The global landscape of esophageal squamous cell carcinoma and esophageal adenocarcinoma incidence and mortality in 2020 and projections to 2040: New estimates from GLOBOCAN 2020

Morgan, E., Soerjomataram, I., Rumgay, H., Coleman, H. G., Thrift, A. P., Vignat, J., Laversanne, M., Ferlay, J., & Arnold, M. (2022). The global landscape of esophageal squamous cell carcinoma and esophageal adenocarcinoma incidence and mortality in 2020 and projections to 2040: New estimates from GLOBOCAN 2020. *Gastroenterology*, *163*(3), 649-658. https://doi.org/10.1053/j.gastro.2022.05.054

Published in:
Gastroenterology

Document Version:
Publisher's PDF, also known as Version of record

The Global Landscape of Esophageal Squamous Cell Carcinoma and Esophageal Adenocarcinoma Incidence and Mortality in 2020 and Projections to 2040: New Estimates From GLOBOCAN 2020

Eileen Morgan,[1] Isabelle Soerjomataram,[1] Harriet Rumgay,[1] Helen G. Coleman,[2,3] Aaron P. Thrift,[4,5] Jérôme Vignat,[1] Mathieu Laversanne,[1] Jacques Ferlay,[1] and Melina Arnold[1]

[1]*Cancer Surveillance Branch, International Agency for Research on Cancer, Lyon, France;* [2]*The Patrick G. Johnston Centre for Cancer Research, Queen's University Belfast, Belfast, UK;* [3]*Centre for Public Health, Queen's University Belfast, Belfast, UK;* [4]*Section of Epidemiology and Population Sciences, Department of Medicine, Baylor College of Medicine, Houston, Texas; and* [5]*Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine, Houston, Texas*

BACKGROUND & AIMS: The aim of this study was to provide an overview of the burden of esophageal cancer in 185 countries in 2020 and projections for the year 2040. **METHODS:** Estimates of esophageal cancer cases and deaths were extracted from the GLOBOCAN database for 2020. Age-standardized incidence and mortality rates were calculated overall, by sex, histologic subtype (adenocarcinoma [AC] and squamous cell carcinoma [SCC]), country, and level of human development for 185 countries. The predicted burden of incidence and mortality in 2040 was calculated based on global demographic projections. **RESULTS:** Globally, there were an estimated 604,100 new cases of, and 544,100 deaths from, esophageal cancer in 2020, corresponding to age-standardized incidence and mortality rates of 6.3 and 5.6 per 100,000, respectively. Most cases were SCCs (85% [512,500 cases]) and 14% (85,700 cases) were ACs. Incidence and mortality rates were 2- to 3-fold higher in male (9.3 and 8.2, respectively) compared with female (3.6 and 3.2, respectively) individuals. Global variations in incidence and mortality were observed across countries and world regions; the highest rates occurred in Eastern Asia and Southern and Eastern Africa and the lowest occurred in Western Africa and Central America regions. If rates remain stable, 957,000 new cases (141,300 AC cases and 806,000 SCC cases) and 880,000 deaths from esophageal cancer are expected in 2040. **CONCLUSIONS:** These updated estimates of the global burden of esophageal cancer represent an important baseline for setting priorities in policy making and developing and accelerating cancer control initiatives to reduce the current and projected burden. Although primary prevention remains key, screening and early detection represent important components of esophageal cancer control in high-risk populations.

Keywords: Esophageal Cancer; Epidemiology; Cancer Prevention.

Esophageal cancer is the eighth most commonly diagnosed cancer and the sixth most common cause of cancer death in the world.[1] Its burden varies greatly across countries and populations, which been linked to differences in the prevalence of underlying risk factors and the distribution of subtypes. Survival from esophageal cancer remains low, in the range of 10%–30% at 5 years post diagnosis in most countries.[2] Recent analyses from high-income countries indicated that although progress has been made over the past 20 years, the 5-year survival rate peaked at 24%[3] in Australia for patients diagnosed during 2010–2014 and at 36% in Japan.[2]

Esophageal cancer can be categorized by 2 main histologic subtypes; adenocarcinoma (AC) and squamous cell carcinoma (SCC), and distinct risk factors have been recognized for these diseases. AC is associated with Barrett's esophagus, history of gastroesophageal reflux disease, obesity, and tobacco smoking, and SCC has been linked with smoking and alcohol consumption.[4–6] Recent studies have highlighted the changing landscape of esophageal cancer, with decreases in SCC and increases in AC observed in Western countries, likely due to changes in risk factor profiles across these countries.[7]

The GLOBOCAN project provides estimates of cancer incidence and mortality in 185 countries or territories across the world to describe the current global burden of cancer and inform policy makers and researchers.[8] With the changing epidemiology and advances in the treatment of esophageal cancer, it is important to provide estimates of the current global burden of this cancer to identify areas where further study and attention are required. As such, we aimed to provide a global update of the current incidence and mortality of esophageal cancer using the most up-to-date cancer estimates. Furthermore, we predict the burden of incidence and mortality in 2040 based on global demographic projections.

Methods

The number of new cases of, and deaths from, cancers of the esophagus (International Classification of Diseases 10th Revision [ICD-10] code C15)[8] were extracted from the GLOBOCAN

Abbreviations used in this paper: **ASR, age-standardized rate; HDI, Human Development Index; M:I, mortality to incidence ratio.**

Most current article

0016-5085
https://doi.org/10.1053/j.gastro.2022.05.054

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Esophageal cancer is the eighth most commonly diagnosed cancer and the sixth most common cause of cancer death in the world. Previous studies have noted changes in the epidemiology of this cancer, much related to changing prevalence of its risk factors.

NEW FINDINGS

Globally, there were approximately 604,000 new cases and 544,000 deaths from esophageal cancer in 2020. We expect this to increase to 957,000 cases and 880,000 deaths annually by 2040.

LIMITATIONS

This study was based on estimates for the year in 2020 with projections to 2040, and results should therefore be interpreted with caution.

IMPACT

The results highlight the current and future impact of esophageal cancer if no further cancer control actions are taken and, therefore, serves as an important evidence base for governments, clinicians, and researchers.

2020 database for 185 countries or territories by sex and 18 age groups (eg, 0–4, 5–9, . . . , 80–84, and 85 years and older).[1,9,10] Corresponding population data for 2020 were extracted from the United Nations website.[11] The data sources and hierarchy of methods used in compiling the cancer estimates have been described in detail elsewhere.[10] In brief, the GLOBOCAN estimates are assembled at the national level using the best available sources of cancer incidence and mortality data within a given country. The methods used to derive the 2020 estimates correspond to those used for previous years[12–14]; when applicable, priority is given to short-term predictions and modeled mortality to incidence (M:I) ratios, and validity is dependent on the degree of representativeness and quality of the source information.[10]

We present tables and figures that are based on the estimated new cases and deaths, as well as 2 summary measures using direct standardization, namely, the age-standardized (incidence or mortality) rate (ASR) per 100,000 person-years based on the 1966 Segi-Doll World standard population[15,16] and the cumulative risk of developing or dying from cancer before the age of 75 years expressed as a percentage, assuming the absence of competing causes of death.[17] These measures allow comparisons between populations adjusted for differences in age structures. To estimate incidence by histologic subtype, we applied subtype-specific proportions published previously[18] to the 2020 GLOBOCAN data. In brief, data on esophageal cancer cases by histology diagnosed in the 2008–2012 period were obtained from 343 cancer registries in 65 countries included in the Cancer Incidence in Five Continents database, volume XI.[19] Sex-, age-, country-, and world region–specific proportions by histology were computed and subsequently multiplied with the total number of esophageal cancer cases in the GLOBOCAN 2020 database. The 2 main histologic subtypes, SCC and AC, were defined according to the third edition of the International Classification of Diseases for Oncology[20]: SCC: 8050–8078 and 8083–8084; AC: 8140–8141, 8143–8145, 8190–8231, 8260–8265, 8310, 8401, 8480–8490, 8550–8552, 8570–8574, and 8576.

