CANCER CARE AND ACCESS TO CANCER DRUGS IN ASIA-PACIFIC

The burden of cancer in Asia-Pacific

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THE BURDEN OF CANCER IN ASIA-PACIFIC

Sup-report 1 of the main report "Cancer care and access to cancer drugs in Asia-Pacific"

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Report summary

The burden of cancer is high in Asia-Pacific, accounting for approximately half of the global cancer deaths. Cancer is currently the leading cause of death in most high-income markets. It will increasingly become a major public health issue in middle-income markets based on current trajectories and experiences from other regions of the world.

The number of newly diagnosed cancer cases has increased from 6.6 million to 7.8 million between 2012 and 2018 in Asia-Pacific. A key driver in this development is population aging, which is taking place at an unprecedented rate across the region. While preventive measures (e.g., tobacco control cessation) could address around 30-50% of all new cancer cases, the provision of high-quality cancer treatment is key to reduce the risk of death for cases that cannot be prevented. Evidence from Europe and the United States shows that health investment in screening and treatment helps to improve outcomes of cancer patients.

Outcomes of cancer patients differ greatly across Asia-Pacific. For every 100 patients diagnosed with cancer, around 50-65 of them survive in high-income markets as compared to 30-40 in middle-income markets, based on estimates derived from mortality-to-incidence ratios. Recent developments also indicate that the situation for cancer patients in high-income markets continues to improve, while patient outcomes in middle-income markets are at best stagnating. A closer analysis of five major cancer types – breast cancer, gastro-esophageal cancer, head and neck cancer, liver cancer, lung cancer – confirms these different patterns observed in high-income and middle-income markets.

Predictions of the future cancer burden indicate increases in the number of newly diagnosed cases and deaths by around 50-60% until 2040 across Asia-Pacific. Advances and investments in all areas of cancer care – prevention, screening, diagnosis, treatment – are needed to meet the challenges brought upon by the demographic development. A clear prioritization of effective and comprehensive cancer control efforts could spare millions of people from getting cancer and simultaneously improve the lives of the millions of cancer patients over the coming decades. To this end, the WHO advocates National Cancer Control Programs (NCCP) to tackle cancer in a strategic way.

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1. The burden of cancer

Cancer is the second-leading cause of death globally, with around 1 in 6 deaths being due to cancer (3). In 2018, there were 18.1 million new cancer cases diagnosed, and 9.6 million cancer deaths worldwide (4). Across the 14 markets in Asia-Pacific[1] studied in this report, there were 7.8 million new cancer cases and 4.8 million cancer deaths. The region, which is home to around 47% of the global total population, thus accounted for almost 50% of the global cancer deaths (1, 2); see Figure 1.

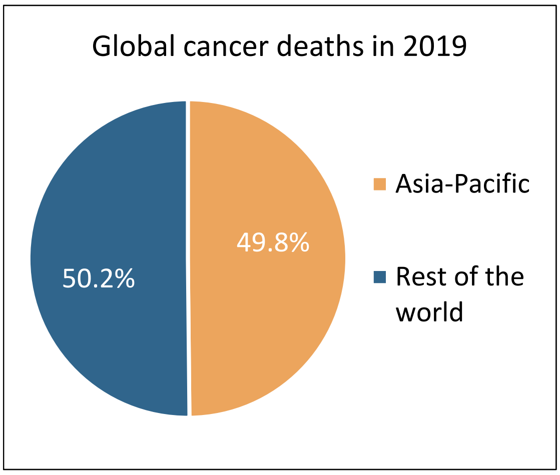

Figure 1: Global distribution of cancer deaths, 2019

Notes: Asia-Pacific consists of the 14 markets considered in this report. All WHO member states and Taiwan are included.
Source: WHO (1) and Taiwan Ministry of Health and Welfare (2).

The global distribution of cancer is uneven. Europe and North America have relatively more new cancer cases in relation to their total population, while Africa has relatively fewer cases. Asia-Pacific falls somewhere in between (4).

The uneven global distribution of cancer points to one of the root causes of cancer: aging. Although cancer can affect people of all ages, the probability of a person to get cancer increases dramatically with age. This is partly because the cellular repair mechanisms become less effective as a person grows older and partly because of an accumulation and exposure to risks[2] over a person's lifetime (3). As people live to older ages and the proportion of elderly increases within a population, naturally the number of cancer incidence would increase. Asia-Pacific has been facing this very scenario of "population aging" in the past decades (5). Since 2000, population aging has been the result of both longer life expectancy (6-year increase in low and lower-middle income countries, 4-year increase in upper-middle and high-income countries) and declining fertility rates (falling from 2.6 to 2.1 per woman of reproductive age). This development is predicted to continue in the coming decades (5), and will exert a substantial upward pressure on cancer numbers (6).

[1] Asia-Pacific consists in this report of 7 high-income markets – Australia, Hong Kong, Japan, New Zealand, Singapore, South Korea, Taiwan – and 7 middle-income markets – China, India, Indonesia, Malaysia, the Philippines, Thailand, Vietnam.
[2] These risks include, for instance, tobacco use, alcohol use, unhealthy diet, physical inactivity, infection with carcinogenic viruses (such as human papillomavirus (HPV) and hepatitis B virus) or with *Helicobacter pylori*, indoor and outdoor air pollution, and ionizing and ultraviolet radiation.

While cancer is a critical public health issue that will become increasingly important to address in Asia Pacific, there is a silver lining. First of all, around 30-50% of all cancer cases are preventable and prevention is key to stem the tide, as emphasized by the World Health Organization (WHO) (3, 7). Second, for all cancer cases that cannot be prevented, the risk of death can be reduced through the provision of high-quality cancer treatment. Evidence from Europe and the United States analyzing the development in recent decades shows that improvements in screening and treatment have helped to improve the prospects of cancer patients (8-11). A clear political commitment, such as the Nixon administration's "War on Cancer" in 1971 in the United States or the Delors Commission's first "Europe Against Cancer" program in 1987 in Europe, was certainly beneficial in this regard (12, 13). Policy makers in Asia-Pacific can learn from these examples and prioritize cancer control efforts to address the challenges ahead. However, a prerequisite for effective cancer control is a good understanding of the magnitude of the burden of cancer.

1.1 Measuring the burden of cancer

Population-level and individual-level measures are needed to characterize the burden of cancer.

- **Population-level measures**: How many new cancer cases and cancer deaths are there in a country?
    - Newly diagnosed cases (**incidence**): The number of new cancer cases diagnosed in a certain year in a specific geographical area; commonly expressed per 100,000 inhabitants ("incidence rate").
    - Deaths (**mortality**): The number of deaths caused by cancer in a certain year in a specific geographical area; commonly expressed per 100,000 inhabitants ("mortality rate").

Incidence rates and mortality rates are presented as "crude rates" in this report, i.e., raw data on incidence and mortality divided by the total local population (per 100,000 inhabitants). Crude rates are needed, because countries differ in population size and also themselves experience changes in population size over time. Crude rates are also a relevant measure for policy makers to look at, as for instance a growing total population per se is not a problem, provided that a growing population entails more income earners and taxpayers who can help finance the health care system.[3]

[3] Age-standardized rates are not considered in this report. In addition to standardizing incidence and mortality numbers by total population size, they take into account different age structures between countries or within the same country over time. This erases the influence of population aging on incidence and mortality statistics. Yet population aging is one of the key challenges in Asia-Pacific, as explained in section 2.

- **Individual-level measures**: Will a patient survive cancer?
    - **5-year survival rate**: The proportion of patients diagnosed with cancer in a certain year that is still alive after five years; commonly expressed in %.
    - **Complement of the mortality-to-incidence ratio** (1–MIR): The number of deaths divided by the number of newly diagnosed cases in a certain year (MIR), with this ratio being subtracted from 1 to make it resemble survival rates; commonly expressed as a raw number.
    - **Disability-adjusted life years** (DALYs) **lost per patient**: One DALY represents one year of healthy life lost (14). DALYs are computed as the sum of two components; Years of Life Lost (YLL) due to premature death caused by a disease and Years of Life Lost to Disability (YLD) due to an impaired health state caused by a disease. In this report, DALYs are standardized by the number of newly diagnosed cancer cases.

The complement of the MIR (1–MIR) is used as a proxy for survival in this report, despite its limitations pointed out in previous literature (15, 16). The ideal measure would be the 5-year survival rate. However, many markets in Asia-Pacific do not have reliable data on this due to the lack of high-quality population-based cancer registries. DALYs lost per patient are used as an additional measure of the cancer burden in this report, as it considers morbidity on top of mortality.

1.2 Aim of the sub-report

The aim of this sub-report is to describe the burden of cancer in Asia-Pacific.

