NEOPLASIA II.

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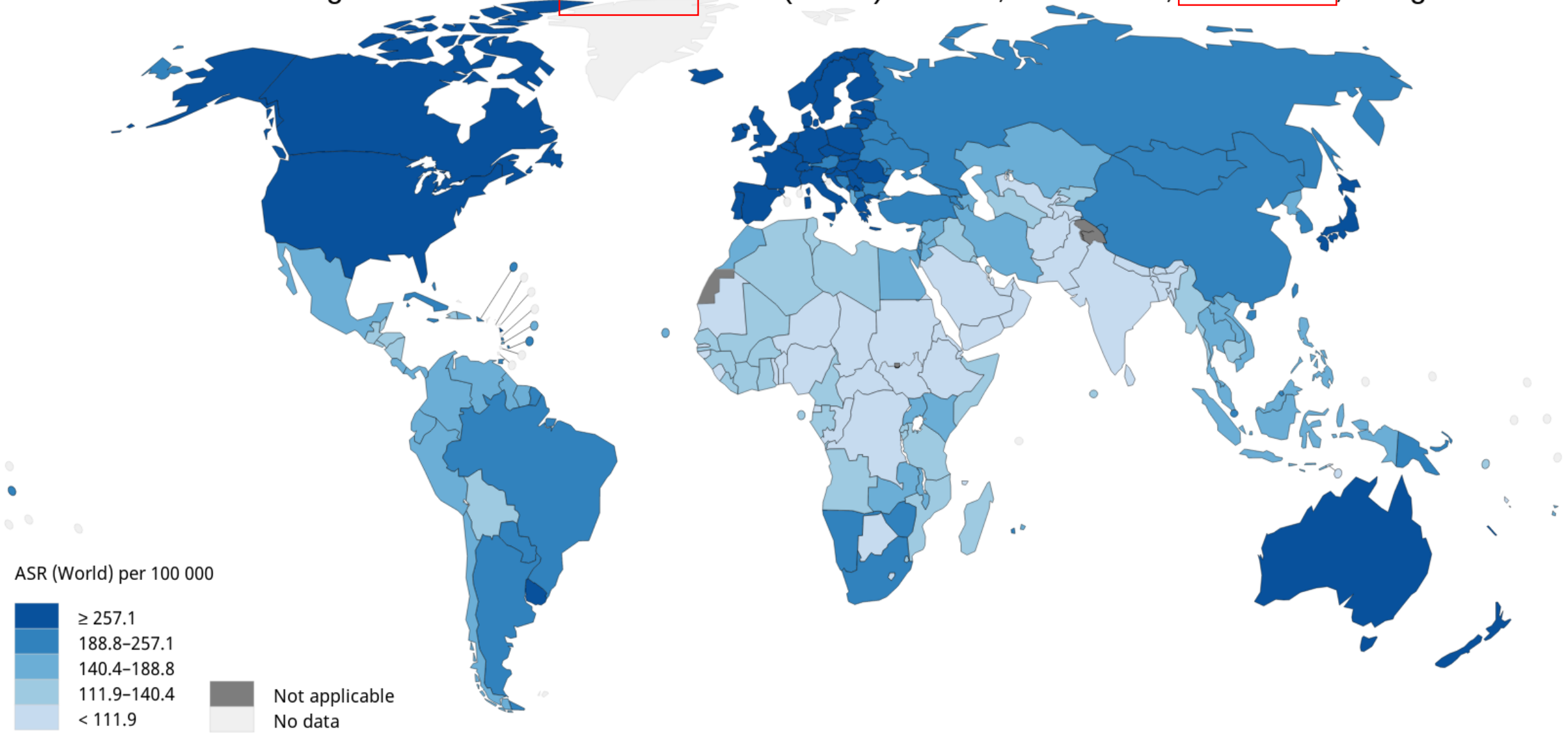
2nd Department of Pathology

11th October 2021

Epidemiology of cancer

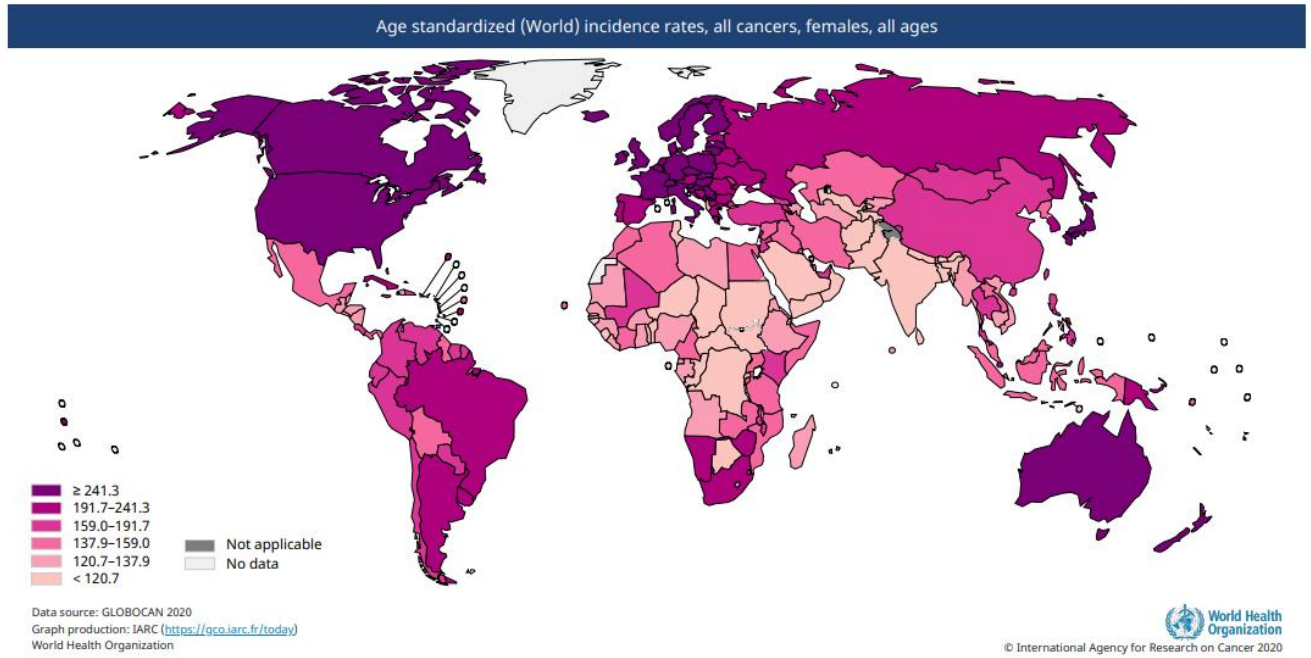
- Incidence
- Mortality
- Age standardized rates (e.g deaths per 100,000 population per year)
- New cancer cases in 2020: 19 292 789 cases
- Cancer death in 2020: : 9 958 133 deaths

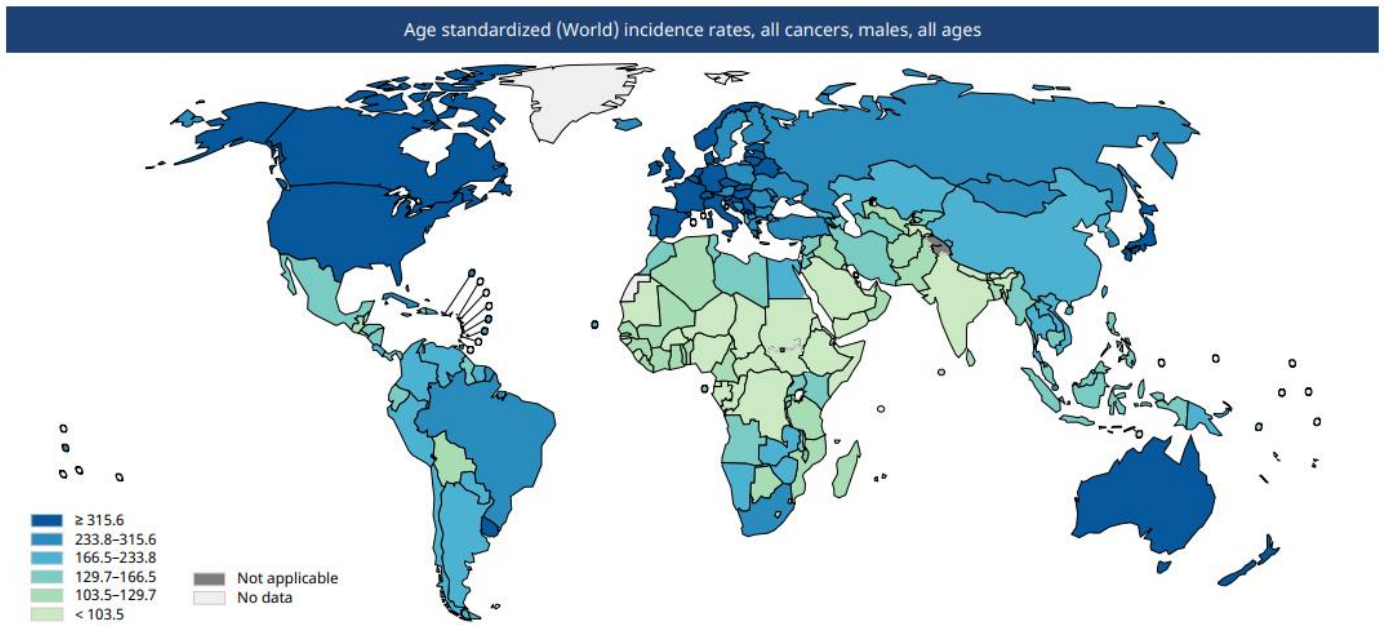
Estimated age-standardized incidence rates (World) in 2020, all cancers, both sexes, all ages



Data source: GLOBOCAN 2020
Graph production: IARC (http://gco.iarc.fr/today)
World Health Organization

World Health Organization


Age standardized (World) incidence rates, all cancers, females, all ages
≥ 241.3
191.7–241.3
159.0–191.7
137.9–159.0
120.7–137.9
< 120.7
Not applicable
No data
Data source: GLOBOCAN 2020
Graph production: IARC (https://gco.iarc.fr/today)
World Health Organization
World Health Organization
© International Agency for Research on Cancer 2020


Age standardized (World) incidence rates, all cancers, males, all ages
≥ 315.6
233.8–315.6
166.5–233.8
129.7–166.5
103.5–129.7
< 103.5
Not applicable
No data

Cancer

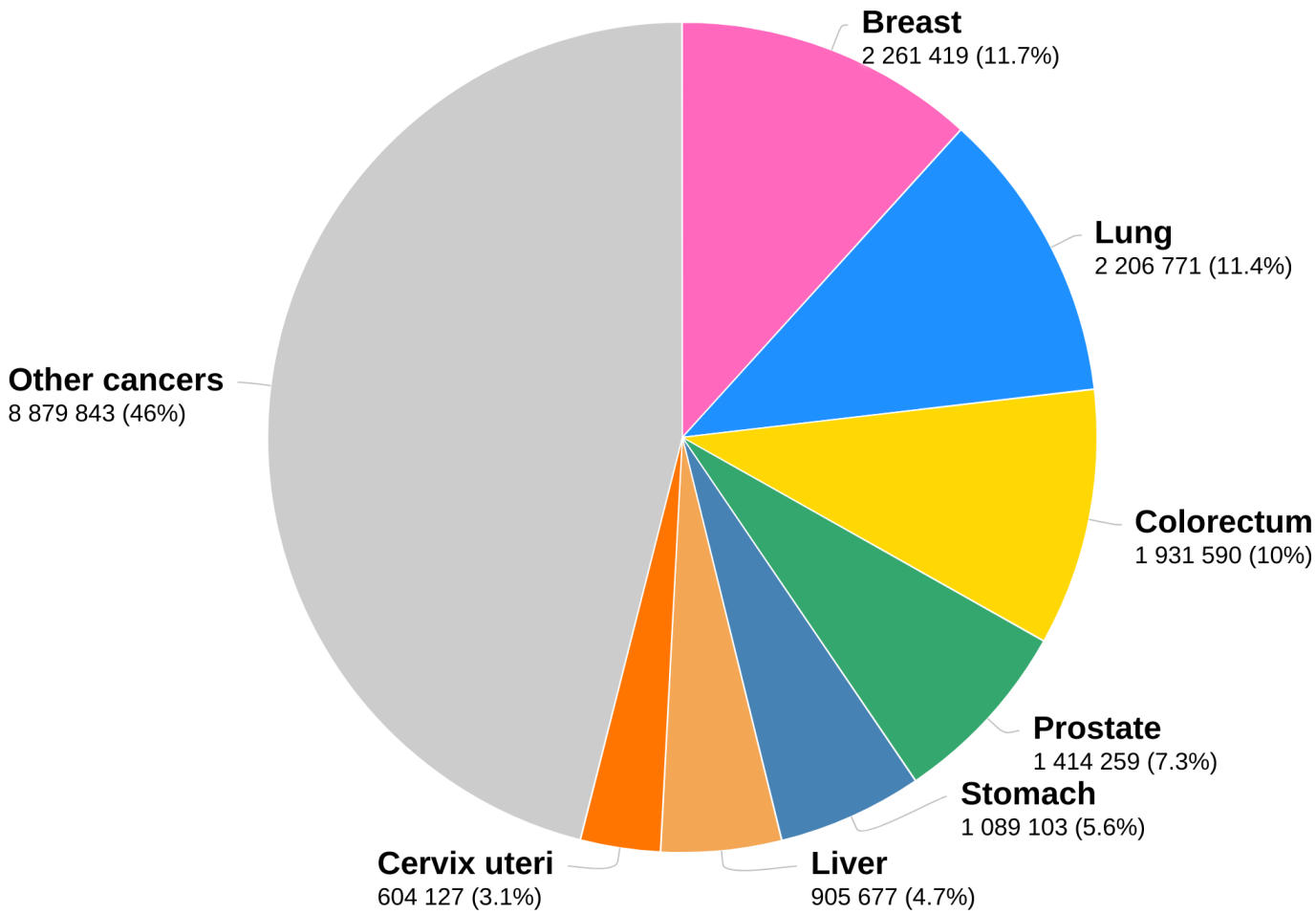
21 September 2021

Key facts

- Approximately 70% of deaths from cancer occur in low- and middle-income countries.
- Around one-third of deaths from cancer are due to tobacco use, high body mass index, alcohol use, low fruit and vegetable intake, and lack of physical activity.
- Cancer-causing infections, such as hepatitis and human papillomavirus (HPV), are responsible for approximately 30% of cancer cases in low- and lower-middle-income countries (3).
- Late-stage presentation and lack of access to diagnosis and treatment are common, particularly in low- and middle-income countries. Comprehensive treatment is reportedly available in more than 90% of high-income countries but less than 15% of low-income countries (4).
- The economic impact of cancer is significant and increasing. The total annual economic cost of cancer in 2010 was estimated at US$ 1.16 trillion (5).

