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TEMPORAL TRENDS OF STOMACH CANCER BETWEEN 2010 AND 2019 IN ASIAN COUNTRIES BY GEOGRAPHICAL REGION AND SOCIO-DEMOGRAPHIC INDEX: A COMPARISON WITH GLOBAL DATA

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ABSTRACT – *Objective:* This study aimed to analyze the trends in stomach cancer (SC) incidence, mortality, and burden in Asia from 2010 to 2019 and compare them with global data.

Materials and Methods: We collected SC data from the 2019 Global Burden of Disease (GBD) study from 2010 to 2019 in 49 countries and territories in Asia. Annual case data and age-standardized rates (ASRs) were used to investigate SC incidence, prevalence, mortality, and disability-adjusted life-years (DALYs) from 2010 to 2019. Comparative variations of age-standardized rates for the indicators studied were shown using the relative difference (%) between years.

Results: In 2019, more than 70% of SC cases and deaths, prevalence, and DALYs occurred in Asian countries. From 2010 to 2019, incidences, deaths, and the prevalence of SC cases increased by 1.1, 1.03, 1.2, and Daly's number decreased by 0.12-fold, in Asia. During this period, the age-standardized incidence rate (ASIR), the age-standardized death rate (ASDR), and the age-standardized DALYs rate (DALYs ASR) of SC decreased by 18%, 23%, and 24%, respectively. The age-standardized prevalence rate (ASPR) increased by 9%. These trends, at the same time, were similar to the trends of global data and other continents. In 2019, age-specific incidence and death cases of SC cancer were peaking at 70-74 years, and prevalence and DALY cases were peaking at 65–69 years. In 2019, the highest ASIR, ASDR, and DALYs ASR of SC were observed in East Asia countries and the highest ASPR in High-income Asia Pacific countries. While all countries experienced a decreasing trend in ASIR and DALYs ASR, the trends for ASPR were increasing in some countries from 2010 to 2019. In 2019, among the high Socio-Demographic Index (SDI) Asian countries, the Republic of Korea had the highest ASIR and ASPR, and Brunei Darussalam had the highest ASDR and DALYs ASR. Among high-middle SDIs, Kazakhstan had the highest ASIR, ASDR, and ASPR, and Georgia had the highest DALYs ASR; among middle SDIs, China had the highest ASIR and ASPR, and Azerbaijan had the highest ASDR and DALYs ASR; among low-middle SDIs, Mongolia had the highest ASIR, ASDR, ASPR, and DALY ASR of SC cancer. Among low SDI Asian countries, Afghanistan had the highest ASIR, ASDR, ASPR, and DALY ASR of SC cancer. For four indicators, in most countries, the ratio of men was higher than women.

Conclusions: Despite the decreasing trend observed in the age-standardized rates of incidence, prevalence, and burden of stomach cancer in Asia, more than 70% of the burden caused by stomach cancer is imposed on Asian countries. Therefore, knowing the risk factors and behavioral habits that lead to the difference in stomach cancer statistics in Asia compared to other countries is pivotal to implement preventive strategies.

KEYWORDS: Stomach cancer, Asia, Incidence, Prevalence, Death, Burden.

INTRODUCTION

In 2020, a total of around 1.1 million new cases of gastric cancer were reported worldwide, making it the fifth most common malignant tumor worldwide. Moreover, with 769,000 deaths in 2020, stomach cancer is the fourth leading cause of cancer death[1,2]. The highest incidence rates for stomach cancer are reported to be in various Asian countries, specifically Japan, China, and Mongolia[2]. Until the age of 74 years, the global cumulative risk for developing stomach cancer is 1.87% in men and 0.79% in women[3,4]. Furthermore, gastric cancer has an estimated five-year survival rate of less than 20%[1].

Various factors can contribute to the development of stomach cancer such as advanced age, male sex, ethnicity, familial history, developing, and genetic factors[5-9], which are non-modifiable and, therefore, cannot be prevented. However, dietary, and behavioral factors such as smoking and alcohol consumption, as well as *Helicobacter pylori* infection[10-13], can be modified and prevented. All things considered, modifiable risk factors should be considered to arrange an effective prevention program[14].

When we look at the geographical distribution of stomach cancer, there is a notable difference between high- and low-risk countries[15]. Over the last century, there has been a decline in the incidence and mortality rates of gastric cancer[16]; however, it is still a major global health issue due to high incidence, poor prognosis, and cellular and molecular heterogeneity[17]. Then again, management per patient is substantially more costly for stomach cancer than other types of cancer[18], thus it is crucial to organize a primary prevention program for gastric cancer that encourages healthy behaviors including ceasing smoking, reducing salt intake, limiting alcohol intake, and increasing fruit and vegetable consumption. Also, high-risk people must participate in cancer screening programs. Gastric cancer screening programs have likely improved the 5-year relative survival rate from 42.8% in 1993–1995 to 76.0% in 2012–2016[19].

As mentioned earlier, gastric cancer is prevalent, especially in Asian countries, including Japan, China, Mongolia, and the Republic of Korea. For instance, 50% of all gastric cancer cases worldwide are reported to be in China, while it is the most prevalent cancer among men in Japan[20]. Thus, this study aims to describe temporal trends of stomach cancer from 2010 to 2019, in Asian countries by geographical region and sociodemographic index, compared with global data.

MATERIALS AND METHODS

Source data

Data on the incidence, mortality, prevalence, and burden (DALY) of SC for 49 Asian countries, six GBD regions, the world and four continents based on year, gender, and SDI from 2010-2019 were extracted from the GBD 2019 study. GBD provides data online and on the data source Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool) based on the International Classification of Diseases 10 (ICD-10) (code C16.9 for SC cancer)[20-22]. These data were compared with other continental and global data. However, because 15 of the 21 GBD countries in North Africa and the Middle East are West Asian countries, we use data for North Africa and the Middle East. Also, two countries of the Southeast Asia region were African[23]. Disability-adjusted life year (DALY) is an international standard form of QALY which developed by GBD and is defined as the sum of the lost year of healthy living due to premature death with years lived with a specified severity and duration of the disability[24].

The expected age at the death of a person is calculated according to the expected mortality for a certain age in a population standardized to the population of Japan, which has the longest lifetime at birth in the world. Thus, “premature” death is defined as a death in an age when one is not expected to die. The total number of DALYs under a given condition in a population is equal to the sum of years of life lost (YLLs) and years of disability with known severity and duration (YLDs)[22,25].

The geometric average of lag-distributed income per capita, average educational attainment of people aged 15 years and older, and the total fertility rate in people aged <25 years is known as SDI[25,26], and reflect

the levels of social and economic conditions which can affect health outcomes in a given location. Based on SDI, countries and territories were categorized into 5 groups: high SDI (≥0·80), high-middle SDI (≥0·69 and <0·80), middle SDI (≥0·61 and <0·69), low-middle SDI (≥0·45 and <0·61), and low SDI (<0·45)[9,27-29].

A weighted average of the age-specific rates per 100,000 persons within the corresponding age groups of the WHO standard population is known as ASR, which was used to omit the differences in the age distribution of the population by applying the rates for each population to a standardized population[30,31].

Ethical considerations

This study was approved by the Ethics Committee of the Jahrom University of Medical Sciences with IR.JUMS.REC.1401.094 code. Informed consent was not required, due to the use of online and anonymous data.

Statistical analysis

We used the age-standardized rates (per 100.000 population) of selected epidemiological indicators to remove the influence of the different age groups composition within populations; for all data, 95% confidence intervals (CI) were reported. Comparative changes in ASRs were shown by the relative changes (%) between years. The relative change is calculated by dividing the value of the absolute difference by the value of the year of origin, which is multiplied by 100 [32]. We calculated the male/female (M/F) ratio by dividing the male ASRs by the female ASRs of each epidemiological index. The definitions used in this study are available at https://www.healthdata.org/terms-defined and https://www.healthdata.org/gbd/.

RESULTS

Incidence rate of SC in Asia

Global data and continents

In Asia, the number of SC incidences increased from 843395 (95% CI: 783577_901300) in 2010 to 930100 (95% CI: 821898_1052240) in 2019, which is over a 1.1-fold increase. In 2019, more than 73% (930100/1269806) of SC cases happened in Asia countries. During this period, the ASIR of SC with an 18% change, decreased from 23.97 (95% CI: 22.21_25.58) per 100.000 in 2010 to 19.77 (95% CI: 17.54_22.28) per 100.000 in 2019, similarly at the same time, this rate globally decreased by 15%, in America by 8%, in Europe by 13%, and in Africa by 9% (**Supplementary Table 1** and Figure 1).

In Asian men, the number of SC incidences increased from 582259 (95% CI: 531463_635901) in 2010 to 642250 (95% CI: 546642_756066) in 2019, which is approximately a 1.1-fold increase. In 2019, more than 69% of Asia SC's new cases, occurred in Asian men which included 75.8% (642250/846872) of global male SC incidence cases. During this period, the ASIR of SC with a 17% change, decreased from 34.61 (95% CI: 31.63_37.59) per 100.000 in 2010 to 28.75 (95% CI: 24.62_33.56) per 100.000 in 2019, while at the same time, this rate globally decreased by 15%, in America by 9%, in Africa by 10%, and in Europe by 14% (**Supplementary Table 2**).

In Asian women, the number of SC incidences increased from 261136 (95% CI: 238970_280741) in 2010 to 287850 (95% CI: 249021_327156) in 2019, which is over a 1.1-fold increase. In 2019, approximately 31% of Asia SC's new cases, occurred in Asian women which included 68.1% (287850/422934) of global female SC incidence cases. During this period, the ASIR of SC with a 18% change, decreased from 14.41 (95% CI: 13.12_15.52) per 100.000 in 2010 to 11.76 (95% CI: 10.15_13.36) per 100.000 in 2019. At the same time, this rate globally decreased by 15%, in Africa by 8%, in Europe by 14%, and in American countries by 7% (**Supplementary Table 3**).

