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CLINICAL ARTICLE

Gynecology

Global incidence and mortality trends of corpus uteri cancer and associations with gross domestic product, human development index, lifestyle, and metabolic risk factors

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Abstract

Objective: To evaluate the worldwide distribution, risk factors, and temporal trends of corpus uteri cancer for different countries and age groups.

Method: Data relating to corpus uteri cancer in 2020 were retrieved from the *Global Cancer Observatory* database. Data from *Cancer Incidence in Five Continents* and *the WHO mortality database* were used for trend analysis. Age-standardized rates (ASR, per 100 000 persons) were calculated for incidence and mortality. Joinpoint regression analysis was used to estimate the 10-year annual average percent change (AAPC).

Results: A total of 417 367 new cases and 97 370 new deaths of corpus uteri cancer were reported globally in 2020. The highest incidence was observed in high-income countries. Higher ASR of mortality of corpus uteri cancer was associated with a higher gross domestic product per capita, higher Human Development Index, and higher prevalence of smoking, alcohol drinking, physical inactivity, obesity, hypertension, diabetes, and lipid disorders. There was a substantial increasing trend of corpus uteri cancer, with the largest AAPC in incidence found in Japan, followed by India, Chile, Korea, and Thailand.

Conclusion: The incidence and mortality of corpus uteri cancer have been increasing substantially for the past 10 years. Intensive lifestyle modifications are needed, especially among younger women.

KEYWORDS
annual average percent change, corpus uteri cancer, incidence, mortality, trends

1 | INTRODUCTION

Corpus uteri cancer is the most common female malignancy in many western countries.[1] Globally, corpus uteri cancer was the third most common cancer and the fourth leading cause of death due to female genital cancer in 2020.[2] There is a wide variation in the incidence and mortality of corpus uteri cancer. Almost two-thirds of all corpus uteri cancer cases occur in high-income regions whereas a lower burden is observed in low-income countries.[3] The vast majority of corpus uteri cancers are adenocarcinomas arising from the endometrium, which can be categorized into two subtypes based on their clinical, tissue, and molecular characteristics.[4] Type I, which occurs in females predominantly after menopause, is estrogen-dependent and accounts for most of all corpus uteri cancers.[4]

Evidence has indicated that menstrually related factors, including giving birth at older ages, use of external hormones (contraceptive pills and hormone replacement therapy), nutrition (alcohol drinking), anthropometrics (overweight, adulthood obesity, and body fat distribution), and unhealthy diet (western diet: low intake of fruit and vegetables and excessive intake of red meat),[5] are important risk factors for corpus uteri cancer, especially in high-income countries.[6] Other risk factors include physical inactivity, diabetes, hypertension, a family history of endometrial cancer,[7] and life expectancy of countries,[8] average educational level,[8] chemical exposure due to migration from low-risk to high-risk areas,[9] granted access to appropriate guideline-based and quality care,[10] and health system from each country.[11]

Information on the most updated distribution, risk factors, and epidemiologic trends of corpus uteri cancer is important for decision making and resource allocation for the reduction of its associated health loss and mortality. However, previous evidence has mainly focused on single countries[12,13] or regions[14] or used relatively old data.[7] The associations between different risk factors and corpus uteri cancer have not been comprehensively evaluated at a country level.[8,15] The present study aimed to present the most updated global incidence and mortality distribution, risk factors, and trend of corpus uteri cancer in different countries, regions, and age groups.

2 | MATERIALS AND METHODS

2.1 | Data sources

The global incidence, mortality, and 5-year prevalence of corpus uteri cancer for 185 countries in 2020 were retrieved from *GLOBOCAN* International Agency for Research on Cancer (IARC), by the World Health Organization (WHO).[16] The IARCs strategy involves not only analyzing, compiling, and using the data from the Agency's collaborators in these estimations but also collaborating with country staff to raise the quality of local data, the coverage of local registries, and the analytical capability of the region.[17] The gross domestic product (GDP) and Human Development Index (HDI) for each country were retrieved from the World Bank and the United Nations, respectively.[18] The *Global Health Data Exchange* database was employed to retrieve the data on the prevalence of smoking, alcohol drinking, unhealthy diet, physical inactivity, hypertension, diabetes, and lipid disorders. Data on the yearly incidence of corpus uteri cancer were extracted from the *Cancer Incidence in Five Continents I-X plus* (*CI5Plus*) for the trend analysis. *CI5*, developed by the IARC, WHO, is a global cancer database where the age- and sex-associated cancer incidence from different countries are available to facilitate direct comparisons based on demographic characteristics.[19] The cancer registries are of high quality and cover a substantial proportion of the world's population. The proportion of cancer cases reported microscopically, the percentage of cancer deaths registered, and the percentage of cancer cases registered were used as the inclusion criteria to evaluate the quality of information by period, gender, and primary cancer sites. Data on corpus uteri cancer mortality were retrieved from the *WHO Mortality database*, where the figures of cancer-related deaths for each year are collected.[20] In the *WHO Mortality database*, only information with a medium or higher quality level was used.[21] To obtain the latest incidence and mortality data of corpus uteri cancer for Northern European countries and the USA specifically, the *Nordic Cancer Registries (NORDCAN)*[22,23] and the *Surveillance, Epidemiology, and End Results (SEER)*[24] were also accessed. A total of 48 countries were divided into nine regions in the trend analysis, including Asia, Oceania, North America, Southern America, Northern Europe, Western Europe, Southern Europe, Eastern Europe, and Africa. To ensure the data were correctly categorized, the extracted incidence and mortality data for corpus uteri cancer in this research adopted the International Classification of Disease and Related Health Problems, 10th revision codes of corpus uteri cancer: Malignant neoplasm of corpus uteri (ICD-10, C54). The Segi-Doll standard population adjustment of age-standardized rates (ASR) per 100 000 were used to ensure such data can be compared overtime.[25]

