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Nowcasting and forecasting global aging and cancer burden: analysis of data from the GLOBOCAN and Global Burden of Disease Study

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ABSTRACT

Objective: To analyze the impact of global population aging on cancer epidemiology, with a focus on the incidence and mortality rates among individuals aged 60 years and above.

Methods: We utilized open-source data, retrieving population age estimates from the United Nations Population Division website. The GLOBOCAN 2020 database provided estimates for cancer cases and deaths in 2020 and 2040, while the Global Burden of Disease 2019 database supplied estimates of new cancer cases worldwide from 2000 to 2019. Inclusion criteria considered individuals aged 60 years and over, focusing on the top five deadliest cancers. The cohort-component method was employed for population prediction, with age-specific incidence and mortality rates estimated for 2020 used to forecast the cancer burden.

Results: In 2021, the global population aged over 60 years accounted for 13.7%, with Europe/North America and Australia/New Zealand having the highest proportions. The older population is predicted to reach 19.2% by 2040. In 2020, of the 19.3 million new cancer cases worldwide, 64% occurred in individuals aged 60 and above, contributing to 71.3% of cancer-related deaths. The five most common cancer sites were the lung, colorectum, prostate, breast, and stomach. Cancer incidence and deaths are projected to rise significantly among older individuals, reaching 20.7 million new cases and 12.7 million deaths by 2040. Older age, tobacco use, dietary factors, alcohol consumption, and high body mass index (BMI) were identified as major risk factors for various cancers in this demographic.

Conclusions: This study reveals a significant rise in cancer incidence and mortality among the elderly due to global population aging. The urgency for targeted interventions in cancer prevention, screening, and treatment for older individuals is emphasized. Despite acknowledged limitations, these findings contribute valuable insights to inform strategies for managing cancer in the elderly amidst evolving demographic trends.

1. Introduction

According to World Population Prospects 2022 reported by the United Nations Population Division,[1] the proportion of the global population aged 60 years and above is 13.9% in 2022. The age structure of the world's population is undergoing a dramatic shift owing to the decreasing fertility rates and increasing life expectancy.[2] Global aging represents advances in public health and medicine; however, it also brings new challenges to public health, especially to cancer burden control.

Advanced age is a well-established risk factor for cancer,[3] characterized by markedly higher incidence and mortality rates in older individuals.[4,5] The lifetime probability of invasive cancer diagnosis reveals a notable age-related discrepancy. In the 60–69 years age group, the likelihood is almost fourfold higher than that in the 49 and below years age group, escalating to nearly tenfold for individuals aged 70 years and above.[5] The year 2020 witnessed a staggering 19.3 million new cancer cases and nearly 10 million cancer-related deaths globally.[6] Alarmingly, more than half of these new cases emerged among older adults, emphasizing the urgency of addressing the intricate intersection between aging and cancer.

Cancer primary prevention, aimed at reducing population exposure to cancer risk factors, represents a cost-effective strategy. The

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Global Burden of Diseases, Injuries, and Risk Factors Study in 2019 is the first comprehensive study to quantify the cancer burden attributable to a broad range of modifiable risk factors. According to the statistics, cancer deaths attributable to all estimated risk factors accounted for 44.4% of all cancer deaths, classified mainly into three categories: environmental and occupational, behavioral, and metabolic risks.[7] Notably, tobacco smoking and alcohol consumption were identified as significant contributors to global cancer mortality.[7,8] However, it is worth noting that there is currently no research focusing on the primary risk factors for elderly cancer patients. As a high-risk population for cancer, it remains unclear whether their risk of developing cancer is more attributable to all estimated risk factors and whether these risk factors differ from those of younger cancer patients.

Despite this alarming trend, limited efforts have been made by countries and regions to implement novel strategies for addressing cancer in older populations. Notably, the World Health Organization (WHO) and the United Nations (UN) established a comprehensive 10-year global action plan in 2020, aiming to ensure a long and healthy life for older individuals.[9] Some nations have also introduced pertinent policies for preventing and treating cancer in the elderly.[10,11] However, the current understanding of the impact and challenges posed by aging on cancer remains insufficient and has not garnered adequate attention.[12,13]

Global aging will further increase the cancer burden, and the intersection of cancer and aging is an emerging global public health challenge. By understanding the impact of population aging on cancer epidemiology, we can formulate better cancer prevention and screening strategies, effectively reduce cancer mortality, and improve the quality of life of older people with cancer. The cohort-component method was utilized to predict population dynamics, incorporating age-specific incidence and mortality rates estimated for 2020 to project the cancer burden. Additionally, we aimed to speculate on the primary risk factors and predict the future trends in cancer incidence and corresponding mortality among the elderly.

2. Materials and methods

2.1. Data sources

We used open-source data from the 2022 Revision of World Population Prospects released by the United Nations (UN) Population Division, GLOBOCAN 2020 statistics released by the International Agency for Research on Cancer, and the Global Burden of Disease (GBD 2019) database released by the Institute for Health Metrics and Evaluation.

The World Population Prospects was collected from primary sources through civil registration and vital statistics systems, population censuses, population registers, and household surveys, whereas GLOBOCAN 2020 and GBD 2019 were modeled. The 2022 Revision of World Population Prospects was based on information from 1758 population and housing censuses for 237 countries or areas. The GLOBOCAN project provided estimates for 2020 on the incidence, mortality, and prevalence of 36 specific types and of all cancer, across 185 countries or regions globally, categorized by sex and age group. The GBD calculated mortality, years of life lost (YLLs) and disability-adjusted life years (DALYs) for 87 risk factors and combinations of risk factors for 204 countries and territories. The corresponding proportion of the older population estimates from 2021 to 2040 was downloaded from the UN website by sex and age. We extracted estimates of cancer cases and deaths for 34 cancer types (including all cancers combined) in 2020 from the GLOBOCAN 2020 database and estimated new cases and deaths of people with cancer aged ≥60 years for the top 5 deadliest cancers in 2040. We collected year-, region-, and age-specific estimates of new cancer cases worldwide between 2000 and 2019 from the GBD 2019 database. We also collected the proportion of risk factors for DALYs by age and cancer type in 2019. DALYs were a crucial measure in public health and epidemiology, as they provide a comprehensive view of the overall disease burden. DALYs were defined as the sum of years lost due to premature death and years lived with disability (YLDs), which were also defined as years of healthy life lost. We acknowledged and consented to the terms set by Institute for Health Metrics and Evaluation (IHME) in their Free-of-Charge Non-Commercial User Agreement.

