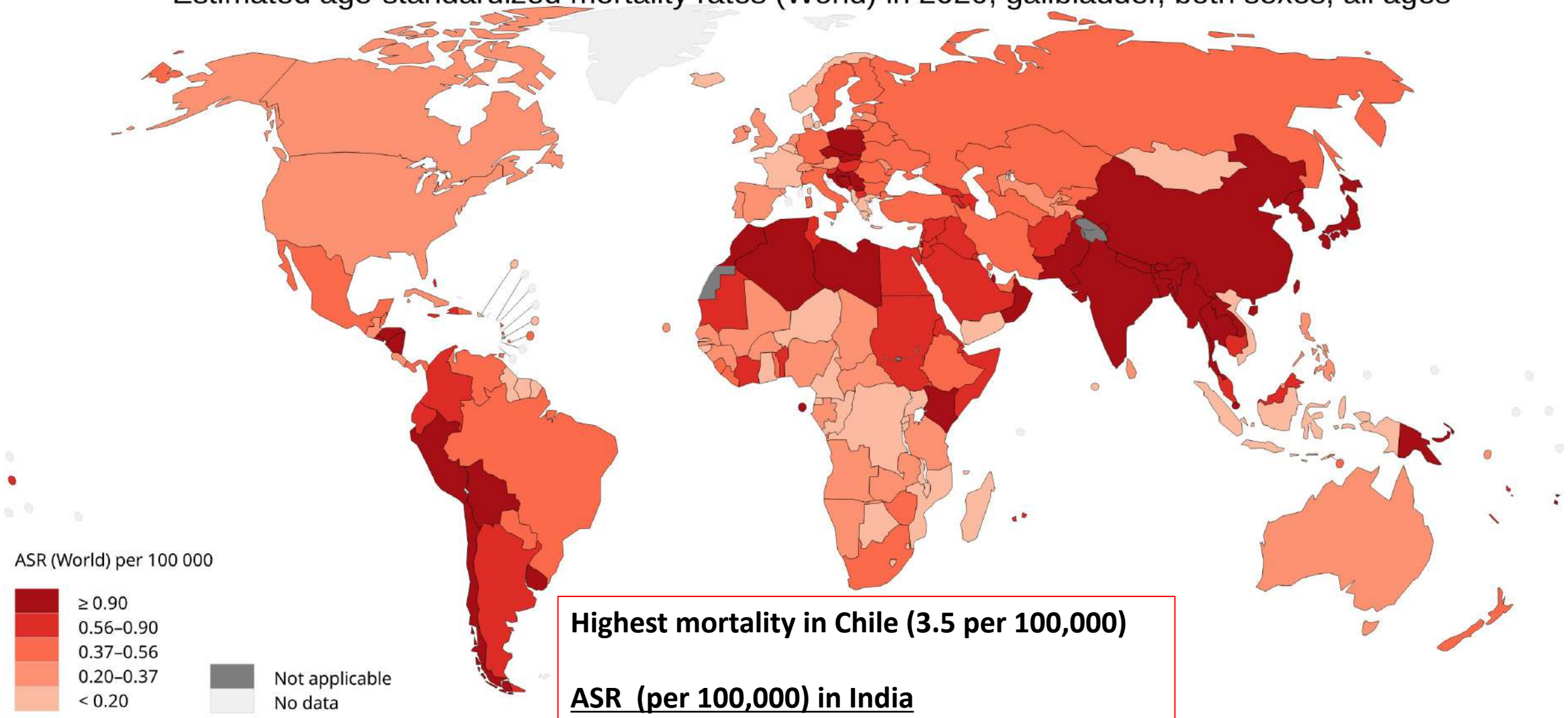
Overall	**1.4**
Males	**0.96**
Females	**1.9**

Population	ASR(W)
Bangladesh	4.9
Nepal	4.1
Korea, Democratic Republic of	2.7
Bhutan	1.8
Myanmar	1.7
Thailand	1.5
India	1.4
Timor-Leste	0.42
Sri Lanka	0.32
Indonesia	0.24
Maldives	0



GLOBOCAN 2020

Estimated age-standardized mortality rates (World) in 2020, gallbladder, both sexes, all ages



Highest mortality in Chile (3.5 per 100,000)

ASR (per 100,000) in India	
Overall	**1.1**
Males	**0.73**
Females	**1.5**

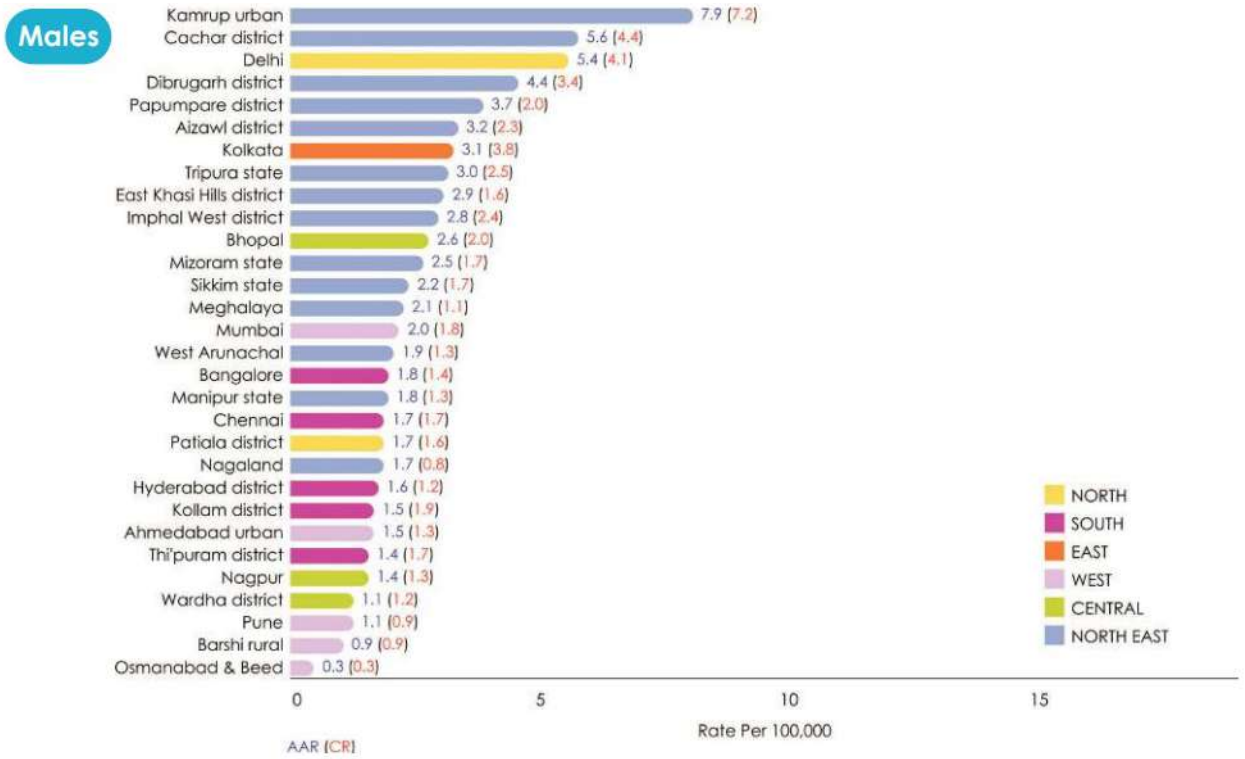
World Health Organization

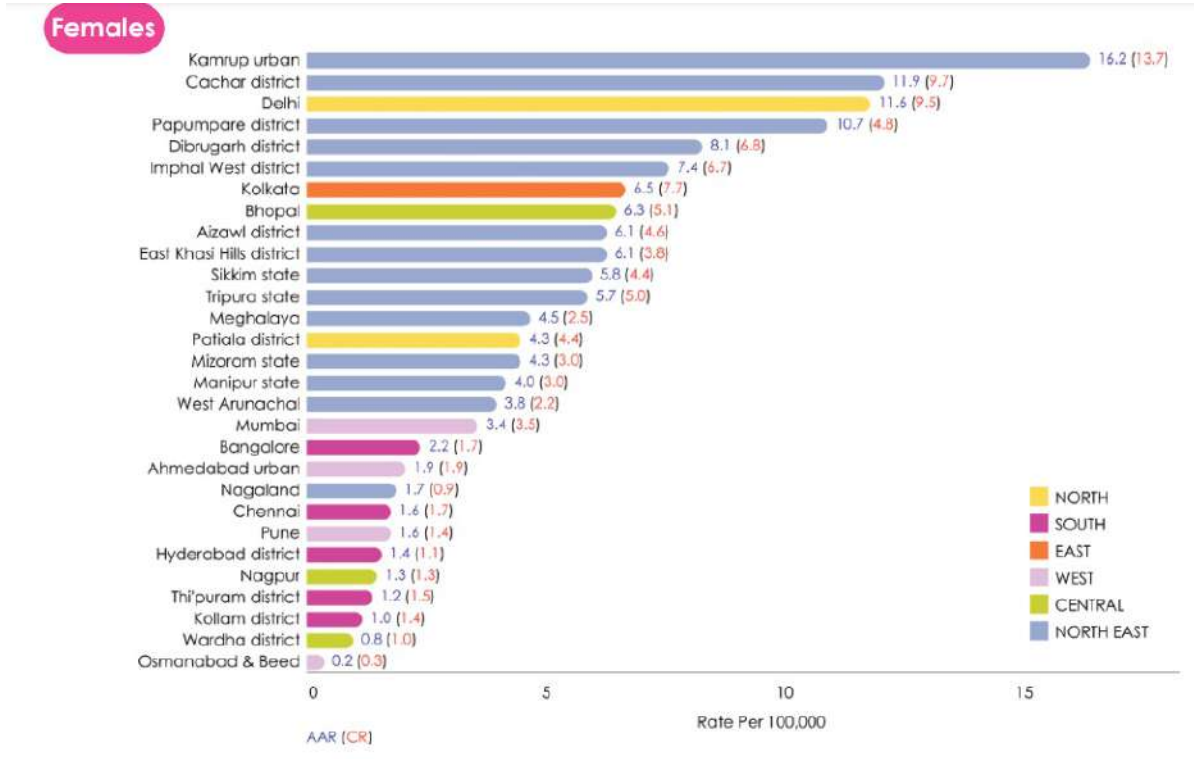
Gall bladder disease in India

- North > South
- Most prevalent in northern and northeastern states of UP, Bihar, Orissa, West Bengal and Assam
- Leading GI cancer in women in northern Indian cities
- Detailed geographic tracking of GBC patients attending TMH Mumbai (1990-95): majority of patients from UP(41.9%) and Bihar (35.8%)

NCRP 2012-16

Ca GB: Comparison of AAR of 28 PBCRs





Districts with highest AAR	Males (AAR)	Females (AAR)
Kamrup urban	7.9	16.2
Cachar	5.6	11.9
Delhi	5.4	11.6
Papumpare		10.7

	Annual percent change	Crude rate 1988	Crude rate 2014
Kamrup urban	Males: +9.7% Females: +7.2%	1.4 8.3	8.4 17.3
Delhi	Males: +4.2% Females: +3.5%	0.9 2.4	4.3 9.5
Dibrugarh	Males: +10.8%	1.7	3.1

Gallbladder Abnormalities in Northern Gangetic Area (GANGA survey)

- Population survey of environmental risk factors for GB disease
- 60 villages of Uttar Pradesh and Bihar, persons aged >30y
- GB diseases surveyed - acute & chronic cholecystitis, solitary & multiple GSD, GB polyps and Ca GB

	Gall bladder disease	Gallstones
Prevalence	6.2% 7.12% with symptoms 2.99% without symptoms	4.15% F 5.59% M 1.99% ($P < 0.05$)

Significant risk factors for GBD	Odd's ratio
Females >50 years	1.703
Multiparity	1.862
Genetic history	1.564
Males with diabetes	4.271
Chickpea consumption	2.546
Drinking unsafe water	2.835

Cluster analysis: positive correlation of nickel, cadmium and chromium in water with a high prevalence of GBD in adjacent villages in Vaishali district, Bihar.