2.2 | Statistical analysis

Two choropleth maps were constructed to describe the worldwide incidence and mortality of corpus uteri cancer. Associations between GDP per capita, HDI, the prevalence of smoking, alcohol drinking, unhealthy diet, physical inactivity, hypertension, diabetes, and lipid and the burden of corpus uteri cancer were examined by univariable linear regression analysis. β coefficients and the corresponding 95% confidence intervals (CI) were estimated from the regression. The β estimates refer to the degree of change in ASR of incidence or mortality of corpus uteri cancer per unit increase in the risk factors. The gathered ASR data of the past decade's trends of incidence and mortality of corpus uteri cancer in the current study were analyzed using a Joinpoint regression (Version 4.8.0.1, April

2020) from the databases mentioned above.[26] The natural logarithm of ASR and binomial approximation of standard errors were employed to expedite the Joinpoint regression analysis. The calculation of Annual Percentage Change (APC) used the corresponding standard errors and natural logarithmic ASR by the Joinpoint regression analysis software and based on the assumption of constant change rate during the whole of the time interval (i.e., 10 years). A maximum of one Joinpoint in the regression was adopted by the software. The changepoint value determined that the segments which were assigned the weighting referred to their length of total time interval proportion. They were then used to calculate the AAPC with 95% CI. The epidemiologic trends of incidence and mortality were indicated by the AAPC, with a positive AAPC meaning an increasing trend and vice versa. The 95% CI can be used as an indicator to evaluate the stability of the trend: an interval overlapping with 0 signifies a stable trend without significant temporal change. This study estimated and analyzed the epidemiologic trends of corpus uteri cancer with females aged 0–85+ years by different age groups (≥50, <50, and <40 years). All values of *P* that were less than or equal to 0.05 were determined as significant results.

2.3 | Ethics approval

The present study was approved by the Survey and Behavioral Research Ethics Committee, the Chinese University of Hong Kong (No. SBRE-20-332). Informed consent was waived, because the present study is based on secondary database analysis.

3 | RESULTS

3.1 | Global incidence of corpus uteri cancer in 2020

Globally, there were 417 367 new case of corpus uteri cancer reported in 2020, with an ASR incidence of 8.7 per 100 000 persons (Figure 1). In 2020, the 5-year cancer prevalence rate was 36.6 per 100 000 persons globally, the highest prevalence was found in Northern America (143.6 per 100 000), Central and Eastern Europe (133.6 per 100 000), and Northern Europe (132.2 per 100 000). Similarly, countries in North America had the highest incidence (ASR = 21.1), followed by Central and Eastern Europe (ASR = 20.2), Northern Europe (ASR = 16.4), Polynesia (ASR = 15.7), and Oceania (ASR = 14.5). The lowest incidence was observed in Middle Africa (ASR = 2.3), followed by South-Central Asia (ASR = 2.7), Eastern Africa (ASR = 3.0), Western Africa (ASR = 3.3), and North Africa (ASR = 3.4). The incidence was higher in high-income (ASR = 15.9) and upper-middle-income (ASR = 8.5) countries compared with low-middle-income (ASR = 3.9) and low-income (ASR = 3.1) countries. Similarly, the highest incidence was reported in regions with very high HDI (ASR = 15.9) and the lowest incidence was reported in low HDI regions (ASR = 2.9).

3.2 | Global mortality of corpus uteri cancer in 2020

Globally, there were 97 370 new deaths of corpus uteri cancer reported in 2020, with an ASR incidence of 1.8 per 100 000 persons. Countries in Polynesia having the highest mortality ASR (ASR = 4.3), followed by Central and Eastern Europe (ASR = 3.7), Caribbean (ASR = 3.5), North America (ASR = 3.1), and Northern Europe (ASR = 2.7). The lowest mortality was observed in North Africa (ASR = 0.72), followed by Middle Africa (ASR = 0.79), South-Central Asia (ASR = 1.0), Eastern Africa (ASR = 1.0), and Western Africa (ASR = 1.2). The mortality rates were higher in countries with high-income (ASR = 2.4) and upper-middle-income (ASR = 1.9) status compared with countries with low-middle-income (ASR = 1.2) and low-income (ASR = 1.0) status.

3.3 | Associations between risk factors and incidence

The associations between risk factors and the incidence of corpus uteri cancer are presented in Figure 2. Higher ASR of incidence of corpus uteri cancer was associated with a higher GDP per capita (β = 1.37, 95% CI 0.94–1.80, P < 0.001), HDI (β = 2.32, 95% CI 1.81 = 2.84, P < 0.001), and higher prevalence of smoking (β = 0.82, 95% CI 0.69–0.97, P < 0.001), alcohol drinking (β = 1.00, 95% CI 0.79–1.21, P < 0.001), physical inactivity (β = 0.62, 95% CI 0.35–0.89, P < 0.001), obesity (β = 0.25, 95% CI 0.18–0.33, P < 0.001), hypertension (β = 0.27, 95% CI 0.17–0.37, P < 0.001), diabetes (β = 0.54, 95% CI 0.37–0.70, P < 0.001), and lipid disorders (β = 0.33, 95% CI 0.27–0.40, P < 0.001).

