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# Global incidence, mortality, and burden of esophageal cancer, and its correlation with SDI, metabolic risks, fasting plasma glucose, LDL cholesterol, and body mass index: An ecological study

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## Abstract

**Background and Aims:** Esophageal cancer (EC) is one of the most common gastrointestinal malignancies. The geographical variation shows the influence of genetic factors, ethnicity, and distribution of various risk factors. Accurate knowledge of EC epidemiology at the global level will help to develop management strategies. Therefore, the present study was conducted to investigate the global and regional disease burden of EC, including the incidence, mortality, and burden of this cancer in 2019.

**Methods:** Incidence, mortality, disability-adjusted life years (DALYs), and age-standardized rates (ASRs) associated with EC in 204 countries in different classifications were extracted from the global burden of disease study. After collecting information on metabolic risks, fasting plasma glucose (FPG), low-density lipoprotein (LDL) cholesterol, and body mass index (body mass index), the relationship between age-standardized incidence rate (ASIR), mortality rate, and DALYs with these variables was determined.

**Results:** In 2019, 534,563 new cases of EC were reported worldwide. The highest ASIR is related to regions with medium sociodemographic index (SDI), and high middle income according to the World Bank, the Asian continent, and the western Pacific region. In 2019, a total of 498,067 deaths from EC were recorded. The highest mortality rate due to ASR is in countries with medium SDI and countries with upper middle income of the World Bank. In 2019, 1,166,017 DALYs were reported due to EC. The ASIR, ASDR, and DALYS ASR of EC showed a significant negative linear correlation with SDI, metabolic risks, high FPG, high LDL cholesterol, and high BMI ($p < 0.05$).

**Conclusions:** The results of this study showed significant gender and geographic variation in the incidence, mortality, and burden of EC. It is recommended to design

and implement preventive approaches based on known risk factors and improve quality and access to efficient and appropriate treatments.

KEYWORDS
burden, epidemiology, esophageal cancer, incidence, mortality

## 1 | INTRODUCTION

Esophageal cancr (EC) is one of the most common gastrointestinal malignancies, with an estimated 0.6 million new cases and 0.54 million deaths in 2020.[1] Despite recent advances in the early detection and treatment of EC, it is still one of the most deadly cancers with a 5-year survival rate of only 10%–15%.[2,3] From the histological point of view, EC appears in one of the two forms of esophageal squamous cell carcinoma (ESCC) and adenocarcinoma (ACE), which are different in terms of occurrence background pattern and etiological factors.[4] Studies have shown that more than 85% of EC cases are ESCC.[5] ESCC has a higher prevalence in developing countries, especially in Southern Europe, East Asia, and South and East Africa, and has a lower incidence in some regions such as North America. In contrast, ACE is increasing in developed countries such as the United States.[6]

The geographical variation shows the influence of genetic factors, ethnicity, and distribution of various risk factors.[4,7] ESCC has a close relationship with lifestyle and environmental factors such as alcohol consumption, tobacco use, and diet,[8,9] while ACE is associated with gastric reflux that leads to Barrett's esophagus, which is a known definitive cause of ACE.[10] ACE is also more prevalent in the male gender, obese persons, current smokers or who had a history of smoking.[3]

Accurate knowledge of EC epidemiology at the global level and identification of high-risk areas in terms of incidence and mortality and associated risk factors will help develop management strategies and wisely allocate limited health resources Lack of up-to-date information, being local, and investigation of special risk factors lead to which available studies could not show an exclusive perspective.[11–13] According to the mentioned considerations, the present study was conducted to investigate the global and regional disease burden of EC, including the incidence, mortality, and DALY based on different SDI regions and also find out its relationship with metabolic risks, fasting plasma glucose (FPG), low-density lipoprotein (LDL) cholesterol, and body mass index (BMI).

## 2 | MATERIALS AND METHODS

### 2.1 | Data sources

Age-standardized incidence rate (ASIR), deaths, disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs) of EC, and targeted risk factors were extracted from the online global burden of disease (GBD) database 2019; which presented the most recent data for epidemiological indexes of diseases at http://ghdx.healthdata.org. In GBD, the epidemiological indexes of 369 diseases and injuries for both sexes in 204 countries and territories based on various divisions of countries were estimated. For an accurate interpretation, we extracted EC data for 204 countries and a variety of classifications based on age groups, sociodemographic index (SDI), World Health Organization (WHO) regions, continents, World Bank regions, and GBD regions.[14–16]

The SDI is the geometric mean of three factors including per capita income, average years of schooling, and total fertility rate; and identifies the position of countries or geographic areas on a scale of development from 0 (lowest) to 1 (highest).[17]

The World Bank categorizes economies for analysis into four income groups; low, medium-low, medium-high, and high. It does this by using per capita gross national income data in US dollars converted into local currency, using the World Bank's Atlas method, which is applied to smooth changes in exchange rates.[18]

DALY is one of the most common summative measures of the health gap in the area of public health and have become the primary measure of quantification of the burden of disease.[19] In GBD, DALY is a developed internationally standardized form of QALY and is defined as the YLL due to premature death and the years lived with a disability of specified severity and duration.[16]

Metabolic risks are important modifiable risk factors for a wide variety of diseases, including cardiovascular disease, cancer, and injury.[20] In GBD, high FPG, high LDL cholesterol, high systolic blood pressure (SBP), high BMI, low bone mineral density (BMD), and kidney dysfunction were considered metabolic risks. The theoretical level of exposure to the minimum risk of a certain risk factor has been defined as the minimum level of death or DALY-weighted multi-cause risk factor curves of previous meta-analysis studies.[21]

TMREL of high BMI was defined as BMI ≥ 25 kg/m$^2$ for adults (ages 20+), and was based on International Obesity Task Force standards for children (ages 1–19)[22]; high FPG as any level above the 4.8–5.4 mmol/L[23]; high LDL cholesterol as LDL-cholesterol above 0.7–1.3 mmol/L[24]; high SBP as SBP above 110–115 mmHg.[25] Kidney dysfunction was defined by urinary albumin to creatinine ratio and estimated glomerular filtration rate as KDIGO classification (CKD stages 1–5).[26] Because bone minerals varied by age and sex, the TMREL of low BMD was defined as the 99th percentile of BMD by age and sex, based on the NHANES study.[21]

## 2.2 | Ethical approaches

This study was approved by the ethics committee of Birjand University of Medical Sciences (ethics committee approval code: IR.BUMS.REC.1400.414). Because no identifiable data were used, informed consent was not necessary for this study.

## 2.3 | Statistical analysis

Data were expressed as values with a 95% confidence interval (CI). Incidence, deaths, DALYs, YLLs, YLDs, and age-standardized rates (ASRs) were expressed as numbers per 100,000 population for the description of the different classifications. To remove the influence of different ages in the patient population and to ensure comparability of statistical indicators, ASRs were expressed in figures per 100,000 population. Then, using SPSS software version 16 and the Pearson correlation coefficient, the correlation between SDI, metabolic risks, FPG, LDL cholesterol, BMI and age-standardized incident rates, death rates, and DALY rates of EC were calculated. A $p$ value of less than 0.05 was considered statistically significant. Definitions of the terminology used in this study can be found at https://www.healthdata.org/terms-defined and https://www.healthdata.org/gbd/.[16]

# 3 | RESULTS

## 3.1 | Incidence rates of EC

In 2019, 534,563 (95% CI: 466,513–595,342) new cases of EC were reported worldwide, of which 388,827 (95% CI: 335,510–444,000) among males and 145,736 (95% CI: 119,952–165,068) among females. The ASIR of EC worldwide was 6.51 (95% CI: 5.69–7.25) per 100,000 inhabitants; 10.13 (95% CI: 8.73–11.56) in males and 3.33 (95% CI: 2.74–3.77) in females.

The highest ASIR per 100,000 people for EC has been reported in Malawi (24.53), Mongolia (21.93), Uganda (15.61), Cabo Verde (15.57), Zimbabwe (15.4), Eswatini (15.14), Lesotho (14.59), China (13.9), and Eritrea (13.2), respectively.

The lowest ASIR per 100,000 people for EC has been reported in Nigeria (0.91), Syrian Arab Republic (0.92), Tunisia (0.96), Algeria (1.08), Palestine (1.1), Jordan (1.14), Nicaragua (1.2), Peru (1.29) and Lebanon (1.3); respectively.

In men, the highest ASIR has been reported in Malawi (33.08), Cabo Verde (30.72), Mongolia (30.48), Eswatini (28.13), Lesotho (23.72), Zimbabwe (22.33), China (21.94), Botswana (20.16), and Taiwan (Province of China) (19.18), respectively. The lowest ASIR has been observed in the Syrian Arab Republic (1.3), Nigeria (1.45), Jordan (1.49), Tunisia (1.5), Algeria (1.56), Iraq (1.64), Palestine (1.66), Morocco (1.84), and Lebanon (1.88), respectively.

In women, the highest ASIR has been reported in Malawi (17.28), Mongolia (16.03), Eritrea (12.96), Uganda (11.18), Kenya (11.17), Zambia (10.92), Somalia (10.8), Burundi (10.36), and Comoros (10.3), respectively. The lowest ASIR has been observed in the Republic of Moldova (0.33), Nigeria (0.42), Guam (0.44), San Marino (0.45), Tunisia (0.45), Ukraine (0.46), Belarus (0.48), Nicaragua (0.51), and Andorra (0.52), respectively.

Statistics show that the highest ASIR for EC occurs in countries with middle SDI (8.42 [95% CI: 6.7–9.75] per 100,000) worldwide. The lowest ASIR occurs in countries with low-middle SDI (4.37 [95% CI: 3.85–6.17] per 100,000 people) worldwide. In men, the highest ASIR for EC occurs in countries with middle SDI (12.7 [95% CI: 10.08–15.16] per 100,000 people). The lowest ASIR occurs in countries with low-middle SDI (5.84 [95% CI: 5.06–8.63] per 100,000 people). In women, the highest ASIR for EC occurs in countries with middle SDI (4.58 [95% CI: 3.13–5.46] per 100,000 people) and low SDI (4.48 [95% CI: 3.65-5.38] per 100,000 people). The lowest ASIR occurs in countries with high SDI (1.93 [95% CI: 1.69–2.16] per 100,000 people).

According to the World Bank classification, the ASIR for EC is highest in the World Bank upper middle income (9.63 [95% CI: 7.68–11.21] per 100,000 people) worldwide and 15.41 (95% CI: 12.08–18.52) per 100,000 people in males; in females in low income (5.91 [95% CI: 4.14–7.4] per 100,000 people) is higher. The lowest rates were seen in lower middle income (3.36 [95% CI: 3.01–4.22] per 100,000 people) worldwide; and 4.29 (95% CI: 3.71–5.54) per 100,000 people in males; in females in high income (1.78 [95% CI: 1.57–1.99] per 100,000 people) is lower.

Among the continents, the highest ASIR was reported in Asia (8.24 [95% CI: 6.96–9.43] per 100,000 people) worldwide, 12.56 (95% CI: 10.28–14.89) per 100,000 people in men, and (4.33 [95% CI: 3.39–5.1] per 100,000 people) in women, while the lowest was observed in America (3.85 [95% CI: 3.48–4.25] per 100,000 people) and Europe (3.95 [95% CI: 3.55–4.38] per 100,000 people) worldwide and among men (6.47 [95% CI: 5.78–7.27] per 100,000 people); in women in America continent (1.61 [95% CI: 1.43–1.79] per 100,000 people) is higher.

The highest ASIR for EC among WHO regions was found in the Western Pacific Region (11.43 [95% CI: 9.1–13.39] per 100,000 people). The lowest was reported in the South-East Asia Region (3.36 [95% CI: 2.92–4.59] per 100,000 people). For men, the highest ASIR was seen in the Western Pacific Region (18.41 [95% CI: 14.51–22.3] per 100,000 people) and the lowest was reported in the South-East Asia Region (4.23 [95% CI: 3.53–6.01] per 100,000 people). For women, the highest ASIR was seen in the Western Pacific Region (5.23 [95% CI: 3.59–6.49] per 100,000 people) and the lowest was reported in the Region of the Americas (1.61 [95% CI: 1.43–1.79] per 100,000 people).

In the GBD regions, the highest ASIR is seen in East Asia (13.72 [95% CI: 10.64–16.25] per 100,000 people) and the lowest in Andean Latin America (1.51 [95% CI: 1.22–1.85] per 100,000 people). For men, the highest ASIR was seen in East Asia (21.7 [95% CI: 16.37–26.61] per 100,000 people) and the lowest was reported in Andean Latin America (2.22 [95% CI: 1.77–2.81] per 100,000 people). For women, the highest ASIR was seen in Eastern

Sub-Saharan Africa (8.56 [95% CI: 6.33–10.86] per 100,000 people) and the lowest was reported in the Andean Latin America (0.85 [95% CI: 0.68–1.06] per 100,000 people).

More details are presented in Tables 1–3 and Figures 1–4.

## 3.2 | Death rates of EC

In 2019, 498,067 (95% CI: 438,411–551,462) death due to EC was reported worldwide, of which 365,554 (95% CI: 315,014–415,028) among males and 132,513 (95% CI: 110,337–150,271) among females.

The age-standardized death rate (ASDR) of EC worldwide was 6.11 (95% CI: 5.38–6.76) per 100,000 inhabitants; 9.68 (95% CI: 8.34–10.96) in males and 3.02 (95% CI: 2.52–3.43) in females.

The highest ASDR per 100,000 people for EC has been reported in Malawi (25.76), Mongolia (24.53), Uganda (16.53), Cabo Verde (16.38), Zimbabwe (16.02), Eswatini (15.86), Lesotho (15.44), Eritrea (13.92), and Kenya (13.72), respectively. The lowest ASDR per 100,000 people for EC has been reported in the Syrian Arab Republic (0.96), Tunisia (0.97), Nigeria (1), Algeria (1.15), Palestine (1.16), Jordan (1.16), Lebanon (1.25), Iraq (1.3), and Nicaragua (1.32), respectively.

