Received: 18 June 2024 | Revised: 14 August 2024 | Accepted: 14 October 2024

DOI: 10.1002/cac2.12622

CANCER COMMUNICATIONS Open Access

LETTER TO THE JOURNAL

The long-term spatiotemporal trends in lung cancer burden and its risk factors at global, regional, and national levels, 1992-2021: The Global Burden of Disease Study 2021

Lung cancer is among the most common types of malignant tumors and continues to be the primary cause of cancer-related death [1]. Despite many striking advances in disease understanding and novel treatment opinions that have occurred in recent years, the survival of lung cancer continues to be low, which causes an important public health and socioeconomic issue [2]. Previous studies have reported estimates of lung cancer burden before 2019 [3, 4]. However, the latest information on lung cancer including data during the COVID-19 pandemic is lacking. It is important to regularly measure the current trends in lung cancer incidence rate, mortality rate, disability-adjusted life-years (DALYs) rate, and risk factors. This information is crucial for updating health policies to adapt to the fast-changing global health landscape during the COVID-19 pandemic.

To address the above issues, we utilized the latest Global Burden of Diseases (GBD) 2021 data to update statistics on lung cancer incidence, mortality, and DALYs at global, regional, and national levels during 1992-2021 (Supplementary Materials and Methods) [5]. On a global scale, there was a 75.60% increase in the estimated number of lung cancer incident cases, a 60.15% increase in death cases, and a 49.88% increase in DALYs from 1992 to 2021 (Supplementary Table S1). However, the corresponding age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), and age-standardized DALYs rate (ASDR) had decreased trends (Supplementary Table S2). We found that the trend was not consistent worldwide. The region with a high-middle socio-demographic index (SDI) had the highest number of lung cancer incident cases, death cases, and DALYs in 2021 (Supplementary Table S1). Only the low-middle SDI region experienced an increasing trend in age-standardized rates (ASRs) from 1992 to 2021 (Supplementary Table S2). Whereas, the highest ASIR, ASMR, and ASDR of lung cancer were in the middle-SDI region (Supplementary Table S1). At the country level, compared with 1992, most countries presented a slight downward trend in ASIR, ASMR, and ASDR in 2021. China ranked first in the incidence of lung cancer cases, followed by the United States of America and Japan in 2021 (Figure 1A, Supplementary Table S3). China, the United States of America, and India ranked in the top 3 in death cases and DALYs in 2021 (Figure 1B-C, Supplementary Tables S4 and S5). Monaco, Greenland, and Montenegro reported the highest ASIR, ASMR, and ASDR in 2021 (Figure 1D-F, Supplementary Tables S3-S5). However, Egypt had the largest increase in ASIR, ASMR, and ASDR from 1992 to 2021, followed by Lesotho and Cabo Verde (Figure 1G-I, Supplementary Tables S3-S5). Additionally, in 2021, the rates of lung cancer incidence, mortality, and DALYs in males were 2.23, 2.36, and 2.31 times higher than those in females (Supplementary Figure S1). The ASIR, ASMR, and ASDR of lung cancer in males presented a decrease from 1992 to 2021, while the ASIR, ASMR, and ASDR of lung cancer in females remain nearly stable (Supplementary Figure S2). The largest proportion of individuals affected by lung cancer are over the age of 50, and there has been an upward trend in the number of cases, mortality, and distribution of DALYs among this age group over the past 30 years (Supplementary Figure S3).

To better understand the impact of age, period, and birth cohort on lung cancer incidence, mortality, and DALY rates over the last 30 years, we next performed age-period-cohort analyses. Our results showed that, globally, a net drift of lung cancer incidence, mortality, and DALYs for the whole population was -1.14%, -1.47%, and -1.46% per year, respectively (Supplementary Figure S4, Supplementary Table S6). The local drifts of lung cancer incidence were above zero for the ages of 75 to 79 (Supplementary

List of abbreviations: AAPC, average annual percentage change; APC, annual percentage change; ASDR, age-standardized DALYs rate; ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; ASR, age-standardized rate; CI, confidence interval; COVID-19, ; DALY, disability-adjusted life-year; GBD, Global Burden of Disease Study; ICD, International Classification of Diseases and Injuries; RR, relative risk; SDI, socio-demographic index; UI, uncertain interval.