Source: https://www.who.int/news-room/fact-sheets/detail/cancer

Estimated number of new cases in 2020, worldwide, both sexes, all ages

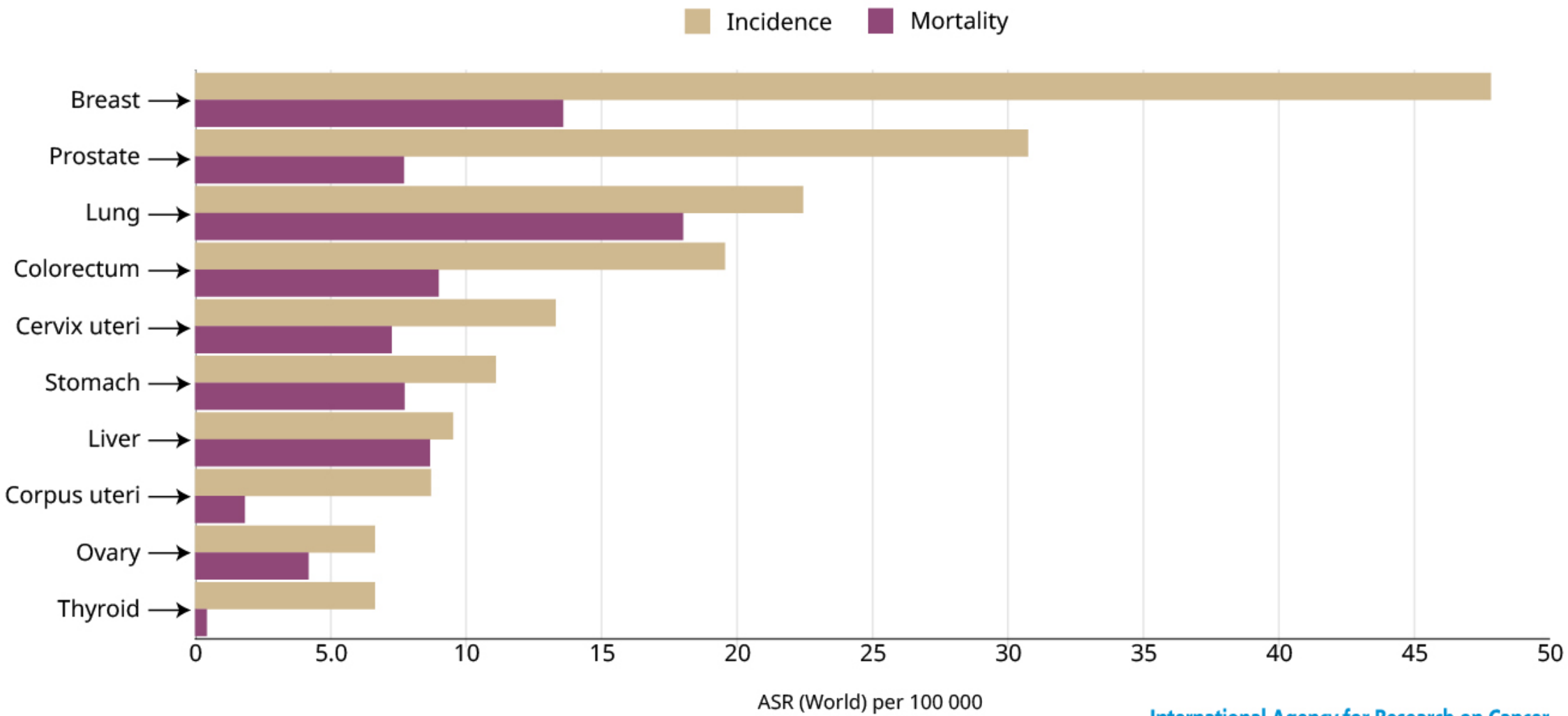


Total : 19 292 789

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

International Agency for Research on Cancer
World Health Organization

Estimated age-standardized (World) incidence and mortality rates (ASR) per 100 000 person-years in 2020 for the 10 most common cancer types, worldwide for both sexes and all ages

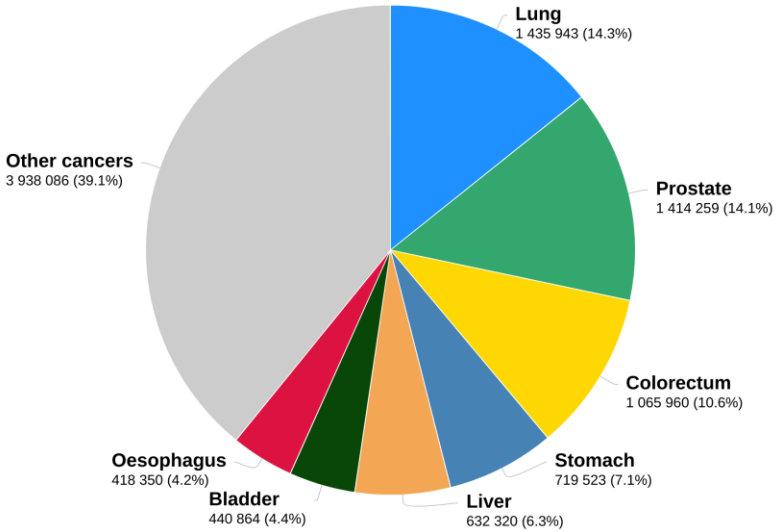


Data source: GLOBOCAN 2020

International Agency for Research on Cancer

World Health Organization

Estimated number of new cases in 2020, worldwide, males, all ages



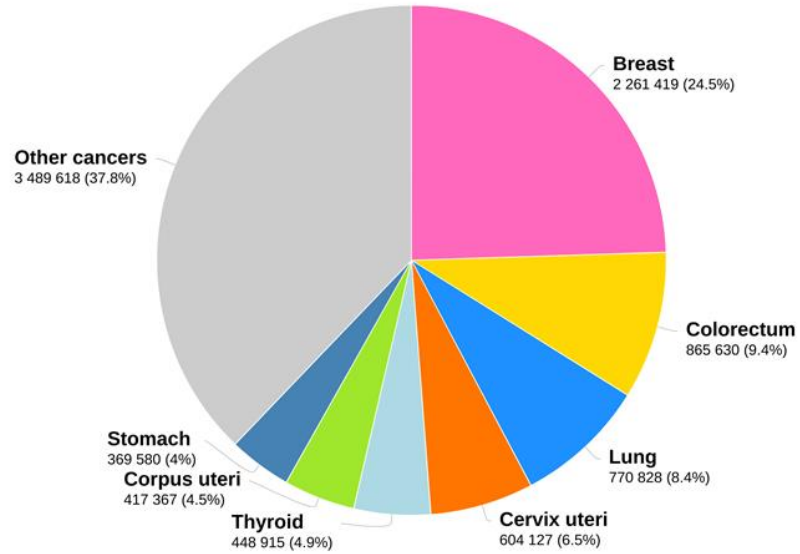
Total : 10 065 305

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

International Agency for Research on Cancer
World Health Organization

Observatory (http://gco.iarc.fr)

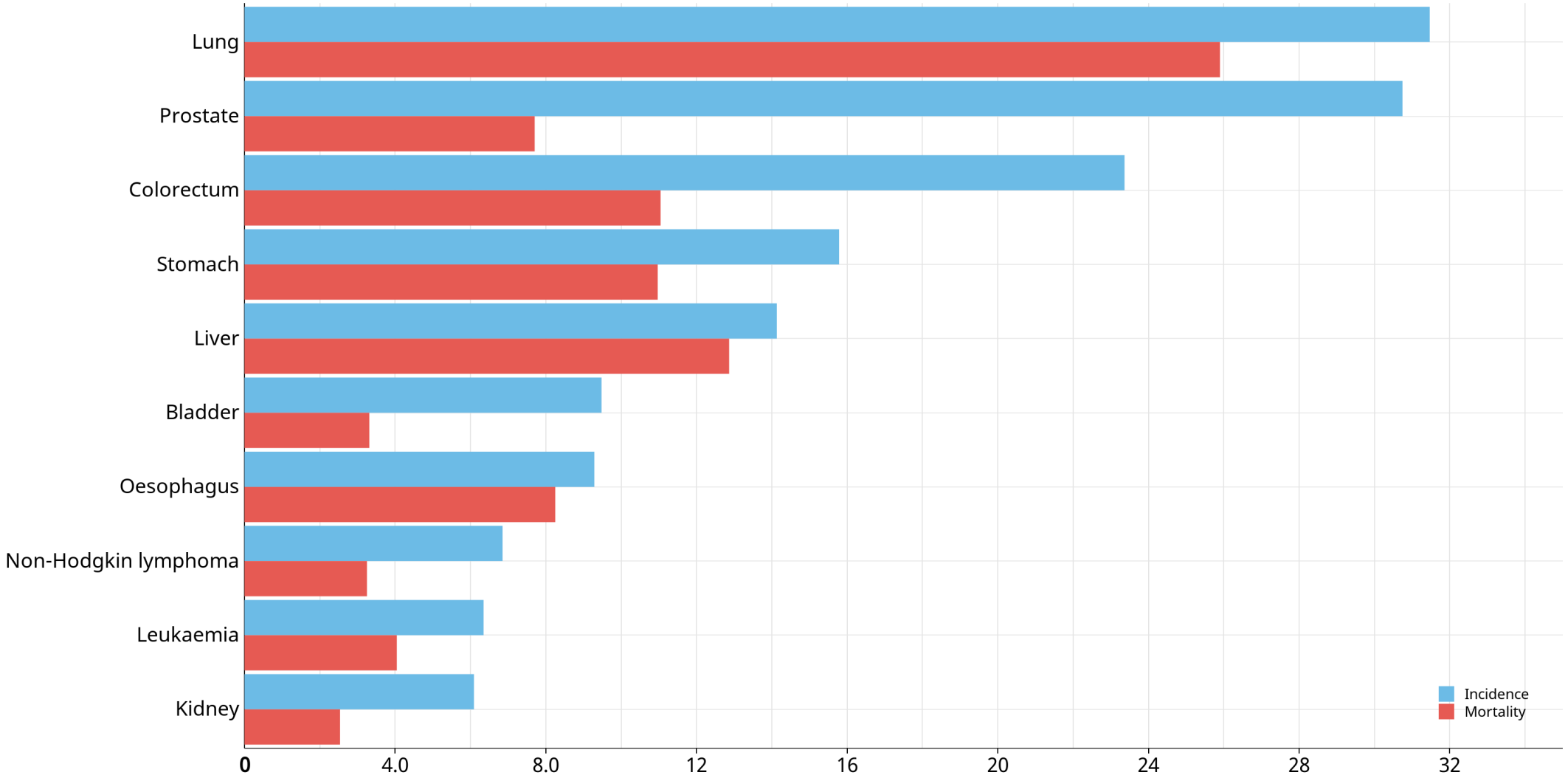
Estimated number of new cases in 2020, worldwide, females, all ages



Total : 9 227 484

International Agency for Research on Cancer
World Health Organization

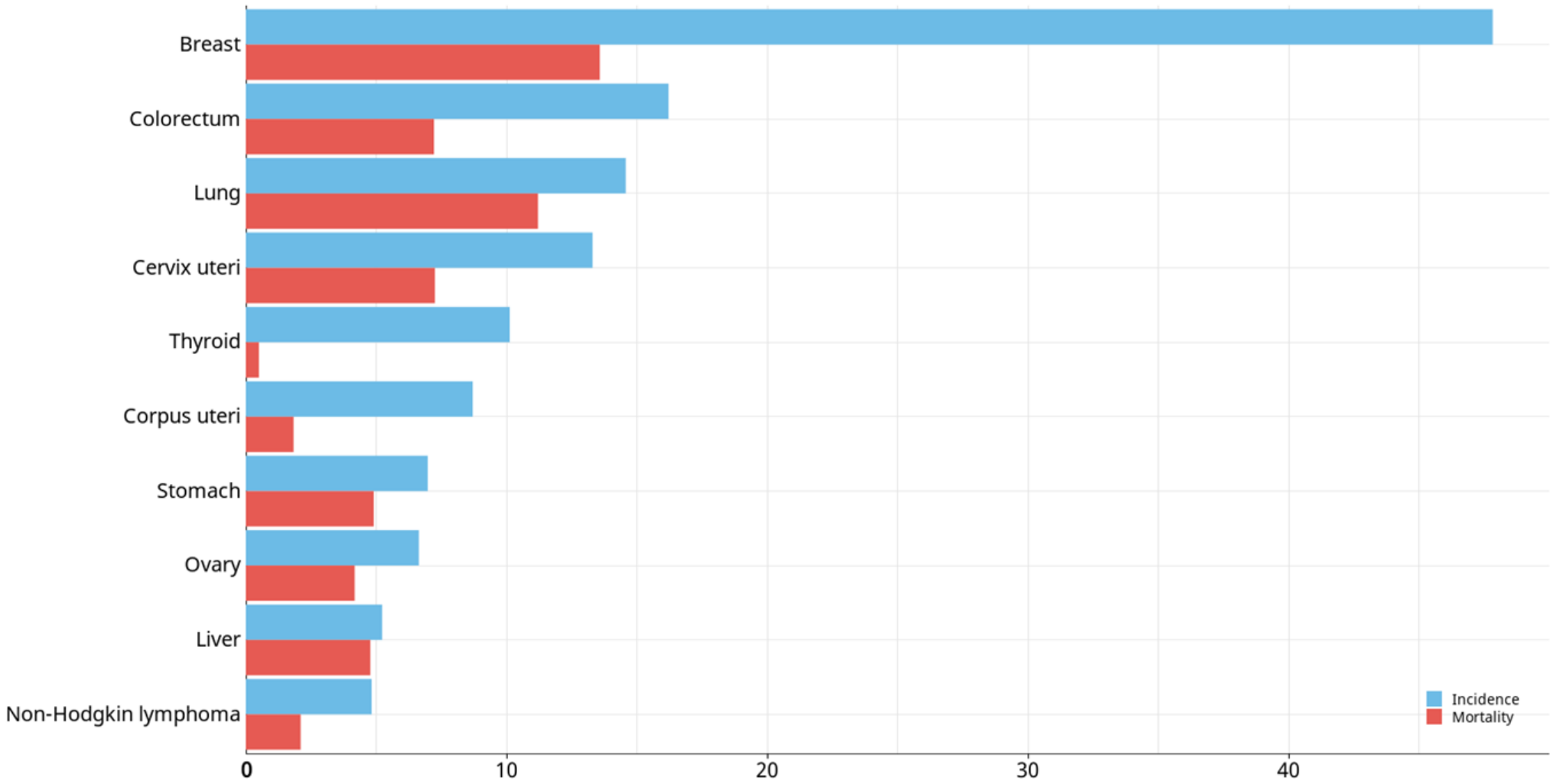
Estimated age-standardized incidence and mortality rates (World) in 2020, worldwide, males, all ages



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

International Agency for Research on Cancer
World Health Organization

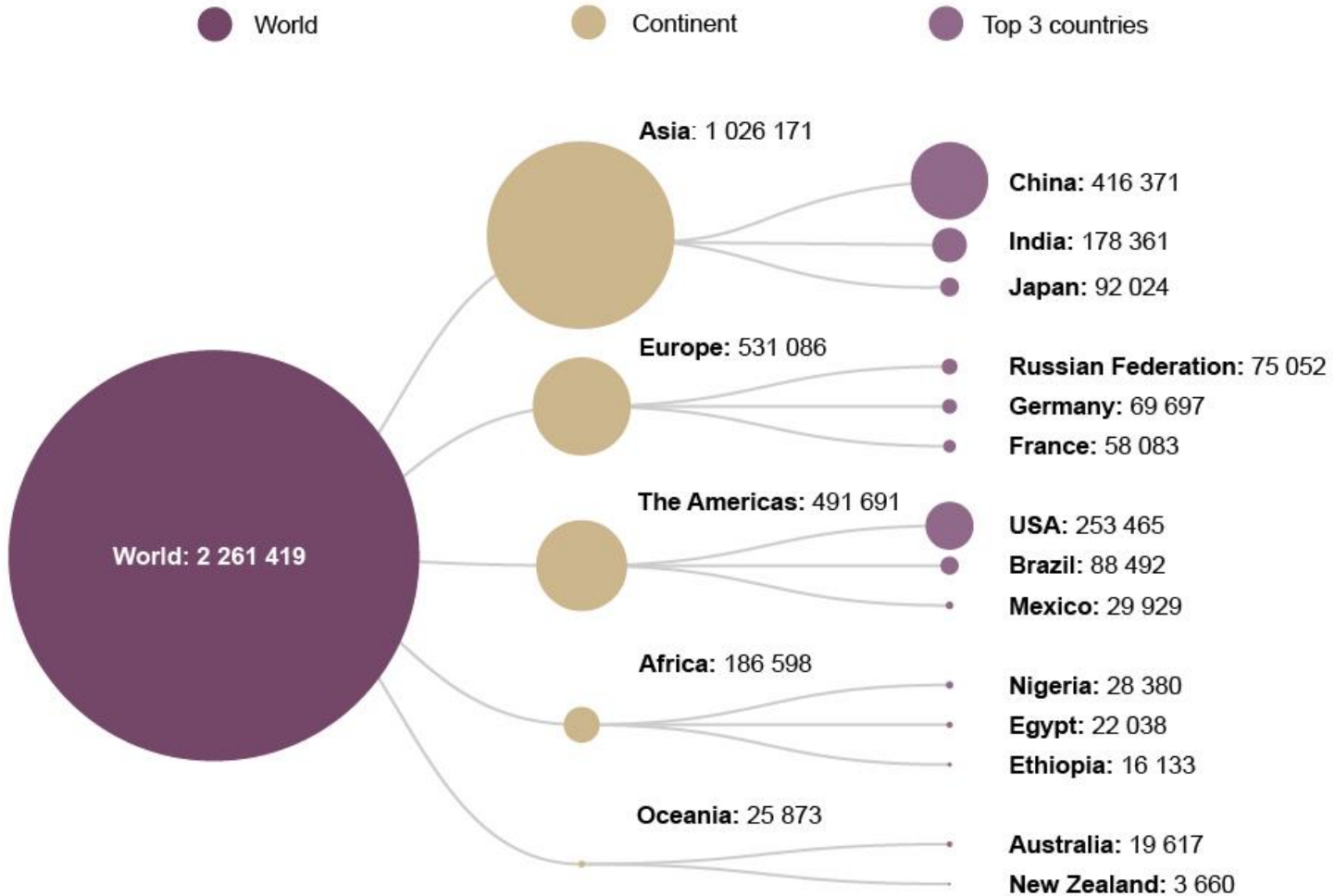
Estimated age-standardized incidence and mortality rates (World) in 2020, worldwide, females, all ages



