# Worldwide patterns and trends in ovarian cancer incidence by histological subtype: a population-based analysis from 1988 to 2017

Yi-Fan Wei,[a,b,l] Li Ning,[c,l] Yi-Lin Xu,[a,b,l] Jing Ma,[d,l] Dong-Run Li,[a,b] Zan-Fei Feng,[d,e] Fang-Hua Liu,[a,b] Yi-Zi Li,[a,b] He-Li Xu,[a,b] Peng Li,[f,g] Yong-Pei Yu,[h] Dong-Hui Huang,[a,b] Xiao-Ying Li,[a,b] Song Gao,[d] Chun-Qing Lin,[i,*] Ting-Ting Gong,[d,**] Qi-Jun Wu,[a,b,d,j,***] and Jing-He Lang[k]

[a]Department of Clinical Epidemiology, Shengjing Hospital of China Medical University, Shenyang, China
[b]Key Laboratory of Precision Medical Research on Major Chronic Disease, Shengjing Hospital of China Medical University, Shenyang, China
[c]Gynecology Oncology, National Clinical Research Center for Cancer, National Cancer Center, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
[d]Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang, China
[e]Department of Epidemiology, School of Public Health, China Medical University, Shenyang, China
[f]Max Planck Institute for Demographic Research, Rostock, Mecklenburg-Vorpommern, Germany
[g]Max Planck – University of Helsinki Center for Social Inequalities in Population Health, Rostock, Germany and Helsinki, Finland
[h]Institute of Advanced Clinical Medicine, Peking University, Beijing, China
[i]National Clinical Research Center for Cancer, National Cancer Center, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
[j]NHC Key Laboratory of Advanced Reproductive Medicine and Fertility (China Medical University), National Health Commission, Shenyang, China
[k]Department of Obstetrics and Gynecology, National Clinical Research Center for Obstetric and Gynaecological Diseases, State Key Laboratory of Common Mechanism Research for Major Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

eClinicalMedicine
2025;79: 102983

Published Online xxx
https://doi.org/10.1016/j.eclinm.2024.102983

## Summary

**Background** Ovarian cancer (OC) is a heterogeneous malignancy with multiple histological subtypes, showing global variability in incidence. Temporal changes in diagnostic criteria and risk factors might influence the incidence and distribution of OC and its subtypes.

**Methods** This study analyzed incidence patterns (2013–2017) and trends (1988–1992 to 2013–2017) of OC and its subtypes across 65 and 40 countries, respectively. Data were extracted from the Cancer Incidence in Five Continents (CI5 XII) and CI5plus databases (accessed in June 2024). Annual percent changes were computed to describe trends in age-standardized rates (ASRs) of OC and its subtypes. Proportions of ASR for each subtype relative to the ASR of OC for individual countries were calculated.

**Findings** The incidence of OC displayed marked disparities across regions and Human Development Index (HDI), with the highest ASRs in Eastern and Central Europe and very high HDI regions, and the lowest in Africa, Asia, and medium HDI regions. Despite stable trend in ASRs of OC globally, notable declines were observed in Europe, America, and Oceania, in contrast to increases in Asian countries like Japan and South Korea. Globally, serous carcinomas remained the most prevalent subtype. European countries exhibited a higher proportion of serous carcinomas, while Asian countries had a higher proportion of endometrioid and clear cell carcinomas. Although trends in subtypes also remained stable, ASRs increased over time for serous carcinomas and germ cell tumor in most countries, while mucinous carcinomas and adenocarcinoma NOS showed a decline.

**Interpretation** Variations in global patterns and trends in OC incidence and its subtypes might be influenced by genetic and reproductive factors. Consequently, region-specific prevention strategies and ongoing surveillance are essential to mitigate the burden of OC.

*Corresponding author. National Clinical Research Center for Cancer, National Cancer Center, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.
**Corresponding author. Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, China.
***Corresponding author. Department of Clinical Epidemiology, Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang, China.
*E-mail addresses:* lincq@cicams.ac.cn (C.-Q. Lin), gongtt@sj-hospital.org (T.-T. Gong), wuqj@sj-hospital.org (Q.-J. Wu).
[l]These authors contributed equally to this work.

**Funding** The National Key Research and Development Program of China (No.2022YFC2704205), the Natural Science Foundation of China (No.82073647, 82373674, and 82103914), Outstanding Scientific Fund of Shengjing Hospital, 345 Talent Project of Shengjing Hospital of China Medical University, the Max Planck – University of Helsinki Center from the Jane and Aatos Erkko Foundation (No.210046), the Max Planck Society (No.5714240218), the University of Helsinki (No.77204227), and the European Union (ERC Synergy, BIOSFER, 101071773).



**Keywords:** Histological subtype; Incidence; Ovarian cancer; Trend; Worldwide

### Research in context

**Evidence before this study**

On June 5, 2024, we conducted a comprehensive, unrestricted PubMed search for English-language articles on ovarian cancer (OC) using specific terms related to the disease and its subtypes. Our search identified only three studies that had previously investigated global patterns or trends in OC incidence by histological subtype, but these were limited by outdated periods, limited national coverage, and a restricted number of subtypes analyzed. Given the evolving diagnostic criteria, changing risk factors, and subtype heterogeneity of OC, there is a critical need for up-to-date, comprehensive epidemiological data to clarify global incidence patterns and trends for OC and its subtypes.

**Added value of this study**

In this study, we updated and extended the assessment of international patterns (2013–2017) and temporal trends (1988–1992 to 2013–2017) in OC incidence overall and by histological subtypes, using data from the Cancer Incidence in Five Continents (CI5 XII) and CI5plus databases across various world regions, countries, and levels of human development. Our findings revealed marked regional disparities in OC incidence and its subtypes, although the global incidence trends remained stable. Serous carcinomas remained the most prevalent subtype worldwide.

**Implications of all the available evidence**

Variations in global patterns and trends of OC incidence overall and by histological subtypes observed in this study might be partially explained by reproductive behaviors, genetic predispositions, advances in diagnostic facilities, and healthcare practices. Thus, region-specific prevention and control strategies, improved access to healthcare, and ongoing surveillance are necessary to effectively mitigate the global burden of OC.

## Introduction

Ovarian cancer (OC), representing malignancies originating from the ovary, ranks as the eighth in terms of both most frequently diagnosed malignancy and leading cause of oncological mortality in women worldwide.[1] In 2022, global incidence estimates reported 324,398 new cases and 206,839 deaths attributed to OC.[1] The burden of OC exhibits marked geographic and ethnic disparities.[2,3] For example, higher incidences have been observed in European and North American regions and among Non-Hispanic White women, whereas lower incidences have been noted in Caribbean and African regions and among Non-Hispanic Black women. Although declining trends in OC incidence rates have been observed over the past few decades, particularly in high-income countries,[4] the prognosis for OC remains dismal, with age-standardized five-year net survival rates varying between 30% and 50% in most countries.[5] Consequently, there is an urgent need for an increased focus on both primary and secondary preventive measures.

OC is a heterogeneous group of neoplasms encompassing multiple histological subtypes with distinct origins. Approximately 90% of OC are epithelial ovarian cancer (EOC), while only 10% are non-EOC, including sex cord-stromal tumor (SCST), germ cell tumor (GCT), and other less common carcinomas.[6] According to the 2020 World Health Organization classification, EOC can be further categorized into five primary histological subtypes: serous, mucinous, endometrioid, clear cell carcinomas, and adenocarcinoma "not otherwise specified" (NOS).[7] These subtypes exhibit distinct morphology, etiology, clinical characteristics, and prognosis.[8–10] Compared to EOC, GCTs generally present at a younger age, tend to be unilateral, and have a more favorable prognosis, while SCSTs are typically diagnosed at an earlier stage, present with endocrine symptoms, and also exhibit a better prognosis.[8,10] Within EOC, although many risk factors overlap such as parity and oral contraceptive use, some are subtype-specific.[11–13] Relative to other subtypes, endometriosis and an older age at menopause are more likely to increase the risk of clear cell and endometrioid carcinomas, while tubal ligation tends to decrease the risk of these subtypes. Additionally, smoking is more strongly correlated with an increased risk of mucinous carcinomas.[12] This heterogeneity emphasizes the necessity for a comprehensive understanding of global patterns and variations across OC subtypes.

To date, three studies have investigated the global patterns or trends in OC incidence, overall and by histological subtypes.[14–16] Coburn et al. evaluated trends in OC incidence overall (1973–1977 to 2003–2007) and by histological subtypes (1988–1992 to 2003–2007), utilizing the Cancer Incidence in Five Continents (CI5) database.[15] Hao and colleagues estimated the pattern and trend for OC incidence from 1973 to 2012, but described only the pattern of OC subtypes during 2008–2012 based on CI5 database.[16] Additionally, Cabasag et al. only focused on the incidence of EOC subtypes from 1995 to 2014 in seven high-income countries.[14] Given the temporal changes in diagnostic techniques and risk factors for OC, along with the limited scopes of the aforementioned studies, up-to-date and comprehensive epidemiological data on global patterns and trends in the incidence of OC and its histological subtypes are still needed.

Herein, we aimed to provide an update and extended assessment of international patterns and temporal trends in OC incidence overall and by histological subtypes, across different world regions, countries, and levels of human development. We incorporated new registries and countries, along with more specific categories, to enhance the scope of our analysis. We have elucidated the incidence patterns of OC and its histological subtypes across 65 separate countries using the most recent CI5 dataset. Additionally, incidence trends for OC and its histological subtypes over a 30-year period from 1988 to 2017 were also analyzed. This research will contribute to a more nuanced understanding of the epidemiology of OC and support the development of effective public health strategies to reduce the global burden of this disease.

## Methods

### Data sources

All data utilized in this analysis were extracted from the most recent (2024) CI5 database (Volume XII)[17] and the CI5plus database.[18] The CI5 series, published every five years since the 1960s by regional and national cancer registries worldwide, contained high-quality information on new cancer cases by registry, site, sex, 5-year age group, and histology (if available), together with age-specific populations. Histological classifications have been reported by registries since 1988. Accordingly, we obtained historical data (1988–2012) from the CI5plus database and the most recent data (2013–2017) from the CI5 database (Volume XII) (accessed in June 2024).

International patterns for the incidence of OC and its histological subtypes were described by world region, country, and human development index (HDI) during 2013–2017, based on registries available in the CI5 database (Volume XII). International trends in the incidence of OC and its histological subtypes were calculated for each 5-year period from 1988–1992 through 2013–2017. Countries were eligible for trend analyses if they had at least 15 consecutive years (3 volumes) of data, and had been included in CI5 Volume XII. For countries providing both national and regional registry data, only the national data were extracted. For countries that provided data solely from one or more regional registries, these data were aggregated to estimate national data. Data from the age-unknown group were excluded from this analysis, as were cases with person-years at risk of zero. Ultimately, sixty-five countries and forty countries from five continents were eligible for the pattern description and trend analysis, respectively. In the trend analysis, changes in OC incidence were evaluated over different time periods for various countries. The period from 1988–1992 to 2013–2017 included Colombia, Costa Rica, Ecuador, Canada, the USA, China, India, Israel, Japan, the Philippines, Thailand, Austria, Croatia, Czech Republic, Denmark, Estonia, France, Germany, Iceland, Italy, the Netherlands, Norway, Slovenia, Spain, Switzerland, the UK, Australia, and New Zealand. Changes from 1993–1997 to 2013–2017 were examined for Uganda, Brazil, South Korea, Ireland, Lithuania, and Malta. For the period from 1998–2002 to 2013–2017, the analysis included Chile, Bahrain, Kuwait, Turkey, Cyprus, and Poland. Notably, since all OC cases in China, Germany and New Zealand were classified as other tumors during the period 1988–1992, the trend analysis of histological subtypes in these three countries was conducted from 1993–1997 to 2013–2017.

According to geographic region and the number of countries included, the world regions were categorized as Asia, Africa, South America, North America, Eastern Europe, Western Europe, Southern Europe, Northern Europe, Central Europe, and Oceania. For histology, OC were categorized as serous carcinoma, mucinous carcinoma, endometrioid carcinoma, clear cell carcinoma, adenocarcinoma NOS, other EOC, SCST, GCT, and other tumors. The HDI, provided by the United Nations Development Programme, is a composite measure based on three fundamental characteristics of human development: a long and healthy life, being knowledgeable, and having a decent standard of living. Countries were divided into four groups (very high, high, medium, and low) based on their HDI values during 2013–2017 to examine the patterns of OC incidence in relation to human development.[19]

### Ethics

This study utilized publicly available, anonymized data extracted from CI5 Volume XII and CI5plus databases, which are provided by the International Agency for Research on Cancer (IARC). The data are aggregated and do not contain any personal identifiers or confidential patient information. Therefore, formal ethical approval and informed consent were not required for this study.

