Chapter 1: The Global Cancer Pandemic: Trends and Disparities

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Kurt Straif provides a historical and global overview on global trends in cancer incidence, disparities, and social inequalities among countries and within countries, with a particular attention given to cancer in children and adolescents. To reduce social inequalities, the author proposes to reexamine research priorities: first, to generate knowledge and monitor progress; second, to expand research focused on prevention; and, third, to focus on equality when implementing and assessing cancer control measures.

Fifty years ago, on December 23, 1971, President Richard M. Nixon signed the National Cancer Act into law. The campaign that was launched was also called “The War on Cancer” and Fort Detrick, the United States Army Futures Command installation for biological warfare facility, located in Frederick, Maryland, was converted into a cancer research center to serve as the headquarter as the Frederick Cancer Research and Development Center. Later, in 2016, President Barack H. Obama launched the Cancer Moonshot Initiative and asked Vice President Joseph R. Biden to lead the initiative to increase research funding and accelerate cancer discoveries. From the start, and reasserted with the Moonshot Initiative, there was a disproportionate focus on finding a cure for cancer. But why had cancer has become such a prominent topic in the 1960s?

Between 1346 and 1352, 25–33 percent of the European population died of the Bubonic plague, also called the “Black Death,” which was believed to be caused by “Miasmas” (from the Greek word for

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“pollution” from noxious vapors and gases from decaying matter and characterized by its foul smell).

Later, in the 18th century, cholera swept into Europe with major epidemics in big cities like London and Paris. Four hundred years after the Black Death, miasmas were still believed to be the cause of the devastating and deadly cholera epidemics. However, with his investigation of the cholera outbreak of 1854 in London, Dr. John Snow (1813–1858) showed that cholera was transmitted by fecal contamination of drinking water. Followed by the identification of Vibrio cholera as a bacterium by the Italian anatomist Filippo Pacini (1812–1883), and the discovery of the German physician and microbiologist Robert Koch (1843–1910) that this bacterium is the cause of cholera, the miasma paradigm was supplanted by the germ theory. In 1882, Koch also discovered the tubercle bacillus that caused tuberculosis, and in 1900 tuberculosis was, together with pneumonia and influenza, one of the two leading causes of death, followed by gastrointestinal infections as the third ranking cause of death in the U.S. Only ranking fourth, heart disease was the first chronic non-communicable disease among the top causes of deaths in 1900. The death rate of cancer—ranking 8th—was only about one fourth that of cardiovascular deaths (Table 1).

With the demographic transition and the epidemiological transition, starting first in high-income countries, this pattern changed radically. The demographic transition is characterized by population-level shifts from a pattern of high birth rates and high death rates to one of low birth rates and low death rates. Changes in mortality rates and causes of death that reflect underlying changes in exposure to risk factors define the epidemiological transition. Specifically, during the past century mortality from infectious diseases declined and led to the dominance of non-communicable diseases (NCD). Among NCD, more recently, and particularly in medium or high-income countries, greater reductions in mortality rates for cardiovascular diseases than for cancer resulted in cancer now figuring as first or second leading cause of premature death (i.e., among adults 30–69 years old) in 134 of 185 countries.
However, cancer is not one disease, but refers to a large, heterogeneous group of diseases that have a common underlying pathology defined by uncontrolled cellular growth. From a global perspective, some cancer types are significantly more frequent than others, but the cancer-specific pattern also varies considerably if we employ the different classic epidemiological measures of disease frequency, incidence (i.e., newly diagnosed cases), mortality, and prevalence. For cancer, the latter is typically (but arbitrarily) estimated based on the five-year survival after the initial diagnosis.