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

International Agency for Research on Cancer
World Health Organization

Estimated number of new cases of female breast cancer in 2020 at all ages



Data source: GLOBOCAN 2020

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World Health Organization

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World Health Organization

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Cancer Prevention Europe

Cancer Prevention Europe (CPE), a consortium of organizations across the whole of Europe, aims to reduce morbidity and mortality from cancer in European populations through prevention and earlier diagnosis of the disease.

https://cancerpreventioneurope.iarc.fr/

Strategies

- **Information-Education-Awareness**
- **Prevention**
  - Goal: to interfere with the development of the disease
  - Vaccination (e.g HPV, Hepatitis B)
  - Surgical preventive strategies (e.g. Preventive bilateral mastectomy in BRCA patients)
- **Screening**
  - Goal: to detect the disease at an early form, that is still amenable to treatment and potential cure
  - Breast cancer screening
  - Cervical PAP smear, HPV testing
  - Colorectal cancer screening
- **Treatment**
  - Make it available to everyone
  - Treat your patient according to state of the art guidelines

Factors contributing in carcinogenesis

- Genetics
- Environmental factors
- Age
- Acquired predisposing conditions to cancer
  - Chronic inflammation
  - Precursor lesions
  - Immunodeficiency

Environmental factors

- **Dominant risk factors**
- Age standardized death rates changed significantly
  - Drop in stomach cancer incidence-refrigeration
  - Drop in lung cancer incidence-changes in smoking habits
  - Increasing incidence of liver cancer-HBV and HCV infection, obesity more common

Environmental factors

- **Smoking** (and second hand smoke)
- **Obesity** (14% of cancer deaths in men and 20% in women related to obesity)
- **Diet** (vegetables and fruits, high fiber intake)
- **Alcohol**
- **Reproductive history** (unopposed estrogen, breastfeeding, HRT)
- **Environmental carcinogens** (UV/sun, sunbed, radon, water pollutant etc.
- **Infections** (HPV, H. Pylori, HBV, HCV, EBV, HTLV-1)

12 WAYS TO REDUCE YOUR CANCER RISK

1A. Tobacco

Do not smoke. Do not use any form of tobacco.
— Dr Maria Leon, IARC

Learn more

2A. Second-hand smoke

Make your home smoke-free. Support smoke-free policies in your workplace.
— Dr Maria Leon, IARC

Learn more

3A. Body weight

Take action to be a healthy body weight.
— Dr Martin Wiseman, WCRF

Learn more

4A. Physical activity

Be physically active in everyday life. Limit the time you spend sitting.
— Dr Martin Wiseman, WCRF

Learn more

5A. Diet

Have a healthy diet. Eat plenty of whole grains, pulses, vegetables and fruits. Limit high-calorie foods (high in sugar or fat) and avoid sugary drinks. Avoid processed meat, limit red meat and foods high in salt.
— Dr Isabelle Romieu, IARC

Learn more

6A. Alcohol

If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention.
— Dr Isabelle Romieu, IARC

Learn more

7A. Sun/UV Exposure

Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds.
— Dr Joachim Schüz, IARC

Learn more

8A. Pollutants

In the workplace, protect yourself against cancer-causing substances by following health and safety instructions.
— Dr Carolina Espina, IARC

Learn more

9A. Radiation

Find out if you are exposed to radiation from naturally high radon levels in your home. Take action to reduce high radon levels.
— Dr Joachim Schüz, IARC

Learn more

10A. Breastfeeding and HRT

For women, breastfeeding reduces the mother's cancer risk, if you can breastfeed your baby. For women, Hormone Replacement Therapy (HRT) increases the risk of certain cancers, limit use of HRT.
— Dr Isabelle Romieu, IARC, and Dr Karen Brown, University of Leicester (UK)

Learn more

11A. Vaccination and infections

Ensure your children take part in vaccination programmes for: Hepatitis B (for newborns), Human Papillomavirus (HPV) (for girls).
— Dr Rolando Herrero, IARC

Learn more

12A. Screening

Take part in organized screening programmes for: Bowel cancer for men and women, breast cancer and cervical cancer for women.
— Dr Paola Armaroli, CPO Piemonte (Italy)

Learn more

The European Code Against Cancer: cancer-code-europe.iarc.fr

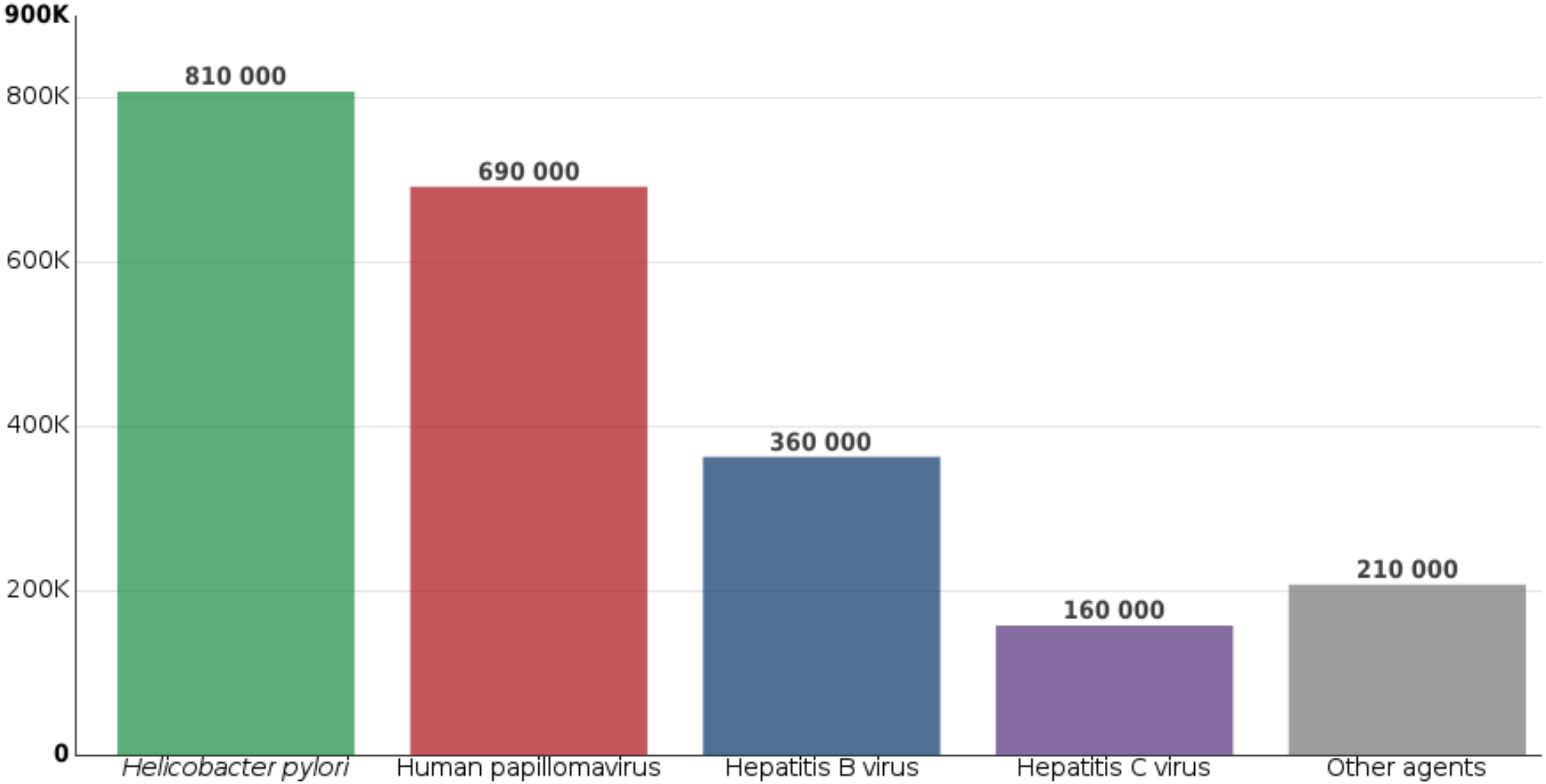
Smoking

Smoking (especially cigarettes) is related to cancer of the

- Mouth
- Pharynx
- Larynx
- Esophagus
- Pancreas
- Urinary bladder
- **LUNG**

Infections

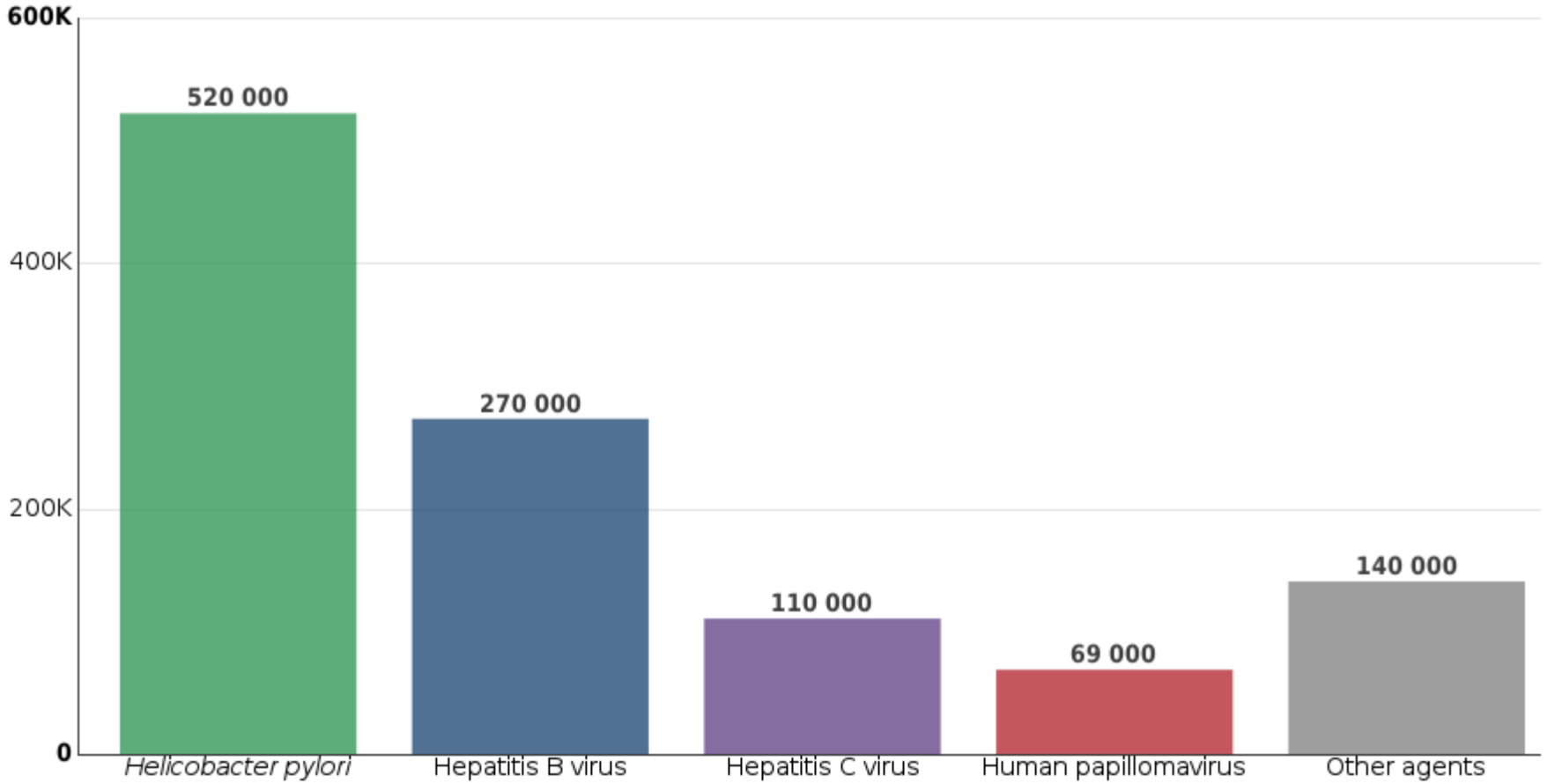
cer cases (all infectious agents) among both sexes in 2018 attributable to infections, in
shown by infectious agents



Data source: de Martel C, Georges D, Bray F, Ferlay J, Clifford GM (2020)
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)

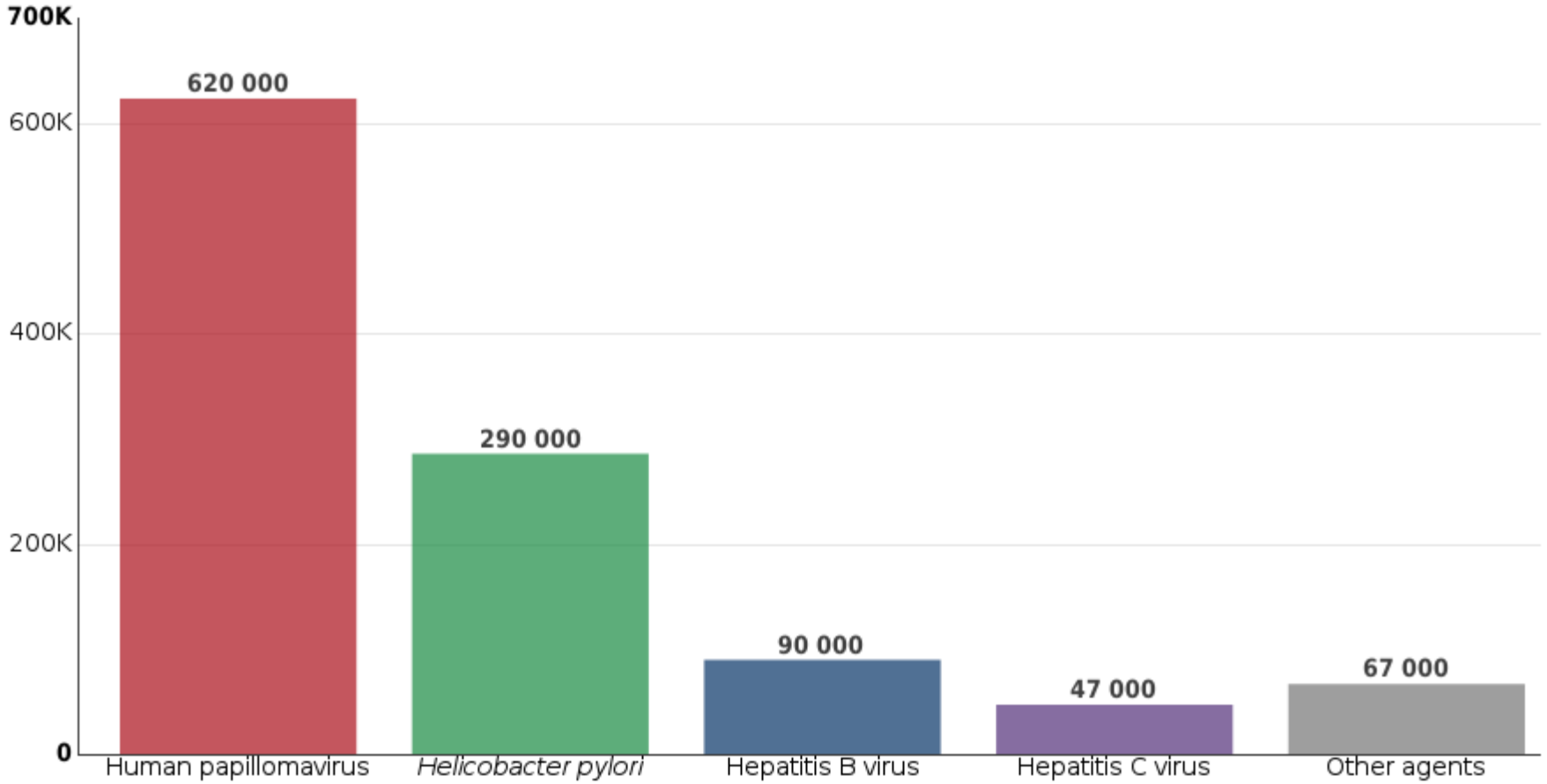
International Agency for Research on Cancer
World Health Organization

er cases (all infectious agents) among males in 2018 attributable to infections, in the wo
by infectious agents



Data source: de Martel C, Georges D, Bray F, Ferlay J, Clifford GM (2020)
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)

r cases (all infectious agents) among females in 2018 attributable to infections, in the w
by infectious agents



