

## Cancer statistics and trends in China: the potential of natural product application

Ting LI, MUYANG HUANG, JINJIAN LU

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•Commentary•

## Cancer statistics and trends in China: the potential of natural product application

LI Ting<sup>1,2\*</sup>, HUANG Muyang<sup>1</sup>, LU Jinjian<sup>1,2,3\*</sup><sup>1</sup> State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao SAR 999078, China;<sup>2</sup> MoE Frontiers Science Center for Precision Oncology, University of Macau, Macao SAR 999078, China;<sup>3</sup> Department of Pharmaceutical Sciences, Faculty of Health Sciences, University of Macau, Macao SAR 999078, China

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Cancer presents a significant global challenge, impacting individuals, communities, and healthcare systems worldwide [1, 2]. Fundamentally, cancer involves the uncontrolled growth and proliferation of cells, driven by genetic and epigenetic alterations orchestrated by a complex array of molecular entities, including oncogenes, tumor suppressor genes, and various regulatory factors [3-5]. This intricate interplay complicates early detection, often resulting in a significant mortality burden. Accounting for nearly 30% of premature deaths globally, cancer is a major barrier to increasing human life expectancy [6, 7]. The urgent need for continued research, innovation, and collaborative efforts highlights the importance of combating this relentless disease.

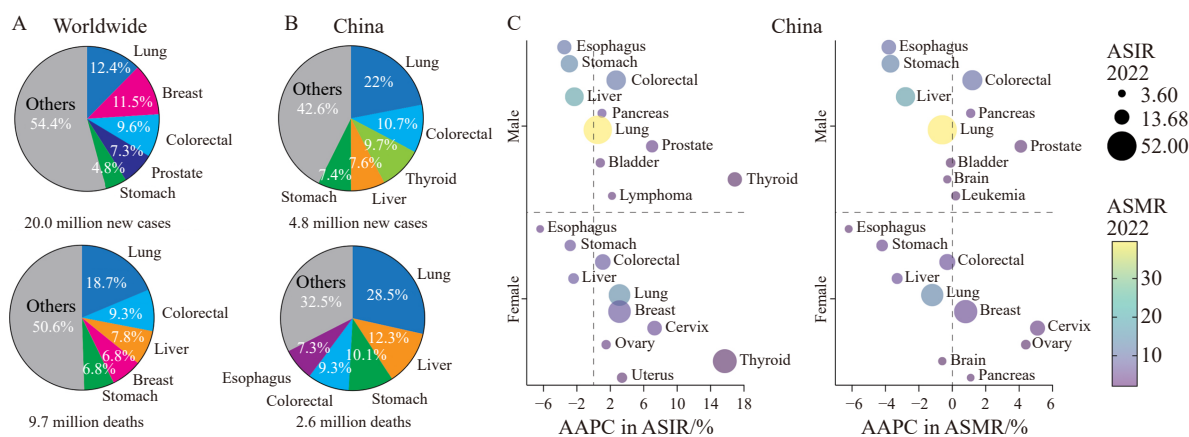
According to the latest estimates from the International Agency for Research on Cancer (IARC) in 185 countries in 2022, there were approximately 20.0 million new cases diagnosed worldwide, resulting in around 9.7 million cancer-related deaths [8]. The top five cancer types in both sexes accounted for 45.6% of newly diagnosed cases and 49.4% of cancer-related deaths. Globally, lung cancer was the most frequently diagnosed, followed by breast cancer, colorectal cancer, prostate cancer, and stomach cancer. Similarly, lung can-

cer was the leading cause of cancer mortality, followed by colorectal cancer, liver cancer, breast cancer, and stomach cancer (Fig. 1A). A recent study by HAN *et al.* based on high-quality data from 700 registries provided comprehensive data on cancer incidence and mortality rates across different regions in China, refining the cancer profile in the country [9]. Projections for 2022 indicate that China will experience over 4.8 million new cancer cases and approximately 2.6 million cancer-related deaths. These figures represent 24.0% and 26.8% of the global totals for new cancer cases and deaths, respectively. The top five cancer types in China—lung, colorectal, thyroid, liver, and stomach cancers—account for 57.4% of new cases. Meanwhile, lung, liver, stomach, colorectal, and esophageal cancers comprise 67.5% of cancer-related deaths (Fig. 1B). Notably, while breast and prostate cancers are predominant globally, thyroid and esophageal cancers are more prevalent in China. These differences in cancer prevalence and mortality between China and the global population underscore the necessity of considering regional variations in cancer epidemiology.