- Section 2 explains the past development of the cancer burden leading up to the current status.
- Section 3 focuses on the past development of five selected cancer types.
- Section 4 provides an outlook of the future development of the cancer burden.

2. The burden of cancer over time

This section describes the burden of cancer in Asia-Pacific with the help of different population-level and individual-level measures. It aims to answer the following questions: What is the size of the cancer burden in relation to other diseases? What is the trend in the cancer burden at the population level? What is the trend in the cancer burden at the individual level?

2.1 Method and data

Different kinds of data sources were combined to obtain relevant information on the burden of cancer. To compare cancer to other diseases, data on the causes of death were obtained. The main source was the "Cause-specific mortality" database maintained by the WHO (1). For Hong Kong and Taiwan, this information was directly obtained from respective local authorities (2, 17).

Information on cancer incidence and cancer mortality was primarily obtained from publicly available national cancer registries or publications that provide estimates on incidence and mortality based on data from regional cancer registries. For countries without such data, estimates from GLOBOCAN (Global Cancer Observatory) – a global database on cancer statistics maintained by the International Agency for Research on Cancer (IARC), part of the WHO – were obtained. Data for the years 2012 and 2018 (or nearest year) were sourced for all 14 markets; see Table A1 in the Appendix for further information and links to sources. Cancer was defined as all malignant cancer sites but non-melanoma skin cancer[4] (ICD-10 C00-C97/C44) wherever possible.

Box 1: Data quality of the national cancer registry in Malaysia

In Malaysia, the national cancer registry publishes reports covering 5-year periods (18). The latest report covers the period 2012-2016 and reported 115,238 incidence cases and 82,601 deaths, up from 103,507 cases and 64,275 deaths, respectively, in the period 2007-2011. The numbers for 2012-2016 correspond to yearly average of 23,048 new cases and 16,520 deaths. In comparison to these yearly averages, GLOBOCAN estimates that there were 43,372 new cases (88% difference) and 26,207 deaths (59% difference) in 2018, based on its own methodology to derive cancer statistics in countries with low-quality data (19). This echoes cautions by the Breast Cancer Welfare Association Malaysia of grave underreporting of cancer cases in Malaysia (20).

The foundation for analyses of trends in the cancer burden are solid data from population-based nationwide cancer registries. Most middle-income markets either lack such cancer registries or have national/regional registries of poor quality; see Box 1. Therefore, results from the analysis of both the size of the cancer burden and trends over time should

[4] Non-melanoma skin cancer is commonly excluded from incidence data (and sometimes also from mortality data), as its registration is often incomplete and inaccurate, as it is usually non-fatal and treated in primary care.

be taken as directional and considered with caution across middle-income markets. Some high-income markets also either publish annual key statistics on cancer with rather long delays (more than 2 years in Australia, New Zealand, and South Korea) or fail to publish comprehensive key statistics (incidence, prevalence, mortality, survival) in annual reports (e.g., South Korea does not include information on mortality). Singapore publishes no annual reports and only covers five-year periods – the latest report covering 2013–2017; see also Box 2.

Box 2: GLOBOCAN data, WHO data, and national cancer registry data in Singapore

In Singapore, the national cancer registry reported 71,265 new cases and 27,730 deaths during 2013-2017 (21), corresponding to yearly averages of 14,253 new cases and 5,546 deaths. The Ministry of Health reported around 29,400 cancer deaths (6% difference) during 2013-2017 (22). GLOBOCAN estimates that there were 25,770 new cases (81% difference) and 13,066 deaths (136% difference) in 2018 (19). GLOBOCAN data seem to seriously overestimate the number of new cases and of deaths. The WHO Global Health Estimates report 7,898 cancer deaths in 2019 compared to 26,834 total deaths (1), which are both higher numbers than reported by the Ministry of Health, but the proportion of cancer deaths is very similar.

Information on disability-adjusted life years (DALY) caused by cancer (defined as malignant neoplasms) were obtained from the WHO (23), and combined with information on newly diagnosed cancer cases from the sources indicated above.

2.2 Results

The burden of cancer in relation to other diseases

Cancer is one of the leading causes of death in Asia-Pacific. During the past two decades, the number of cancer deaths has increased from 3.2 million in 2000 to 4.7 million in 2019.[5] In 2000, cancer was already the leading cause of death in three high-income markets (Hong Kong, Japan, Taiwan) and one middle-income market (Thailand); see Figure 2. In 2019, cancer had become the leading cause of death (accounting for 29-31% of all deaths) in all high-income markets except in Singapore where cardiovascular diseases are still narrowly leading. Across all middle-income markets, the proportion of deaths attributed to cancer has also expanded between 2000 and 2019; it ranged from 9% of deaths in the Philippines to 25% of deaths in China in 2019.

The development in Asia-Pacific parallels the development in Europe in recent decades. While cancer is still the second-leading cause of death behind cardiovascular disease across the continent, in some countries (Denmark, France, Netherlands, and the UK) cancer is already the major killer

[5] Estimated numbers of cancer deaths differ from source to source. As noted in section 1, there were 4.8 million deaths in 2018 based on data from national cancer registries and GLOBOCAN, whereas the estimate of 4.7 million deaths in 2019 here is based on data from the WHO and the local authorities in Taiwan.

(24). With the shifting demographics and changing lifestyles, there is an urgent need to address growing demands in health care to maintain the well-being of the population.

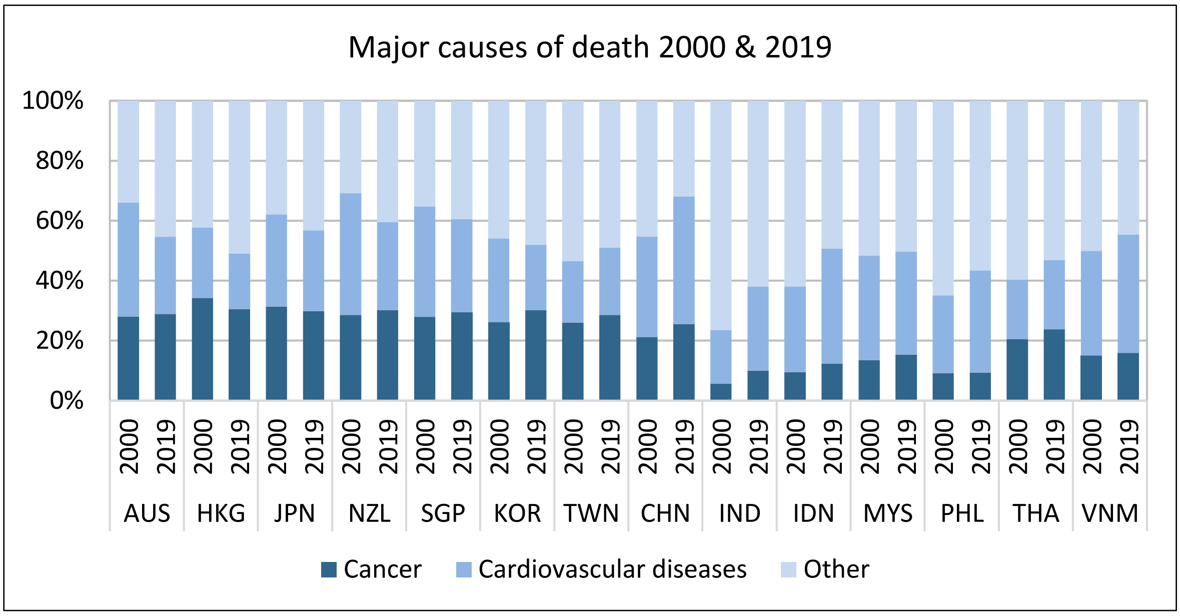

Figure 2: Major causes of death, 2000 and 2019

Notes: Cancer is defined as malignant neoplasms in all markets. Cardiovascular diseases (ICD-10: I00-I99) are somewhat underestimated in HKG (only include ICD-10: I00-I09, I11, I13, I20-I51, I60-I69) and in TWN (only include ICD-10: I01-I02.0, I05-I09, I10-I15, I20-I25, I27, I30-I52, I60-I69, I71). Numbers in 2000 in HKG and TWN refer to 2001 due to lack of data.
Source: WHO (1), except for HKG (17) and TWN (2).