Data source: de Martel C, Georges D, Bray F, Ferlay J, Clifford GM (2020)
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)

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World Health Organization

Human Papillomavirus

Histopathology

Histopathology 2020, **76**, 6–10. DOI: 10.1111/his.13992

REVIEW

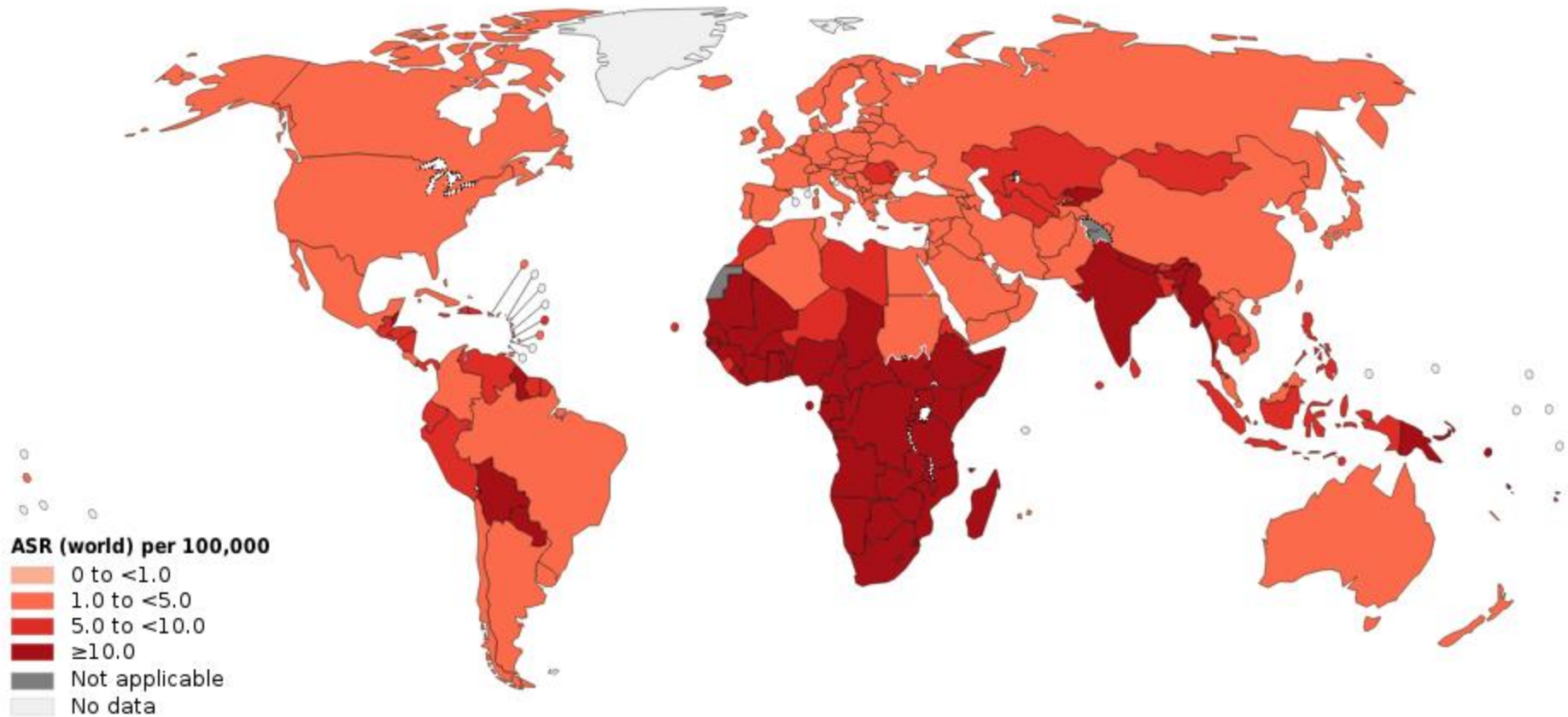
The most important discoveries of the past 50 years in gynaecological pathology

Steven G Silverberg[1] & C Blake Gilks[2]

[1]*University of Maryland Medical System, Baltimore, MD, USA, and* [2]*Department of Pathology and Laboratory Medicine, Vancouver General Hospital, Vancouver, BC, Canada*

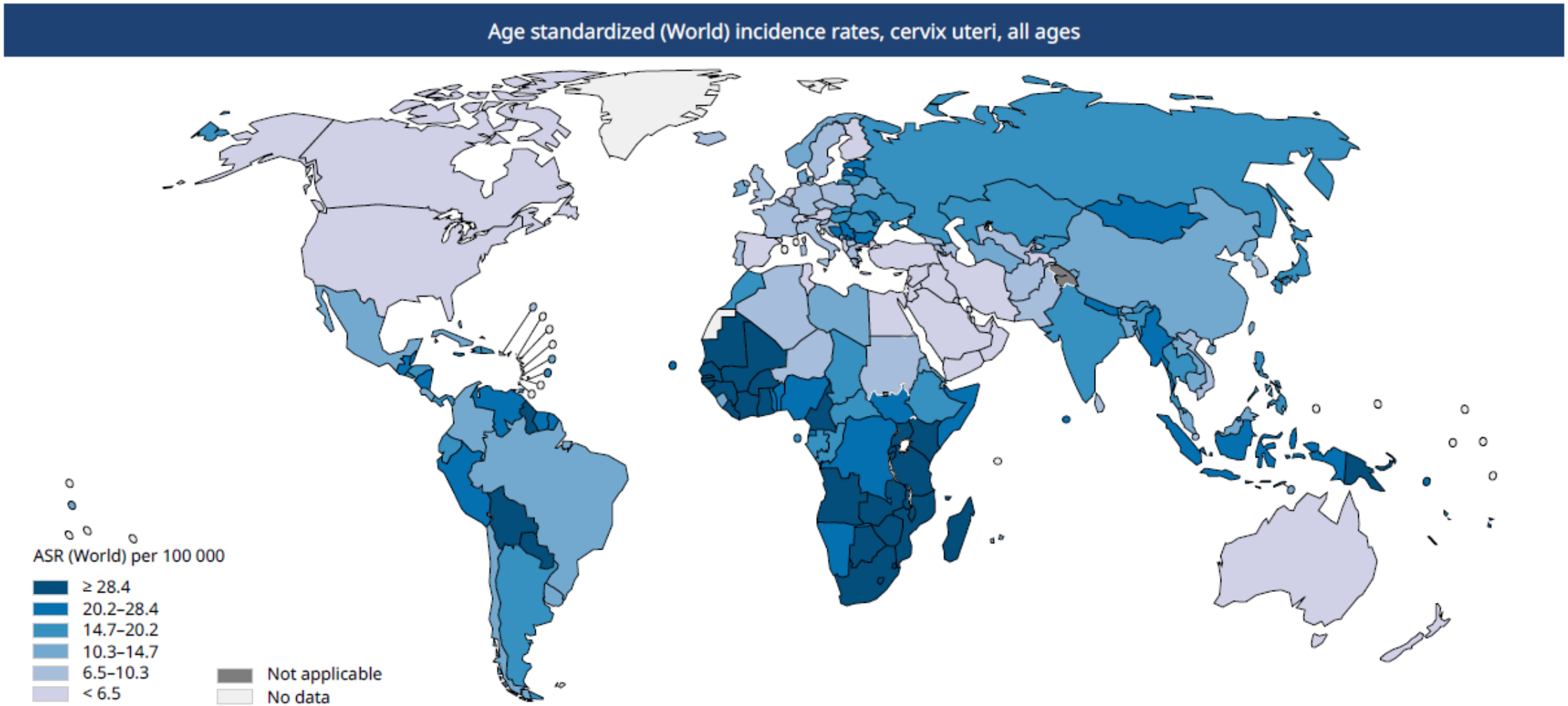
Number 1: Discovery of the role of human papillomavirus (HPV) in the aetiology of carcinoma of the lower genital tract

Age-standardized rates (worldwide) per 100 000 individual in 2018 attributable to infections (Human papillomavirus), by country

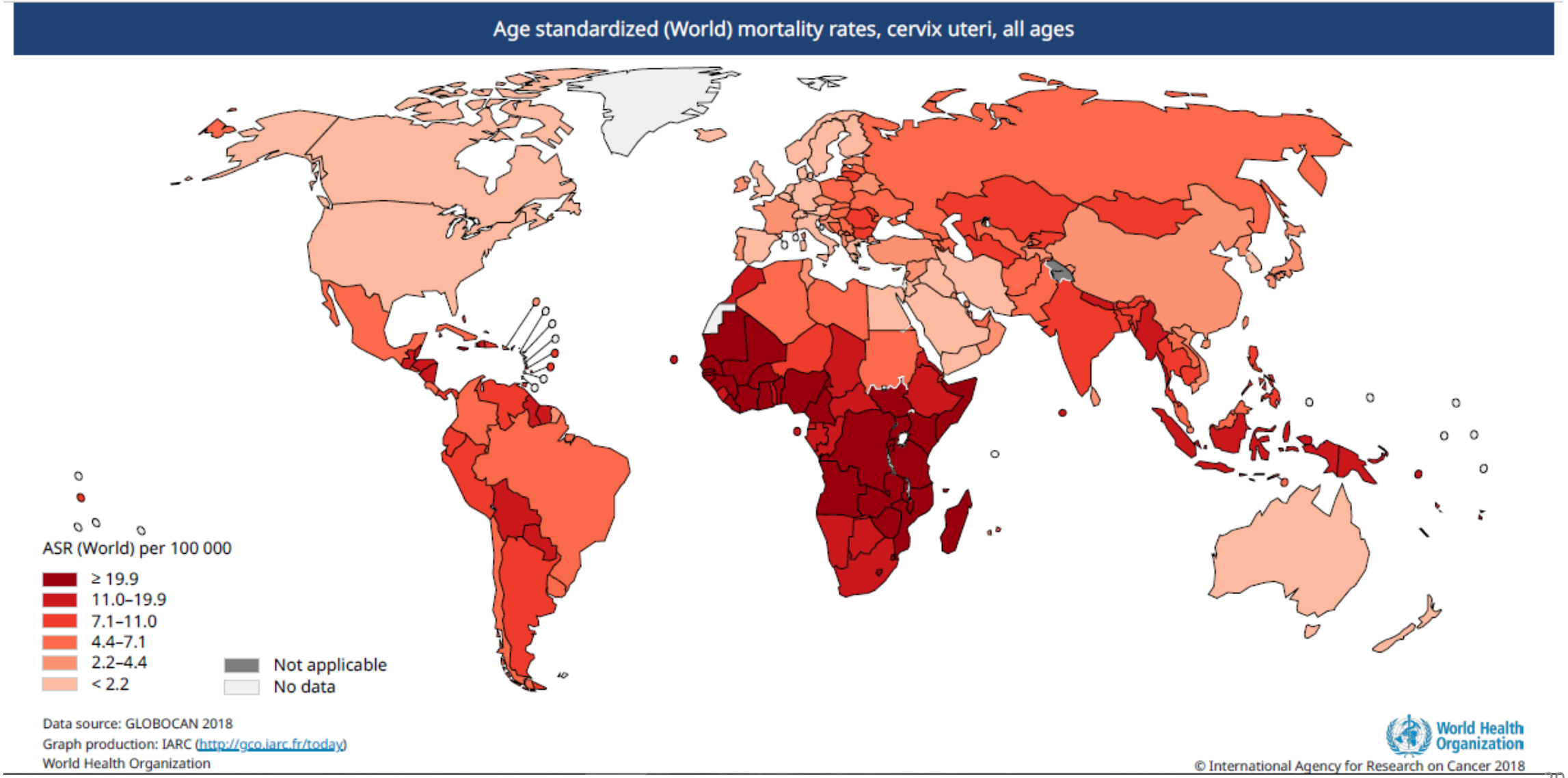


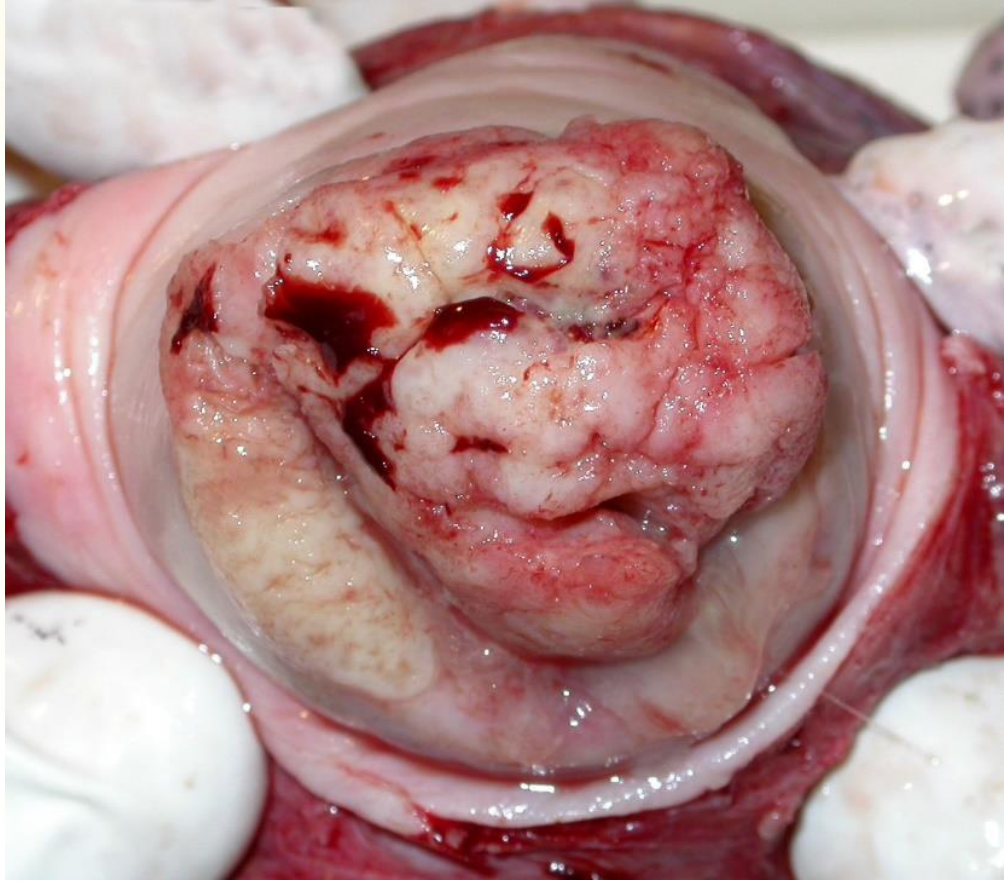
- Over 200 HPV types
- 14 types considered high risk (oncogenic)
- High risk (oncogenic) HPV- squamous cell carcinoma of vulva, vagina, cervix, penis, anus, tonsilla and oropharynx
- MOST IMPORTANT: HPV 16 and 18
- Other high risk HPVs: 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, (66, and 68)
- Co-carcinogens in cervical cancer:
  - Multiple sexual partners
  - Young age at first intercourse
  - High parity
  - Immunosuppression, HIV co-infection
  - Oral contraceptives
  - Smoking