### Statistics

Incidence rates (per 100,000 person-years) for OC overall and by histological subtypes were calculated and age-standardized to the world standard population using 5-year age groups ranging from 0–4 to 85+.[20,21] To evaluate the changes in age-standardized rates (ASRs) over time by country, the annual percent change (APC) or average annual percent change (AAPC) was calculated using Joinpoint Regression Program Version 5.1.0 (Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute). APC assesses the internal trends, while AAPC estimates the overall average change trend across multiple intervals. When no joinpoint is observed, AAPC equals APC. Generally, 7–11 consecutive observations are required to detect one joinpoint.[22] Given that this analysis only included six consecutive observations from 1988–1992 to 2013–2017, the APC and 95% confidence intervals (CIs) were employed to describe trends in ASRs over the 30-year period. Nevertheless, we performed a sensitivity analysis allowing one joinpoint for countries with six consecutive observations. In addition to plotting the ASR trend for OC on the original scale, ASR trends for histological subtypes were plotted on a semi-log scale to facilitate the comparison of temporal trends and magnitudes across regions and countries.[23] Additionally, the proportions of the ASR for each histological subtype relative to the overall ASR of OC were displayed graphically in bars to visualize the variation of different subtypes across regions compared with the international distribution. Furthermore, to examine the international age distribution of OC by histological subtypes, age-specific incidence rates were calculated based on 5-year age groups and plotted by subtypes on a semi-log scale. Last, age-specific incidence rates by four HDI levels were also plotted by subtypes on a semi-log scale.

### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study, and the corresponding authors had final responsibility for the decision to submit for publication.

## Results

### International patterns and trends of OC

In the most recent period (2013–2017), ASRs of OC were highest in Eastern Europe, followed by Central Europe and Southern Europe (Table 1 and Fig. 1). For specific countries, the highest ASRs of OC occurred in Latvia (15.53 per 100,000 person-years), followed by Lithuania (13.28). Intermediate ASRs of OC were seen in Northern Europe, Western Europe, Oceania, North America, and South America, with one exception being Ireland (10.78). Conversely, the lowest ASRs of OC were detected in Africa and Asia, except for Brunei, the Philippines, and Singapore (12.20, 11.12, and 10.10, respectively). The lowest ASR of OC was recorded in Benin (3.26). When describing international patterns of OC incidence by HDI, we found that the highest ASR of OC occurred in very high HDI regions (8.22), while the lowest ASR was seen in regions with medium HDI values (5.52).

Different trends in ASRs of OC were detected among populations in Europe, the Americas, Asia, and Oceania (Table 1 and Figs. 1 and 2). During the period 1988–2017, significant decreases in ASRs of OC were noted in 19 out of 40 countries, with APC ranged from −0.46 to −2.87. For all countries examined in Northern Europe, Western Europe, and Oceania, ASRs decreased from high to intermediate rates, with marked declines in Iceland (APC: −2.87, 95% CI: −4.80, −0.90) from 11.29 in 1988–1992 to 5.98 in 2013–2017, the Netherlands (APC: −1.75, 95% CI: −2.86, −0.63) from 10.01 in 1989–1992 to 6.95 in 2013–2017, and New Zealand (APC: −1.66, 95% CI: −2.35, −0.96) from 10.51 in 1988–1992 to 7.01 in 2013–2017. The ASRs in Eastern Europe, North America and South America tended to be steadily decreasing over time; there were substantial reductions in Estonia (APC: −0.56, 95% CI: −1.04, −0.09), Canada (APC: −0.80, 95% CI: −1.03, −0.56), the USA (APC: −1.47, 95% CI: −1.71, −1.23), and Colombia (APC: −1.00, 95% CI: −1.91, −0.08).

In Southern Europe and Central Europe, the temporal trends of ASRs varied, with some countries maintaining a steady trend while others experiencing significant declines. Noteworthy decreases were observed in Italy (APC: −0.46, 95% CI: −0.78, −0.15), Malta (APC: −1.35, 95% CI: −2.59, −0.09), Austria (APC: −2.40, 95% CI: −3.22, −1.57), Germany (APC: −1.15, 95% CI: −1.93, −0.37), and Switzerland (APC: −1.22, 95% CI: −1.58, −0.86). In contrast, Asian regions mostly exhibited stable temporal trends, although several countries showed significant upward trends, including Japan (APC: 1.90, 95% CI: 1.32, 2.50) and South Korea (APC: 1.18, 95% CI: 0.82, 1.53). Distinctly, Israel demonstrated a significant decrease in ASR of OC from 1988–1992 to 2013–2017 (APC: −1.98, 95% CI: −2.42, −1.54). In the sensitivity analysis, the overall trend of OC incidence remained consistent in most countries (Supplementary Table S1).

### International patterns and trends of OC by histological subtypes

Among all histological subtypes of OC, serous carcinomas consistently exhibited the highest ASRs in most countries assessed (Table 2). Especially in Europe, ASRs of serous carcinomas were relatively high, with Lithuania recording the highest ASR at 6.59 per 100,000 person-years. ASRs of mucinous carcinomas were relatively high in several Asian countries such as Brunei (2.59), the Philippines (1.12), and Singapore (1.12), with Brunei having the highest ASR of mucinous carcinomas globally. Furthermore, ASRs of endometrioid and clear cell carcinomas were also higher in Asian regions, with

| | Historical period | | Recent period (2013–2017) | | APC (95% CI) |
|---|---|---|---|---|---|
| | Cases | ASR | Cases | ASR | |
| Asia | | | | | |
| Bahrain | 46 (1998–2002) | 6.17 | 107 | 7.73 | 1.37 (–1.18, 3.97) |
| Brunei | – | – | 128 | 12.20 | – |
| China | 1270 (1988–1992) | 5.54 | 33,780 | 5.50 | –0.58 (–1.64, 0.49) |
| India | 384 (1988–1992) | 5.02 | 20,191 | 5.24 | –0.44 (–2.37, 1.53) |
| Iran | – | – | 231 | 5.09 | – |
| Israel | 1310 (1988–1992) | 10.70 | 1772 | 6.83 | **–1.98 (–2.42, –1.54)** |
| Japan | 2749 (1988–1992) | 6.17 | 30,949 | 9.22 | **1.90 (1.32, 2.50)** |
| Kuwait | 63 (1998–2002) | 5.27 | 237 | 4.45 | –0.59 (–4.27, 3.24) |
| The Philippines | 690 (1988–1992) | 9.05 | 1674 | 11.12 | 0.18 (–1.10, 1.48) |
| Qatar | – | – | 36 | 7.42 | – |
| South Korea | 1445 (1993–1997) | 5.38 | 12,720 | 6.61 | **1.18 (0.82, 1.53)** |
| Singapore | – | – | 1489 | 10.10 | – |
| Thailand | 149 (1988–1992) | 4.32 | 2615 | 5.89 | 0.58 (–0.18, 1.35) |
| Turkey | 676 (1998–2002) | 5.70 | 3139 | 6.52 | 0.64 (–1.36, 2.68) |
| Africa | | | | | |
| Algeria | – | – | 161 | 5.21 | – |
| Benin | – | – | 25 | 3.26 | – |
| Kenya | – | – | 289 | 8.03 | – |
| Mauritius | – | – | 278 | 6.53 | – |
| Morocco | – | – | 559 | 4.72 | – |
| Seychelles | – | – | 16 | 5.49 | – |
| South Africa | – | – | 56 | 3.37 | – |
| Uganda | 73 (1993–1997) | 5.50 | 225 | 6.26 | –0.14 (–2.64, 2.43) |
| Zimbabwe | – | – | 274 | 8.31 | – |
| North America | | | | | |
| Canada | 7146 (1988–1992) | 10.29 | 13,395 | 8.55 | **–0.80 (–1.03, –0.56)** |
| Costa Rica | 289 (1988–1992) | 5.07 | 508 | 4.88 | –0.29 (–0.79, 0.21) |
| Trinidad and Tobago | – | – | 255 | 9.67 | – |
| The USA | 12,134 (1988–1992) | 11.06 | 107,319 | 7.90 | **–1.47 (–1.71, –1.23)** |
| South America | | | | | |
| Argentina | – | – | 726 | 8.86 | – |
| Brazil | 99 (1993–1997) | 5.10 | 1827 | 6.19 | –0.38 (–3.29, 2.63) |
| Chile | 79 (1998–2002) | 8.32 | 141 | 5.88 | –2.10 (–4.75, 0.62) |
| Colombia | 266 (1988–1992) | 8.49 | 1026 | 7.15 | **–1.00 (–1.91, –0.08)** |
| Ecuador | 131 (1988–1992) | 5.89 | 957 | 6.54 | –0.08 (–1.36, 1.21) |
| Peru | – | – | 1271 | 7.82 | – |
| Uruguay | – | – | 1124 | 8.20 | – |
| Northern Europe | | | | | |
| Denmark | 2823 (1988–1992) | 13.73 | 2539 | 9.10 | **–1.65 (–2.43, –0.86)** |
| Finland | – | – | 2356 | 7.92 | – |
| Iceland | 90 (1988–1992) | 11.29 | 81 | 5.98 | **–2.87 (–4.80, –0.90)** |
| Norway | 2159 (1988–1992) | 13.28 | 1959 | 8.60 | **–1.71 (–2.56, –0.85)** |
| Sweden | – | – | 2990 | 6.90 | – |
| Western Europe | | | | | |
| Belgium | – | – | 3913 | 7.04 | – |
| France | 1754 (1988–1992) | 9.62 | 5436 | 7.10 | **–1.37 (–1.89, –0.85)** |
| Ireland | 1167 (1994–1997) | 12.30 | 1988 | 10.78 | **–0.70 (–1.33, –0.07)** |
| The Netherlands | 4496 (1989–1992) | 10.01 | 5796 | 6.95 | **–1.75 (–2.86, –0.63)** |
| The UK | 2869 (1988–1992) | 13.40 | 29,675 | 9.46 | **–1.36 (–1.53, –1.19)** |

(Table 1 continues on next page)

| | Historical period | | Recent period (2013–2017) | | APC (95% CI) |
|---|---|---|---|---|---|
| | Cases | ASR | Cases | ASR | |
| (Continued from previous page) | | | | | |
| Eastern Europe | | | | | |
| Belarus | – | – | 4298 | 10.66 | – |
| Estonia | 772 (1988–1992) | 12.29 | 749 | 10.60 | **−0.56 (−1.04, −0.09)** |
| Latvia | – | – | 1518 | 15.53 | – |
| Lithuania | 2000 (1993–1997) | 13.94 | 1981 | 13.28 | −0.31 (−1.20, 0.59) |
| The Russian Federation | – | – | 5807 | 11.50 | – |
| Ukraine | – | – | 17,392 | 11.43 | – |
| Southern Europe | | | | | |
| Croatia | 1807 (1988–1992) | 10.00 | 2122 | 10.23 | 0.10 (−1.69, 1.91) |
| Cyprus | 189 (1998–2002) | 8.08 | 308 | 8.75 | 0.93 (−2.94, 4.94) |
| Italy | 1133 (1988–1992) | 8.85 | 17,447 | 8.40 | **−0.46 (−0.78, −0.15)** |
| Malta | 159 (1993–1997) | 12.16 | 188 | 9.06 | **−1.35 (−2.59, −0.09)** |
| Portugal | – | – | 53 | 7.44 | – |
| Spain | 1366 (1988–1992) | 7.50 | 3276 | 7.62 | −0.17 (−0.71, 0.38) |
| Central Europe | | | | | |
| Austria | 299 (1988–1992) | 12.69 | 3463 | 7.87 | **−2.40 (−3.22, −1.57)** |
| Czech Republic | 4912 (1988–1992) | 12.91 | 5174 | 10.14 | −1.15 (−2.50, 0.21) |
| Germany | 514 (1988–1992) | 9.92 | 24,640 | 8.63 | **−1.15 (−1.93, −0.37)** |
| Liechtenstein | – | – | 14 | 8.29 | – |
| Poland | 532 (1998–2002) | 11.28 | 638 | 11.12 | 0.05 (−3.12, 3.31) |
| Slovenia | 736 (1988–1992) | 10.16 | 788 | 7.67 | −0.80 (−1.89, 0.30) |
| Switzerland | 718 (1988–1992) | 10.35 | 2898 | 7.68 | **−1.22 (−1.58, −0.86)** |
| Oceania | | | | | |
| Australia | 4164 (1988–1992) | 8.98 | 6790 | 6.81 | **−1.07 (−1.34, −0.79)** |
| New Zealand | 1151 (1988–1992) | 10.51 | 1369 | 7.01 | **−1.66 (−2.35, −0.96)** |
| Human development index | | | | | |
| Very High | – | – | 313,791 | 8.22 | – |
| High | – | – | 60,118 | 6.57 | – |
| Medium | – | – | 22,713 | 5.52 | – |
| Low | – | – | 524 | 6.90 | – |

APC, annual percent change; ASR, age-standardized rate; UK, United Kingdom; USA, United States of America. [a]Values in bold indicate statistically significant results.

