



Global burden of lung cancer: implications from current evidence

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Lung cancer, including trachea and bronchus cancer, is widely regarded as a threat to global health, causing a heavy burden on individuals and families with significant impacts in terms of economic expenditure and resource use (1-6). Lung cancer control should be a main target to improve global health, especially to achieve the reduction by one-third premature mortality from non-communicable diseases (NCDs) by 2030—one of the United Nations (UN) Sustainable Development Goals (SDGs) (7). For global responses to further control lung cancer, in this editorial commentary we summarize the key characteristics of global lung cancer epidemiology and discuss the implications.

Global epidemiology of lung cancer

Supported by the Global Burden of Disease (GBD) Study, several recently published articles report cancer statistics, including incidence, mortality and disability-adjusted-life-years (DALYs), for 195 countries and territories from 1990 to 2017 (1-5). Overall, lung cancer was the second most common cancer, after non-melanoma skin cancer, with

2.2 million incident cases in 2017 (1). Lung cancer was also the most common cause of cancer death and DALYs for males, and the second leading common cause of cancer death and DALYs for females—with a total of 1.9 million deaths and 40.9 million DALYs in both sexes (1).

From 2007 to 2017, the incidence of lung cancer increased by 37% (1). The increase was mainly due to changing age structure, population growth and changes in age-specific incidence rates, accounting for 19%, 13% and 5%, respectively. The trends and drivers differ substantially by a country's socio-demographic index (SDI), an important composite indicator of level of income, educational attainment and total fertility rate in countries/regions. In high-SDI countries, lung cancer cases increased by 17%; changing age structure was the major driver (16%). In middle-SDI countries, cases increased by 62% (29% due to changing age structure and 23% due to changes in age-specific incidence rates). In low-SDI countries, cases increased by 49%, due to population growth (24%), changing age structure (14%) and changes in age-specific incidence rates (11%) (1). With respect to lung cancer risk

factors, the recent GBD study emphasizes the critical role of smoking as a driver of lung cancer incidence. The study found the relative risk of lung cancer from smoking is 3.4 at 10 pack-years and 6.5 at 20 pack-years, which is very high, “far more likely to be causal than an exposure with a relative risk of 1.1” (8).

Lung cancer has been the leading cause of cancer death for decades (2). Between 2007 and 2017, the number of deaths attributable to lung cancer increased by nearly 30%, while the age-standardized mortality rate (ASMR) decreased by 2% (1). The changes in number of deaths due to lung cancer varied by age group: for those aged 15 to 49, the number of deaths decreased by 1%, while those aged 50 to 69 and over 70 years old, the number of deaths increased by 40% and 30%, respectively (1). The leading risk factors for lung cancer deaths were smoking (male: 75.4%; female: 36.6%) and ambient particulate matter pollution (male: 14.5%; female: 13.0%) (3). Notably, in males, the proportion of the lung cancer ASMR attributable to occupational exposure to asbestos was high (global: 14.0%; high-SDI countries: 27.8%). Among both sexes, in low-SDI countries the proportions of the ASMR attributable to household air pollution from solid fuels were also considerable (male: 21.7%; female: 29.9%), compared to the global level (male: 4.0%; female: 5.4%) (3).

As mentioned, there were 40.9 million DALYs attributable to lung cancer in 2017 (1), a 61% increase from 1990. Although most of the increase in DALYs were in the age group of 50–69 (4), the age-standardized DALY rate decreased (estimated annual percentage change: -0.74). During the past 28 years, the leading attributable factor for DALYs was smoking, followed by ambient particulate matter pollution, occupational carcinogens, dietary risks, metabolic risks, and other environmental risks (4). Among DALYs, 99% were due to years of life lost (YLLs) and 1% due to years lived with disability (YLDs) (1). With respect to YLLs, a measure of premature death, lung cancer still ranked number one among all types of neoplasm (from 2007 to 2017). During the same decade, absolute YLLs increased by 25%, but the age-standardized YLL rate decreased by 4% (1).

