



Hormozgan University of Medical Sciences

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Tobacco and Health

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Bladder cancer & Tobacco



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Bladder cancer is the most common malignancy involving the urinary system and the **ninth** most common malignancy worldwide . Bladder cancer (BC) is the **seventh** most commonly diagnosed cancer in the male population worldwide.

Worldwide, there are over **500,000** cases of bladder cancer and almost **200,000** deaths related to bladder cancer each year . There is highest rates of incidence in Europe, North America, Western Asia, and Northern Africa.

Bladder cancer is typically diagnosed in older individuals. A majority (73%) of patients with bladder cancer are **older than 65** years of age. The median age at diagnosis is **69** years in males and **71** years in females .(tobacco smoking and environmental carcinogen)



- Three-quarters of new cases occur in men , yet women have greater disease-specific mortality.
- Furthermore, **women** have been shown to have a **higher stage** at BC diagnosis. However, women have also been shown to have **poorer survival outcomes** when adjusted for all stages . This may represent differences in treatment efficacy and cancer biology and drug interactions.

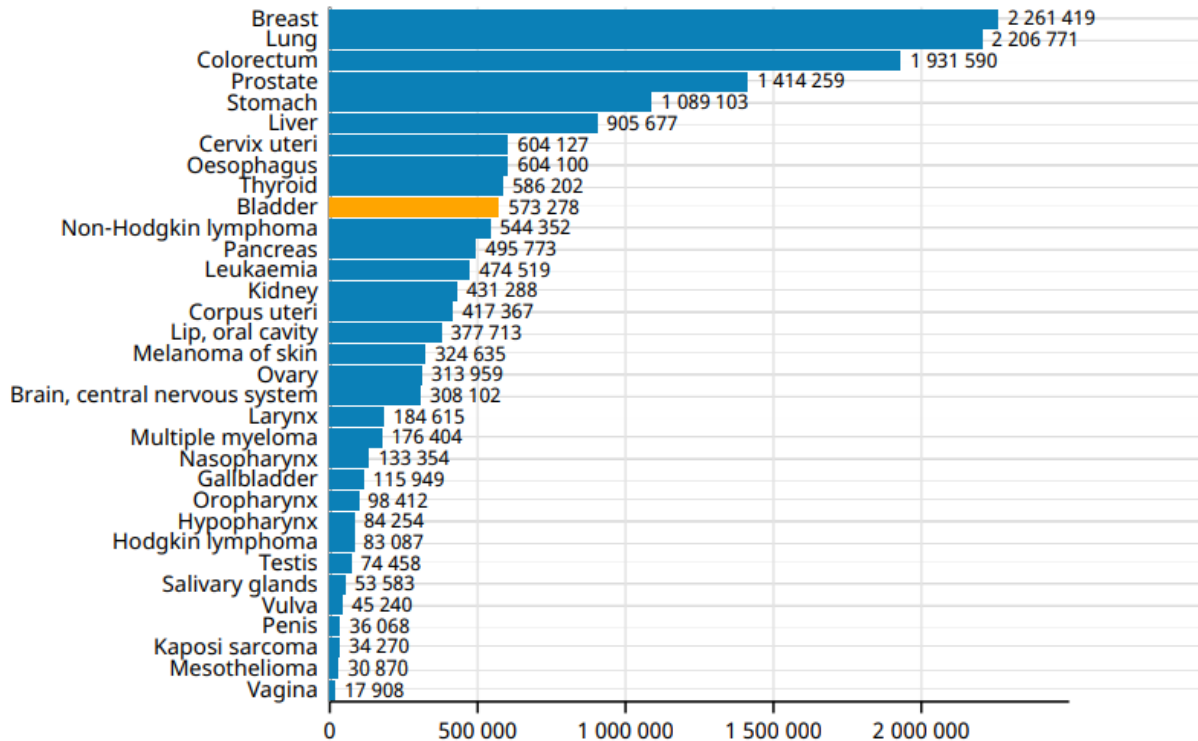


Bladder

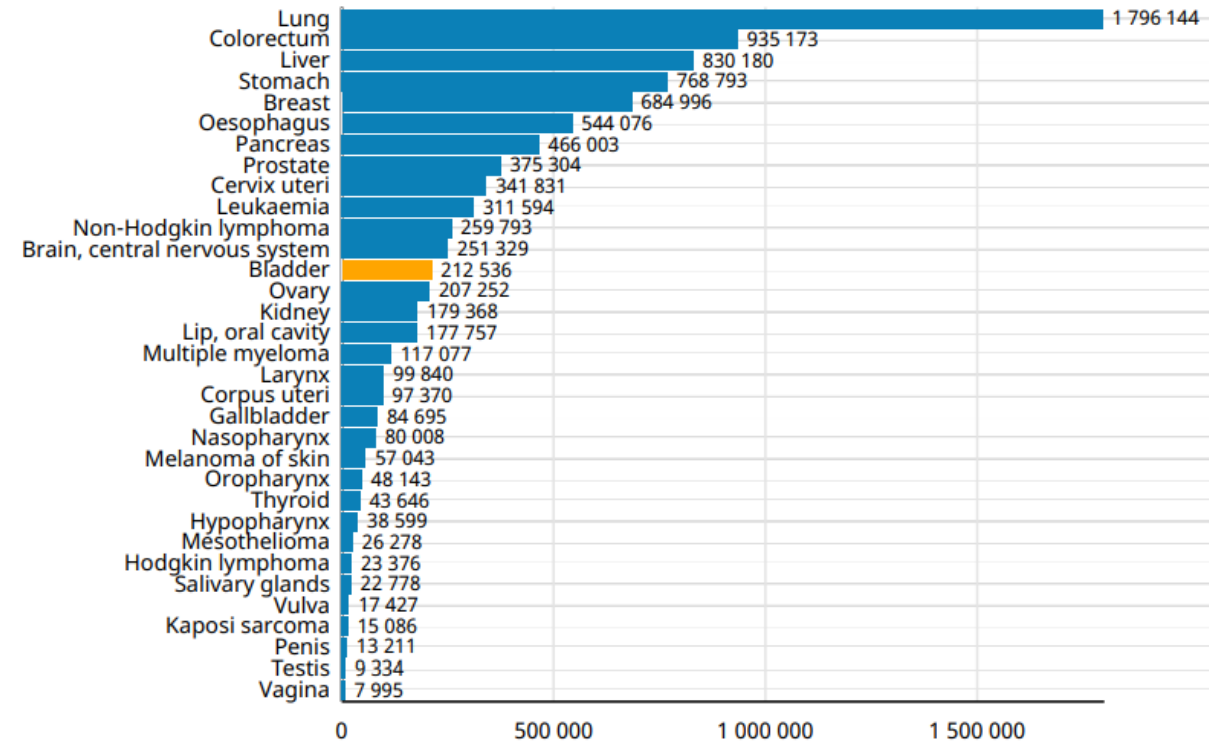
Source: Globocan 2020



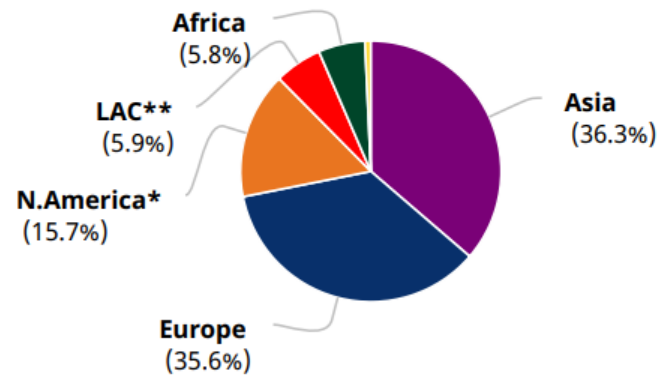
Number of new cases in 2020, both sexes, all ages