For each measure, and for both sexes combined, somewhat different top five cancers constituted about half of all cancers among middle-aged adults in 2018. Total cancer incidence was 18.1 million, and the leading causes were lung and breast cancer, followed by colorectal cancer and prostate cancer. In contrast, for cancer mortality, lung cancer was by far the leading cancer, breast cancer was only fifth, and prostate cancer did not make it into the top five. Instead, liver cancer showed and ranked fourth, closely after stomach cancer. Total cancer mortality was about half of the incidence, i.e., 9.6 million deaths.\(^{10}\)

The percentage distribution differs for the estimated 43.8 million prevalent 5-year cancer survivors. Here (see Figure 2), breast cancer leads and lung cancer barely shows up among the top 5 cancer survivors. Prostate cancer is back and ranked third, and thyroid cancer emerges as one of the top

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\(^{10}\) Jemal, Torre, Soerjomataram, and Bray, *The Cancer Atlas.*
five cancers among 5-year survivors. Only colorectal cancer has a similar percentage of about 10 percent across all three frequency measures.

There are important differences by sex for the ranking of most frequent cancers, and these differences vary further by region. For cancer incidence among women, globally breast cancer is the number one ranking cancer in most countries. However, cancer of the cervix uteri is most common in several low and medium-income countries (LMIC), particularly in Africa. In terms of mortality, cancer of the cervix ranks first in even more countries and in all Sub-Saharan Africa. In many high-income countries (HIC) and in China, lung cancer leads the mortality rates. In Mongolia, liver cancer is the most frequent cancer in terms of incidence and mortality.

Among men, liver cancer is also the most frequent cancer in Mongolia. Moreover, this is true in several countries in South-East Asia and Africa. In terms of incidence, prostate cancer ranks number one in the Americas, Australia, European and African countries, while lung cancer leads in many Asian countries. For mortality, lung cancer takes the lead before prostate cancer, with notable exceptions in several countries of Africa and Central and South America. Only in the Indian sub-continent, cancers of the lip and oral cavity are the most frequent cancers, for both incidence and mortality.\(^\text{11}\)

On a finer grid, there is even more important variation across cancer registries. Even when restricted to the variation between the 10\(^\text{th}\) and 90\(^\text{th}\) percentile, the relative magnitude of cancer incidence varies more than fifty times for melanoma of the skin with lowest rates among Qataris and highest in Georgia, USA. The incidence of cancers of the prostate and testis varies by about 15 times globally, with lowest rates in Maanshan, China, and Chennai, India, and highest rates in Limousin, France, and Wales, respectively. The age-standardized rates depict the absolute variations. Closer to the highest rate of prostate cancer, lung cancer incidence in Chelyabinsk, Russia, and colorectal cancer in Trento, Italy,

\(^{11}\) Jemal, Torre, Soerjomataram, and Bray, *The Cancer Atlas.*
The smallest relative variation among the depicted 22 cancer types is leukemia and is still more than twofold.\textsuperscript{12}

There have been substantial trends over time as illustrated with sex-specific cancer mortality rates in the United States from 1930 to 2011. Lung cancer—today’s top-leading cause of cancer death—was only one of the less frequent cancers in the 1930, before age-standardized lung cancer death rates among men increased by more than ten times and peaked around 1990. However, lung cancer was still by far the leading cause of cancer death in 2011. A similar trend, but later and less pronounced, was observed among women, starting to increase in the late 1960s, and its decline is showing only recently. In contrast, stomach cancer was the leading cause of cancer deaths in the early twentieth century, but monotonically decreased in both sexes over the last century.\textsuperscript{13}

Trends over time may differ noticeably even over shorter times, between neighboring countries and in different age groups among adults. Trends of colorectal cancer incidence in Canada from 1980 to 2010 among adults 50 years and older are relatively stable, while in the United States, after a peak in the mid-1980s, an almost monotonic decline has now resulted in incidence rates that are lower than those in Canada. In contrast, in both countries, among adults less than 50 years old the incidence of cancers of the colorectum (and the uterine corpus) started to increase in the early 1990s.\textsuperscript{14}

**Cancers in Childhood and Adolescence**

Cancers occurring in childhood and adolescence differ markedly from the cancer patterns in adults. Globally, the most common cancers in children are leukemia and lymphoma, while major cancers that are


\textsuperscript{13} Based on data from Max Roser and Hannah Ritchie, “Cancer,” *Our World in Data*, 2019, ourworldindata.org/cancer.