We also provide a prediction of the future number of esophageal cancer cases and deaths worldwide for the year 2040 based on demographic projections and scenarios of uniformly increasing (by 1%, 2%, or 3%), stable, or decreasing (by 1%, 2%, or 3%) rates annually from the baseline year of 2020. We avoided using scenarios of rates changing by ±5% or more, given that such changes would be unlikely to occur in real life.

The results are presented by country and aggregated across 19 United Nations–defined world regions[11] and according to the United Nations' 4-tier Human Development Index (HDI) in 2020[21]; the latter is a means to assess cancer burden at varying levels of development (low, medium, high, and very high HDI). Throughout, we use the terms *transitioning*, *emerging*, and *lower HDI countries/economies* as synonyms for nations classified as low or medium HDI, and *transitioned* or *higher HDI countries/economies* for those classified as high or very high HDI.

The Global Cancer Observatory (https://gco.iarc.fr) includes facilities for the tabulation and graphical visualization of the GLOBOCAN database, including explorations of the current[9] and future[22] burdens for 36 cancer types and all cancers combined, including nonmelanoma skin cancer (ICD-10 code C44, excluding basal cell carcinomas).[8]

Results

Incidence: Worldwide

Globally, an estimated 604,100 people were diagnosed with esophageal cancer in 2020, corresponding to an age-standardized incidence rate of 6.3 per 100,000. It is the eighth most commonly diagnosed cancer, accounting for 3% of all cancer cases. More male (n = 418,350) than female (n = 185,750) patients were diagnosed with esophageal cancer in 2020 (age-standardized incidence rates, 9.3 vs 3.6 per 100,000).

Incidence by World Region and Country

Of all cases, 59.2% occurred in Eastern Asia—53.7% in China alone (Table 1, Figure 1). Incidence rates for male individuals varied across regions and were generally lowest in Western Africa, Central America, Northern Africa, and Western Asia, with rates of fewer than 6 per 100,000 observed in these regions, and were highest in Eastern Asia, Southern and Eastern Africa, and Northern Europe (Supplementary Figure 1, Supplementary Table 1). At the national level, incidence rates in male individuals were highest in Cape Verde (21.6), Mongolia (20.7), and Malawi (20.3). Similar patterns were observed for female individuals, with incidence rates lowest in Central America and Micronesia/Polynesia regions, and highest in Eastern Asia and Eastern Africa, although rates were up to 8 times lower than for their male counterparts across all countries. Figure 2 shows the age-standardized incidence rates of male and female individuals by world region with reference to the threshold of rare cancer definition (fewer than 6 cases

Table 1. New Cases, Deaths, Age-Standardized Incidence Rates, and Mortality Rates (per 100,000 Person-Years) for Esophageal Cancer by Histologic Subtype,[a] World Region, and Human Development Index, 2020

	Incidence						Mortality	
	AC		SCC		All cases		All deaths	
World region	Cases	ASR	Cases	ASR	Cases	ASR	Deaths	ASR
Eastern Africa	1916	0.9	14,168	6.4	16,137	7.3	15,188	7
Middle Africa	246	0.3	1885	2.2	2136	2.5	2030	2.4
Northern Africa	1032	0.5	2156	1.0	3254	1.5	3152	1.5
Southern Africa	430	0.8	3169	5.9	3610	6.7	3449	6.4
Western Africa	283	0.2	2119	1.1	2409	1.3	2278	1.2
Caribbean	535	0.9	1076	1.8	1703	2.8	1647	2.7
Central America	577	0.3	1157	0.6	1779	0.9	1704	0.9
South America	4510	0.8	10,902	2.0	15,529	2.8	14,448	2.6
Northern America	13,540	1.9	6643	0.9	20,806	2.9	18,480	2.4
Eastern Asia	30,311	1.0	324,443	11.2	357,779	12.3	319,118	10.7
All but China	1675	0.3	31,163	5.6	33,357	6	17,983	3
China	28,636	1.2	293,280	12.5	324,422	13.8	301,135	12.7
South Eastern Asia	1486	0.2	12,781	1.8	14,439	2	13,695	1.9
South Central Asia	8103	0.4	96,427	5.2	105,034	5.6	97,436	5.2
All but India	3531	0.7	38,124	7.2	41,854	7.9	39,094	7.4
India	4572	0.3	58,303	4.3	63,180	4.7	58,342	4.3
Western Asia	1208	0.5	2985	1.2	4300	1.7	4114	1.7
Central Eastern Europe	2446	0.4	12,847	2.4	15,435	2.9	14,120	2.6
Northern Europe	8129	3.4	4445	1.8	12,968	5.3	10,985	4.2
Southern Europe	1786	0.5	4380	1.3	6307	1.8	5564	1.5
Western Europe	7885	1.7	10,008	2.3	18,283	4.1	14,842	3
Australia/New Zealand	1099	1.8	769	1.2	1916	3.1	1564	2.4
Melanesia/Micronesia/ Polynesia	149	1.9	109	1.4	276	3.3	262	3.2
HDI								
Low	2446	0.5	15,920	3.2	18,457	3.7	17,558	3.6
Medium	9068	0.4	101,904	4.9	111,582	5.3	103,722	5
High	36,625	0.9	322,941	8.1	362,576	9.1	337,168	8.3
Very high	37,534	1.2	71,704	2.3	111,343	3.5	85,497	2.6
World	85,672	0.9	512,469	5.4	604,100	6.3	544,076	5.6

[a]Other carcinomas are not presented separately and therefore the sum of the subtypes will not equate to the total cases reported.

per 100,000). Most regions are below the threshold for classifying esophageal cancer as a rare cancer, particularly in women (18 of 20 regions in women and 14 of 20 regions in men with incidence rates of fewer than 6 per 100,000).