Number of deaths in 2020, both sexes, all ages

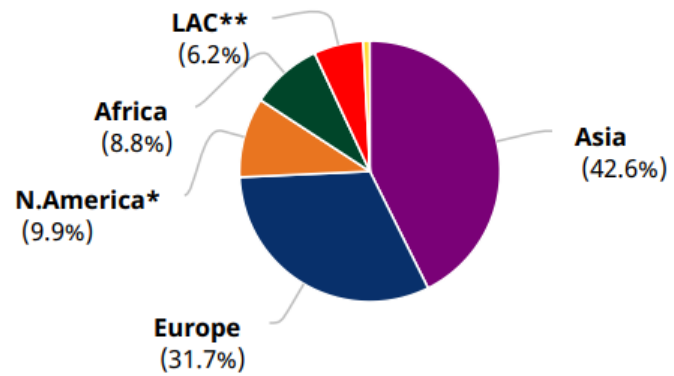


Incidence, both sexes



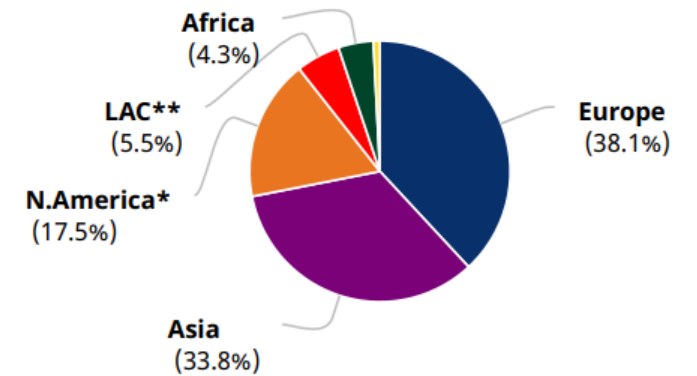
| | Population | Number |
|-----------------------------------|------------|--------|
| Asia | 208 091 | |
| Europe | 203 983 | |
| *Northern America | 89 997 | |
| **Latin America and the Caribbean | 33 840 | |
| Africa | 33 196 | |
| Oceania | 4 171 | |
| Total | 573 278 | |

Mortality, both sexes



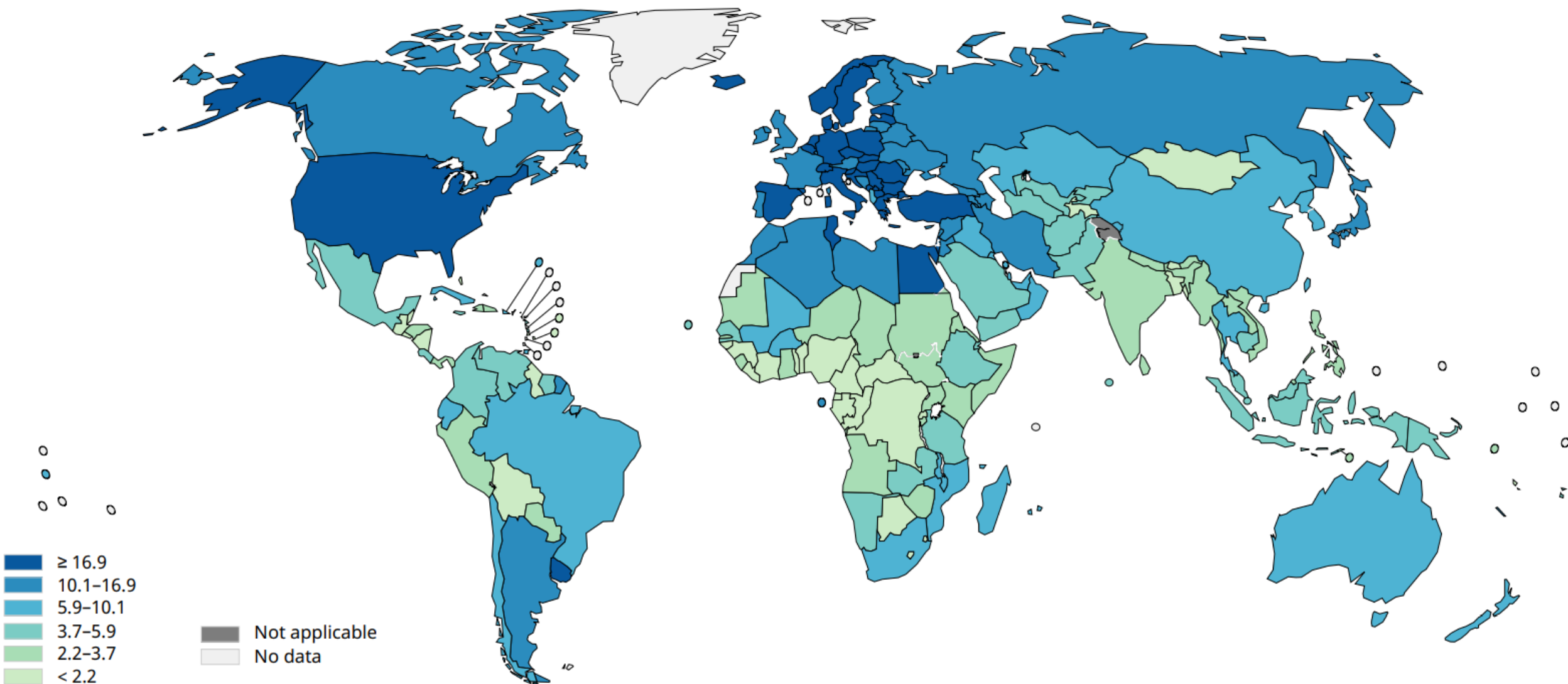
| | Population | Number |
|-----------------------------------|------------|--------|
| Asia | 90 610 | |
| Europe | 67 289 | |
| *Northern America | 21 045 | |
| Africa | 18 747 | |
| **Latin America and the Caribbean | 13 100 | |
| Oceania | 1 745 | |
| Total | 212 536 | |