Unisa S, et al. Population-based study to estimate prevalence and determine risk factors of gallbladder diseases in the rural Gangetic basin of North India. HPB (Oxford). 2011

3-y prospective study for Ca GB (KGMU Lucknow)

- Peak incidence: 31-50 y
- Male: Female = 1: 4.83
- On average, females were 5 years younger than males at diagnosis
- 68% patients: low socioeconomic strata - Kuppuswamy classes IV, V (lower class)
- 84% consumed mustard oil (home made/loose packed) as predominant cooking medium
- Age of menarche <14y (83%), Age at FCB <20y (56%), Parity >2 (57%)– higher incidence
- >70% were postmenopausal
- 80% had gallstones
- 32% had incidental GBC diagnosis, 52% presented with distant mets

➔**Contribution of lifestyle, cultural, dietary factors**

➔**Balanced diet, prevention of malnutrition/adulteration, tobacco prevention and early intervention for cholelithiasis may help decrease incidence**

Gupta S, Kori C, Kumar V, Misra S, Akhtar N. Epidemiological Study of Gallbladder Cancer Patients from North Indian Gangetic Planes--a High-Volume Centre's Experience. J Gastrointest Cancer. 2016 Mar;47(1):27-35.

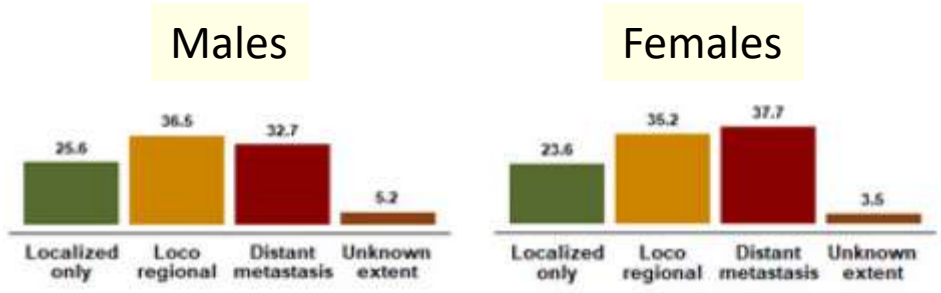
Case control study at TMH Mumbai

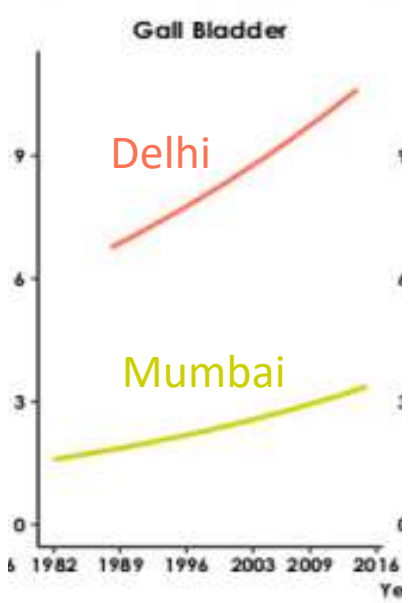
- Role of cooking with mustard oil and other dietary factors in relation to Ca GB in high- and low-incidence regions of India
- Increased risk of Ca GB
  - High consumption of mustard oil in both high-risk (OR 1.33) and low-risk regions (OR = 3.01)
  - Deep frying of fresh fish in mustard oil (OR = 1.57)
- Protective association
  - Consumption of leafy vegetables, fruits, onion and garlic
- No association
  - Consumption of meat, spicy food, turmeric, pulses
  - Any other oil as cooking medium

Mhatre S, et al. Mustard oil consumption, cooking method, diet and gallbladder cancer risk in high- and low-risk regions of India. Int J Cancer. 2020

NCRP HBCR data – GI cancers

- 58 HBCRs
- GB cancers constitute 10% of GI cancers in males (rank 4) and 23.8% in females (rank 2)
- 80% GB malignancies were adenocarcinomas
- Younger age (45-49 years) in women compared to other cancers
- ~70% have locally advanced or metastatic disease
- For the period 1982-2016, annual percentage change in AAR was
  - 1.76% for Delhi
  - 2.31% for Mumbai





S ST, et al. Asian Pac J Cancer Prev. 2022

Hepatocellular carcinoma

- HCC and Intrahepatic cholangio - 6th most common cancer
- HCC – 3rd most common cause of mortality, second most lethal tumor (5y S 18%)
- Increasing incidence and mortality: North America, Latin America, and central Europe (recent decline or plateau in deaths due to increased detection of localised HCC)

Hepatocellular carcinoma – Risk factors

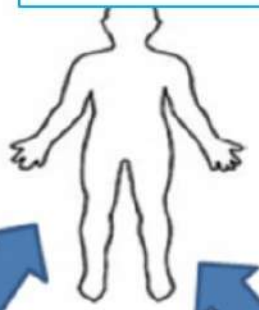
Susceptible host

Gender
- M > F

Diabetes mellitus

Obesity

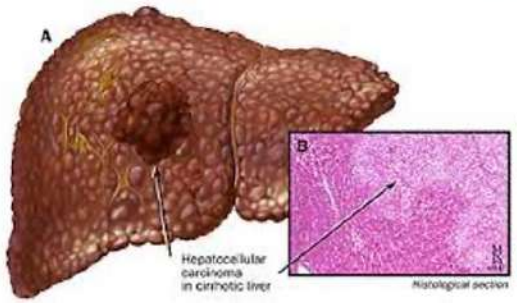
Genetic susceptibility
- Hereditary hemochromatosis
- Alpha-1 antitrypsin deficiency
- Acute intermittent porphyria
- Porphyria cutanea tarda



Pancreatic cancer

Environment / lifestyle

Local factors



- Cirrhosis due to any cause
- Non-alcoholic fatty liver disease

Infections – HBV, HCV, HDV

Lifestyle factors – Alcohol, tobacco
- Tobacco

Toxins — synergistic effect
- Aflatoxin B1 - parts of Africa & Asia
- Betel nut chewing
- Iron overload - non-dietary sources (eg, chronic transfusion of RBCs for hereditary anemia)
- Contaminated drinking water (China - algal toxin Microcystin)

Hepatocellular carcinoma – Risk factors

Cirrhosis

- Cirrhosis from any etiology increases HCC risk
- Nearly 1/3 cirrhotic patients develop HCC during their lifetime (annual incidence rate 1-8%)
- Causes of cirrhosis
  - Cryptogenic (NASH)
  - Viral hepatitis
  - Alcoholic liver disease
- Distribution of these causes varies worldwide

Hepatocellular carcinoma – Risk factors

Viral hepatitis

50% HCC cases – HBV, 20% - chronic HCV

- **Hepatitis B virus** — Factors other than cirrhosis include:
  - High viral load (ie, HBV DNA levels >10^6 copies /mL)
  - HBeAg positivity (an indicator of a prolonged replication phase)
  - HBsAg levels >1000 IU/mL in patients with HBeAg negative chronic HBV with low viral load (ie, inactive chronic HBV)
  - HBV genotype C
  - Male sex (for patients who are HBsAg positive)
  - Viral coinfection (HCV or hepatitis D virus)
  - Coinfection with HEV reduces risk compared to HBV alone
  - HBsAg clearance – does not eliminate the risk of HCC but lower compared to HBsAg positive

- Contributing factors in addition to HBV
  - Age – Young age of HBV acquisition or older age among those with chronic infection
  - Lifestyle factors – Alcohol or tobacco use.
  - Blood group B (in males only)
  - Family history of HCC

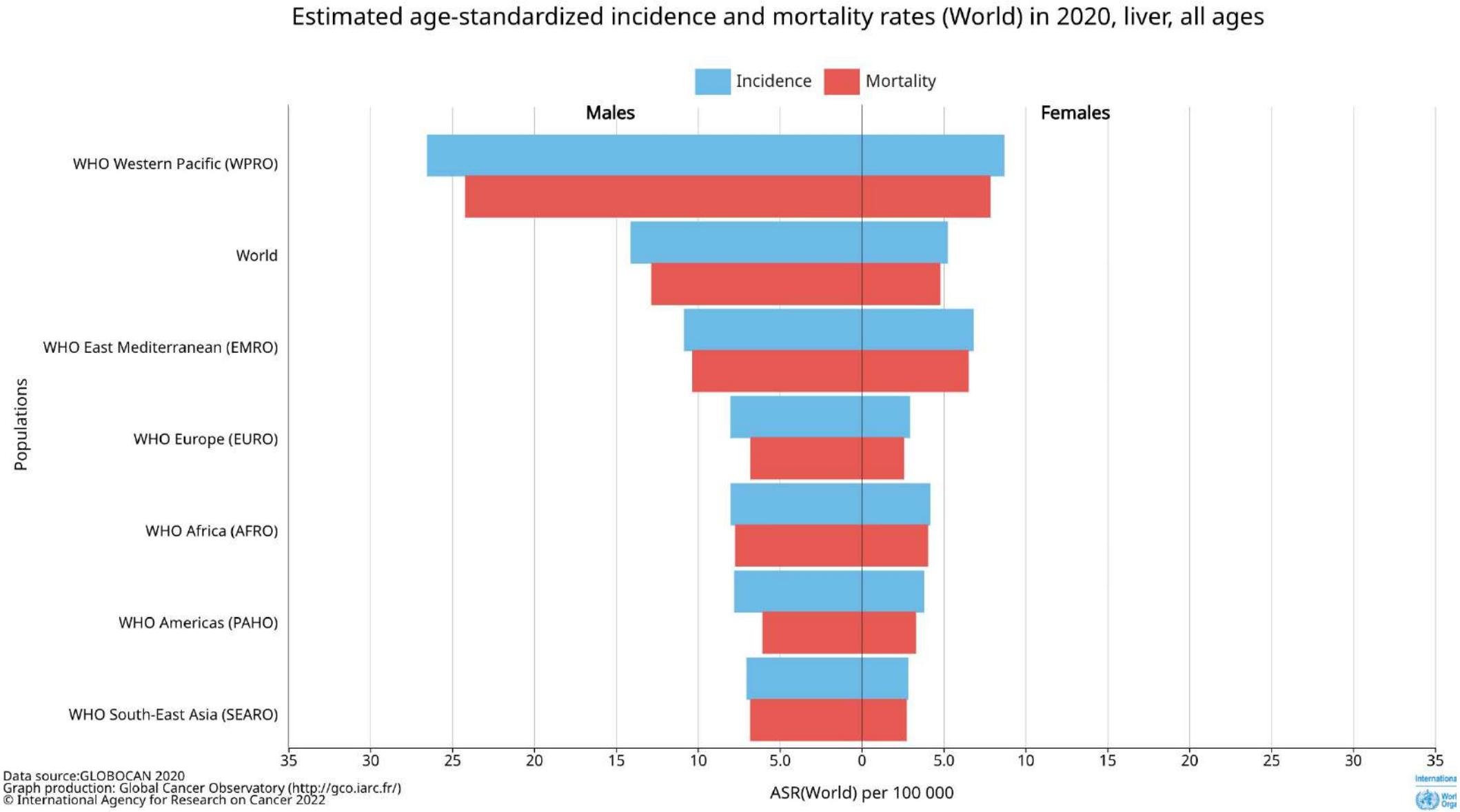
Hepatocellular carcinoma – Risk factors

- **Hepatitis C virus** - cirrhosis as well as other risk factors:
  - Genotype – HCV genotype 1b, compared with genotypes 2a/c)
  - Viral coinfection (HBV or human immunodeficiency virus infection)
  - Lifestyle factors – Alcohol or tobacco use
  - Metabolic factors – Diabetes mellitus, obesity
- **Hepatitis D virus** — coinfection with HBV increases risk