2.2. Inclusion and exclusion criteria of the selected datasets

The 2022 Revision of World Population Prospects used the latest census or registry data, projected to 2022 with updated information on birth rates, death rates, and international migration petterns. These data (https://population.un.org/wpp/Methodology/) were rigorously checked and adjusted for accuracy and consistency. GLOBOCAN 2020 published cancer incidence and mortality in 185 countries or territories of the world in 2020. These estimates were derived from the latest data obtained through collaborations with cancer registries, the WHO, or from online public sources. Institute for Health Metrics and Evaluation collected data from surveys, censuses, and other methods worldwide. They acquired the dataset either by downloading it from public sources or through agreements with the data collectors. This individual data was then transformed into regional estimates and published as research projects like the GBD. We included data by selecting variables in these datasets based on demand. The website of World Population Prospects 2022 offers the option of downloading population by age and sex directly. The Global Cancer Observatory website has modules such as CANCER TODAY or CANCER TOMORROW with the option to download 2020 and 2040 cancer data. We can download Global Burden of Disease Results by choosing ‘Measure’, ‘Metric’, ‘Cause’, ‘Location’, ‘Age’, ‘Sex’, ‘Year’ option on GBD Results website. We searched these dataset from 6th October to 28th November in 2022.

2.3. Definitions

People aged 60 years and over are defined as older adults in this study, as endorsed by WHO, and allowed for comparability with other studies on cancer in older adults. Population aging is when the population over 60 years accounts for no less than 10% of the total population in a country or region. We defined tumors with the top five estimated deaths as the five major cancer types. Finally, we defined the income level of each region using the World Bank country classification.

2.4. Statistical analysis

We used population data estimated from the results of 1758 national population censuses conducted between 1950 and 2022 and information from vital registration systems, and 2890 nationally representative sample surveys. The population was assessed based on data from 237 countries or areas underpinned by analyses of historical demographic trends. The DALYs rates were calculated as the sum of years of life lived with disability and years of life lost. Cancer prediction was based on estimates of the incidence, mortality, and prevalence of 36 specific cancer types and all cancer sites combined in 185 countries or territories of the world in 2020, by sex and age group, as part of the GLOBOCAN project. We utilized the cohort-component method to project the population, employing age-specific incidence and mortality rates estimated for 2020 to calculate the expected population for the years 2025–2040. Specific statistical methods can be found at https://population.un.org/wpp/Download/ Standard/Population/ and https://gco.iarc.fr. Analyses were performed using R software (version 4.2.1 R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/).

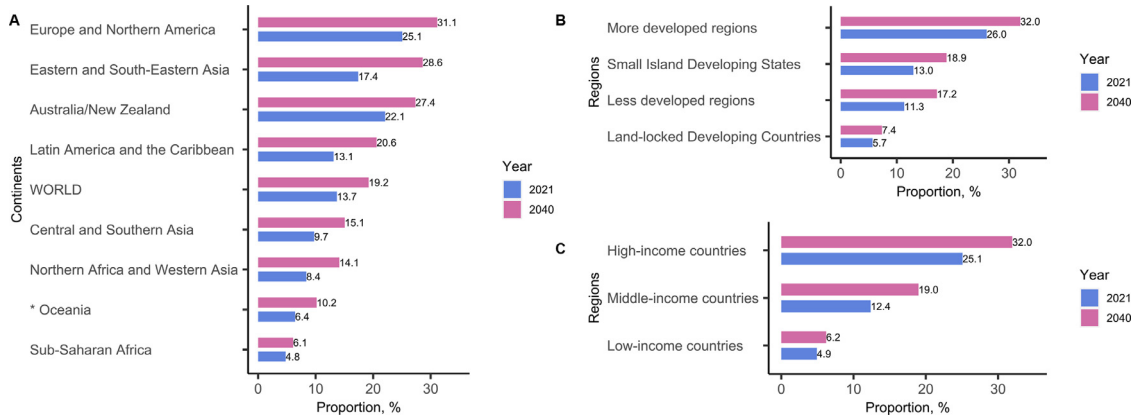

Fig. 1. Proportion of the older population in different continents developed and developing countries, and countries with varying income levels in 2021 and 2040. (A) Proportion of older population in different continents. (B) Proportion of older population in developed and developing countries. (C) Proportion of older population in countries with varying income levels.*, Oceania excluding Australia and New Zealand; less-developed regions excluding China.

3. Results

3.1. Aging population in the world

In 2021, the global population aged over 65 and 60 years reached 761,272,597 and 1,083,211,047, respectively. Those aged ≥60 years accounted for 13.7% of the total population. Europe/North America and Australia/New Zealand had the highest proportions of older people, at 25.1% and 22.1%, respectively (Fig. 1A), followed by Eastern and South-Eastern Asia (17.4%), Latin America and the Caribbean (13.1%), Central and Southern Asia (9.7%), and Northern Africa and Western Asia (8.4%). Sub-Saharan Africa and Oceania (excluding Australia and New Zealand) had the lowest proportions of older people, at 4.8% and 6.4%, respectively. Concerning the degree of economic development, the more developed regions had the highest proportion of older adults (26.0%), whereas the land-locked developing countries (LLDC) had the lowest proportion (5.7%) (Fig. 1B). Similarly, high-income countries/regions had the highest proportion of older adults (25.1%), whereas the proportion of older people in middle-income and low-income countries was 12.4% and 4.9%, respectively (Fig. 1C).

In 2021, the UN Population Division assessed the population of different age groups in 236 countries/regions, among which 138 (58.5%) countries/regions met the aging criteria (Supplementary Table 1). In addition, 132 (55.9%) countries/regions had more than 7% of their population aged ≥65 year (Supplementary Table 1). The older population in Italy, Japan, Monaco, and Saint Helena accounted for more than 30% of their total population.

It is predicted that by 2040, the number of older adults will reach 1,766,075,374, accounting for 19.2% of the global population. The number of countries/regions globally meeting the aging criteria will increase to 180 (Supplementary Table 1). Additionally, the number of countries/regions with an older population ratio of more than 30% will reach 63, with Japan (42.5%) and Hong Kong of China (42.4%) having the highest proportion. Similarly, the older population in more developed and less developed regions will increase to 32.0% and 17.2% of the total population, respectively. The proportion of the older population in LLDC will increase to 7.4%, and in low-income countries, it will increase to 6.2%.

3.2. New cancer cases and deaths in older people in 2020

In 2020, the number of new cancer cases worldwide was 19,292,789, with 9,958,133 deaths (Table 1). In total, 12,355,723 older adults were newly diagnosed with cancer, accounting for 64.0% of the new cancer cases. A total of 7,096,380 older adults died from cancer, accounting for 71.3% of new cancer deaths. The five most common cancer sites were the lung, colorectum, prostate, breast, and stomach. Lung, colorectum, stomach, liver, and breast malignancies were the top five causes of cancer-related deaths. Of these, 1,420,411 older adults died of lung cancer.