In men, the highest ASDR has been reported in Malawi (34.44), Mongolia (27), Cabo Verde (32.4), Eswatini (29.61), Lesotho (25.18), Zimbabwe (23.45), Uganda (22.06), Botswana (21.08), and Greenland (18.55), respectively. The lowest ASDR has been observed in the Syrian Arab Republic (1.35), Jordan (1.54), Tunisia (1.55), Nigeria (1.59), Algeria (1.65), Iraq (1.75), Maldives (1.78), Lebanon (1.87), and Saudi Arabia (1.93), respectively.

In women, the highest ASDR has been reported in Malawi (18.45), Mongolia (18.22), Eritrea (13.75), Kenya (13.4), Uganda (12.03), Somalia (11.62), Zambia (11.57), Comoros (10.95), and Zimbabwe (10.75), respectively. The lowest ASDR has been observed in San Marino (0.35), the Republic of Moldova (0.35), Andorra (0.37), Ukraine (0.43), the Republic of Korea (0.44), Tunisia (0.44), Guam (0.45), Libya (0.49), and Belarus (0.5), respectively

Statistics show that the highest ASDR for EC occurs in countries with Middle SDI (6.54 (95% CI: 3.85–6.17) per 100,000 people). The lowest ASDR occurs in countries with High SDI (4.18 [95% CI: 3.93–4.38] per 100,000 people). In men, the highest ASDR for EC occurs in countries with Middle SDI (12.62 [95% CI: 10.12–15.04] per 100,000 people) and the lowest ASDR occurs in countries with Low-middle SDI (6.04 [95% CI: 5.29–8.88] per 100,000 people). In women, the highest ASDR for EC occurs in countries with Low SDI (4.76 [95% CI: 3.87–5.75] per 100,000 people) and the lowest ASDR occurs in countries with High SDI (1.51 [95% CI: 1.36–1.61] per 100,000 people).

According to the World Bank classification, the ASDR for EC is highest in the Upper Middle Income (9.15 [95% CI: 7.41–10.66] per 100,000 people) worldwide and 15.12 (95% CI: 12.06–18.11) per 100,000 people in males; in females in Low Income (6.27 (95% CI: 4.37–7.93) per 100,000 people) is higher. The lowest rates were seen in Lower Middle Income (3.5 [95% CI: 3.13–4.35] per 100,000 people) worldwide; in men, the lowest rate was observed in Lower Middle Income (4.47 [95% CI: 3.9–5.74] per 100,000 people) and women in high-income countries with 1.4 (95% CI: 1.27-1.5) per 100,000 population.

Among the continents, the highest ASDR was reported in Asia (7.73 [95% CI: 6.57–8.8] per 100,000 people), while the lowest was observed in Europe (3.49 [95% CI: 3.27–3.68] per 100,000 people) worldwide. For men, the highest ASDR was reported in Asia (12.03 [95% CI: 9.93–14.17] per 100,000 people), and the lowest rate in Europe (6.14 [95% CI: 5.76–6.49] per 100,000 people). For women, the highest ASDR was reported in Africa (4.56 [95% CI: 3.39–5.58] per 100,000 people) and the lowest rate in Europe (1.39 [95% CI: 1.27–1.48] per 100,000 people).

The highest ASDR for EC among WHO regions was found in the Western Pacific Region (10.41 [95% CI: 8.36–12.26] per 100,000 people). The lowest was reported in the South-East Asia Region (3.48 [95% CI: 3.05–4.71] per 100,000 people). For men, the highest ASDR was seen in the Western Pacific Region (17.29 [95% CI: 13.62–20.94] per 100,000 people) and the lowest was reported in the South-East Asia Region (4.39 [95% CI: 3.67–6.16] per 100,000 people). For women, the highest ASDR was seen in the African Region (5.21 [95% CI: 3.89–6.43] per 100,000 people) and the lowest was reported in the Region of the Americas (1.51 [95% CI: 1.38–1.6] per 100,000 people).

In the GBD regions, the highest ASDR was seen in East Asia (12.96 [95% CI: 10.19–15.37] per 100,000 people) and the lowest in Andean Latin America (1.63 [95% CI: 1.33–2] per 100,000 people). For men, the highest ASDR was seen in East Asia (21.34 [95% CI: 16.45–26.2] per 100,000 people) and the lowest was reported in Andean Latin America (2.44 [95% CI: 1.94–3.06] per 100,000 people). For women, the highest ASDR was seen in Eastern Sub-Saharan Africa (9.36 [95% CI: 6.82–11.83] per 100,000 people) and the lowest was reported in Eastern Europe (0.89 [95% CI: 0.75–1.06] per 100,000 people).

More details are presented in Tables 1–3 and Figures 1–4.

## 3.3 | The burden of EC

In 2019, 11,666,017 (95% CI: 10,378,747–12,938,949) DALYs due to EC were reported worldwide, of which 11,515,943 (95% CI: 10,243,446–12,787,773) cases were related to YLLs and 150,074 (95% CI: 107,070–195,662) cases were related to YLDs.

The number of DALYs due to EC in men was reported at 8,821,716 (95% CI: 7,626,694–10,090,930), of which 8,714,068 (95% CI: 7,522,778–9,973,749) cases were related to YLLs and 107,649 (95% CI: 76,287–142,652) cases were related to YLDs.

For women, the number of DALYs due to EC was reported at 2,844,300 (95% CI: 2,434,410–3,195,247), of which 2,801,875 (95% CI: 2,391,555–3,157,407) cases were related to YLLs and 42,425 (95% CI: 29,237–56,389) cases were related to YLDs.

**TABLE 1** Esophageal cancer incidence cases, age-standardized incidence rate, deaths, age-standardized mortality rate, DALYs, age-standardized DALY rates, YLLs, age-standardized YLLs rates, YLDs, and age-standardized YLDs rates in 2019 (both sexes).

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| Global | 534,563 | 6.51 | 498,067 | 6.11 | 11,666,017 | 139.79 | 11,515,943 | 137.98 | 150,074 | 1.82 |
| | (466,513–595,342) | (5.69-7.25) | (438,411–551,462) | (5.38–6.76) | (10,378,747–12,938,949) | (124.44–154.98) | (10,243,446–12,787,773) | (122.84–153.13) | (107,070–195,662) | (1.3–2.37) |
| **SDI** | | | | | | | | | | |
| High SDI | 95,911 | 5.20 | 79,088 | 4.18 | 1,653,972 | 95.82 | 1,624,350 | 94.18 | 29,623 | 1.64 |
| | (86,719–105,092) | (4.71–5.7) | (73,600–83,089) | (3.93–4.38) | (1,570,861–1,731,345) | (91.39–100.45) | (1,542,691–1,699,854) | (89.9–98.55) | (21,314–38,245) | (1.18–2.11) |
| High-middle SDI | 145,267 | 7.06 | 135,757 | 6.62 | 3,105,596 | 151.03 | 3,065,318 | 149.07 | 40,278 | 1.96 |
| | (113,247–169,316) | (5.5–8.22) | (108,339–156,606) | (5.29–7.62) | (2,487,365–3,596,286) | (121.17–174.68) | (2,451,806–3,550,219) | (119.4–172.55) | (27,243–54,660) | (1.32–2.65) |
| Middle SDI | 205,237 | 8.42 | 193,720 | 8.15 | 4,485,644 | 175.17 | 4,429,457 | 172.91 | 56,186 | 2.26 |
| | (164,588–237,934) | (6.7–9.75) | (157,830–223,774) | (6.54–9.39) | (3,737,169–5,192,821) | (145.44–202.51) | (3,685,983–5,144,017) | (143.68–199.99) | (38,520–75,152) | (1.54–3.03) |
| Low-middle SDI | 59,864 | 4.37 | 60,670 | 4.53 | 1,611,655 | 111.27 | 1,595,286 | 110.09 | 16,369 | 1.18 |
| | (52,707–84,056) | (3.85–6.17) | (53,987–85,565) | (4.02–6.39) | (1,433,392–2,250,321) | (99.04–155.69) | (1,417,742–2,230,246) | (97.94–154.26) | (11,416–23,584) | (0.82–1.69) |
| Low SDI | 28,132 | 5.39 | 28,684 | 5.69 | 805,543 | 141.09 | 797,969 | 139.67 | 7575 | 1.41 |
| | (23,219–33,412) | (4.48–6.4) | (23,834–34,252) | (4.75–6.75) | (662,160–973,246) | (116.53–168.89) | (655,600–961,449) | (115.41–167.23) | (5104–10,699) | (0.95–1.98) |
| **World Bank Income Level** | | | | | | | | | | |
| High Income | 104,139 | 4.73 | 87,040 | 3.85 | 1,823,035 | 88.72 | 1,791,011 | 87.24 | 32,024 | 1.48 |
| | (94,002–114,160) | (4.27–5.2) | (81,129–91,280) | (3.63–4.02) | (1,737,674–1,899,653) | (84.78–92.32) | (1,705,814–1,868,887) | (83.38–90.98) | (22,880–41,494) | (1.06–1.92) |
| Upper Middle Income | 325,584 | 9.63 | 304,832 | 9.15 | 6,940,368 | 200.00 | 6,851,066 | 197.39 | 89,302 | 2.61 |
| | (260,177–379,969) | (7.68–11.21) | (248,449–356,550) | (7.41–10.66) | (5,739,489–8,141,316) | (165.89–233.85) | (5,647,779–8,047,522) | (163.21–231.32) | (61,308–120,705) | (1.79–3.53) |
| Lower Middle Income | 80,310 | 3.36 | 81,222 | 3.50 | 2,209,932 | 86.65 | 2,187,738 | 85.74 | 22,193 | 0.91 |
| | (71,920–100,297) | (3.01–4.22) | (72,568–100,689) | (3.13–4.35) | (1,971,695–2,701,416) | (77.42–107) | (1,951,501–2,669,450) | (76.54–105.6) | (15,464–29,702) | (0.64–1.23) |
| Low Income | 24,378 | 7.77 | 24,825 | 8.19 | 689,059 | 200.96 | 682,548 | 198.94 | 6511 | 2.02 |
| | (18,184–29,539) | (5.86–9.37) | (18,577–30,000) | (6.2–9.87) | (506,292–838,680) | (150–244.17) | (502,644–830,292) | (148.62–241.86) | (4225–9255) | (1.33–2.88) |
| **Continents** | | | | | | | | | | |
| Africa | 34,646 | 5.53 | 35,585 | 5.90 | 978,849 | 141.90 | 969,588 | 140.47 | 9261 | 1.43 |
| | (27,041–41,426) | (4.34–6.54) | (27,594–42,273) | (4.61–6.98) | (755,057–1,174,509) | (109.85–169.3) | (747,076–1,163,860) | (108.68–167.66) | (6154–13,100) | (0.96–2.02) |
| America | 49,140 | 3.85 | 47,551 | 3.71 | 1,087,393 | 86.37 | 1,073,756 | 85.30 | 13,636 | 1.07 |
| | (44,339–54,202) | (3.48–4.25) | (44,855–49,561) | (3.5–3.87) | (1,042,551–1,128,835) | (82.83–89.68) | (1,028,399–1,113,422) | (81.72–88.48) | (9476–17,853) | (0.75–1.4) |

(Continues)