Asian regions

In 2019, the highest ASIR of SC was observed in East Asia countries (30.24 (95% CI: 25.55_35.54)) with a 17% decrease compared with 2010. All Asian regions experienced a decreasing trend from 4% (North Africa and Middle East) to 24% (High-income Asia Pacific) from 2010 to 2019 (Figure 2).

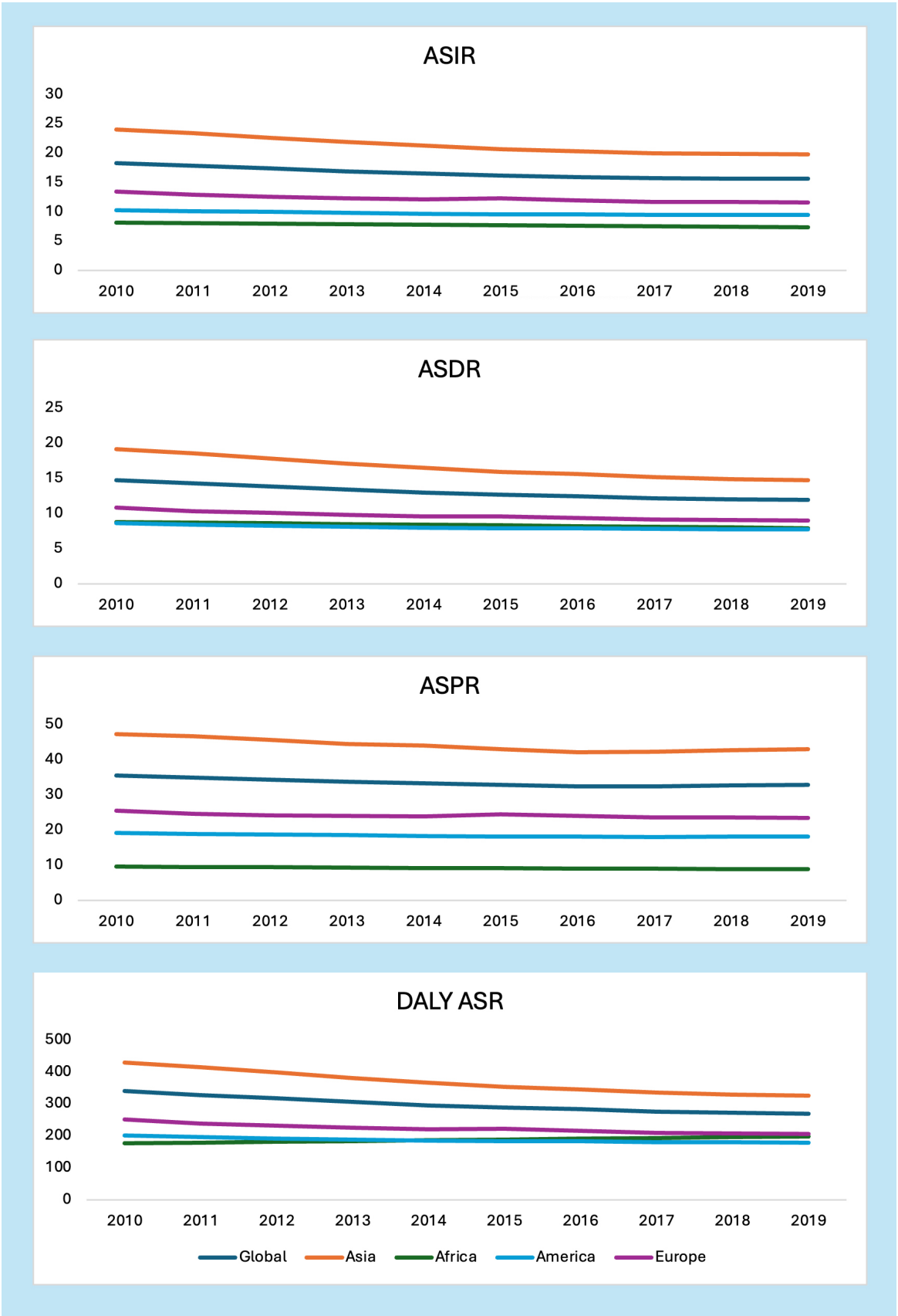

Figure 1. Temporal trend of incidence, prevalence, death and DALYs age standard rates (per 100.000 population) of stomach cancer in ASIA comparison with global data and other continents from 1990 to 2019.

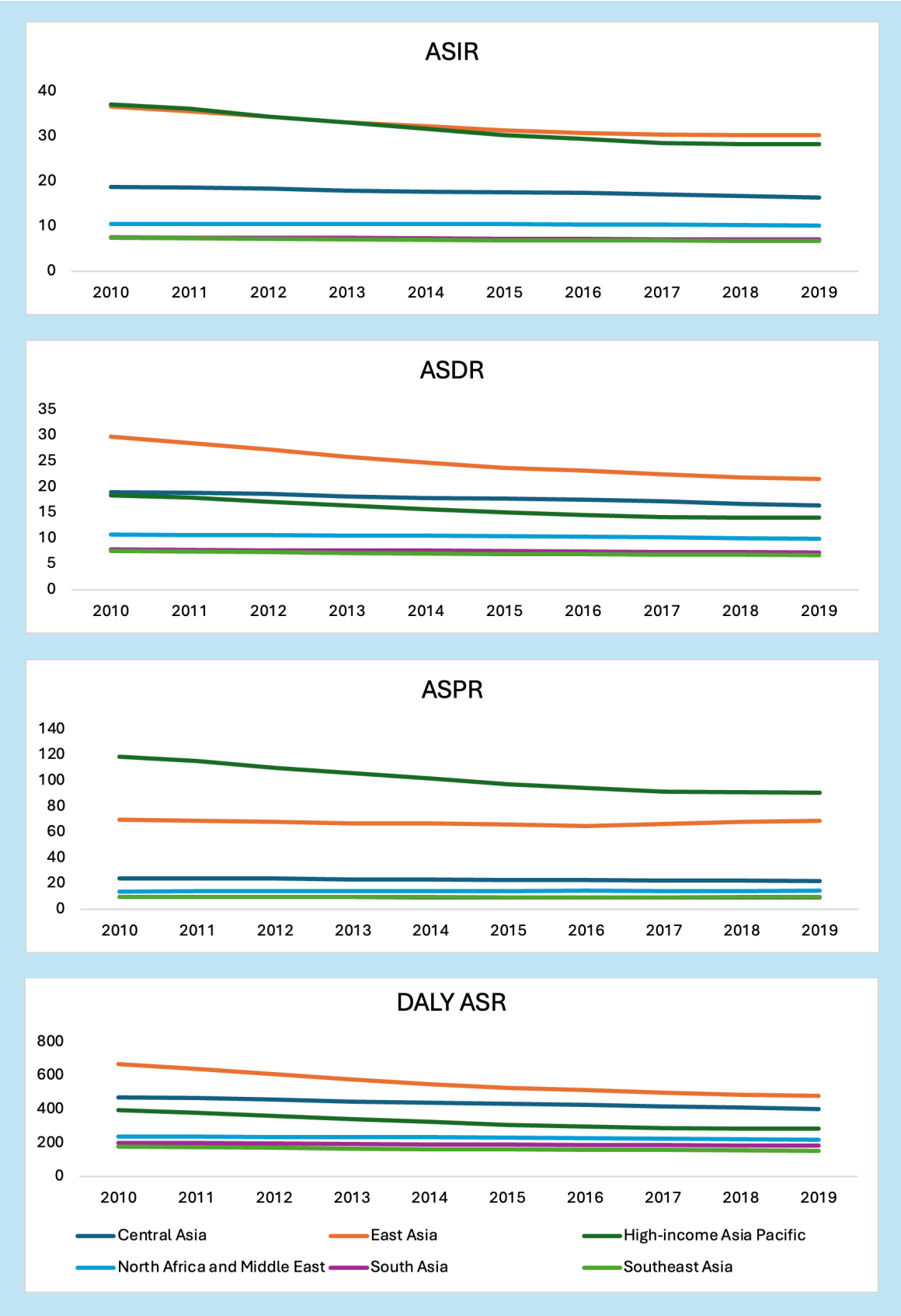

Figure 2. Temporal trend of incidence, prevalence, death and DALYs age standard rates (per 100.000 population) of stomach cancer in Asian regions from 1990 to 2019.

In men, the highest ASIR of SC was observed in East Asia countries (46.67 (95% CI: 37.62_56.82)) with a 15% decrease compared with 2010. All Asian regions experienced a decreasing trend from 4% (North Africa and Middle East) to 26% (High-income Asia Pacific) from 2010 to 2019. In women, the highest ASIR of SC was observed in High-income Asia Pacific countries (16.97 (95% CI: 13.95_19.98)), with a 21% decrease compared with 2010. Also, other Asian regions experienced a decreasing trend from 4% (North Africa and Middle East) to 22% (East Asia), and the South Asia region experienced a stable trend from 2010 to 2019.

Age distribution

In 2019, age-specific incidence cases of SC were peaking at 70-74 years generally, 65-69 years in males, and 70-74 in females. In all age groups, the incidence cases of SC in males was higher (Figure 3).