Incidence by Histologic Subtype

There were an estimated 85,700 AC cases and 512,500 SCC cases (ASRs of 0.9 and 5.4 per 100,000, respectively) and 6000 remaining cases of other histologic subtypes diagnosed worldwide in 2020. Globally, SCC was the most common subtype in both male and female patients, contributing to 85% of all esophageal cancer cases, with incidence rates of 7.8 and 3.2 per 100,000, respectively. Although AC represented only 14% of all esophageal cancers worldwide, and was also much more common in male patients relative to female patients (ASRs of 1.4 and 0.4, respectively), it was the dominant subtype in 21 mostly highly developed countries, including Australia, Canada,

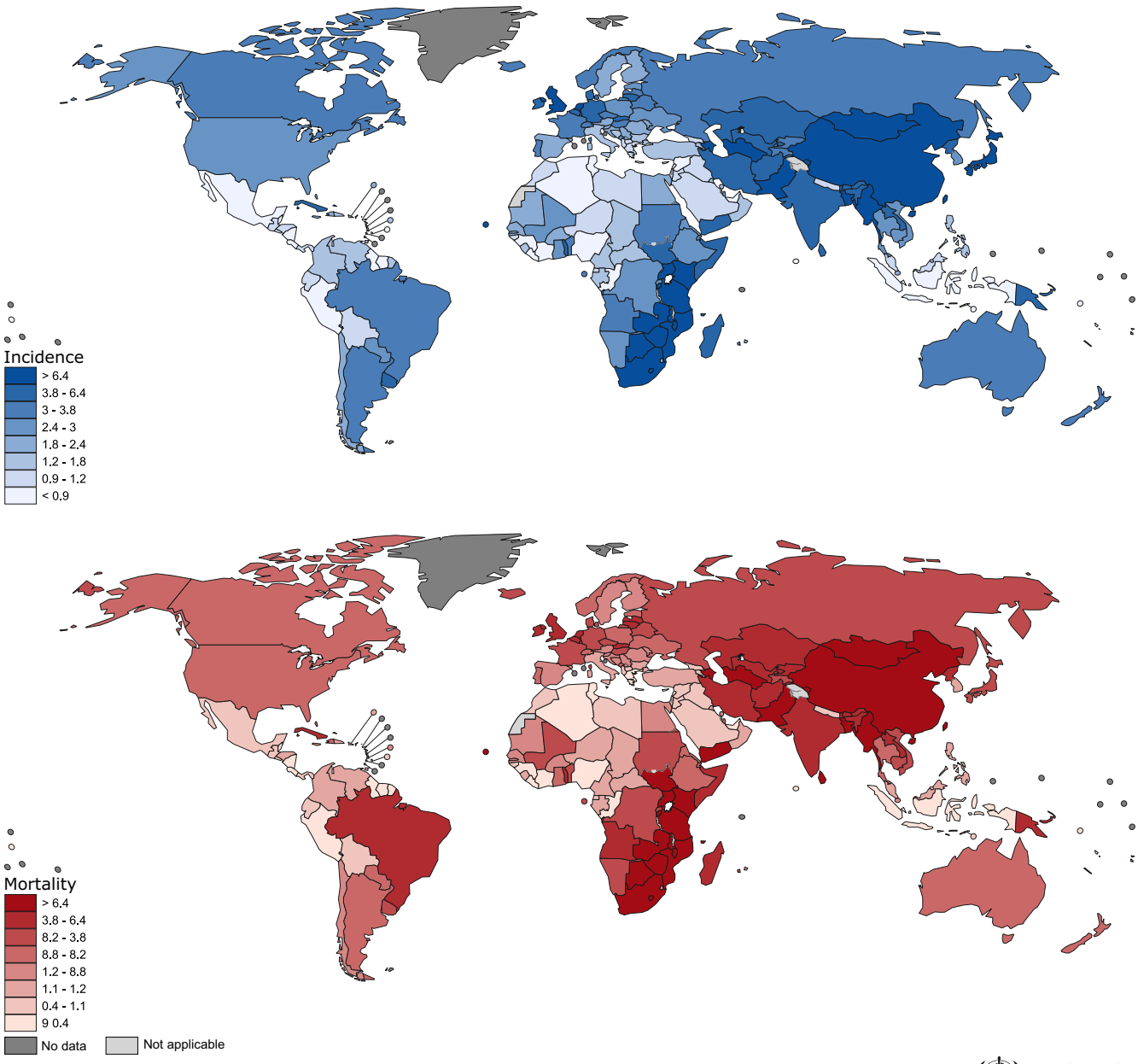


Figure 1. Worldwide esophageal cancer incidence and mortality rates (age-adjusted according to the world standard population, per 100,000), both sexes combined, in 2020.

several countries in Northern and Western Europe, as well as the United States. In consequence, distinct regional differences in incidence were observed between the 2 subtypes, with AC incidence rates highest in Northern Europe and North America and SCC rates highest in Eastern and South Central Asia and South Africa (Table 1, Figure 3).

Mortality: Worldwide

In the same year, there were approximately 544,100 (ASR of 5.6 per 100,000) deaths due to esophageal cancer (Table 1). Mortality was higher in male than female patients, with 375,000, and almost 170,000 deaths corresponding to age-standardized mortality rates of 8.2 and 3.2 per 100,000, respectively (Supplementary Table 1). Compared with other cancer sites, esophageal cancer is the sixth most common cause of cancer mortality, contributing to 6% of all cancer-related deaths in 2020.

Mortality by World Region and Country

Esophageal cancer is the third most common cause of cancer deaths in several countries, including Bangladesh, Pakistan, Sri Lanka, Tanzania, Kenya, Malawi and Uganda, Sudan, and Botswana. Of all esophageal cancer-related deaths, 58.7% occurred in Eastern Asia; 55.3% of all