We used the five cancers that caused the most deaths to analyze the relationship between population aging, cancer incidence and deaths in the older population. Trends in the incidence of all cancers and five major cancer types in the different age groups are shown in Fig. 2. We observed that the number of people with cancer in all age groups has gradually increased in recent years. Moreover, there was a spike in cancer incidence in people aged ≥60 years compared with the other age groups. For example, from 2005 to 2019, the incidence of liver cancer in people aged ≥60 years significantly increased.

Fig. 3 showed the changing trend in the proportion of people ≥60 years affected with all cancers and the five major cancer types and that of people aged ≥60 years in the world. The global population aged ≥60 years is consistent with the growing trend of people with cancer for all five major cancer types. Moreover, compared with that for other cancers, the growth speed of older people with liver cancer has gradually slowed down.

3.3. Ranking of risk factors for cancer by age group

The ranking of absolute deaths due to various causes by age in 2019 is presented in Fig. 4. Cancer ranked 2nd in absolute deaths of all causes in all age groups and higher among all causes of death with increasing age (11th at 0–20, 5th at 30–34, and 2nd at 35–89 years). The same trend was observed for absolute deaths in 2018 and absolute DALYs in 2019 (Supplementary Figs. 1–2).

The proportions of the five major cancer types by DALYs, attributable to the risk factors for cancer in 2019 between all ages and the 60–89 years age group, are shown in Fig. 5. The proportion of risk factors for the five major cancers was slightly higher in the 60–89 years age group than in all age groups. For patients in the 60–89 years age group, tobacco was a common factor associated with all five major cancer types; it was the leading risk factor for DALYs in people with lung cancer of different sexes (80% for men, 47% for women). Dietary risk contributed the most to DALYs in elderly colon and rectum cancer patients (34% for men, 33% for women). Alcohol use, covering 14% of DALYs, was the main risk factor in women with liver cancer, whereas tobacco and alcohol use were the main risk factors for liver cancer patients in men, covering 26% of DALYs. The risk factor of high BMI contributed 14% and 10% to the DALYs of men and women patients with liver cancer, respectively. Tobacco was the main risk factor in male patients with stomach cancer, explaining 28% of DALYs. High BMI was a major risk factor for female breast cancer, explaining 10% of DALYs.

Table 1
Estimated new cancer cases and deaths of elderly cancer patients in 2020.

ICD	Cancer site*	Estimated new cases			Estimated deaths		
		Number	Crude rate	ASR	Number	Crude rate	ASR
C00-97	All cancers	12,355,723	1177	1105	7,096,380	676	619.1
C33-34	Lung	1,683,169	160.3	151.3	1,420,411	135.3	126.1
C18-21	Colorectum	1,403,008	133.7	123.9	748,192	71.3	62.7
C16	Stomach	786,013	74.9	70.1	577,278	55	50.8
C22	Liver	564,754	53.8	51.4	527,317	50.2	47.7
C50	Breast	1,027,785	181.7	178.8	402,255	71.1	65.2
C15	Oesophagus	422,376	40.2	38.9	395,505	37.7	35.7
C25	Pancreas	396,844	37.8	34.2	380,747	36.3	32.6
C61	Prostate	1,216,139	251.3	240.6	358,301	74	66.7
C67	Bladder	464,119	44.2	40	189,059	18	15.2
C82-86, C96	Non-Hodgkin lymphoma	320,446	30.5	28.5	176,809	16.8	15.1
C91-95	Leukaemia	231,937	22.1	20.4	176,342	16.8	15.1
C53	Cervix uteri	194,195	34.3	35.1	157,641	27.9	27.8
C64-65	Kidney	268,220	25.6	24.4	135,931	12.9	11.7
C70-72	Brain, central nervous system	137,654	13.1	12.7	130,822	12.5	12
C56	Ovary	148,463	26.2	25.6	127,217	22.5	21.5
C88+C90	Multiple myeloma	131,152	12.5	11.6	94,233	9	8.1
C00-06	Lip, oral cavity	193,855	18.5	18.1	94,087	9	8.7
C54	Corpus uteri	232,489	41.1	41.3	73,699	13	11.9
C32	Larynx	118,113	11.3	11.2	70,769	6.7	6.5
C23	Gallbladder	84,374	8	7.3	62,555	6	5.4
C43	Melanoma of skin	202,174	19.3	17.8	41,857	4	3.5
C11	Nasopharynx	45,327	4.3	4.4	37,654	3.6	3.6
C73	Thyroid	166,921	15.9	16.2	33,282	3.2	2.8
C09-10	Oropharynx	53,764	5.1	5.2	29,422	2.8	2.8
C12-13	Hypopharynx	49,150	4.7	4.7	24,718	2.4	2.3
C45	Mesothelioma	24,682	2.4	2.1	22,003	2.1	1.8
C07-08	Salivary glands	29,225	2.8	2.6	15,550	1.5	1.4
C51	Vulva	31,495	5.6	4.9	13,688	2.4	2
C81	Hodgkin lymphoma	22,323	2.1	2	10,841	1	1
C60	Penis	22,427	4.6	4.5	8359	1.7	1.6
C52	Vagina	10,950	1.9	1.8	5236	0.9	0.8
C62	Testis	6552	1.4	1.3	2582	0.5	0.5
C46	Kaposi sarcoma	6937	0.7	0.6	2535	0.2	0.2

* The order of the cancer sites is sorted by the number of deaths from the most to the least.
Abbreviations: ASR, age-standardized rate; ICD, International Classification of Diseases.

3.4. Proportion of older cancer patients by income level

The proportion of people ≥60 years with cancer increased gradually from 2000 to 2019 worldwide. The proportion of colorectal cancer patients over ≥60 years has grown more slowly than that of patients over ≥60 years with other cancer types. Lung cancer has accounted for the highest proportion of people ≥60 years with cancer since 2003. From 2000 to 2019, the proportion of breast cancer patients ≥60 years was the lowest among the five cancers that caused the most deaths. The proportion of people ≥60 years with cancer was significantly higher in high-income countries than that in low-income countries. Furthermore, the proportion of people with cancer aged ≥60 years in high-income countries has increased significantly since 2005, whereas that of patients over ≥60 years in low-income countries has stabilized or even decreased from 2000 to 2019. The same trend remained consistent across different cancer types (Fig. 6).