5-year prevalence, both sexes

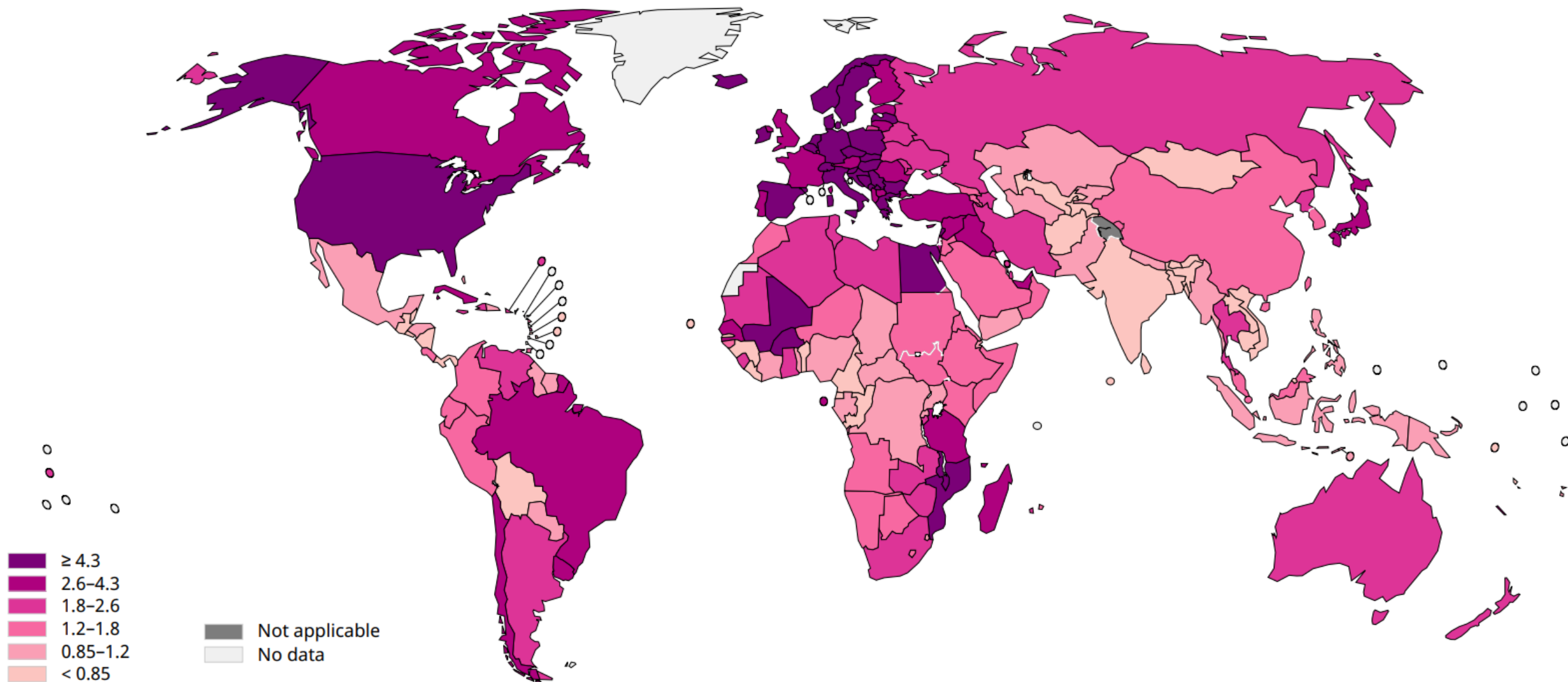


| | Population | Number |
|-----------------------------------|------------|--------|
| Europe | 655 264 | |
| Asia | 582 090 | |
| *Northern America | 300 556 | |
| **Latin America and the Caribbean | 94 169 | |
| Africa | 74 691 | |
| Oceania | 13 855 | |
| Total | 1 720 625 | |

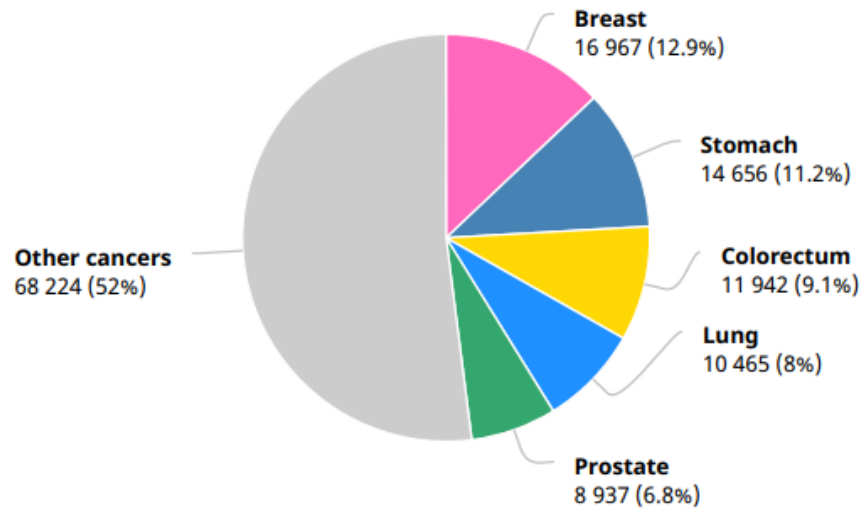
Age standardized (World) incidence rates, bladder, males, all ages