In 2022, the crude incidence rate and age-standardized incidence rate (ASIR) for all cancer types in China were 341.75 and 201.61 per 100 000, respectively. The crude mortality rate and age-standardized mortality rate (ASMR) for all cancers were 182.34 and 96.47 per 100 000, respectively. From 2000 to 2018, there was a notable 1.4% average annual percentage change (AAPC) increase in the ASIR for all cancers, primarily driven by a 2.6% rise in females, particularly due to increases in thyroid and cervical cancers. Conversely, during this period, the ASMR for all cancers combined decreased by approximately 1.3% annually. This overall decline was largely attributed to reductions in esophageal, stom-

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**Fig. 1** Cancer statistics and trends in China, 2022. Pie charts illustrate the distribution of new cases and deaths for the top five cancers worldwide (A) and in China (B) in 2022. (C) Bubble plots visually depict the average annual percentage change (AAPC) in age-standardized incidence rates (ASIR) and age-standardized mortality rates (ASMR) for selected cancers by sex in China. As the X-axis extends to the right, increasing trends for the selected cancers become more prominent. The size of each bubble corresponds to the ASIR in 2022, with larger bubbles indicating higher incidence rates. The color of each bubble indicates the ASMR in 2022, with yellow shading denoting higher mortality rates.

ach, and liver cancers in both males and females. However, the ASMR for prostate, colorectal, and pancreatic cancers in males, as well as cervical and ovarian cancers in females, showed increases during the same period. Notably, prostate cancer exhibited the highest annual increase at 4.1%, while cervical cancer showed a 5.1% annual increase (Fig. 1C). The study also highlights a significant rise in thyroid cancer incidence, potentially due to increased cancer awareness, improved healthcare access, and more frequent thyroid ultrasound screenings. Conversely, the rising incidence and mortality rates of prostate, cervical, and ovarian cancers, which are not currently among the top five most common cancers, underscore the critical need for enhanced screening efforts and the development of more effective treatments for these cancer types.

Despite the transformative impact of targeted therapies and immunotherapies on cancer treatment over the past decade, finding optimal and effective treatment options remains a persistent challenge<sup>[10]</sup>. Natural products, such as artemisinin, arsenic trioxide, and paclitaxel, have a well-documented history in clinical treatment. Currently, over 400 novel molecular entities derived from natural products or plants have been approved for drug therapy<sup>[11, 12]</sup>. These compounds, with their diverse structures and abundant sources, present promising candidates for combating cancer. Icarin, a flavonoid extracted from *Epimedium brevicornum* Maxim, has shown significant promise in treating solid tumors and received clinical approval for hepatocellular carcinoma treatment in China in 2022<sup>[10, 13]</sup>. Additionally, indirubin, a compound sourced from traditional Chinese medicine and notably found in Indigo Naturalis within the formula Danggui Longhui Wan, has demonstrated efficacy in treating leukemia, leading to its approval for medical use in China<sup>[14]</sup>.

To maximize the potential and efficacy of natural products in cancer therapy, it is crucial to explore several fu-

ture research directions: (1) Continued efforts are needed to discover and isolate novel compounds with unique structures and activities. For instance, bulbocodin D and bulbocodin C, two bibenzyls derived from *Pleione bulbocodioides* (Franch.) Rolfe<sup>[15]</sup>, show potential in contributing to cancer treatment. (2) Promoting clinical studies that combine natural products with conventional cancer therapies can enhance treatment efficacy and reduce side effects<sup>[16]</sup>. For example, combining ginsenoside Rh2 from ginseng with existing anticancer approaches, such as targeted therapies like everolimus<sup>[17]</sup> or immunotherapies like anti-PD-L1 antibodies<sup>[18]</sup>, has demonstrated enhanced therapeutic effects and provides valuable insights for future clinical research. (3) Exploring novel treatment modalities, such as toxic natural product-based antibody-drug conjugates<sup>[19]</sup>, bioactive natural product-based PROTACs<sup>[20]</sup>, and molecular glues<sup>[21]</sup>, may lead to groundbreaking natural product-derived medications. (4) Integrating traditional Chinese medicine with modern pharmaceutical approaches, such as using ginseng extracts (total ginsenosides) and specific ginsenoside (Rg3, CK, Rd, etc.), to develop natural product self-assembly systems for drug delivery, targeted accumulation, and efficient anticancer effects, holds significant promise for revolutionary advancements<sup>[22, 23]</sup>. (5) Strengthening research into the mechanisms of action using cutting-edge technologies, such as CRISPR-Cas9 gene editing, multiomics, and bioinformatics, will facilitate clinical translation and personalized applications of natural products in cancer therapy.

In summary, HAN's research<sup>[9]</sup> offers a comprehensive overview of current cancer statistics in China, highlighting the persistent challenges posed by lung cancer. However, it is equally important to address other cancer types, such as prostate and cervical cancer, which are exhibiting significant upward trends despite not being the most prevalent. The urgent need for effective cancer control measures underscores the

potential of natural products as a promising area for future research and clinical development.

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