3.4 | Associations between risk factors and mortality

The associations between risk factors and mortality of corpus uteri cancer are presented in Figure 3. Higher ASR of mortality of corpus uteri cancer was associated with a higher GDP per capita (β = 0.15, 95% CI 0.05–0.25, P < 0.001), HDI (β = 0.35, 95% CI 0.22–0.48, P < 0.001), and higher prevalence of smoking (β = 0.12, 95% CI 0.08–0.15, P < 0.001), alcohol drinking (β = 0.12, 95% CI 0.07–0.17, P < 0.001), physical inactivity (β = 0.12, 95% CI 0.06–0.18, P < 0.001), obesity (β = 0.06, 95% CI 0.04–0.07, P < 0.001), hypertension (β = 0.04, 95% CI 0.02–0.07, P < 0.001), diabetes (β = 0.13, 95% CI 0.09–0.16, P < 0.001), and lipid disorders (β = 0.46, 95% CI 0.03–0.06, P < 0.001).

3.5 | Temporal trends of corpus uteri cancer

The incidence and mortality trends of corpus uteri cancer for each country are shown in Figure S1 and their corresponding analysis results of joinpoint regression are shown in Figure S2. Overall, there was a substantial increasing trend of corpus uteri cancer irrespective of age group and geographical region.

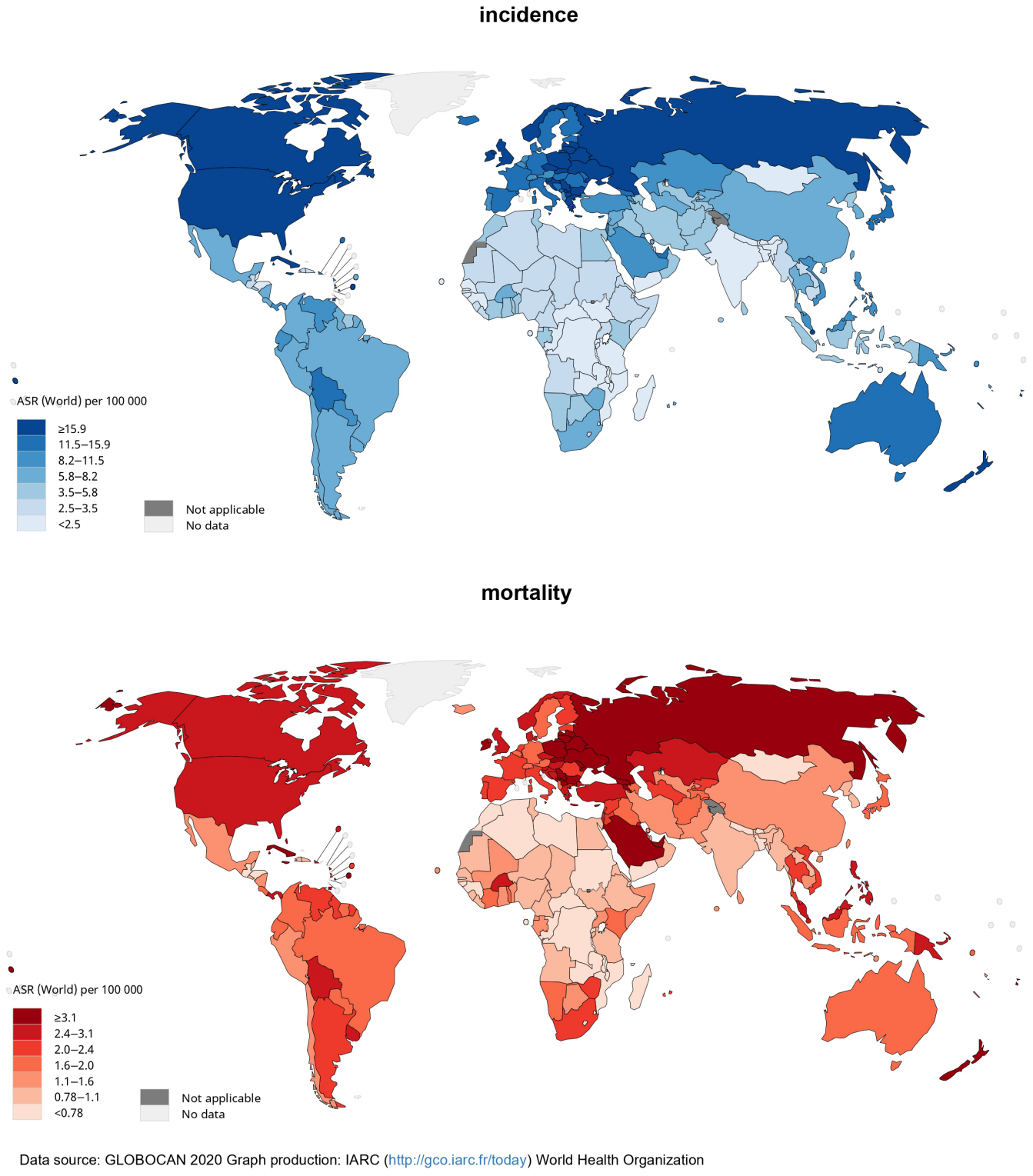

FIGURE 1 Global incidence and mortality of corpus uteri cancer, all ages, in 2020.