Age standardized (World) incidence rates, bladder, females, all ages

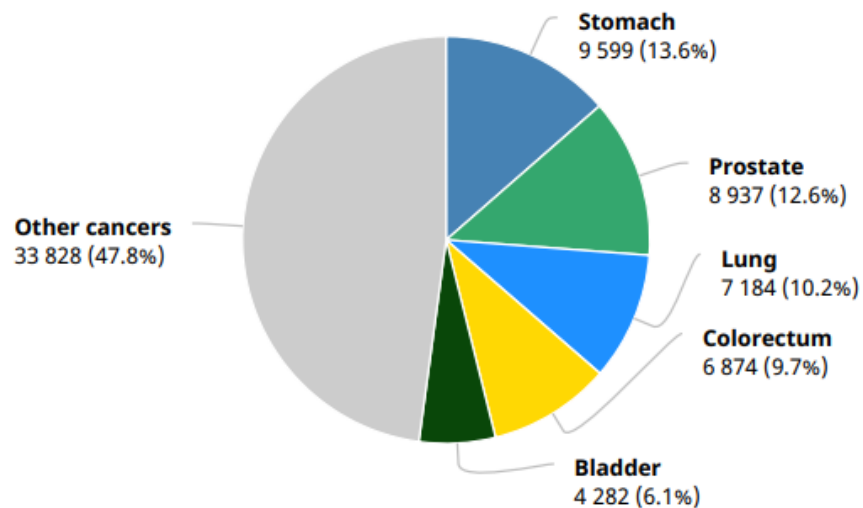


Number of new cases in 2020, both sexes, all ages



Total: 131 191

Number of new cases in 2020, males, all ages



Total: 70 704

Geography



Numbers at a glance

Total population

83 992 953

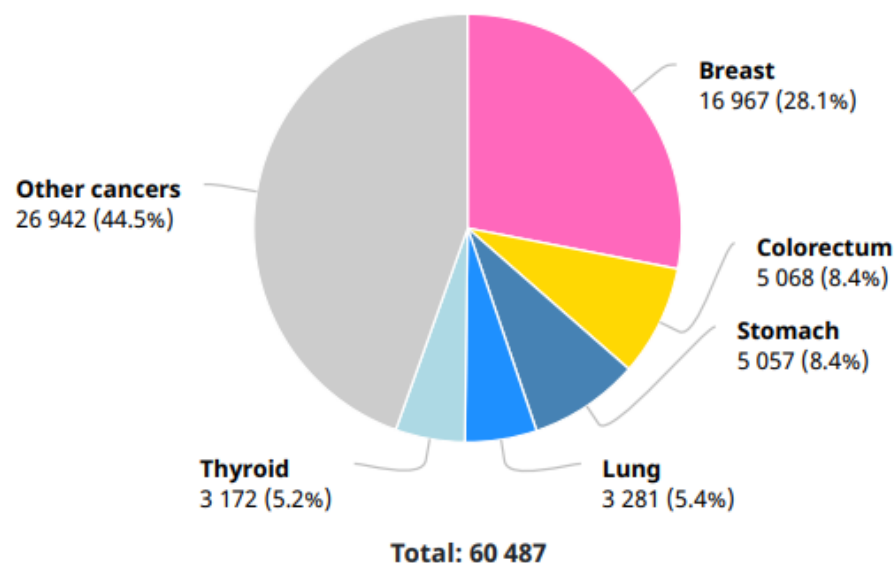
Number of new cases

131 191

Number of deaths

79 136

Number of new cases in 2020, females, all ages



Summary statistic 2020

| | Males | Females | Both sexes |
|--|---|---|---|
| Population | 42 408 406 | 41 584 547 | 83 992 953 |
| Number of new cancer cases | 70 704 | 60 487 | 131 191 |
| Age-standardized incidence rate (World) | 165.0 | 139.0 | 152.7 |
| Risk of developing cancer before the age of 75 years (%) | 16.1 | 13.4 | 14.7 |
| Number of cancer deaths | 46 436 | 32 700 | 79 136 |
| Age-standardized mortality rate (World) | 107.9 | 78.9 | 94.0 |
| Risk of dying from cancer before the age of 75 years (%) | 10.1 | 7.7 | 8.9 |
| 5-year prevalent cases | 161 810 | 157 930 | 319 740 |
| Top 5 most frequent cancers excluding non-melanoma skin cancer (ranked by cases) | Stomach Prostate Lung Colorectum | Breast Colorectum Stomach Lung | Breast Stomach Colorectum Lung |

Number of prevalent cases (5-year)

319 740

Data source and methods

Incidence

Country-specific data source: Local

Method: Weighted/simple average of the most recent local rates applied to 2020 population

Mortality

Country-specific data source: National (WHO)

Method: Most recent rates from one source applied to 2020 population

Prevalence

Computed using sex-; site- and age-specific incidence to 1-;3- and 5-year prevalence ratios from Nordic countries for the period (2006-2015), and scaled using Human Development Index (HDI) ratios.