***Table 1:*** **Age-standardized ovarian cancer incidence rates per 100,000 person-years from 1988–2002 to 2013–2017, by countries and human development indices.[a]**

Singapore displaying the highest ASRs for both endometrioid (1.53) and clear cell carcinomas (2.01).

With respect to adenocarcinoma NOS, the highest ASRs occurred in Eastern Europe, with the Russian Federation recording the highest ASR (4.91), followed by Ukraine (4.14) and Latvia (4.02). For other EOC, the highest ASR was noted in Latvia (2.60). Notably, the ASRs of SCST and GCT were generally lower than those of the EOC. Belarus recorded the highest ASR for SCST (0.84), while Liechtenstein had the highest ASR for GCT (1.91). The highest ASR for other tumors was observed in Trinidad and Tobago (4.23), followed by Uganda (3.61) and the Philippines (3.47).

Regarding human development, in very high HDI regions, serous carcinomas (3.50) remained the most common histological subtypes, followed by other tumors (0.79), endometrioid carcinomas (0.77), and adenocarcinoma NOS (0.75) (Table 2 and Fig. 3). In high HDI regions, adenocarcinoma NOS had the highest ASR (1.55), followed by other tumors (1.51) and serous carcinomas (1.45). Notably, in region with medium or low HDI values, other tumors were the most frequent subtype with ASRs of 1.40 and 3.32, respectively. The second most frequent subtypes were adenocarcinoma NOS with an ASR of 1.35 in medium HDI regions and serous carcinomas with an ASR of 1.15 in low HDI regions.

The ASRs of histological subtypes as proportions of the total OC ASR by continents and countries are illustrated in Fig. 4. Globally, serous carcinomas constituted 37.66% of the total OC ASR, followed by other tumors (13.17%), adenocarcinoma NOS (12.77%),

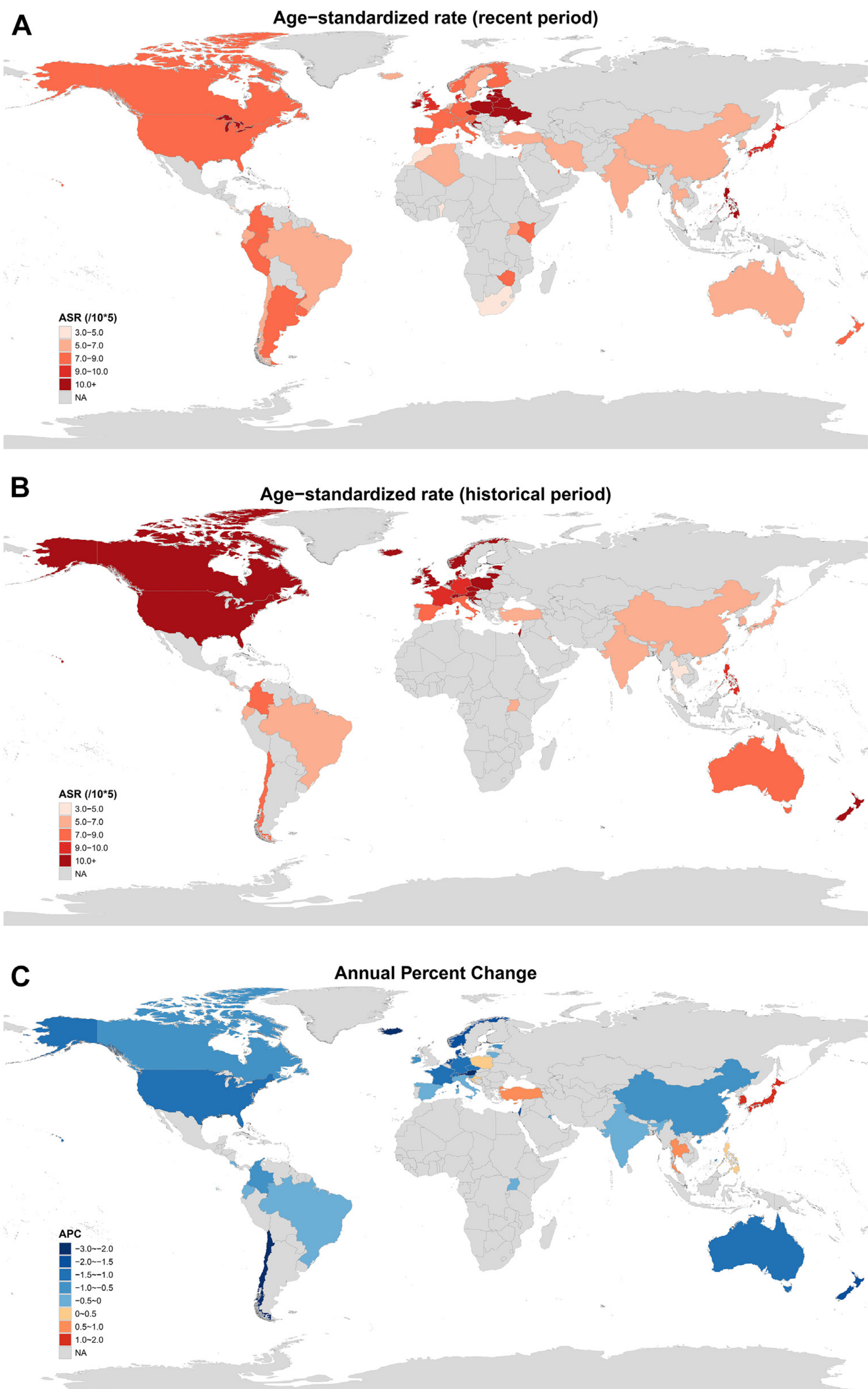


*Fig. 1:* Global age-standardized rates of ovarian cancer in recent periods (A) and historical periods (B) and annual percent change of ovarian cancer incidence (C).

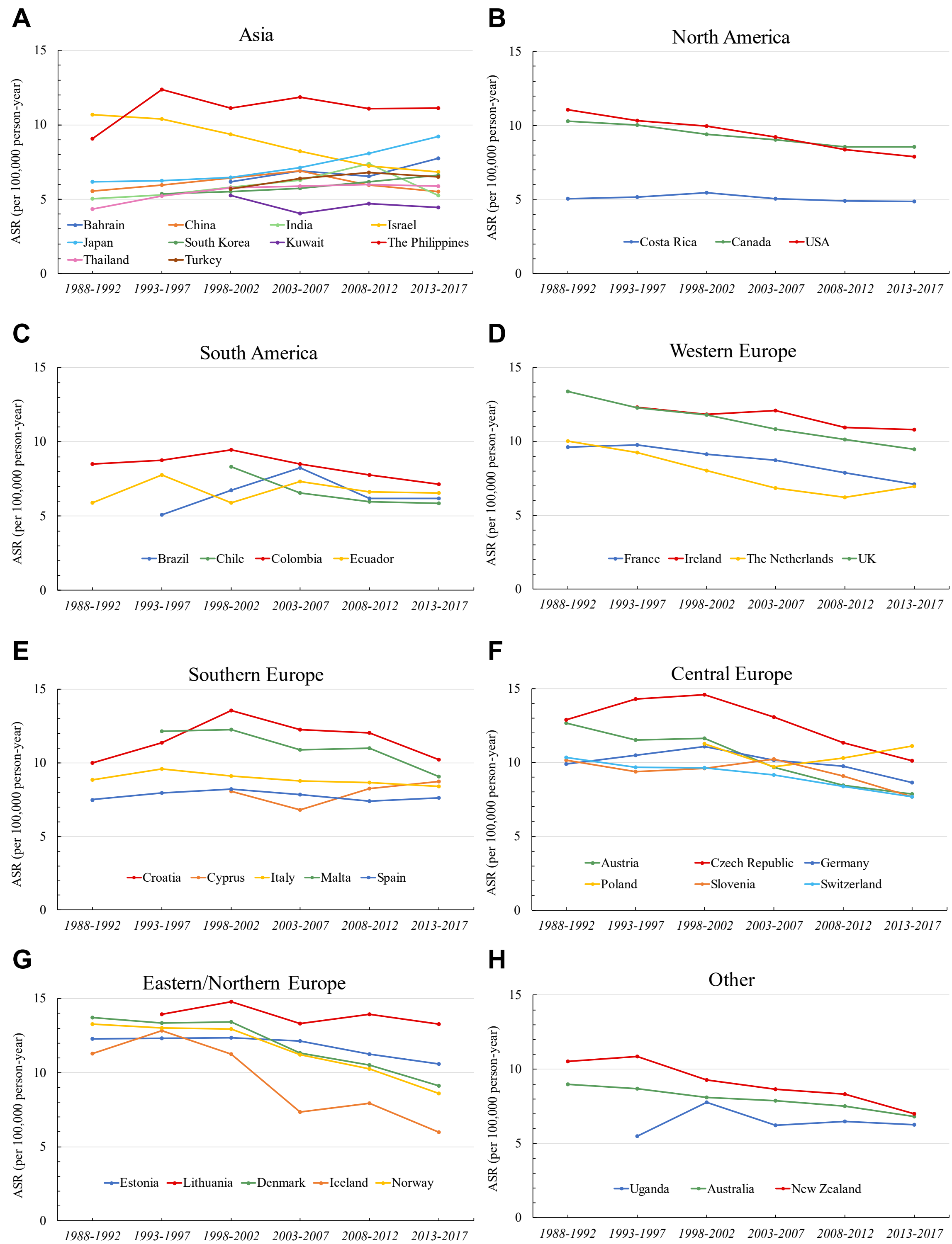


***Fig. 2:* Trends in ovarian cancer ASRs (per 100,000 person-years) by continents and countries from 1988–1992 to 2013–2017.** A, Asia; B, North America; C, South America; D, Western Europe; E, Southern Europe; F, Central Europe; G, Eastern/Northern Europe; H, Other.