The burden of cancer at the population level

The number of newly diagnosed cancer cases has increased from 6.6 million to 7.8 million between 2012 and 2018 in Asia-Pacific. To take into account the influence of overall population growth in this period, Figure 3 shows incidence rates of cancer per 100,000 inhabitants for all 14 markets. There are two key observations to be made. First, incidence rates differ largely in magnitude between markets, ranging from below 100 new cases per 100,000 inhabitants in India and Malaysia to over 800 new cases per 100,000 inhabitants in Japan in 2018. In comparison, the crude incidence rate in Europe was just below 600 in 2018 (24). The differences in magnitude are largely explained by differences in the age-specific composition of the population in the different markets. The incidence of cancer rises dramatically with age (3), meaning that a population consisting of a larger proportion of older people will record more cancer cases. In fact, Figure 4 shows that the proportion of people aged 65 years or above ranged from around 6-7% in India, Indonesia, Malaysia, and the Philippines to 28% in Japan in 2020. This four-fold difference should be kept in mind when seeing the eight-fold difference in incidence rates between Japan and middle-income markets in Figure 3.

The second key observation from Figure 3 is that the number of newly diagnosed cancer cases has been increasing between 2012 and 2018 in all markets, despite the limited time period. Increases were minimal in South Korea, New Zealand, and Australia during this period, yet a look further back in time in the respective national cancer registries reveals large increases (e.g., 110% increase in the crude rate between 2000 and 2017 in South Korea) (25-27). This is also similar to the situation in some of the Nordic countries in Europe which have experienced shorter periods of stagnating cancer incidence rates, whereas long-term trends are unambiguously going up (28).

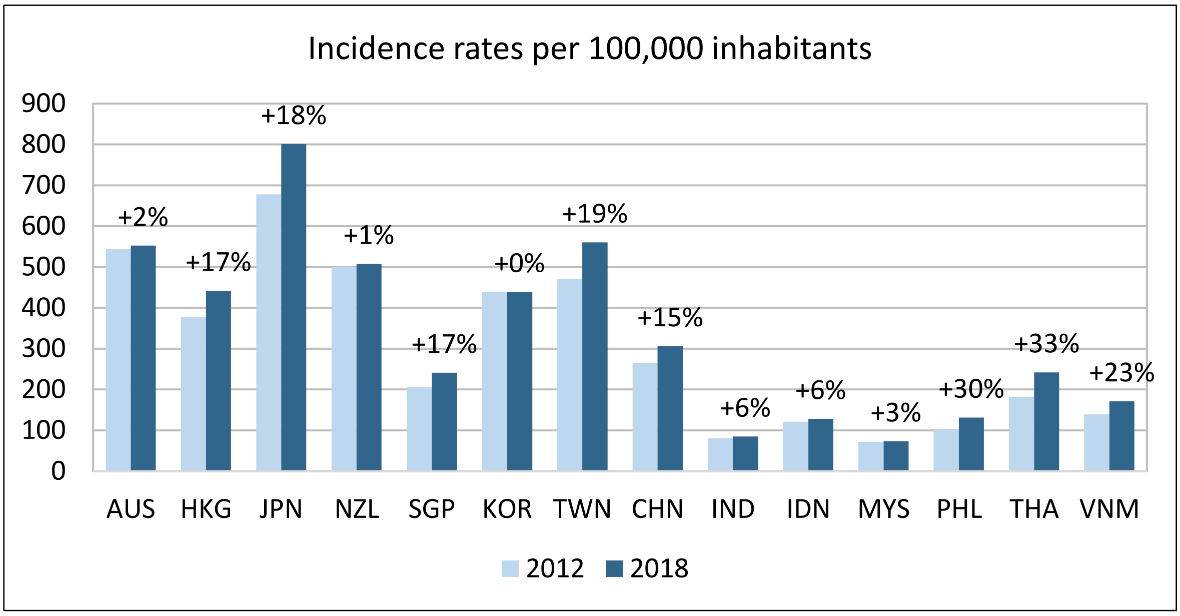

Figure 3: Cancer incidence per 100,000 inhabitants (crude rates), 2012 and 2018

Source: National cancer registries and GLOBOCAN; see Table A1 in the Appendix.

In general, increases in cancer incidence in Asia over time have been documented before (29). Major factors explaining increasing cancer incidence rates are as follow:

- **Population aging**: As the risk of getting cancer increases with age, an aging population contributes to an increasing number of cancer cases. Figure 4 shows the age structure of all 14 markets in 2000 and 2020. The proportion of people aged 65 years or above has been increasing considerably in all markets. In several markets the proportion more than doubled.
- **Risk factors**: Several lifestyle factors are linked to cancer (7).[6] The WHO estimates that around 30-50% of all newly diagnosed cancer cases relate to these factors and are therefore

[6] The latest World Cancer Report of the WHO lists tobacco consumption, infectious agents (e.g., *Helicobacter pylori*, human papillomaviruses, hepatitis B and C viruses), alcohol consumption, sunlight and ultraviolet radiation, ionizing radiation (from both natural sources and artificial sources such exposure to medical radiation), diet and nutrition (high intake of processed meat and red meat and low intake of fruits and

assumed to be preventable (3). Not all risk factors are equally carcinogenic. Smoking is the most important risk factor globally (7). In fact, recent studies for Sweden, the UK, and the US show that cigarette smoking is responsible for almost half of all preventable cancer cases (30-32). Recent studies for East Asia also point to smoking as major public health problem (33). Changing smoking behaviors and changing patterns in all other risk factors (e.g., obesity, HPV infection rates) over time will eventually affect cancer incidence rates. However, several decades may pass between the exposure to a carcinogen and the diagnosis of cancer (called latency period) (34).

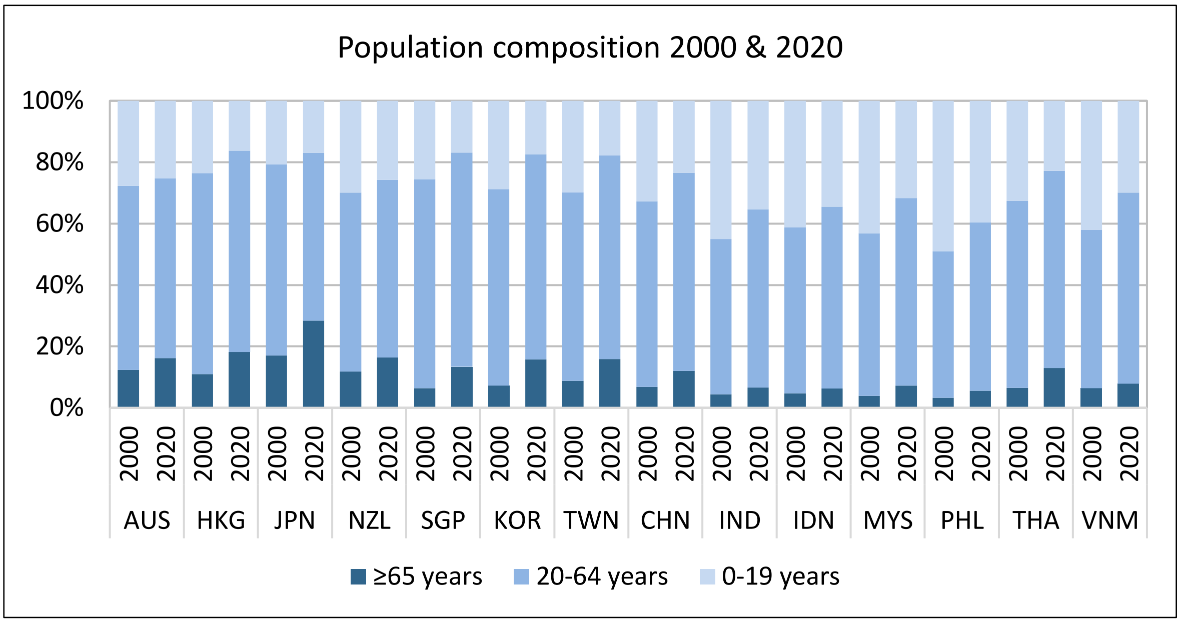

Figure 4: Population composition by age group, 2000 and 2020

Notes: Numbers for 2020 are based on the "medium fertility variant". Source: United Nations (35).

- **Screening**: Established screening methods are available for some cancer types; breast cancer, cervical cancer, colorectal cancer, lung cancer, prostate cancer. In high-income markets in Asia, population-based screening programs for breast cancer exist and opportunistic screening is also done in middle-income markets (36). Similarly, opportunistic prostate cancer screening is common in some markets (37). Lung cancer screening for people who are or have been heavy smokers is comparatively new and has been trialed mostly in China, Japan, and South Korea (38). Even though screening is vital for early detection of

vegetables), physical inactivity, obesity, dietary carcinogens (e.g., aflatoxin and aristolochic acid), contamination of air (airborne particulate matter originating from, e.g., fuel combustion for transportation or and domestic heating and cooking.), water, soil, and food (e.g., through arsenic), occupational carcinogens (e.g., asbestos, polycyclic aromatic hydrocarbons, heavy metals), pharmaceutical drugs (e.g., hormonal contraceptives) (7).

cancer, some screening methods – mammography for breast cancer and PSA testing for prostate cancer – also lead to the detection of a considerable proportion of cases of latent disease that never would have become symptomatic, i.e., overdiagnosis (39, 40). The implementation of such screening programs or greater participation and use of screening in general inflates cancer incidence rates over time.