Hepatocellular carcinoma – Epidemiology

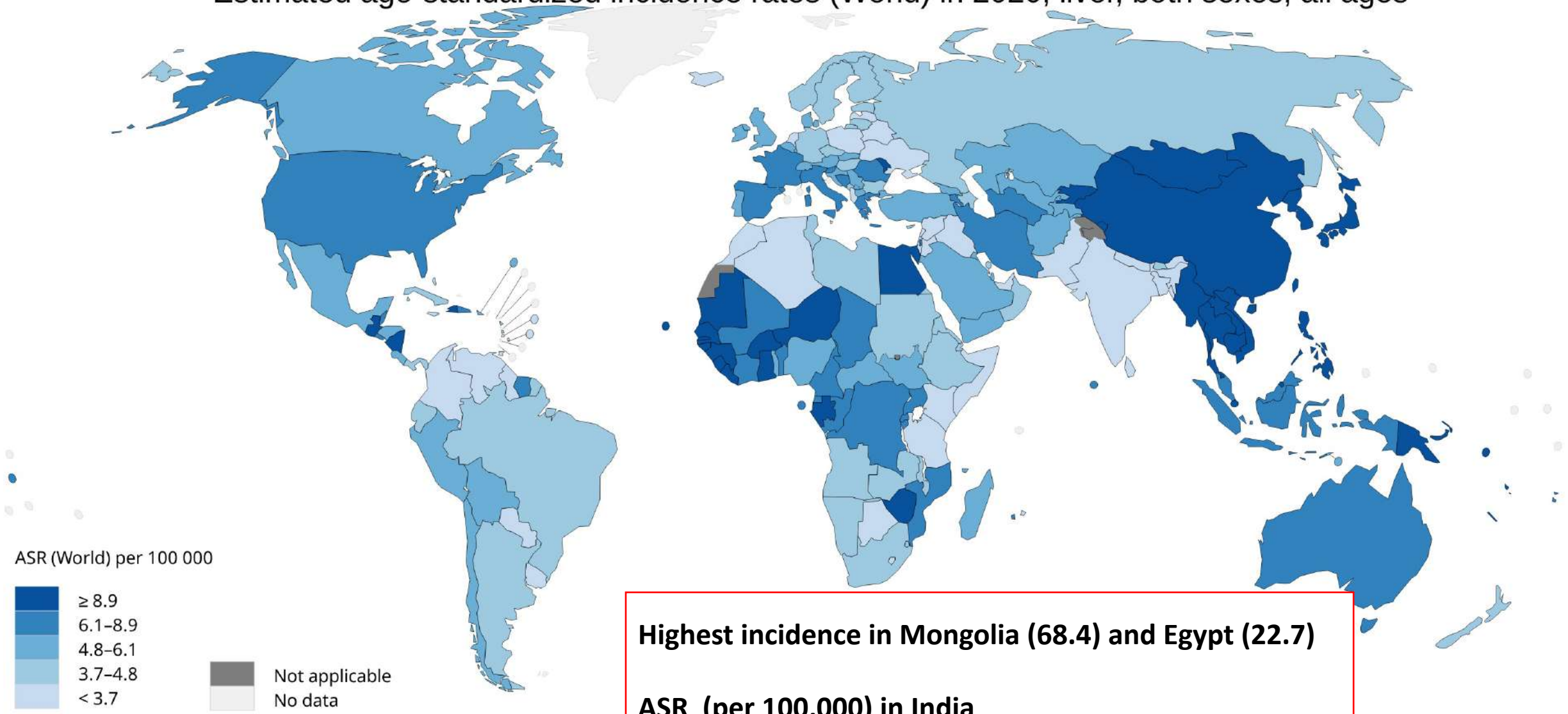
- Geographic variation
  - Asia (72%), Europe (10%), Africa (8%), North America (5%), Latin America (5%)
  - Highest incidence - Mongolia (93.7 per 100,000)
  - Different exposure to viruses and environmental agents
- Sex and race
  - Men > Women (3:1)
  - In USA, incidence in Asia-Pacific Islanders (7.8) > Black Americans (4.2) > Native Americans/Alaska Natives (3.2) > White Americans (2.6)
  - Year of birth - HCV highest prevalence in birth years 1945-65 – highest mortality for liver cancer

GLOBOCAN 2020



GLOBOCAN 2020

Estimated age-standardized incidence rates (World) in 2020, liver, both sexes, all ages



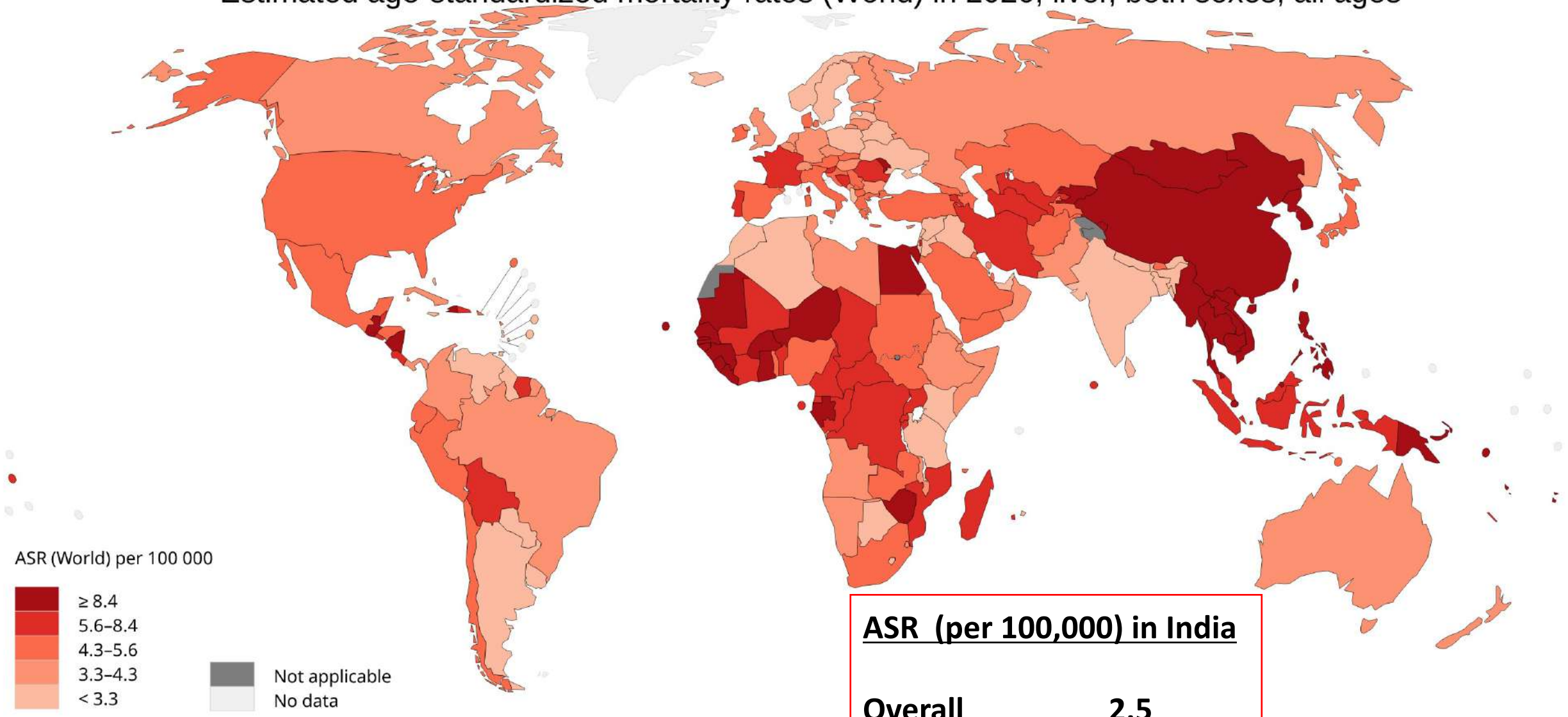
Highest incidence in Mongolia (68.4) and Egypt (22.7)

ASR (per 100,000) in India

Overall	**2.6**
Males	**3.6**
Females	**1.6**

GLOBOCAN 2020

Estimated age-standardized mortality rates (World) in 2020, liver, both sexes, all ages