CERVICAL CANCER IS A MAJOR GLOBAL HEALTH ISSUE



CERVICAL CANCER IS A MAJOR GLOBAL HEALTH ISSUE

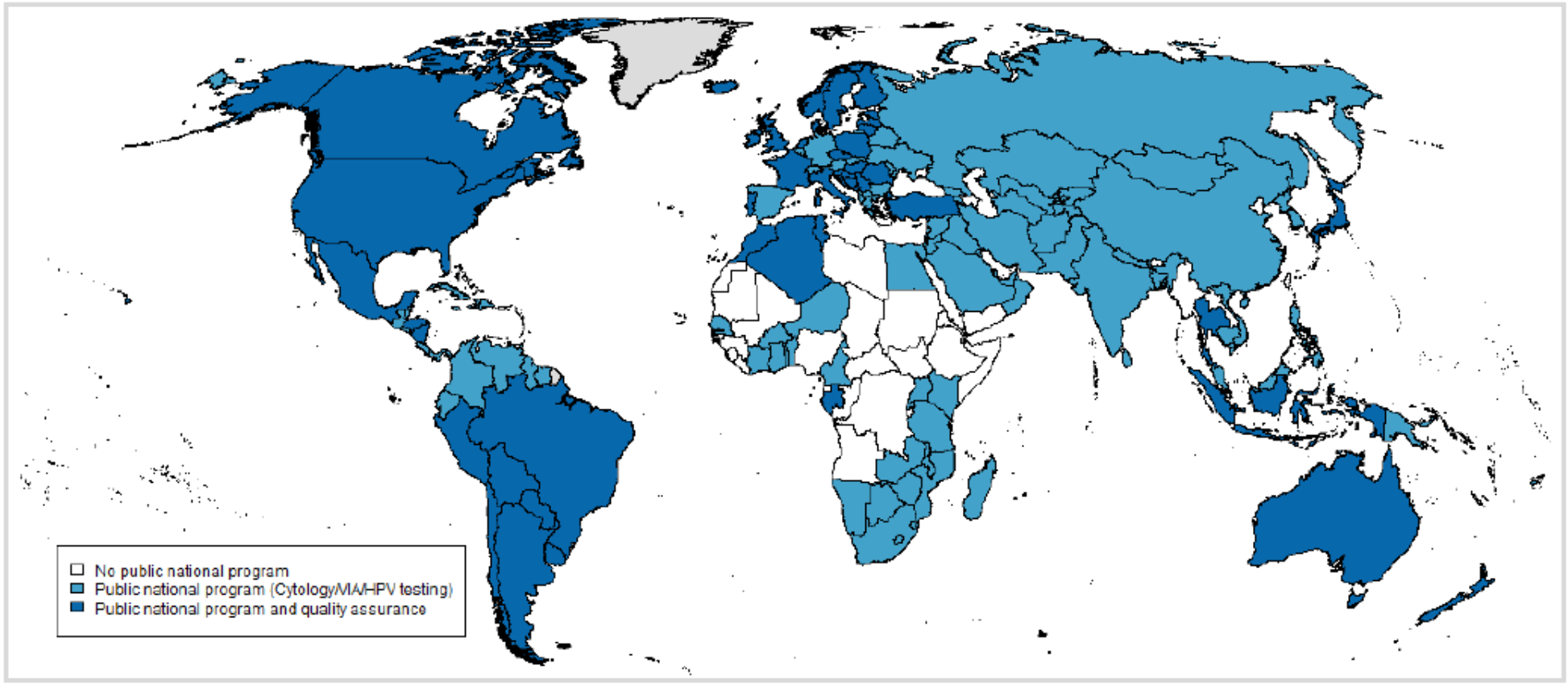




Cervical cancer-squamous cell carcinoma
from the archive of the 2nd Dept. Of Pathology, Semmelweis University, Budapest, Hungary

Cervical cancer- Squamous cell carcinoma
from the archive of the 2nd Dept. Of Pathology, Semmelweis University, Budapest, Hungary

Worldwide status of cervical cancer screening programmes



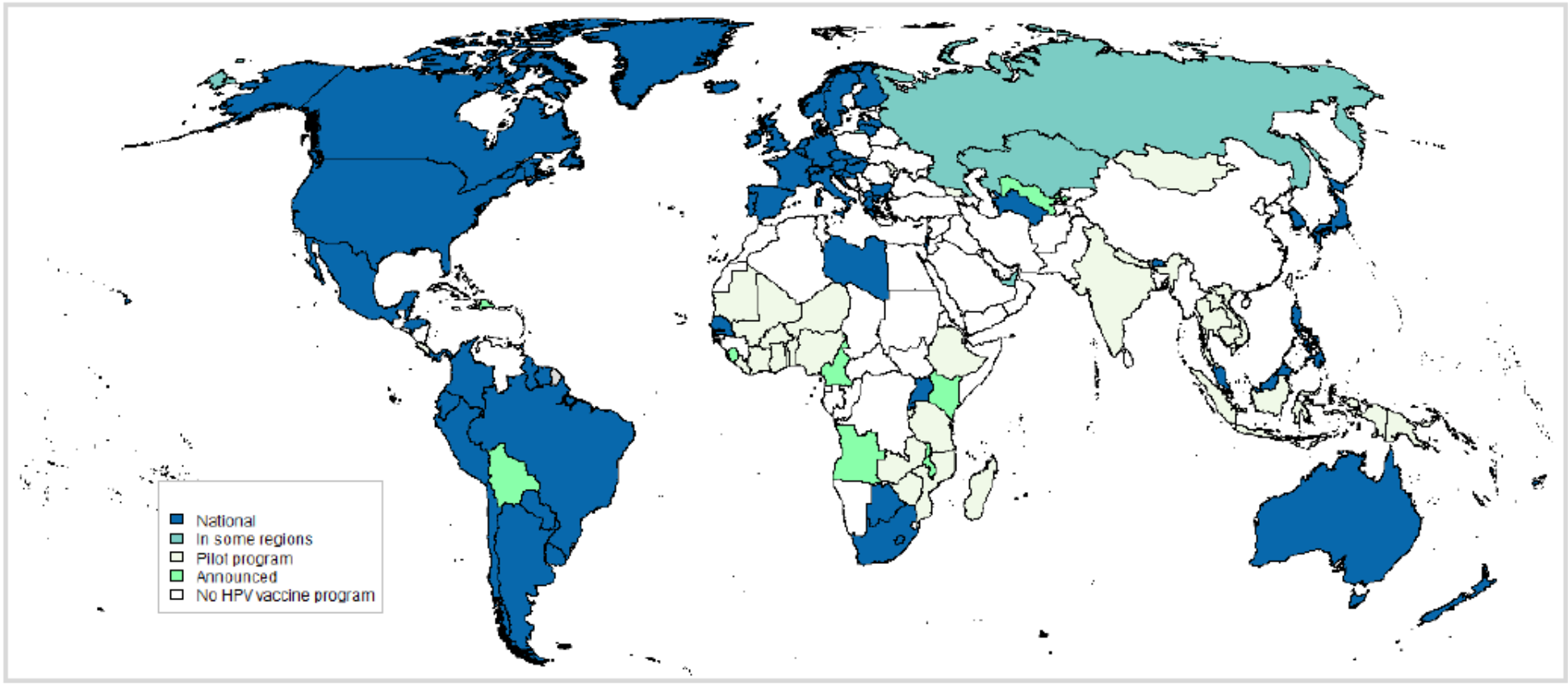
Data accessed on 31 Dec 2016.

www.hpvcenter.net

Prevention-vaccination

- Quadrivalent vaccine: Gardasil® (HPV 6, 11, 16, and 18)
  - The L1 capsid proteins are produced in yeast cells (*Saccharomyces cerevisiae*) and mixed with an aluminum adjuvant.
  - For both males and females who are 9–26 years of age
  - three doses at 0, 2, and 6 months.
- Bivalent vaccine: Cervarix® (HPV 16 and 18)
  - The VLPs in this preparation are generated in insect cells with baculovirus and an adjuvant with ASO_4 and monophosphoryl lipid A via bacterial cell walls
  - For girls and women 10–25 years of age and is given in three doses at 0, 1, and 6 months.
- Nonavalent vaccine: Gardasil 9® (HPV 16, 18, 31, 33, 45, 52, and 58) and (HPV 6, 11)
  - protection from 70 to 90% of cervical cancer-causing HPV infections

Worldwide status of HPV vaccination programmes



Data accessed on 31 Dec 2016.

www.hpvcenter.net

A cervical cancer-free future: First-ever global commitment to eliminate a cancer

17 November 2020 News release

To eliminate cervical cancer as a public health problem, all countries must reach and maintain an incidence rate of fewer than 4 new cases of cervical cancer per 100 000 women per year. Achieving that goal rests on three key pillars and their corresponding targets:

Vaccination: 90% of girls fully vaccinated with the HPV vaccine by the age of 15 years;
Screening: 70% of women screened using a high-performance test by the age of 35 years, and again by the age of 45 years;
Treatment: 90% of women with pre-cancer treated and 90% of women with invasive cancer managed.

Each country should meet the 90–70–90 targets by 2030 to get on the path towards eliminating cervical cancer by the end of this century.

Sources: https://www.who.int/news/item/17-11-2020-a-cervical-cancer-free-future-first-ever-global-commitment-to-eliminate-a-cancer

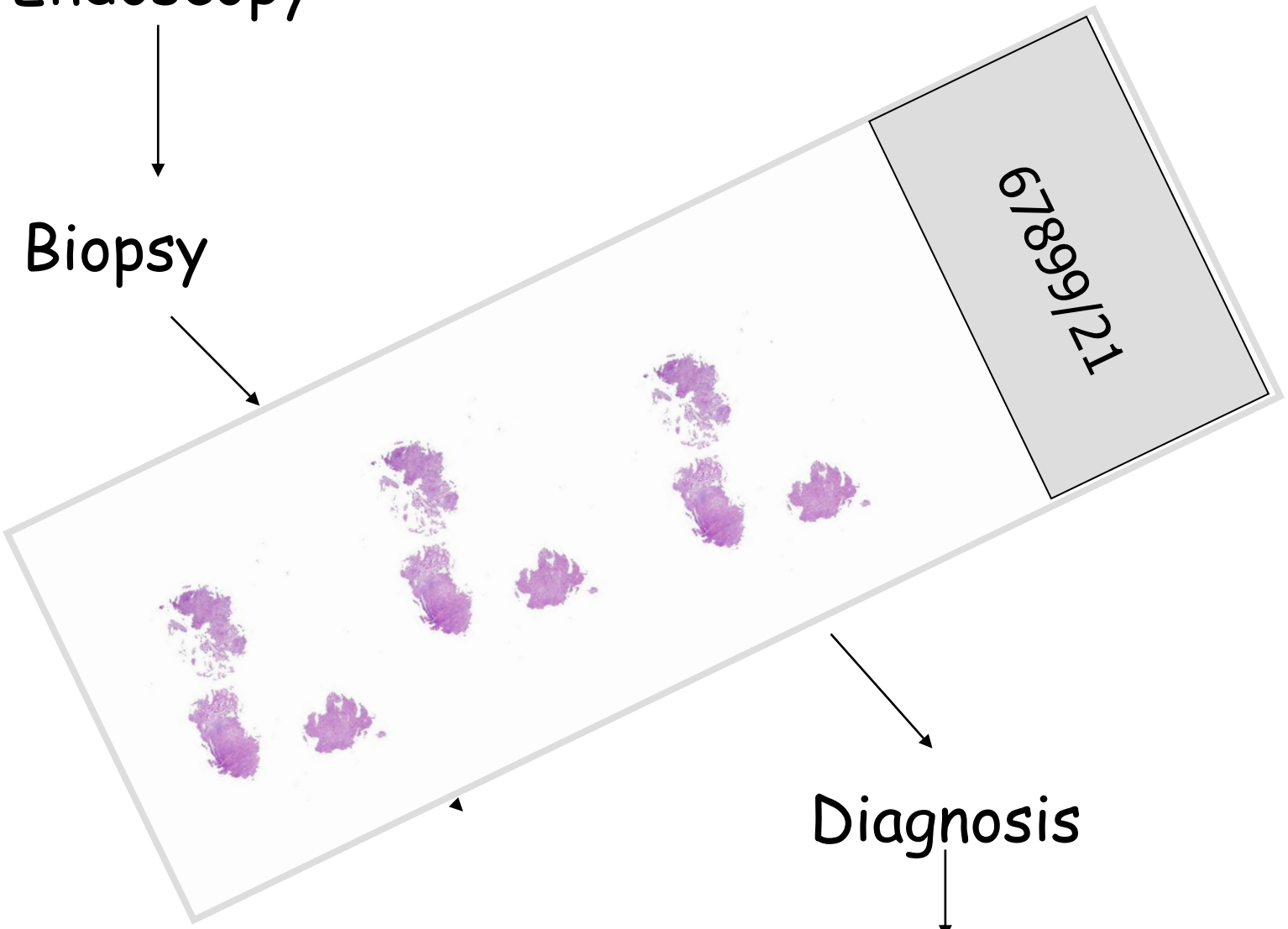
Helicobacter pylori

H.pylori

- 1983. Campylobacter pylori
- Gram negative rods
- its role in chronic gastritis (antrum), peptic ulcer disease, gastric carcinoma, gastric MALT lymphoma