- **Competing risks of death**: The risk of getting cancer is influenced by the epidemiological development in other diseases. More people are nowadays surviving previously fatal diseases (e.g., myocardial infarction) as a result of improvements in health care and medicine. This is especially true for many cardiovascular diseases; see the declining share of cardiovascular diseases in Figure 2 in most high-income markets. As more people reach an advanced age, this leaves more people at risk of getting cancer (41).

The number of cancer deaths has increased from 3.8 million to 4.8 million between 2012 and 2018 in Asia-Pacific. Figure 5 shows mortality rates of cancer per 100,000 inhabitants for all 14 markets. These numbers should not be interpreted in isolation but rather interpreted together with the numbers for incidence rates in Figure 3. There are two observations to be made. First, mortality rates differ largely in magnitude between markets, ranging from around 50 deaths per 100,000 inhabitants in India and Malaysia to 300 deaths per 100,000 inhabitants in Japan in 2018. In comparison, the crude mortality rate in Europe was 275 in 2018 (24). A high mortality rate of a market does not necessarily indicate something about that country's effectiveness of cancer care. As Japan had by far the highest incidence rate in 2018, it is not surprising to find that it also had the highest mortality rate, and vice versa for India and Malaysia.

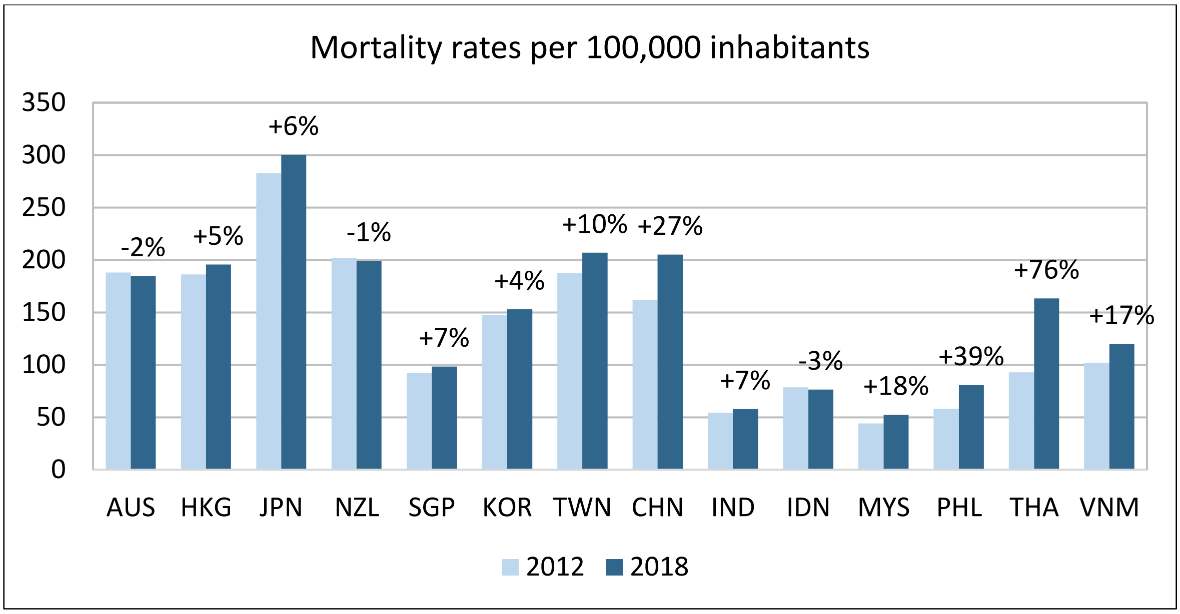

Figure 5: Cancer mortality per 100,000 inhabitants (crude rates), 2012 and 2018

Source: National cancer registries and GLOBOCAN; see Table A1 in the Appendix.

The second observation from Figure 5 is that the number of cancer deaths has been increasing between 2012 and 2018 in most markets. This mirrors the observed development for incidence rates, as more new cancer cases imply, ceteris paribus, more deaths. Trends in explaining incidence (population aging, risk factors, screening programs, epidemiological development in other diseases) are thus also relevant for explaining trends in mortality. In addition, trends in the quality of cancer care (diagnostics and treatment) influence trends in mortality. Australia and New Zealand managed to achieve small reductions in mortality rates between 2012 and 2018.[7] Such small reductions have also been observed in several countries in Europe between 1995 and 2018 (24). Trends in middle-income markets, such as the small reduction in Indonesia and the massive increase in Thailand, should be interpreted with caution, as changes to GLOBOCAN's methodology and data inputs to estimate cancer cases might heavily affect the results (42, 43). Yet, despite the data limitations, the trajectories in middle-income markets are undoubtedly increasing; see also section 4.

[7] South Korea is an example where mortality rates increased slightly despite a stagnation in incidence rates. Such patterns are rather unusual and do not necessarily indicate that the quality of cancer treatment has become worse. An explanation could be shifting proportions in cancer types with different survival profiles, such as an increase in the incidence of pancreatic cancer and an equally large decrease in the incidence of breast cancer.

The burden of cancer at the individual level

The cancer burden at the population level is also a reflection of the burden at the individual level. Success in the fight against cancer is often judged by looking at survival rates, which indicate the proportion of diagnosed patients that are still alive after a certain period of time (typically after 5 years as an indication of being "cured"). In the absence of comparable data on survival rates across all 14 markets in Asia-Pacific, the complement of the mortality-to-incidence ratio (1–MIR) is considered as a proxy. A higher 1–MIR implies a higher survival rate.

Figure 6 shows the 1–MIR for all 14 markets in 2012 and in 2018. Both levels and trends in the 1–MIR are noteworthy. All high-income markets achieve much higher 1–MIRs than the middle-income markets. For every 100 patients diagnosed with cancer, around 50-65 of them would survive in high-income markets as compared to 30-40 in middle-income markets. In China, India, Malaysia, Thailand, and Vietnam around twice as many newly diagnosed patients die from cancer as in Australia and South Korea. These vast differences can also be observed for actual 5-year survival rates shown in Figure A1 in the Appendix for a selected number of cancer types and markets with available data in the CONCORD-3 study (44). This study concluded that patients in the USA and Canada in the Americas, in Australia and New Zealand in Oceania, and in Finland, Iceland, Norway, and Sweden in Europe tended to have the highest survival for most cancers around the world in patients diagnosed in 2010 to 2014.

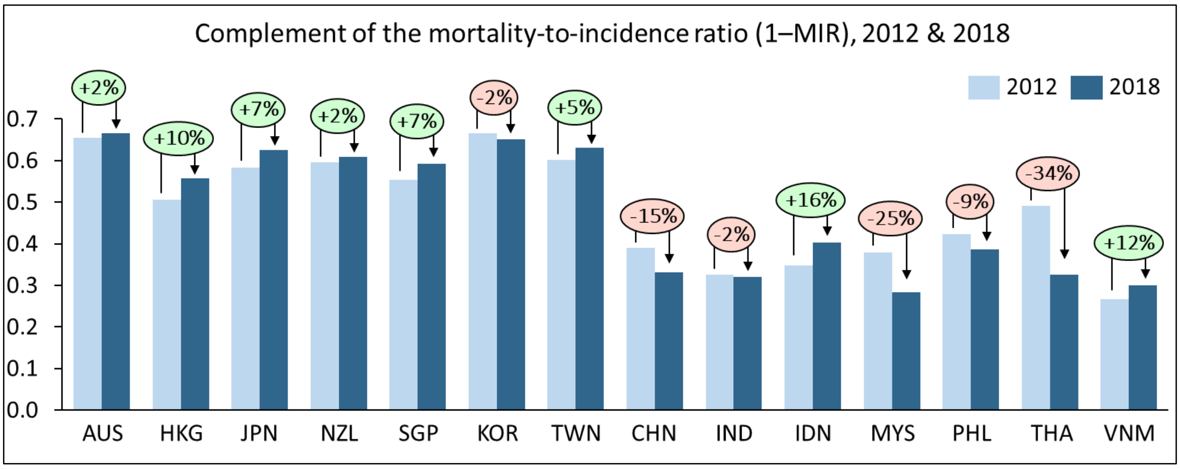

Figure 6: Complement of the mortality-to-incidence ratio of cancer, 2012 and 2018

Notes: Numbers in ellipses show relative changes. Differences in the frequency of common cancer types with differing survival rates impede market comparisons.
Source: National cancer registries and GLOBOCAN; see Table A1 in the Appendix.