According to the latest CONCORD program report from 290 registries in 61 countries and regions, the age-standardized 5-year net survival rate of lung cancer in 2010–2014 was 10–19% in most countries/regions—still very low compared to the rates of other neoplasm types (6). There were only 13 countries/regions with a lung cancer 5-year survival rate greater than 20%; these are, in descending

order: Japan, Israel, Korea, USA, Canada, Taiwan, Latvia, Mauritius, Switzerland, Iceland, China, Austria, Sweden. Four countries had a 5-year survival rate less than 10% (Thailand, Brazil, Bulgaria and India). The global survival trends of lung cancer between 1995–1999 and 2000–2014 were similar; however, the net survival increased by over 5% in 23 countries, among which survival increased by 10% in two countries (China and South Korea) (6).

Implications for lung cancer control

Lung cancer is characterized by its aggressive nature and lack of early noticeable symptoms, leading to diagnostic/treatment delays and consequent poor outcomes. Disparities of the above lung cancer statistics between countries/regions reflect their different development stages of population and society including the capacity of lung cancer control (1–6,9). In response to global lung cancer epidemiology, overall, countries need to be prepared for the increasing burden from this disease, given the growing incidence of lung cancer in many countries. Specifically, several low- to middle-SDI countries are encountering the shift of disease burden from communicable diseases to NCDs (e.g., lung cancer), due to changing age structure and population growth, and advances in controlling communicable, maternal, neonatal, and nutritional (CMN) diseases (9); while most high-SDI countries are dealing with an aging population leading to increased lung cancer cases. Furthermore, lung cancer mortality rate, YLLs and survival at the global level are unlikely to improve quickly mainly given the challenges in diagnostics and costs of treatment. However, survival improvement in many countries reflects the progress of lung cancer control at population level (6,10), especially the progress in diagnosis and treatment.

To conquer lung cancer for all, it is crucial to keep translating research into real-world practice, enhance prevention policies, support equitable access to healthcare, improve the timeliness and effectiveness of healthcare services, and increase public awareness about lung cancer, its prevention, early detection and survivorship. Transdisciplinary efforts (11) across socio-ecological levels (individual, interpersonal, organizational, community, and public policy) should be emphasized. Control activities should span the cancer continuum, including primary prevention (e.g., tobacco control and cessation, control of air pollution and other environmental exposures), secondary prevention and diagnosis (e.g., cancer screening

in high-risk populations), treatment (e.g., development of new treatments, comprehensive approaches involving surgery, chemotherapy, radiotherapy, targeted therapy and immunotherapy to different cancer stages), survivorship care (e.g., smoking cessation, surveillance strategies to detect recurrence, or second primary cancers, improvement of quality of life), and cancer supporting/end-of-life care (e.g., palliative care). Also, efforts should be made via improving the services especially at health system and public policy (e.g., governmental administration, health insurance) (12) and community levels (e.g., education, social campaigns) (13).

To reduce the burden of lung cancer via the process mentioned above, global, national and regional organizations including the World Health Organization (WHO) and respective Departments of Health, as well as non-governmental organizations in cancer areas like the International Association for the Study of Lung Cancer (IASLC) and the Union for International Cancer Control (UICC) should work together to lead universal efforts. The universal efforts include the promotion of key policy initiatives to control cigarette smoking (especially strengthening administration and implementation as guided by the WHO Framework Convention for Tobacco Control) and air pollution, the agreement on essential cancer drugs based on universal health coverage (14,15), fairer methods for pricing cancer medicines and reducing development costs (15), the development of nationally appropriate clinical practice guidelines and international/regional research & educational programs for healthcare professionals and the public, as well as the improvement of health equity via addressing disparities in cancer care and cancer outcomes (mainly due to the intersected impacts of gender, race/ethnicity, geographic and socioeconomic factors). Pharmaceutical and other health service companies can also play a role to identify appropriate markets to invest and develop services in countries/regions; social media and academic communication platforms are important to disseminate high-quality evidence to impact social change and improve public health.