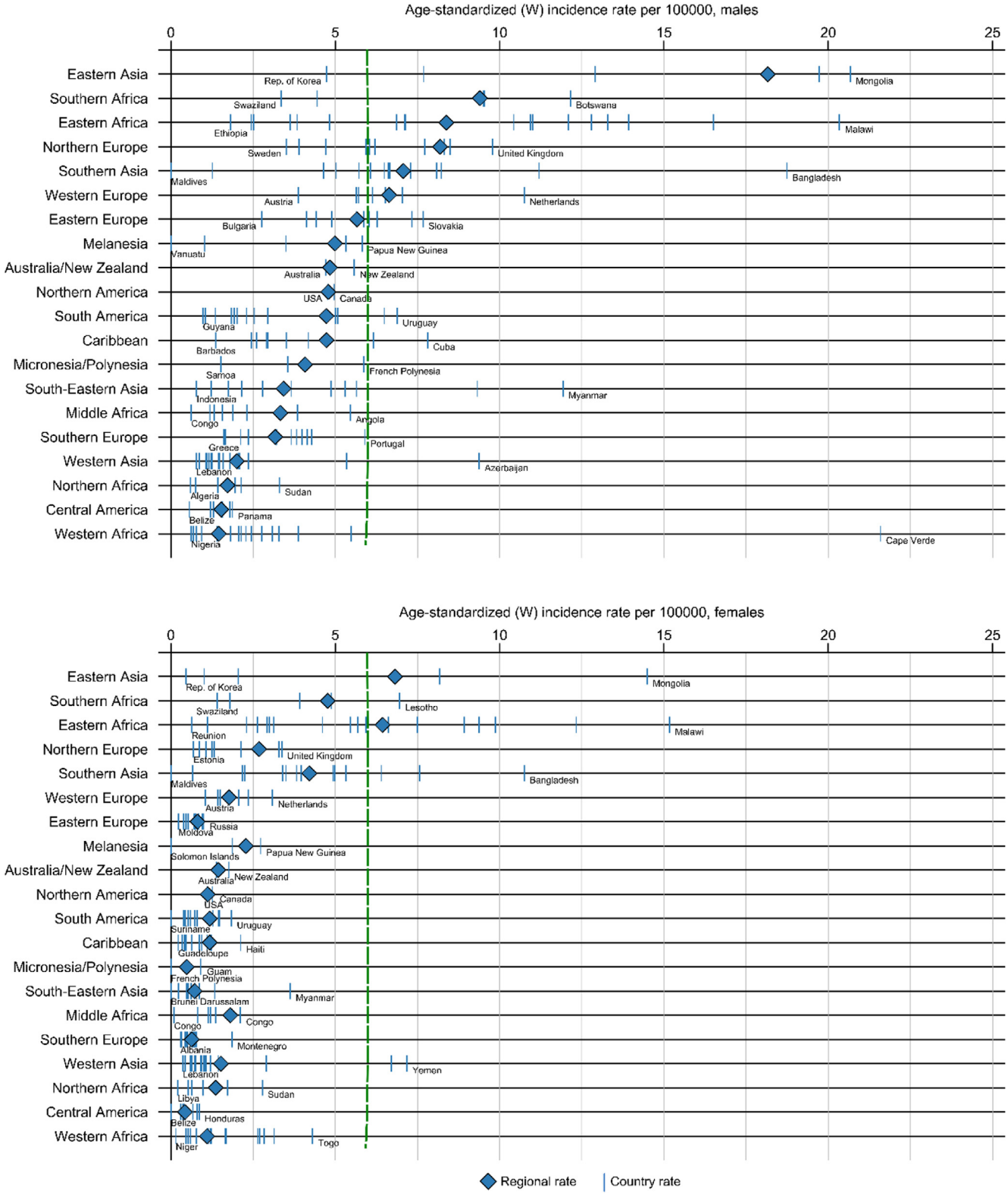


Figure 2. Age-standardized incidence rates of esophageal cancer in male (*top*) and female (*below*) individuals by world region. Ordered according to descending incidence rates by world region in male individuals. The *dashed green line* indicates the threshold of rare cancer definition (fewer than 6 per 100,000).[23]

deaths were in China alone (Table 1 and Figure 1). Mortality rates for male patients were highest in high-incidence regions, including Eastern Asia and Southern and Eastern Africa, and lowest in low-incidence regions, including Western Africa, Central America, and Northern Africa (Supplementary Figure 1, Supplementary Table 1). In terms

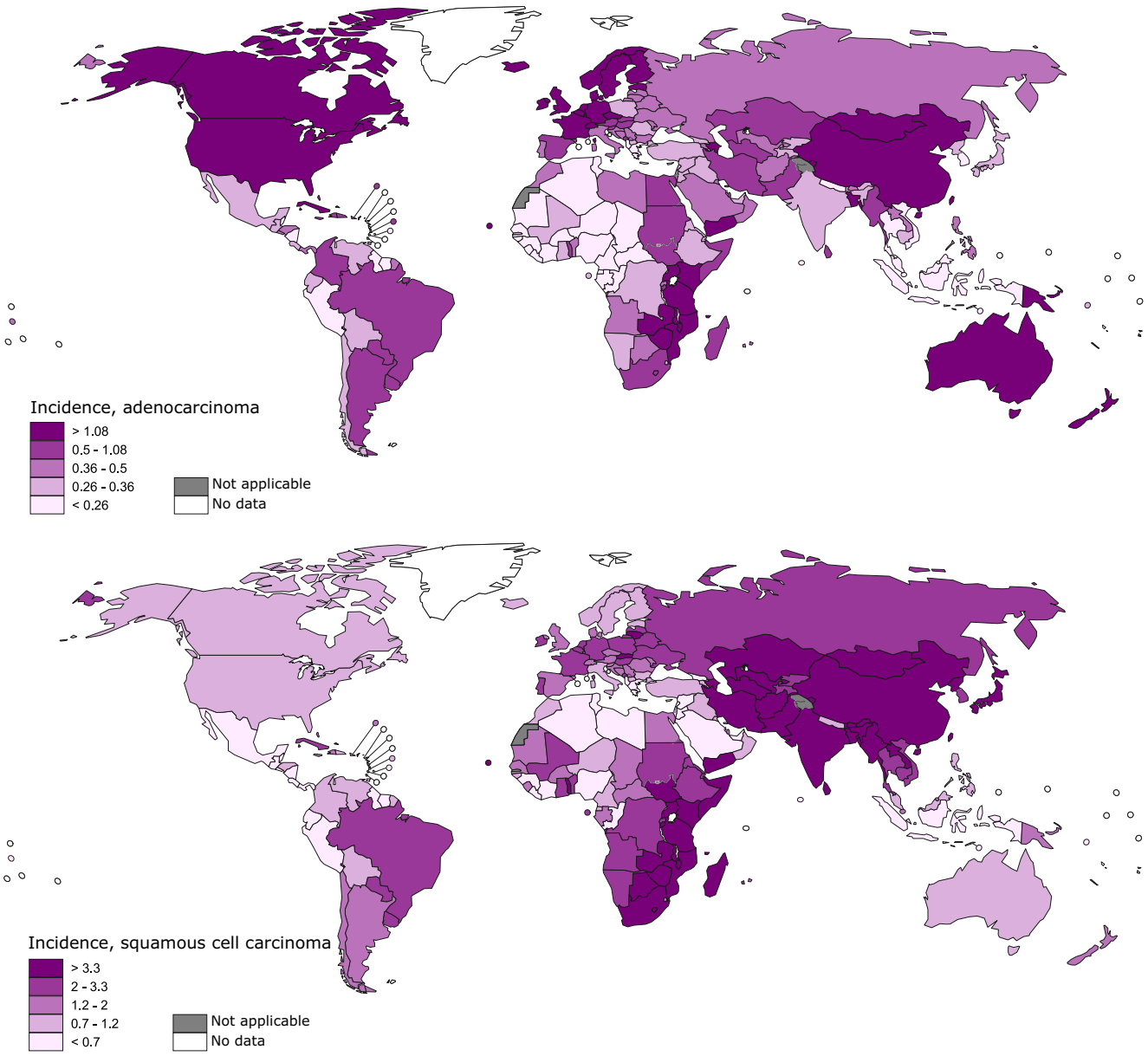


Figure 3. Worldwide esophageal AC and SCC incidence rates (age-adjusted according to the world standard population, per 100,000) in 2020.

of country level, mortality rates in male patients were highest in Cape Verde (20.8), Mongolia (20.3), and Malawi (19.5). Similar patterns were observed in female mortality rates, with mortality rates as much as 8-fold lower than in male patients in some Eastern Asian countries.

Incidence and Mortality by Human Development Index

Supplementary Figure 2 shows the relationship between incidence and mortality of esophageal cancer across countries for 4 HDI subgroups. Due to its high fatality, strong linear correlations were observed between incidence and mortality rates across regions for both sexes for all HDI categories except for male patients in Japan, which had a much lower mortality rate (4.9) compared with its higher incidence (12.9). At a regional level, M:I ratios were highest in Northern Africa, the Caribbean, and Micronesia (M:I, 0.97) and lowest in Western Europe (M:I, 0.81).