Trends in the 1–MIR between 2012 and 2018 in Figure 6 suggest improvements in cancer treatment in most high-income markets. This resembles the development in Europe where the 1–MIR increased slightly by 2% in relative terms during the same period (24). Trends in middle-income markets[8] need to be interpreted with caution in the absence of data from nationwide population-based cancer registries. Nonetheless, the decrease in the 1–MIR in middle-income markets foreshadows difficulties in maintaining even modest quality levels in cancer treatment in the face of the increasing patient numbers shown in Figure 3. Comprehensive cancer control plans and actions are required to halt this negative development.

Another measure to gauge the burden of cancer at the individual level is DALYs lost per patient. Figure 7 shows results for this measure and both levels and trends are again noteworthy. In all high-income markets fewer DALYs are lost per patient than in the middle-income markets. This is in line with the findings from the 1–MIR-analysis, where middle-income markets have lower 1–MIR. However, a lower burden in terms of DALYs per patient can be the result of both longer survival and higher quality-of-life. Trends over time indicate a stagnating cancer burden in most high-income markets, whereas the picture is more mixed in middle-income markets.

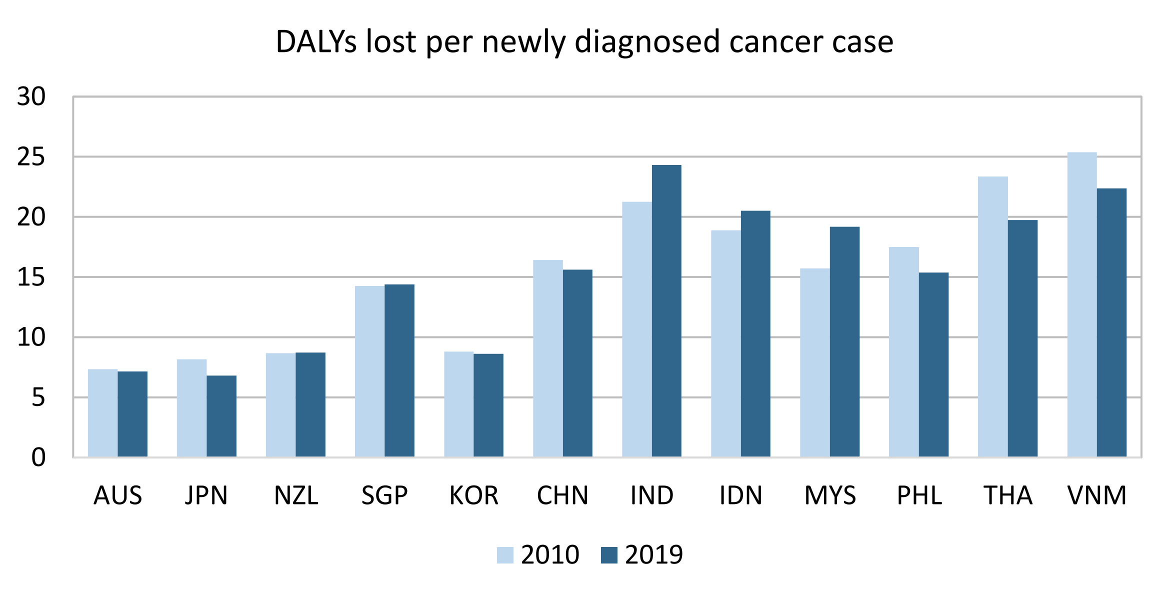

Figure 7: DALYs of cancer lost per newly diagnosed cancer case, 2010 and 2019

Notes: No comparable data for DALYs are available for HKG and TWN. In SGP, DALYs might be overestimated and cancer incidence underestimated (see Box 2), resulting in a too high estimate in this figure. Estimates of cancer incidence from 2012 and 2018 (see Table A1 in the Appendix) were used to standardize total DALYs in 2010 and 2019, respectively. Source: WHO for DALYs (23), and national cancer registries and GLOBOCAN for incidence; see Table A1 in the Appendix.

[8] In China, the latest national estimates based on data from regional registries indicate that the 1–MIR has remained unchanged at 0.39 between 2012 (45) and 2015 (46). This might indicate that the GLOBOCAN estimate of 0.33 for 2018, and hence the 15% relative decrease in Figure 6, is overestimated.

3. The burden of selected cancer types

Cancer is the collective name of a group of over 100 diseases that are characterized by uncontrolled growth and division of cells. This section describes the burden of five major cancer types – breast cancer, gastro-esophageal cancer, head and neck cancer, liver cancer, lung cancer – in Asia-Pacific with the help of different population-level and individual-level measures. It aims to answer the following questions: What is the extent of the disease burden from these cancer types in relation to other cancer types? What is the trend in the burden of these cancer types at the individual level?

3.1 Method and data

Five major cancer types that are responsible for around half of all cancer cases across Asia-Pacific were selected for a deeper analysis in this and subsequent sub-reports. These are breast cancer (ICD-10 C50), gastro-esophageal cancer (C15-C16), head and neck cancer (C00-C14, C30-C32)[9], liver cancer (C22), and lung cancer (C33-34). Information on cancer incidence and cancer mortality was obtained from national cancer registries and GLOBOCAN as described in section 2.1; see also Table A1 in the Appendix for further information and links to sources.

3.2 Results

Cancers are commonly classified based on their primary site, i.e., based on the organ where the first tumor forms. Some cancer types are much more common than others, and the proportion of different cancer types may vary both across countries and within a country over time. Figure 8 shows the proportions of five major cancer types across the 14 markets for both incidence and mortality in 2018. Even though a diverse pattern is discernable, there are some similarities. Lung cancer and breast cancer each account for 6-18% of incidence, while lung cancer is responsible for around 20% of deaths in most markets. The five cancer types are jointly responsible for two thirds of deaths in China and Vietnam, but only about one third of deaths in Australia and New Zealand.

There are several noticeable patterns in Figure 8 that previous studies have related to differences in risk factors between markets.

[9] Some national cancer registries and GLOBOCAN do not report small sub-types of head and neck cancer. In Japan, C30-31 is missing; in New Zealand C30-32; in GLOBOCAN C14 and C30-31.

- Liver cancer is particularly common (more than 5% of total incidence and mortality) in China, Hong Kong, the Philippines, South Korea, Taiwan, Thailand, and Vietnam and has been linked to high infection rates with hepatitis B virus and hepatitis C virus (47, 48).
- Gastric cancer is particularly common in China, Hong Kong, India, Japan, Malaysia, South Korea, Singapore, Taiwan, Thailand, Vietnam and has been linked to high prevalence of *Helicobacter pylori* infection, higher consumption of salt and salt-preserved foods, as well as smoking (in men) (49, 50).
- Esophageal cancer is particularly common in China and almost half of all newly diagnosed cases globally occur there, but conclusive evidence on risk factors (such as indoor air pollution, exposure to polycyclic aromatic hydrocarbons) has not been reached yet (51-53).
- Head and neck cancer is particularly common in India. Head and neck cancer is generally associated with tobacco consumption, alcohol consumption, and human papillomavirus infection (54, 55), but the high rates in India have been linked to chewing of the "betel quid" containing the carcinogenic areca nut (56, 57).

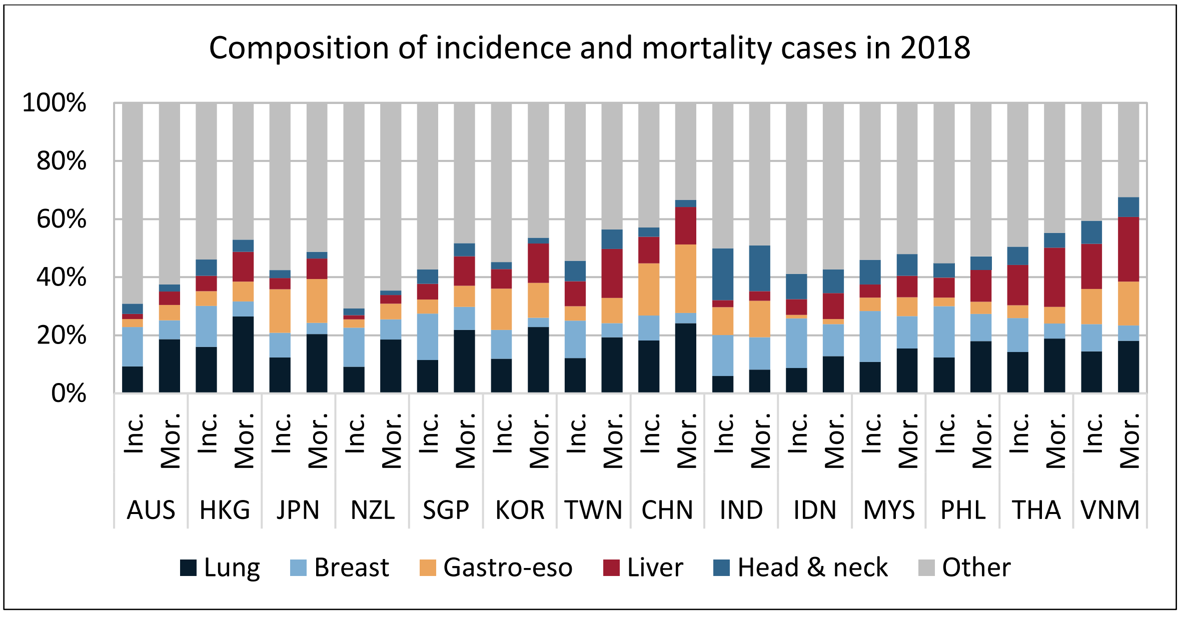

Figure 8: Proportion of selected cancer types in cancer incidence and mortality, 2018