| | Serous | | Mucinous | | Endometrioid | | Clear cell | | NOS[a] | | Other EOC | | SCST | | GCT | | Other | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR |
| Asia | | | | | | | | | | | | | | | | | | |
| Bahrain | 15 | 1.22 | 11 | 0.70 | 6 | 0.40 | 5 | 0.31 | 38 | 2.95 | 13 | 0.89 | 6 | 0.38 | 6 | 0.35 | 7 | 0.53 |
| Brunei | 23 | 2.34 | 29 | 2.59 | 14 | 1.31 | 6 | 0.52 | 22 | 2.14 | 11 | 1.04 | 1 | 0.09 | 9 | 0.76 | 13 | 1.40 |
| China | 7964 | 1.28 | 1767 | 0.31 | 1250 | 0.21 | 1323 | 0.21 | 7015 | 1.11 | 3305 | 0.54 | 320 | 0.05 | 1127 | 0.29 | 9709 | 1.50 |
| India | 3566 | 0.93 | 1038 | 0.26 | 325 | 0.08 | 238 | 0.06 | 5326 | 1.39 | 3780 | 0.98 | 182 | 0.05 | 742 | 0.19 | 4994 | 1.30 |
| Iran | 71 | 1.63 | 20 | 0.41 | 5 | 0.10 | 0 | 0 | 25 | 0.58 | 26 | 0.54 | 4 | 0.09 | 14 | 0.32 | 66 | 1.44 |
| Israel | 1057 | 4.05 | 62 | 0.27 | 101 | 0.43 | 27 | 0.11 | 146 | 0.51 | 164 | 0.59 | 26 | 0.11 | 59 | 0.30 | 130 | 0.45 |
| Japan | 7462 | 2.16 | 2747 | 0.94 | 4124 | 1.42 | 5535 | 1.88 | 2883 | 0.66 | 1124 | 0.34 | 124 | 0.04 | 1069 | 0.74 | 5881 | 1.04 |
| Kuwait | 117 | 2.31 | 20 | 0.21 | 4 | 0.04 | 8 | 0.10 | 20 | 0.43 | 21 | 0.44 | 6 | 0.07 | 11 | 0.11 | 30 | 0.75 |
| The Philippines | 307 | 2.10 | 181 | 1.12 | 144 | 0.95 | 98 | 0.64 | 90 | 0.62 | 285 | 1.97 | 4 | 0.03 | 38 | 0.22 | 527 | 3.47 |
| Qatar | 12 | 2.18 | 0 | 0 | 1 | 0.33 | 2 | 0.33 | 13 | 2.97 | 3 | 0.84 | 0 | 0 | 2 | 0.22 | 3 | 0.55 |
| South Korea | 5452 | 2.69 | 1394 | 0.81 | 925 | 0.49 | 1189 | 0.62 | 731 | 0.31 | 638 | 0.30 | 335 | 0.19 | 605 | 0.61 | 1451 | 0.58 |
| Singapore | 471 | 3.03 | 155 | 1.12 | 221 | 1.53 | 301 | 2.01 | 73 | 0.41 | 81 | 0.53 | 16 | 0.14 | 63 | 0.77 | 108 | 0.57 |
| Thailand | 493 | 1.08 | 221 | 0.51 | 316 | 0.68 | 440 | 0.95 | 305 | 0.65 | 154 | 0.34 | 38 | 0.09 | 140 | 0.49 | 508 | 1.11 |
| Turkey | 1661 | 3.41 | 168 | 0.35 | 187 | 0.40 | 134 | 0.28 | 153 | 0.31 | 272 | 0.55 | 63 | 0.14 | 129 | 0.35 | 372 | 0.73 |
| Africa | | | | | | | | | | | | | | | | | | |
| Algeria | 63 | 2.13 | 7 | 0.21 | 17 | 0.57 | 0 | 0 | 27 | 0.84 | 9 | 0.29 | 4 | 0.14 | 8 | 0.20 | 26 | 0.83 |
| Benin | 0 | 0 | 1 | 0.07 | 0 | 0 | 0 | 0 | 10 | 1.15 | 2 | 0.33 | 0 | 0 | 0 | 0 | 12 | 1.71 |
| Kenya | 59 | 1.82 | 13 | 0.15 | 2 | 0.07 | 1 | 0.05 | 54 | 1.58 | 28 | 1.01 | 9 | 0.19 | 16 | 0.18 | 107 | 2.97 |
| Mauritius | 21 | 0.49 | 9 | 0.21 | 3 | 0.07 | 3 | 0.07 | 60 | 1.41 | 106 | 2.53 | 5 | 0.12 | 3 | 0.10 | 68 | 1.54 |
| Morocco | 167 | 1.38 | 64 | 0.54 | 23 | 0.18 | 9 | 0.07 | 119 | 1.02 | 79 | 0.68 | 24 | 0.20 | 10 | 0.09 | 64 | 0.55 |
| Seychelles | 0 | 0 | 2 | 0.62 | 0 | 0 | 2 | 0.89 | 2 | 0.47 | 3 | 0.91 | 2 | 0.40 | 2 | 1.14 | 3 | 1.08 |
| South Africa | 7 | 0.39 | 6 | 0.35 | 0 | 0 | 0 | 0 | 5 | 0.20 | 34 | 2.20 | 1 | 0.07 | 2 | 0.10 | 1 | 0.06 |
| Uganda | 15 | 0.64 | 8 | 0.23 | 0 | 0 | 3 | 0.08 | 34 | 0.90 | 20 | 0.52 | 4 | 0.13 | 17 | 0.15 | 124 | 3.61 |
| Zimbabwe | 55 | 1.88 | 19 | 0.56 | 2 | 0.05 | 2 | 0.07 | 35 | 1.29 | 10 | 0.30 | 15 | 0.38 | 21 | 0.35 | 115 | 3.42 |
| North America | | | | | | | | | | | | | | | | | | |
| Canada | 6437 | 4.03 | 734 | 0.58 | 1125 | 0.85 | 810 | 0.59 | 1115 | 0.55 | 959 | 0.61 | 122 | 0.09 | 370 | 0.45 | 1723 | 0.79 |
| Costa Rica | 136 | 1.35 | 26 | 0.25 | 11 | 0.11 | 11 | 0.10 | 42 | 0.39 | 32 | 0.31 | 3 | 0.02 | 28 | 0.29 | 219 | 2.06 |
| Trinidad and Tobago | 55 | 2.18 | 10 | 0.35 | 7 | 0.31 | 1 | 0.04 | 9 | 0.36 | 49 | 1.84 | 3 | 0.12 | 6 | 0.25 | 115 | 4.23 |
| The USA | 48,298 | 3.43 | 5692 | 0.50 | 8779 | 0.75 | 5429 | 0.45 | 11,065 | 0.65 | 10,926 | 0.79 | 2576 | 0.25 | 2938 | 0.40 | 11,616 | 0.68 |
| South America | | | | | | | | | | | | | | | | | | |
| Argentina | 221 | 2.75 | 70 | 0.89 | 61 | 0.80 | 10 | 0.13 | 105 | 1.25 | 84 | 1.01 | 19 | 0.26 | 29 | 0.45 | 127 | 1.32 |
| Brazil | 490 | 1.67 | 152 | 0.53 | 65 | 0.22 | 45 | 0.15 | 406 | 1.38 | 162 | 0.54 | 18 | 0.07 | 48 | 0.25 | 441 | 1.39 |
| Chile | 65 | 2.75 | 12 | 0.52 | 6 | 0.24 | 3 | 0.13 | 16 | 0.61 | 11 | 0.39 | 8 | 0.35 | 6 | 0.36 | 14 | 0.53 |
| Colombia | 329 | 2.37 | 70 | 0.49 | 42 | 0.29 | 26 | 0.18 | 88 | 0.60 | 117 | 0.80 | 29 | 0.21 | 41 | 0.37 | 284 | 1.85 |
| Ecuador | 317 | 2.23 | 94 | 0.62 | 31 | 0.21 | 18 | 0.13 | 135 | 0.95 | 86 | 0.60 | 12 | 0.08 | 123 | 0.78 | 141 | 0.94 |
| Peru | 360 | 2.27 | 114 | 0.69 | 75 | 0.46 | 68 | 0.43 | 92 | 0.57 | 88 | 0.56 | 10 | 0.06 | 62 | 0.41 | 402 | 2.37 |
| Uruguay | 417 | 3.17 | 136 | 1.13 | 60 | 0.51 | 32 | 0.29 | 91 | 0.67 | 85 | 0.55 | 16 | 0.14 | 29 | 0.36 | 258 | 1.36 |
| Northern Europe | | | | | | | | | | | | | | | | | | |
| Denmark | 1604 | 5.41 | 192 | 0.90 | 180 | 0.67 | 90 | 0.38 | 187 | 0.53 | 25 | 0.08 | 30 | 0.12 | 55 | 0.40 | 155 | 0.40 |
| Finland | 1185 | 3.84 | 180 | 0.81 | 202 | 0.81 | 112 | 0.45 | 113 | 0.25 | 81 | 0.24 | 99 | 0.47 | 38 | 0.33 | 346 | 0.72 |
| Iceland | 47 | 3.63 | 5 | 0.47 | 8 | 0.65 | 1 | 0.08 | 3 | 0.17 | 9 | 0.40 | 1 | 0.09 | 2 | 0.31 | 5 | 0.18 |
| Norway | 476 | 2.01 | 141 | 0.75 | 148 | 0.78 | 105 | 0.52 | 660 | 2.68 | 82 | 0.34 | 87 | 0.46 | 48 | 0.42 | 212 | 0.64 |
| Sweden | 1681 | 3.62 | 245 | 0.65 | 291 | 0.71 | 210 | 0.53 | 165 | 0.30 | 60 | 0.11 | 164 | 0.49 | 77 | 0.32 | 97 | 0.17 |
| Western Europe | | | | | | | | | | | | | | | | | | |
| Belgium | 2461 | 4.29 | 283 | 0.62 | 270 | 0.53 | 187 | 0.37 | 162 | 0.20 | 156 | 0.28 | 50 | 0.11 | 88 | 0.33 | 256 | 0.31 |
| France | 3029 | 3.94 | 320 | 0.55 | 325 | 0.49 | 181 | 0.27 | 674 | 0.68 | 257 | 0.31 | 69 | 0.13 | 130 | 0.39 | 451 | 0.34 |
| Ireland | 933 | 5.13 | 129 | 0.86 | 167 | 1.04 | 93 | 0.59 | 266 | 1.27 | 98 | 0.53 | 3 | 0.02 | 41 | 0.37 | 258 | 0.96 |
| The Netherlands | 3079 | 3.59 | 460 | 0.71 | 395 | 0.55 | 338 | 0.46 | 816 | 0.71 | 129 | 0.17 | 47 | 0.07 | 142 | 0.35 | 390 | 0.33 |
| The UK | 13,894 | 4.34 | 2019 | 0.83 | 2136 | 0.83 | 1441 | 0.55 | 3018 | 0.82 | 2247 | 0.62 | 463 | 0.19 | 666 | 0.45 | 3791 | 0.82 |

(Table 2 continues on next page)

| | Serous | | Mucinous | | Endometrioid | | Clear cell | | NOS[a] | | Other EOC | | SCST | | GCT | | Other | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR | Cases | ASR |
| (Continued from previous page) | | | | | | | | | | | | | | | | | | |
| Eastern Europe | | | | | | | | | | | | | | | | | | |
| Belarus | 1508 | 3.93 | 319 | 0.80 | 281 | 0.73 | 117 | 0.28 | 1208 | 2.75 | 179 | 0.42 | 306 | 0.84 | 67 | 0.32 | 313 | 0.58 |
| Estonia | 415 | 5.96 | 61 | 0.99 | 41 | 0.75 | 11 | 0.21 | 45 | 0.50 | 41 | 0.55 | 21 | 0.35 | 11 | 0.34 | 103 | 0.95 |
| Latvia | 342 | 3.95 | 107 | 1.21 | 23 | 0.27 | 12 | 0.14 | 392 | 4.02 | 239 | 2.60 | 37 | 0.47 | 15 | 0.33 | 351 | 2.54 |
| Lithuania | 921 | 6.59 | 67 | 0.54 | 124 | 0.98 | 53 | 0.46 | 203 | 1.29 | 84 | 0.58 | 30 | 0.24 | 25 | 0.36 | 474 | 2.23 |
| The Russian Federation | 1163 | 2.33 | 292 | 0.61 | 261 | 0.54 | 73 | 0.16 | 2511 | 4.91 | 483 | 0.93 | 292 | 0.63 | 79 | 0.32 | 653 | 1.07 |
| Ukraine | 2985 | 2.09 | 973 | 0.69 | 485 | 0.32 | 233 | 0.15 | 6391 | 4.14 | 2263 | 1.51 | 844 | 0.62 | 238 | 0.32 | 2980 | 1.58 |
| Southern Europe | | | | | | | | | | | | | | | | | | |
| Croatia | 754 | 3.83 | 80 | 0.43 | 103 | 0.58 | 60 | 0.34 | 212 | 0.93 | 135 | 0.73 | 54 | 0.37 | 34 | 0.39 | 690 | 2.63 |
| Cyprus | 151 | 4.39 | 21 | 0.67 | 26 | 0.75 | 3 | 0.11 | 56 | 1.42 | 13 | 0.30 | 5 | 0.16 | 8 | 0.41 | 25 | 0.55 |
| Italy | 7477 | 3.77 | 854 | 0.48 | 1351 | 0.79 | 653 | 0.37 | 1692 | 0.70 | 1672 | 0.71 | 136 | 0.09 | 294 | 0.38 | 3318 | 1.11 |
| Malta | 56 | 2.50 | 20 | 1.07 | 14 | 0.83 | 8 | 0.49 | 47 | 2.02 | 14 | 0.77 | 1 | 0.15 | 4 | 0.41 | 24 | 0.82 |
| Portugal | 17 | 2.18 | 5 | 0.84 | 6 | 0.80 | 2 | 0.31 | 9 | 1.24 | 5 | 0.77 | 1 | 0.28 | 1 | 0.16 | 7 | 0.85 |
| Spain | 1530 | 3.68 | 223 | 0.59 | 318 | 0.84 | 197 | 0.52 | 301 | 0.57 | 237 | 0.48 | 23 | 0.06 | 71 | 0.38 | 376 | 0.50 |
| Central Europe | | | | | | | | | | | | | | | | | | |
| Austria | 1421 | 3.39 | 120 | 0.35 | 155 | 0.42 | 56 | 0.14 | 547 | 1.13 | 262 | 0.54 | 36 | 0.09 | 55 | 0.31 | 811 | 1.49 |
| Czech Republic | 2571 | 5.19 | 303 | 0.66 | 338 | 0.74 | 126 | 0.29 | 542 | 1.02 | 381 | 0.73 | 131 | 0.32 | 63 | 0.23 | 719 | 0.98 |
| Germany | 12,132 | 4.37 | 1111 | 0.49 | 1400 | 0.59 | 551 | 0.24 | 2447 | 0.74 | 2307 | 0.69 | 352 | 0.16 | 320 | 0.28 | 4020 | 1.07 |
| Liechtenstein | 9 | 4.47 | 0 | 0 | 0 | 0 | 1 | 0.74 | 2 | 0.70 | 1 | 0.47 | 0 | 0 | 1 | 1.91 | 0 | 0 |
| Poland | 307 | 5.24 | 33 | 0.52 | 52 | 1.09 | 27 | 0.53 | 82 | 1.27 | 33 | 0.49 | 14 | 0.29 | 13 | 0.59 | 77 | 1.11 |
| Slovenia | 503 | 5.07 | 33 | 0.36 | 69 | 0.75 | 26 | 0.31 | 40 | 0.31 | 36 | 0.28 | 2 | 0.01 | 10 | 0.17 | 69 | 0.41 |
| Switzerland | 1557 | 4.16 | 175 | 0.54 | 219 | 0.71 | 123 | 0.42 | 313 | 0.60 | 121 | 0.27 | 39 | 0.12 | 62 | 0.38 | 289 | 0.48 |
| Oceania | | | | | | | | | | | | | | | | | | |
| Australia | 3274 | 3.20 | 505 | 0.61 | 528 | 0.62 | 388 | 0.44 | 615 | 0.46 | 436 | 0.36 | 137 | 0.17 | 279 | 0.51 | 628 | 0.43 |
| New Zealand | 617 | 3.05 | 93 | 0.60 | 142 | 0.84 | 74 | 0.45 | 104 | 0.43 | 60 | 0.33 | 19 | 0.13 | 45 | 0.44 | 215 | 0.75 |
| HDI | | | | | | | | | | | | | | | | | | |
| Very High | 136,877 | 3.50 | 19,636 | 0.62 | 25,194 | 0.77 | 18,811 | 0.57 | 33,912 | 0.75 | 24,324 | 0.60 | 5970 | 0.20 | 8075 | 0.43 | 40,971 | 0.79 |
| High | 13,236 | 1.45 | 3461 | 0.40 | 2300 | 0.25 | 2169 | 0.24 | 14,593 | 1.55 | 6385 | 0.70 | 1290 | 0.15 | 1836 | 0.33 | 14,848 | 1.51 |
| Medium | 4099 | 1.00 | 1296 | 0.30 | 494 | 0.12 | 346 | 0.08 | 5589 | 1.35 | 4172 | 1.02 | 219 | 0.05 | 806 | 0.19 | 5692 | 1.40 |
| Low | 70 | 1.15 | 28 | 0.37 | 2 | 0.02 | 5 | 0.06 | 79 | 1.11 | 32 | 0.40 | 19 | 0.24 | 38 | 0.23 | 251 | 3.32 |