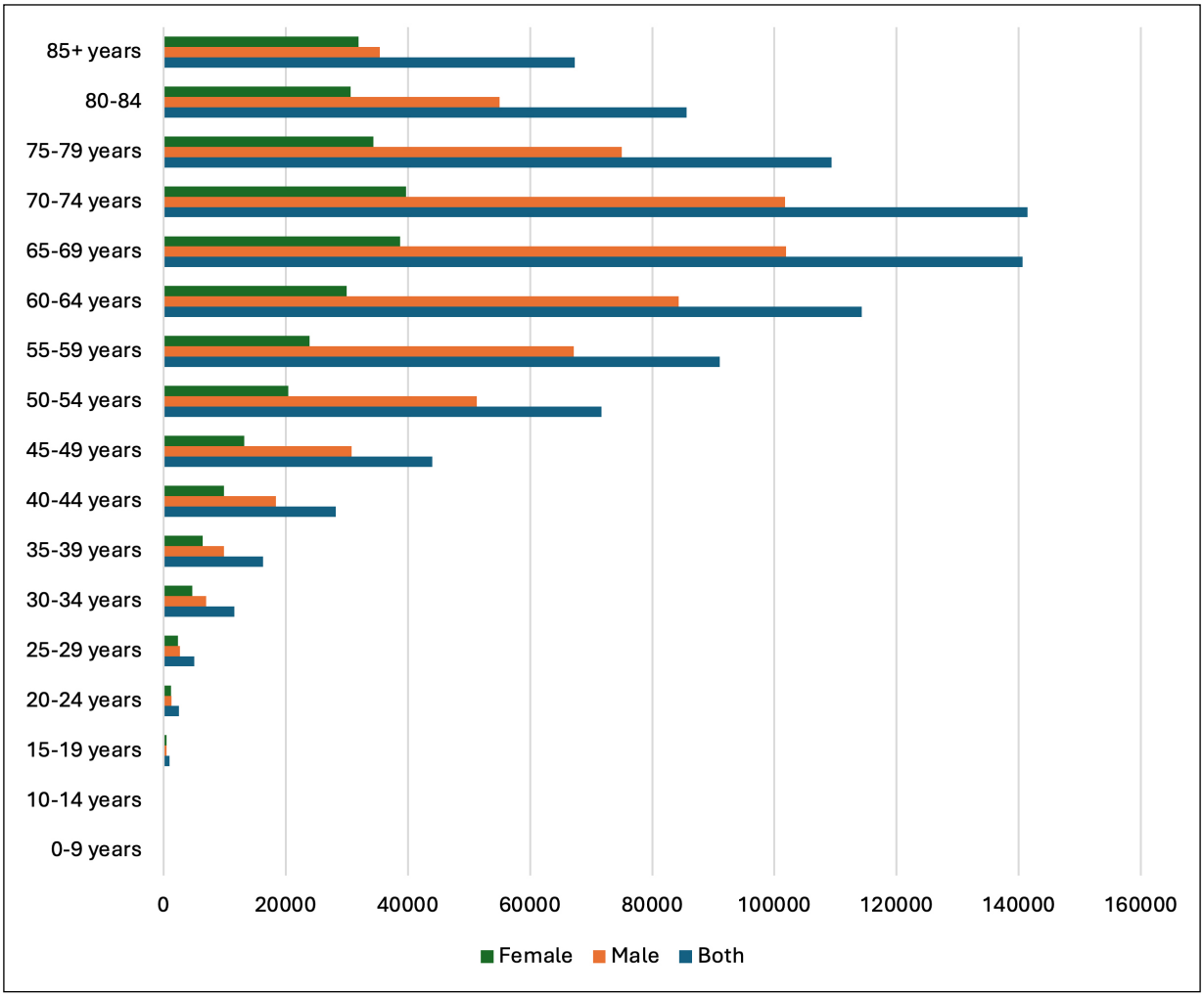

Figure 3. Age-specific incidence cases of stomach cancer among genders in Asia, 2019.

SDI

Among high SDI Asian countries, the Republic of Korea (28.67) and Japan (28.29) have the highest ASIR of SC, and Qatar (3.94) and Saudi Arabia (4.40) have the lowest rate. In this group, all countries reported a downward trend of 8 to 30% from 2010 to 2019. Among high-middle SDI Asian countries, Kazakhstan (14.63) and Georgia (14.67) have the highest ASIR of SC, and Sri Lanka (5.43) has the lowest rate. In this group, all countries reported a downward trend of 5 to 26% from 2010 to 2019. Among middle SDI Asian countries, China (30.64) has the highest ASIR of SC, and the Philippines (4.38) has the lowest rate. In this group, Iran (Islamic Republic of) and Iraq recorded an upward trend of 1 to 2%. Other countries had a downward trend from 3 (Vietnam) to 17% (China) from 2010 to 2019. Among low-middle SDI Asian coun-

tries, Mongolia (43.70) has the highest ASIR of SC, and Maldives (3.79) has the lowest rate. In this group, all countries had a downward trend from 2 (Democratic People's Republic of Korea) to 33% (Palestine) from 2010 to 2019; except Timor-Leste which experienced an upward trend of 8%. Among low SDI Asian countries, Afghanistan (27.69) has the highest ASIR of SC, and Pakistan (6.45) has the lowest rate. In this group, Afghanistan and Pakistan experienced a downward trend, Nepal reported an upward trend of 0.6%, and Yemen reported a stable trend from 2010 to 2019. More details are presented in **Supplementary Table 4.**

National comparison

Among Asian countries, 44 countries experienced a decreasing trend in the SC morbidity rate between 2010 and 2019; the greatest decrease was detected in the Republic of Korea (decrease in ASIR = -0.3 (95% CI: -0.41_-0.17)) and the greatest increase was detected in the Timor-Leste (increase in ASIR = 0.08 (95% CI: -0.12_0.27)) (Figure 4).

In 2019, the highest ASIR (per 100.000) of SC was reported in Mongolia (43.7), China (30.64), the Republic of Korea (28.67), Japan (28.29), and Afghanistan (27.69). The lowest ASIR of SC was reported in Maldives (3.79), Kuwait (3.94), Philippines (4.38), Saudi Arabia (4.4), and the Syrian Arab Republic (4.97).

In 2019, the highest ASIR (per 100.000) of SC in men was reported in Mongolia (66.04), China (47.35), Japan (42.16), the Republic of Korea (42.09), and the Democratic People's Republic of Korea (35.73). The lowest ASIR of SC was reported in Maldives (4), Kuwait (4.78), Saudi Arabia (5.02), the Syrian Arab Republic (5.62), and the Philippines (5.76).

In 2019, the highest ASIR (per 100.000) of SC in women was reported in Mongolia (28.18), Afghanistan (24.74), the Republic of Korea (18.1), Tajikistan (18.01), and Japan (16.86). The lowest ASIR of SC was reported in Kuwait (2.66), the Philippines (3.21), Saudi Arabia (3.48), Maldives (3.55), and Thailand (4.27). Results in detail are presented in **Supplementary Table 4** and Figure 5.

Male/ female ratio

The ASIR of SC in Qatar was reported to be higher in women than in men. In other countries, the incidence of SC in men was higher than in women. The highest ratio was reported in China (3.00-fold) and the lowest ratio was recorded in Qatar (0.78-fold). While, in 2010, this ratio in Qatar and the United Arab Emirates only in men was higher than in women (Figure 6).

Death rates of SC in Asia

Global data and continents

In Asia, the number of SC deaths increased from 651321 (95% CI: 606240_693416) in 2010 to 672825 (95% CI: 596995_746918) in 2019, which is over a 1.03-fold increase. In 2019 more than 70% (672825/957185) of SC deaths happened in Asia countries. During this period, the ASDR of SC with 23% change, decreased from 19.15 (95% CI: 17.75_20.37) per 100.000 in 2010 to 14.67 (95% CI: 13.04_16.23) per 100.000 in 2019. Also, at the same time, this rate globally decreased by 19%, in America and Africa by 10%, and in Europe by 17% (Figure 1 and **Supplementary Table 1**).

In Asian men, the number of SC deaths increased from 435291 (95% CI: 398888_470381) in 2010 to 443843 (95% CI: 379854_509606) in 2019, which is over a 1.02-fold increase. In 2019, more than 66% of Asia SC death occurred in Asian men which included 72.6% (443843/611504) of global male SC death cases. During this period, the ASDR of SC with a 24% change decreased from 27.09 (95% CI: 24.92_29.19) per 100.000 in 2010 to 20.7 (95% CI: 17.83_23.58) per 100.000 in 2019, while at the same time, this rate globally decreased by 20%, in Europe by 18%, in America by 11%, in Africa by 10% (**Supplementary Table 2**).

In Asian women, the number of SC deaths increased from 216030 (95% CI: 197462_233531) in 2010 to 228982 (95% CI: 198549_261516) in 2019, which is over a 1.06-fold increase. In 2019, approximately 34% of Asia SC deaths occurred in Asian women which included 66.24% (228982/345681) of global female SC death cases. During this period, the ASIR of SC with 22% changes, decreased from 12.22 (95% CI: 11.13_13.25) per 100.000 in 2010 to 9.48 (95% CI: 8.22_10.82) per 100.000 in 2019. At the same time, this rate globally decreased by 18%, in Europe by 17%, and in America and Africa by 9% (**Supplementary Table 3**).