3.6 | Overall incidence trends of corpus uteri cancer

Among 48 countries/economies, 18 countries showed a significantly increased trend of corpus uteri cancer incidence (Figure 4). Within these countries, the largest AAPC was found in Japan (AAPC = 8.66, 95% CI 6.71–10.65, $P < 0.001$), followed by India (AAPC = 8.18, 95% CI 5.16–11.30, $P < 0.001$), Chile (AAPC = 6.23, 95% CI 2.20–10.42, $P = 0.007$), Korea (AAPC = 5.16, 95% CI 3.92–6.41, $P < 0.001$), and Thailand (AAPC = 4.38, 95% CI 0.97–7.90, $P = 0.018$). By contrast, only three countries showed significant decreases in the AAPC trend of corpus uteri incidence rate: the Philippines (AAPC = −3.89,

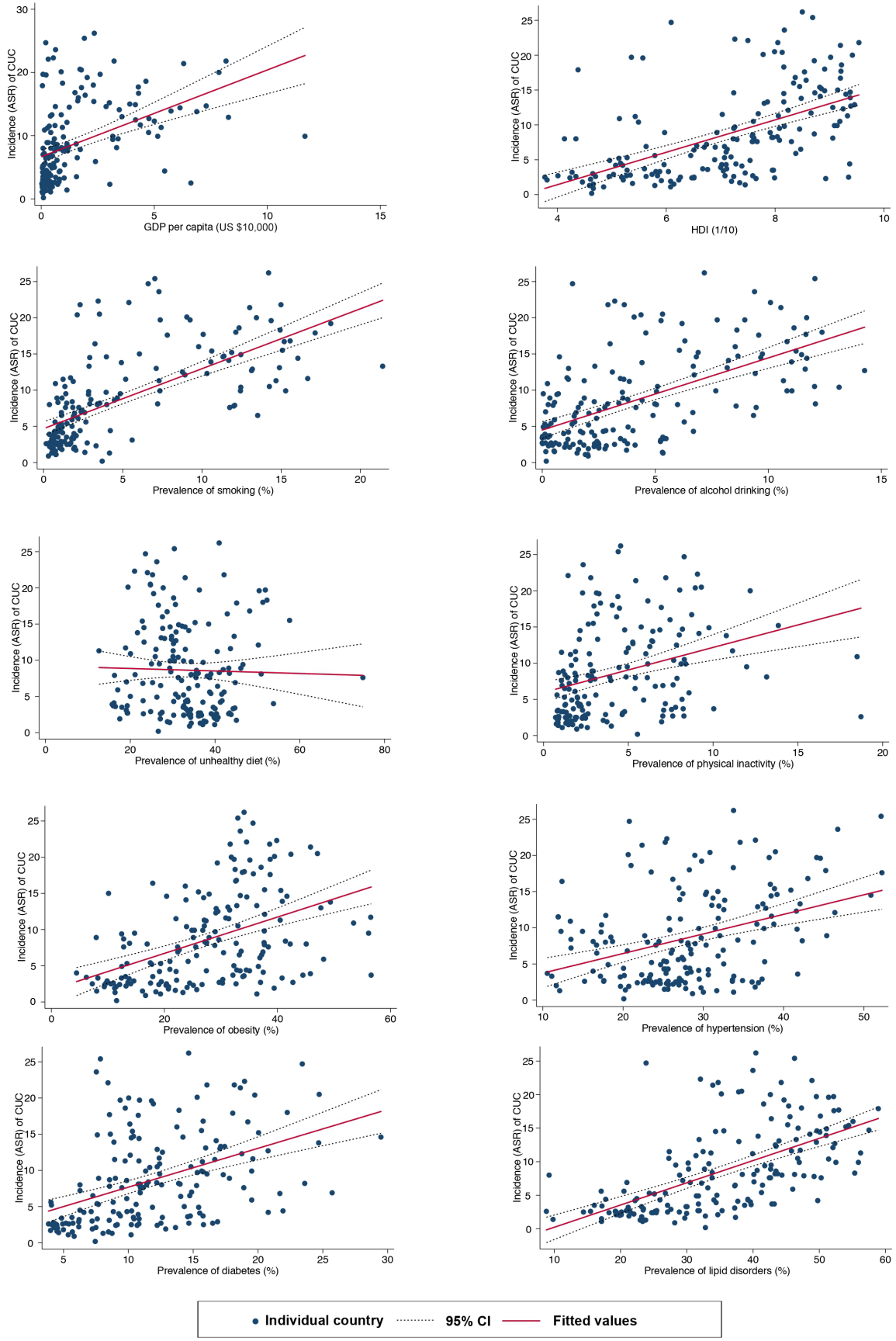

FIGURE 2 Associations between risk factors and incidence of corpus uteri cancer.