ASR, age-standardized rate; EOC, epithelial ovarian cancer; GCT, germ cell tumor; HDI, human development index; SCST, sex cord-stromal tumor; UK, United Kingdom; USA, United States of America. [a]NOS represents adenocarcinoma, NOS.

***Table 2:*** **Age-standardized ovarian cancer incidence rates per 100,000 person-years by histological subtypes, countries, and human development indices, 2013–2017.**

other EOC (8.64%), endometrioid carcinomas (7.76%), mucinous carcinomas (7.00%), clear cell carcinomas (5.94%), GCT (4.78%), and SCST (2.25%).

In Asian region, several countries exhibited distinctly higher proportions of mucinous, endometrioid, and clear cell carcinomas compared to the global distribution. Specifically, Brunei had a higher proportion of mucinous carcinomas, while Japan, Singapore, and Thailand presented higher proportions of both endometrioid and clear cell carcinomas. The proportions of other EOC and other tumors in Africa were noticeably higher than the global distribution, with South Africa showing a higher proportion of other EOC, and Uganda and Benin exhibiting higher proportions of other tumors.

The proportions of each subtype in South America, North America, and Oceania were largely similar to the global distribution, except for elevated proportions of other tumors in Costa Rica and Trinidad and Tobago. Regarding European regions, the proportion of serous carcinomas exceeded the global distribution, especially in Northern, Western, and Central Europe. Additionally, in Eastern Europe, the proportions of adenocarcinoma NOS and SCST in some nations were visibly higher than the global distribution, with the Russian Federation displaying a higher proportion of adenocarcinoma NOS and Belarus showing a larger proportion of SCST.

Fig. 5 shows the ASRs of histological subtypes as proportions of the total OC ASR by HDI. Regions with very high HDI values exhibited markedly elevated proportions of serous, endometrioid, and clear cell carcinomas compared to regions with high, medium, and low HDI. Conversely, the proportion of adenocarcinoma NOS was notably reduced in very high HDI regions compared to the other three regions. The highest proportion of mucinous carcinomas was observed in very

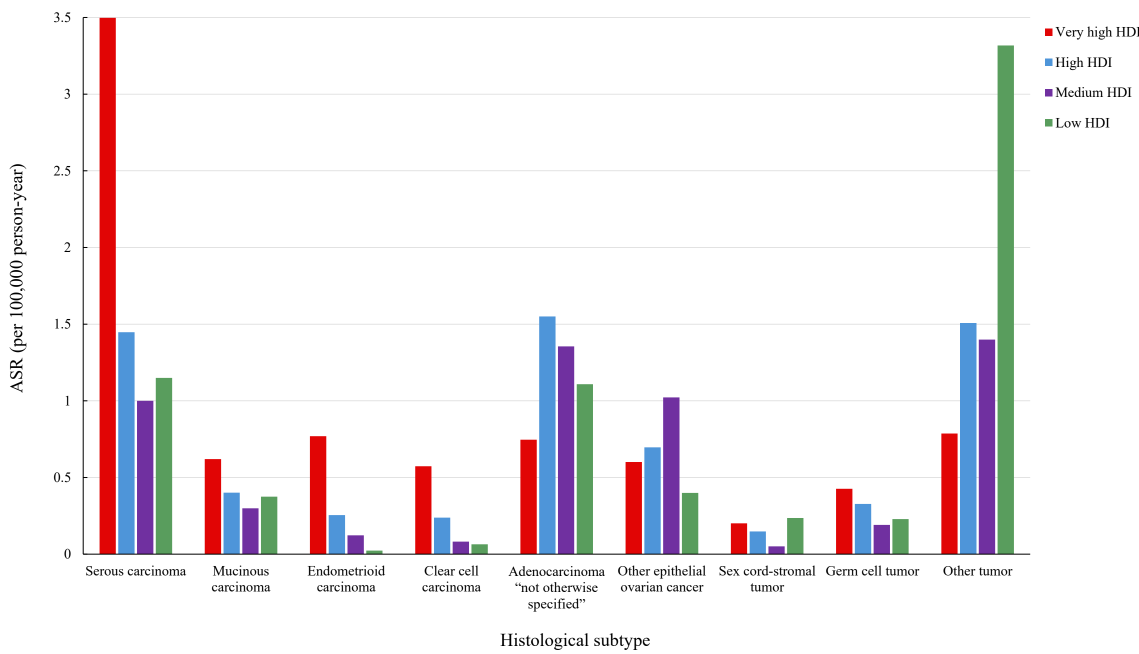


***Fig. 3:* ASRs (per 100,000 person-years) of ovarian cancer by histological subtypes and human development indices, 2013–2017.** HDI, human development index.

high HDI regions, followed by high, low and medium HDI regions, respectively. Other EOC was most prevalent in medium HDI regions, followed by high, very high, and low HDI regions. The proportions of SCST in medium HDI regions was obviously lower than in the other three regions. The proportions of GCT were comparable in very high and high HDI regions and exceeded those in medium and low HDI regions. Although the proportion of other tumors was distinctly higher in low HDI regions than that in very high, high, and medium HDI regions, it remained relatively elevated in high and medium HDI regions.

Notable temporal trends in histological subtypes were observed across the countries examined (Table 3). In populations from Asia, Western Europe, Eastern Europe, Southern Europe, and Central Europe, significant increases in the ASRs of serous carcinomas were recorded over time (Supplementary Fig. S1). The most pronounced rise in ASRs for serous carcinomas occurred in Croatia (APC: 6.69, 95% CI: 1.18, 12.50), followed by South Korea (APC: 3.33, 95% CI: 2.47, 4.20). Conversely, the ASRs of mucinous carcinomas exhibited significant decreases in Asia, North America, Europe, and Oceania, with the most rapid decline in Austria (APC: −7.73, 95% CI: −10.99, −4.34), followed by Malta (APC: −5.51, 95% CI: −8.42, −2.51) and New Zealand (APC: −5.32, 95% CI: −9.76, −0.67) (Supplementary Fig. S2).

The ASRs of endometrioid carcinomas also significantly decreased in Asian, American, Northern European, Western European, Central European, and Oceanian regions, except for Japan, which exhibited an increase (APC: 6.09, 95% CI: 5.01, 7.18) (Supplementary Fig. S3). The most substantial declines were seen in Kuwait (APC: −16.53, 95% CI: −28.98, −1.90). There were variable trends in the ASRs of clear cell carcinomas across Asia, Northern Europe, Eastern Europe, Southern Europe, Central Europe, and Oceania (Supplementary Fig. S4). For instance, Croatia showed a substantial increase in ASRs (APC: 9.62, 95% CI: 0.46, 19.61), whereas Norway exhibited a significant decrease (APC: −2.94, 95% CI: −4.87, −0.98).

For adenocarcinoma NOS, ASRs demonstrated a steady decline over time in 24 out of 40 countries, with Slovenia experiencing the fastest decrease (APC: −8.22, 95% CI: −9.70, −6.70) (Supplementary Fig. S5). With respect to other EOC, temporal trends of ASRs varied. There was a substantial increase in China (APC: 9.19, 95% CI: 2.72, 16.06), in contrast to a notable reduction in Germany (APC: −7.64, 95% CI: −14.04, −0.77) (Supplementary Fig. S6). Similar to other EOC, SCST showed variable trends across different countries. The most striking increase in ASR occurred in Croatia (APC: 6.69, 95% CI: 2.49, 11.07), whereas the most rapid decline was observed in Costa Rica (APC: −6.64, 95% CI: −11.46, −1.56) (Supplementary Fig. S7).

The ASRs of GCT showed significant upward trends in Asia, South America, Western Europe, Central Europe, and Oceania, with Japan experiencing the largest rise (APC: 3.72, 95% CI: 2.55, 4.90), followed by Ecuador (APC: 3.69, 95% CI: 0.74, 6.72) (Supplementary Fig. S8). As for other tumors, the ASRs increased most

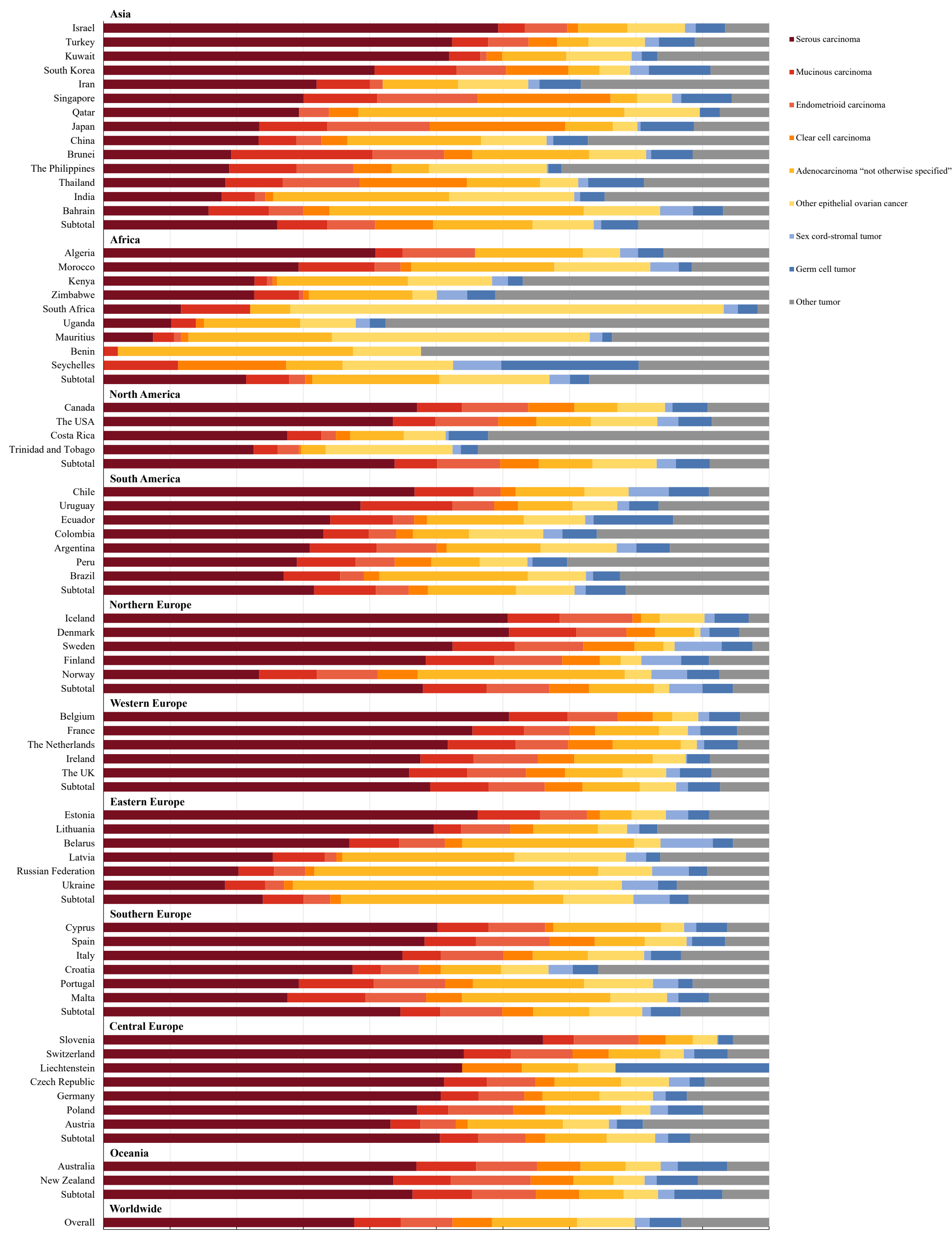


*Fig. 4:* Proportion of the ASRs (per 100,000 person-years) of ovarian cancer by histological subtypes across regions and countries, 2013–2017.