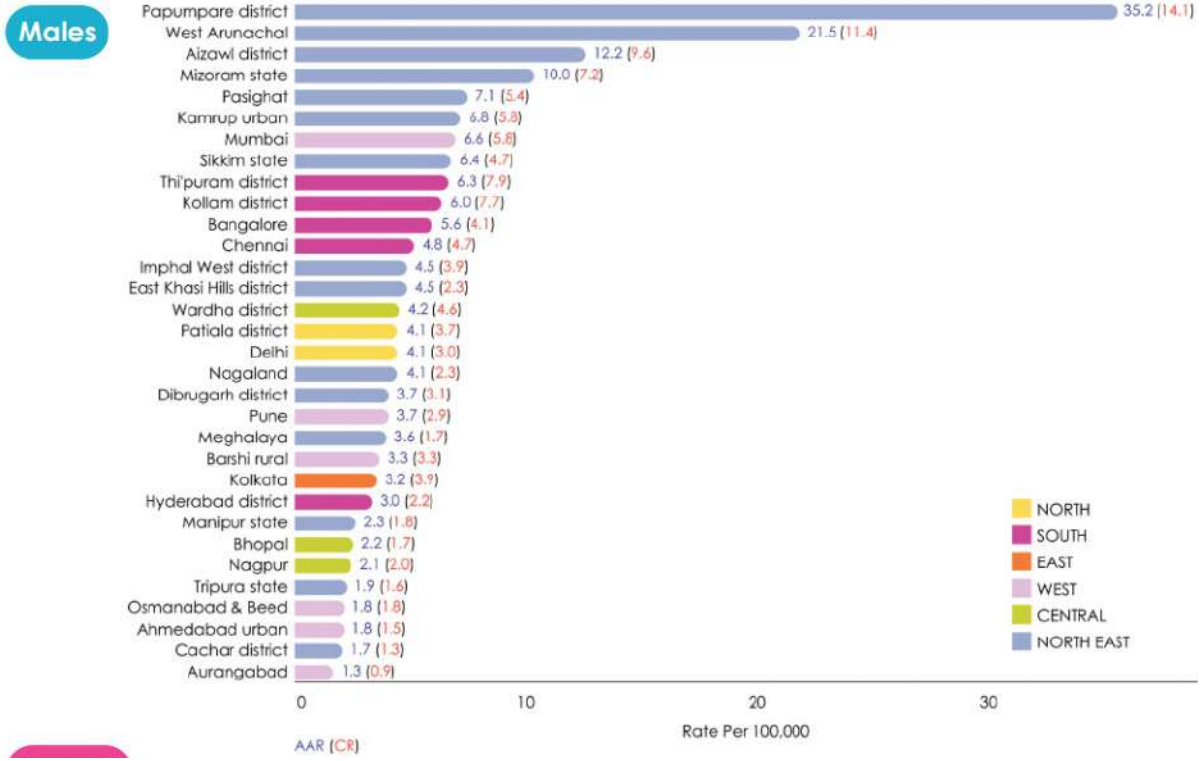


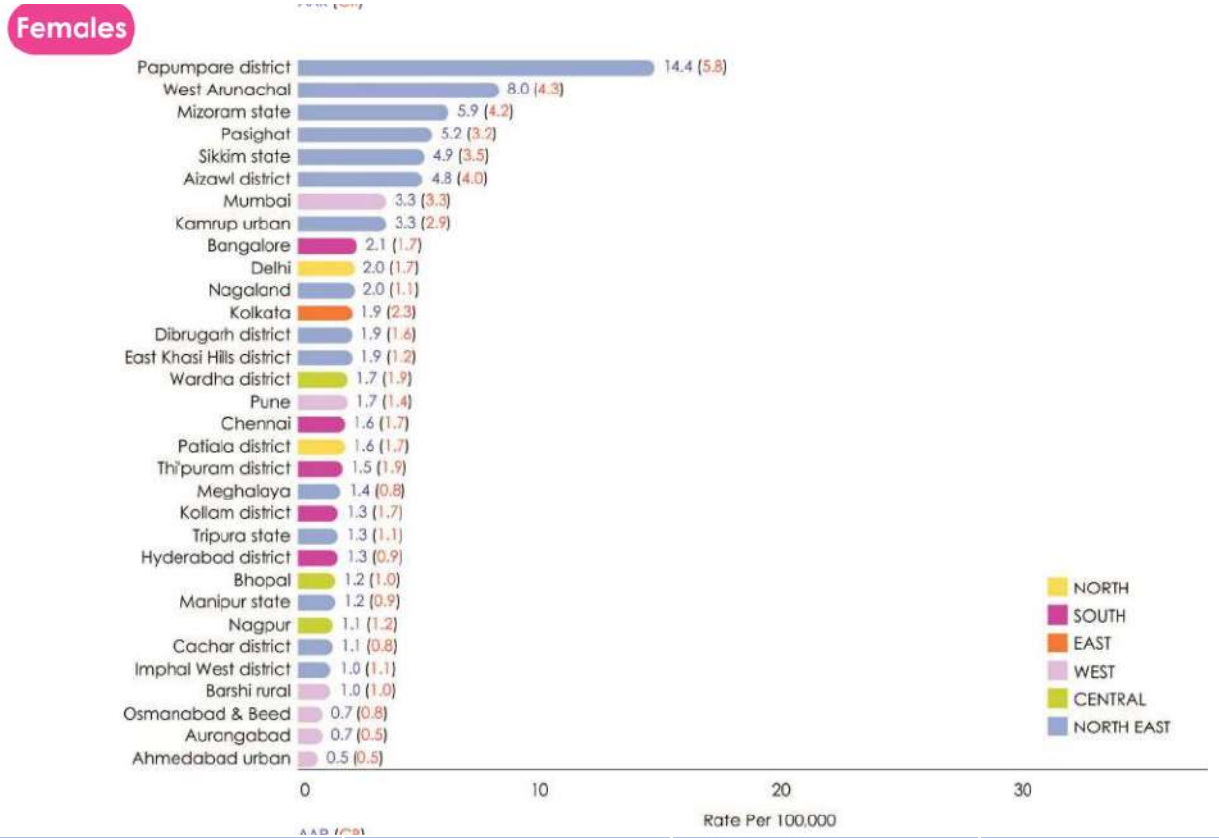
ASR (per 100,000) in India

Overall	**2.5**
Males	**3.5**
Females	**1.5**

World Health Organization

Liver: Comparison of AAR of 28 PBCRs





Districts with highest AAR	Males (AAR)	Females (AAR)
Papumpare	35.2	14.4
West Arunachal	21.5	8.0
Aizawl	12.2	
Mizoram	10.0	5.9

	Annual percent change	Crude rate 1988	Crude rate 2014
Kamrup urban	Males: +11.0%	2.5	6.2
Thiruvananthapuram	Males: +7.2%	4.5	9.3
Mumbai	Males: +4.0% Females: +4.2%	2.1 1.4	4.8 3.2

3y observational study on HCC patients: KMC Manipal

- 73.2% had cirrhosis
- Diabetes mellitus (DM) was present in 44.2%
- BCLC stages C and D - 62.4%
- Only 26.6% of cirrhotic HCC patients were diagnosed during surveillance
- Patients in non-cirrhotic HCC group
  - higher age
  - larger lesion size
  - lower MELD score

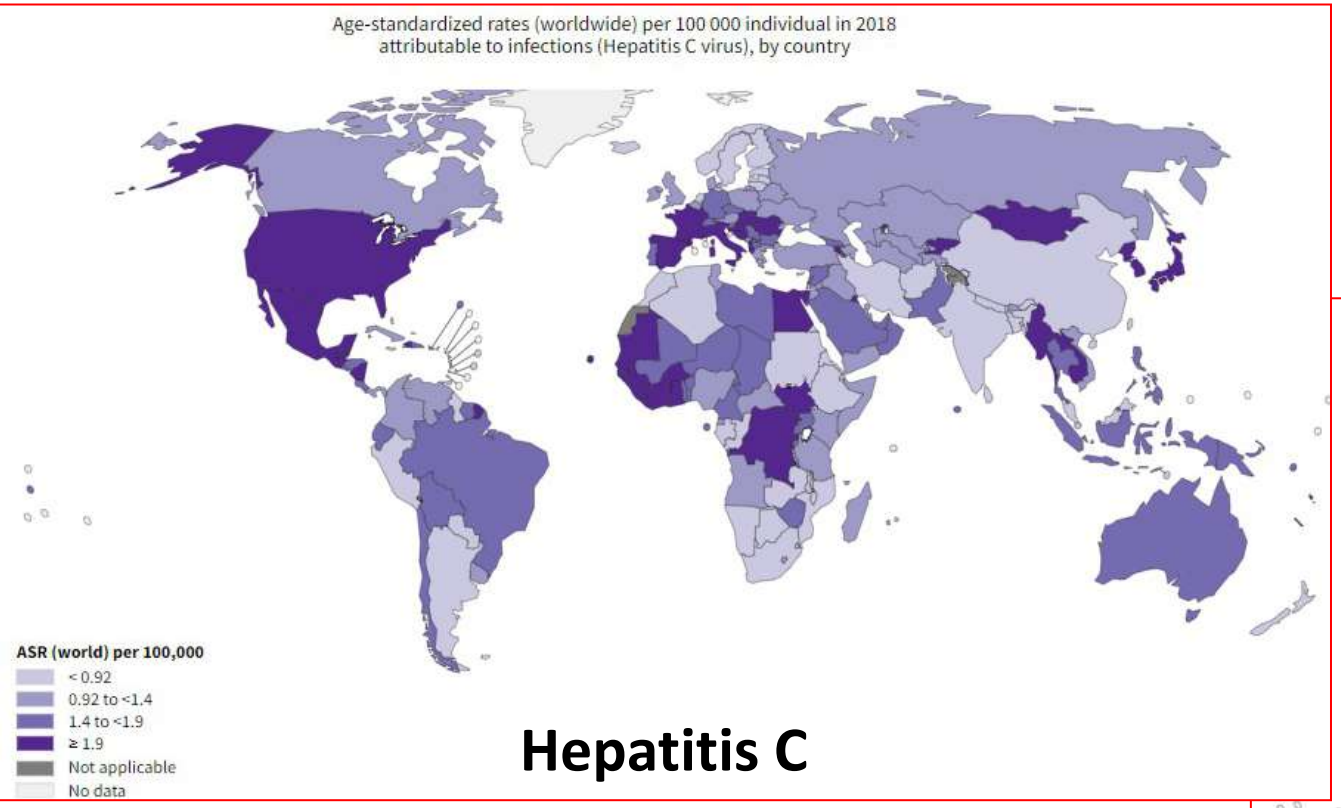
Etiology	Percentage
Cryptogenic	51.3
Alcohol	19.4
Hepatitis B	17.4
Hepatitis C	5.8

Musunuri B, et al. Profile of patients with hepatocellular carcinoma: An experience from a tertiary care center in India. Indian J Gastroenterol. 2022

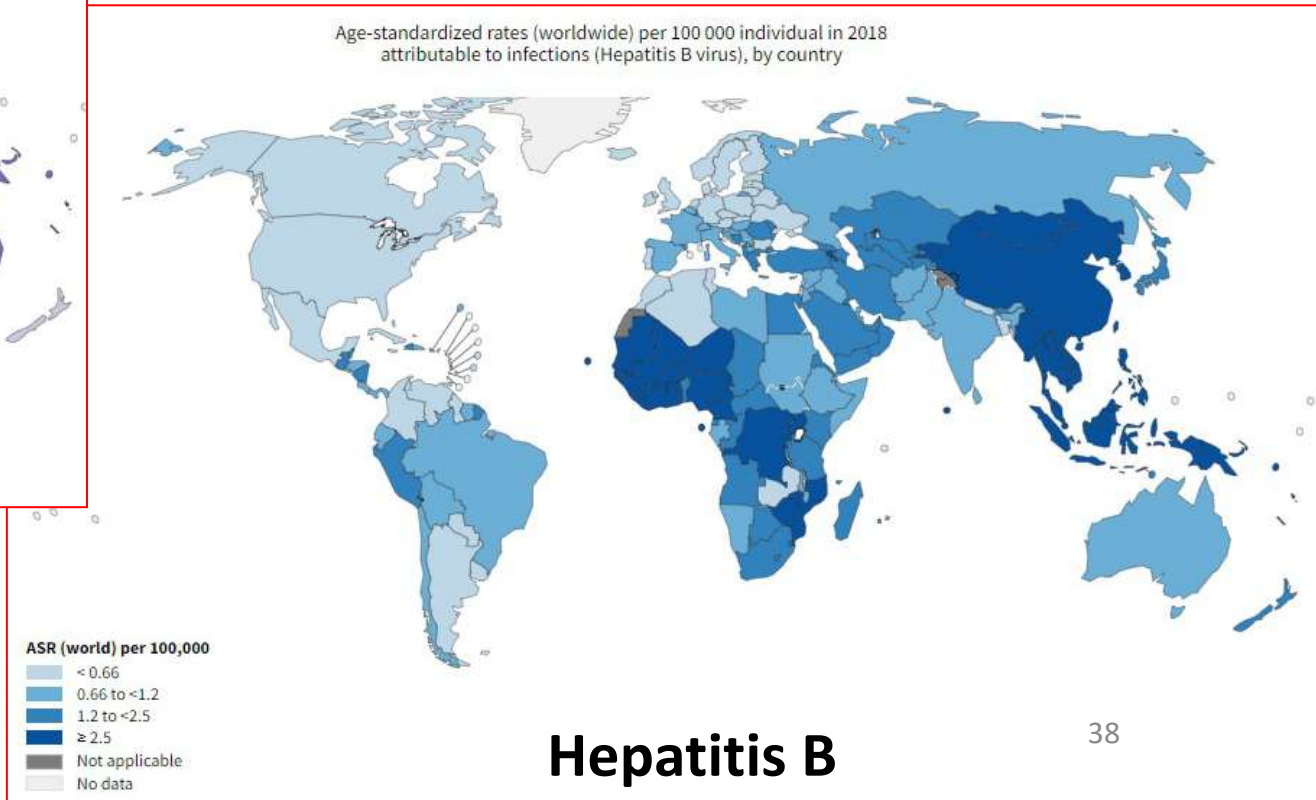
Hepatocellular carcinoma - Protective factors

- **Vaccination against HBV**
- **Antiviral therapy for viral hepatitis** due to HBV or HCV
- **Medications**
  - **Statins** (hydroxymethylglutaryl CoA reductase inhibitors) – OR 0.63; 95% CI 0.52-0.76 - effect most profound in East Asian males with chronic HBV
  - **Aspirin and other NSAIDs**
  - **Metformin**
- **Lifestyle factors**
  - Coffee – possibly due to antioxidants
  - **Diet** – consumption of white meat, fish, omega-3 fatty acids, vegetables, dietary intake of Vit E
  - **Physical activity** –effect of exercise on glucose or lipid metabolism or on improving NAFLD
  - Other factors — For patients with NASH & obesity, **bariatric surgery** has lower HCC rates

Hepatitis C has greater contribution in West while Hepatitis B in East Asia and Africa