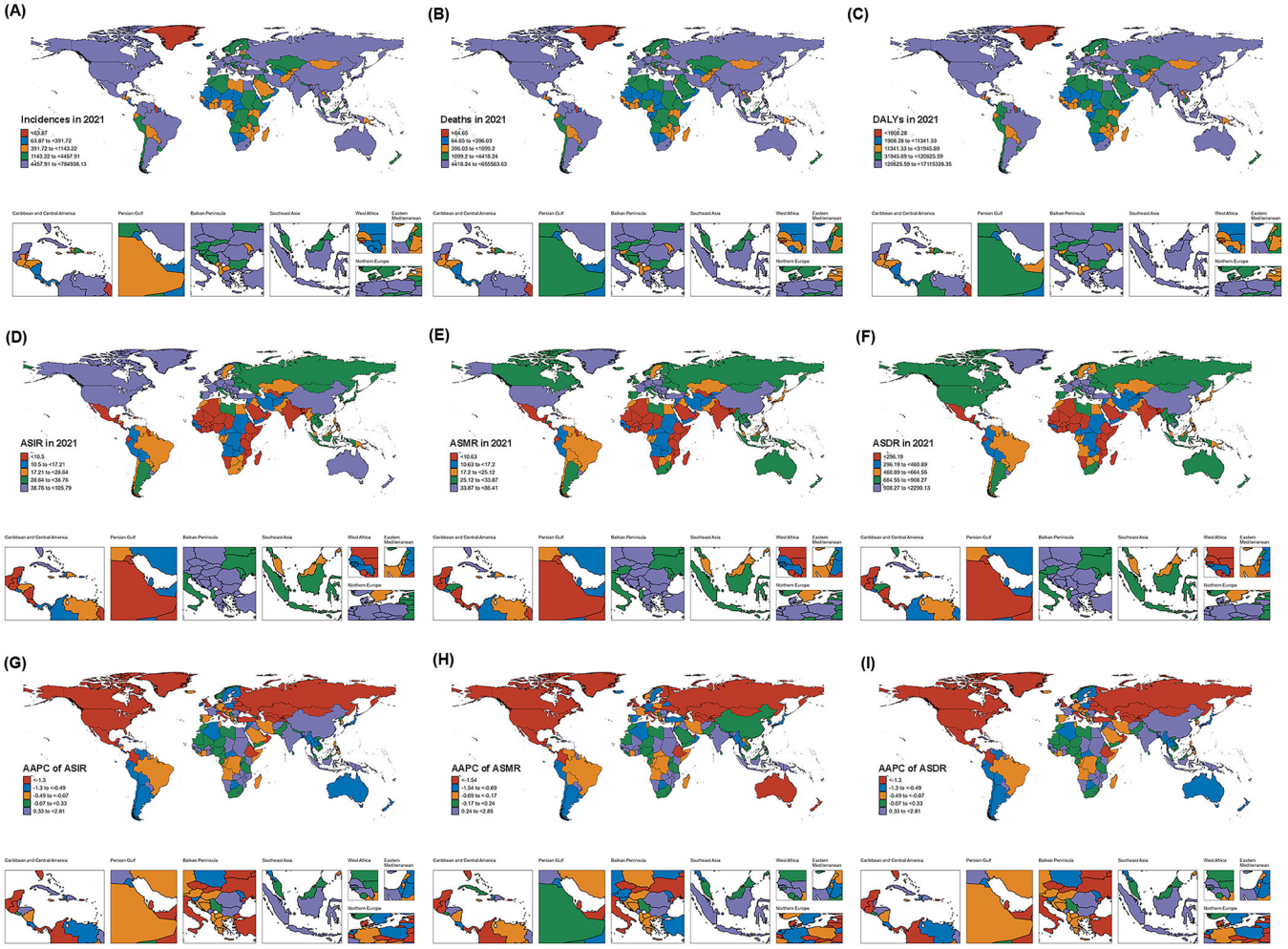

FIGURE 1 The incidences (A), Deaths (B), and DALYs (C) of lung cancer across 204 countries and territories in 2021, the ASIR (D), ASMR (E), and ASDR (F) of lung cancer across 204 countries and territories in 2021, and the AAPC of ASIR (G), ASMR (H), and ASDR (I) during 1992-2021. Abbreviations: ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized DALYs rate; AAPC, average annual percentage change.