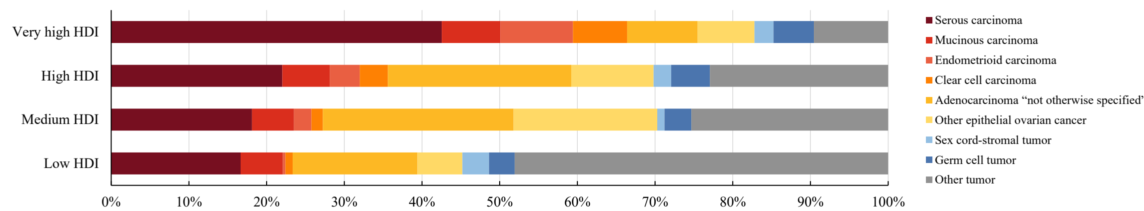


***Fig. 5:*** **Proportion of the ASRs (per 100,000 person-years) of ovarian cancer by histological subtypes across human development indices, 2013–2017.** HDI, human development index.

rapidly in Brazil (APC: 5.41, 95% CI: 1.64, 9.33), while China showed the most pronounced decline (APC: −6.71, 95% CI: −10.10, −3.19) (Supplementary Fig. S9). In the sensitivity analysis of temporal trends across nine subtypes, the overall trends in most countries and subtypes remained consistent with the main findings (Supplementary Tables S2–S10). However, when a joinpoint was included, we observed significant increasing trends for endometrioid carcinomas in Italy and clear cell carcinomas in Costa Rica, contrasting with non-significant declining trends without a joinpoint. Conversely, for GCT in the USA, a non-significant increasing trend was noted without a joinpoint, but a significant declining trend emerged when a joinpoint was allowed.

### International incidence of OC by histological subtypes and age groups

The international incidence rates of OC (per 100,000 person-years) by histological subtypes and age groups are depicted in Fig. 6. The incidence rates for all subtypes remained relatively low until the age group of 35–39 years. The incidence rates of serous carcinomas exhibited a steady increase with age, reaching a peak of 16.30 in women aged 70–74, followed by a slight decline to 8.06 in women aged 85+. Similarly, steady increases with age were observed in adenocarcinoma NOS, other EOC, and other tumors. The incidence rates for adenocarcinoma NOS peaked at 6.48 in the age group of 80–84, while other EOC and other tumors peaked at 4.11 and 15.96, respectively, in the oldest age group. The age-specific incidence rates for mucinous carcinomas, endometrioid carcinomas, and clear cell carcinomas followed similar patterns, initially increasing and then decreasing, and the decline nodes occurred at ages 65–69, 50–54, and 55–59, respectively. For both SCST and GCT, the incidence rates were consistently low across all age groups.

When further classified by the HDI, the results are depicted in Supplementary Fig. S10. The age-specific incidence rates of all subtypes in very high HDI regions generally aligned with the international incidence trends described above. For example, the incidence rates of serous carcinomas, adenocarcinoma NOS, other EOC, and other tumors increased steadily with age, all peaking in the oldest age groups. Similarly, the incidence rates of mucinous carcinomas, endometrioid carcinomas, and clear cell carcinomas first increased and then declined with age, while the incidence rates for SCST and GCT remained low.

However, in high HDI regions, the incidence rates for all subtypes, except GCT and other tumors, exhibited a pattern of increasing with age and then declining. The incidence rates of GCT peaked in the youngest age groups and subsequently declined, while the incidence rates for other tumors increased steadily with age. Notably, the incidence rates for all subtypes, except GCT, increased with age and then declined, peaking at ages 50–59 or 60–69, in the medium HDI regions. In contrast, GCT incidence peaked in the 0–39 age group and subsequently declined. Due to the inclusion of only three countries and the small number of OC cases, detailed age-specific incidence trends in low HDI regions were not described.

## Discussion

This population-based analysis provided the most recent global estimations of patterns and trends in OC incidence overall and by histological subtypes. The global incidence of OC exhibited substantial variability across different regions, countries, and socioeconomic strata. This disparity might arise from a multitude of factors, including genetic predispositions, reproductive behaviors, and the accessibility of healthcare resources. Within regions categorized by different HDI values, notable variations in ASRs of OC were observed. This variability might be partially attributed to fewer diagnostic facilities and inadequate healthcare infrastructures in regions with medium or low HDI values.[24,25] In addition, higher women's health awareness in very high HDI regions might partly account for the higher ASRs of OC compared with medium or low HDI regions, as increased health awareness could promote earlier diagnosis of OC, potentially leading to statistically higher incidence rates. Given the vital role of early diagnosis and timely treatment in improving outcomes, public health education to enhance health awareness is critical, especially in areas with medium and low HDI values.[26,27]

| | Serous | Mucinous | Endometrioid | Clear cell | NOS[a] | Other EOC | SCST | GCT | Other |
|---|---|---|---|---|---|---|---|---|---|
| Asia | | | | | | | | | |
| Bahrain (1998) | −0.74 (−24.10, 29.82) | 58.27 (−71.38, 775.25) | −3.63 (−15.70, 10.16) | 69.00 (−93.08, 4025.11) | 1.42 (−8.93, 12.94) | 1.80 (−21.15, 31.44) | −0.40 (−17.44, 20.16) | −1.32 (−17.74, 18.38) | 3.82 (−11.58, 21.91) |
| China (1993) | 4.24 (−5.26, 14.70) | −2.10 (−12.11, 9.05) | −8.66 (−22.68, 7.90) | −6.05 (−26.31, 19.77) | 3.19 (−4.37, 11.35) | **9.19 (2.72, 16.06)** | 2.31 (−8.39, 14.25) | 0.65 (−12.13, 15.30) | **−6.71 (−10.10, −3.19)** |
| India (1988) | **2.01 (0.64, 3.39)** | 0.17 (−2.95, 3.39) | −0.42 (−5.53, 4.97) | −0.11 (−4.50, 4.48) | −0.99 (−3.09, 1.16) | 0.84 (−4.25, 6.20) | **−4.01 (−5.64, −2.35)** | −2.26 (−4.71, 0.26) | **−1.86 (−3.40, −0.29)** |
| Israel (1988) | −0.14 (−1.07, 0.80) | **−4.19 (−6.65, −1.67)** | **−4.54 (−6.78, −2.25)** | −2.20 (−4.95, 0.62) | **−4.75 (−6.18, −3.30)** | **−2.68 (−3.86, −1.48)** | −0.62 (−6.40, 5.51) | −0.38 (−2.05, 1.33) | **−3.88 (−6.64, −1.04)** |
| Japan (1988) | **2.57 (2.07, 3.08)** | 0.94 (−0.22, 2.12) | **6.09 (5.01, 7.18)** | **6.35 (5.09, 7.63)** | **−2.08 (−3.49, −0.65)** | 0.34 (−0.25, 0.92) | −0.07 (−1.94, 1.83) | **3.72 (2.55, 4.90)** | −2.05 (−4.06, 0.00) |
| South Korea (1993) | **3.33 (2.47, 4.20)** | −1.21 (−4.68, 2.38) | 0.37 (−1.07, 1.84) | **6.25 (3.25, 9.34)** | **−2.47 (−4.27, −0.65)** | −0.38 (−1.70, 0.95) | 2.68 (−2.15, 7.74) | **1.80 (1.09, 2.51)** | **−2.70 (−3.97, −1.42)** |
| Kuwait (1998) | 4.29 (−0.18, 8.95) | −4.08 (−17.85, 11.98) | **−16.53 (−28.98, −1.90)** | −1.68 (−86.96, 641.21) | **−5.79 (−11.00, −0.28)** | −4.08 (−27.48, 26.85) | 47.86 (−81.93, 1109.87) | −5.60 (−25.18, 19.11) | 2.95 (−26.71, 44.62) |
| The Philippines (1988) | 1.67 (−0.19, 3.56) | −1.74 (−4.45, 1.04) | −3.13 (−7.63, 1.59) | 1.20 (−2.16, 4.69) | **−1.98 (−2.85, −1.09)** | −0.31 (−5.70, 5.37) | −8.10 (−16.14, 0.73) | −2.05 (−6.01, 2.07) | 2.11 (−1.77, 6.15) |
| Thailand (1988) | 1.02 (−0.91, 3.00) | **−4.22 (−6.17, −2.24)** | 2.52 (−0.53, 5.66) | **5.56 (3.49, 7.67)** | 0.63 (−1.42, 2.73) | **2.37 (0.74, 4.03)** | −0.80 (−4.20, 2.72) | 0.83 (−0.61, 2.30) | −0.05 (−1.16, 1.08) |
| Turkey (1998) | **2.81 (0.97, 4.69)** | −3.02 (−12.62, 7.63) | −5.00 (−10.49, 0.83) | −0.05 (−8.95, 9.73) | −1.89 (−8.71, 5.45) | 1.70 (−4.43, 8.21) | 1.43 (−10.12, 14.46) | 0.21 (−0.88, 1.31) | −0.01 (−11.32, 12.75) |
| Africa | | | | | | | | | |
| Uganda (1993) | 86.58 (−25.69, 368.43) | 47.03 (−39.02, 254.48) | 0.00 (−0.00, 0.00) | 80.00 (−44.74, 486.30) | −3.03 (−11.21, 5.90) | −3.24 (−9.13, 3.04) | 27.57 (−67.84, 406.03) | −0.90 (−11.72, 11.24) | 0.62 (−2.35, 3.67) |
| North America | | | | | | | | | |
| Canada (1988) | 0.26 (−0.95, 1.47) | **−3.69 (−5.95, −1.39)** | **−1.77 (−3.29, −0.23)** | 0.54 (−0.15, 1.23) | **−3.74 (−5.95, −1.48)** | −0.02 (−2.00, 2.00) | −2.07 (−4.87, 0.80) | 0.60 (−0.20, 1.40) | 0.19 (−3.98, 4.53) |
| Costa Rica (1988) | 0.87 (−0.97, 2.74) | −1.36 (−5.90, 3.39) | −2.32 (−7.70, 3.38) | −0.79 (−7.44, 6.34) | −1.79 (−4.79, 1.31) | −3.09 (−6.26, 0.18) | **−6.64 (−11.46, −1.56)** | −1.26 (−3.61, 1.16) | 1.72 (−2.07, 5.66) |
| The USA (1988) | −0.64 (−1.29, 0.02) | **−3.02 (−4.47, −1.55)** | **−2.75 (−3.49, −2.01)** | −0.01 (−0.61, 0.60) | **−5.46 (−6.10, −4.82)** | −0.91 (−2.50, 0.70) | **1.74 (0.23, 3.27)** | 0.11 (−0.74, 0.97) | 0.36 (−1.20, 1.94) |
| South America | | | | | | | | | |
| Brazil (1993) | 3.47 (−4.34, 11.93) | −1.55 (−9.04, 6.55) | −2.83 (−9.31, 4.12) | −0.83 (−9.18, 8.29) | **−4.21 (−7.01, −1.33)** | −4.17 (−8.49, 0.35) | −1.85 (−7.55, 4.21) | 1.60 (−4.66, 8.26) | **5.41 (1.64, 9.33)** |
| Chile (1998) | 3.36 (−1.25, 8.19) | −2.89 (−21.96, 20.84) | **−13.21 (−24.27, −0.53)** | −6.96 (−17.88, 5.42) | −0.76 (−5.66, 4.39) | **−4.72 (−7.43, −1.94)** | −2.91 (−22.53, 21.68) | −1.38 (−13.12, 11.93) | **−5.17 (−7.58, −2.69)** |
| Colombia (1988) | 0.17 (−0.39, 0.73) | −2.04 (−5.52, 1.56) | −4.09 (−9.02, 1.11) | 1.39 (−3.87, 6.93) | −2.98 (−6.42, 0.59) | **−1.39 (−2.11, −0.65)** | 1.41 (−0.85, 3.73) | 0.49 (−0.64, 1.63) | −0.99 (−4.14, 2.28) |
| Ecuador (1988) | 2.25 (−0.48, 5.06) | 2.77 (−0.32, 5.96) | −0.95 (−6.76, 5.23) | 0.31 (−2.47, 3.17) | **−2.48 (−4.76, −0.14)** | **−3.39 (−5.57, −1.16)** | −5.47 (−11.08, 0.48) | **3.69 (0.74, 6.72)** | −1.46 (−4.97, 2.18) |
| Northern Europe | | | | | | | | | |
| Denmark (1988) | 0.38 (−0.51, 1.27) | **−2.63 (−4.04, −1.21)** | **−3.79 (−5.73, −1.80)** | −1.74 (−3.55, 0.11) | **−4.84 (−7.92, −1.66)** | **−7.23 (−10.34, −4.01)** | −3.46 (−9.54, 3.02) | −0.18 (−2.29, 1.98) | −1.46 (−3.91, 1.05) |
| Iceland (1988) | −1.69 (−4.03, 0.70) | **−4.91 (−8.70, −0.96)** | −1.50 (−6.71, 4.00) | −4.16 (−10.20, 2.28) | **−7.49 (−11.00, −3.85)** | −2.92 (−10.59, 5.40) | −33.77 (−73.79, 67.33) | −3.99 (−12.63, 5.51) | −4.11 (−9.07, 1.12) |
| Norway (1988) | −2.80 (−10.52, 5.59) | **−2.89 (−4.39, −1.37)** | **−2.55 (−4.22, −0.86)** | **−2.94 (−4.87, −0.98)** | −4.69 (−11.39, 2.52) | **−2.41 (−4.09, −0.69)** | 0.28 (−5.62, 6.55) | 1.48 (−1.64, 4.69) | −0.59 (−1.73, 0.57) |