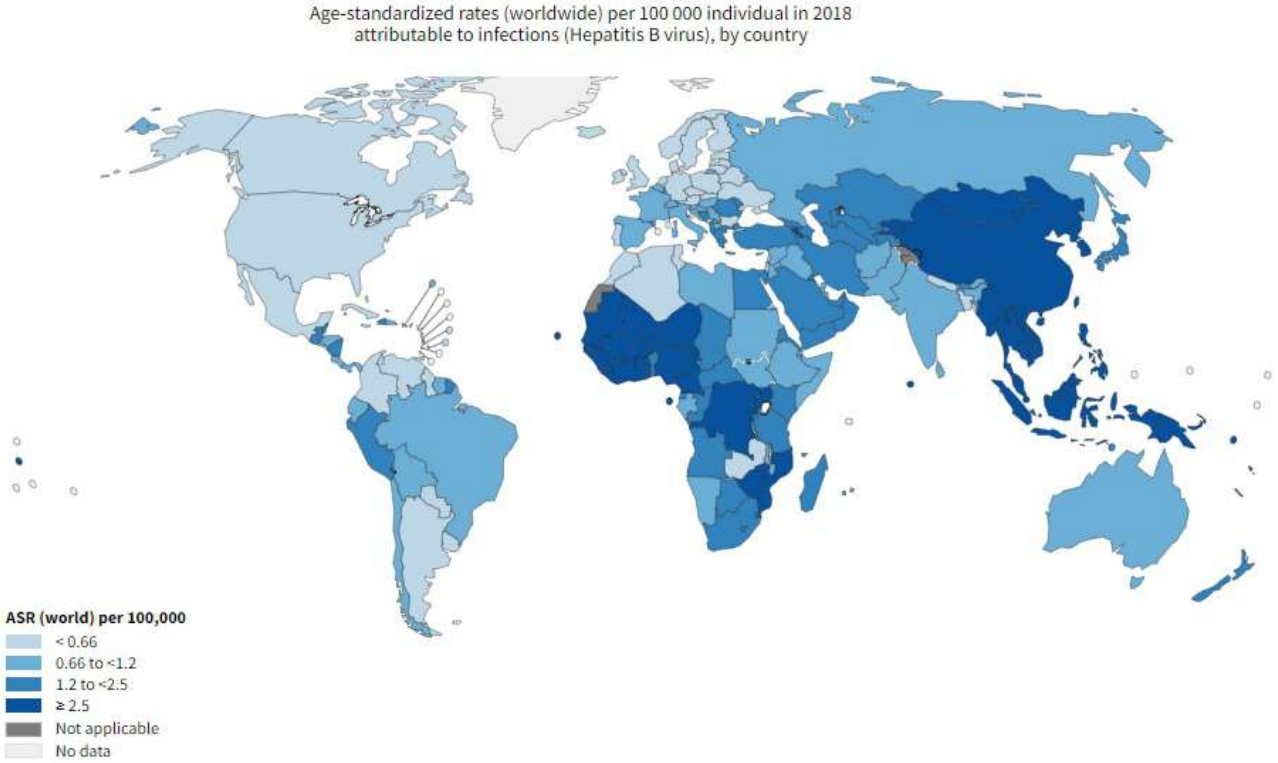


Hepatitis C



Hepatitis B

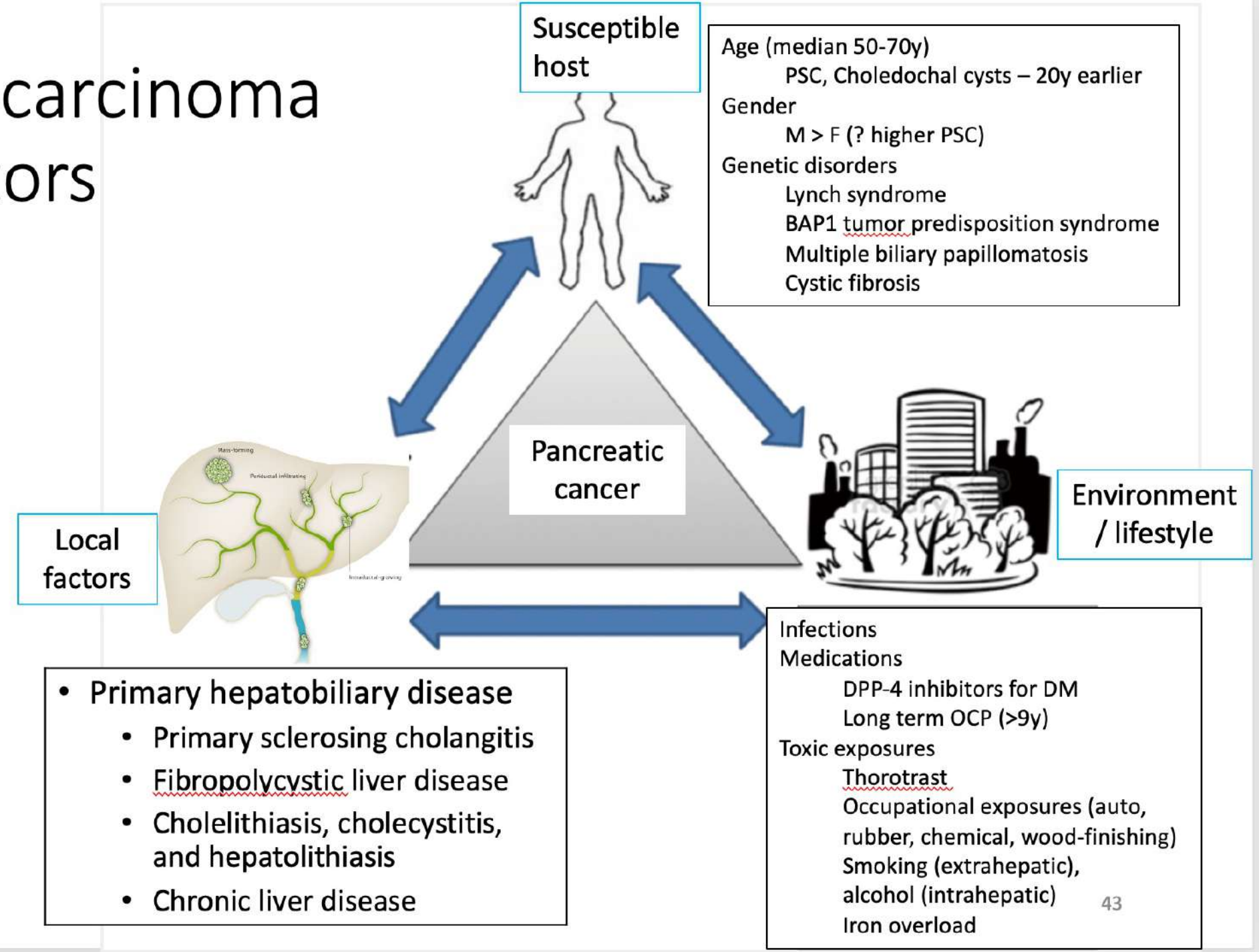
HBV-associated cancer incidence correlates inversely with HBV vaccination coverage



Cholangiocarcinoma

- 3% of all GI cancers
- Incidence – difficult to interpret, usually clubbed with liver (intrahepatic) or GB (extrahepatic)
  - Highest in Thailand, China (40-fold higher than USA)
  - US SEER data
    - 15% of intrahepatic and 33% of extrahepatic lesions are cholangiocarcinomas
    - Incidence 1.26 per 100,000 (2/3 are intrahepatic)
  - Incidence increasing for both intra- and extrahepatic
  - Factors: higher detection, concomitant increase in risk factors (cirrhosis, alcoholic liver disease, HCV)

Cholangiocarcinoma – Risk factors



Cholangiocarcinoma – Risk factors

Primary hepatobiliary disease

- **Primary sclerosing cholangitis** — leads to strictures of intrahepatic and/or extrahepatic bile ducts
  - Contribute to 30% cholangio
  - Lifetime risk of cholangio 5-15% (0.6-1.5% per annum)
  - Age of diagnosis younger than other cholangio (30-50 years) and diagnosis is difficult
  - Risk unrelated to duration of inflammation (30% diagnosed within 2 years of PSC diagnosis)
  - History of smoking and alcohol increase risk of cholangio

- **Fibropolycystic liver disease**
  - Congenital abnormalities of the biliary tree (Caroli syndrome, congenital hepatic fibrosis, choledochal cysts)
  - 15% risk of malignant change (average age at diagnosis 34y)

Cholangiocarcinoma – Risk factors

- **Cholelithiasis, cholecystitis, and hepatolithiasis**
  - Risk of cholangio lower than Ca GB for GSD
  - Hepatolithiasis or recurrent pyogenic cholangitis – higher incidence in Southeast Asia than West. 50-70% cholangios in Taiwan and 6-18% in Japan have associated hepatolithiasis
  - Diagnosis of cholangio should be suspected in a patient >40y who has a long history of hepatolithiasis, weight loss, high SAP, CEA >4.2 ng/mL, and hepatolithiasis in either the right or both lobes of the liver

- **Chronic liver disease** - more for intrahepatic cholangio
  - HCV (3.5% at 10y, RR 2.55)
  - HBV (less common than HCV)
  - Cirrhosis regardless of etiology
  - Alcoholic liver disease
  - **Precursor lesions** —intraductal papillary neoplasm of bile ducts, intraductal tubulopapillary neoplasm of the bile ducts (rare), and biliary intraepithelial neoplasia

Cholangiocarcinoma – Risk factors

Infections

- **Parasitic infection** — Liver flukes (Clonorchis, Opisthorchis) in Thailand through consumption of undercooked fish – intrahepatic/
  - Carcinogens produced by bacteria in fish and other foods, smoking, alcohol, and HBV infection may act as cofactors
- **HIV infection**
- **H. pylori infection**

Other factors

- **Elevated blood glucose** — DM (RR 1.60) – both intrahepatic and extrahepatic cholangiocarcinomas. High risk in higher sugar consumption in Swedish registries (HR 1.69).
- **Obesity** — intrahepatic cholangiocarcinoma
- **Metabolic syndrome** — intrahepatic cholangiocarcinoma (OR 1.56)