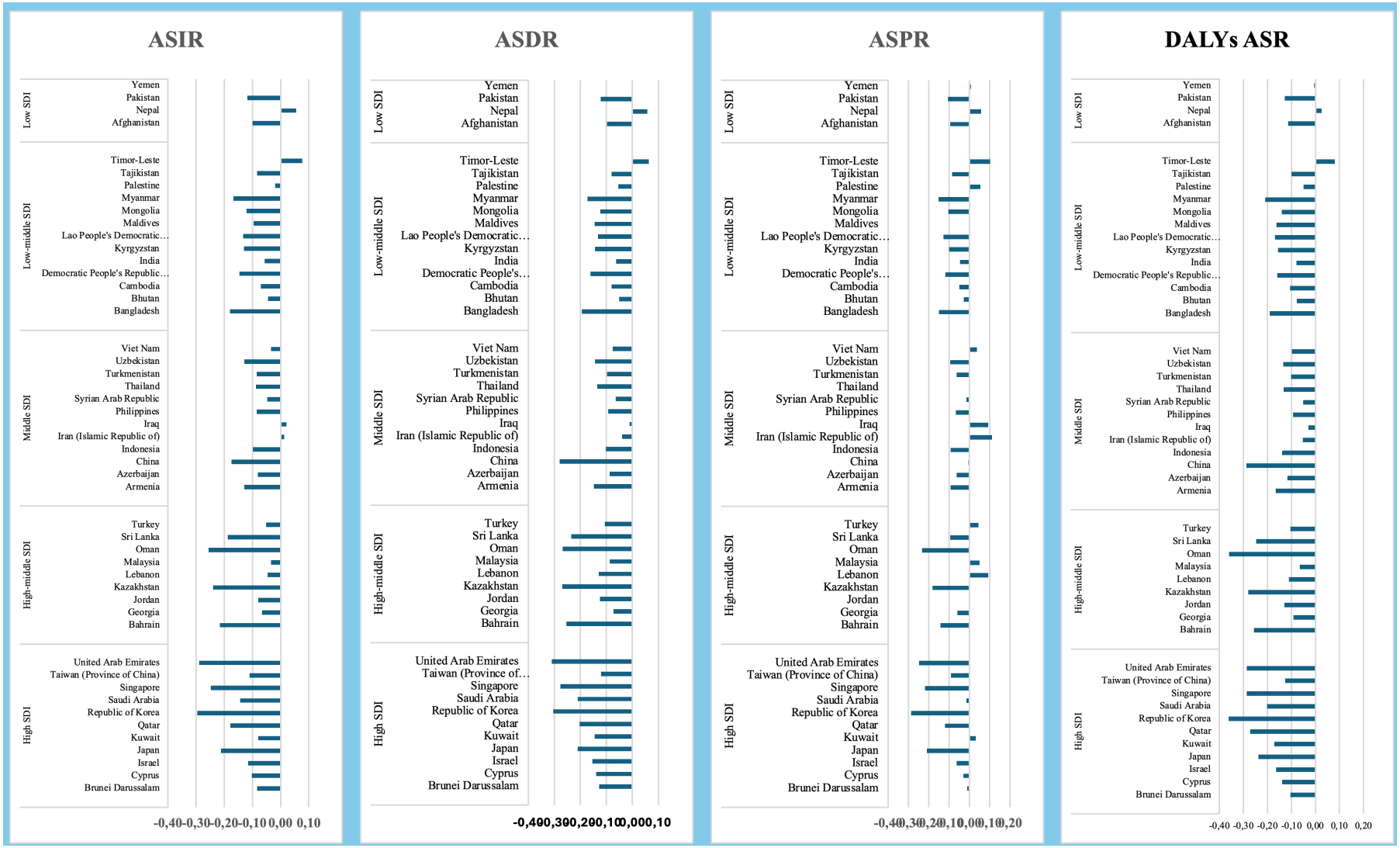

Figure 4. The relative change (%) in age-standardized incidence rate (ASIR), age-standardized death rate (ASMR), age-standardized DALYs rate (DALYs ASR), and age-standardized prevalence rate (ASPR) of stomach cancer in Asian countries from 2010 to 2019.

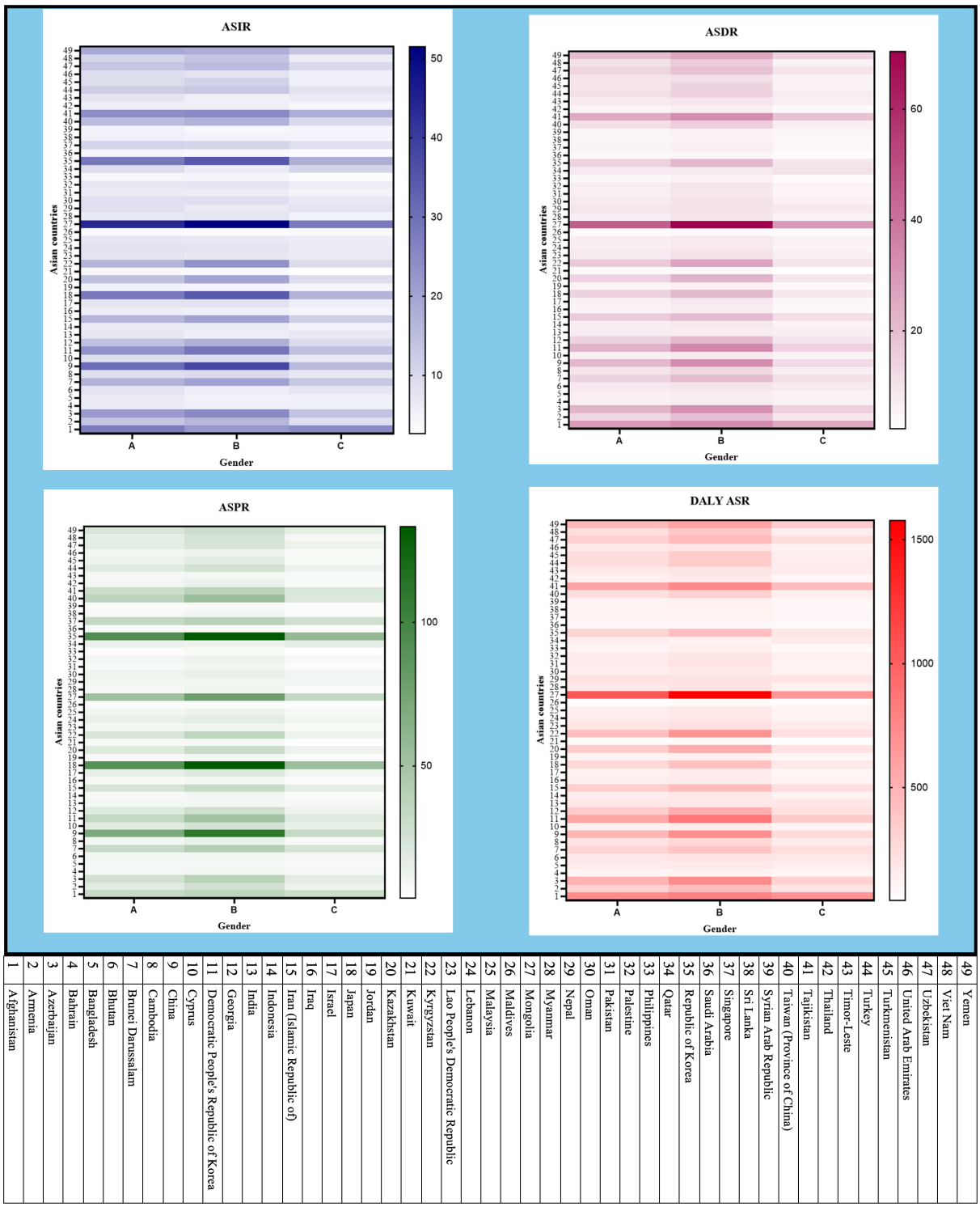

Figure 5. The distribution of age-standardized incidence rate (ASIR), age-standardized death rate (ASMR), age-standardized DALYs rate (DALYs ASR), and age-standardized prevalence rate (ASPR) of stomach cancer in Asian countries in 2019 based on gender (A: Both genders, B: Male, and C: Female).

Asian regions

In 2019, the highest ASDR of SC was observed in East Asia regions (21.51 (95% CI: 18.23_24.95)), with a 28% decrease compared with 2010. Also, in this period, all Asian regions had a decreasing trend of 7% (North Africa and Middle East) to 28% (East Asia) (Figure 2 and **Supplementary Table 1**).