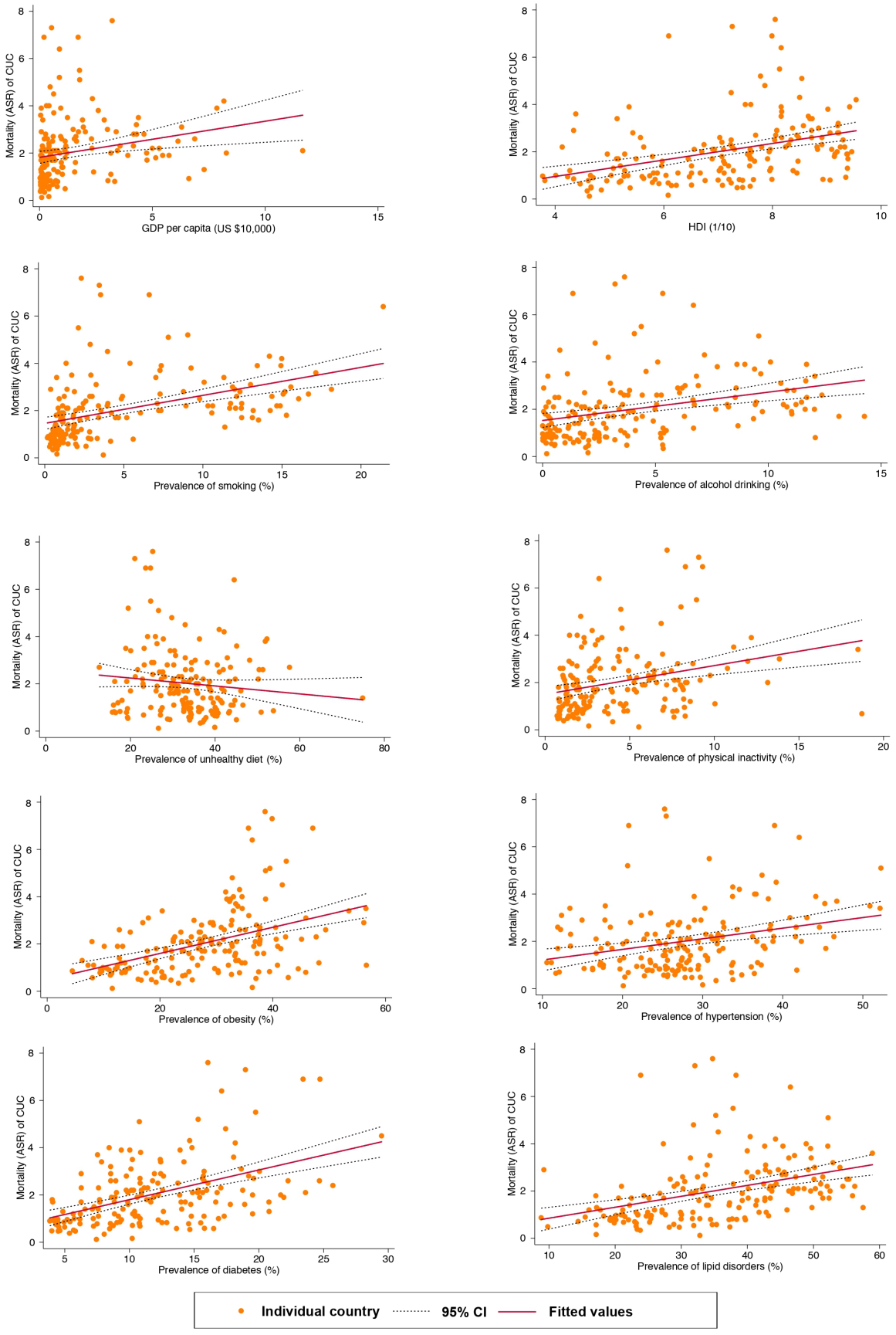

FIGURE 3 Associations between risk factors and mortality of corpus uteri cancer.