\textsuperscript{14} Jemal, Torre, Soerjomataram, and Bray, *The Cancer Atlas*. 
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typical among adults—such as cancers of the lung, breast, or colon—are extremely rare in children. Among the younger children (ages 0–14) leukemia and tumors of the central nervous system are most frequent and lymphoma is third, while in adolescents (ages 15–19), incidence rates of lymphoma surpass those of leukemia and tumors of the central nervous system. Further, epithelial tumors and melanoma emerge in this older age group. Overall, cancer in children is about ten times less frequent than in adults, but, as in adults, important variations are seen across regions and ethnicities.

Social Inequalities in Cancer
Descriptive cancer epidemiology provides numerous illustrations of major structural inequalities, for instance when one considers survival from acute lymphoblastic leukemia, the most frequent cancer in children. Figure 1 depicts the 5-year survival from this cancer based on results of cohort studies. The size of the circles indicates the number of cases from available cohorts that contributed to the region-specific survival data. Therefore, these numbers are not valid for incidence or mortality comparison between regions. However, the survival data by region highlight the poor survival in LMIC. While survival in HIC was 90 percent and higher, survival in Africa was only 43 percent. Particularly in LMIC such survival data likely represent the upper end of survival (e.g., among children who were diagnosed and treated in a major specialized cancer hospital, and later followed-up in a cohort), while in the poorest countries only 10 percent of children can hope to survive.

Inequalities are not only prominent across countries of different income but also within countries. Figure 2 summarizes age-standardized mortality rates per 100,000 by deprivation quintile in England for all cancers combined for the period 2007–2011. While these all-cancer mortality rates are generally higher in men than in women, in both sexes a significant trend with increased mortality by increasing deprivation

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quintile is documented. All-cancer mortality in the most deprived quintile is 50 percent higher than in the least deprived, for both men and women.

Many important disparities by race or ethnicity have been revealed. Female breast and colorectal cancer mortality ratio by race in the U.S. illustrates this structural problem. Cancer mortality rates for female The descriptive illustration of social inequalities in cancer concludes with an example of incidence and mortality of cancer of the cervix uteri—one of the most frequent cancers in women—by country income level. For both incidence and mortality, there is a strong trend across country income levels with highest occurrence in low-income countries. Moreover, the ratio

Figure 1. 5-year age-standardized net survival (percent) observed in the available cohorts of cases diagnosed with lymphoid leukemia
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of mortality to incidence strongly increases from high to low-income countries.¹⁶

Many more illustrations of social inequalities in cancer can be explored in the International Agency for Research on Cancer’s Reducing Social Inequalities in Cancer: Evidence and Priorities for Research.¹⁷ This publication is the outcome of an international workshop convened by the Agency in April 2018. The book introduces the concept of cancer as a disease of disparities and how global public health addresses social inequalities in cancer. The chapters provide an overview of social

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inequalities in cancer between and within countries, factors and mechanisms contributing to these inequalities, and real-world examples of interventions that reduce these social inequalities. The workshop also recommended research priorities to reduce social inequalities in cancer: first, generating knowledge and monitoring progress; second, expanding research focused on prevention; and, third, focusing on equality when implementing and assessing cancer control measures.

At Boston College, Kurt Straif, MD, PhD., is currently Visiting Professor of Epidemiology and co-director of the Global Observatory on Pollution at Health with the Schiller Institute for Integrated Science and Society. Since 2001, he had leading positions at the International Agency for Research on Cancer (IARC), as a senior epidemiologist, Head of the IARC Monographs Programme, to classify carcinogenic hazards of all kinds of environmental exposures (chemical, biological, physical agents, and personal habits), Acting Head of a large epidemiological research group, and initiator of large international projects. In 2014, he relaunched the IARC Handbooks of Cancer Prevention with a broad perspective on prevention (i.e., breast cancer screening, avoidance of obesity, and colorectal cancer screening). Since 2017 he also supervises the World Health Organization’s Classification of Tumours (“Blue Books”). In 2016, he received the Champion of Environmental Health Research Award in commemoration of fifty years of Environmental Health Research by the National Institutes of Health. In 2018, he presented the Distinguished Lecture in Occupational and Environmental Cancer at the U.S. National Cancer Institute.