Future Projections: Cases and Deaths

Worldwide, an estimated 957,000 new esophageal cancer cases (141,300 AC and 806,000 SCC) are projected to occur in 2040, an increase of 58.4% compared with the 604,000 cases diagnosed in 2020, if national rates in 2020

remain constant (Figure 4). If rates were to decrease by 1% per year as a result of changes in the prevalence of risk factors, projected cases for the year 2040 could be reduced to 780,000 worldwide. Similarly, the number of deaths from esophageal cancer is projected to increase by 61.8% from 2020 to 880,000 deaths by 2040, if current mortality rates were to remain stable (Figure 4). If mortality rates decreased by 1% each year, there would be 720,000 deaths projected by 2040. It would require a ≥3% decrease in rates to achieve fewer cases and deaths in the future than what is observed today.

Discussion

This article provides an overview of the burden of esophageal cancer incidence and mortality in 185 countries worldwide in 2020. Approximately 604,000 new esophageal cancer cases and 545,000 deaths occurred in 2020, with considerable variation across countries and regions. Although it can be considered rare (incidence rates fewer than 6 per 100,000) in many regions,[23] globally it is the eighth most common cancer diagnosed (3% of all cases) and the sixth most common cause of cancer-related deaths (6% of all deaths). Globally, most new cases (85%) were SCCs and the minority were ACs (14%), both with very distinct geographical patterns. The highest incidence rates were documented in Eastern Asia, followed by Southern and Eastern Africa, regions where SCC dominates the esophageal cancer burden. In addition to tobacco and alcohol, other risk factors might also contribute to the high incidence in these regions, including consumption of hot beverages, opium smoking, low fruit and vegetable consumption, drinking unpiped water, and exposure to air pollution.[24–26] Dental fluorosis and oral health have been associated with increased risks in East Africa.[27] Other contributors to the high incidence observed in some countries, including the so-called central Asian esophageal cancer belt[28] and Eastern Africa's esophageal cancer corridor,[29] remain to be explored.

Due to very distinct etiologies of the 2 main histologic subtypes of esophageal cancer, it remains crucial to investigate histology-specific incidence patterns and trends to better understand the contribution of underlying risk factors. Representing 85% of all esophageal cancers globally, SCC remains by far the most common subtype, particularly in high-incidence regions. SCC incidence rates were highest in Eastern Africa and Eastern and South Central Asia regions, which likely reflects exposures to specific carcinogens, including tobacco smoking, hot beverage consumption, and indoor air pollution. In contrast, incidence rates of AC exceeded those of SCC in historically low-incidence countries that have shown both declines in smoking prevalence (a risk factor for SCC) and increases in obesity (a risk factor for AC).[30] The dominance of AC has been documented in a number of populations, particularly in male individuals in North America, Northern and Western Europe, and Oceania, which may be attributable to changes in the prevalence of AC risk factors, such as gastroesophageal reflux disease, Barrett's esophagus, and abdominal obesity, and decreases in *Helicobacter pylori* infection over time.[7] The higher incidence in male compared with female individuals that has been observed in this study and in previous histologic-

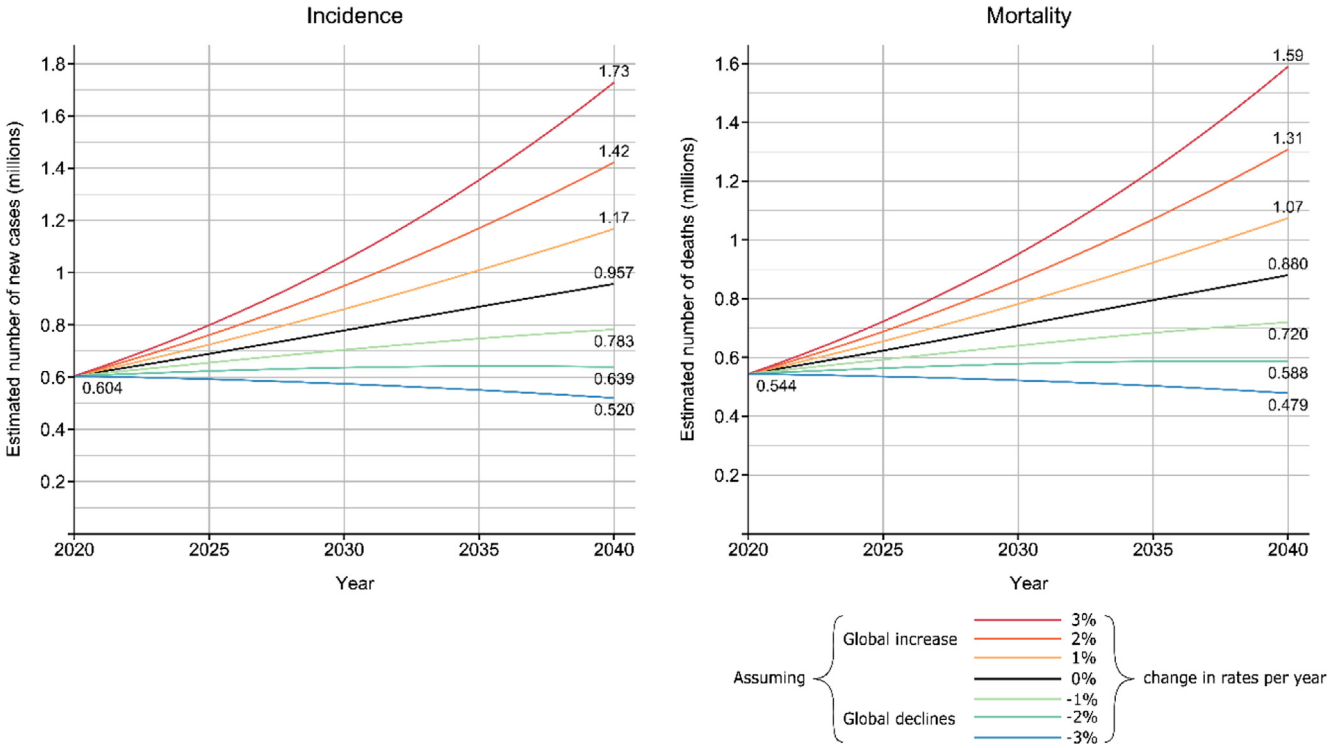


Figure 4. Projected number of cases and deaths of esophageal cancer worldwide from 2020 to 2040.

specific studies could reflect differences in risk factor prevalence. Targeted interventions and studies on high-risk groups are warranted to close the gap and reduce the excess risk among male individuals.

The most important prognostic factors determining survival from esophageal cancer is stage at diagnosis. Yet, most esophageal cancer cases tend to be diagnosed at an advanced stage, when treatment options are limited, and survival remains low even in high-income countries. Mortality patterns and rates, therefore, often closely mimic those of incidence in many world regions, particularly in Bangladesh, Pakistan, Sri Lanka, Tanzania, Kenya, Malawi and Uganda, Sudan, and Botswana, where esophageal cancer is among the top 3 causes of cancer deaths. Recent trials, such as the CheckMate 649 and KEYNOTE-590, have shown promising results for new chemotherapy treatment regimens and extending survival in patients with advanced metastatic cancer.[31,32] With this in mind, attention should be focused on the observed survival inequality across regions where more advanced cases and limited access to such treatments are likely to occur.