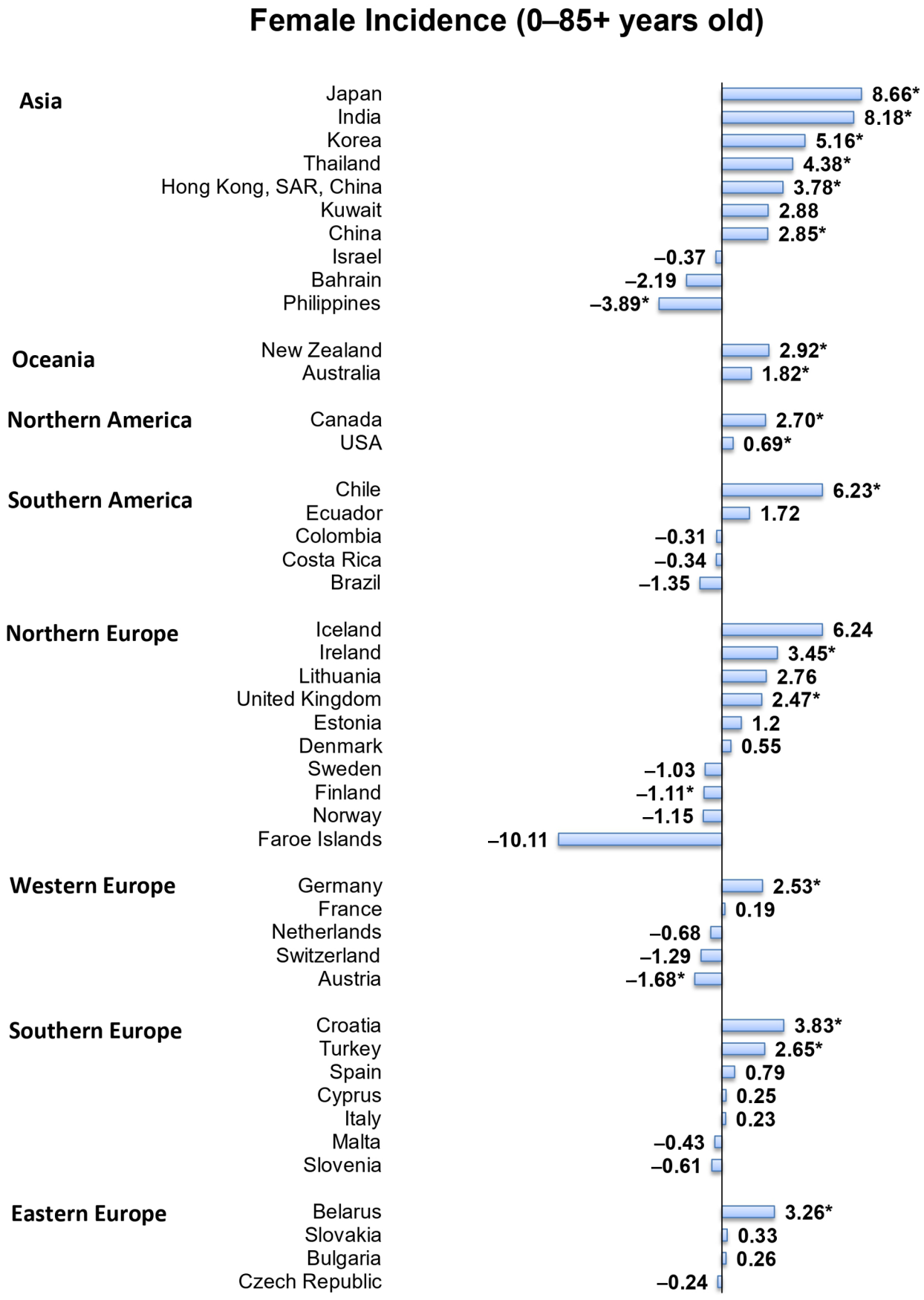

FIGURE 4 Annual average percent change (AAPC) of incidence of corpus uteri cancer in females aged 0 to 85+ years.

95% CI −5.53 to −2.21, $P<0.001$), Austria (AAPC = −1.68, 95% CI −2.47 to −0.88, $P<0.001$), and Finland (AAPC = −1.11, 95% CI −1.93 to −0.29, $P=0.015$).

3.7 | Overall mortality trends of corpus uteri cancer

Among 48 countries/economies, 18 showed a significantly increased trend of corpus uteri cancer mortality (Figure 5). Among these 18 countries/economies, the highest AAPC was observed in Thailand (AAPC = 22.05, 95% CI 15.80–28.63, $P<0.001$), followed by Ecuador (AAPC = 13.71, 95% CI 10.69–16.81, $P<0.001$), Slovenia (AAPC = 6.94, 95% CI 2.59–11.47, $P=0.006$), the Philippines (AAPC = 5.53, 95% CI 3.78–7.31, $P<0.001$), and Hong Kong (AAPC = 5.48, 95% CI 3.09–7.92, $P<0.001$). In contrast, only one country showed a significantly decreased trend of corpus uteri cancer mortality: Denmark (AAPC = −4.00, 95% CI −6.98 to −0.93, $P=0.017$).

3.8 | Incidence trends of corpus uteri cancer in females aged 50 and older

Among all populations aged 50 years and older, 17 countries had a statistically significant increase in the incidence of corpus uteri cancer. India had the largest increase in this trend (AAPC = 9.39, 95% CI 6.35–12.52, $P<0.001$), followed by Japan (AAPC = 8.21, 95% CI 6.58–9.86, $P<0.001$), Korea (AAPC = 5.15, 95% CI 3.79–6.53, $P<0.001$), Ireland (AAPC = 3.77, 95% CI 2.04–5.53, $P<0.001$), and Croatia (AAPC = 3.72, 95% CI 2.38–5.08, $P<0.001$). In contrast, four countries showed a significantly declining incidence trend of corpus uteri cancer, including the Philippines (AAPC = −3.57, 95% CI −5.38 to −1.72, $P=0.002$), Austria (AAPC = −1.77, 95% CI −2.43 to −1.10, $P<0.001$), Sweden (AAPC = −1.66, 95% CI −2.36 to −0.96, $P<0.001$), and Finland (AAPC = −1.32, 95% CI −2.41 to −0.23, $P=0.024$).

3.9 | Incidence trends of corpus uteri cancer in females aged below 50

Among all populations younger than 50 years, nine countries showed an increasing trend of incidence of corpus uteri cancer. Japan had the highest incidence increase (AAPC = 9.81, 95% CI 4.86–14.99, $P=0.002$), followed by New Zealand (AAPC = 5.93, 95% CI 3.28–8.64, $P<0.001$), Croatia (AAPC = 5.16, 95% CI 0.84–9.66, $P=0.024$), Korea (AAPC = 4.74, 95% CI 2.87–6.64, $P<0.001$), and Hong Kong (AAPC = 4.68, 95% CI 2.53–6.87, $P<0.001$). In contrast, three countries showed a decreasing trend in incidence, including the Philippines (AAPC = −4.52, 95% CI −7.26 to −1.69, $P=0.006$), France (AAPC = −4.05, 95% CI −7.21 to −0.78, $P=0.022$), and Israel (AAPC = −3.15, 95% CI −5.50 to −0.74, $P=0.017$).

3.10 | Incidence trends of corpus uteri cancer in females aged below 40

Among all populations younger than 40 years, nine countries demonstrated an increasing trend of corpus uteri cancer incidence, including Costa Rica (AAPC = 13.57, 95% CI 4.95–22.89, $P=0.006$), Japan (AAPC = 11.29, 95% CI 5.41–17.50, $P=0.002$), Bahrain (AAPC = 9.95, 95% CI 3.75–15.67, $P=0.005$), Belarus (AAPC = 7.92, 95% CI 3.85–12.14, $P=0.002$), and Hong Kong (AAPC = 6.75, 95% CI 1.66–12.11, $P=0.015$). In contrast, only one country showed a significantly decreasing trend in incidence (the Philippines: AAPC = −6.26, 95% CI −10.09, −2.27, $P=0.007$).