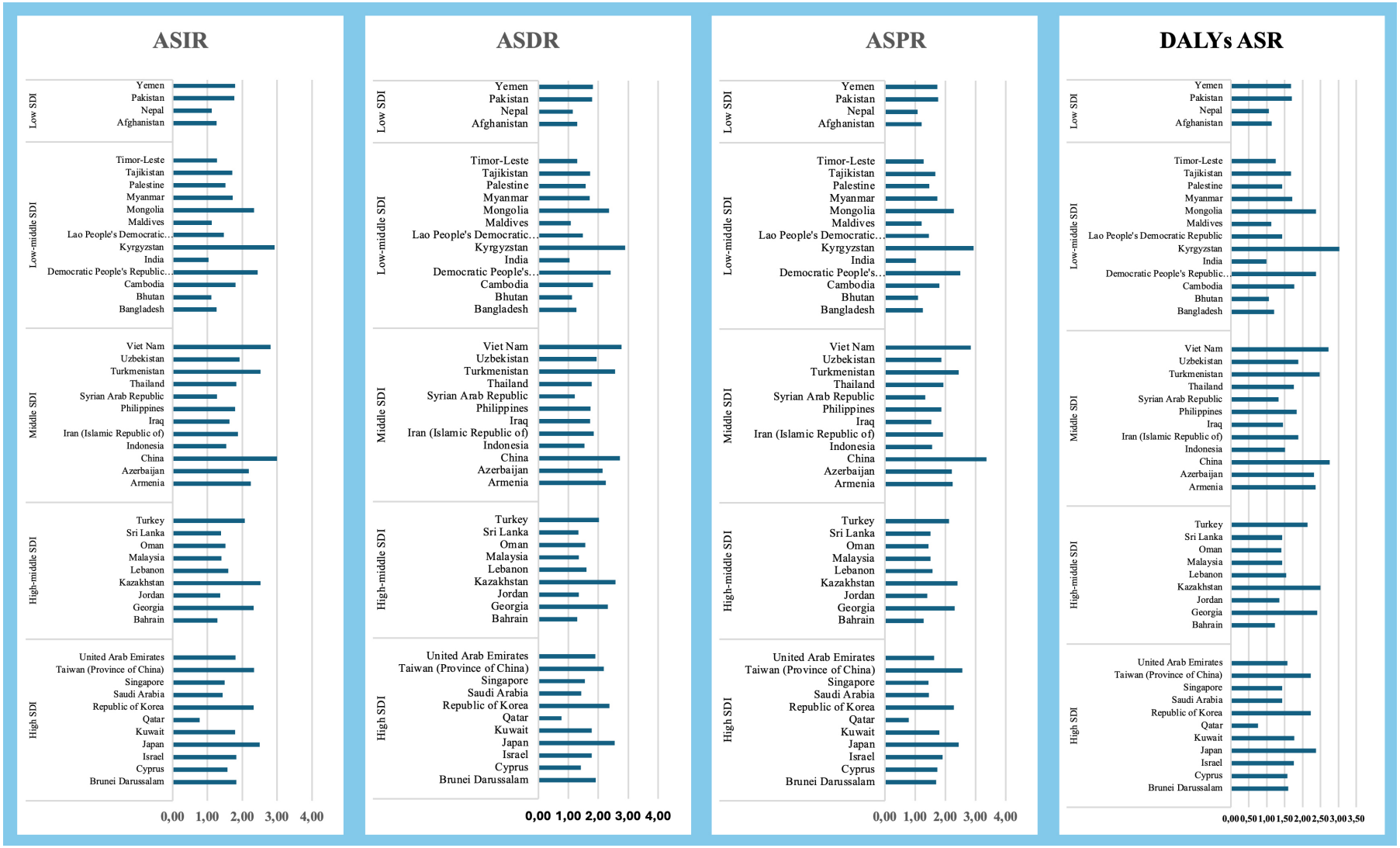

Figure 6. The male/female ratio of age-standardized incidence rate (ASIR), the age-standardized death rate (ASDR), age-standardized DALYs rate (DALYs ASR), and age-standardized prevalence rate (ASPR) of stomach cancer in Asian countries based on sociodemographic index (SDI), 2019.

In men, the highest ASDR of SC was observed in East Asia countries (32.73 (95% CI: 26.48_39.29)); with a 26% decrease compared with 2010. Also, in this period, all Asian regions had a decreasing trend of 8% (North Africa and Middle East) to 26% (East Asia and High-income Asia Pacific).

In women, the highest ASDR of SC was observed in East Asia countries (12.13 (95% CI: 9.89_14.73)), with a 30% decrease compared with 2010. Also, in this period, all Asian regions had a decreasing trend of 1% (South Asia) to 30% (East Asia) (**Supplementary Table 3**).

Age distribution

In 2019, age-specific death cases of SC were peaking at 70–74 years generally and in males, and 85 years and higher in females. In all age groups, death cases of SC in males were higher than in females, except in ages <30 years which in females was higher (Figure 7).

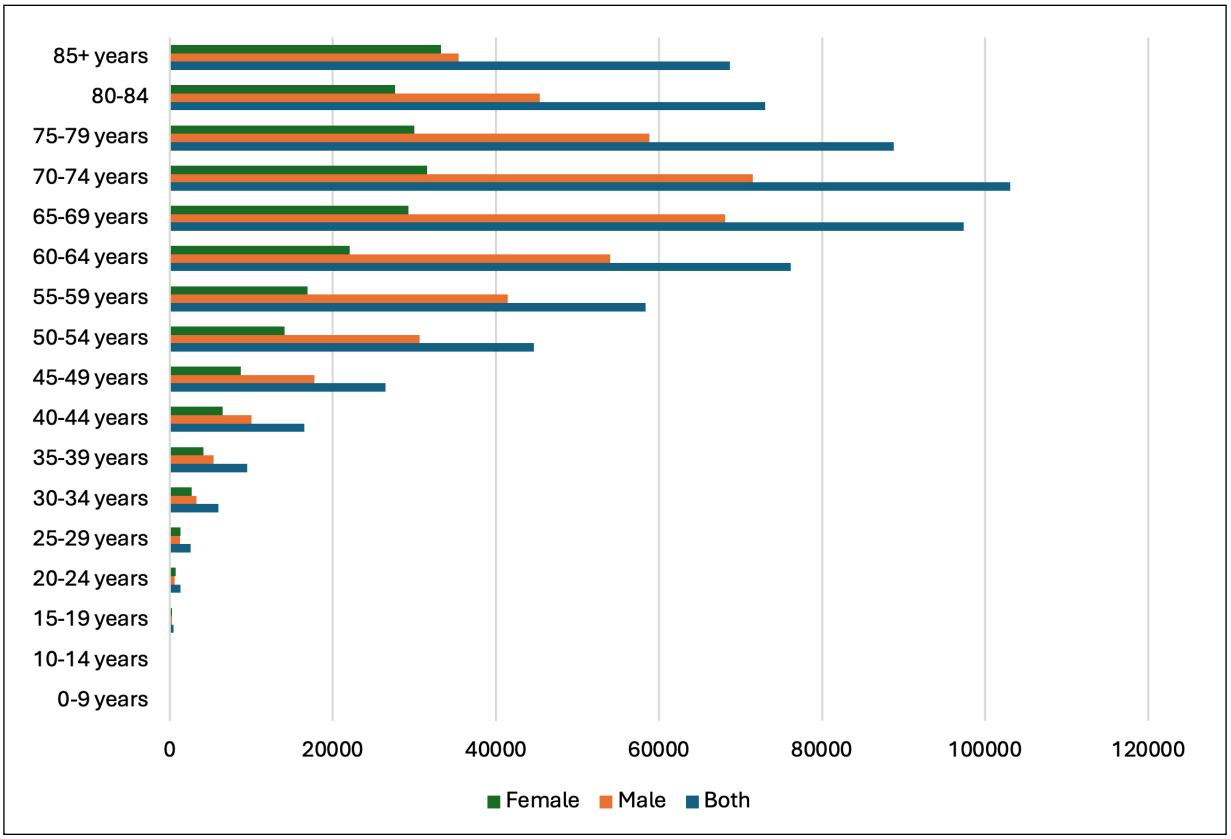

Figure 7. Age-specific death cases of stomach cancer among genders in Asia, 2019.

SDI

In 2019, among high SDI Asian countries, Brunei Darussalam (14.11), the Republic of Korea (14.09), and Japan (14.07) have the highest ASDR of SC, and Kuwait (3.45) has the lowest rate. In this classification, between 2010 and 2019, all countries recorded a downward trend between 12% (Taiwan (Province of China)) to 31% (United Arab Emirates). Among high-middle SDI Asian countries, Kazakhstan (14.11) and Georgia (14.07) have the highest ASDR of SC, and Sri Lanka (5.04) has the lowest rate. In this classification, between 2010 and 2019, all countries recorded a downward trend between 7% (Georgia) and 17% (Kazakhstan and Oman). Among middle SDI Asian countries, Azerbaijan (22.48) and China (21.72) have the highest ASDR of SC, and the Philippines (4.50) have the lowest rate. In this group, all countries recorded a downward trend between 1% (Iraq) to 28% (China) from 2010 to 2019. Among low-middle SDI Asian countries, Mongolia (46.04) has the highest ASDR of SC, and Maldives (3.60) has the lowest rate. In this group, only Timor-Leste (6%) experienced an upward trend, other countries reported a down-

ward trend from 5 (Bhutan and Palestine) to 19% (Bangladesh) from 2010 to 2019. Among low SDI Asian countries, Afghanistan (29.30) has the highest ASDR of SC, and Pakistan (6.87) has the lowest rate. In this group, 2 countries experienced a downward trend, 1 country reported an upward trend and 1 stable trend from 2010 to 2019. More details are presented in **Supplementary Table 5**.

National comparison

Among Asian countries, 47 countries experienced a decreasing trend in the SC death rate between 2010 and 2019; the greatest increase was detected in Timor-Leste (increase in ASDR = 0.06 (95% CI: -0.13_0.25)) and the greatest decrease was detected in the United Arab Emirates (decrease in ASDR = -0.31 (95% CI: -0.43_-0.17)) (Figure 4).

In 2019, the highest ASDR (per 100.000) of SC was reported in Mongolia (46.04), Afghanistan (29.3), Tajikistan (25.26), Democratic People's Republic of Korea (22.49), and Azerbaijan (22.48). The lowest ASDR of SC was reported in Kuwait (3.45), Maldives (3.6), Saudi Arabia (4.1), the Philippines (4.5), and the Syrian Arab Republic (4.97).

Among Asian men, the highest ASDR (per 100.000) of SC was reported in Mongolia (70.4), the Democratic People's Republic of Korea (34.54), Afghanistan (33.45), China (33.14), and Tajikistan (32.65). The lowest ASDR of SC was reported in Maldives (3.73), Kuwait (4.17), Saudi Arabia (4.67), the Syrian Arab Republic (5.54), and Sri Lanka (5.84).

Among Asian women, the highest ASDR (per 100.000) of SC was reported in Mongolia (29.86), Afghanistan (25.8), Tajikistan (18.87), Azerbaijan (14.99), and Yemen (14.42). The lowest ASDR of SC was reported in Kuwait (2.34), Saudi Arabia (3.27), the Philippines (3.37), Maldives (3.45), and Thailand (3.86). Results in detail are presented in **Supplementary Table 5** and Figure 5.

Male/female ratio

In 2010 and 2019, the ASDR of SC in Qatar is reported to be higher in women than in men. In other countries, the ASDR of SC in men was higher than in women. In 2019, the highest ratio was reported in Vietnam (2.78-fold) and the lowest ratio was recorded in Qatar (0.77-fold). Results in detail are presented in **Supplementary Table 5** and Figure 6.

Prevalence of SC in Asia

Global data and continents

In Asia, the number of cases who lived with SC increased from 1743263 (95% CI: 1618395_1871582) in 2010 to 2089176 (95% CI: 1823365_2391043) in 2019, which is a 1.2-fold increase. In 2019, more than 77% (2089176/2711657) of SC prevalence happened in Asian countries. During this period, the ASPR of SC with a 9% change, decreased from 47.26 (95% CI: 43.77_50.65) per 100.000 in 2010 to 42.98 (95% CI: 37.64_48.97) per 100.000 in 2019. Also, at the same time, this rate globally increased by 7%, in America by 5%, and in Europe and Africa by 8% (Figure 1 and **Supplementary Table 1**).