Notes: Inc. = Incidence, Mor. = Mortality, Lung = NSCLC, Breast = breast cancer, Gastro-eso = gastro-esophageal cancer, Liver = liver cancer, Head & neck = head and neck cancer, Other = all remaining malignant cancer types.
Source: National cancer registries and GLOBOCAN; see Table A1 in the Appendix.

The burden of the five cancer types at the individual level differs considerably. Figure 9 shows the 1–MIR for the five types in all 14 markets. Breast cancer has the highest 1–MIR (indicating highest survival; see also Figure A1 in the Appendix) in all markets, whereas liver cancer has the lowest 1–

MIR in almost all markets closely followed by lung cancer and gastro-esophageal cancer.[10] The 1–MIRs for all cancer types are higher in high-income markets than in middle-income markets, indicating better cancer treatment in high-income markets in line with the results in section 2.2. A noticeable outlier among the high-income markets is gastro-esophageal cancer, with Japan and South Korea recording much higher 1–MIRs. This has been attributed to specific clinical factors, particularly earlier stage at diagnosis (58, 59).

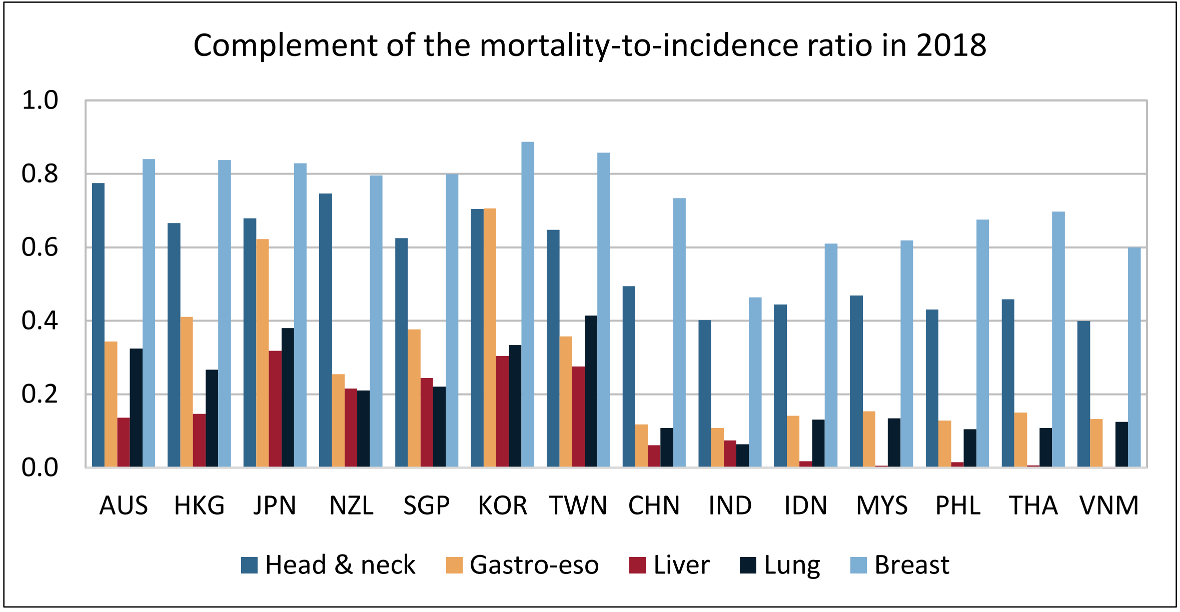

Figure 9: Complement of the mortality-to-incidence ratio of selected cancer types, 2018

Notes: Lung = NSCLC, Breast = breast cancer, Gastro-eso = gastro-esophageal cancer, Liver = liver cancer, Head & neck = head and neck cancer.
Source: National cancer registries and GLOBOCAN; see Table A1 in the Appendix.

Developments in the 1–MIR for the five cancer types between 2012 and 2018 are shown in Figure 10 (high-income markets) and Figure 11 (middle-income markets). Lung cancer and breast cancer experienced improvements (i.e., increase in the 1–MIR) in nearly all high-income markets, whereas 1–MIRs stagnated in Japan and New Zealand during this period; see Figure 10. Improved breast cancer screening leading to early detection and better treatment have been suggested as reasons behind the recent improvement in these markets (36). For lung cancer, screening was not available during this period but several drug treatments targeting a common genomic alteration (EGFR) in Asian lung cancer patients were introduced during this period (60); see sub-report 3. By contrast, the magnitudes of improvements made in liver cancer and head and neck cancer were smaller (especially

[10] The 1–MIR and the 5-year survival rate match quite closely for most cancer types. For example, Australia recorded 5-year survivals of 91% in breast cancer, 31% in gastric cancer, 22% in esophageal cancer, 71% in head and neck cancer, 20% in liver cancer, and 19% in lung cancer in the period 2012-2016 (25).

if compared the low baseline 1–MIR), which might be explained by a lack of clinical advancement with more effective treatment modalities (61-63).

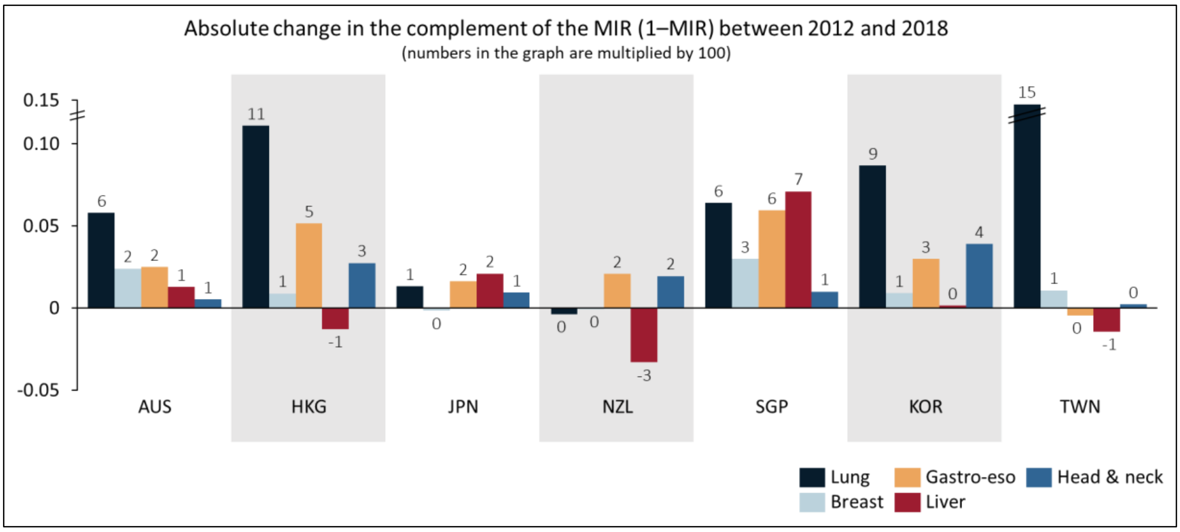

Figure 10: Absolute change in the complement of the mortality-to-incidence ratio between 2012 and 2018 in high-income markets

Notes: Lung = NSCLC, Breast = breast cancer, Gastro-eso = gastro-esophageal cancer, Liver = liver cancer, Head & neck = head and neck cancer. Numbers next to bars are multiplied by 100.
Source: National cancer registries and GLOBOCAN; see Table A1 in the Appendix.