4 | DISCUSSION

This study presents the most updated worldwide incidence, mortality, risk factors, and epidemiologic trends of corpus uteri cancer by age and country using global and national cancer registries. There were several main findings. First, the highest incidence and mortality rates of corpus uteri cancer were observed in high-income regions, including North America, Europe, and Oceania. Second, higher incidence and mortality of corpus uteri cancer were associated with a higher GDP per capita, higher HDI, and increased prevalence of smoking, alcohol drinking, physical inactivity, obesity, hypertension, diabetes, and lipid disorders. Finally, there was a substantial increasing trend of corpus uteri cancer for the recent past decade irrespective of age groups and geographical region.

There was wide variation in the distribution of corpus uteri cancer across different countries in 2020. We observed the highest incidence of corpus uteri cancer in North America, Europe, and Oceania. The study also found that the incidence and mortality of corpus uteri cancer were associated with GDP per capita and HDI at the country level. These results are generally consistent with previous research which showed that the burden of corpus uteri cancer was associated with HDI.[8] The regional variation in the disease burden of corpus uteri cancer might be related to the reproductive factors and endogenous estrogen exposure associated with the socioeconomic level for different countries. According to the World Population Prospects 2022, fertility rates were relatively low in the more developed regions, the average number of births per woman was 1.5 for Europe and Northern America and 4.6 for Sub-Saharan Africa in 2021.[27] The risk of developing corpus uteri cancer decreases with an increase in the number of children a woman has given birth to (three to four children: relative risk [RR] 0.36, 95% CI 0.32–0.40, ref: 0 children).[28] The previous study proposed that high-protein diets in high-income countries, such as excessive consumption of red meat, may raise the chance of corpus uteri cancer because it may trigger earlier menarche (under the age of 12), which lengthens the time of exposure to estrogen.[29] It should be noted that the risk factor of estrogen exposure was linked to the more prevalent type I cases

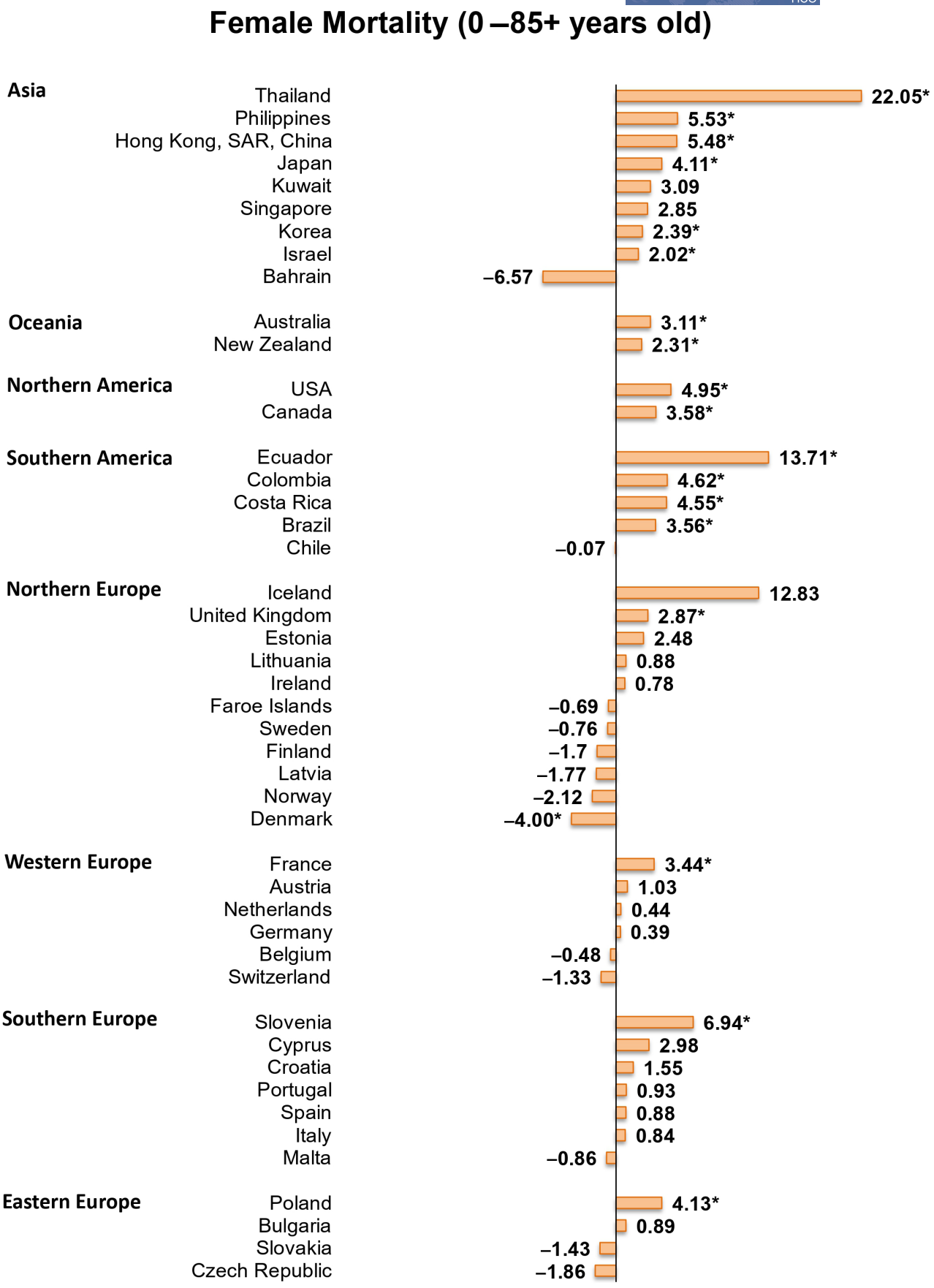

FIGURE 5 Annual average percent change (AAPC) of mortality of corpus uteri cancer in females aged 0 to 85+ years.