If current rates continue, the projected number of cases of esophageal cancer is expected to increase to 957,000 by 2040, with deaths rising to 880,000 in the same year due to population growth and aging. There is a need for future planning to expand the health care workforce capacity and resource availability to manage these predicted increases, particularly for provision of neoadjuvant radiotherapy, which is a key element to improved survival rates observed in countries with very high HDI.[33] Although our projections show an expected increase in the number of cases, the opportunity to reduce the future burden of this disease lies in primary prevention, with a need for focus on reducing population levels of obesity, tobacco, and alcohol. Furthermore, given differences in risk factors and survival, particularly by stage and histologic subtype, with SCC showing lower survival than AC,[33] future research should focus on histologic-specific outcomes. Yet, many existing studies are based on data from high-income countries and therefore it is difficult to assess the situation in low- and middle-income countries. As such, population-based cancer registries, particularly in low- and middle-income countries, should be supported and encouraged in their efforts to collect detailed data (including information on histology), that will allow for such analyses to be conducted in areas of the world with the greatest burden of esophageal cancer.

Despite its high incidence, Japan had much lower mortality rates for esophageal cancer than other countries with similar incidence. High survival rates for esophageal cancer in Japan are likely an effect of the long-standing national endoscopic screening program for gastric cancer, which aims to detect early-stage cancers, when curative endoscopic treatments can be performed. Heightened public awareness in Japan may also play a role in the detection of early cancers. Although endoscopic screening has proved to be successful,[34] the high cost and risk of complications hinder its implementation at a national level, particularly in low-income settings.[35] Recent breakthroughs in less invasive, more cost-effective methods (such as sponges originally trialed to detect Barrett's esophagus) show promise for novel methods for the detection of treatable dysplasia and early esophageal cancer.[36,37] It is important for in-depth investigations of disparities in incidence and mortality across countries to be conducted to understand the roles of social health determinants and histologic subtype. Disparities between and within countries have been investigated previously, for example, racial disparities were observed in the United States with higher incidence rates of SCC among Black individuals and AC more pronounced in White men.[38]

Some limitations should be noted in relation to this work. Although these results are based on the best-available and high-quality data from population-based cancer registries, caution is warranted when interpreting estimates from countries with limited coverage from population-based cancer registries and where proxy data were used to obtain national estimates.[10] Indeed, the accuracy of estimates in some low- and middle-income countries is likely to be reduced due to limited or no availability of surveillance systems; however, the estimation methods used have been refined in past decades and are still considered the reference standard for global cancer statistics.[10] This inequity in cancer registration is being addressed through the ongoing Global Initiative for Cancer Registry Development (https://gicr.iarc.fr) led by the International Agency for Research on Cancer. Furthermore, data do not reflect the impact of the COVID-19 pandemic on cancer diagnosis, as they are based on extrapolations of cancer data collected in earlier years. In the main scenario, the predictions of the future burden of esophageal cancer in 2040 do not take into account changes in background incidence over time and by histologic subtype, and solely reflect transitions in population growth and aging between 2020 and 2040. Given the previously reported ongoing changes in incidence rates, especially by subtype,[7,30] the forecasted estimates presented here should be interpreted with caution. Finally, incidence estimates by histologic subtype were based on data from the most recent volume of the Cancer Incidence in the Five Continents series referring to the 2008–2012 period and may not represent current patterns. However, in the absence of more recent histology-specific data, the estimates presented here provide insight into global incidence patterns by subtype.

In this article, we provided a snapshot of the geographical variation of esophageal cancer incidence and mortality in 2020 and an outlook into 2040 by sex and HDI in 185 countries. This overview allows governments and researchers to prioritize funding and research in cancer control according to current regional and national estimates on the burden of esophageal cancer. Our results highlight the international burden of esophageal cancer with regions of Eastern Asia and Southern and Eastern Africa as having the highest incidence in the world. Further epidemiological studies and surveillance by histologic subtype are warranted and increased efforts for esophageal cancer control are required, particularly in terms of primary prevention, with many modifiable risk factors of this highly fatal cancer identified.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at http://doi.org/10.1053/j.gastro.2022.05.054.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209–249.
2. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 2018; 391:1023–1075.
3. Arnold M, Rutherford MJ, Bardot A, et al. Progress in cancer survival, mortality, and incidence in seven high-income countries 1995-2014 (ICBP SURVMARK-2): a population-based study. Lancet Oncol 2019; 20:1493–1505.
4. Rustgi AK, El-Serag HB. Esophageal carcinoma. N Engl J Med 2014;371:2499–2509.
5. El-Serag HB, Hashmi A, Garcia J, et al. Visceral abdominal obesity measured by CT scan is associated with an increased risk of Barrett's oesophagus: a case-control study. Gut 2014;63:220–229.
6. Coleman HG, Xie S-H, Lagergren J. The epidemiology of esophageal adenocarcinoma. Gastroenterology 2018; 154:390–405.
7. Rumgay H, Arnold M, Laversanne M, et al. International trends in esophageal squamous cell carcinoma and adenocarcinoma incidence. Am J Gastroenterol 2021; 116:1072–1076.
8. World Health Organization. International Classification of Diseases 10th Revision (ICD-10). Available at: http://www.who.int/classifications/icd/en/. Accessed July 22, 2022.
9. Ferlay J, Laversanne M, Ervik M, et al. Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer, 2020. Available at: https://gco.iarc.fr/today/home. Accessed April 30, 2021.
10. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: an overview. Int J Cancer 2021;149:778–789.
11. United Nations Statistics Division. Standard country or area codes for statistical use (M49). Available at: https://unstats.un.org/unsd/methodology/m49/. Accessed April 30, 2021.
12. Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 2019; 144:1941–1953.
13. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136:E359–E386.
14. Ferlay J, Shin HR, Bray F, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127:2893–2917.
15. Segi M. Cancer Mortality for Selected Sites in 24 Countries (1950-1957). Department of Public Health, Tohoku University of Medicine, 1960.
16. Doll R, Payne P, Waterhouse J. Cancer Incidence in Five Continents - A Technical Report. 1st ed. Springer, 1966.
17. Day NE. Cancer Incidence in Five Continents. Cumulative rate and cumulative risk. IARC Sci Publ 1992;120:862–864.
18. Arnold M, Ferlay J, Van Berge Henegouwen MI, et al. Global burden of oesophageal and gastric cancer by histology and subsite in 2018. Gut 2020;69:1564–1571.
19. Bray F, Colombet M, Mery L, et al. Cancer Incidence in Five Continents. Volume XI. International Agency for Research on Cancer, 2017.
20. World Health Organization. International Classification of Diseases for Oncology, 3rd edition (ICD-O-3). Available at: https://www.who.int/standards/classifications/other-classifications/international-classification-of-diseases-for-oncology. Accessed June 11, 2022.
21. United Nations Development Programme. Human Development Report 2020. United Nations, 2020.
22. Ferlay J, Laversanne M, Ervik M, et al. Global Cancer Observatory: Cancer Tomorrow. International Agency for Research on Cancer, 2020. Available at: https://gco.iarc.fr/tomorrow/en. Accessed April 30, 2021.
23. Gatta G, van der Zwan JM, Casali PG, et al. Rare cancers are not so rare: the rare cancer burden in Europe. Eur J Cancer 2011;47:2493–2511.
24. Middleton DRS, Menya D, Kigen N, et al. Hot beverages and oesophageal cancer risk in western Kenya: findings from the ESCCAPE case–control study. Int J Cancer 2019;144:2669–2676.
25. Sheikh M, Poustchi H, Pourshams A, et al. Individual and combined effects of environmental risk factors for esophageal cancer based on results from the Golestan Cohort Study. Gastroenterology 2019;156:1416–1427.
26. Sheikh M, Shakeri R, Poustchi H, et al. Opium use and subsequent incidence of cancer: results from the Golestan Cohort Study. Lancet Glob Heal 2020;8:e649–e660.
27. Menya D, Maina SK, Kibosia C, et al. Dental fluorosis and oral health in the African Esophageal Cancer Corridor: findings from the Kenya ESCCAPE case–control study and a pan-African perspective. Int J Cancer 2019; 145:99–109.
28. Semnani SH, Besharat S, Abdolahi N, et al. Esophageal cancer in northeastern Iran [1]. Indian J Gastroenterol 2005;24:224.
29. van Loon K, Mwachiro MM, Abnet CC, et al. The African Esophageal Cancer Consortium: a call to action. J Glob Oncol 2018;4:1–9.
30. Arnold M, Laversanne M, Brown LM, et al. Predicting the future burden of esophageal cancer by histological subtype: international trends in incidence up to 2030. Am J Gastroenterol 2017;112:1247–1255.
31. Kato K, Sun J-M, Shah MA, et al. LBA8_PR Pembrolizumab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced esophageal