(Table 3 continues on next page)

| | Serous | Mucinous | Endometrioid | Clear cell | NOS[a] | Other EOC | SCST | GCT | Other |
|---|---|---|---|---|---|---|---|---|---|
| (Continued from previous page) | | | | | | | | | |
| Western Europe | | | | | | | | | |
| France (1988) | 0.42 (−0.35, 1.20) | **−3.33 (−4.46, −2.19)** | −2.35 (−5.25, 0.64) | 0.64 (−0.69, 1.99) | **−4.96 (−6.35, −3.55)** | **−4.34 (−5.20, −3.48)** | 0.28 (−1.78, 2.38) | 1.47 (−1.25, 4.26) | −0.87 (−1.89, 0.16) |
| Ireland (1994) | **2.02 (1.41, 2.63)** | **−3.44 (−4.96, −1.89)** | 0.38 (−1.50, 2.29) | 1.52 (−4.10, 7.47) | **−4.17 (−5.95, −2.36)** | −2.66 (−6.39, 1.22) | −4.52 (−16.70, 9.45) | 1.55 (−0.87, 4.03) | **−2.22 (−3.75, −0.67)** |
| The Netherlands (1989) | 2.70 (−0.09, 5.56) | **−3.83 (−4.87, −2.77)** | **−2.25 (−4.04, −0.41)** | −0.11 (−0.50, 0.27) | **−5.98 (−7.08, −4.87)** | **−5.14 (−6.68, −3.57)** | **−3.34 (−5.39, −1.24)** | 0.91 (−0.79, 2.64) | **−1.39 (−2.69, −0.07)** |
| The UK (1988) | **1.78 (1.41, 2.16)** | **−2.77 (−4.34, −1.18)** | **−2.10 (−3.66, −0.52)** | 0.55 (−0.82, 1.94) | **−5.62 (−8.02, −3.16)** | **−5.10 (−7.23, −2.91)** | 1.35 (−2.05, 4.87) | **2.47 (1.32, 3.64)** | 0.23 (−0.30, 0.77) |
| Eastern Europe | | | | | | | | | |
| Estonia (1988) | **2.00 (0.29, 3.74)** | −0.12 (−3.36, 3.23) | 2.16 (−0.23, 4.60) | −1.05 (−4.12, 2.11) | **−4.04 (−5.97, −2.06)** | −1.52 (−6.55, 3.79) | −2.12 (−5.68, 1.56) | −0.71 (−3.58, 2.24) | **−5.63 (−7.95, −3.25)** |
| Lithuania (1993) | 9.83 (−2.84, 24.16) | 3.23 (−8.55, 16.53) | 7.56 (−4.91, 21.68) | **7.88 (4.00, 11.90)** | −7.45 (−14.64, 0.34) | **−7.30 (−9.85, −4.68)** | −3.08 (−6.53, 0.50) | 0.85 (−3.09, 4.96) | −3.89 (−7.91, 0.30) |
| Southern Europe | | | | | | | | | |
| Croatia (1988) | **6.69 (1.18, 12.50)** | 0.73 (−6.12, 8.09) | 2.39 (−5.00, 10.35) | **9.62 (0.46, 19.61)** | −2.61 (−6.24, 1.16) | **−5.39 (−9.99, −0.57)** | **6.69 (2.49, 11.07)** | 1.20 (−3.29, 5.90) | −1.14 (−4.07, 1.87) |
| Cyprus (1998) | 3.13 (−1.87, 8.39) | 0.76 (−5.10, 6.99) | 1.00 (−13.29, 17.65) | −3.14 (−22.12, 20.46) | −0.26 (−2.03, 1.55) | **−5.16 (−6.32, −3.98)** | −8.57 (−24.78, 11.13) | 3.59 (−4.19, 12.01) | 0.16 (−7.46, 8.41) |
| Italy (1988) | **1.75 (1.31, 2.20)** | **−3.01 (−4.47, −1.53)** | −0.47 (−2.40, 1.49) | **2.28 (0.66, 3.93)** | **−5.17 (−6.72, −3.59)** | **−1.30 (−2.18, −0.42)** | −2.69 (−5.60, 0.31) | 0.93 (−0.58, 2.46) | −0.18 (−1.37, 1.02) |
| Malta (1993) | −1.38 (−2.16, −0.61) | **−5.51 (−8.42, −2.51)** | 1.25 (−10.78, 14.91) | −2.30 (−7.56, 3.25) | −0.37 (−3.25, 2.61) | 1.21 (−2.11, 4.64) | −23.98 (−77.64, 158.47) | −3.04 (−6.18, 0.20) | 0.24 (−4.25, 4.95) |
| Spain (1988) | **2.32 (1.64, 3.02)** | **−2.98 (−3.87, −2.08)** | −0.59 (−1.81, 0.64) | **1.96 (0.40, 3.53)** | **−3.06 (−4.92, −1.15)** | **−1.79 (−3.19, −0.37)** | −1.18 (−2.45, 0.10) | 0.30 (−1.53, 2.16) | −1.57 (−3.67, 0.56) |
| Central Europe | | | | | | | | | |
| Austria (1988) | 0.03 (−1.22, 1.30) | **−7.73 (−10.99, −4.34)** | **−4.17 (−6.40, −1.90)** | −0.27 (−4.43, 4.08) | **−5.28 (−8.72, −1.71)** | **−6.21 (−11.48, −0.63)** | −2.28 (−9.33, 5.32) | −1.96 (−5.36, 1.55) | **2.48 (0.08, 4.93)** |
| Czech Republic (1988) | **1.23 (0.58, 1.89)** | **−4.13 (−6.70, −1.49)** | −1.47 (−5.59, 2.84) | 1.30 (−0.48, 3.11) | −1.59 (−4.87, 1.79) | −2.64 (−5.99, 0.83) | **−2.82 (−4.52, −1.08)** | −1.70 (−3.54, 0.17) | **−3.18 (−3.97, −2.38)** |
| Germany (1993) | **1.30 (0.15, 2.47)** | −3.74 (−7.59, 0.27) | −0.80 (−2.06, 0.48) | **1.75 (0.10, 3.43)** | **−6.75 (−12.56, −0.56)** | **−7.64 (−14.04, −0.77)** | 2.63 (−4.49, 10.27) | −0.44 (−4.70, 4.01) | −1.08 (−11.25, 10.26) |
| Poland (1998) | 3.60 (−0.58, 7.97) | −2.38 (−14.15, 11.00) | −0.12 (−9.02, 9.65) | 3.87 (−15.14, 27.15) | −4.61 (−9.90, 0.99) | 2.00 (−6.03, 10.73) | −4.35 (−10.19, 1.88) | −1.18 (−12.69, 11.86) | **−2.88 (−4.91, −0.81)** |
| Slovenia (1988) | 1.85 (−0.07, 3.80) | −1.93 (−5.52, 1.80) | −1.71 (−4.73, 1.41) | 0.14 (−2.37, 2.72) | **−8.22 (−9.70, −6.70)** | **−4.26 (−6.68, −1.77)** | −4.46 (−11.85, 3.55) | −0.44 (−6.12, 5.58) | −0.73 (−2.59, 1.17) |
| Switzerland (1988) | 0.19 (−0.76, 1.15) | **−3.05 (−5.34, −0.71)** | −1.57 (−4.36, 1.30) | −0.00 (−1.94, 1.97) | **−4.85 (−7.34, −2.29)** | **−3.75 (−6.77, −0.63)** | −0.05 (−2.82, 2.79) | **1.16 (0.15, 2.18)** | −0.99 (−3.37, 1.46) |
| Oceania | | | | | | | | | |
| Australia (1988) | −0.13 (−1.03, 0.79) | **−3.01 (−4.89, −1.09)** | **−1.16 (−1.51, −0.81)** | **−0.60 (−1.09, −0.10)** | **−4.44 (−5.45, −3.42)** | **−2.15 (−3.35, −0.93)** | 1.35 (−2.79, 5.68) | **1.58 (0.55, 2.63)** | −0.27 (−2.83, 2.36) |
| New Zealand (1993) | 0.42 (−2.49, 3.42) | **−5.32 (−9.76, −0.67)** | −0.20 (−2.09, 1.73) | 0.98 (−3.24, 5.39) | **−6.65 (−8.52, −4.74)** | **−6.25 (−11.05, −1.20)** | 0.66 (−8.45, 10.67) | −0.01 (−3.99, 4.15) | −3.53 (−7.27, 0.36) |

APC, annual percent change; CI, confidence interval; EOC, epithelial ovarian cancer; GCT, germ cell tumor; SCST, sex cord-stromal tumor; UK, United Kingdom; USA, United States of America. [a]NOS represents adenocarcinoma, NOS. [b]Values in bold indicate statistically significant results.

***Table 3*: The annual percent change (APC) and 95% confidence interval (CI) in ovarian cancer incidence by histological subtypes from 1988 to 2017.**[b]

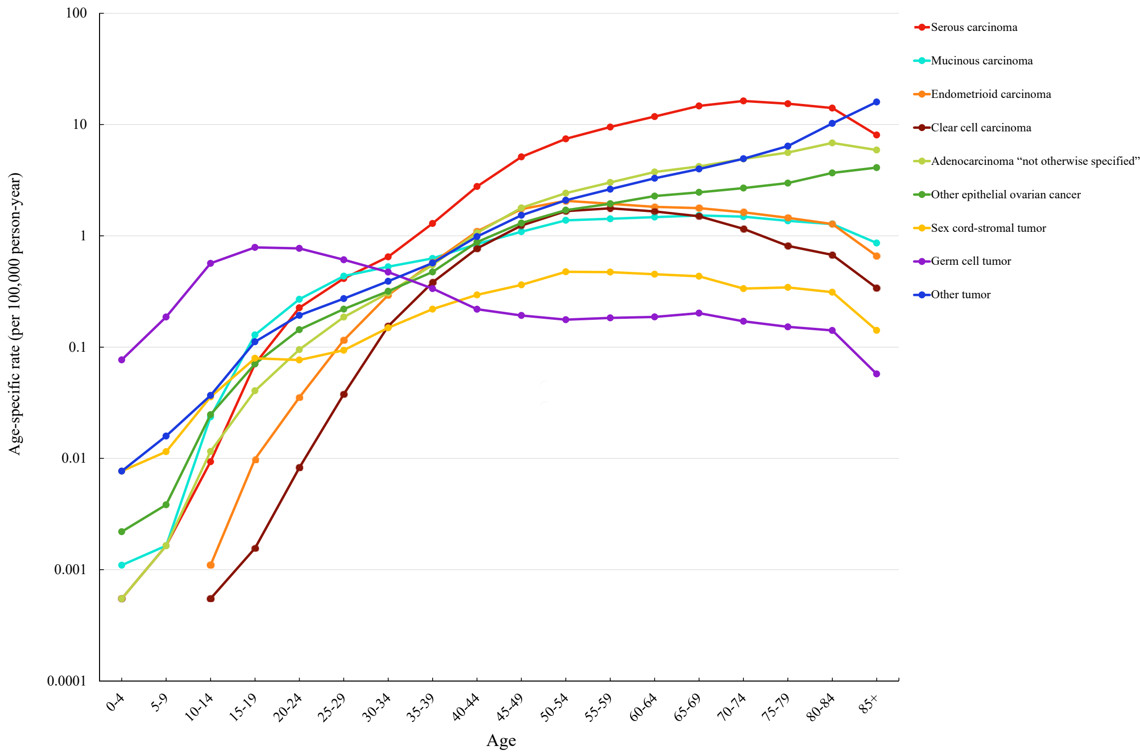


***Fig. 6:*** **Age-specific incidence (per 100,000 person-years) of ovarian cancer by histological subtypes and 5-year age groups, 2013–2017**.