**TABLE 1** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| Asia | 391,200 | 8.24 | 361,124 | 7.73 | 8,409,032 | 170.51 | 8,299,317 | 168.23 | 109,714 | 2.28 |
| | (332,573–449,273) | (6.96–9.43) | (307,593–411,840) | (6.57–8.8) | (7,201,261–9,643,913) | (145.87–194.85) | (7,096,881–9,518,470) | (143.8–192.42) | (77,489–145,528) | (1.6–3.02) |
| Europe | 59,228 | 3.95 | 53,459 | 3.49 | 1,183,004 | 83.68 | 1,165,639 | 82.51 | 17,365 | 1.18 |
| | (53,028–65,651) | (3.55–4.38) | (49,924–56,436) | (3.27–3.68) | (1,117,175–1,248,122) | (79.13–88.37) | (1,100,137–1,229,645) | (78.03–87.15) | (12,271–22,682) | (0.83–1.54) |
| **WHO regions** | | | | | | | | | | |
| African Region | 31,224 | 6.42 | 32,134 | 6.87 | 883,245 | 164.69 | 874,938 | 163.03 | 8307 | 1.66 |
| | (24,361–37,615) | (5.02–7.69) | (25,328–38,613) | (5.44–8.2) | (690,974–1,077,309) | (129.02–198.52) | (683,795–1,066,258) | (128.01–196.86) | (5514–11,901) | (1.11–2.35) |
| Eastern Mediterranean Region | 18,083 | 4.24 | 18,135 | 4.43 | 504,856 | 106.16 | 499,900 | 105.04 | 4956 | 1.12 |
| | (13,996–20,736) | (3.32–4.82) | (14,048–20,788) | (3.46–5.05) | (386,997–583,808) | (82.37–121.97) | (382,661–578,516) | (81.42–120.85) | (3360–6630) | (0.76–1.5) |
| European Region | 62,866 | 4.03 | 57,136 | 3.60 | 1,279,951 | 86.50 | 1,261,601 | 85.31 | 18,350 | 1.19 |
| | (56,401–69,532) | (3.62–4.45) | (53,452–60,403) | (3.37–3.79) | (1,207,920–1,349,261) | (81.74–91.29) | (1,190,007–1,330,460) | (80.66–90.06) | (12,990–23,979) | (0.84–1.56) |
| Region of the Americas | 49,140 | 3.85 | 47,551 | 3.71 | 1,087,393 | 86.37 | 1,073,756 | 85.30 | 13,636 | 1.07 |
| | (44,339–54,202) | (3.48–4.25) | (44,855–49,561) | (3.5–3.87) | (1,042,551–1,128,835) | (82.83–89.68) | (1,028,399–1,113,422) | (81.72–88.48) | (9476–17,853) | (0.75–1.4) |
| South-East Asia Region | 57,969 | 3.36 | 58,479 | 3.48 | 1,560,535 | 85.38 | 1,544,422 | 84.46 | 16,113 | 0.92 |
| | (50,204–78,946) | (2.92–4.59) | (51,027–79,004) | (3.05–4.71) | (1,357,972–2,087,267) | (74.31–114.42) | (1,344,746–2,072,813) | (73.5–113.56) | (11,091–22,495) | (0.63–1.29) |
| Western Pacific Region | 314,131 | 11.43 | 283,479 | 10.41 | 6,325,670 | 226.88 | 6,237,272 | 223.68 | 88,397 | 3.20 |
| | (248,990–368,906) | (9.1–13.39) | (228,271–335,523) | (8.36–12.26) | (5,153,182–7,565,317) | (185.13–270.81) | (5,061,881–7,472,393) | (181.86–267.23) | (60,806–119,141) | (2.2–4.3) |
| **GBD Region** | | | | | | | | | | |
| **East Asia and Pacific – WB** | 327,119 | 10.40 | 296,407 | 9.52 | 6,658,835 | 207.22 | 6,566,769 | 204.31 | 92,066 | 2.90 |
| | (262,700–382,322) | (8.36–12.14) | (240,766–348,022) | (7.71–11.14) | (5,450,341–7,884,574) | (169.96–244.61) | (5,366,345–7,785,749) | (167.11–241.91) | (63,395–124,071) | (2–3.91) |
| East Asia | 284,908 | 13.72 | 263,307 | 12.96 | 5,922,865 | 275.44 | 5,844,616 | 271.73 | 78,249 | 3.71 |
| | (220,166–338,886) | (10.64–16.25) | (209,014–314,860) | (10.19–15.37) | (4,733,467–7,156,234) | (221.92–331.75) | (4,655,173–7,079,836) | (218.22–327.93) | (53,499–106,306) | (2.53–5.01) |
| Oceania | 147 | 2.15 | 147 | 2.30 | 4213 | 53.58 | 4172 | 52.99 | 42 | 0.59 |
| | (110–196) | (1.66–2.89) | (111–197) | (1.78–3.05) | (3133–5650) | (40.42–71.74) | (3100–5587) | (39.94–70.95) | (26–63) | (0.36–0.89) |
| Southeast Asia | 15,543 | 2.54 | 15,330 | 2.59 | 403,725 | 61.73 | 399,275 | 61.01 | 4450 | 0.71 |
| | (13,193–18,202) | (2.18–2.97) | (13,164–17,964) | (2.24–3.05) | (342,843–472,284) | (52.74–72.38) | (339,139–466,894) | (52.14–71.63) | (3024–6070) | (0.48–0.97) |

**TABLE 1** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Sub-Saharan Africa – WB** | 32,572 (25,083–39,197) | 6.82 (5.24–8.16) | 33,517 (25,981–40,075) | 7.30 (5.67–8.7) | 923,414 (708,273–1,117,711) | 175.05 (135.67–210.26) | 914,751 (702,598–1,107,530) | 173.29 (133.97–207.93) | 8663 (5720–12,345) | 1.76 (1.16–2.48) |
| Central Sub-Saharan Africa | 4431 (2378–6020) | 8.41 (4.48–11.59) | 4509 (2426–6141) | 8.98 (4.79–12.41) | 127,510 (68,514–172,764) | 215.22 (115.53–294) | 126,328 (67,898–171,069) | 213.06 (114.67–290.28) | 1183 (592–1810) | 2.16 (1.07–3.3) |
| Eastern Sub-Saharan Africa | 16,391 (12,431–20,713) | 10.03 (7.71–12.6) | 16,940 (12,941–21,344) | 10.77 (8.28–13.48) | 476,744 (361,802–608,685) | 263.43 (200.49–332.94) | 472,395 (359,070–602,637) | 260.86 (198.62–329.79) | 4349 (2818–6523) | 2.57 (1.68–3.82) |
| Southern Sub-Saharan Africa | 5941 (5316–6943) | 10.66 (9.56–12.29) | 6095 (5489–7002) | 11.30 (10.23–12.77) | 159,882 (142,561–188,481) | 267.11 (239.24–310.78) | 158,340 (141,234–186,505) | 264.41 (236.57–307.53) | 1542 (1093–2068) | 2.70 (1.92–3.59) |
| Western Sub-Saharan Africa | 4986 (3776–5992) | 2.71 (2.06–3.21) | 5135 (3916–6146) | 2.89 (2.2–3.42) | 137,923 (104,912–167,521) | 67.83 (51.54–81.61) | 136,559 (104,056–165,639) | 67.11 (51.13–80.71) | 1364 (888–1866) | 0.72 (0.47–0.98) |
| **South Asia – WB** | 55,491 (48,269–73,744) | 3.81 (3.33–5.07) | 56,114 (48,993–73,980) | 3.97 (3.47–5.22) | 1,528,466 (1,338,674–1,987,169) | 99.01 (86.59–129.39) | 1,513,183 (1,324,789–1,965,928) | 97.98 (85.82–128.01) | 15,283 (10,535–21,002) | 1.03 (0.71–1.42) |
| South Asia | 53,488 (46,152–72,051) | 3.78 (3.27–5.1) | 54,161 (46,992–72,771) | 3.93 (3.41–5.25) | 1,476,590 (1,282,692–1,962,191) | 98.29 (85.53–131.08) | 1,461,864 (1,271,162–1,942,404) | 97.27 (84.6–129.94) | 14,726 (10,085–20,579) | 1.02 (0.7–1.43) |
| **Latin America and Caribbean – WB** | 23,173 (21,154–25,321) | 3.47 (3.16–3.79) | 23,597 (22,052–24,998) | 3.56 (3.32–3.77) | 566,841 (535,333–599,388) | 83.47 (78.78–88.27) | 560,528 (528,976–592,578) | 82.53047694 (77.9–87.28) | 6313 (4466–8251) | 0.94 (0.67–1.23) |
| Andean Latin America | 827 (670–1021) | 1.51 (1.22–1.85) | 889 (723–1090) | 1.63 (1.33–2) | 18,839 (15,081–23,638) | 33.43 (26.85–41.96) | 18,611 (14,920–23,382) | 33.02099184 (26.52–41.49) | 229 (150–323) | 0.41 (0.27–0.58) |
| Caribbean | 1920 (1641–2200) | 3.69 (3.15–4.23) | 1923 (1649–2197) | 3.70 (3.17–4.23) | 47,316 (40,107–54,718) | 90.70 (76.86–104.79) | 46,787 (39,657–54,047) | 89.68888693 (76–103.48) | 529 (366–723) | 1.02 (0.7–1.38) |
| Central Latin America | 3869 (3281–4511) | 1.66 (1.41–1.94) | 4021 (3391–4707) | 1.74 (1.47–2.04) | 90,775 (76,781–107,044) | 37.96 (32.14–44.75) | 89,687 (75,737–105,875) | 37.49947879 (31.72–44.25) | 1088 (743–1477) | 0.46 (0.32–0.63) |
| Tropical Latin America | 12,684 (11,993–132,94) | 5.17 (4.87–5.42) | 12,767 (11,996–13,448) | 5.25 (4.92–5.53) | 32,8430 (311,722–345,187) | 131.03 (124.29–137.7) | 324,988 (308,541–341,521) | 129.6409398 (123.04–136.29) | 3442 (2426–4437) | 1.39 (0.98–1.8) |

(Continues)

**TABLE 1** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Middle East and North Africa – WB** | 7233 (5761–8120) | 2.31 (1.87–2.58) | 7193 (5743–8056) | 2.40 (1.94–2.67) | 183,960 (144,033–208,700) | 52.92 (42.01–59.45) | 181,919 (142,372–206,486) | 52.29130952 (41.53–58.65) | 2041 (1387–2714) | 0.63 (0.43–0.84) |
| North Africa and Middle East | 10,024 (7415–11,436) | 2.36 (1.79–2.66) | 9968 (7385–11,383) | 2.44 (1.85–2.75) | 259,488 (183,343–301,673) | 55.58 (40.51–63.78) | 256,660 (181,010–298,509) | 54.9339228 (39.98–63.11) | 2828 (1857–3791) | 0.65 (0.43–0.86) |
| **Europe and Central Asia – WB** | 62,616 (56,190–69,203) | 4.05 (3.65–4.48) | 56,895 (53,229–60,120) | 3.62 (3.39–3.81) | 127,5126 (120,3533–1,344,332) | 87.06 (82.28–91.88) | 1,256,851 (1,185,741–1,325,374) | 85.86 (81.18–90.66) | 18,275 (12,945–23,875) | 1.20 (0.85–1.57) |
| Central Asia | 4834 (4274–5679) | 6.70 (5.95–7.75) | 4924 (4359–5769) | 7.08 (6.32–8.15) | 129,818 (114,167–153,552) | 164.79 (145.56–193.06) | 128,525 (113,094–152,195) | 163.06 (144.16–191.08) | 1294 (902–1759) | 1.74 (1.22–2.36) |
| Central Europe | 5853 (5109–6664) | 2.89 (2.52–3.3) | 5856 (5124–6670) | 2.86 (2.49–3.25) | 143,701 (124,717–164,319) | 74.70 (64.49–85.35) | 142,075 (123,152–162,108) | 73.89 (63.8–84.54) | 1626 (1122–2174) | 0.81 (0.56–1.09) |
| Eastern Europe | 11,086 (9669–12,604) | 3.25 (2.83–3.69) | 10,655 (9298–12,077) | 3.10 (2.71–3.51) | 27,7541 (240,922–316,272) | 83.49 (72.58–95.11) | 274,446 (238,217–313,336) | 82.57 (71.71–94.21) | 3095 (2123–4149) | 0.91 (0.63–1.23) |
| **High Income** | 97,631 (87,948–107,607) | 4.73 (4.28–5.21) | 81,439 (75,807–85,169) | 3.84 (3.61–4) | 1,660,656 (1,582,744–1,726,083) | 86.63 (82.96–89.94) | 1,630,616 (1,552,587–1,695,748) | 85.15 (81.51–88.38) | 30,040 (21,468–38,790) | 1.4888042 (1.07–1.93) |
| Australasia | 2192 (1767–2707) | 4.41 (3.55–5.46) | 2035 (1830–2218) | 4.02 (3.65–4.39) | 39,885 (36,426–43,385) | 85.18 (78.02–92.42) | 39,263 (35,936–42,640) | 83.91 (77.07–91.15) | 622 (412–871) | 1.27 (0.85–1.79) |
| Asia Pacific | 25,159 (21,213–29,616) | 5.71 (4.83–6.76) | 16,337 (14,650–17,795) | 3.53 (3.22–3.84) | 306,118 (281,921–333,763) | 75.76 (70.65–82.63) | 297,167 (273,876–323,419) | 73.66 (68.74–80.33) | 8952 (6299–12,189) | 2.10 (1.47–2.88) |
| North America | 26,162 (22,461–30,594) | 4.22 (3.63–4.96) | 24,152 (22,876–25,147) | 3.84 (3.65–3.99) | 524,630 (503,915–544,030) | 88.30 (84.99–91.37) | 517,253 (496,691–535,626) | 87.09 (83.86–90.13) | 7377 (5020–9874) | 1.21 (0.82–1.62) |
| Southern Latin America | 3945 (3158–4943) | 4.70 (3.75–5.89) | 4067 (3769–4359) | 4.82 (4.47–5.15) | 83,206 (77,617–89,098) | 101.08 (94.41–108.18) | 82,161 (76,601–88,018) | 99.83 (93.2–106.84) | 1045 (687–1479) | 1.25 (0.82–1.78) |
| Western Europe | 40,174 (35,133–45,706) | 4.64 (4.06–5.29) | 34,847 (32,416–36,620) | 3.87 (3.64–4.06) | 706,817 (669,630–741,655) | 88.65 (84.34–92.92) | 694,772 (657,345–728,064) | 87.21 (82.93–91.38) | 12,044 (8460–15,996) | 1.44 (1.01–1.91) |

Abbreviations: ASR, Age-standardized rate; CI, confidence interval; DALY, disability-adjusted life year; SDI, sociodemographic index; YLD, year lived with disability; YLL, year of life lost.

**TABLE 2** Esophageal cancer incidence cases, age-standardized incidence rate, deaths, age-standardized mortality rate, DALYs, age-standardized DALY rates, YLLs, age-standardized YLLs rates, YLDs, and age-standardized YLDs rates in 2019 men.