(80%–90%), whereas type II cancer is estrogen-independent with no known risk factor.[30] Other factors may include a higher prevalence of environmental, lifestyle, and metabolic risk factors, and more advanced technology and capacity of detection for corpus uteri cancer in wealthy countries. Our study identified some modifiable and common lifestyle and metabolic risk factors associated with the incidence and mortality of corpus uteri cancer at a country level, including smoking, alcohol drinking, physical inactivity, obesity, hypertension, diabetes, and lipid disorders. The findings are generally supported by previous individual-level observational studies on their associations. For instance, in a prospective study of 367 903 women from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, an increased risk of corpus uteri cancer with cigarette smoking in premenopausal women was reported (RR 1.10, 95% CI 0.80–1.51). However, the effect on postmenopausal women (RR 0.62, 95% CI 0.30–1.30) and perimenopausal women (RR 1.00, 95% CI 0.44–2.27) was relatively minor.[31] Some studies suggest that nicotines anti-estrogenic effect may potentially reduce the risk of corpus uteri cancer.[32] Compared with non-drinkers, women consuming two or more drinks/day had a multivariate RR of 2.01 (95% CI 1.30–3.11) for corpus uteri cancer.[33] Compared with women with low lifetime physical activity, those with greater activity throughout life had the highest reduction in risk (odds ratio [OR] 0.62, 95% CI 0.44–0.88) for corpus uteri cancer.[34] In a study of 454 women with corpus uteri cancer, the ORs were 3.83 for obesity, 1.77 for hypertension, 2.18 for diabetes, and 1.20 for hyperlipidemia.[35]

There was an overall increasing trend of corpus uteri cancer over the past 10 years. Several factors may have contributed to this trend, including the general increasing prevalence of obesity, metabolic syndrome, estrogen exposure, and nulliparity among women. It was estimated that there was a global increase in overweight/obesity in women between 1980 and 2013 from 30% to 38%.[36] The proportion of women with high body mass index (calculated as weight in kilograms divided by the square of height in meters) increased even faster than the global average in wealthy countries.[37] A study from China found that the prevalence of metabolic syndrome rose more rapidly in women (from 7.9% to 30.7%) than in men (9.4% to 27.2%) from 1991–1995 to 2011–2015.[38] Large increases in the use of hormones were reported in the 1990s when more than 30% of postmenopausal women age 45–64 years used hormones in western countries.[39] In parallel, nulliparity has more than doubled since the 1990s in Austria, Japan, Spain, and Thailand.[40]

The present study reports the most recent information on the incidence, mortality, and risk factors of corpus uteri cancer worldwide. The data were collected from high-quality cancer registries with more than 1 million cases. Accurate and representative cancer statistics are provided by population-based cancer registries, through various sources, such as hospitals, diagnostic laboratories, and vital statistics agencies.[41] The profile of cancer, globally and by world region, is built up using the best available sources of cancer incidence and mortality data within a given country. Therefore, the validity of the national estimates depends on the degree of representativeness and quality of the source information. There are several limitations to the current analysis. First, there could be under-reporting of the cases and deaths of corpus uteri cancer in the less developed regions because of the underdevelopment of infrastructure and mechanism of cancer registries in these places. Second, incidence and mortality might have been overestimated for some populations as their figures were represented by cancer registries in the major states or cities. Third, a direct comparison between different geographical locations could be difficult as the cancer reporting infrastructure could have changed across time. However, this limitation is of less concern when it comes to the trends of corpus uteri cancer according to age groups within the same population. In addition, there was a lack of analysis on the trends of incidence and mortality of the different subtypes of corpus uteri cancer. The incidence, mortality, risk factors, and epidemiologic trends could vary by different histologic subtypes of corpus uteri cancer, this information bears some implications for the prevention of corpus uteri cancer.

In conclusion, the incidence and mortality of corpus uteri cancer have been increasing substantially for the past decade, likely due to the increasing prevalence of obesity, metabolic syndrome, estrogen exposure, and nulliparity among females. We expect that these trends will continue due to population growth, economic development, and lifestyle transitions, especially in low-income regions. Intensive lifestyle modifications are needed, especially among younger females, including further promotion of alcohol control, physical activity, weight control, and optimal management of metabolic syndrome. For secondary and tertiary prevention, it is also imperative to improve early detection, treatment, surveillance, and quality of life for females with corpus uteri cancer. Follow-up studies are warranted to further explore the reasons behind these epidemiologic trends and provide more insights into the specific etiology and prognosis of corpus uteri cancer by histologic subtypes.

AUTHOR CONTRIBUTIONS

Junjie Huang and Martin C. S. Wong participated in the conception of the research ideas, study design, interpretation of the findings, writing of the first draft of the manuscript, and provided intellectual input to the translational aspects of the study. Wing Chung Chan, Chun Ho Ngai, and Veeleah Lok retrieved information from the relevant databases, performed the statistical analysis, and presented the methodology and results. Mellissa Withers, Lin Zhang, Don Eliseo Lucero-Prisno III, Wanghong Xu, Zhi-Jie Zheng, and Edmar Elcarte made critical revisions to the manuscripts and provided expert opinions on implications of the study findings.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data used for the analyses are publicly available from the World Health Organization websites (https://gco.iarc.fr/; https://apps.who.int/gho/data/node.main).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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