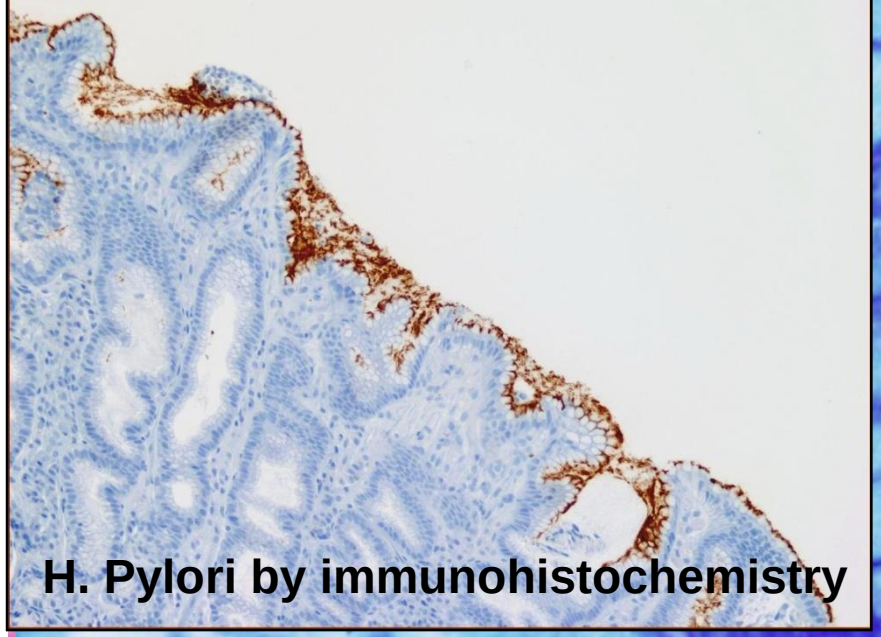
Endoscopy

Biopsy

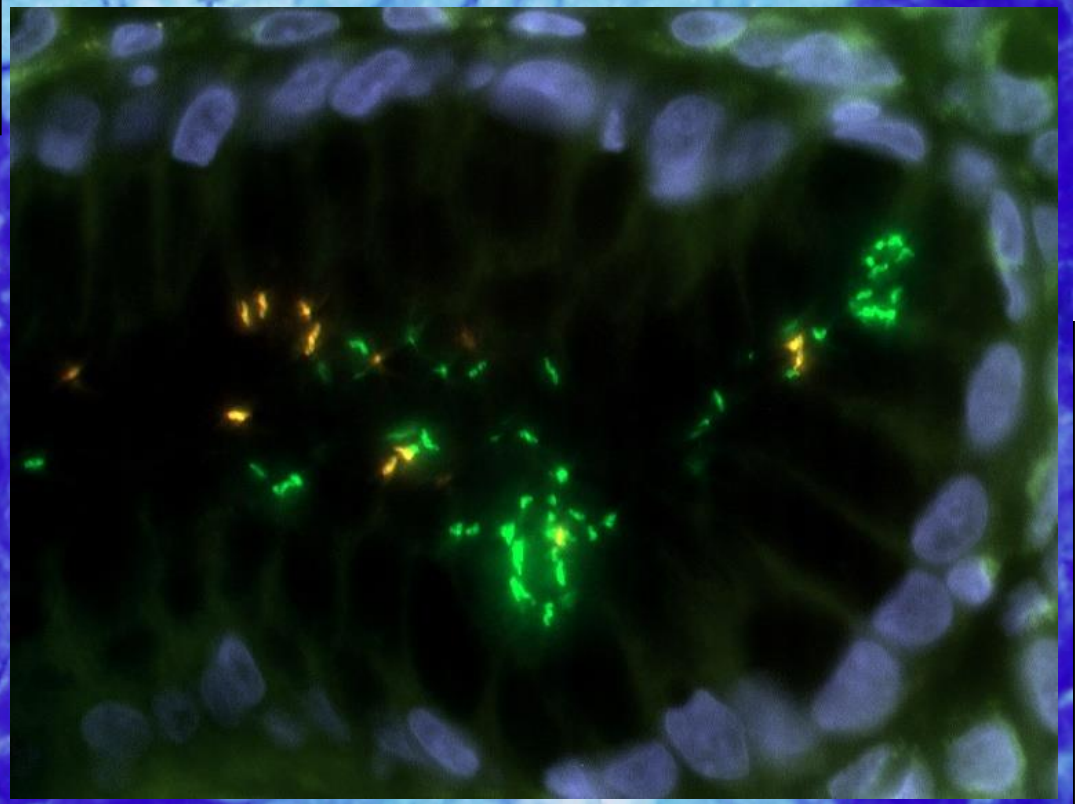


Diagnosis

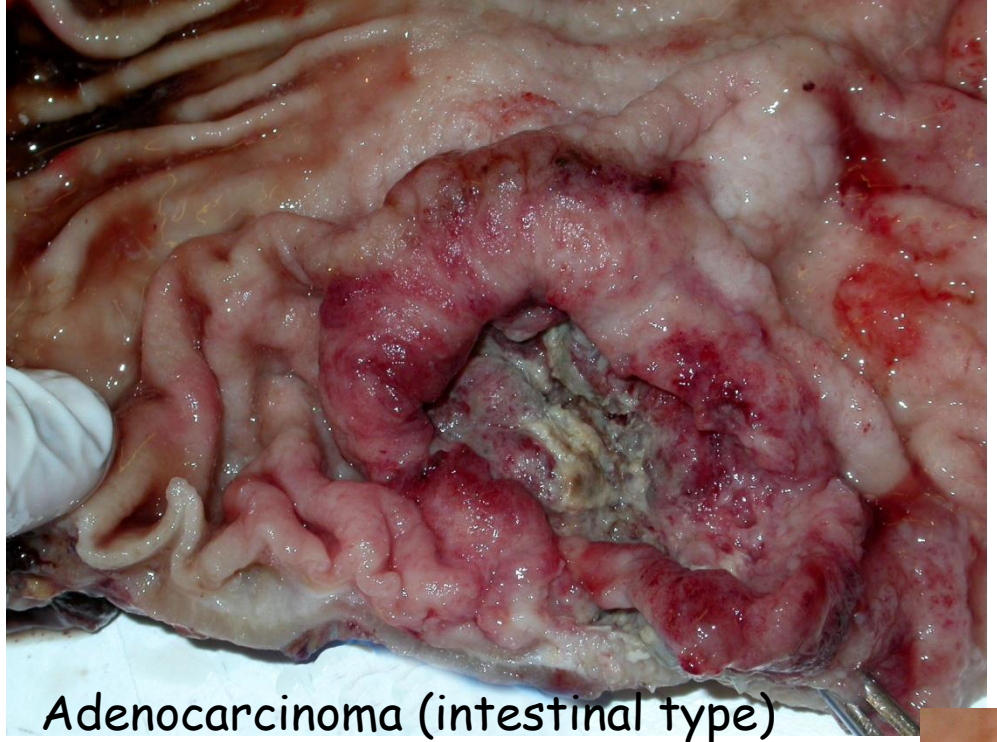
Therapy



H. Pylori by immunohistochemistry

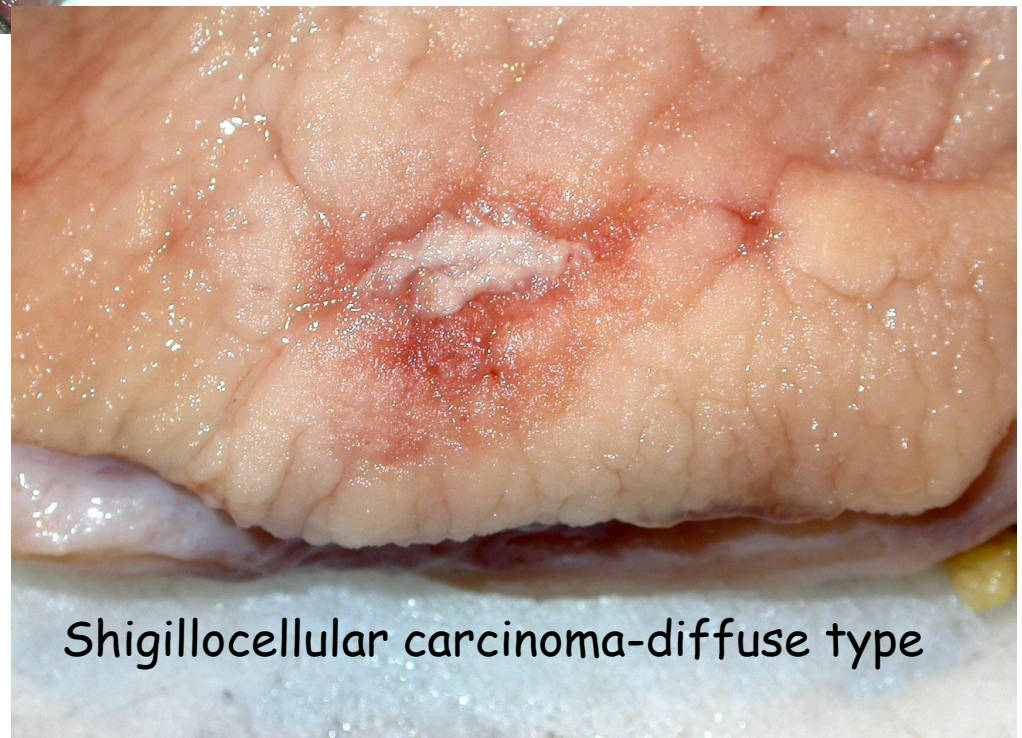


H.pylori-Giemsa



Adenocarcinoma (intestinal type)

Shigillocellular cc-diffuse type



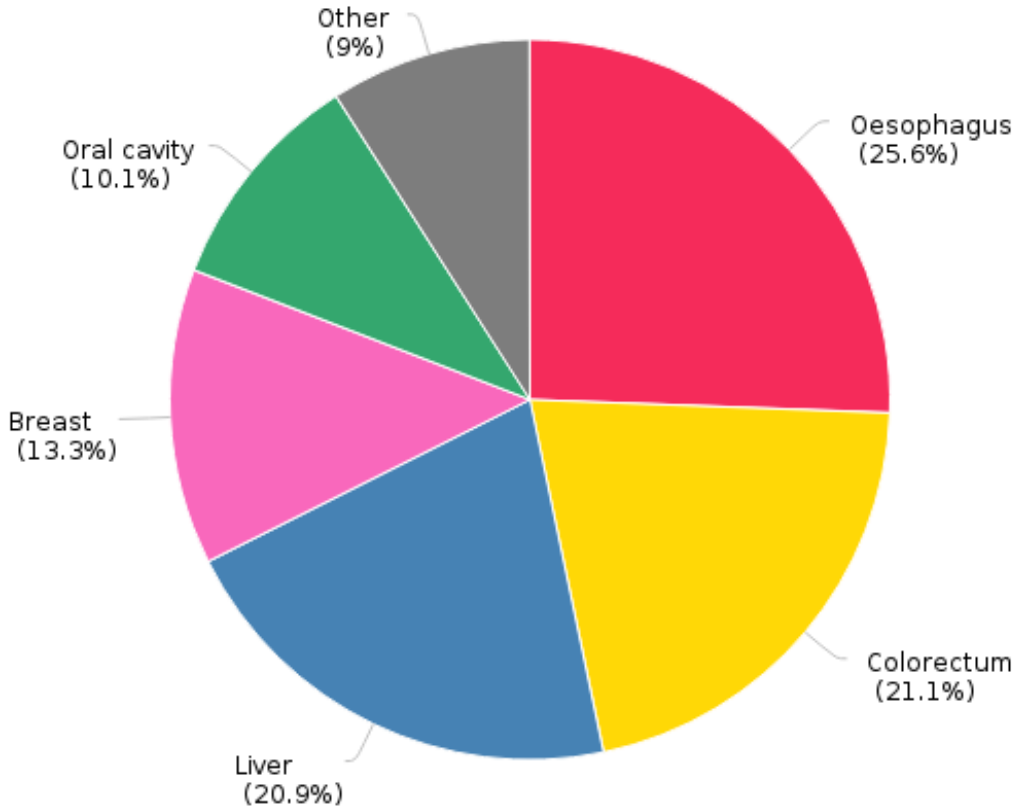
Shigillocellular carcinoma-diffuse type

Other oncogenic viruses

- **Human T-Cell Leukemia Virus Type 1 (HTLV-1)**
  - A retrovirus endemic in Japan, the Caribbean, South America and Africa
  - causes adult T-cell leukemia/lymphoma.
- **Epstein Barr Virus (EBV)**
  - ubiquitous herpesvirus
  - Burkitt lymphomas, B-cell lymphomas in patients with T-cell immunosuppression (HIV infection, transplant recipients) , other cancers
- **Hepatitis B Virus and Hepatitis C Virus (HBV and HCV**)
  - 70% to 85% of hepatocellular carcinomas

Alcohol

Estimated number of new cancer cases in 2020 attributable to alcohol drinking, World, both sexes



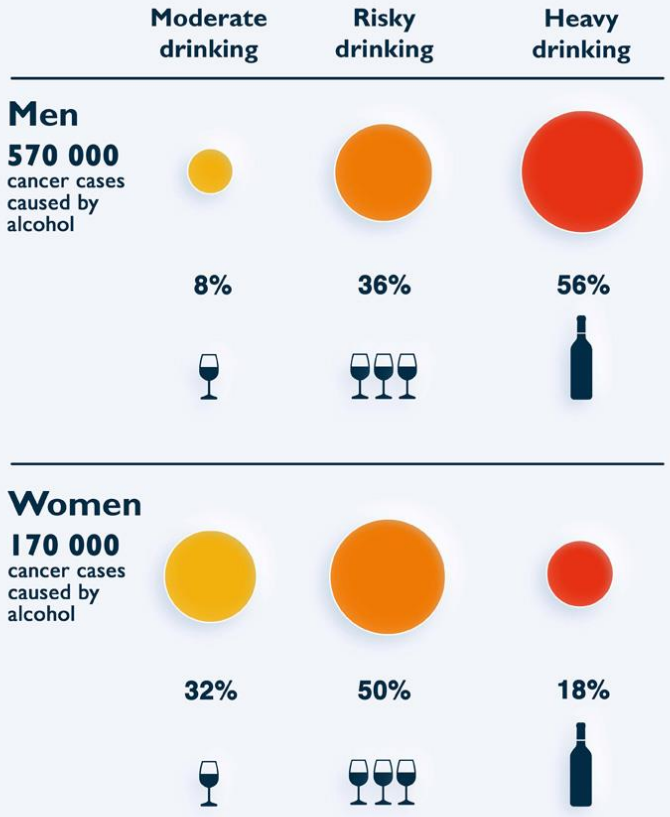
Total number of attributable cases: 740 000

Data source: GLOBOCAN 2012
Graph production: IARC
World Health Organization

International Agency for Research on Cancer

World Health Organization

Contribution of different levels of alcohol drinking to the global alcohol-attributable cancer burden in 2020



Moderate drinking: less than 20 grams of pure alcohol per day

Risky drinking: 20–60 grams of pure alcohol per day

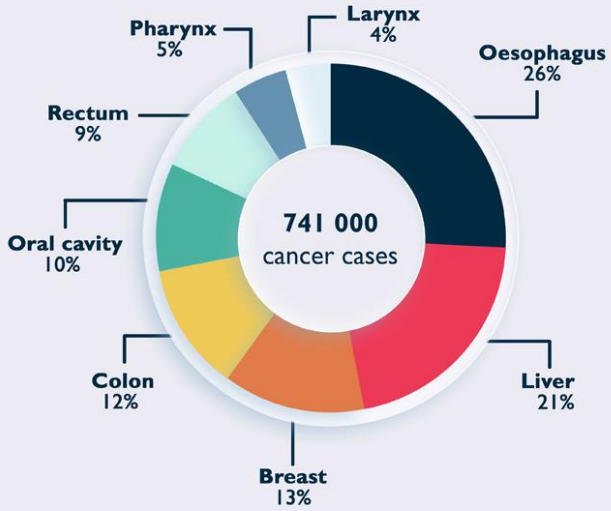
Heavy drinking: more than 60 grams of pure alcohol per day

International Agency for Research on Cancer

World Health Organization

Alcohol drinking caused more than 740 000 cases of cancer globally in 2020.

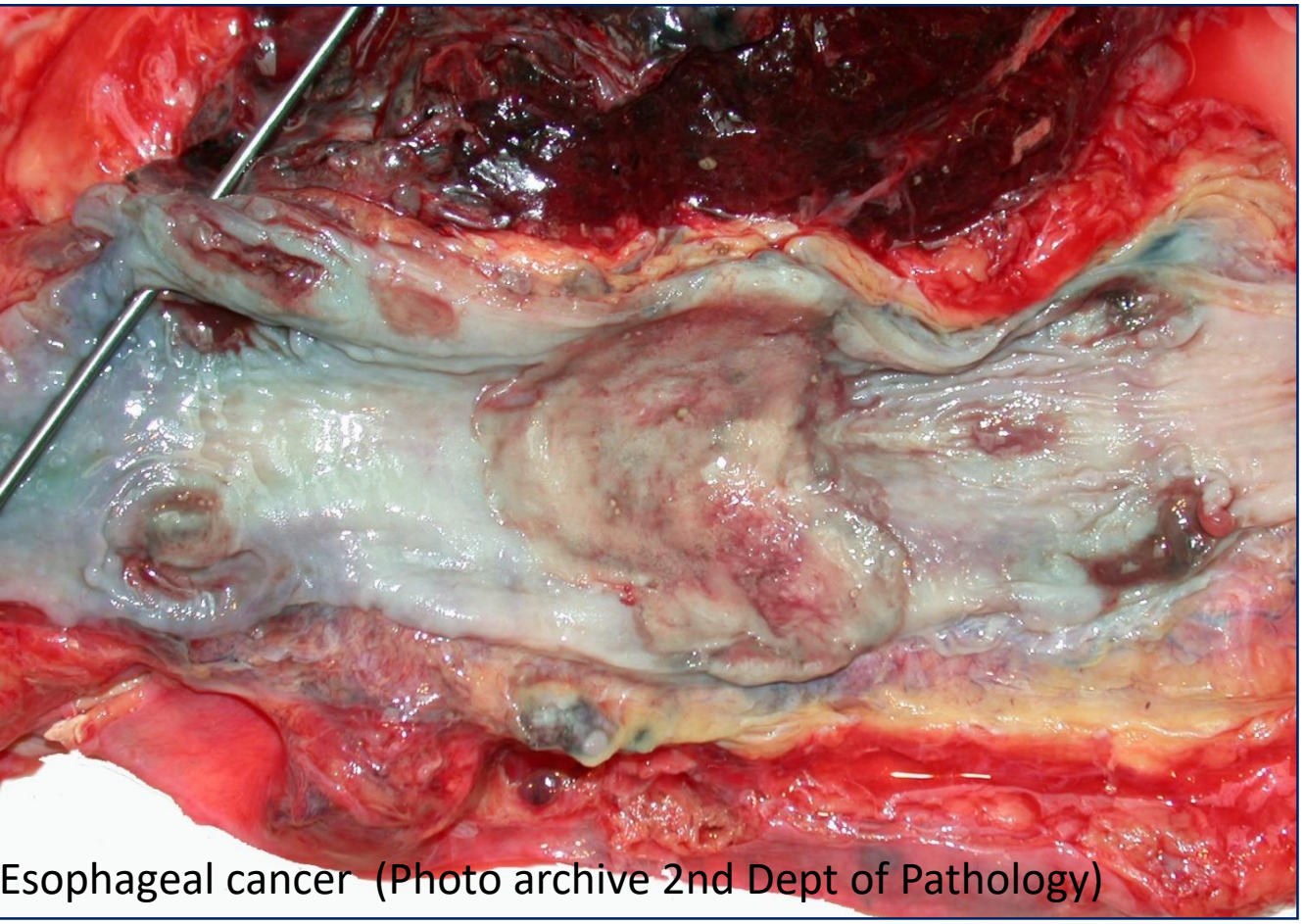
Which cancer types contributed to the total number of cases caused by alcohol drinking?



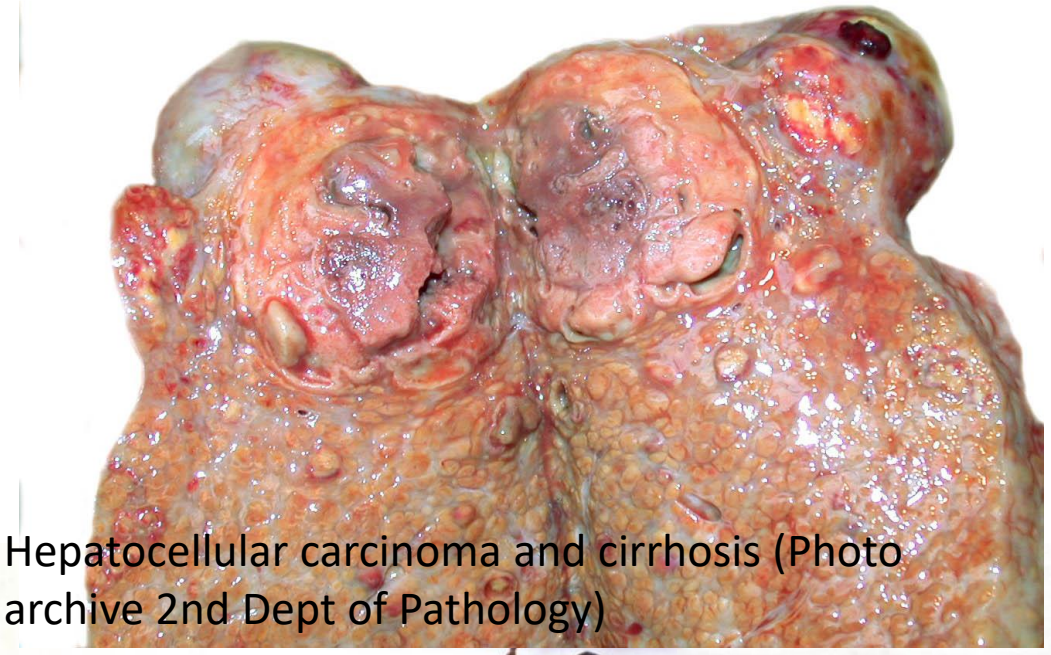
Even **light and moderate drinking*** can cause cancer and accounted for more than 100 000 new cases worldwide in 2020.