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| Global | 388,827 | 10.13 | 365,554 | 9.68 | 8,821,716 | 221.38 | 8,714,068 | 218.61 | 107,649 | 2.77 |
| | (335,510–444,000) | (8.73–11.56) | (315,014–415,028) | (8.34–10.96) | (7,626,694–10,090,930) | (191.21–252.21) | (7,522,778–9,973,749) | (188.83–249.68) | (76,287–142,652) | (1.97–3.66) |
| **SDI** | | | | | | | | | | |
| High SDI | 75,555 | 8.92 | 62,182 | 7.28 | 1,355,369 | 165.92 | 1,332,334 | 163.18 | 23,035 | 2.74 |
| | (68,055–83,454) | (8.03–9.84) | (58,793–65,202) | (6.89–7.64) | (1,291,167–1,422,052) | (158.24–174.16) | (1,270,699–1,397,106) | (155.75–171.32) | (16,575–29,748) | (1.97–3.55) |
| High-middle SDI | 110,145 | 11.86 | 104,879 | 11.47 | 2,511,455 | 262.66 | 2,481,501 | 259.47 | 29,954 | 3.19 |
| | (84,183–132,597) | (9.09–14.21) | (81,479–124,518) | (8.91–13.59) | (1,989,952–2,994,090) | (208.04–311.91) | (1,965,209–2,956,114) | (205.49–308.5) | (20,087–41,423) | (2.15–4.39) |
| Middle SDI | 147,987 | 12.70 | 142,742 | 12.62 | 3,423,855 | 276.14 | 3,384,157 | 272.82 | 39,697 | 3.32 |
| | (118,092–177,284) | (10.08–15.16) | (114,729–170,896) | (10.12–15.04) | (2,774,900–4,107,393) | (223.66–330.77) | (2,744,031–4,059,097) | (220.78–327.5) | (27,184–54,081) | (2.29–4.45) |
| Low-middle SDI | 38,549 | 5.84 | 38,884 | 6.04 | 1,047,436 | 148.95 | 1,036,947 | 147.39 | 10,489 | 1.56 |
| | (33,348–56,842) | (5.06–8.63) | (33,930–56,641) | (5.29–8.88) | (911,007–1,508,225) | (129.75–214.45) | (902,310–1,491,867) | (128.44–212.43) | (7182–15,882) | (1.06–2.37) |
| Low SDI | 16,481 | 6.30 | 16,760 | 6.63 | 480,895 | 168.62 | 476,454 | 166.97 | 4,442 | 1.65 |
| | (13,025–20,221) | (4.98–7.7) | (13,269–20,714) | (5.29–8.19) | (376,519–598,266) | (133.03–209.38) | (372,978–591,886) | (131.74–206.95) | (2,913–6,369) | (1.09–2.35) |
| **World Bank Income Level** | | | | | | | | | | |
| High Income | 81,487 | 8.10 | 68,008 | 6.71 | 1,487,664 | 153.84 | 1,462,947 | 151.36 | 24,717 | 2.48 |
| | (73,416–89,933) | (7.29–8.96) | (64,272–71,045) | (6.35–7.01) | (1,420,226–1,551,792) | (147.09–160.55) | (1,398,094–1,525,678) | (144.63–157.86) | (17,662–32,022) | (1.78–3.22) |
| Upper Middle Income | 242,745 | 15.41 | 232,378 | 15.12 | 5,519,636 | 334.55 | 5,454,400 | 330.48 | 65,236 | 4.06 |
| | (189,957–293,156) | (12.08–18.52) | (184,790–280,234) | (12.06–18.11) | (4,445,498–6,692,272) | (268.87–404.18) | (4,382,759–6,626,111) | (265.1–400.06) | (43,859–89,364) | (2.74–5.55) |
| Lower Middle Income | 49,681 | 4.29 | 50,072 | 4.47 | 1,381,428 | 111.03 | 1,367,728 | 109.87 | 13,700 | 1.16 |
| | (42,931–63,844) | (3.71–5.54) | (43,583–63,819) | (3.9–5.74) | (1,199,203–1,750,154) | (96.61–140.75) | (1,187,763–1,732,051) | (95.61–139.37) | (9464–18,833) | (0.8–1.6) |
| Low Income | 14,803 | 9.82 | 14,988 | 10.31 | 430,269 | 260.08 | 426,304 | 257.53 | 3965 | 2.55 |
| | (10,880–18,626) | (7.29–12.25) | (11,069–18,782) | (7.71–12.82) | (314,868–544,284) | (191.4–327.98) | (312,199–540,146) | (189.5–323.87) | (2506–5711) | (1.63–3.68) |
| **Continents** | | | | | | | | | | |
| Africa | 21,560 | 6.94 | 21,945 | 7.32 | 624,213 | 183.35 | 618,440 | 181.54 | 5774 | 1.81 |
| | (16,606–26,094) | (5.34–8.3) | (16,762–26,550) | (5.62–8.74) | (473,688–763,542) | (139.98–222.51) | (469,259–756,242) | (138.58–220.57) | (3789–8111) | (1.19–2.53) |
| America | 37,837 | 6.47 | 36,806 | 6.32 | 869,566 | 147.83 | 859,292 | 146.07 | 10,274 | 1.75 |
| | (33,771–42,519) | (5.78–7.27) | (35,045–38,302) | (6–6.58) | (836,474–903,429) | (142.2–153.53) | (827,058–892,455) | (140.61–151.75) | (7173–13,455) | (1.23–2.3) |

(Continues)

**TABLE 2** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| Asia | 284,642 | 12.56 | 266,188 | 12.03 | 6,378,988 | 265.89 | 6,300,277 | 262.48 | 78,711 | 3.41 |
| | (233,255–339,631) | (10.28–14.89) | (218,454–315,018) | (9.93–14.17) | (5,255,579–7,615,340) | (219.88–314.77) | (5,183,411–7,522,929) | (216.82–311.19) | (54,550–107,244) | (2.36–4.62) |
| Europe | 44,522 | 6.79 | 40,349 | 6.14 | 942,815 | 147.25 | 929,999 | 145.28 | 12,817 | 1.97 |
| | (39,733–49,673) | (6.06–7.57) | (37,858–42,649) | (5.76–6.49) | (886,885–1,001,854) | (138.28–156.52) | (873,986–987,289) | (136.32–154.31) | (9,012–16,767) | (1.38–2.57) |
| **WHO regions** | | | | | | | | | | |
| African Region | 19,397 | 8.22 | 19,753 | 8.69 | 563,605 | 216.99 | 558,435 | 214.86 | 5170 | 2.13 |
| | (14,914–23,804) | (6.35–10.01) | (15,126–24,294) | (6.65–10.56) | (428,799–702,717) | (166.2–267.79) | (425,245–695,432) | (164.96–264.99) | (3389–7382) | (1.39–3.03) |
| Eastern Mediterranean Region | 10,407 | 4.69 | 10,501 | 4.93 | 292,803 | 118.37 | 289,952 | 117.13 | 2851 | 1.24 |
| | (7927–12,413) | (3.58–5.52) | (7750–12,410) | (3.7–5.75) | (211,080–350,489) | (87.1–140.35) | (209,170–347,629) | (85.98–139.19) | (1861–3885) | (0.82–1.68) |
| European Region | 46,650 | 6.82 | 42,487 | 6.21 | 999,854 | 148.88 | 986,465 | 146.91 | 13,389 | 1.97 |
| | (41,734–51,876) | (6.11–7.59) | (39,915–44,939) | (5.83–6.57) | (939,680–1,063,166) | (139.78–158.33) | (928,481–1,046,864) | (138.22–155.98) | (9439–17,547) | (1.39–2.57) |
| Region of the Americas | 37,837 | 6.47 | 36,806 | 6.32 | 869,566 | 147.83 | 859,292 | 146.07 | 10,274 | 1.75 |
| | (33,771–42,519) | (5.78–7.27) | (35,045–38,302) | (6–6.58) | (836,474–903,429) | (142.2–153.53) | (827,058–892,455) | (140.61–151.75) | (7173–13,455) | (1.23–2.3) |
| South-East Asia Region | 35,555 | 4.23 | 35,822 | 4.39 | 972,036 | 108.39 | 962,192 | 107.24 | 9,844 | 1.15 |
| | (29,472–50,655) | (3.53–6.01) | (29,809–50,066) | (3.67–6.16) | (803,335–1,343,251) | (89.88–150.49) | (795,554–1,328,329) | (88.97–148.73) | (6,689–14,194) | (0.78–1.66) |
| Western Pacific Region | 238,106 | 18.41 | 219,303 | 17.29 | 5,104,340 | 379.54 | 5,038,457 | 374.52 | 65,883 | 5.03 |
| | (185,744–290,278) | (14.51–22.3) | (172,453–267,695) | (13.62–20.94) | (4,036,216–6,288,845) | (301.22–465.59) | (3,968,233–6,219,232) | (296.55–460.51) | (45,264–90,491) | (3.45–6.88) |
| **GBD Region** | | | | | | | | | | |
| **East Asia and Pacific – WB** | 247,149 | 16.74 | 228,274 | 15.79 | 5,344,957 | 345.87 | 5,276,526 | 341.31 | 68,430 | 4.56 |
| | (194,726–299,242) | (13.28–20.14) | (181,162–277,015) | (12.55–19.04) | (4,268,207–6,523,621) | (276.92–420.56) | (4,200,274–6,451,808) | (272.59–415.8) | (46,963–93,833) | (3.13–6.23) |
| East Asia | 213,576 | 21.70 | 202,627 | 21.34 | 4,762,730 | 456.24 | 4,705,325 | 450.55 | 57,405 | 5.69 |
| | (161,490–263,961) | (16.37–26.61) | (156,174–251,212) | (16.45–26.2) | (3,693,718–5,949,237) | (356.28–566.73) | (3,633,608–5,888,088) | (350.88–560.71) | (37,834–79,578) | (3.77–7.84) |
| Oceania | 111 | 3.14 | 111 | 3.35 | 3203 | 78.83 | 3172 | 77.97 | 32 | 0.86 |
| | (81–158) | (2.28–4.4) | (81–158) | (2.44–4.68) | (2319–4485) | (57.18–111.28) | (2291–4437) | (56.59–110.18) | (19–49) | (0.53–1.33) |
| Southeast Asia | 10,990 | 3.84 | 10,823 | 3.94 | 295,010 | 94.94 | 291,879 | 93.87 | 3131 | 1.06 |
| | (9179–13,033) | (3.23–4.55) | (9081–12,957) | (3.33–4.73) | (245,807–348,668) | (79.03–113.21) | (242,652–345,235) | (78.23–112) | (2076–4343) | (0.71–1.46) |

**TABLE 2** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Sub-Saharan Africa – WB** | 20,125 (15,268–24,595) | 8.71 (6.58–10.51) | 20,501 (15,375–25,044) | 9.22 (6.95–11.14) | 585,624 (439,965–724,517) | 229.55 (172.68–281.19) | 580,262 (436,402–718,667) | 227.31 (170.92–278.91) | 5362 (3489–7628) | 2.25 (1.46–3.18) |
| Central Sub-Saharan Africa | 2683 (1485–3779) | 11.14 (6.13–15.66) | 2718 (1509–3826) | 11.91 (6.53–16.85) | 79,146 (44,186–111,330) | 286.69 (159.4–402.9) | 78,431 (43,842–110,307) | 283.86 (157.47–398.89) | 715 (366–1114) | 2.83 (1.44–4.43) |
| Eastern Sub-Saharan Africa | 9340 (6894–12,414) | 11.51 (8.58–15.09) | 9523 (7104–12,549) | 12.15 (9.13–15.8) | 279,056 (204,866–369,904) | 311.61 (232.29–410.48) | 276,565 (203,089–366,481) | 308.63 (230.4–407.17) | 2492 (1532–3800) | 2.98 (1.84–4.54) |
| Southern Sub-Saharan Africa | 3899 (3429–4872) | 16.49 (14.63–20.16) | 3952 (3526–4887) | 17.50 (15.65–21) | 109,927 (97,126–138,273) | 419.56 (373.33–520.53) | 108,914 (96,078–137,004) | 415.44 (369.42–514.59) | 1013 (706–1393) | 4.13 (2.88–5.63) |
| Western Sub-Saharan Africa | 3672 (2649–4468) | 4.06 (2.9–4.89) | 3760 (2670–4522) | 4.31 (3.03–5.14) | 103,822 (74,478–126,665) | 104.94 (74.4–126.96) | 102,823 (73,840–125,529) | 103.87 (73.71–125.56) | 999 (632–1,372) | 1.08 (0.68–1.48) |
| **South Asia – WB** | 32,228 (26,489–45,128) | 4.49 (3.69–6.33) | 32,610 (27,008–44,970) | 4.68 (3.89–6.4) | 895,446 (738,369–1,230,333) | 116.92 (96.84–160.72) | 886,602 (731,768–1,216,395) | 115.71 (95.54–158.8) | 8844 (5991–12,591) | 1.20 (0.81–1.74) |
| South Asia | 31,250 (25,409–44,454) | 4.46 (3.65–6.39) | 31,647 (26,005–44,168) | 4.65 (3.84–6.45) | 869,512 (709,751–1,206,889) | 116.47 (95.56–161.69) | 860,938 (703,447–1,193,180) | 115.27 (94.56–159.98) | 8574 (5763–12,369) | 1.21 (0.82–1.73) |
| **Latin America and Caribbean – WB** | 17,307 (15,903–18,883) | 5.64 (5.18–6.16) | 17,573 (16,445–18,659) | 5.81 (5.43–6.17) | 439,901 (414,961–466,602) | 139.04 (131.1–147.39) | 435,237 (410,727–461,291) | 137.54 (129.72–145.8) | 4664 (3318–6114) | 1.51 (1.08–1.97) |
| Andean Latin America | 581 (460–738) | 2.22 (1.77–2.81) | 629 (501–790) | 2.44 (1.94–3.06) | 13,304 (10,515–17,301) | 49.28 (38.91–63.52) | 13,145 (10,388–17,097) | 48.68 (38.49–62.6) | 159 (103–228) | 0.60 (0.39–0.86) |
| Caribbean | 1503 (1274–1740) | 6.12 (5.21–7.07) | 1501 (1281–1729) | 6.16 (5.24–7.08) | 37,973 (31,966–44,298) | 152.39 (128.56–177.49) | 37,564 (31,648–43,807) | 150.74 (127.28–175.52) | 408 (284–568) | 1.65 (1.15–2.3) |
| Central Latin America | 2759 (2312–3247) | 2.58 (2.17–3.02) | 2872 (2400–3394) | 2.72 (2.27–3.21) | 66,715 (55,519–79,291) | 60.09 (49.97–71.25) | 65,944 (54,806–78,383) | 59.38 (49.29–70.49) | 771 (521–1,053) | 0.71 (0.48–0.97) |
| Tropical Latin America | 9843 (9277–10,396) | 8.77 (8.26–9.26) | 9861 (9294–10,449) | 8.94 (8.39–9.48) | 263,422 (248,867–278,494) | 226.28 (214–239.33) | 260,780 (246,149–276,122) | 223.96 (211.66–236.98) | 2642 (1864–3401) | 2.32 (1.65–2.99) |