3.5. Estimated new cases and deaths of older people with cancer in 2040

The cancer incidence among older people is expected to increase from 12.4 million in 2020 to 20.7 million in 2040 (Fig. 7A). Moreover, an estimated 12.7 million older adults will die of cancer in 2040, a 78.9% increase from 2020 (Fig. 7B).

By 2040, older people with tracheal, bronchial, and lung cancer will have the highest number of new cases, followed by colorectal, prostate, gastric, breast, liver, and esophageal cancers. New cases and deaths from tracheal, bronchial, lung, breast, liver, intrahepatic bile duct, stomach, colorectal, esophageal, and prostate cancers will significantly increase from 2020 to 2040 (Figs. 7C and D). The number of new tracheal, bronchial, and lung cancer cases will reach 2.9 million, an increase of 71.2%, by 2040.

4. Discussion

We analyzed the magnitude and relevance of global population aging and cancer burden for the older population from demographic and epidemiological perspectives. Our analysis of population aging and cancer burden in the older population was based on the latest data from the UN Population Division, GLOBOCAN, and Global Burden of Disease (GBD) databases. To the best of our knowledge, this is the first analysis to provide an in-depth view of the current state and future challenges of global aging and cancer as a crosscutting public health issue. Our research findings revealed that, at present and even in the next two decades, the increasing trends in the global incidence and mortality of cancer are primarily attributed to the elderly population.

With substantial improvements in health care and advances in pharmaceutical research,[14,15] the average life expectancy increased to 73.5 years in 2019.[2] Mortality rates among older adults are falling rapidly,[16] and life expectancy will continue to increase in most countries.[17] By 2030, there is a 50% probability that women will live beyond 90 years.[17] In addition, the global total fertility rate fell from 2.72 in 2000 to 2.31 in 2019.[2] In 2019, people older than 65 years outnumbered children under 5 years of age for the first time in human history.[1] It is estimated that by 2050, the proportion of older adults will be more than double that of children under the age of 5 years.[1] The global population is aging quickly. More than 1083 million people are aged 60 years and above, accounting for 13.7% of the global population. In economically developed Europe and North America, a quarter of the population is aged 60

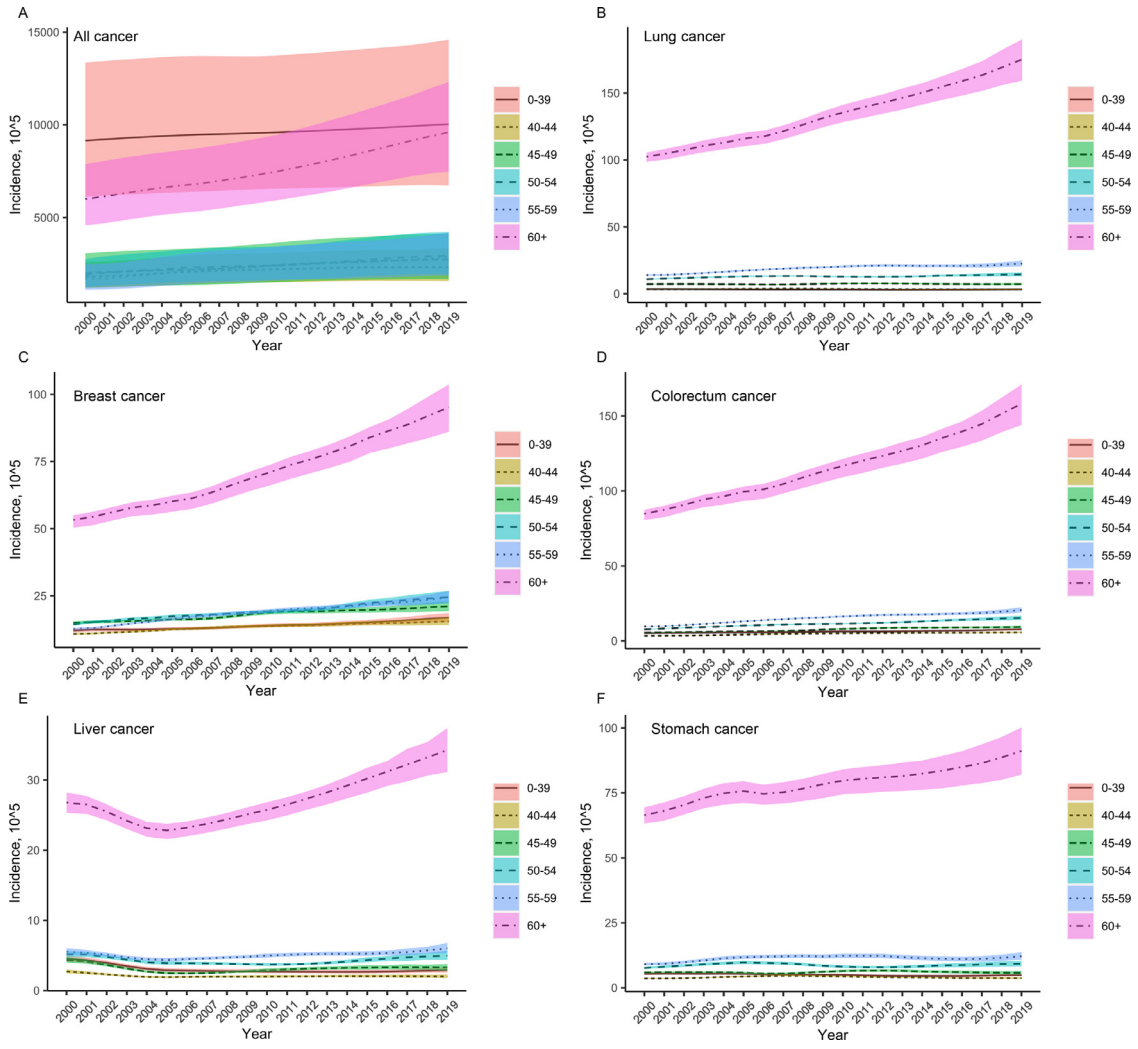

Fig. 2. Trend of cancer incidence in different age groups and the top five cancer types. (A) Incidence trends of all cancer types across different age groups. (B) Incidence trends of lung cancer across different age groups. (C) Incidence trends of Breast Cancer across different age groups. (D) Incidence trends of colorectal cancer across different age groups. (E) Incidence trends of liver cancer across different age groups. (F) Incidence trends of stomach cancer across different age groups.

years and above. Moreover, this phenomenon has not reached its peak, but will intensify. Although population aging has started in high-income countries, low- and middle-income countries are also transitioning towards aging. For example, the proportion of the older population in the Lao People's Democratic Republic was 6.9% in 2020, but it will exceed to 10% in 2040. Similarly, low- and middle-income countries such as Kyrgyzstan, Egypt, and Honduras will also enter the ranks of aging countries in 2040.