cancer: the phase 3 KEYNOTE-590 study. Ann Oncol 2020;31:S1192–S1193.
32. Moehler M, Shitara K, Garrido M, et al. LBA6_PR Nivolumab (nivo) plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer (GC/GEJC)/esophageal adenocarcinoma (EAC): first results of the CheckMate 649 study. Ann Oncol 2020;31:S1191.
33. Morgan E, Soerjomataram I, Gavin AT, et al. International trends in oesophageal cancer survival by histological subtype between 1995 and 2014. Gut 2021;70:234–242.
34. Wei WQ, Chen ZF, He YT, et al. Long-term follow-up of a community assignment, one-time endoscopic screening study of esophageal cancer in China. J Clin Oncol 2015;33:1951–1957.
35. Lao-Sirieix P, Fitzgerald RC. Screening for oesophageal cancer. Nat Rev Clin Oncol 2012;9:278–287.
36. Fitzgerald RC, di Pietro M, O'Donovan M, et al. Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial. Lancet 2020;396:333–344.
37. Sami SS, Moriarty JP, Rosedahl JK, et al. Comparative cost effectiveness of reflux-based and reflux-independent strategies for Barrett's esophagus screening. Am J Gastroenterol 2021;116:1620–1631.
38. Xie SH, Rabbani S, Petrick JL, et al. Racial and ethnic disparities in the incidence of esophageal cancer in the United States, 1992–2013. Am J Epidemiol 2017;186:1341–1351.

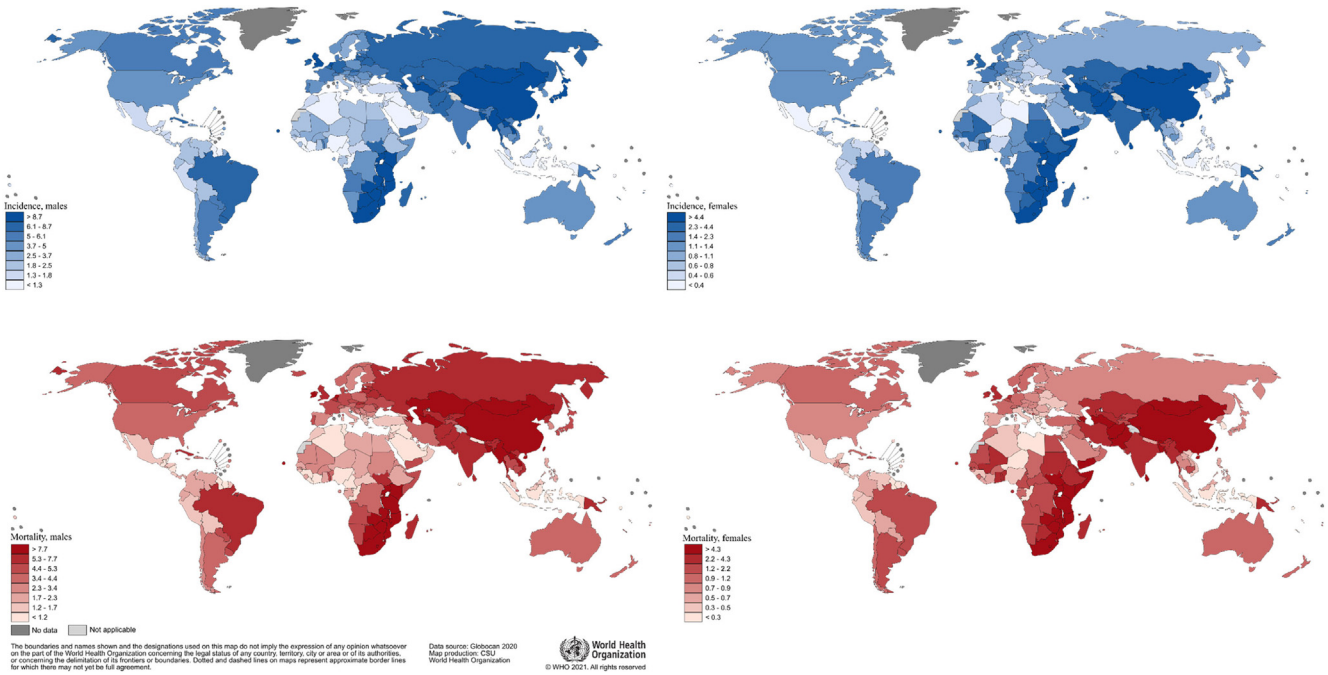
Received November 9, 2021. Accepted May 30, 2022.

Correspondence
Address correspondence to: Eileen Morgan, PhD, Cancer Surveillance Branch, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon CEDEX 08, France. e-mail: morgane@iarc.who.int.