(Continues)

**TABLE 2** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Middle East and North Africa – WB** | 4704 (3674–5381) | 2.89 (2.25–3.27) | 4739 (3681–5395) | 3.03 (2.35–3.41) | 122,767 (92,034–142,706) | 67.52 (52.51–77.45) | 121,452 (91,090–141,143) | 66.74014663 (51.83–76.58) | 1315 (869–1756) | 0.78 (0.52–1.04) |
| North Africa and Middle East | 6259 (4554–7272) | 2.90 (2.17–3.33) | 6310 (4603–7341) | 3.04 (2.26–3.48) | 164,791 (116,101–195,254) | 69.00 (49.77–80.63) | 163,042 (114,984–193,361) | 68.21301487 (49.22–79.89) | 1750 (1126–2370) | 0.79 (0.52–1.06) |
| **Europe and Central Asia – WB** | 46,483 (41,597–51,684) | 6.87 (6.15–7.64) | 42,324 (39,761–44,759) | 6.25 (5.87–6.61) | 996,355 (936,234–1,059,555) | 149.93 (140.75–159.46) | 983,014 (925,123–1,043,436) | 147.95 (139.18–157.12) | 13,341 (9411–17,478) | 1.98 (1.4–2.59) |
| Central Asia | 2929 (2551–3627) | 9.51 (8.37–11.53) | 2958 (2582–3657) | 10.09 (8.9–12.2) | 79,409 (68,672–98,503) | 229.67 (200.63–282.88) | 78,627 (68,034–97,633) | 227.24 (198.38–280.29) | 782 (542–1086) | 2.44 (1.69–3.34) |
| Central Europe | 4748 (4087–5457) | 5.23 (4.51–6.02) | 4686 (4029–5382) | 5.17 (4.44–5.93) | 120,455 (103,127–138,584) | 135.18 (115.8–155.4) | 119,142 (102,066–137,073) | 133.72 (114.5–153.79) | 1313 (909–1759) | 1.46 (1–1.95) |
| Eastern Europe | 9149 (7793–10,615) | 6.68 (5.71–7.74) | 8678 (7367–10,022) | 6.42 (5.46–7.4) | 236,390 (200,136–273,269) | 170.26 (144.04–197.12) | 233,849 (197,847–270,359) | 168.41 (142.39–194.78) | 2541 (1733–3415) | 1.85 (1.26–2.48) |
| **High Income** | 75,535 (68,101–83,866) | 8.06 (7.25–8.94) | 62,898 (59,283–65,482) | 6.64 (6.28–6.91) | 1,336,852 (1,277,918–1,389,090) | 149.07 (142.88–154.8) | 1,313,929 (1,256,576–1,365,252) | 146.59 (140.36–152.28) | 22,923 (16,302–29,690) | 2.47 (1.76–3.21) |
| Australasia | 1507 (1208–1870) | 6.56 (5.24–8.12) | 1461 (1330–1594) | 6.30 (5.76–6.86) | 30,353 (27,829–32,879) | 137.37 (126.42–148.3) | 29,943 (27,522–32,456) | 135.56 (124.96–146.54) | 410 (264–583) | 1.81 (1.18–2.53) |
| Asia Pacific | 21,385 (17,785–25,794) | 10.68 (8.87–12.89) | 13,641 (12,441–14,825) | 6.66 (6.11–7.25) | 263,572 (243,999–288,037) | 139.04 (129.26–153.24) | 255,995 (237,514–279,651) | 135.18 (125.68–148.42) | 7577 (5283–10,337) | 3.86 (2.7–5.29) |
| North America | 20,683 (17,315–24,930) | 7.26 (6.07–8.75) | 19,387 (18,475–20,136) | 6.77 (6.46–7.03) | 43,3015 (416,528–448,910) | 154.95 (149.16–160.45) | 427,363 (410,606–442,756) | 152.96 (147.09–158.35) | 5651 (3779–7647) | 2.00 (1.34–2.7) |
| Southern Latin America | 2677 (2116–3356) | 7.35 (5.84–9.21) | 2766 (2567–2967) | 7.67 (7.11–8.22) | 59,880 (55,503–64,283) | 162.18 (150.31–173.79) | 59,181 (54,876–63,509) | 160.27 (148.68–171.63) | 699 (447–998) | 1.91 (1.22–2.72) |
| Western Europe | 29,282 (25,318–33,497) | 7.47 (6.46–8.56) | 25,642 (24,147–26,950) | 6.42 (6.06–6.75) | 550,033 (522,570–577,836) | 147.86 (140.71–155.47) | 541,447 (514,578–568,606) | 145.62 (138.79–152.84) | 8586 (6036–11,502) | 2.23 (1.56–2.98) |

Abbreviations: ASR, Age-standardized rate; CI, confidence interval; DALY, disability-adjusted life year; SDI, sociodemographic index; YLD, year lived with disability; YLL, year of life lost.

**TABLE 3** Esophageal cancer incidence cases, age-standardized incidence rate, deaths, age-standardized mortality rate, DALYs, age-standardized DALY rates, YLLs, age-standardized YLLs rates, YLDs, and age-standardized YLDs rates in 2019 women.

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| Global | 145,736 | 3.33 | 132,513 | 3.02 | 2,844,300 | 65.29 | 2,801,875 | 64.32 | 42,425 | 0.97 |
| | (119,952–165,068) | (2.74–3.77) | (110,337–150,271) | (2.52–3.43) | (2,434,410–3,195,247) | (55.83–73.33) | (2,391,555–3,157,407) | (54.9–72.49) | (29,237–56,389) | (0.67–1.29) |
| **SDI** | | | | | | | | | | |
| High SDI | 20,356 | 1.93 | 16,907 | 1.51 | 298,603 | 31.19 | 292,016 | 30.55 | 6587 | 0.65 |
| | (17,601–22,788) | (1.69–2.16) | (14,919–18,275) | (1.36–1.61) | (274,365–317,994) | (29.25–33.02) | (268,964–310,946) | (28.65–32.35) | (4621–8717) | (0.45–0.86) |
| High-middle SDI | 35,122 | 3.06 | 30,879 | 2.66 | 594,140 | 53.07 | 58,3816 | 52.16 | 10,324 | 0.91 |
| | (24,900–44,192) | (2.18–3.84) | (22,628–38,241) | (1.96–3.29) | (452,624–719,107) | (40.59–64.07) | (445,733–709,621) | (39.97–63.26) | (6711–14,402) | (0.59–1.27) |
| Low SDI | 11,652 | 4.48 | 11,924 | 4.76 | 324,648 | 113.69 | 321,515 | 112.52 | 3133 | 1.17 |
| | (9460–14,072) | (3.65–5.38) | (9645–14,363) | (3.87–5.75) | (258,063–391,364) | (90.95–137.43) | (255,542–387,542) | (89.85–136.06) | (2,097–4,363) | (0.78–1.63) |
| Low-middle SDI | 21,316 | 3.01 | 21,786 | 3.15 | 564,219 | 75.85 | 558,339 | 75.03 | 5880 | 0.82 |
| | (18,319–28,823) | (2.58–4.1) | (18,852–30,095) | (2.72–4.39) | (488,216–762,040) | (65.68–102.82) | (482,696–752,562) | (64.9–101.7) | (3974–8391) | (0.55–1.16) |
| Middle SDI | 57,250 | 4.58 | 50,977 | 4.18 | 1,061,789 | 81.80 | 1,045,300 | 80.51 | 16,489 | 1.29 |
| | (39,583–68,442) | (3.13–5.46) | (36,525–60,575) | (2.96–4.95) | (788,270–1,259,769) | (60.14–96.89) | (777,211–1,242,805) | (59.27–95.55) | (10,788–22,627) | (0.84–1.77) |
| **World Bank Income Level** | | | | | | | | | | |
| High Income | 22,652 | 1.78 | 19,033 | 1.40 | 335,371 | 29.20 | 328,064 | 28.61 | 7307 | 0.60 |
| | (19,521–25,293) | (1.57–1.99) | (16,795–20,470) | (1.27–1.5) | (308,867–355,599) | (27.42–30.82) | (303,046–347,741) | (26.82–30.18) | (5123–9652) | (0.42–0.79) |
| Low Income | 9575 | 5.91 | 9837 | 6.27 | 258,790 | 146.42 | 256,244 | 144.89 | 2546 | 1.53 |
| | (6665–12,101) | (4.14–7.4) | (6810–12,372) | (4.37–7.93) | (178,829–330,108) | (101.96–185.86) | (176,966–327,115) | (100.85–183.89) | (1596–3607) | (0.96–2.15) |
| Lower Middle Income | 30,630 | 2.50 | 31,150 | 2.61 | 828,504 | 63.57 | 820,011 | 62.89 | 8494 | 0.68 |
| | (26,448–37,726) | (2.17–3.1) | (26,892–38,870) | (2.26–3.29) | (715,637–1,020,072) | (55.09–78.45) | (707,130–1,011,714) | (54.44–77.53) | (5761–11,545) | (0.47–0.93) |
| Upper Middle Income | 82,839 | 4.62 | 72,454 | 4.08 | 1,420,732 | 78.49 | 1,396,666 | 77.16 | 24,067 | 1.33 |
| | (58,241–101,142) | (3.24–5.65) | (52,606–88,254) | (2.95–4.98) | (1,078,318–1,718,017) | (59.4–94.92) | (1,056,182–1,694,824) | (58.18–93.69) | (15,676–33,022) | (0.87–1.83) |
| **Continents** | | | | | | | | | | |
| Africa | 13,086 | 4.19 | 13,640 | 4.56 | 354,636 | 102.49 | 351,148 | 101.41 | 3487 | 1.08 |
| | (9777–16,167) | (3.14–5.14) | (10,152–16,857) | (3.39–5.58) | (263,690–440,459) | (76.29–126.52) | (261,219–436,502) | (75.52–125.34) | (2277–4909) | (0.7–1.51) |
| America | 11,303 | 1.61 | 10,744 | 1.51 | 217,826 | 32.13 | 214,464 | 31.64 | 3362 | 0.48 |
| | (10,030–12,605) | (1.43–1.79) | (9802–11,415) | (1.38–1.6) | (204,835–229,712) | (30.3–33.89) | (201,515–226,075) | (29.83–33.37) | (2384–4424) | (0.34–0.64) |

(Continues)

**TABLE 3** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| Asia | 106,558 | 4.33 | 94,936 | 3.91 | 2,030,044 | 80.86 | 1,999,040 | 79.61 | 31,003 | 1.25 |
| | (83,567–125,405) | (3.39–5.1) | (76,397–111,530) | (3.13–4.59) | (1,698,323–2,364,559) | (67.5–94.12) | (1,672,038–2,331,829) | (66.53–92.63) | (21,108–41,739) | (0.85–1.68) |
| Europe | 14,707 | 1.64 | 13,110 | 1.39 | 240,189 | 29.44 | 235,640 | 28.92 | 4548 | 0.52 |
| | (12,944–16,563) | (1.45–1.85) | (11,855–14,083) | (1.27–1.48) | (223,255–256,126) | (27.59–31.39) | (218,563–251,272) | (27.1–30.8) | (3178–6060) | (0.37–0.7) |
| **WHO regions** | | | | | | | | | | |
| African Region | 11,827 | 4.78 | 12,380 | 5.21 | 319,640 | 116.73 | 316,504 | 115.50 | 3137 | 1.23 |
| | (8895–14,706) | (3.58–5.93) | (9319–15,417) | (3.89–6.43) | (239,456–403,791) | (87.92–145.35) | (237,070–399,977) | (87.06–144.07) | (2060–4456) | (0.81–1.74) |
| Eastern Mediterranean Region | 7676 | 3.76 | 7634 | 3.90 | 212,053 | 92.89 | 209,949 | 91.90 | 2104 | 0.99 |
| | (5733–9294) | (2.78–4.49) | (5775–9266) | (2.95–4.67) | (160,114–262,519) | (70.48–113.56) | (158,370–260,469) | (69.67–112.54) | (1380–2901) | (0.65–1.36) |
| European Region | 16,217 | 1.76 | 14,649 | 1.52 | 280,097 | 33.50 | 275,136 | 32.95 | 4961 | 0.55 |
| | (14,331–18,136) | (1.57–1.96) | (13,306–15,735) | (1.4–1.63) | (260,133–299,193) | (31.18–35.92) | (255,214–293,648) | (30.68–35.2) | (3463–6570) | (0.39–0.74) |
| Region of the Americas | 11,303 | 1.61 | 10,744 | 1.51 | 217,826 | 32.13 | 214,464 | 31.64 | 3362 | 0.48 |
| | (10,030–12,605) | (1.43–1.79) | (9802–11,415) | (1.38–1.6) | (204,835–229,712) | (30.3–33.89) | (201,515–226,075) | (29.83–33.37) | (2384–4424) | (0.34–0.64) |
| South-East Asia Region | 22,414 | 2.54 | 22,656 | 2.63 | 588,499 | 63.38 | 582,230 | 62.68 | 6269 | 0.70 |
| | (18,778–29,626) | (2.13–3.4) | (18,900–30,640) | (2.2–3.56) | (487,931–789,434) | (52.71–85.13) | (482,750–781,968) | (52.05–84.34) | (4229–8914) | (0.47–0.99) |
| Western Pacific Region | 76,025 | 5.23 | 64,175 | 4.41 | 1,221,330 | 84.23 | 1,198,815 | 82.68 | 22,515 | 1.55 |
| | (52,143–94,397) | (3.59–6.49) | (44,701–79,676) | (3.07–5.47) | (889,214–1,514,041) | (61.4–104.32) | (868,312–1,488,336) | (59.95–102.54) | (14,488–31,088) | (1–2.14) |
| **GBD Region** | | | | | | | | | | |
| **East Asia and Pacific – WB** | 79,970 | 4.81 | 68,133 | 4.11 | 1,313,878 | 78.90 | 1,290,243 | 77.48 | 23,635 | 1.42 |
| | (55,891–98,430) | (3.36–5.92) | (48,412–83,501) | (2.91–5.03) | (982,399–1,604,939) | (58.94–96.34) | (965,244–1,582,556) | (57.91–94.99) | (15,369–32,422) | (0.92–1.95) |
| East Asia | 71,332 | 6.67 | 60,680 | 5.78 | 1,160,135 | 106.42 | 1,139,292 | 104.49 | 20,844 | 1.93 |
| | (47,153–89,703) | (4.39–8.38) | (41,265–75,995) | (3.9–7.24) | (828,882–1,451,416) | (75.55–133.05) | (810,780–1,429,114) | (73.98–130.84) | (13,036–29,147) | (1.2–2.69) |
| Oceania | 36 | 1.11 | 36 | 1.21 | 1010 | 26.54 | 1000 | 26.24 | 10 | 0.30 |
| | (27–48) | (0.85–1.46) | (27–48) | (0.93–1.59) | (735–1379) | (19.93–35.62) | (729–1366) | (19.7–35.3) | (6–15) | (0.19–0.44) |
| Southeast Asia | 4553 | 1.43 | 4508 | 1.46 | 108,715 | 32.29 | 107,396 | 31.89 | 1319 | 0.41 |
| | (3747–5461) | (1.19–1.71) | (3707–5483) | (1.2–1.77) | (89,146–131,593) | (26.6–38.95) | (87,985–129,981) | (26.28–38.5) | (894–1821) | (0.28–0.56) |