- Urothelial (previously known as transitional cell [TCC]) carcinoma is the predominant histologic type in the United States and Western Europe, where it accounts for approximately **90 percent** of bladder cancers.
- The surface epithelium (urothelium) that lines the mucosal surfaces of the entire urinary tract is exposed to potential carcinogens that are either excreted in the urine or activated from precursors in the urine by hydrolyzing enzymes. This "**field cancerization**" effect is one hypothesis to explain the **multifocal occurrence**.
- Studies of urothelial bladder cancer have identified multiple risk factors, the most important of which are cigarette smoking and various occupational exposures .



- Smoking tobacco is by far the greatest risk factor for bladder cancer, accounting for approximately **50–65%** of new cases each year. Smoking has been shown to increase the risk of bladder cancer by **three to four times**.
- **The relative risk for bladder cancer mortality due to smoking is second only to lung cancer, which is the number one cause of cancer death in the world.**
- An almost **linear increase** in BCa risk has been observed with **smoking duration**, from approximately a twofold increase after 20 to a more than a fivefold increase after 60 years of exposure .



- Tobacco smoke contains known carcinogens such as beta-naphthylamine and polycyclic aromatic hydrocarbons. These particles promote inflammation, and their metabolism, in the bladder and throughout the body, culminates in DNA-adduct formation and permanent genetic mutation. Such mutations can activate oncogenes or suppress tumor suppressor genes, promoting carcinogenesis.
- Certain inherited genotypes associated with **abnormal detoxification** enzymes have been shown to **increase the susceptibility to cancer** among those who smoke.