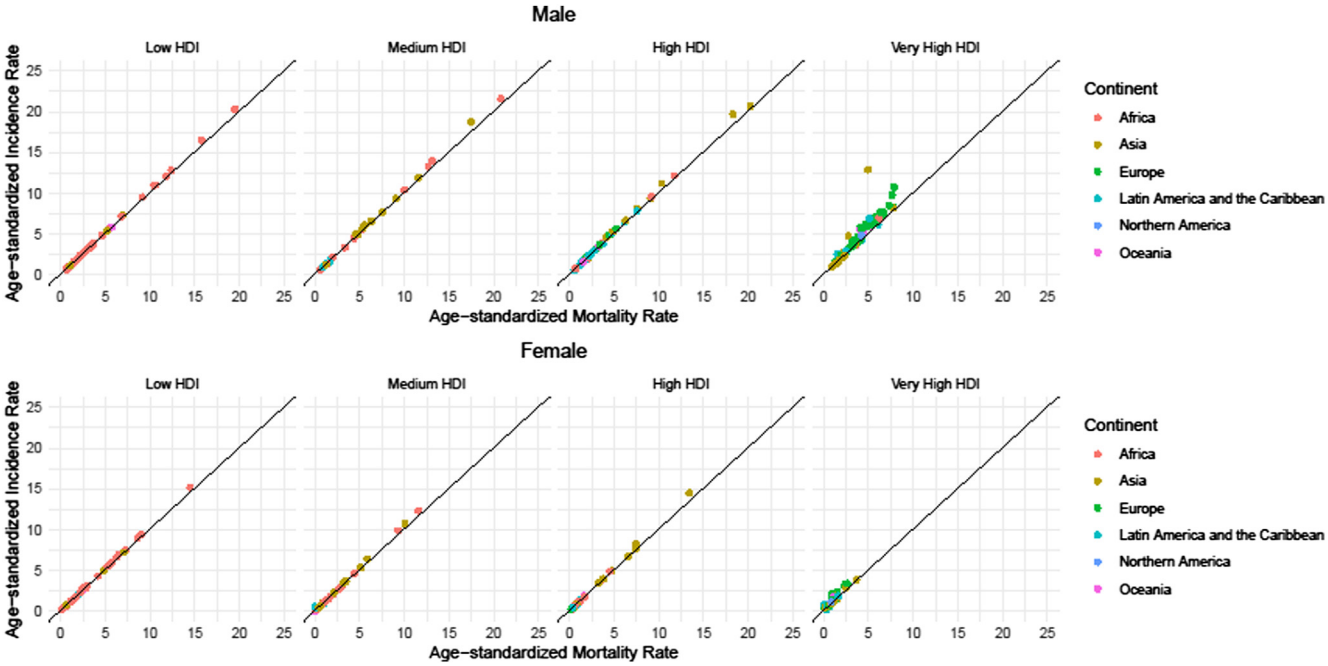
CRediT Authorship Contributions
Eileen Morgan, PhD (Data curation: Equal; Investigation: Lead; Project administration: Equal; Writing – original draft: Lead; Writing – review & editing: Lead).
Isabelle Soerjomataram, MSc, PhD, MD (Conceptualization: Lead; Investigation:Equal; Writing – review & editing: Equal).
Harriet Rumgay, BSc (Writing – review & editing: Equal).
Helen G. Coleman, PhD (Writing – review & editing: Equal).
Aaron P. Thrift, PhD (Writing – review & editing: Equal).
Jérôme Vignat, MSc (Data curation: Equal; Formal analysis: Equal; Investigation:Equal; Methodology: Equal; Visualization: Equal; Writing – review & editing: Equal).
Mathieu Laversanne, MSc (Formal analysis: Equal; Investigation: Equal; Methodology: Equal; Visualization: Lead; Writing – review & editing: Equal).
Jacques Ferlay, MSc (Data curation: Lead; Formal analysis: Lead; Investigation: Equal; Methodology: Lead; Visualization: Equal; Writing – review & editing: Equal).
Melina Arnold, PhD (Conceptualization: Equal; Data curation: Equal; Investigation:Equal; Supervision: Lead; Visualization: Supporting; Writing – original draft: Equal; Writing – review & editing: Equal).

Disclaimer
The authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy, or views of the International Agency for Research on Cancer/World Health Organization.

Conflicts of interest
The authors disclose no conflicts.



Supplementary Figure 1. Worldwide esophageal cancer incidence and mortality rates (age-adjusted according to the world standard population, per 100,000) in male and female individuals in 2020.



Supplementary Figure 2. Relationship between age-standardized esophageal cancer mortality and incidence rates per 100,000 people worldwide by sex, continent, and HDI in 2020.

Supplementary Table 1. New Cases, Deaths, Age-Standardized Incidence Rates, and Mortality Rates (per 100,000 Person-Years) for Esophageal Cancer by Sex, World Region, and Human Development Index, 2020

	Incidence				Mortality				
	Male		Female		Male		Female		
World region	Cases, n	ASR	Cases, n	ASR	Deaths, n	ASR	Deaths, n	ASR	M:I ratio
Eastern Africa	8514	8.4	7623	6.4	8028	8.0	7160	6.1	0.94
Middle Africa	1343	3.3	793	1.8	1275	3.2	755	1.7	0.95
Northern Africa	1750	1.7	1504	1.4	1694	1.7	1458	1.3	0.97
Southern Africa	2109	9.4	1501	4.8	2049	9.1	1400	4.5	0.96
Western Africa	1318	1.5	1091	1.1	1240	1.4	1038	1.1	0.95
Caribbean	1311	4.7	392	1.2	1267	4.6	380	1.1	0.97
Central America	1315	1.5	464	0.4	1249	1.5	455	0.4	0.96
South America	11,779	4.7	3750	1.2	10,992	4.4	3456	1.0	0.93
Northern America	16,298	4.8	4508	1.1	14,800	4.2	3680	0.8	0.89
Eastern Asia	251,456	18.2	106,323	6.8	221,846	15.8	97,272	6.0	0.89
All but China	28,412	11.1	4945	1.5	15,066	5.6	2917	0.7	0.54
China	223,044	19.7	101,378	8.2	206,780	18.3	94,355	7.4	0.93
South-Eastern Asia	11,576	3.4	2863	0.7	10,999	3.3	2696	0.7	0.95
South Central Asia	65,281	7.1	39,753	4.2	60,429	6.6	37,007	3.9	0.93
All but India	25,098	9.6	16,756	6.3	23,519	9.0	15,575	5.9	0.93
India	40,183	6.1	22,997	3.4	36,910	5.6	21,432	3.2	0.92
Western Asia	2309	2.0	1991	1.5	2194	1.9	1920	1.5	0.96
Central-Eastern Europe	12,517	5.7	2918	0.8	11,435	5.1	2685	0.7	0.91
Northern Europe	9070	8.2	3898	2.7	7717	6.6	3268	2.0	0.85
Southern Europe	4892	3.2	1415	0.6	4355	2.6	1209	0.5	0.88
Western Europe	13,938	6.6	4345	1.8	11,403	5.2	3439	1.2	0.81
Australia/New Zealand	1387	4.8	529	1.4	1164	3.9	400	1.0	0.82
Melanesia	161	5.0	86	2.3	152	4.8	82	2.2	0.95
Micronesia/Polynesia	26	4.1	3	0.5	25	3.9	3	0.5	0.97
HDI									
Low	10,060	4.3	8397	3.2	9569	4.1	7989	3.1	0.95
Medium	70,828	6.9	40,754	3.8	65,815	6.4	37,907	3.5	0.93
High	250,143	13.3	112,433	5.2	232,396	12.3	104,772	4.8	0.93
Very high	87,210	6.1	24,133	1.3	66,433	4.5	19,064	0.9	0.77
World	418,350	9.3	185,750	3.6	374,313	8.2	169,763	3.2	0.90