**TABLE 3** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Sub-Saharan Africa – WB** | 12,447 (9190–15,473) | 5.11 (3.75–6.3) | 13,016 (9611–16,222) | 5.56 (4.09–6.87) | 337,790 (248,260–424,465) | 125.17 (92.36–155.7) | 334,489 (245,836–419,594) | 123.86 (91.59–153.77) | 3301 (2132–4673) | 1.31 (0.85–1.85) |
| Central Sub-Saharan Africa | 1748 (831–2556) | 6.23 (2.97–9.01) | 1791 (854–2607) | 6.68 (3.2–9.63) | 48,364 (22,703–71,244) | 154.77 (73.31–226.52) | 47,896 (22,533–70,645) | 153.16 (72.63–224.49) | 468 (203–746) | 1.60 (0.71–2.61) |
| Eastern Sub-Saharan Africa | 7051 (5163–8999) | 8.56 (6.33–10.86) | 7417 (5416–9483) | 9.36 (6.82–11.83) | 197,687 (145,382–254,347) | 216.51 (158.04–276.05) | 195,830 (143,713–252,611) | 214.33 (156.83–273.96) | 1857 (1192–2701) | 2.18 (1.41–3.16) |
| Southern Sub-Saharan Africa | 2042 (1733–2402) | 6.49 (5.53–7.58) | 2142 (1824–2487) | 6.98 (5.93–8.05) | 49,955 (42,397–58,817) | 150.74 (128.27–176.63) | 49,426 (42,016–58,174) | 149.09 (126.67–174.79) | 529 (367–728) | 1.65 (1.14–2.26) |
| Western Sub-Saharan Africa | 1315 (1026–1587) | 1.46 (1.14–1.74) | 1376 (1075–1646) | 1.59 (1.24–1.88) | 34,101 (26,435–41,495) | 33.81 (26.5–40.65) | 33,736 (26,153–41,063) | 33.41 (26.15–40.19) | 365 (242–508) | 0.40 (0.26–0.55) |
| **South Asia – WB** | 23,263 (119,952–165,068) | 3.17 (2.74–3.77) | 23,504 (110,337–150,271) | 3.28 (2.52–3.43) | 633,020 (2,434,410–3,195,247) | 81.45 (55.83–73.33) | 626,581 (2,391,555–3,157,407) | 80.59 (54.9–72.49) | 6439 (29,237–56,389) | 0.86 (0.67–1.29) |
| South Asia | 22,238 (119,952–165,068) | 3.11 (2.74–3.77) | 22,514 (110,337–150,271) | 3.24 (2.52–3.43) | 607,078 (2,434,410–3,195,247) | 80.40 (55.83–73.33) | 600,926 (2,391,555–3,157,407) | 79.55 (54.9–72.49) | 6152 (29,237–56,389) | 0.85 (0.67–1.29) |
| **Latin America and Caribbean – WB** | 5866 (119,952–165,068) | 1.62 (2.74–3.77) | 6024 (110,337–150,271) | 1.66 (2.52–3.43) | 126,940 (2,434,410–3,195,247) | 34.99 (55.83–73.33) | 125,291 (2,391,555–3,157,407) | 34.53 (54.9–72.49) | 1649 (29,237–56,389) | 0.46 (0.67–1.29) |
| Andean Latin America | 246 (119,952–165,068) | 0.85 (2.74–3.77) | 260 (110,337–150,271) | 0.91 (2.52–3.43) | 5536 (2,434,410–3,195,247) | 18.81 (55.83–73.33) | 5466 (2,391,555–3,157,407) | 18.57 (54.9–72.49) | 70 (29,237–56,389) | 0.24 (0.67–1.29) |
| Caribbean | 417 (119,952–165,068) | 1.51 (2.74–3.77) | 422 (110,337–150,271) | 1.52 (2.52–3.43) | 9343 (2,434,410–3,195,247) | 34.25 (55.83–73.33) | 9223 (2,391,555–3,157,407) | 33.82 (54.9–72.49) | 120 (29,237–56,389) | 0.44 (0.67–1.29) |
| Central Latin America | 1110 (119,952–165,068) | 0.88 (2.74–3.77) | 1149 (110,337–150,271) | 0.92 (2.52–3.43) | 24,061 (2,434,410–3,195,247) | 18.83 (55.83–73.33) | 23,743 (2,391,555–3,157,407) | 18.58 (54.9–72.49) | 318 (29,237–56,389) | 0.25 (0.67–1.29) |
| Tropical Latin America | 2840 (2597–3052) | 2.13 (1.95–2.29) | 2906 (2637–3120) | 2.19 (1.98–2.35) | 65,008 (60,249–69,587) | 48.56 (45.02–51.99) | 64,208 (59,519–68,795) | 47.96 (44.44–51.37) | 800 (566–1,053) | 0.60 (0.42–0.79) |

(Continues)

**TABLE 3** (Continued)

| | Incidence cases (95% CI) | Incidence ASR per $10^5$ (95% CI) | Deaths cases (95% CI) | Deaths ASR per $10^5$ (95% CI) | DALYs number (95% CI) | DALYs ASR per $10^5$ (95% CI) | YLLs number (95% CI) | YLLs ASR per $10^5$ (95% CI) | YLDs number (95% CI) | YLDs ASR per $10^5$ (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Middle East and North Africa – WB** | 2529 (1978–2865) | 1.70 (1.34–1.91) | 2453 (1917–2772) | 1.73 (1.36–1.94) | 61,193 (46,770–70,475) | 37.13 (28.82–42.28) | 60,467 (46,242–69,673) | 36.66 (28.38–41.73) | 726 (498–976) | 0.47 (0.33–0.64) |
| North Africa and Middle East | 3765 (2647–4391) | 1.81 (1.32–2.09) | 3659 (2593–4292) | 1.83 (1.32–2.11) | 94,696 (62,662–113,396) | 41.58 (28.49–49.12) | 93,618 (62,035–112,190) | 41.07 (28.19–48.55) | 1078 (694–1465) | 0.50 (0.33–0.69) |
| **Europe and Central Asia – WB** | 16,133 (14,254–18,041) | 1.77 (1.58–1.97) | 14,570 (13,236–15,656) | 1.53 (1.41–1.64) | 278,771 (259,046–297,836) | 33.67 (49.77–36.11) | 273,837 (254,041–292,223) | 33.12 (30.84–35.39) | 4935 (3447–6533) | 0.56 (0.39–0.74) |
| Central Asia | 1904 (1690–2158) | 4.70 (4.19–5.29) | 1966 (1748–2222) | 5.00 (4.48–5.6) | 50,410 (44,435–57,482) | 116.04 (102.83–131.58) | 49,898 (43,922–56,976) | 114.81 (101.56–130.46) | 512 (358–698) | 1.23 (0.86–1.66) |
| Central Europe | 1105 (950–1269) | 0.92 (0.79–1.06) | 1169 (1008–1347) | 0.94 (0.81–1.09) | 23,246 (19,981–26,899) | 21.14 (18.14–24.62) | 22,933 (19,658–26,567) | 20.88 (17.92–24.3) | 313 (211–424) | 0.26 (0.18–0.36) |
| Eastern Europe | 1937 (1636–2298) | 0.89 (0.75–1.07) | 1977 (1665–2337) | 0.89 (0.75–1.06) | 41,151 (34,614–49,314) | 20.31 (16.96–24.47) | 40,597 (34,134–48,774) | 20.05 (16.7–24.26) | 554 (377–763) | 0.26 (0.18–0.36) |
| **High Income** | 22,096 (18,982–24,734) | 1.86 (1.63–2.09) | 18,541 (16,432–19,925) | 1.46 (1.33–1.56) | 323,804 (297,967–342,961) | 30.32 (28.49–31.91) | 316,687 (291,862–335,054) | 29.69 (27.87–31.26) | 7117 (4995–9414) | 0.62 (0.44–0.83) |
| Australasia | 685 (542–852) | 2.46 (1.95–3.06) | 574 (490–644) | 1.97 (1.71–2.2) | 9532 (8409–10,526) | 36.96 (33.02–40.64) | 9320 (8239–10,298) | 36.17 (32.38–39.67) | 212 (140–299) | 0.79 (0.51–1.12) |
| Asia Pacific | 3773 (2925–4592) | 1.46 (1.16–1.78) | 2697 (2149–3061) | 0.93 (0.79–1.03) | 42,547 (36,443–47,498) | 19.04 (17.09–20.91) | 41,172 (35,357–45,848) | 18.48 (16.61–20.35) | 1375 (937–1939) | 0.56 (0.38–0.78) |
| North America | 5479 (4607–6487) | 1.59 (1.34–1.9) | 4764 (4340–5048) | 1.34 (1.23–1.41) | 91,615 (86,053–95,946) | 28.50 (27.02–29.75) | 89,889 (84,618–94,135) | 27.99 (26.59–29.2) | 1726 (1205–2340) | 0.51 (0.36–0.69) |
| Southern Latin America | 1267 (1016–1583) | 2.61 (2.08–3.28) | 1301 (1184–1415) | 2.61 (2.38–2.84) | 23,326 (21,421–25,250) | 50.36 (46.45–54.39) | 22,980 (21,146–24,859) | 49.63 (45.77–53.74) | 346 (225–487) | 0.72 (0.47–1.02) |
| Western Europe | 10,892 (9353–12,548) | 2.16 (1.87–2.49) | 9205 (8168–9914) | 1.67 (1.52–1.79) | 156,784 (144,026–166,820) | 34.48 (32.26–36.51) | 153,326 (140,973–163,069) | 33.76 (31.58–35.78) | 3458 (2370–4633) | 0.72 (0.5–0.98) |

Abbreviations: ASR, Age-standardized rate; CI, confidence interval; DALY, disability-adjusted life year; SDI, sociodemographic index; YLD, year lived with disability; YLL, year of life lost.

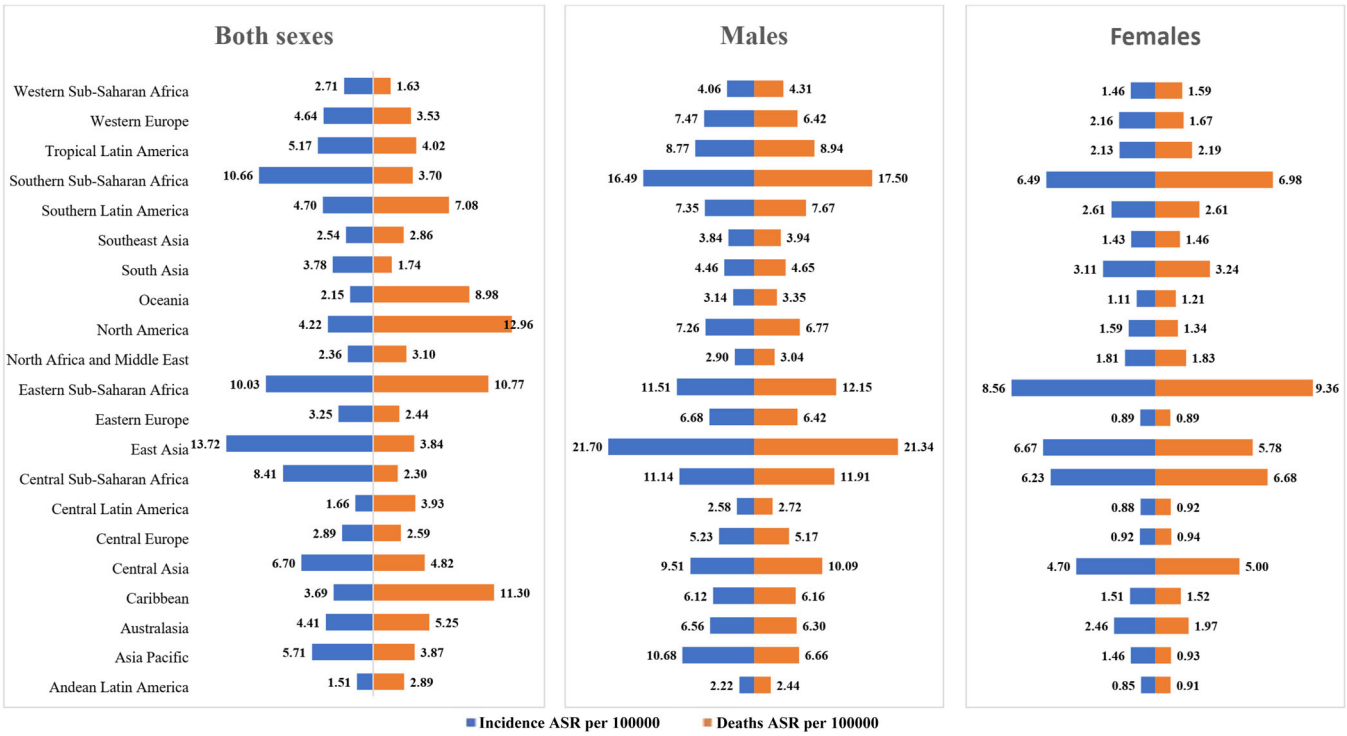


**FIGURE 1** Age-standardized incidence (ASIR) and death rate of EC in GBD regions by sex, in 2019. EC, esophageal cancer; GBD, global burden of disease; LDL, low-density lipoprotein; SDI, sociodemographic index.