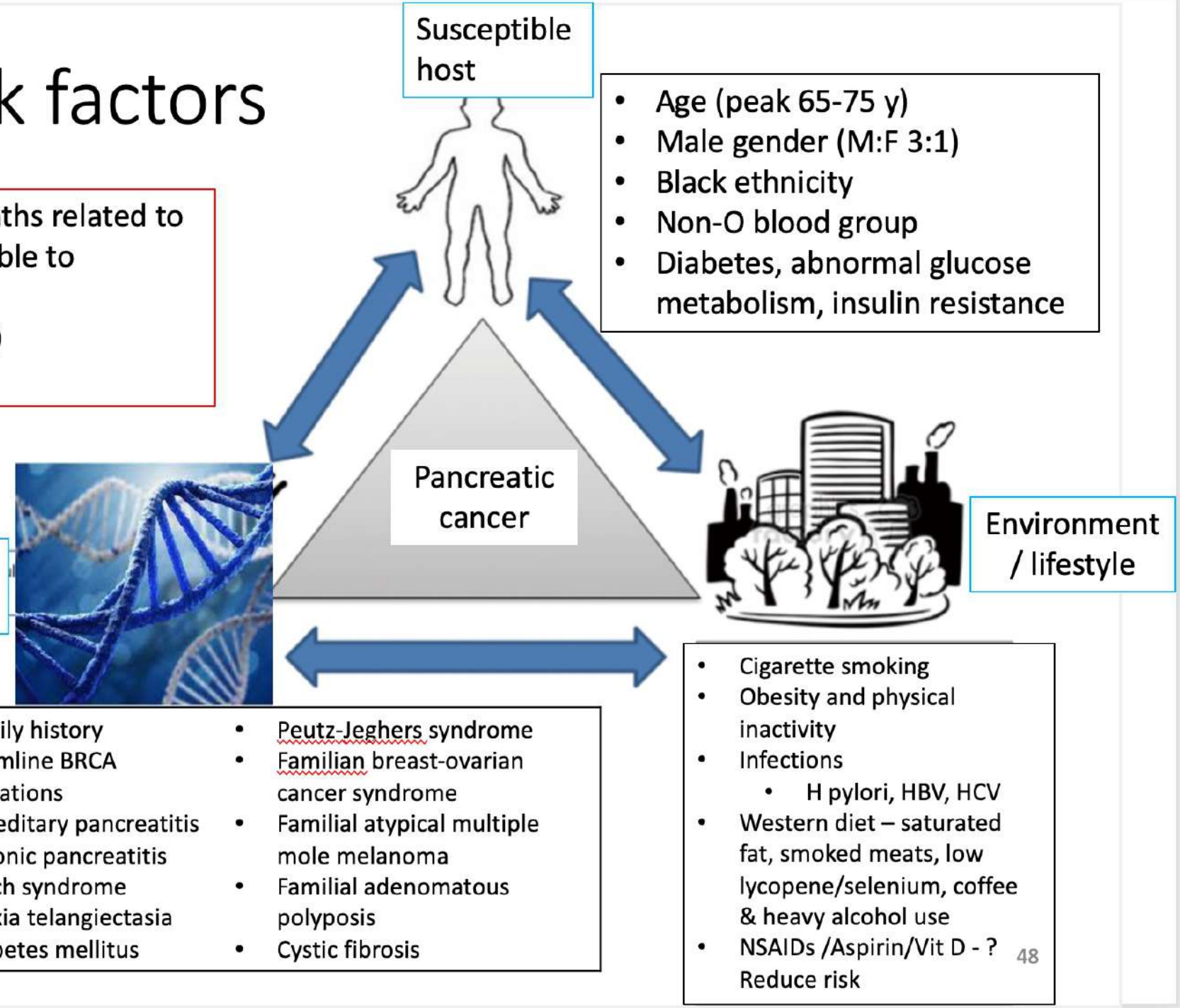
Pancreatic adenocarcinoma

- Worldwide, pancreatic cancer is the 7th leading cause of cancer deaths in both men and women (4^{th} in USA)
- Deemed a disease of developed world
- Early diagnosis in Western countries
  - Average age at diagnosis lower by 3.5 y
  - More cancers detected in IA stage
  - Improved OS in early stage
    - OS in IA: 45% (2004) → 84% (2012)

Pancreas – Risk factors

2017 Global Burden of Disease Study: deaths related to pancreatic cancer were primarily attributable to

- Smoking (21%)
- High fasting plasma glucose (8.9%)
- High body mass index (6.2 %)



- Age (peak 65-75 y)
- Male gender (M:F 3:1)
- Black ethnicity
- Non-O blood group
- Diabetes, abnormal glucose metabolism, insulin resistance

80% cancers – sporadic mutations

- Family history
- Germline BRCA mutations
- Hereditary pancreatitis
- Chronic pancreatitis
- Lynch syndrome
- Ataxia telangiectasia
- Diabetes mellitus
- Peutz-Jeghers syndrome
- Familian breast-ovarian cancer syndrome
- Familial atypical multiple mole melanoma
- Familial adenomatous polyposis
- Cystic fibrosis

- Cigarette smoking
- Obesity and physical inactivity
- Infections
  - H pylori, HBV, HCV
- Western diet – saturated fat, smoked meats, low lycopene/selenium, coffee & heavy alcohol use
- NSAIDs /Aspirin/Vit D - ? Reduce risk

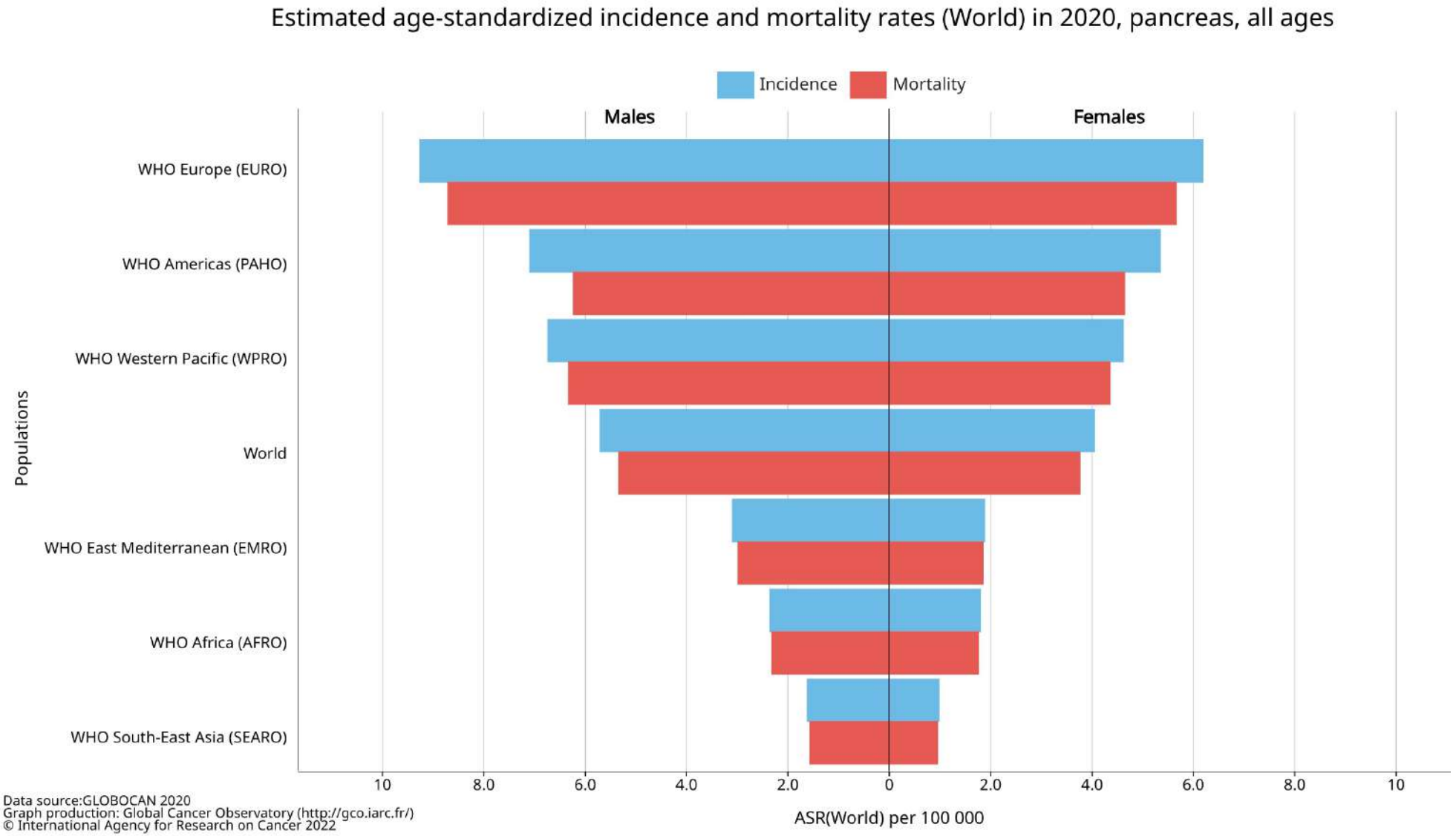
Pancreas - Epidemiology

- Age
  - Pancreatic cancer is rare before the age of 45. Peak incidence in men is at age 65-69 and in women at 75-79
  - Median age in USA 79 years
  - In India, the disease peaks in the 6th decade
- Gender
  - In India, M:F ratio is 1.5-2 : 1
  - Gender differences confounded by habits like smoking; undiscovered genetic factors may contribute
- Extent
  - Most cases are locoregionally advanced; only 15-20% are potentially resectable at presentation
- Geography
  - Highest incidence in high-income North America, high-income Asia Pacific, and Western and Central Europe
  - Lowest incidence in South Asia and eastern and central Sub-Saharan Africa
  - USA: African-Americans > Caucasians > Asian Americans and Pacific Islanders

Pancreas – Risk factors

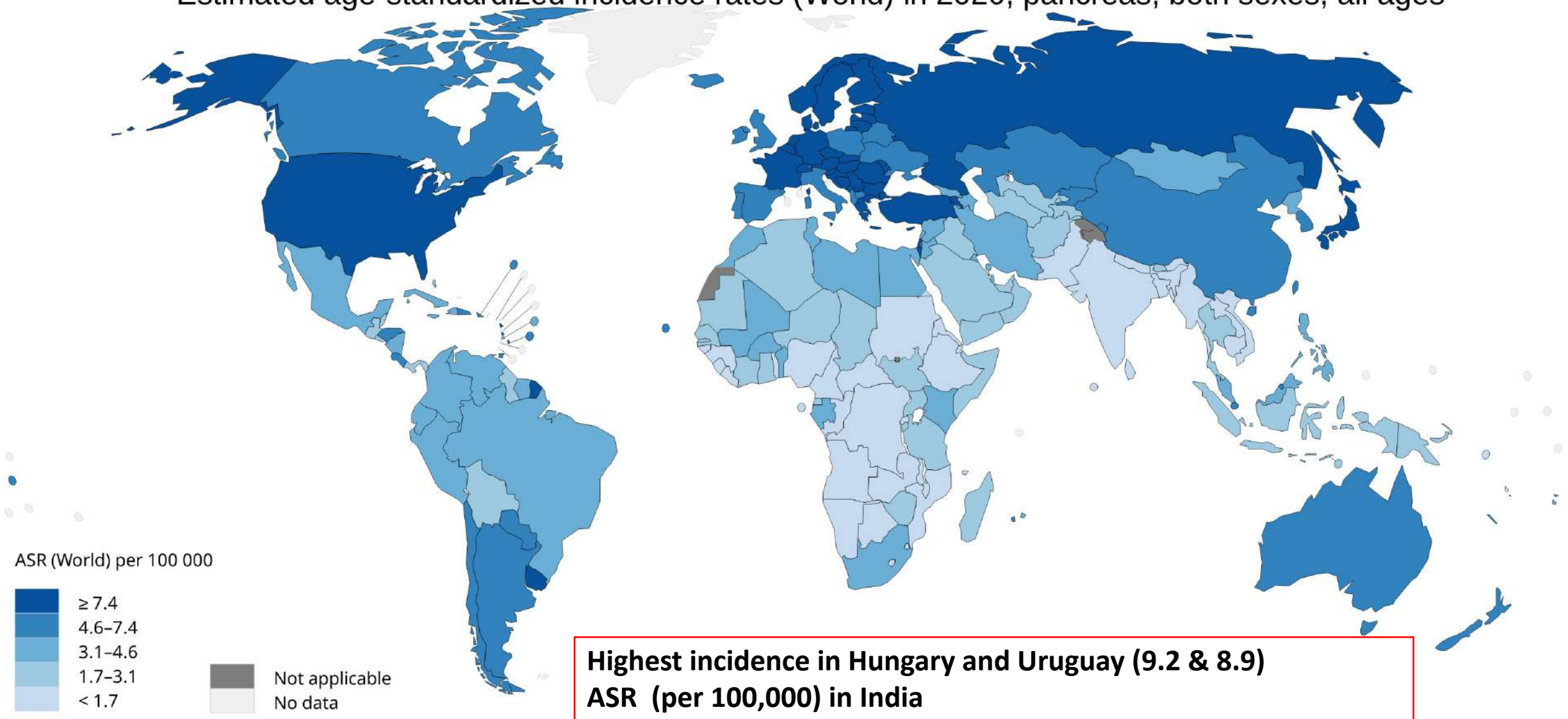
- Genetic factors
  - African Americans
    - Advanced disease, lesser access to surgery
    - Genetic predisposition
      - higher rates of K-ras mutations to valine
      - lower rates of K-ras mutations to cysteine
      - lower expression of Fas
      - trend towards higher HER2 positivity
  - Chinese patients
    - different expressions of K-ras and p53 than Western or Japanese patients
  - Asian patients
    - less aggressive tumors and better survival rate than non-Asian patients