With the popularization of tumor etiology research and screening, the rate of early cancer diagnosis and effective treatment has significantly improved, along with the 5-year survival rate.[18] However, the 2019 Global Burden of Disease Study showed that over the past decade, the number of new cancer cases has increased by 26.3%, and the number of deaths has increased by 20.9%.[19] From our analysis, we observed that the increase in cancer incidence and deaths is mainly attributable to cancer in older adults. More than half of the newly diagnosed people with cancer in 2021 were aged 60 years and above, and nearly three-quarters of the deaths occurred in older adults. Except for liver cancer, the incidence of other cancers (including lung, breast, colorectal, and gastric cancers) continues to increase in older adults. The incidence of liver cancer showed a trend of first decreasing and then increasing, which may be attributed to the fact that the global coverage of the hepatitis B vaccine has reduced the risk of liver cancer.[20,21]

Population aging is a primary factor contributing to the current increase in new cancer cases and new death cases. The aging population will further exacerbate the incidence and mortality of cancer among the elderly, especially in low- and middle-income countries. To alleviate the global burden of cancer, the reduction of both the incidence and mortality of cancer in the elderly should be set as a priority.

Cancer can occur at any age; however, the incidence of most cancers increases markedly in the older population.[5] Factors such as poor lifestyle choices, exposure to air pollution, and engagement in occupations with carcinogenic risks contribute to prolonged exposure to risk factors among older adults, potentially increasing their susceptibility to cancer development. In light of these considerations, our study aimed to delve into the specific risk exposure factors that contribute to the elevated incidence of cancer in the elderly, with the ultimate goal of formulating targeted intervention measures. It is worth highlighting that the 60–89 years age group exhibited a slightly higher prevalence of the five major cancer risk factors compared to all age groups combined. This observation underscores the notion that the elevated cancer incidence in the older population is, in part, attributable to the cumulative impact of multiple risk factors.[22] Tobacco use and dietary choices emerge as prominent contributors to cancer-related mortality, with lung cancer in older men being notably influenced by tobacco consumption, followed by air pollution, occupational hazards, and dietary factors in descend-

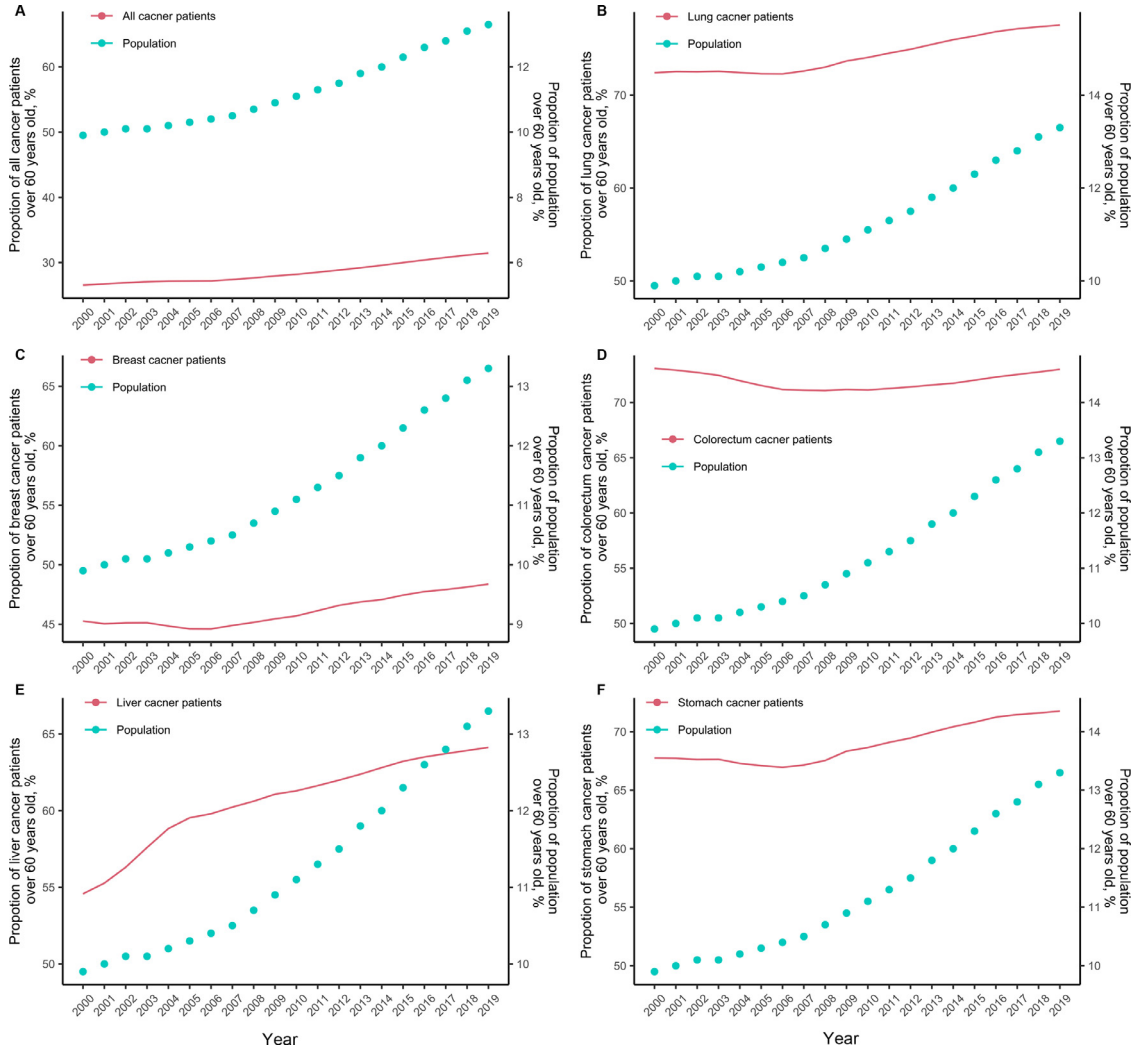

Fig. 3. Comparison between the proportion of people with cancer and the world population aged ≥60 years. (A-F) Comparative analysis the prevalence of all cancers (A), lung cancers (B), breast cancers (C), colorectum cancers (D), liver cancers (E), stomach cancers (F) in people aged 60 years or older versus the global population.