The age-standardized DALYs rate (ASR of DALYs) of EC worldwide was 139.79 (95% CI: 124.44–154.98) per 100,000 inhabitants; 221.38 (95% CI: 191.21–252.216) in males and 65.29 (95% CI: 55.83–73.33) in females.

Worldwide, the highest ASR of DALYs has been reported in Malawi (651.57), Mongolia (486.69), Eswatini (409.37), Uganda (403.54), Zimbabwe (400.7), Lesotho (398.1), Cabo Verde (388.77), Eritrea (347.49), and Somalia (339.06), respectively. The lowest ASR of DALYs has been observed in Tunisia (21.41), Syrian Arab Republic (21.75), Nigeria (21.87), Algeria (24.24), Palestine (25.53), Jordan (26.16), Cyprus (26.58), Lebanon (27.83), and Peru (28.57), respectively.

In men, the highest ASR of DALYs has been reported in Malawi (900.59), Cabo Verde (770.5), Eswatini (756.95), Mongolia (680.59), Lesotho (653), Zimbabwe (600), Uganda (561.42), Zambia (473.35), and China (458.55), respectively. The lowest ASR of DALYs has been observed in the Syrian Arab Republic (30.88), Tunisia (33.96), Jordan (34.59), Nigeria (35.64), Algeria (35.9), Kuwait (37.51), Palestine (37.62), Iraq (39.53), and Peru (41.86), respectively.

In women, the highest ASR of DALYs has been reported in Malawi (432.87), Mongolia (343.15), Eritrea (332.32), Kenya (301.32), Somalia (288.11), Zambia (278), Uganda (271.01), Comoros (258.99), and Madagascar (254.35), respectively. The lowest ASR of DALYs has been observed in San Marino (7.6), the Republic of Korea (8.09), the Republic of Moldova (8.09), Andorra (8.25), Guam (9.35), Tunisia (9.46), Nigeria (9.63), Ukraine (10.59), and Nicaragua (10.77), respectively.

Statistics show that the highest ASR of DALYs for EC occurs in countries with Middle SDI (175.17 [95% CI: 145.44–202.51] per 100,000 people) and the lowest rates occur in countries with High SDI (95.82 [95% CI: 91.39–100.45] per 100,000 people). In men, the highest ASR of DALYs for EC occurs in countries with Middle SDI (276.14 [95% CI: 223.66–330.77] per 100,000 people) and the lowest rates occur in countries with Low-middle SDI (148.95 [95% CI: 129.75–214.45] per 100,000 people). In women, the highest ASR of DALYs for EC occurs in countries with Low SDI (113.69 [95% CI: 90.95–137.43] per 100,000 people) and the lowest rates occur in countries with High SDI (31.19 [95% CI: 29.25–33.02] per 100,000 people).

According to the World Bank classification, the ASR of DALYs for EC is highest in the Low Income and Upper Middle-Income categories worldwide, Upper Middle Income (334.55 [95% CI: 268.87–404.18] per 100,000 people) in males, and Low Income (146.42 [95% CI: 101.96–185.86] per 100,000 people) in females. The lowest rates were seen in Lower Middle- and Low-Income countries worldwide, Lower Middle Income (111.03 [95% CI: 96.61–140.75] per 100,000 people) in men and women in High Income (29.2 [95% CI: 27.42–30.82] per 100,000 people).

Among the continents, the highest ASR of DALYs was reported in Asia (170.51 [95% CI: 145.87–194.85] per 100,000 people), while the lowest was observed in Europe (83.68 [95% CI: 79.13–88.37] per 100,000 people) worldwide. For men, the highest ASR of DALYs was reported in Asia (265.89 [95% CI: 219.88-314.77] per 100,000 people) and the lowest rate in Europe (147.25 [95% CI: 138.28–156.52] per 100,000 people) and America (147.83 [95% CI: 142.2–153.53] per 100,000 people). For women, the highest ASDR was reported in Africa (102.49 [95% CI: 76.29–26.52] per 100,000

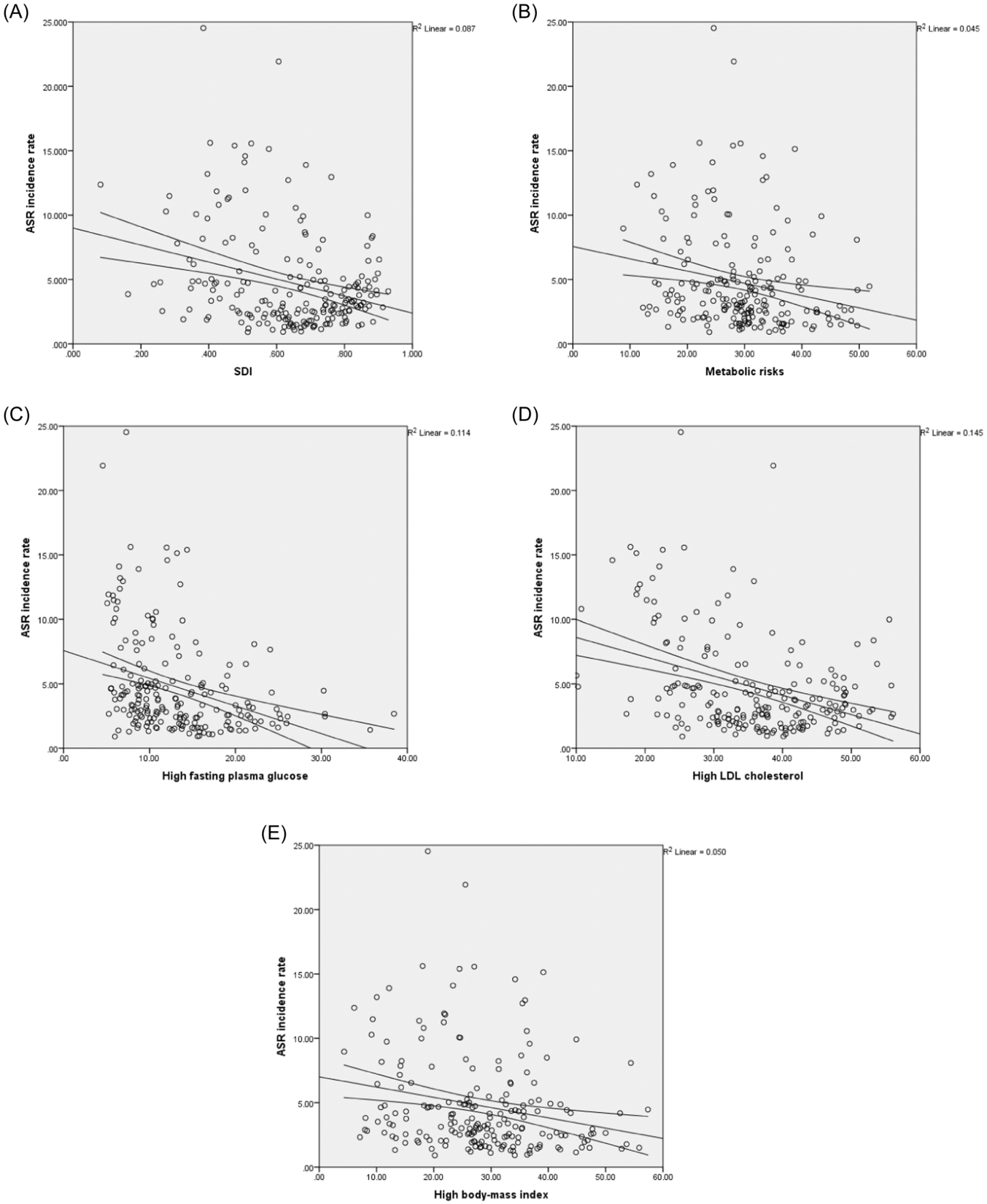


**FIGURE 2** (A–E) Correlation between age-standardized incidence rate of EC and (A) SDI, (B) metabolic risks, (C) high fasting plasma glucose (FPG), (D) high LDL cholesterol, and (E) high body mass index (BMI). EC, esophageal cancer; LDL, low-density lipoprotein; SDI, sociodemographic index.

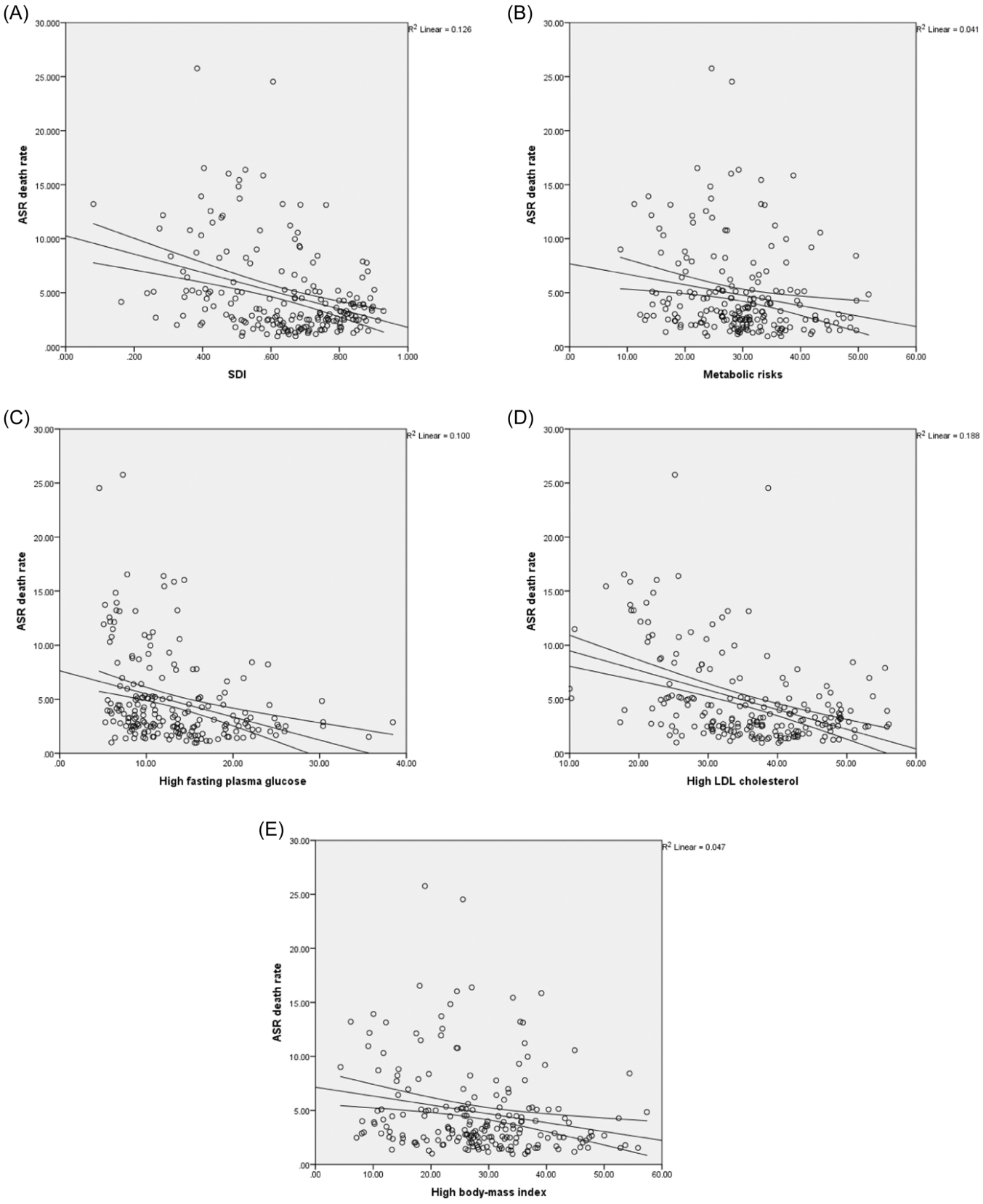


**FIGURE 3** (A–E) Correlation between age-standardized death rate of EC and (A) SDI, (B) metabolic risks, (C) high fasting plasma glucose (FPG), (D) high LDL cholesterol, and (E) high body mass index (BMI). The age-standardized DALYs rates of EC decreased with using of SDI ($r = -0.374$, $p < 0.0001$), metabolic risks ($r = -0.220$, $p = 0.002$), high FPG ($r = -0.322$, $p < 0.0001$), high LDL cholesterol ($r = -0.448$, $p < 0.0001$), high BMI ($r = -0.235$, $p < 0.001$). DALY, disability-adjusted life year; EC, esophageal cancer; LDL, low-density lipoprotein; SDI, sociodemographic index.