GLOBOCAN 2020



GLOBOCAN 2020

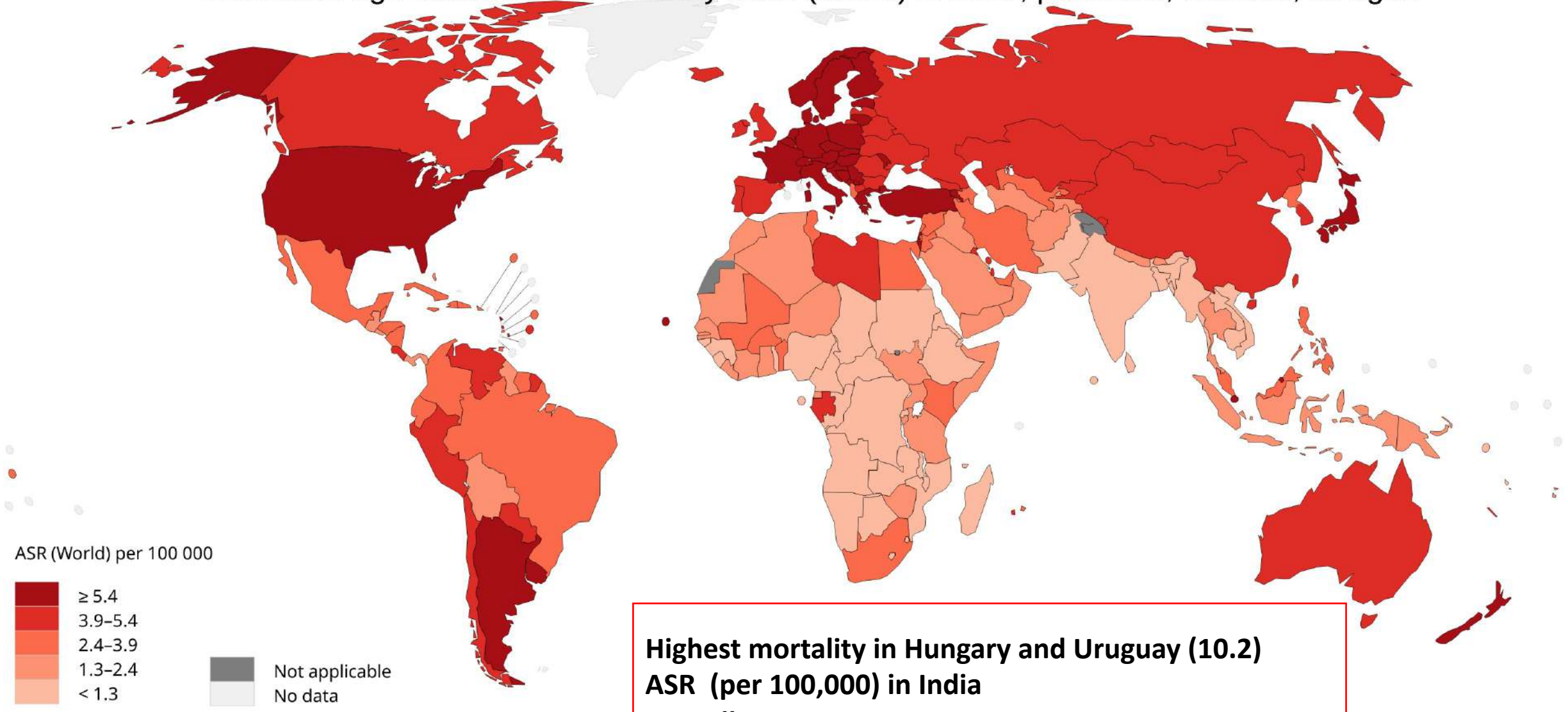
Estimated age-standardized incidence rates (World) in 2020, pancreas, both sexes, all ages



Highest incidence in Hungary and Uruguay (9.2 & 8.9)
ASR (per 100,000) in India
Overall 0.94
Males 1.2
Females 0.69

GLOBOCAN 2020

Estimated age-standardized mortality rates (World) in 2020, pancreas, females, all ages



Highest mortality in Hungary and Uruguay (10.2)
ASR (per 100,000) in India
Overall 0.90
Males 1.1
Females 0.66

World Health Organization

ILBS data

Table 2: Distribution by diagnosis of registered patients (*n*=502)

Diagnosis	Number of patients, *n* (%)
Carcinoma gall bladder	149 (29.7)
HCC	87 (17.3)
Cholangiocarcinoma	44 (8.8)
Periampullary carcinoma	31 (6.2)
Carcinoma pancreas	35 (6.8)
NET	11 (2.2)

Ca GB: 75% stage IV, 44% had gallstones, M:F ratio 1 : 1.6
HCC: 65.5% were BCLC C, M:F ratio 7.7 : 1

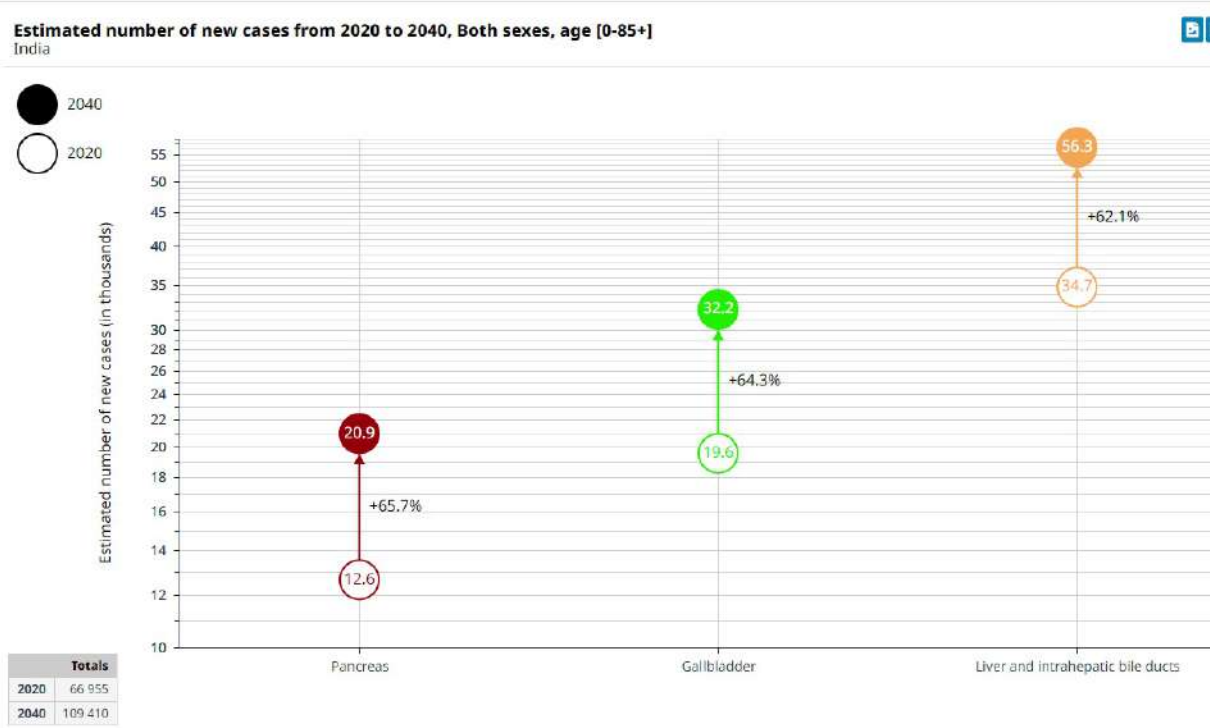
6m OS was 56.5% for biliary cancers, 71.4% for HCC

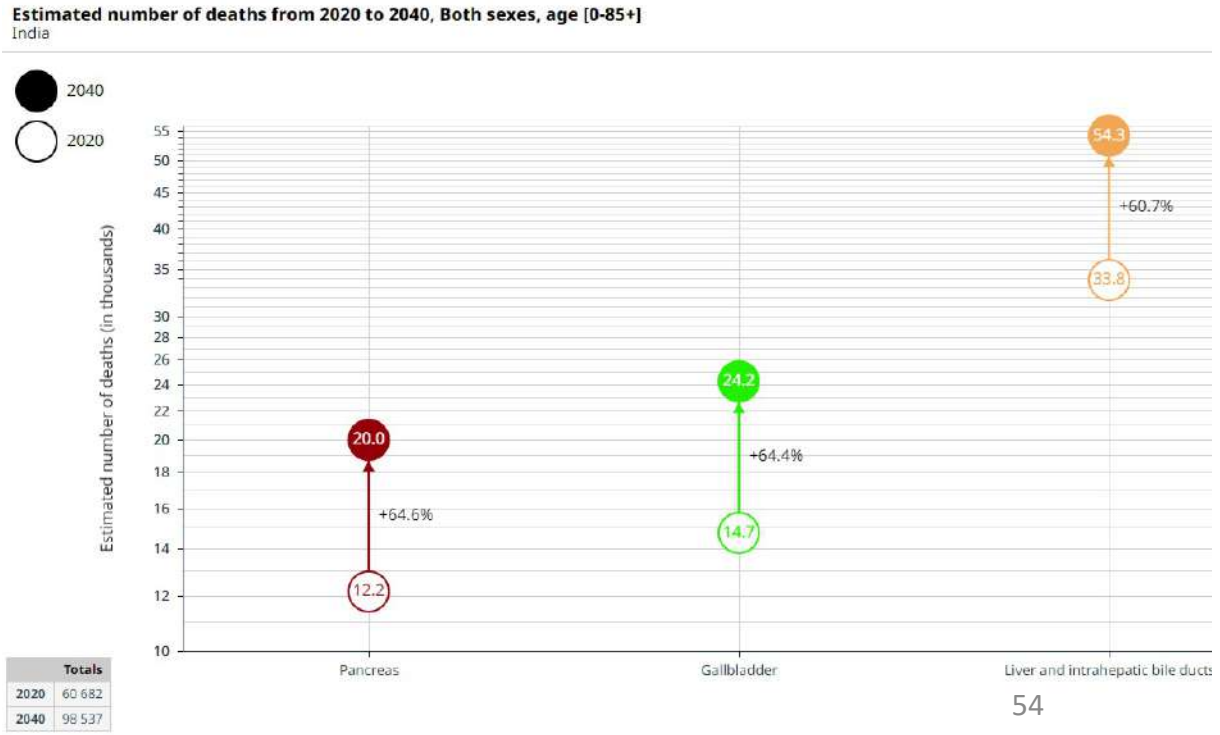
WHO Encyclopedia of carcinogens IARC monographs

- To date, IARC has classified 120 agents as carcinogenic to humans
- Agents classified in 4 groups
- Group 1: carcinogenic to humans