** up to two alcoholic drinks per day*

Men accounted for about **three quarters of the total cases** of cancer caused by alcohol drinking.



Esophageal cancer (Photo archive 2nd Dept of Pathology)

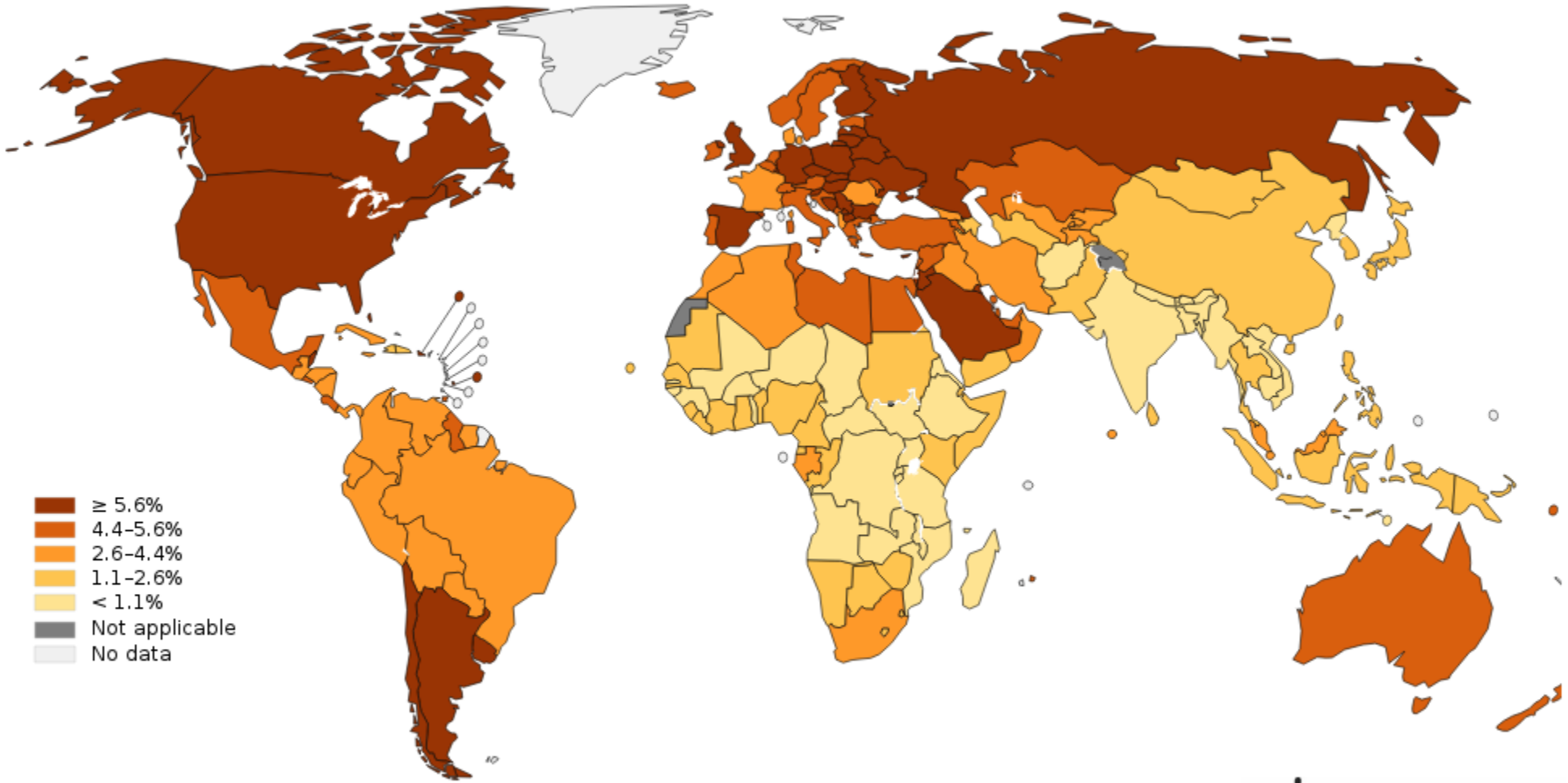


Hepatocellular carcinoma and cirrhosis (Photo archive 2nd Dept of Pathology)

Pancreatic cancer (Photo archive 2nd Dept of Pathology)

Obesity

Fraction (%) of all cancer cases (at all anatomical sites) among both sexes (worldwide) in 2012 attributable to excess body mass index, by country

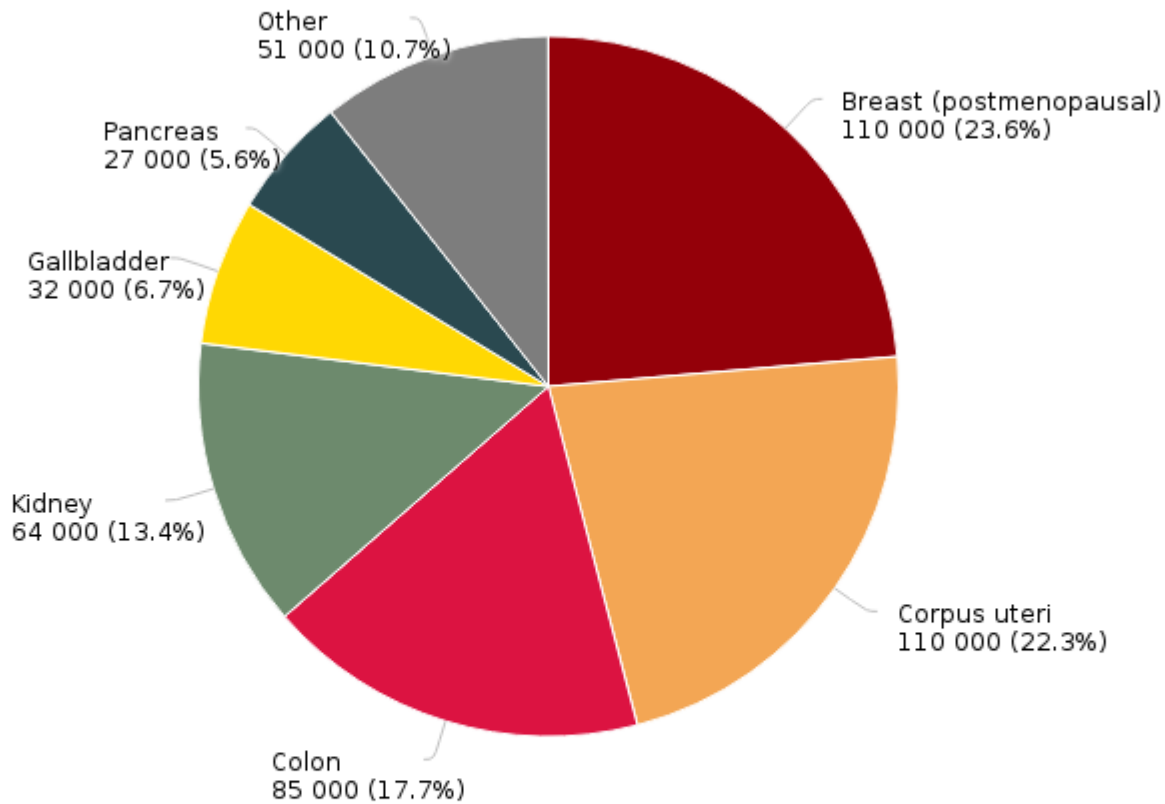


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: GLOBOCAN 2012
Map production: IARC
World Health Organization

World Health Organization

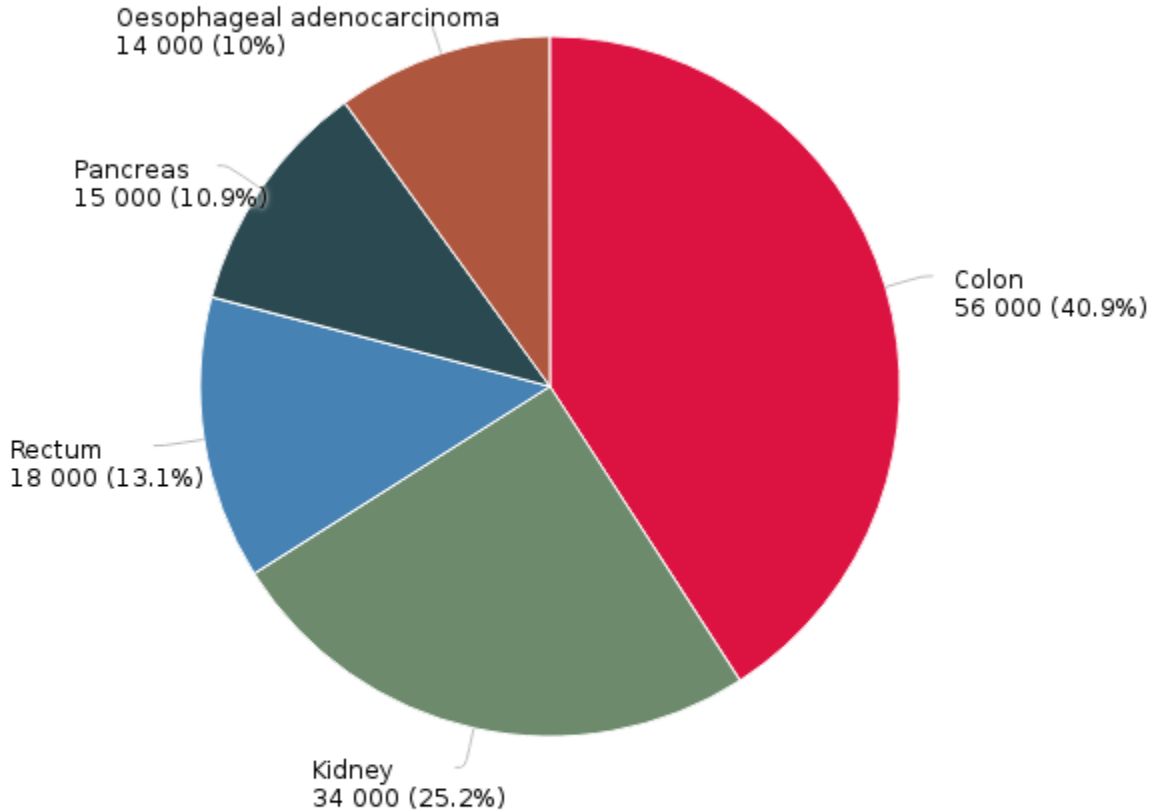
Cancer (at all anatomical sites) among both sexes (worldwide) in 2012 attributable to excess body mass index, shown by anatomical site as percentages of the total number of all such attributable cases at all anatomical sites in this population



Data source: GLOBOCAN 2012
Graph production: IARC World Health Organization

World Health Organization

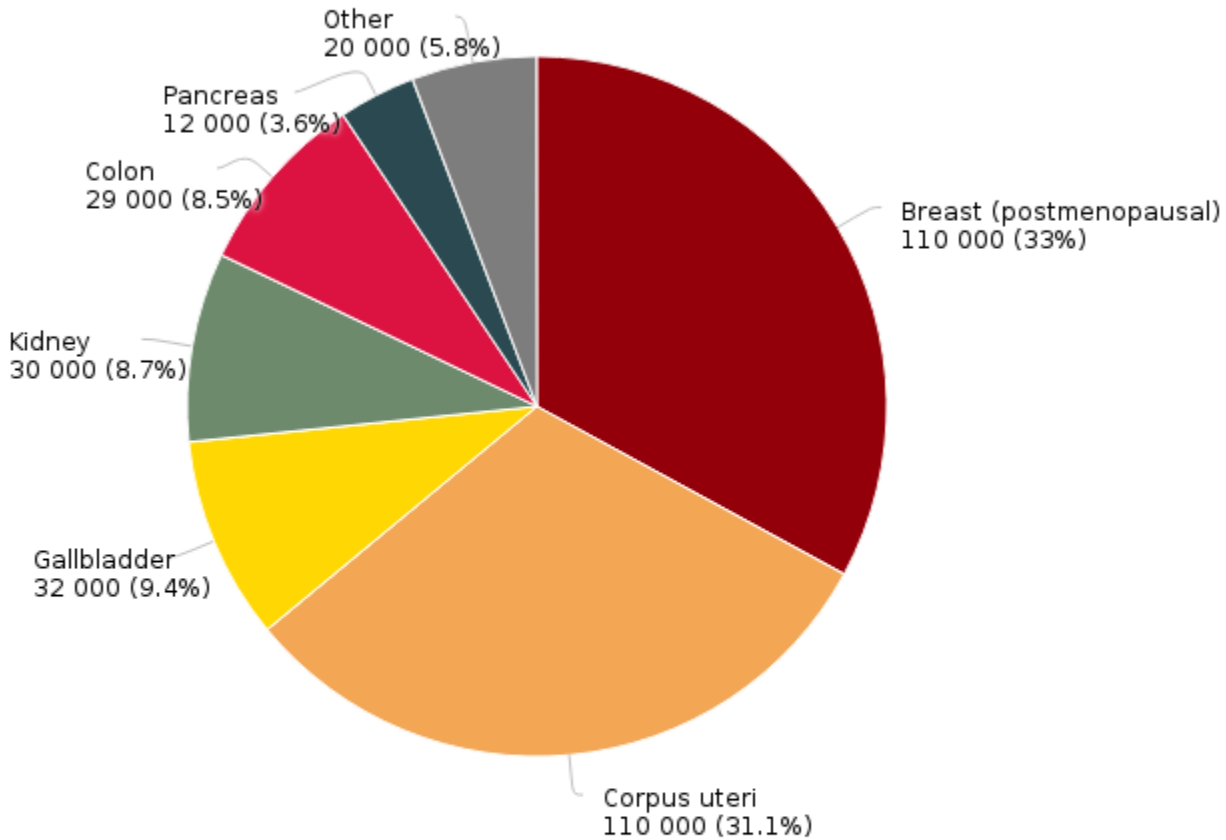
ancer cases (at all anatomical sites) among males (worldwide) in 2012 attributable to excess body mass index, shown by anatomical site as percentages of the total number of all such attributable cases at all anatomical sites in this population



Data source: GLOBOCAN 2012
Graph production: IARC World Health Organization

World Health Organization

ıncer cases (at all anatomical sites) among females (worldwide) in 2012 attributable to excess body mass index, shown by anatomical site as percentages of the total number of all such attributable cases at all anatomical sites in this population