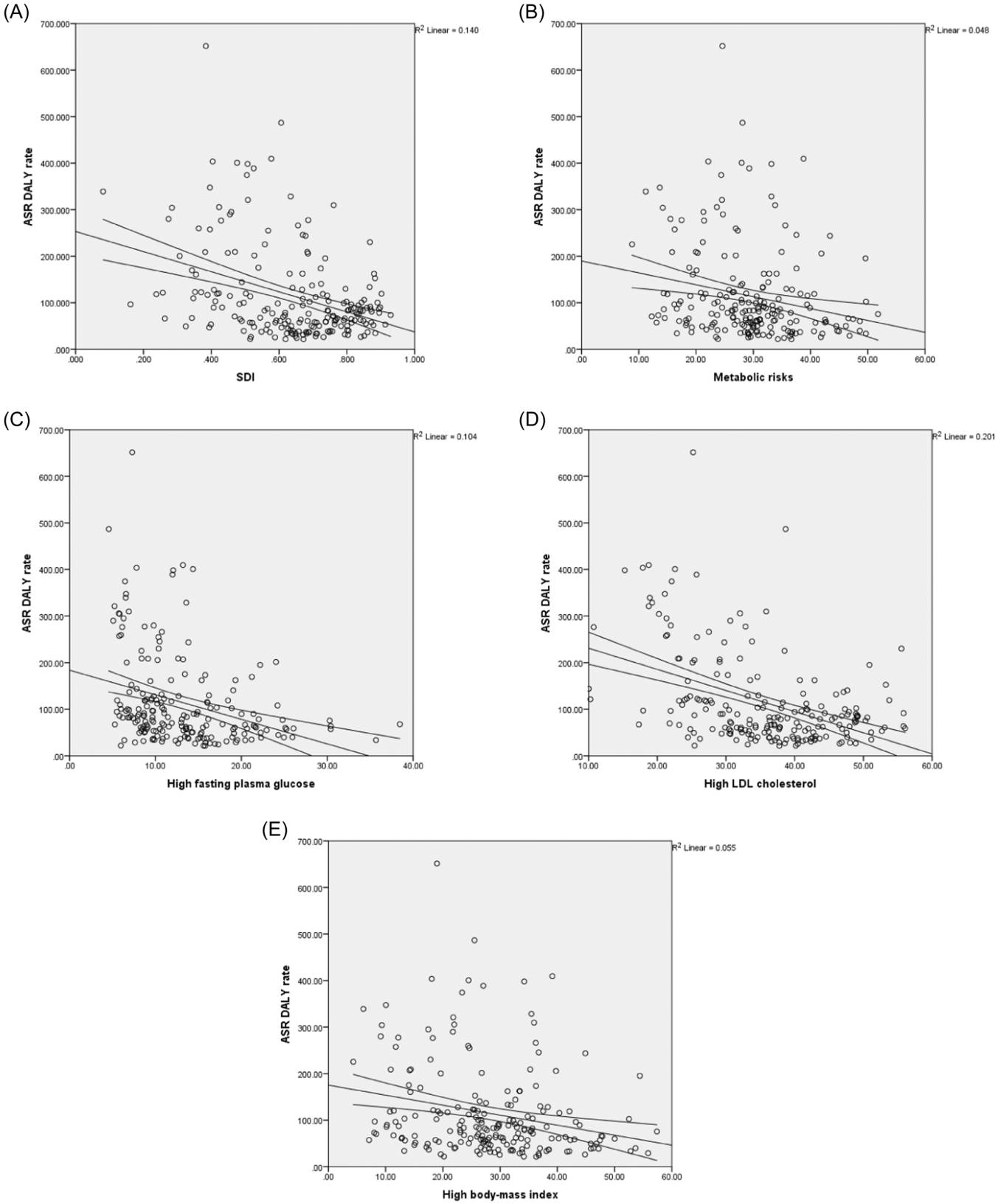


**FIGURE 4** (A–E) Correlation between age-standardized DALYs rate of EC and (A) SDI, (B) metabolic risks, (C) high fasting plasma glucose, (D) high LDL cholesterol, and (E) high body mass index.

people) and the lowest rate in Europe (29.44 [95% CI: 27.59–31.39] per 100,000 people).

The highest ASR of DALYs for EC among WHO regions was found in the Western Pacific Region (226.88 [95% CI: 185.13–270.81] per 100,000 people). The lowest was reported in the South-East Asia Region (85.38 [95% CI: 74.31–114.42] per 100,000 people). For men, the highest ASR of DALYs was seen in the Western Pacific Region (379.54 [95% CI: 301.22–465.59] per 100,000 people) and the lowest was reported in the South-East Asia Region (108.39 [95% CI: 89.88–150.49] per 100,000 people). For women, the highest ASR of DALYs was seen in the African Region (116.73 [95% CI: 87.92–145.35] per 100,000 people) and the lowest was reported in the Region of the Americas (32.13 [95% CI: 30.3–33.89] per 100,000 people).

In the GBD regions, the highest ASR of DALYs was seen in East Asia (275.44 [95% CI: 221.92–331.75] per 100,000 people) and the lowest in Andean Latin America (33.43 [95% CI: 26.85–41.96] per 100,000 people). For men, the highest ASR of DALYs was seen in East Asia (456.24 [95% CI: 356.28–566.73] per 100,000 people) and the lowest was reported in Andean Latin America (49.28 [95% CI: 38.91–63.52] per 100,000 people). For women, the highest ASR of DALYs was seen in Eastern Sub-Saharan Africa (216.51 [95% CI: 158.04–276.05] per 100,000 people) and the lowest was reported in Andean Latin America (18.81 [95% CI: 14.86–23.57] per 100,000 people). More details are presented in Tables 1–3 and Figures 1–4.

### 3.4 | The correlation between global EC incidence, mortality, SDI, metabolic risks, fasting plasma glucose, LDL cholesterol, and body mass index

The age-standardized incidence rates of EC decreased with using of SDI ($r = -0.295$, $p < 0.001$), metabolic risks ($r = -0.211$, $p = 0.002$), high fasting plasma glucose ($r = -0.338$, $p < 0.0001$), high LDL cholesterol ($r = -0.381$, $p < 0.0001$), high body mass index ($r = -0.224$, $p = 0.002$) (Figure 2A–E).

The age-standardized death rates of EC decreased with using of SDI ($r = -0.355$, $p < 0.001$), metabolic risks ($r = -0.202$, $p = 0.004$), high fasting plasma glucose ($r = -0.316$, $p < 0.0001$), high LDL cholesterol ($r = -0.434$, $p < 0.0001$), high body mass index ($r = -0.217$, $p = 0.002$) (Figure 3A–E).

The age-standardized DALYs rates of EC decreased with using of SDI ($r = -0.374$, $p < 0.0001$), metabolic risks ($r = -0.220$, $p = 0.002$), high fasting plasma glucose ($r = -0.322$, $p < 0.0001$), high LDL cholesterol ($r = -0.448$, $p < 0.0001$), high body mass index ($r = -0.235$, $p < 0.001$) (Figure 4A–E).

## 4 | DISCUSSION

This study was conducted to investigate the incidence, mortality, and disease burden of EC based on ASIR, ASDR, and DALY, and also to examine the relationship between EC and metabolic risks, FPG, BMI, and LDL cholesterol using the latest data of GBD 2019. The results showed that the burden of disease, mortality, and incidence of EC is 3–3.4 times higher in men than that in women. The present study revealed high geographical diversity in the burden of EC. In some regions of Asia, such as China and Mongolia, which are known as the "esophageal cancer belt," high ASR was observed. We also found that EC has a high incidence and death in some regions of East, West, and South Africa. So that the ASIR of EC in the East Asia region and Southern Sub-Saharan Africa region is more than nine and seven times that of the Andean Latin America region, respectively. However, the quality of reported data is not the same in different regions and the reported data should be interpreted with caution.[28]

As reported in previous studies,[29] ASDR, ASIR, and DALY in men were higher than in women, so the ASIR in men was reported to be almost three times higher than that of women. However, according to studies that investigated the trend of EC, the decrease in the incidence of EC in men was higher than in women, and this has been attributed to the increasing trend of smoking in women.[30] Various factors have been mentioned to justify this gender difference in the burden of EC: First, the prevalence of known risk factors for EC differs in men and women. Second, women seek treatment in the early stages of the disease, and as a result of receiving treatment at lower stages, they have a better prognosis than men.[31]

In this study, SDI is used to reflect socioeconomic status, another factor related to the incidence of EC. Based on the observed geographic variation, the ASIR of EC is higher in high SDI and medium to high SDI countries and regions, which is consistent with other studies that have shown low socioeconomic status has an inverse relationship with EC.[32,33] So that the ASIR of EC in the High-middle SDI and Middle SDI countries are more than 1.6 and 1.9 times that of the Low-middle SDI countries, respectively. In general, the incidence of EC is higher in less developed and developing countries.[34] Various studies have shown an inverse relationship between ESCC and high socioeconomic status, and a direct relationship between EAC and higher socioeconomic status.[27,35] However, some studies that have been conducted using regional economic indicators do not confirm this relationship.[36,37] In any case, the observed relationship can be because the low socioeconomic status of people leads to delayed diagnosis and treatment and less access to medical services.[38] Also, the prognosis of EC may be different in patients with different socioeconomic statuses. A study by Kuo et al. in China showed that low socioeconomic status was strongly associated with an increased risk of mortality caused by EC.[39] In countries with a higher prevalence of EC such as China, increasing endoscopic screening in at-risk populations is recommended for early detection of EC.

Studies have shown that metabolic syndrome is an important risk factor for the development of malignancies[40] and a positive relationship between metabolic syndrome and EC has been reported.[41–43] Metabolic syndrome can lead to an increased risk of EC in three ways (insulin resistance, activation of pro-inflammatory factors, and deregulation of leptin).[44–46] In the meta-analysis study conducted by Zhang et al., results showed that among the components of hyperglycemic metabolic syndrome, high blood pressure, and BMI were more correlated to EC.[47] Although no study

has directly examined the relationship between EC and high blood pressure, some studies have shown that high blood pressure is associated with the occurrence of malignancies.[48]

High FPG is another factor related to EC, which according to the results of the present study, has an inverse relationship with EC. Hyperglycemia (FPG > 180) leads to respiratory dysfunction and eventually, increases the anaerobic respiration of body cells (hypoxia). When body cells are subjected to hypoxia for a long time, the possibility of cell mutation and eventually, turning into cancer cells increases.[49] Furthermore, hyperglycemia leads to the induction of tumorigenesis by indirectly increasing the function of IGF-1. It also directly causes an increase in hyperinsulinemia.[50]

High BMI is associated with EC,[51–53] but it has a different mechanism in two types of EC. Obesity is considered a risk factor but in ESCC, it reduces the risk.[54,55] According to studies, obesity can increase the risk of EAC in two ways: First, obesity, especially abdominal obesity, leads to an increase in the internal pressure of the abdomen, and as a result, it leads to an increase in gastric reflux, which is one of the main risk factors for EAC.[56,57] Second, obesity affects the growth of tumors with a specific mechanism such as increasing the level of hormones such as IGF.[58] However, obesity has an inverse relationship with ESCC, so it reduces the risk of ESCC. The reason for this phenomenon has not yet been determined, but it seems that since smokers have a lower BMI and on the other hand, one of the known risk factors for ESCC is smoking, this relationship can be justified.

A high level of LDL cholesterol is one of the other factors correlated to EC. Studies have shown that abnormal plasma lipid levels are associated with an increased risk of cancers, especially gastrointestinal cancers.[59] Furthermore, several epidemiological studies have shown an inverse relationship between plasma LDL cholesterol and the risk of cancer-related mortality.[60–62] However, the results of a meta-analysis of data from three trials did not confirm any relationship between LDL cholesterol and increased risk of cancer.[63] Evidence shows that cancer cells need higher amounts of cholesterol synthesis and mediators of the cholesterol biosynthesis pathway to perform and maintain a high level of proliferation, compared to normal body cells.[64,65] However, further studies are needed to investigate this relationship, and also to identify accurate biomarkers to improve diagnostic methods and treat patients.

## 5 | CONCLUSION

The GBD 2019 data were used in the present study to provide the most up-to-date information related to EC and some of its risk factors. The results of this study showed significant gender and geographic variation in the incidence, mortality, and burden of EC. It is recommended to design and implement preventive approaches based on known risk factors and improve quality and access to efficient and appropriate treatments.

### 5.1 | Limitations

One of the limitations of this study was the nonuniformity of the cancer registration system and data quality in different regions, especially regions with lower SDI. As an example, the information recorded in the African Sahara region had inappropriate quality in GBD's opinion, and according to GBD's quality measurement criteria, it has not received any stars. Also, among other challenges of using GBD data, we can mention the delay in accessing data, changes in the coding method, and other biases. Finally, according to the mentioned considerations, the results should be interpreted with caution.

## AUTHOR CONTRIBUTIONS

**Afrooz Mazidimoradi**: Conceptualization; data curation; formal analysis; investigation; methodology; validation; writing—original draft; writing—review and editing. **Fatemeh Ghavidel**: Conceptualization; data curation; investigation; methodology; writing—original draft; writing—review and editing. **Zohre Momenimovahed**: Conceptualization; data curation; investigation; methodology; resources; writing—original draft; writing—review and editing. **Leila Allahqoli**: Conceptualization; data curation; investigation; project administration; writing—original draft; writing—review and editing. **Hamid Salehiniya**: Conceptualization; data curation; formal analysis; investigation; methodology; supervision; validation; writing—original draft; writing—review and editing.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data presented in this study are available on request from the corresponding author.

## ETHICS STATEMENT

The study was approved by the ethics committee of the Birjand University of Medical Sciences (ethics committee approval code IR.BUMS.REC.1400.414). As the authors used routinely collected anonymized electronic data, patient consent was not required. In this study, informed consent was not necessary because of the use of an online database.

## TRANSPARENCY STATEMENT

The lead author Hamid Salehiniya affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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