	Absolute deaths (95% CI)	All age rank	<20 rank	20-24 rank	25-29 rank	30-34 rank	35-39 rank	40-44 rank	45-49 rank	50-54 rank	55-59 rank	60-89 rank
Cardiovascular diseases	18562510 (17079965 - 19721374)	1	14	5	3	2	1	1	1	1	1	1
Cancers	**10079637 (9412881 - 10661852)**	**2**	**11**	**6**	**7**	**5**	**2**	**2**	**2**	**2**	**2**	**2**
Chronic respiratory diseases	3974315 (3581757 - 4303823)	3	17	17	17	16	13	11	10	6	6	3
Respiratory infections and tuberculosis	3683098 (3382547 - 4011672)	4	2	4	4	6	6	5	4	5	5	5
Diabetes and kidney diseases	2988924 (2772621 - 3183100)	5	15	13	11	10	9	9	6	4	4	4
Digestive diseases	2557689 (2389929 - 2716340)	6	13	10	8	8	7	4	3	3	3	7
Neurological disorders	2221323 (1027903 - 4759829)	7	16	16	16	17	17	17	16	15	12	6
Maternal and neonatal disorders	2078910 (1783925 - 2451711)	8	1	7	9	9	10	13	17	20	NA	NA
Unintentional injuries	1774600 (1546391 - 1947532)	9	7	3	6	7	8	8	9	8	7	8
Enteric infections	1748251 (1286411 - 2416192)	10	3	9	10	12	12	12	12	11	11	9
Transport injuries	1278879 (1130883 - 1392622)	11	9	2	2	3	5	7	7	7	8	11
Self-harm and interpersonal violence	1245962 (1160945 - 1330179)	12	10	1	1	1	4	6	8	9	9	12
Other non-communicable diseases	1137247 (1008396 - 1297377)	13	4	14	14	15	16	15	14	14	14	10
HIV/AIDS and sexually transmitted infections	953728 (849269 - 1108382)	14	8	8	5	4	3	3	5	10	10	17
Neglected tropical diseases and malaria	747344 (406562 - 1247138)	15	5	11	13	13	14	14	13	13	15	14
Other infectious diseases	730486 (605256 - 904684)	16	6	12	15	14	15	16	15	16	16	13
Substance use disorders	296097 (273032 - 311105)	17	19	15	12	11	11	10	11	12	13	18
Nutritional deficiencies	251577 (221150 - 289040)	18	12	18	18	18	18	19	19	18	17	15
Musculoskeletal disorders	117543 (94835 - 136051)	19	20	19	19	19	19	18	18	17	18	16
Skin and subcutaneous diseases	98522 (75116 - 123949)	20	18	20	20	20	20	20	20	19	19	19
Mental disorders	318 (286 - 386)	21	21	21	21	21	21	21	21	NA	NA	NA

Fig. 4. Ranking of absolute deaths due to cancer compared to other causes by age group in 2019. CI, confidence interval; NA, not available.

ing order of significance. No significant differences were reported in the risk factors among all age groups and older people with cancer for colorectal, liver, and gastric cancers. Dietary risk is the leading cause of colorectal cancer, and alcohol consumption and high BMI are the main causes of liver cancer. These findings align with the primary risk factors for colorectal and liver cancers across all age groups.[7,8]

Although hepatitis B vaccination reduces the incidence of liver cancer, the risk from alcohol consumption is still steadily increasing. Among older women with breast cancer, the proportion of those with a high BMI was significantly higher than that in all age groups. Numerous studies have consistently shown that a higher BMI is not only linked to an increased risk of breast cancer but also associated with worse clinical

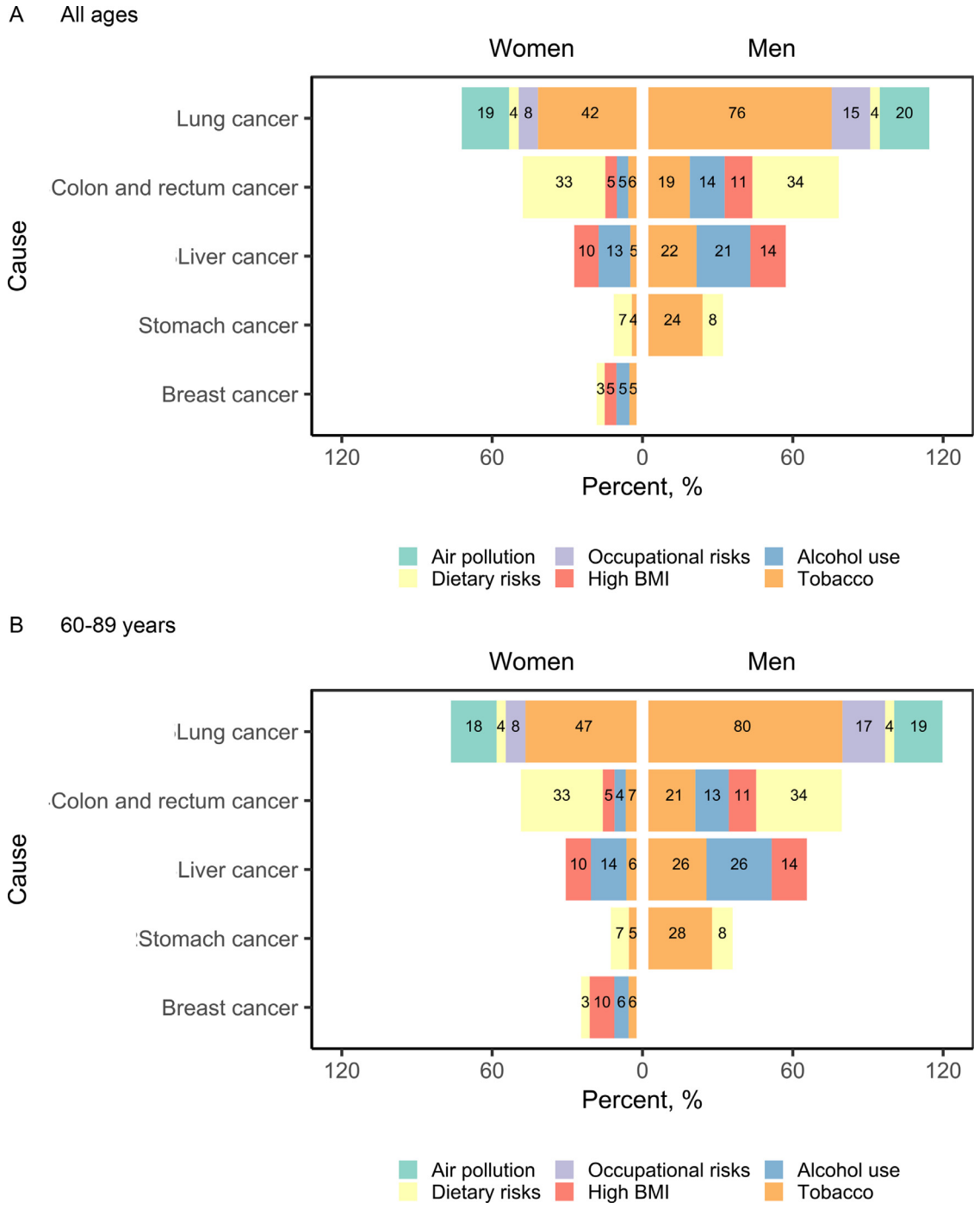

Fig. 5. Comparison of the proportion of risk factors among all age groups (A) and the 60–89 years-age group (B) by cancer type in the world in 2019. BMI, body mass index.