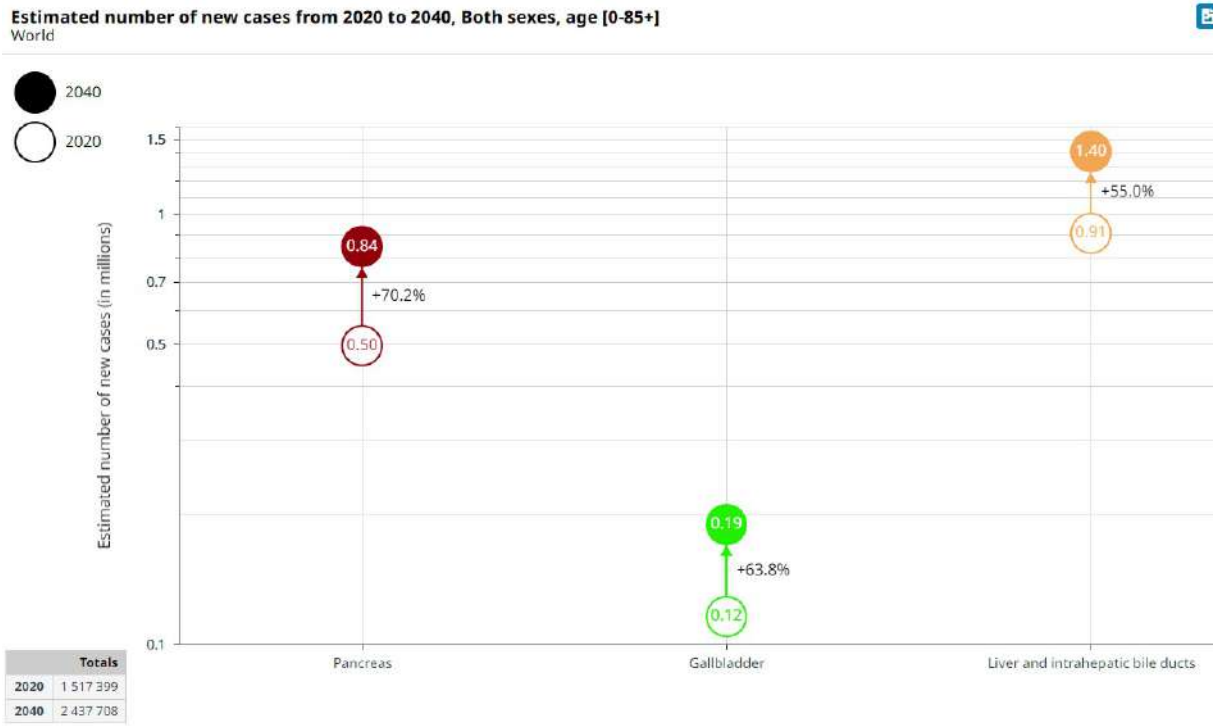
LIVER (HEPATOCELLULAR CARCINOMA) Aflatoxins Alcoholic beverages Estrogen-progestogen contraceptives Hepatitis B virus Hepatitis C virus Plutonium Thorium-232 and its decay products Tobacco smoking (in smokers and in smokers' children) LIVER (ANGIOSARCOMA) Vinyl chloride	GALLBLADDER Thorium-232 and its decay products BILIARY TRACT Chlonorchis sinensis 1,2-Dichloropropane Opisthorchis viverrini PANCREAS Smokeless tobacco Tobacco smoking

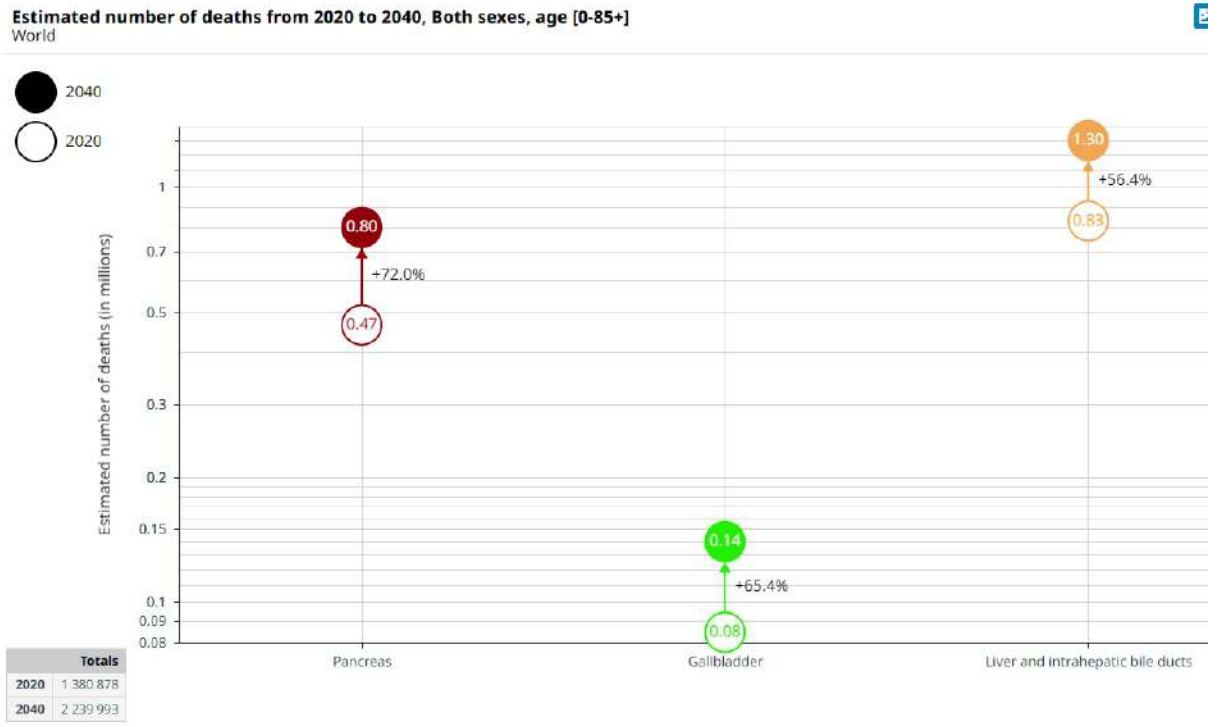
Both incidence and mortality in India expected to rise in next 20 years



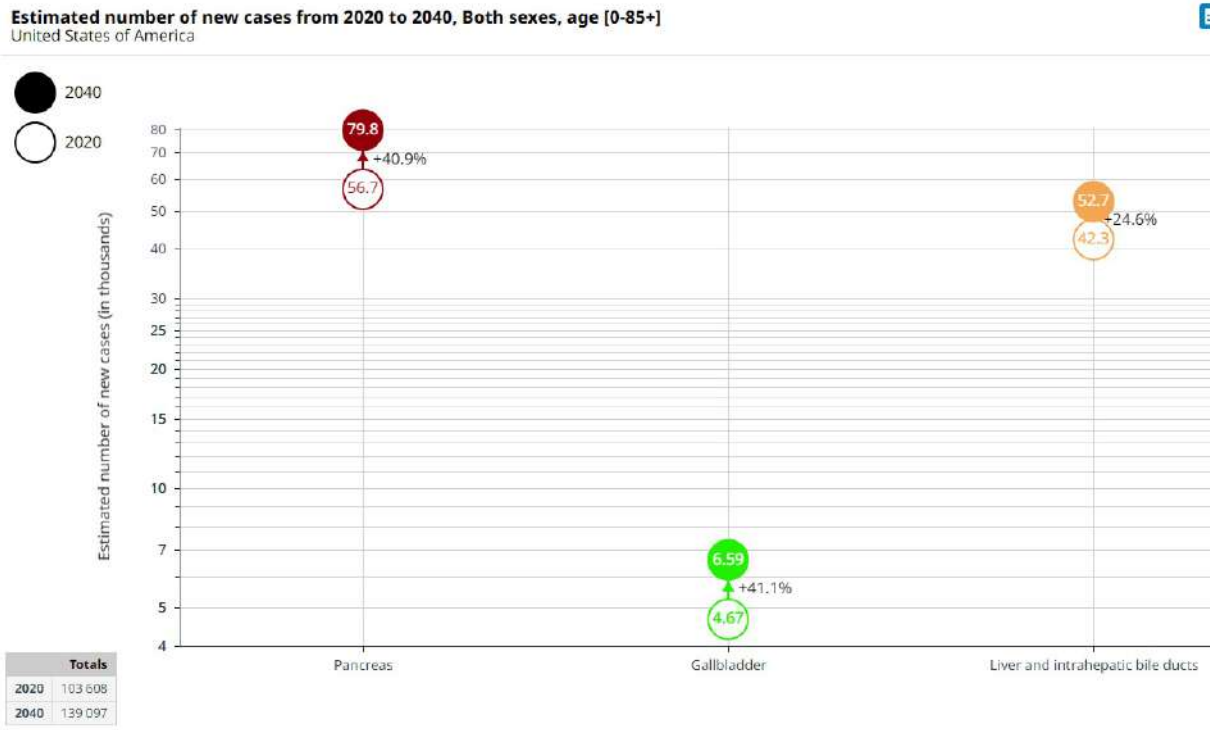


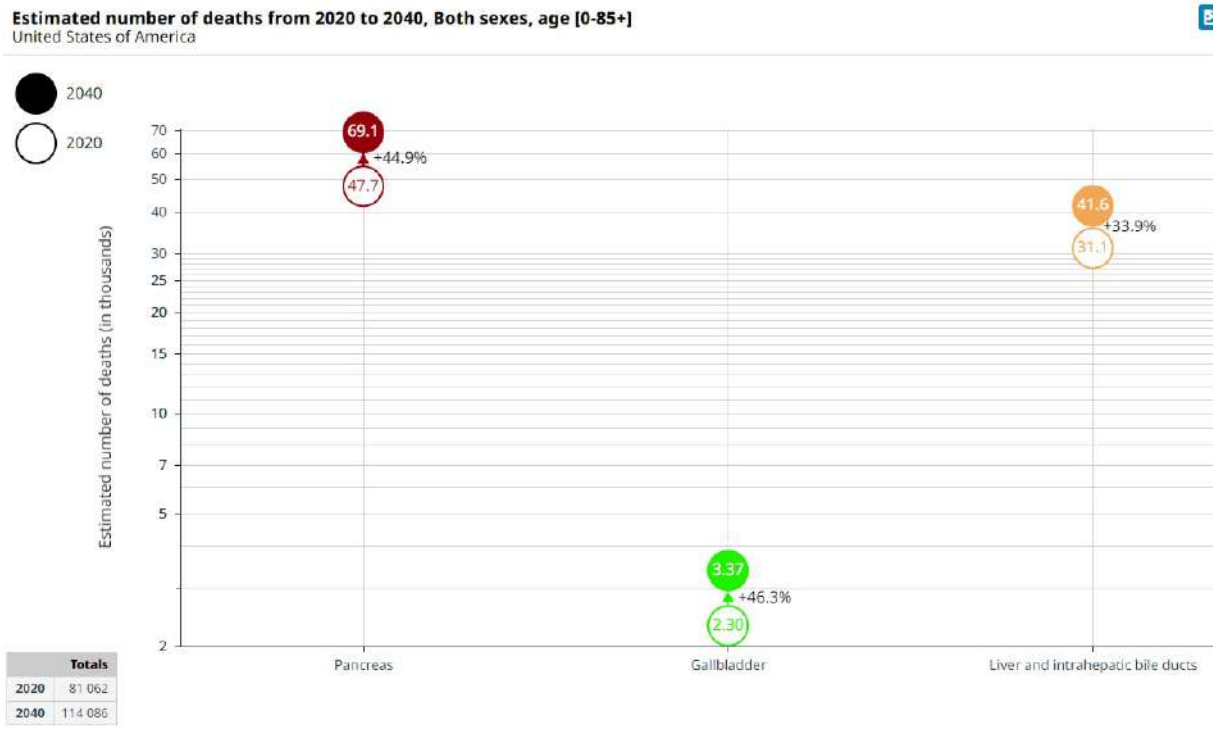
Similar trends in World





Relatively smaller rise in USA





Conclusion

- Complex interplay of host and environmental factors for disease risk and epidemiology
- All HPB malignancies rising in the World as well as India
- No screening programme – only surveillance for high risk populations
- Ca GB – small problem for the World but of high relevance in North India – high incidence, advanced stage, rarely curable
- Possible remedies
  - Ca GB: improve socioeconomic conditions, access to cholecystectomy for GB disease
  - HCC: Discourage alcohol, Hepatitis B vaccination
  - Cholangiocarcinoma: surveillance of high risk patients
  - Pancreas: Discourage smoking, control DM/obesity, healthy diet