We are concerned about the potential impact of the COVID-19 pandemic to worsen lung cancer outcomes. Internationally we are witnessing reductions in cancer incidence during the pandemic reflecting delays in presentation to healthcare and reduced access to diagnosis and treatment (16,17). At the same time, routine lung cancer services have been interrupted by the pandemic, including the conversion from hospital visit to consultation

by phone or video, and treatment plans have been changed (e.g., switch to oral treatments, treatment delay and discontinuation) (18,19). Furthermore, current evidence indicates that COVID-19 patients with lung cancer have a relatively high mortality rate (33%) (20,21), and that delays in cancer diagnosis and treatment are projected to cause substantial increases of avoidable cancer deaths and life-years lost (22,23). It is possible that we may see a worsening of outcomes during and for some time after the COVID-19 pandemic. Therefore, healthcare organizations and relevant regulatory bodies should take action to provide effective healthcare services (24). Specifically, the focus should be on conducting accurate assessment of COVID-19 burden, enhancing the use of telehealth, optimizing the workflows of primary and specialty care, identifying patients at risk, and activating patients' outreach and education (16). At the same time, interventions in diagnosis and treatment pathways to minimize the exposure and poorer outcomes from COVID-19 infection should be implemented to protect patients and clinical practitioners; also, healthcare organizations should be well-prepared and capable to provide services for a potential surge in the number of cancer patients due to the backlog of diagnosis and treatment delays caused by the pandemic (24).

Lastly, we emphasize the importance of cancer surveillance. Comparative assessments based on population level statistics can be instrumental in tracking the progress of disease control, and guiding further policy and health system design, globally and locally. Considering the global burden of lung cancer, countries and regional governments are encouraged to improve the quality and timeliness of reporting including higher population coverage and better data completeness to guide future global initiatives to control lung cancer (6,25). Along with the improvement, surveillance based on lung cancer statistics by subtype may become possible, since the nature and patient outcomes are distinct for non-small-cell compared to small-cell lung cancer. In addition, measures with greater precision, like incidence-based mortality, might be feasible (10). With such improvement, the public, policymakers and medical professionals should have greater benefit from cancer surveillance in order to advance resource allocation and healthcare effectiveness, especially during the time of unexpected social change (e.g., disease pandemic, financial crisis).

Conclusions

Lung cancer is the leading cause of cancer death worldwide.

In this editorial commentary, we summarize the key characteristics of global lung cancer epidemiology and discuss the implications to further control lung cancer. In brief, the key characteristics are: (I) growing incident cases and deaths, (II) only a small reduction in global mortality rate, (III) lung cancer deaths and DALYs mainly attributable to smoking and ambient particulate matter pollution, (IV) low 5-year survival rate (10–19%) in most countries but improved in many countries, (V) disparities in measures by country/region and their sociodemographic development status. Therefore, key implications are: (I) countries need to be well prepared to face the increasing lung cancer burden; (II) challenges are still significant in controlling lung cancer, especially given its aggressive nature and lack of early noticeable symptoms; (III) to conquer lung cancer, it will be crucial to implement strong tobacco control policies, enhance access to healthcare services, improve the timeliness and effectiveness of the services, and increase public awareness about lung cancer; for that, (IV) transdisciplinary efforts across socio-ecological levels on disease control need to be emphasized along the cancer care continuum; (V) global, national and regional organizations should lead universal efforts to reduce the burden; (VI) healthcare services need to respond to the impact of the COVID-19 pandemic on diagnosis and treatment delays and worsening lung cancer outcomes; (VII) lung cancer surveillance with comparative assessments is instrumental in tracking the progress of disease control, guiding further policy, resource allocation and health system design, globally and locally.

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