In Asian men, the number of SC prevalence increased from 1251037 (95% CI: 1144652_1365365) in 2010 to 1516586 (95% CI: 1275092_1804339) in 2019, which is over a 1.21-fold increase. In 2019, approximately 73% of patients who lived with SC in Asia, were men which included 79.7% (1516586 /1902034) of global male SC prevalence cases. During this period, the ASPR of SC with an 8% change, decreased from 69.75 (95% CI: 63.78_75.87) per 100.000 in 2010 to 64.5 (95% CI: 54.51_76.29) per 100.000 in 2019; at the same time, this rate globally decreased by 6%, in America by 6%, and in Europe and Africa by 2% (**Supplementary Table 2**).

In Asian women, the number of SC prevalence increased from 492227 (95% CI: 452401_528986) in 2010 to 572590 (95% CI: 491621_657076) in 2019, which is approximately a 1.16-fold increase. In 2019, approximately 27% of patients who lived with SC in Asia were women, which included 71% (572590/809623) of global female SC prevalence cases. During this period, the ASPR of SC with a 12% change, decreased from 26.19 (95% CI: 23.89_28.14) per 100.000 in 2010 to 23.01 (95% CI: 19.73_26.42) per 100.000 in 2019; at the same time, this rate globally decreased by 10%, in America by 4%, in Africa by 7%, and in Europe by 8% (**Supplementary Table 3**).

Asian regions

In 2019, the highest ASPR of SC was observed in High-income Asia Pacific countries (90.58 (95% CI: 78.34_103.7)) with a 23% decrease compared with 2010. While all Asian regions experienced a decreasing trend of 1 (Central Asia) and 23% (South Asia), North Africa and the Middle East had an increasing trend of 3% (Figure 2).

In men, the highest ASPR of SC was observed in High-income Asia Pacific countries (132.02 (95% CI: 111.92_156.19)) with a 26% decrease compared with 2010. Also, Central Asia, South Asia, and Southeast Asia regions experienced a decreasing trend of 1 (Central Asia) and 23% (South Asia); East Asia and North Africa and Middle East regions experienced an increasing trend of 2 to 3%, respectively (**Supplementary Table 2**).

In women, the highest ASPR of SC was observed in High-income Asia Pacific countries (132.02 (95% CI: 111.92_156.19)), with a 26% decrease compared with 2010. Also, Central Asia, South Asia, and Southeast Asia regions experienced a decreasing trend of 1 (Central Asia) and 23% (South Asia); East Asia and North Africa and Middle East regions experienced an increasing trend of 2 to 3%, respectively (**Supplementary Table 3**).

Age distribution

In 2019, age-specific prevalence cases of SC were peaking at 65–69 years generally, in males, and females. In all age groups, the prevalence cases of SC in males was higher than in females (Figure 8).

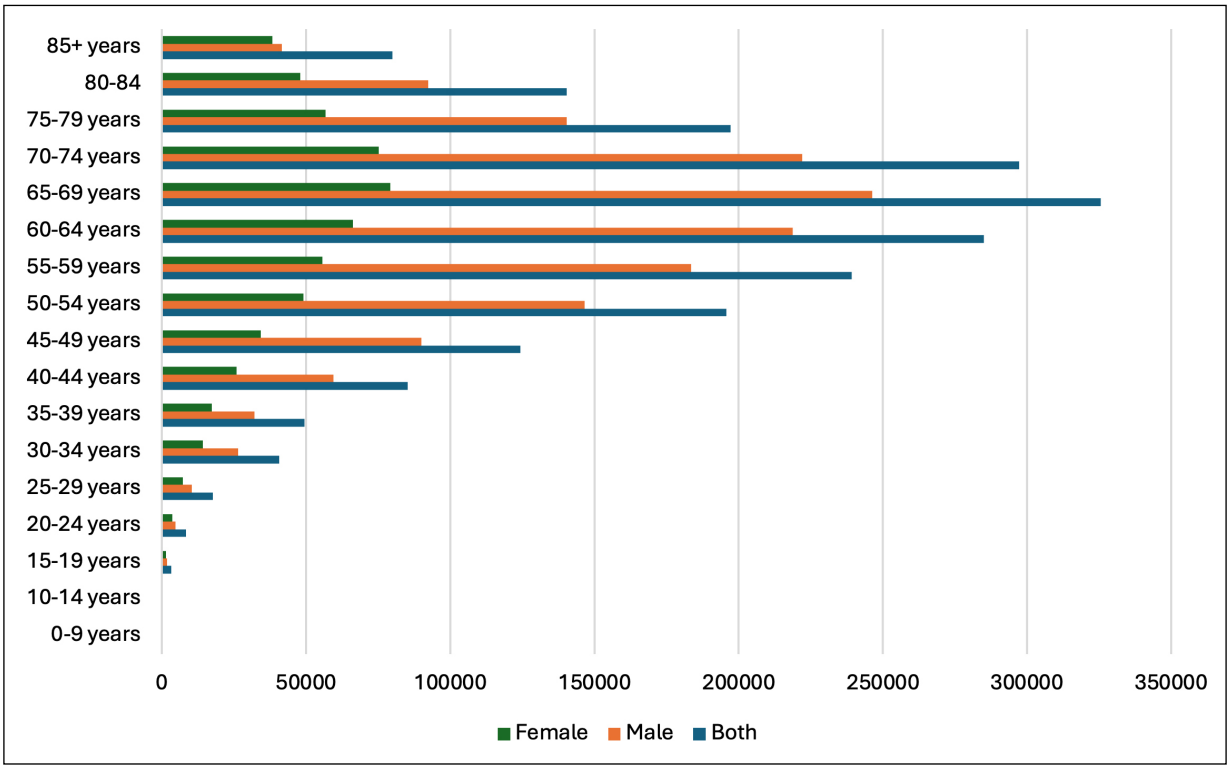

Figure 8. Age-specific prevalence cases of stomach cancer among genders in Asia, 2019.

SDI

Among high SDI Asian countries, the Republic of Korea (92.73) and Japan (90.70) have the highest ASPR of SC, and Saudi Arabia (6.69) has the lowest rate. In this group, Kuwait experienced an upward trend of 3%, and other countries reported a downward trend from 1 (Brunei Darussalam) to 29% (Republic of Korea) from 2010 to 2019. Among high-middle SDI Asian countries, Kazakhstan (20.28) had the highest ASPR of SC, and Jordan (7.85) had the lowest rate. In this group, 5 countries experienced a downward

trend from 6 to 23%, 3 countries reported an upward trend from 4 to 9%, and one had a stable trend from 2010 to 2019. Among middle SDI Asian countries, China (70.06) has the highest ASPR of SC, and the Philippines (5.63) has the lowest rate. In this group, 8 countries experienced a downward trend from 1 to 9%, 3 countries reported an upward trend from 4 to 11%, and one had a stable trend from 2010 to 2019. Among low-middle SDI Asian countries, Mongolia (53.02) has the highest ASPR of SC, and Maldives (5.80) has the lowest rate. In this group, 10 countries experienced a downward trend from 3 to 15%, 2 countries reported an upward trend from 5 to 10%, and one had a stable trend from 2010 to 2019. Among low SDI Asian countries, Afghanistan (33.37) has the highest ASPR of SC, and Pakistan (7.81) has the lowest rate. In this group, 2 countries experienced an upward trend of 1 to 6%, and 2 countries recorded a downward trend of 9 to 11% from 2010 to 2019. More details are presented in **Supplementary Table 6**.

National comparison

Among Asian countries, 37 countries experienced a decreasing trend in the SC prevalence rate between 2010 and 2019; the greatest increase was detected in Iran (Islamic Republic of) (increase in ASPR = 0.11 (95% CI: 0.04_0.19)) and the greatest decrease was detected in the Republic of Korea (decrease in ASPR = -0.29 (95% CI: -0.4_-0.14)) (Figure 4).

In 2019, the highest ASPR (per 100.000) of SC was reported in the Republic of Korea (92.73), Japan (90.7), China (70.06), Mongolia (53.02), and Taiwan (Province of China) (37.22). The lowest ASPR of SC was reported in the Philippines (5.63), Maldives (5.8), Saudi Arabia (6.69), Syrian Arab Republic (6.79), and Kuwait (6.83).

In Asian men, the highest ASPR (per 100.000) of SC was reported National distribution of SC among men Republic of Korea (133.3), Japan (132.59), China (109.61), Mongolia (78.12), and Taiwan (Province of China) (54.81). The lowest ASPR (per 100.000) of SC was reported in Maldives (6.3), Philippines (7.48), Saudi Arabia (7.64), Syrian Arab Republic (7.8), and Kuwait (8.29).

In women, the highest ASPR (per 100.000) of SC was reported in the Republic of Korea (58.19), Japan (54.37), Mongolia (34.26), China (32.59), and Afghanistan (30.44). The lowest ASPR (per 100.000) of SC was reported in the Philippines (4), Kuwait (4.6), Maldives (5.18), Saudi Arabia (5.24), and Pakistan (5.59). Results in detail are presented in **Supplementary Table 6** and Figure 5.

Male/ female ratio

In 2010, in Qatar and the United Arab Emirates only, the ASPR of SC in males was higher than in women, and in 2019, the ASPR of SC in Qatar was reported to be higher in women than in men. In other countries, the prevalence of SC in men was higher than in women. The highest ratio was reported in China (3.36-fold) and the lowest ratio was recorded in Qatar (0.77-fold) (Figure 6).

Burden of SC in Asia

Global data and continents

In Asia, the number of SC DALYs decreased from 16135847 (95% CI: 15071264_17225747) in 2010 to 15889630 (95% CI: 14119891_17684444) in 2019, which is a 0.12-fold decrease. In 2019, more than 71.5% (15889630/22220980) of SC DALYs happened in Asian countries. During this period, the DALYs ASR of SC with a 24% change, decreased from 428.68 (95% CI: 400.03_457.11) per 100.000 in 2010 to 324.66 (95% CI: 288.65_360.64) per 100.000 in 2019. In the same period, this rate globally decreased by 21%, in America and Africa by 11%, and in Europe by 18% (Figure 1 and **Supplementary Table 1**).