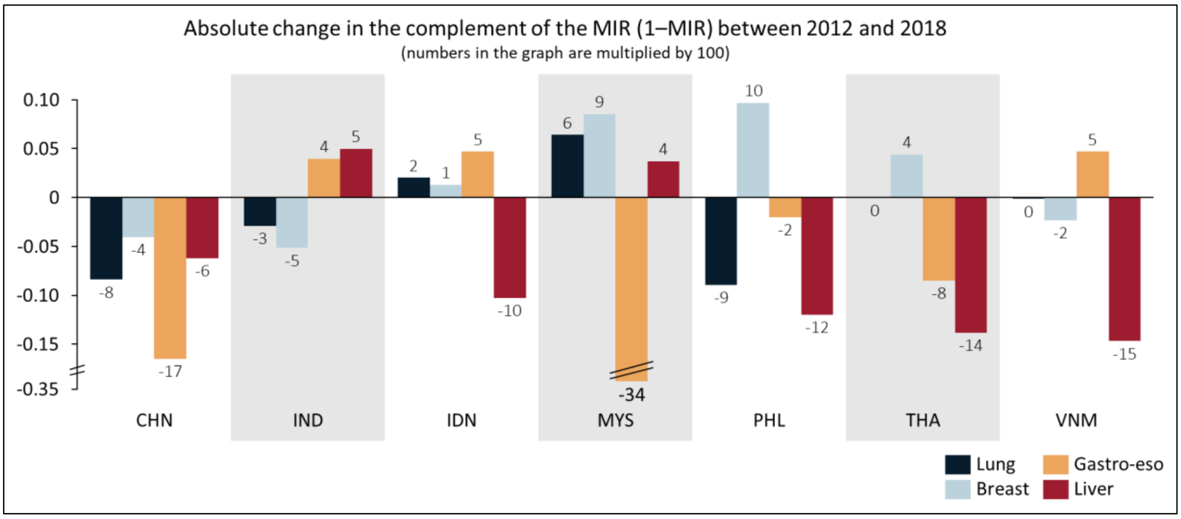

Figure 11: Absolute change in the complement of the mortality-to-incidence ratio between 2012 and 2018 in middle-income markets

Notes: Lung = NSCLC, Breast = breast cancer, Gastro-eso = gastro-esophageal cancer, Liver = liver cancer, Head & neck = head and neck cancer. No data available for head and neck cancer in any market in 2012. Numbers next to bars are multiplied by 100.
Source: National cancer registries and GLOBOCAN; see Table A1 in the Appendix.

As mentioned in section 2.2, trends in the 1–MIR in middle-income markets need to be interpreted with caution in the absence of data from nationwide population-based cancer registries. Recent developments in the 1–MIR, shown in Figure 11, suggest limited improvements across the considered cancer types. The only notable exception is breast cancer in Malaysia, the Philippines, and Thailand which showed significant improvements. This might be explained by increased awareness among women, decreased belief in ineffective traditional and alternative therapies, as well as improved treatment options (e.g., trastuzumab became available to patients in these markets during this period; see sub-report 3), although robust studies on this are lacking (36).

4. Future development of the cancer burden

This section provides an outlook of the future development of the cancer burden in Asia-Pacific. It aims to answer the following question: What might be the size of the cancer burden in 2040?

4.1 Method and data

Predictions of the future cancer burden are naturally uncertain. GLOBOCAN provides a tool to gauge the future development until 2040 in terms cancer incidence and cancer mortality (6). It uses two inputs in its predictions. First, national age-specific cancer incidence/mortality rates for the base year (here 2020) are calculated. It is assumed that these rates do not change in the prediction period until 2040. Thus, changes in risk factors associated with cancer such as smoking habits, obesity levels, etc. are not incorporated. Second, data from the United Nations on predicted changes in total population size and age structure until 2040 are used.[11] The expected number of new cancer cases or deaths in a country are computed by multiplying the age-specific incidence/mortality rates with the corresponding expected population sizes of different age groups in 2040. The predictions thus capture only the effect of the expected demographic development.

To better understand the underlying demographic development until 2040, data from the United Nations were also obtained (35).

4.2 Results

The expected demographic development in the 14 markets between 2020 and 2040 is depicted in Table 1 and Figure 12. In most high-income and middle-income markets, the total population is expected to grow by around 10-20%, while population numbers are expected to stagnate in South Korea, Taiwan, China, and Thailand and to decrease by 10% in Japan; see Table 1. A growing/declining population will accelerate/slow down the growth in the cancer burden. However, the changing composition of all populations in Asia-Pacific is much more important for the future development of the cancer burden. Figure 12 shows that the share of elderly people aged 65 years and above will increase in all markets. In China, Indonesia, Singapore, South Korea, Thailand, and Vietnam population aging will proceed at a noticeably rapid pace, with the proportion of elderly people expected to double within the course of the next 20 years. In Hong Kong, Japan, and South

[11] These numbers are based on the "medium fertility variant".

Korea around one third of the population will be aged 65 years and above in 2040. This means that a considerable proportion of the population is of an age when the risk to get cancer is very high.

Table 1: Forecasted change in total population size between 2020 and 2040

	AUS	HKG	JPN	NZL	SGP	KOR	TWN
Relative change 2020 to 2040	+20%	+9%	-10%	+13%	+10%	-3%	-1%
	CHN	**IND**	**IDN**	**MYS**	**PHL**	**THA**	**VNM**
Relative change 2020 to 2040	+1%	+15%	+16%	+20%	+24%	-1%	+11%

Notes: Numbers for 2020 and 2040 are based on the "medium fertility variant".
Source: United Nations (35).

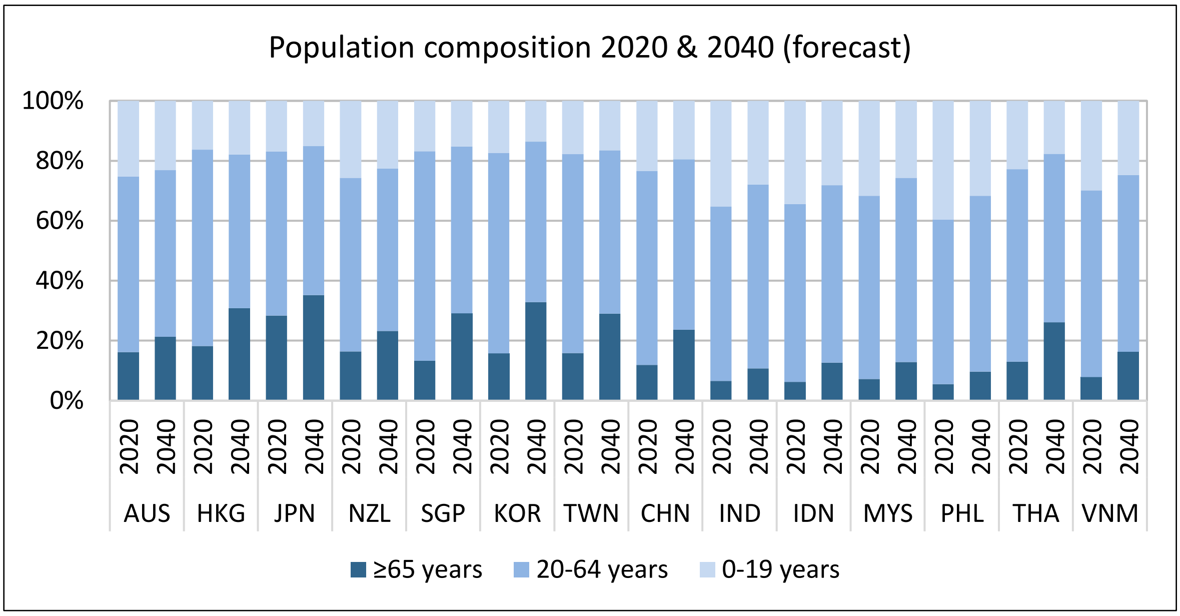

Figure 12: Forecasted population composition by age group, 2020 and 2040

Notes: Numbers for 2020 and 2040 are based on the "medium fertility variant".
Source: United Nations (35).