The extent of **cigarette smoking** appears to be related to the **aggressiveness** of bladder cancer. Heavy smokers (≥ 30 pack years) were more likely to have a high-grade tumor and to have muscle-invasive disease at their original presentation compared with nonsmokers .

Patients who **continue** to smoke at the time of treatment for bladder cancer also can experience **worsened clinical outcomes**, such as increased risk of recurrent disease, decreased response to chemotherapy, and higher mortality rates .

Among those patients undergoing surgery, smokers have a significantly increased risk of **perioperative complications**. Getting patients to quit smoking may be the most impactful intervention for improving quality and duration of life among patients with bladder cancer.



- There was a small but statistically significant increase in the incidence of bladder cancer among males who smoked a **pipe or cigars** but not cigarettes (HR 1.29).
- Pure tobacco **cigarette smokers** (95% confidence interval (CI) **2.9–4.2**) were at greater risk than pure **pipe smokers** (**1.2–3.1**) or pure tobacco **cigar smokers** (**1.6–3.5**). These latter forms of smoking are also associated with a lesser risk of lung and head and neck cancer, likely because they reach lower temperatures than cigarettes, contain fewer chemicals, and result in not as much inhalation of carcinogenic particles .



- Recently the use of electronic cigarettes is on the rise in most high-income countries.
- The e-liquid commonly includes a propylene glycol/nicotine/flavouring mix. They are perceived as offering the health benefit of not involving tar and harmful combustion by-products. At inception, the regulation of the constituents of e-cigarettes was relaxed and there were concerns regarding the inclusion of known bladder carcinogens such as arsenic in small quantities. However, the e-cigarette components are now more stringent. At present, **there are no RCT or high evidence level studies to show harmful** health effects from e-cigarettes and indeed they are endorsed as a healthier alternative to traditional cigarettes, and are considered a stepping-stone to smoking cessation.

Smoking cessation



- Smoking cessation decreases but does not eliminate the increased risk of bladder cancer .
- The older age of onset of bladder cancer suggests a latency period of approximately 30 years from the initiation of smoking to the cancer diagnosis. However, smoking cessation has been shown to reduce the risk of bladder cancer by approximately **40% within only 1–4 years**, and complete return to **baseline risk by 20 years**, suggesting a non-linear relationship between incidence and pack-years .

- A meta-analysis that included data from 88 studies found that the relative risks of bladder cancer for **all smokers**, **current smokers**, and **former smokers** compared with nonsmokers were **2.62** (95% CI 2.43-2.83), **3.49** (3.13-3.88), and **2.07** (1.84-2.33), respectively . Smoking cessation also appears to decrease the recurrence rate for patients with non-muscle-invasive bladder cancer even after the diagnosis .

Secondhand smoke

- Exposure to secondhand cigarette smoke appears to be a risk factor for the development of bladder cancer .
- Females who **lived with two or more smokers** during childhood had a **threefold** increased risk of bladder cancer compared with those without a childhood exposure to secondhand smoke, while females with a domestic partner who smoked for **10 or more years had a twofold increased** risk compared with those without such exposure.
- A meta-analysis of 14 studies by Yan et al. showed that there was **22% increased risk of bladder cancer** for lifetime secondhand smoking exposure in nonsmoking patients compared with unexposed nonsmoking population



- BC is often considered as three disease entities owing to the difference in oncological natural histories; low grade non-muscle invasive (LG-NMIBC, the most indolent), high grade non-muscle invasive (HG-NMIBC, grade 3 pTis, PTa or pT1 cancers) and muscle invasive BC (MIBC, \geq T2) . Patients will then be started on a treatment pathway depending on the aggressiveness of the pathology found (as determined by histological grade and TNM staging).



- Since the 1970s, **the five-year survival** rate for those diagnosed with bladder cancer has **improved** to approximately 80 percent .
- Many bladder cancer patients do not die of their disease but do experience multiple recurrences. As a consequence, there are a relatively large number of people alive with a history of bladder cancer
- **BC is the most expensive cancer to treat**, with the cost of MIBC approaching \$150,000 per capita .



Thank you for your attention