prognosis.[23,24] This emphasizes the importance of considering lifestyle factors in understanding cancer risks in older populations. Primary prevention strategies play a pivotal role in mitigating the cancer burden in older adults. Encouraging healthy lifestyle choices, implementing environmental interventions, expanding vaccine coverage, and making ecological improvements collectively contribute to a comprehensive approach in reducing cancer incidence among the elderly.[25] However, risk factors such as smoking, alcohol consumption, and high BMI are not the primary drivers of the increased incidence of cancer in the elderly, at least not observed significantly different from non-elderly cancers. This observation leads us to speculate that advanced age itself may serve as a crucial risk factor for cancer development. Although the intricate interplay between these two processes remains elusive, the mechanisms underlying the aging-cancer relationship have been identified.[26] Age exerts influence on the quantity of somatic mutations in tumor cells, with a consistent mutation rate of 0.077 mutations per megabase per year, contributing to the evolution of cancer cells over time.[27] The occurrence and development of cancer involve long-term processes marked by the continuous accumulation of pathogenic somatic mutations, transitioning from quantitative to qualitative changes.[28] Research by Shah et al. sheds light on the dysregulated molecular aging phenotype observed in tumors of younger individuals, which is associated with hallmarks

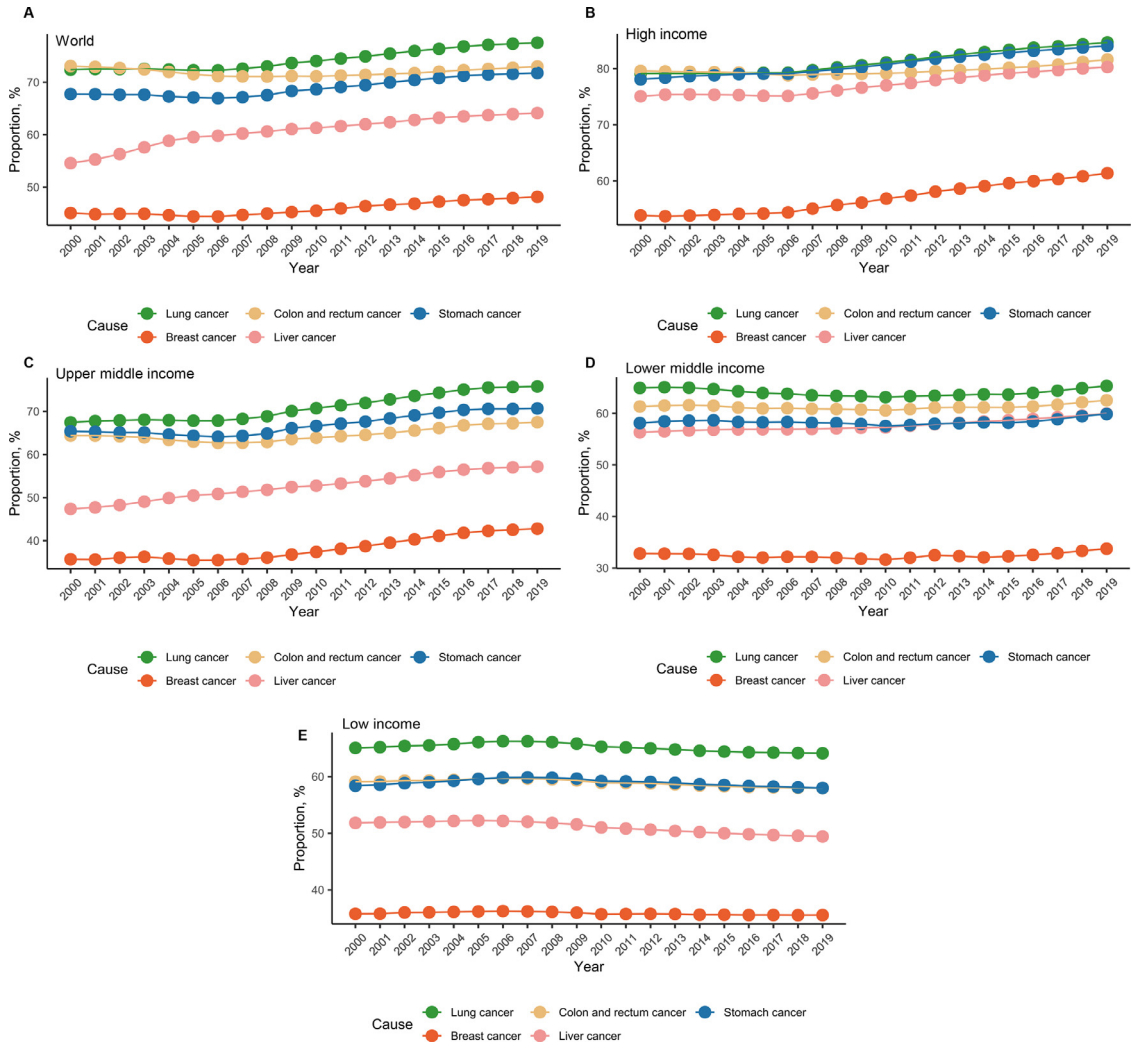

Fig. 6. Proportion of cancer incidence in people above 60 years in the world and regions with different income levels. (A) Cancer incidence rates among individuals above 60 years in worldwide. (B) Cancer incidence rates among individuals above 60 years in regions with high income levels. (C) Cancer incidence rates among individuals above 60 years in regions with upper middle income levels. (D) Cancer incidence rates among individuals above 60 years in regions with lower middle income. (E) Cancer incidence rates among individuals above 60 years in regions with low income.

of premature senescence.[29] Additionally, the immune function of older adults is weakened, leading to a reduction in immune-infiltrating cells in the tumor microenvironment, which is associated with an unfavorable prognosis for cancer.[29,30] In summary, the increased susceptibility to cancer among the elderly is attributed to factors such as advanced age, compromised immune function associated with aging, and the accumulation of detrimental pathological changes.