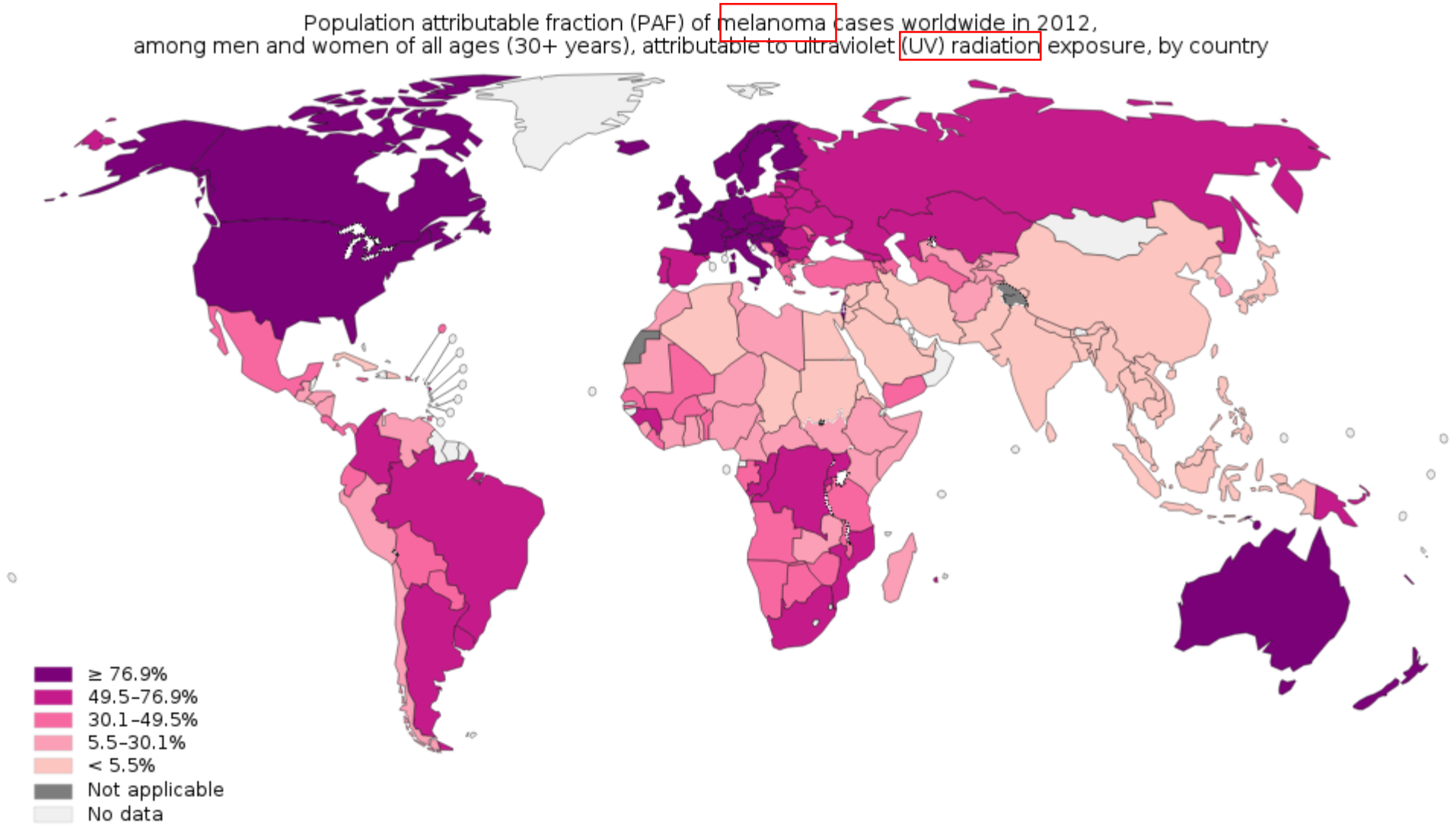


Data source: GLOBOCAN 2012
Graph production: IARC World Health Organization

World Health Organization

SUN/UV exposure

- Ionizing radiation causes chromosome breakage, translocations, and point mutations, leading to genetic damage and carcinogenesis.
- UV rays induce the formation of pyrimidine dimers within DNA, leading to mutations.
- UV rays can give rise to skin cancers. Basal cell carcinoma, Squamous cell carcinoma and Melanoma.
- xeroderma pigmentosa individuals have defects in the repair of pyrimidine dimers and are at particularly high risk.


Population attributable fraction (PAF) of melanoma cases worldwide in 2012,
among men and women of all ages (30+ years), attributable to ultraviolet (UV) radiation exposure, by country
≥ 76.9%
49.5–76.9%
30.1–49.5%
5.5–30.1%
< 5.5%
Not applicable
No data

Environmental carcinogens

Agents or Groups of Agents	Human Cancers for Which Reasonable Evidence Is Available	Typical Use or Occurrence
Arsenic and arsenic compounds	Lung carcinoma, skin carcinoma	By-product of metal smelting; component of alloys, electrical and semiconductor devices, medications and herbicides, fungicides, and animal dips
Asbestos	Lung, esophageal, gastric, and colon carcinoma; mesothelioma	Formerly used for many applications because of fire, heat, and friction resistance; still found in existing construction as well as fire-resistant textiles, friction materials (i.e., brake linings), underlayment and roofing papers, and floor tiles
Benzene	Acute myeloid leukemia	Principal component of light oil; despite known risk, many applications exist in printing and lithography, paint, rubber, dry cleaning, adhesives and coatings, and detergents; formerly widely used as solvent and fumigant
Beryllium and beryllium compounds	Lung carcinoma	Missile fuel and space vehicles; hardener for lightweight metal alloys, particularly in aerospace applications and nuclear reactors
Cadmium and cadmium compounds	Prostate carcinoma	Uses include yellow pigments and phosphors; found in solders; used in batteries and as alloy and in metal platings and coatings
Chromium compounds	Lung carcinoma	Component of metal alloys, paints, pigments, and preservatives
Nickel compounds	Lung and oropharyngeal carcinoma	Nickel plating; component of ferrous alloys, ceramics, and batteries; by-product of stainless-steel arc welding
Radon and its decay products	Lung carcinoma	From decay of minerals containing uranium; potentially serious hazard in quarries and underground mines
Vinyl chloride	Hepatic angiosarcoma	Refrigerant; monomer for vinyl polymers; adhesive for plastics; formerly inert aerosol propellant in pressurized containers

From Robbins Pathologic basis of diseases 10th edition

Chemical carcinogenesis

- Scrotal skin cancer in chimney sweeps due to chronic exposure to soot- described by Sir Percival Pott in London
- Danish Chimney Sweeps Guild ruled that its members must bathe daily
- Chemical carcinogens have highly reactive electrophile groups that directly damage DNA, leading to mutations and cancer

- Direct-acting agents do not require metabolic conversion to become carcinogenic
- Indirect-acting agents are not active until converted to an ultimate carcinogen by endogenous metabolic pathways. Hence, polymorphisms of endogenous enzymes such as cytochrome P-450 may influence carcinogenesis
- After exposure of a cell to a mutagen or an initiator, tumorigenesis can be enhanced by exposure to promoters, which stimulate proliferation of the mutated cells.

- Human carcinogens
  - direct-acting agents (e.g., alkylating agents used for chemotherapy)
  - indirect-acting agents (e.g., benzo[*a*]pyrene, azo dyes, aflatoxin)
  - promoters or agents that cause pathologic hyperplasias of the endometrium or regenerative activity in the liver

Age

- Cancer incidence rises with increasing age
- Cancer is the leading cause of death in women aged 40-79 and in men 60-79
- Childhood cancer

Acquired Predisposing Conditions to cancer

- Chronic inflammation
- Precursor lesions
- Immunodeficiency

Chronic inflammation

Modified from Tlsty TD, Coussens LM: Tumor stroma and regulation of cancer development, *Ann Rev Pathol Mech Dis* 1:119, 2006.

Pathologic Condition	Associated Neoplasm(s)	Etiologic Agent(s)
Asbestosis, silicosis	Mesothelioma, lung carcinoma	Asbestos fibers, silica particles
Inflammatory bowel disease	Colorectal carcinoma	
Lichen sclerosis	Vulvar squamous cell carcinoma	
Pancreatitis	Pancreatic carcinoma	Alcoholism, germline mutations (e.g., in the trypsinogen gene)
Chronic cholecystitis	Gallbladder cancer	Bile acids, bacteria, gallbladder stones
Reflux esophagitis, Barrett esophagus	Esophageal carcinoma	Gastric acid
Sjögren syndrome, Hashimoto thyroiditis	MALT lymphoma	
Opisthorchis, cholangitis	Cholangiocarcinoma, colon carcinoma	Liver flukes (*Opisthorchis viverrini*)
Gastritis/ulcers	Gastric adenocarcinoma, MALT lymphoma	*Helicobacter pylori*
Hepatitis	Hepatocellular carcinoma	Hepatitis B and/or C virus
Osteomyelitis	Carcinoma in draining sinuses	Bacterial infection
Chronic cervicitis	Cervical carcinoma	Human papillomavirus
Chronic cystitis	Bladder carcinoma	Schistosomiasis

MALT, Mucosa-associated lymphoid tissue.

Precursor lesions

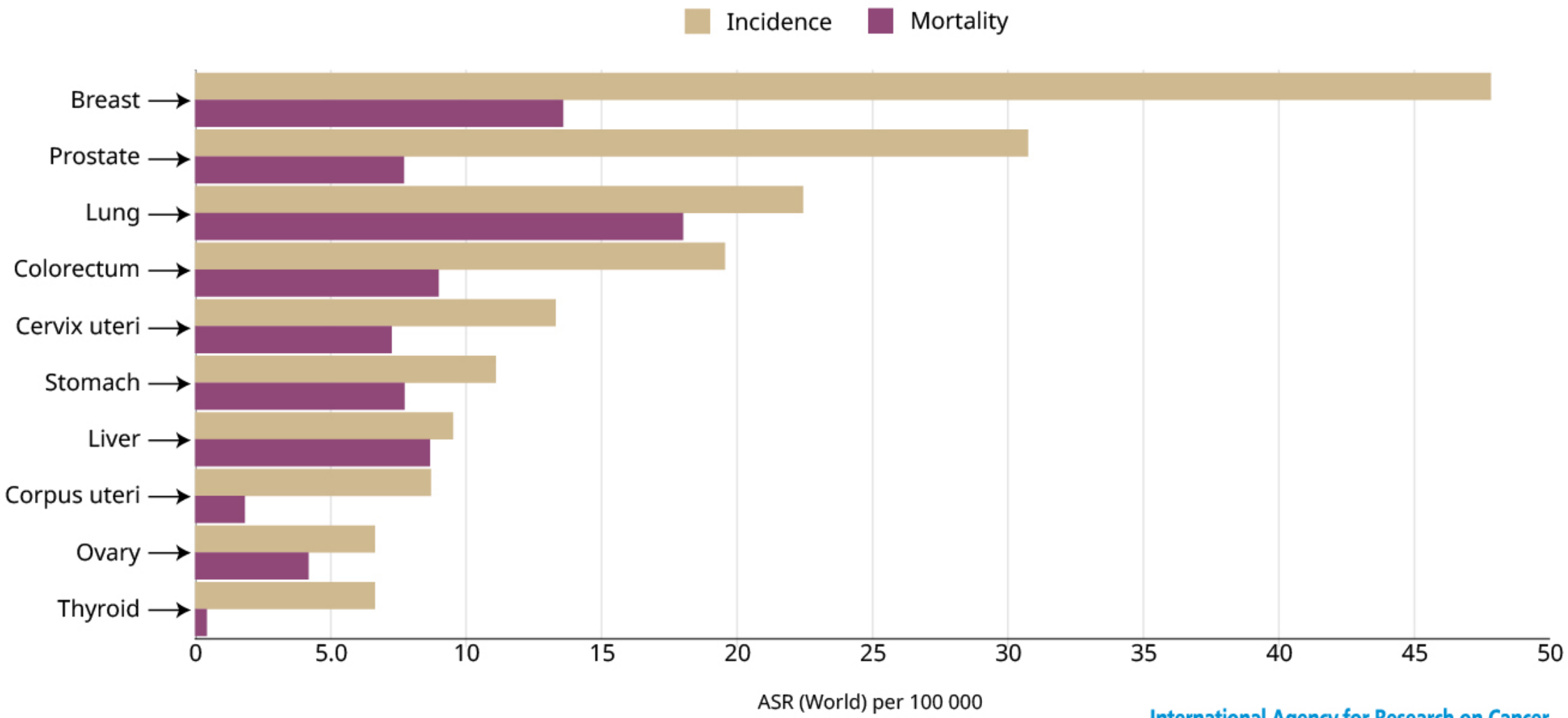
- Metaplasia e.g. Barrett mtpl and esophageal adenocarcinoma
- Dysplasia e.g. HSIL and cervical cancer
- Hyperplasia e.g endometrial hyperplasia and endometrioid carcinoma

Immunodeficiency

- deficits in T-cell immunity  increased risk for cancer
- Oncogenic viruses
- Lymphoma, carcinoma, sarcoma

3 important issues to remember

Estimated age-standardized (World) incidence and mortality rates (ASR) per 100 000 person-years in 2020 for the 10 most common cancer types, worldwide for both sexes and all ages

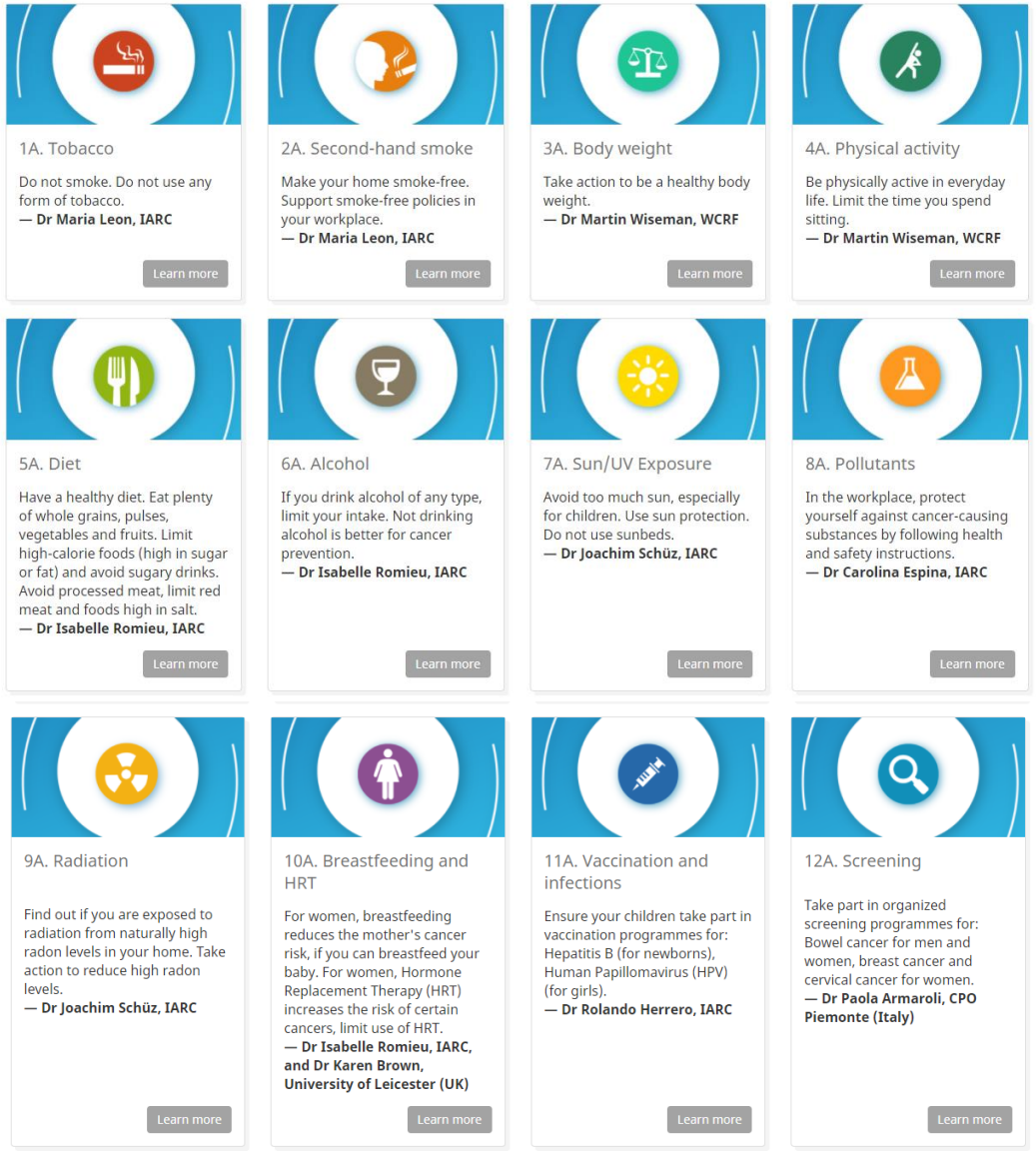


Data source: GLOBOCAN 2020

International Agency for Research on Cancer

World Health Organization

12 WAYS TO REDUCE YOUR CANCER RISK



The European Code Against Cancer: cancer-code-europe.iarc.fr

A cervical cancer-free future: First-ever global commitment to eliminate a cancer

17 November 2020 News release

To eliminate cervical cancer as a public health problem, all countries must reach and maintain an incidence rate of fewer than 4 new cases of cervical cancer per 100 000 women per year. Achieving that goal rests on three key pillars and their corresponding targets:

Vaccination: 90% of girls fully vaccinated with the HPV vaccine by the age of 15 years;
Screening: 70% of women screened using a high-performance test by the age of 35 years, and again by the age of 45 years;
Treatment: 90% of women with pre-cancer treated and 90% of women with invasive cancer managed.

Each country should meet the 90–70–90 targets by 2030 to get on the path towards eliminating cervical cancer by the end of this century.

Sources: https://www.who.int/news/item/17-11-2020-a-cervical-cancer-free-future-first-ever-global-commitment-to-eliminate-a-cancer