In Asian men, the number of SC DALYs decreased from 10961978 (95% CI: 10030961_11915833) in 2010 to 10640023 (95% CI: 9057419.44_12271049.01) in 2019, which is over a 0.97-fold decrease. In 2019, approximately 67% of SC DALYs in Asia, occurred in men which included 73.3% (10640023/14521172) of global male SC DALYs cases. During this period, the DALYs ASR of SC with a 25% change, decreased from 599.01 (95% CI: 550.49_648.97) per 100.000 in 2010 to 449.18 (95% CI: 384.56_514.94) per 100.000 in 2019, in the same period, this rate globally decreased by 22%, in Europe by 18%, and in America and Africa by 11% (**Supplementary Table 2**).

In Asian women, the number of SC DALYs increased from 5173869 (95% CI: 4783919_5586183) in 2010 to 5249607 (95% CI: 4581016_6016801) in 2019, which is approximately a 1.02-fold increase. In 2019, more than 33% of DALYs related to SC in Asia were women, which included 68.2% (5249607/7699808) of global female SC DALYs cases. During this period, the DALYs ASR of SC with a 22% change, decreased from 269.06 (95% CI: 248.81_290.27) per 100.000 in 2010 to 209.7 (95% CI: 183.24_239.92) per 100.000 in 2019. At the same time, this rate globally decreased by 19%, in American and African countries by 10%, and in European countries by 18% (**Supplementary Table 3**).

Asian regions

In 2019, the highest DALYs ASR of SC was observed in East Asia countries (477.93 (95% CI: 402.48_560.38)); with a 28% decrease compared with 2010. All regions recorded a decreasing trend of 9 (South Asia) to 28% (East Asia and High-income Asia Pacific) (Figure 2 and **Supplementary Table 1**).

In men, the highest DALYs ASR of SC was observed in East Asia countries (713.07 (95% CI: 570.7_867.76)) with a 27% decrease compared with 2010. All regions recorded a decreasing trend of 9 (North Africa and Middle East) to 30% (High-income Asia Pacific) (**Supplementary Table 2**).

In women, the highest DALYs ASR of SC was observed in Central Asia countries (261.49 (95% CI: 236.71_290.35)); with a 15% decrease compared with 2010. All regions recorded a decreasing trend of 9 (North Africa and the Middle East) to 30% (East Asia) (**Supplementary Table 3**).

Age distribution

In 2019, DALY cases of SC were peaking at 65–69 years generally, in males, and females. In all age groups, DALY cases of SC in males were higher than in females, except in ages <30 years and higher which in females was higher (Figure 9).

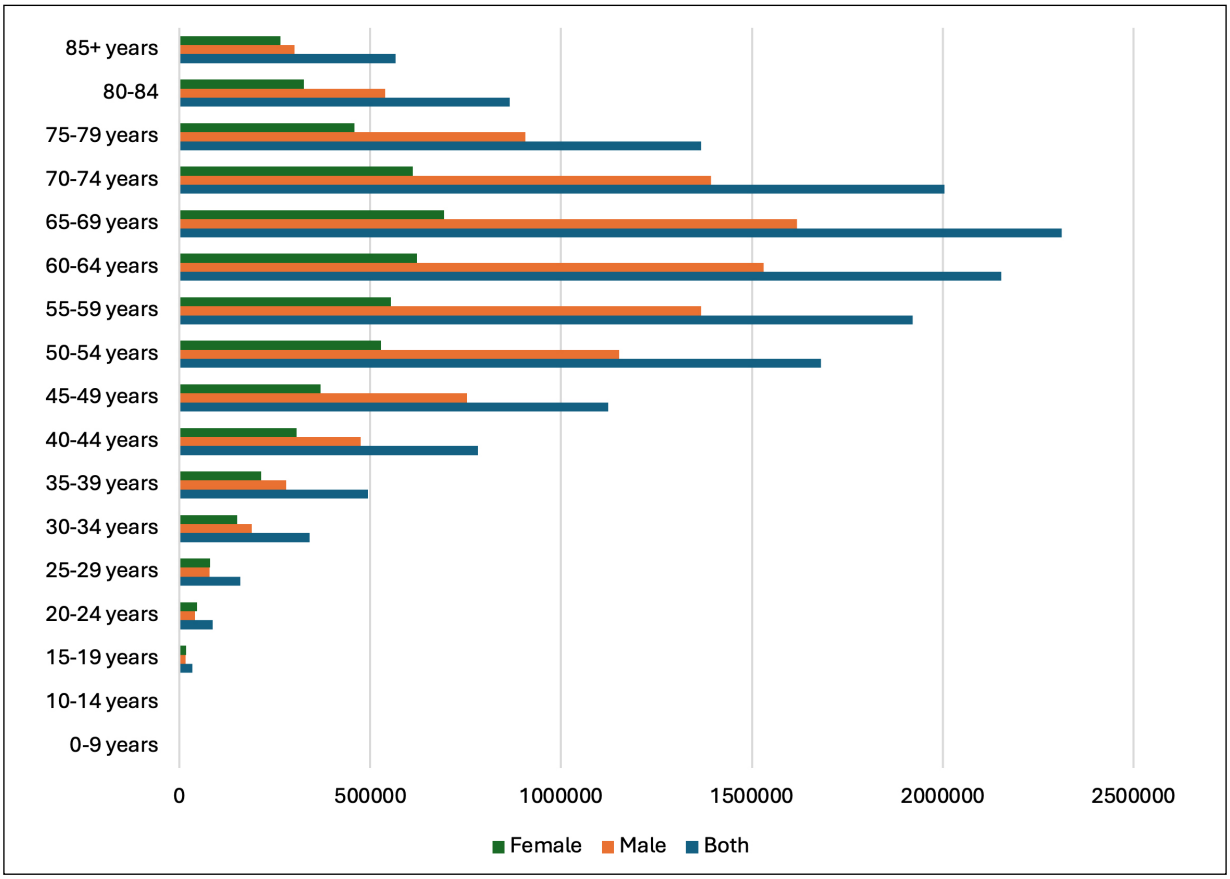

Figure 9. Age-specific DALYs cases of stomach cancer among genders in Asia, 2019.

SDI

In 2019, among high SDI Asian countries, Brunei Darussalam (299.66) and the Republic of Korea (298.70) have the highest DALYs ASR of SC, and Kuwait (64.88) has the lowest rate. In this group, all countries experienced a downward trend from 10 (Brunei Darussalam) to 36% (Republic of Korea) from 2010 to 2019. Among high-middle SDI Asian countries, Georgia (355.53) and Kazakhstan (345.97) have the highest DALYs ASR of SC, and Sri Lanka (107.38) has the lowest rate. In this group, all countries experienced a downward trend from 7 (Malaysia) to 28% (Kazakhstan) from 2010 to 2019. In middle SDI Asian countries, Azerbaijan (502.49) and China (481.15) have the highest DALYs ASR of SC, and the Syrian Arab Republic (107.16) and the Philippines (107.44) have the lowest rate. In this group, all countries experienced a downward trend from 3 (Iraq) to 29% (China) from 2010 to 2019.

Among low-middle SDI Asian countries, Mongolia (1059.24) has the highest ASPR of SC, and Maldives (68.10) has the lowest rate. In this group, only Timor-Leste experienced an upward trend of 8%, other countries reported a downward trend from 5 (Palestine) to 21% (Myanmar) from 2010 to 2019. Among low SDI Asian countries, Afghanistan (728.70) has the highest DALY ASR of SC, and Pakistan (162.70) has the lowest rate. In this group, Nepal reported an increasing trend of 3%, and other countries experienced a downward trend of 1 to 13% from 2010 to 2019. More details are presented in **Supplementary Table 7**.

National comparison

Among Asian countries, 47 countries experienced a decreasing trend in the SC DALYs ASR between 2010 and 2019; the greatest increase was detected in Timor-Leste (increase in DALYs ASR = 0.08 (95% CI: -0.13_0.31)) and the greatest decrease was detected in Republic of Korea (decrease in DALYs ASR = -0.36 (95% CI: -0.42_-0.3)) (Figure 4).

In 2019, the highest DALYs ASR (per 100.000) of SC was reported in Mongolia (1059.24), Afghanistan (728.7), Tajikistan (590.16), Democratic People's Republic of Korea (577.22), and Azerbaijan (502.49). The lowest DALY ASR of SC was reported in Kuwait (64.88), Maldives (68.1), Saudi Arabia (86.23), Singapore (105.97), and the Syrian Arab Republic (107.16).

In Asian men, the highest DALYs ASR (per 100.000) of SC was reported in Mongolia (1577.24), Democratic People's Republic of Korea (856.33), Afghanistan (784.67), Tajikistan (749.13), and Azerbaijan (731.28). The lowest DALY ASR (per 100.000) of SC was reported in Maldives (71.95), Kuwait (78.41), Saudi Arabia (97.9), Syrian Arab Republic (122.74), and Bahrain (125.14).

In women, the highest DALYs ASR (per 100.000) of SC was reported in Afghanistan (690.4), Mongolia (665.19), Tajikistan (445.18), Democratic People's Republic of Korea (360.56), and Yemen (353.39). The lowest DALY ASR (per 100.000) of SC was reported in Kuwait (44.38), Maldives (63.62), Saudi Arabia (68.48), Philippines (77.16), and Singapore (88.28). Results in detail are presented in **Supplementary Table 7** and Figure 5.

Male/female ratio

In 2010, only in Qatar and the United Arab Emirates, the DALYs ASR of SC in males was higher than in women, and in 2019, the DALYs ASR of SC in Qatar and India were reported to be higher in women than in men. In other countries, the incidence of SC in men was higher than in women. The highest ratio was reported in China (3.02-fold) and the lowest ratio was recorded in Qatar (0.75-fold) (Figure 6).