Population aging slows global economic growth, especially in developed countries, and contributes to the shrinkage of the working population. In addition, global aging will substantially increase the number of people with complex care needs.[31] Therefore, governments in various countries and regions must make economic and social adjustments to address the impact of population aging.[32] Society and medical institutions should pay more attention to the older population, especially in cancer screening, treatment, and care of older people with cancer.[13,33] A wealth of evidence supports the utilization of selected cancer screening techniques as a method for controlling cancer in middle-aged and elderly populations. The target population for screening is progressively transitioning from high-risk groups to the general population. Most older people have other health problems that affect the choice of surgery, treatment regimens, and their eligibility to participate in clinical trials.[34] Cardiovascular disease is the leading cause of death for all ages, followed by cancer and chronic respiratory diseases. Additionally, many age-related diseases, including chronic organ and oral health damage caused by aging, further contribute to an increased risk of cancer. For instance, conditions such as periodontitis and oral diseases can elevate the low chronic burden in the development of oral cancer.[35,36]

While leveraging data from reputable sources such as the UN Population Division, GLOBOCAN, and GBD databases, this study is not without limitations. Firstly, the reliance on available data introduces potential reporting variations across regions. Additionally, the analysis, primarily focused on overarching trends and associations, may overlook specific nuances in individual cases or regional disparities. The study's depth is further constrained by a lack of exploration into additional potential factors, such as genetic predisposition or regional variations in healthcare quality, limiting a more nuanced understanding of the subject.

In conclusion, this is the first study designed to provide a global estimate of the impact of population aging on cancer incidence and mortality. The urgency for targeted interventions in cancer prevention, screening, and treatment for older individuals is underscored. However, acknowledging the limitations, especially regarding data constraints and a lack of exploration into certain influencing factors, emphasizes

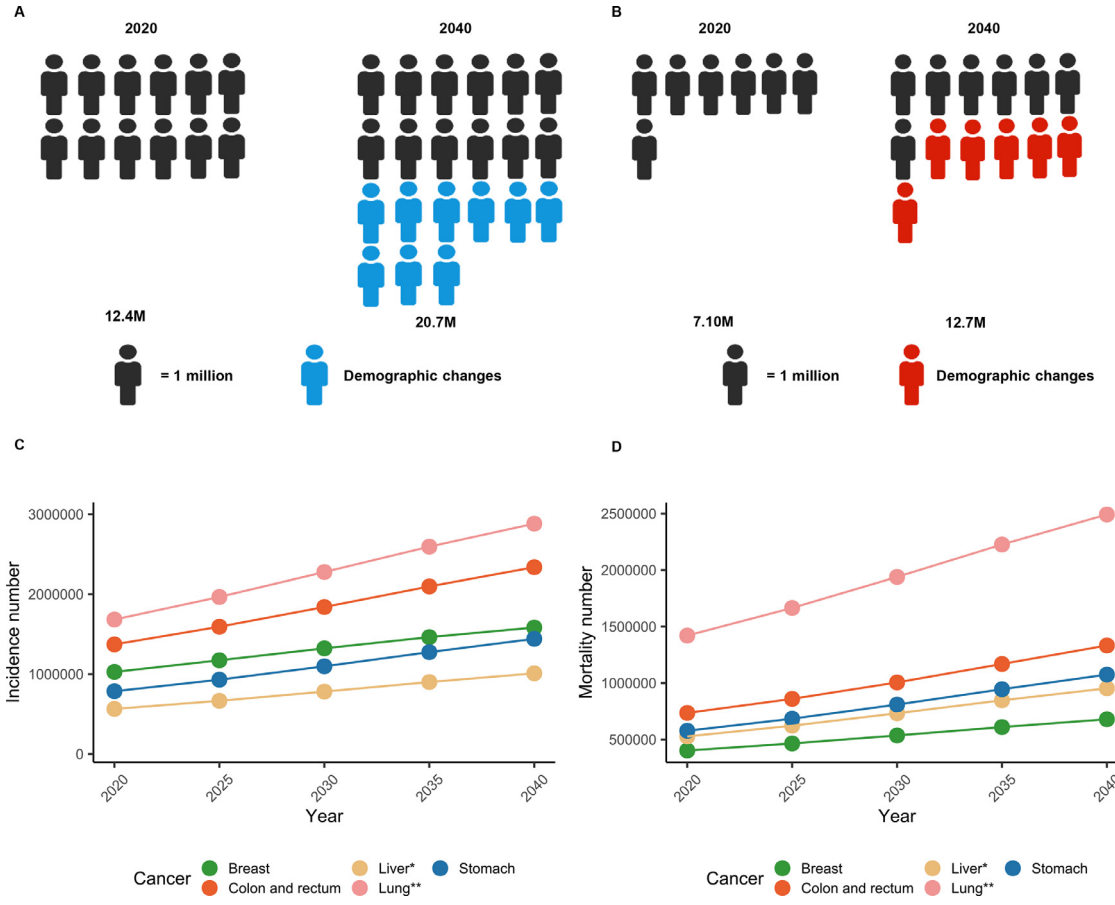

Fig. 7. Estimated new cases and deaths of older people with cancer in 2040. (A) Visualization of estimated cancer incidence among the elderly in 2020 and 2040. (B) Visualization of estimated cancer-related deaths among the elderly in 2020 and 2040. (C) Estimated new cases of older people with cancer in 2040. (D) Estimated deaths of older people with cancer in 2040. M, million. *, lung cancer included trachea, bronchus, and lung cancer; **, liver cancer included liver and intrahepatic bile ducts cancer.

the need for further research. These findings contribute to shaping more comprehensive and precise strategies for managing cancer in the elderly, ensuring adaptability to the evolving demographic landscape.

Declarations of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

L.L. and F.M. completed conceptualization. T.S. and D.Z were responsible for data curation. L.L., T.S. and D.Z. handled fornal analysis. L.L. and T.S. conducted investigation. L.L., T.S. and D.Z. contributed to methodology. F.M. provided funding acquisition and managed project administration. T.S. and L.L. worked on software. L.L. and F.M. provided supervision. L.L. and T.S. conducted validation. L.L., T.S. and D.Z. handled visualization. L.L., T.S. and D.Z. were responsible for writing-original draft. L.L. and F.M. contributed to writing-review & editing.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jncc.2024.05.002.

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