Figure S4, Supplementary Table S7). Similar age trends of lung cancer were observed across different SDI quintiles. Generally, the risk for lung cancer significantly grew with age and the age effects for females were significantly lower than for males (Supplementary Figure S5). Period effects showed different patterns across different SDI quintiles over the study period (Supplementary Figure S6). At the global level and in high-SDI countries, the period effect of incidence, mortality, and DALYs rate decreased over time, and the reduction in risk over time was less for females compared to males. Only in regions with low-middle SDI did the incidence rate continue to increase from 1992 to 2021. When looking at the cohort effect, there is a significant decrease in Cohort trends of lung cancer, particularly in the global, middle-SDI, high-middle SDI, and high-SDI regions (Supplementary Figure S7). From the earlier birth cohort to the later birth cohort, there was an upward trend in females in regions with low-middle SDI, while males in low-middle SDI remained nearly constant. In low SDI, females show a trend of rising, and males show a trend of declining.

We further estimated the lung cancer burden caused by risk factors to prioritize public health interventions (Supplementary Figures S8 and S9). From 1992 to 2021, the proportion of high fasting plasma glucose and ambient particulate matter pollution steadily increased as global risk factors for lung cancer. Smoking still remains the highest proportion in 2021, followed by occupational exposure to asbestos. However, over time, the proportion of smoking and occupational exposure to asbestos has gradually decreased. The changing trend of the proportion of risk factors in lung cancer presented different trends in different SDI regions. In high SDI areas, occupational exposure to asbestos and high fasting plasma glucose are higher than those in other areas and the proportion of occupational exposure to silica is decreas-

ing year by year. In the high middle SDI area, smoking, secondhand smoke, and residential radon make up a relatively high proportion. In the middle SDI area, the proportion of ambient particulate matter pollution was higher than those in other areas. In regions with low SDI and low-middle SDI, the highest proportion was a diet low in fruits and household air pollution from solid fuels.

In conclusion, over the past 30 years, despite a global downward trend in ASIR, ASMR, and ASDR of lung cancer, it remains a significant burden worldwide. The significant differences in ASIR, ASMR, ASDR, and risk factors among countries and territories remained a key epidemiological characteristic of lung cancer. This suggests that each government should adopt flexible health policies and allocate medical resources reasonably to improve their healthcare systems in order to address the diverse needs related to lung cancer. Global strategies for improving air quality, tobacco control, promoting clean cooking fuels, and reducing occupational hazards are vital for reducing the burden of lung cancer. All comprehensive and comparable estimates provided in this study can serve as a data basis for further scientific research and facilitate valid comparisons among different areas.

AUTHOR CONTRIBUTIONS

Zegui Tu: conceptualization, data curation, formal analysis, visualization, project administration, and writing-original draft. Shuangsi Liao: resources, data curation, formal analysis, investigation, methodology, and writing-original draft. Caini Chen: resources, data curation, writing-original draft. Caili Li: resources, validation, visualization, and writing-original draft. Qipeng Hu: validation, visualization, methodology, and writing-review and editing. Chengzhi Cai: validation, and writing-review and editing. Yang Yu: data curation, writing-review and editing. Jieyan Luo: resource, and writing-review and editing. Meijuan Huang: conceptualization, project administration, and writing-review and editing. All authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

We would like to express our gratitude to the collaborators who contributed to the Global Burden of Disease Study 2021.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

FUNDING INFORMATION

Not applicable.

DATA AVAILABILITY STATEMENT

The source data of this study can be freely accessed at the Global Health Data Exchange GBD Results Tool. The datasets used and analyzed during this study are available from the article or supplemental materials.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.