DISCUSSION

This study aims to investigate the temporal trend of incidence, mortality, and burden of SC from 2010 to 2019 in 49 Asian countries based on geographic region and SDI and compare them with global data. According to the results, from 2010 to 2019, the number of new cases of SC has increased 1.1 times. The number of deaths has also increased by 1.03 times, and the prevalence of SC has increased by 1.2 times. At this time, the DALY of SC has decreased by 0.98 times. Also, from 2010 to 2019, ASIR, ASDR, ASPR, and DALYs ASR have all decreased by 18%, 23%, 9%, and 24%, respectively.

In 2019, more than 73% of SC cases occurred in Asian countries. From 2010 to 2019, the number of new SC cases has increased 1.1 times in both men and women. In the surveyed countries, from 2010 to 2019, the ASIR of SC has decreased by almost 18%. This decrease has been more in women (18%) than men (17%). Meanwhile, the ASIR of SC has also decreased globally, in America, Europe and Africa. In terms of age, the newest cases of SC were observed in men aged 65-69 and in women aged 70-74. In 2019, the highest ASIR of SC was observed in East Asia countries in general, men of East Asia countries and women of high-income Asia Pacific countries.

SC is a multifactorial disease[14,33,34]. Risk factors contributing to SC include lifestyle and environmental factors, *Helicobacter pylori (H. pylori*) infection, low socio-economic status, dietary factors such as excessive consumption of salty and smoked foods and low intake of fibers (fruits and vegetables), current and former smoking, current and former alcohol abuse, low physical activity, obesity, radiation, gastroesophageal reflux disease, positive familial history and genetic predisposition. Moreover, a notable association between dietary acid load and the risk of gastric cancer was revealed. Consumption of animal-based foods (mostly meat) can lead to a higher dietary acid load while plant-based foods are inversely linked to dietary acid load[35].

The results of a systematic review and meta-analysis showed that *Helicobacter pylori* is the most important risk factor[14]. In 1994, the International Agency for Research on Cancer announced *H. pylori* as a carcinogen and reconfirmed it in 2009[36]. Chronic *H. pylori* infection is the main cause of SC, which accounts for about 89% of distal SC cases worldwide[37-39]. Most *H. Pylori* infections are acquired in childhood and if not treated, they usually remain. The prevalence of *H. Pylori* infection in adults is more than 50% in many industrialized countries. It must be considered that the prevalence of this bacterial infection differs from region to region. The regions with the highest prevalence of *H. pylori* infections are Africa and South America, and the regions with the lowest prevalence are Oceania and Western Europe[40]. In a systematic review, it was revealed that the prevalence of *H. pylori* infection is 50.8% in developing countries and 34.7% in developed countries. Moreover, the global infection rate was 42.7% in women and 46.3% in men[41].

It has been shown that more than 2 billion *H. pylori*-positive patients and about 75% of SC cases in the world live in Asia[40]. Considering that *H. pylori* infection is known as an infectious disease, it is recommended that regardless of the symptoms, infected people be treated to prevent serious complications and transmission[42].

According to the results, from 2010 to 2019, SC ASDR decreased by 23% in the 49 countries studied. This decrease was more in men than women (24% *vs.* 22%). In 2019, more than 70% of SC deaths occurred in Asian countries. In the same year, the ASDR of SC was 20.7 per 100,000 individuals in men and 9.48 per 100,000 individuals in women. Meanwhile, the ASDR of SC had also decreased globally, in America, Europe and Africa, although the decrease observed in Asian countries was more substantial. According to the age distribution, most cases of SC deaths were observed in men aged 70-74 and women aged 85 and older. In the total population, the highest ASDR of SC was reported in East Asian countries. Altogether, improvements in medical treatment may have contributed to the reduction in gastric cancer mortality[43]. Further advances in the treatment of gastric cancer and *H. pylori* infections may be important to maintain the decline in gastric cancer mortality in the future[44]. On the other hand, as mentioned, the ASIR of SC also decreased during the period of study, yet the ASDR of SC decreased at a greater pace (23% *vs.* 18%), which indicates a decrease in mortality. SC mortality has also decreased in European countries, and it was shown that a major factor in reducing SC mortality is reducing exposure to *H. pylori* infection[44].

In this study, it was discovered that from 2010 to 2019, the prevalence of SC had increased 1.2 times in Asian countries, which was higher in men than in women (1.21 *vs.* 1.16). Also, the ASPR of SC had decreased by 9% in all the studied countries. The ASPR decreased more in women (12%) than in men (8%). Also, the ASPR of SC has increased globally, in America, Europe, and Africa. In 2019, more than 77% of SC prevalence was reported in Asian countries. According to the results, the ASPR of SC peak was reported in men and women aged 65-69. The highest ASPR of SC in the total population was reported in men and women of high-income Asia Pacific countries. Although, from 2010 to 2019, the ASPR of SC decreased in high-income Asia-Pacific countries. The reduction of ASPR SC can be due to changes in lifestyle and public health interventions such as reducing *H. pylori* infection, improving living conditions and better food storage methods[40], which lead to a decrease in the incidence and consequently the prevalence of SC. Of course, the survival rate of SC should also be considered. The results of a study in Korea showed that the 5-year overall relative survival rate of SC patients increased from 55.7% in the period of 19999-2005 to 77.0% in the period of 2013-2019[45]. Major risk factors to determine disease-free survival are shown by Safari at el[46] to be a stage, tumor grade, radiotherapy, tumor site, surgery, and age.

As previously noted, most contributing factors of stomach cancer are closely related to the level of socioeconomic development[47]. For instance, improved hygiene and better food preservation as well as an increase in fresh vegetable intake[48]. In the meantime, the prevalence of *H. pylori* infection as a major confirmed cause of gastric cancer is closely linked with economic development and better living conditions can undoubtedly reduce the prevalence of *H. pylori* infection[49]. All things considered, we should pay attention to the role of economic development in reducing *H. pylori* and thus reducing SC. Moreover, we should consider the fact that economically developed countries have more resources and can afford better health insurance policies for the screening and treatment of *H. pylori* infection. In the 1990s, American and European countries developed national plans to contain the prevalence of *H. pylori* through screening and treatment[50,51] which led to a notable decrease in the incidence rates of gastric cancer compared to economically developing countries.

The results have shown that the number of SC DALY has decreased 0.98 times. Although it has reduced, in 2019, a total of 71.5% of SC DALYs were reported in Asian countries. In this time, DALYs ASR of SC have decreased in of both men and women with more reduction in men (22% *vs.* 25%). Similar to Asian countries, the reduction in DALYs ASR of SC has been seen globally, in Europe, America and Africa from 2010 to 2019, but the drop was more significant in Asian countries. To consider the age distribution of this study, the peak for DALY cases of SC in 2019 was in men and women 65-69 years old. In 2019, most DALYs ASR of SC in the whole population and in men was in East Asian countries and women were in Central Asian countries. Since in this period, ASPR, ASIR, and ASDR of stomach cancer have decreased from 9 to 23 %, it would cause a reduction in DALYs ASR by 24%.

H. pylori serology screening should be done in geographical areas with a high incidence of SC, especially in individuals younger than 50 years old[52]. The potential effectiveness of a gastric cancer prevention program that includes *H. pylori* screening and treatment depends on the patient's risk factors for gastric cancer at the time of *H. pylori* eradication and the screening method used[52]. There are various assumptions about the effectiveness and the cost that support population-based screening for *H. pylori* and eradication of infection as an affordable approach[53-55]. Many epidemiological studies have shown that gastric cancer screening can effectively reduce cancer incidence and mortality by enabling early detection and treatment in high-risk populations. SC screening, early detection and treatment are considered secondary cancer prevention measures and are the primary focus of current SC prevention programs worldwide[54,56,57]. As of now, population-based *H. pylori* screening and treatment programs appear to be the most promising measures to reduce the incidence of gastric cancer[55]. To improve social awareness of stomach cancer modifiable risk factors, it is important to encourage screening programs and educational interventions, especially in high-risk communities.

Limitations

Considering that online data was used in this study, one of the most important limitations of the study is possible errors in data recording. Also, the quality of data is not the same in all countries, including countries with low SDI.

CONCLUSIONS

Despite the decreasing trend observed in the age-standardized rates of incidence, prevalence, and burden of stomach cancer in Asia, more than 70% of the burden caused by stomach cancer is imposed on Asian countries. It is hoped that due to the high rate of decline observed in the last decade, we will observe a decrease in this amount to the level of global statistics. In Asia, the regions of East Asia and the High-income Asia Pacific have the highest amount. Therefore, knowing the risk factors and behavioral habits that lead to the difference in stomach cancer statistics in Asia compared to other countries, and implementing preventive strategies seem necessary. Also, by implementing appropriate educational programs in the field of gastric cancer symptoms and encouraging early referral when symptoms are observed, the death burden of this disease can be reduced.

Ethics approval and consent to participate:

This study was approved by the Ethics Committee of the Jahrom University of Medical Sciences with IR.JUMS.REC.1401.094 code. Informed consent was not required, due to the use of online and anonymous data.

Conflict of interest statement:
The authors have no conflict of interest to declare.

Consent for publication:
Written informed consent for publication was not required, due to the use of online and anonymous data.

Availability of data and material:
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Conceptualization: Hamid Salehiniya, Afrooz Mazidimoradi, and Fatemeh Rezaei; Formal analysis: Hamid Salehiniya, Leila Allahqoli, and Afrooz Mazidimoradi; Data curation: Hamid Salehiniya, Afrooz Mazidimoradi, Leila Allahqoli, and Fatemeh Rezaei; Project administration: Hamid Salehiniya, Afrooz Mazidimoradi, Fatemeh Rezaei, and Ali Rayatinejad; Writing-original draft: all authors contributed to writing-original draft; Writing-review and editing: all authors contributed in editing the final proof.

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