Against the backdrop of the expected demographic development (population aging in all markets and changing overall population sizes in some markets), Figure 13 illustrates the expected development of the cancer burden between 2020 and 2040. It shows what would happen if the status quo (base year 2020) remains, i.e., in the absence of further improvements in cancer treatment and prevention. All markets would be expected to record increases in incidence cases, ranging from 9% in Japan to 93% in Singapore, and in deaths, ranging from 23% in Japan to 139% in Singapore. Across the 12 markets in Figure 13, an additional 3.93 million incidence cases (up from 8.25 to 12.18 million) and 3.29 million deaths (up from 5.01 to 8.30 million) are expected to occur in 2040 compared to 2020.[12]

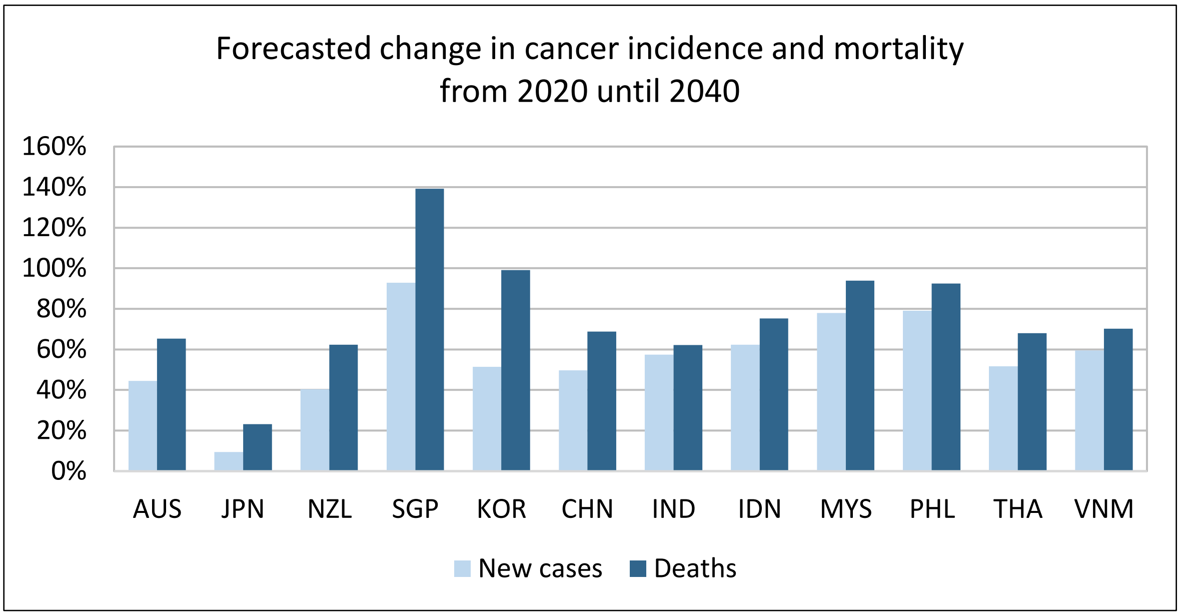

Figure 13: Forecasted change in total cancer incidence and cancer mortality between 2020 and 2040

Notes: Changes refer to total number of cases. "Cancer" refers to all cancers excl. non-melanoma skin cancer. No comparable data are available for HKG and TWN.
Source: GLOBOCAN (6).

The forecasted development in Figure 13 prompts urgent action by all governments across Asia-Pacific. Advances and investments in all areas of cancer care – prevention, screening, diagnosis, treatment – are needed to meet the challenges brought upon by the demographic development and to achieve a lasting turnaround in cancer incidence and mortality. A clear prioritization of effective and comprehensive cancer control efforts could spare millions of people from getting cancer and simultaneously improve the lives of the millions of cancer patients over the coming decades. To this end, the WHO advocates National Cancer Control Programs (NCCP) to tackle cancer in a strategic way (64).

[12] There is a larger relative increase in deaths than in incidence cases in all markets. This would suggest that the 1–MIR becomes worse in the future, contrary to the recent development observed in high-income markets in section 2. GLOBOCAN forecasts are based on age-specific incidence and mortality rates in 2020. The shape of the age-specific incidence/mortality curves differs particularly at older ages, when mortality increases much faster than incidence (opposite at middle ages). Together with the forecasted rapid increase of the elderly population, this leads to larger increases for mortality.

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Appendix

Table A1: Sources for cancer incidence and cancer mortality

	Market	Incidence		Mortality	
		2012	**2018**	**2012**	**2018**
HIGH-INCOME MARKETS	Australia	National registry (25)	National registry (25)	National registry (25)	National registry (25)
	Hong Kong	National registry (65)	National registry (65)	National registry (65)	National registry (65)
	Japan	National registry (66)	National registry (66)	National registry (66)	National registry (66)
	New Zealand	National registry (26)	National registry (26); 2017	National registry (26)	National registry (26); 2017
	Singapore	National registry (21); average in 2008-2012	National registry (21); average in 2013-2017	National registry (21); average in 2008-2012	National registry (21); average in 2013-2017
	South Korea	National registry (67)	National registry (68); 2017	National registry (67)	National registry (68); 2017
	Taiwan	National registry (69)	National registry (69)	National registry (69)	National registry (69)
MIDDLE-INCOME MARKETS	China	National estimate from regional registries (45)	GLOBOCAN (19)	National estimate from regional registries (45)	GLOBOCAN (19)
	India	GLOBOCAN (70)	GLOBOCAN (19)	GLOBOCAN (70)	GLOBOCAN (19)
	Indonesia	GLOBOCAN (70)	GLOBOCAN (19)	GLOBOCAN (70)	GLOBOCAN (19)
	Malaysia	National registry (18); average in 2007-2011*	National registry (18); average in 2012-2016*	National registry (18); average in 2007-2011*	National registry (18); average in 2012-2016*
	Philippines	GLOBOCAN (70)	GLOBOCAN (19)	GLOBOCAN (70)	GLOBOCAN (19)
	Thailand	GLOBOCAN (70)	GLOBOCAN (19)	GLOBOCAN (70)	GLOBOCAN (19)
	Vietnam	GLOBOCAN (70)	GLOBOCAN (19)	GLOBOCAN (70)	GLOBOCAN (19)

Notes: Total numbers on incidence and mortality were obtained from the sources cited in the table. These numbers were combined with information on the total population from the World Bank (71) and from the Department of Household Registration in Taiwan (72) to calculate crude rates in a standardized manner across all markets. * Data from the registry in Malaysia were only used in section 2, whereas data from GLOBOCAN were used in section 3.

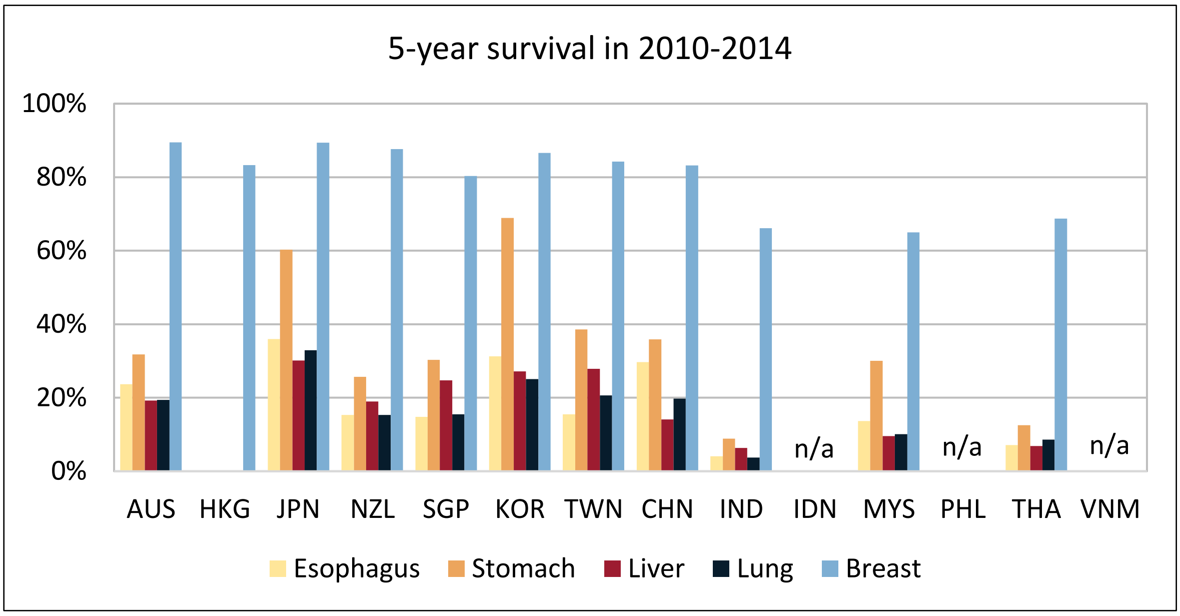

Figure A1: 5-year age-standardized net survival rates in adult patients (15–99 years), 2010–2014

Notes: Esophagus = esophageal cancer, Stomach = gastric cancer, Liver = liver cancer, Lung = lung cancer, Breast = breast cancer. No data are available for head and neck cancer. n/a = no data available. For HKG, only data for breast cancer are available. Coverage of the underlying population is 100% in AUS, HKG, NZL, SGP, KOR, TWN, 40.6% in JPN, 2.3% in CHN, 0.1% in IND, 5.2% in MYS, 20.3% in THA.
Source: CONCORD-3 (44).

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