ASRs of OC also varied across regions and countries, with higher levels in Eastern, Central and Southern Europe and relatively lower levels in Africa and Asia. These disparities might reflect regional differences in screening and diagnostic practices, reproductive factors (such as fertility rates and contraceptive use), genetic susceptibility, and lifestyle factors.[28–31]

Temporal trends in ASRs of OC might reflect changes in the prevalence of risk factors. Increased use of oral contraceptives and shifts in reproductive behaviors might partially explain the declines of ASRs observed in several regions. For example, the widespread use of oral contraceptives in the UK during the 1960s coincided with substantial reductions in OC incidence over time.[32] Although the protective effect of oral contraceptives wanes over time since last use, benefits are still seen at least 30 years after discontinuation.[33] Parity is a protective factor against OC risk,[34] so a lower ASR of OC might be seen in countries with more live births per woman such as India and China.[35]

There is convincing evidence that infertility increases the risk of OC.[36,37] In the current analysis, gradual increases in ASRs of OC were noticed in Japan and South Korea over time, which paralleled a decline in the total fertility rate during the same period.[38] Furthermore, menopausal hormone therapy use is associated with increased OC risk,[39] and its decreased use might have contributed to the decline in ASRs of OC in recent years. For instance, the dramatic reduction in menopausal hormone therapy use following the Women's Health Initiative report in 2002 has been linked to a significant decline in OC incidence in the USA.[40] Prophylactic surgeries, such as bilateral salpingo-oophorectomy and salpingectomy, can effectively reduce the risk of OC.[41,42] In several developed countries, such as the USA and the Netherlands, the declining trends in ASRs of OC might be partially attributable to the increased rate of prophylactic surgeries.[43,44]

Histological subtypes of OC also exhibit distinct patterns across geographic areas and HDI levels. These variations might be attributable to the heterogeneity in genetic and lifestyle risk factors within different populations, which differentially affect each histological subtype. For genetic factors, particularly *BRCA1* and *BRCA2* mutations, have been identified as risk factors for high-grade serous carcinomas.[45,46] Although serous carcinomas could not be subdivided into high or low grade in the present analysis, approximately 90% of serous carcinomas cases were high-grade.[47] Thus, the notably higher ASRs and proportions of serous carcinomas in Israel than other Asian countries might still be attributed to the large proportion of Ashkenazi Jews in Israel, who have a higher prevalence of *BRCA1* and *BRCA2* mutations.[48–50]

In terms of mucinous carcinomas, the ASR was relatively high in several Asian countries, such as Brunei, the Philippines, and Singapore. This might be related to unhealthy lifestyle habits (such as smoking and alcohol consumption) and increasing body mass index in these regions.[51–54] Additionally, with improved diagnostic criteria and techniques for mucinous carcinomas, a high proportion of cases previously classified as mucinous OC is now believed to be metastases from other anatomical sites (usually the gastrointestinal tract, e.g., Krukenberg tumors). This might partly explain the significant reduction in ASRs of mucinous carcinomas in most countries.[55–57]

Other risk factors such as endometriosis might also influence the distribution of histological subtypes, particularly endometrioid and clear cell carcinomas.[12] In this analysis, the relatively low ASR and proportion of serous carcinomas were offset by higher rates of endometrioid and clear cell carcinomas in Japan and Singapore. This phenomenon might be partly attributed to the higher prevalence of endometriosis among Asian women.[58] Of note, the significance of endometriosis as a risk factor for both endometrioid and clear cell carcinomas might elucidate the observed age-specific incidence patterns, wherein the incidence of these histological subtypes reached the highest around menopausal age.

Non-EOC, particularly GCTs, are typically diagnosed at a younger age, which is consistent with the age-specific incidences depicted in our study. The ASRs and proportions of non-EOC in Northern European and Eastern European regions were much higher than those in other regions, which might be due to distinct gene mutations and a younger age distribution within these populations.[59] Regarding other tumors, the ASRs and proportions in the Netherlands were notably lower than those in other countries, potentially indicating a more accurate classification of OC. This was supported by the temporal trends observed in the Netherlands, where the ASRs of other tumors have significantly decreased over time.

Differences in the ASRs and proportions of histological subtypes across four HDI regions might be partly explained by disparities in the availability and accessibility of healthcare services, diagnostic technologies, and lifestyle factors. For instance, in regions with lower HDI values, limited healthcare resources might lead to a higher proportion of diagnoses classified as other EOC and other tumors.[25] Additionally, poor diagnostic technologies and healthy lifestyle related to lower HDI values, such as pathological diagnostic technique, obesity rates, and smoking status, might explain gradually decreased the proportion of mucinous carcinomas across four HDI levels.[25,60,61]

When considering the temporal trends in ASRs of subtypes, due to insufficient data in the Joinpoint model, trend estimates for certain time periods and subtypes in some countries might be unstable, including Uganda, China, Bahrain, Kuwait, Iceland, and Malta, thus requiring special attention when interpreting these results. In Uganda and China (1993–1997), cases of most subtypes were rare or absent, possibly due to the small number of regional registries, only one for Uganda and two for China (1993–1997). The sparse number of cases for Bahrain (mucinous and clear cell carcinomas) and Kuwait (clear cell carcinomas, SCST, and other tumors) might be attributed to the low incidence of these cancers themselves or to the fact that only Bahrainis and Kuwaitis, respectively, were included in these datasets, ignoring other foreign residents. Regarding the rare case of SCST in Iceland and Malta, this was likely caused by the low incidence of this subtype in these two regions.

Given the instability of trend estimates due to sparse data, as observed in certain subtypes and countries within our study, it might be beneficial to consider alternative statistical methods that are more robust in the presence of limited data, such as Bayesian models, non-parametric models, and spline models. A more common approach is the use of Bayesian methods, which are advantageous for handling sparse datasets by incorporating prior information and borrowing strength across parameters or time periods. Bayesian models might provide more stable estimates in situations with small sample sizes and allow for a probabilistic interpretation of the results, naturally accounting for uncertainty.[62] For example, Bayesian joinpoint regression models have been developed to detect changes in trends while appropriately accounting for uncertainty in the number and locations of joinpoints, which is especially beneficial with sparse data.[63] Such models might improve the reliability of trend analyses in regions with limited case numbers and provide clearer insights into the epidemiology of these subtypes. Future studies could explore the application of Bayesian modeling to our data, potentially enhancing the robustness of our findings in areas where traditional joinpoint models might be unstable due to data limitations.

The strengths of the present study lie in its extensive data coverage and detailed subtype analysis. Firstly, the study utilized the CI5 database, which covers high-quality OC incidence data from five continents, thereby providing comprehensive patterns and trends of OC incidence on a global scale. Secondly, the study not only analyzed the overall incidence of OC by regions and HDI, but also explored in depth the incidence patterns and temporal trends of different histological subtypes. This was crucial for understanding the etiology and potential risk factors for specific subtypes and tailoring prevention and treatment strategies. Furthermore, examining the variation in OC incidence across different HDI regions could inform targeted public health interventions and resource allocation.

However, the study also has several limitations. One major limitation was the relatively small sample size in trend analyses of subtypes for certain countries such as Uganda, Bahrain, and Kuwait, which might result in instability of trend estimation and wide 95% CIs. Therefore, these findings should be interpreted with caution. Additionally, data for low HDI regions included only three countries, potentially compromising the comprehensiveness and representation of results for these regions. Third, in a limited number of countries, such as Chile, Israel, the Philippines, and Uganda, cases in the 80–84 or 85+ age groups were excluded due to the absence of corresponding person-years at risk, which might lead to an underestimation of incidence in these countries. Nevertheless, the effect of this underestimation might be negligible owing to the very limited number of cases in these age groups. Fourth, although histological grade was very important for serous carcinomas, we were unable to subdivide the serous subtype into high-grade and low-grade serous carcinomas due to the deficiencies in the CI5 database. Fifth, there were only 6 continuous observations for trend analyses in this study, potentially introducing bias in the estimation of APC. Despite advancements in diagnostic level and technology of OC over time with scientific and technological progress, pathological diagnosis remains the definitive diagnostic criterion.[64] Consequently, the diagnostic criteria for OC have not changed significantly, which might alleviate concerns about this bias. The study was also limited by the absence of national cancer registries in several countries. In these countries, regional cancer registries were combined to approximate the national profiles, which might result in relative underrepresentation for these countries.

In summary, there were notable variations in ASRs of OC across countries, with higher ASRs identified in Latvia, Lithuania, Brunei, and the Russian Federation and lower ASRs in Benin, South Africa, Kuwait, and Morocco. Although the ASR of OC has remained relatively stable globally, marked declines were observed among European, American, and Oceania populations, while certain Asian countries (Japan and South Korea) have experienced increases. Globally, serous carcinomas remain the most common histological subtype of OC. Despite the stability in worldwide ASRs of subtypes, most countries exhibited consistent increases in serous carcinomas and GCT, while mucinous carcinomas and adenocarcinoma NOS demonstrated consistent declines.

The higher incidence rates of OC and its histological subtypes observed in this study might be partially explained by genetic predispositions, reproductive behaviors, healthcare resources, and health awareness. It is suggested that countries with high incidence should strengthen public health education, actively screen for susceptibility genes, address adverse reproductive factors and lifestyles, and improve medical conditions to achieve primary and secondary prevention of OC. Further research is necessary to definitively identify the specific factors driving these variations in OC incidence across different countries, ultimately enabling the development of region-specific prevention and control strategies to effectively mitigate the global burden of this disease.

#### Contributors
Y-FW, LN, C-QL, T-TG, Q-JW, and J-HL contributed to the study design. Y-FW, Y-LX, JM, D-RL, and Z-FF collection of data. Y-FW, Y-LX, JM, D-RL, and Z-FF analysis of data. Y-FW, LN, Y-LX, JM, D-RL, Z-FF, F-HL, Y-ZL, H-LX, PL, Y-PY, D-HH, X-YL, SG, C-QL, T-TG, Q-JW, and J-HL wrote the first draft of the manuscript and edited the manuscript. All authors read and approved the final manuscript. Y-FW, LN, Y-LX, and JM contributed equally to this work. Y-FW, Y-LX, JM, D-RL, and Q-JW have viewed and verified the underlying data.

#### Data sharing statement
The Cancer Incidence in Five Continents data are publicly available at: https://ci5.iarc.fr/Default.aspx. Processed datasets used in the analysis are available from the corresponding author upon reasonable request.

#### Editor note
The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

#### Declaration of interests
The authors declare no competing interests.

#### Acknowledgements
This work was supported by the National Key Research and Development Program of China (No.2022YFC2704205 to Wu QJ), the Natural Science Foundation of China (No.82073647 and No.82373674 to Wu QJ and No.82103914 to Gong TT), Outstanding Scientific Fund of Shengjing Hospital (Wu QJ), 345 Talent Project of Shengjing Hospital of China Medical University (Gong TT), the Max Planck – University of Helsinki Center from the Jane and Aatos Erkko Foundation (No.210046 to Li P), the Max Planck Society (No.5714240218 to Li P), the University of Helsinki (No.77204227 to Li P), and the European Union (ERC Synergy, BIOSFER, 101071773 to Li P).

#### Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102983.

#### References

1 Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229–263.
2 Huang J, Chan WC, Ngai CH, et al. Worldwide burden, risk factors, and temporal trends of ovarian cancer: a global study. *Cancers*. 2022;14(9).
3 Phung MT, Pearce CL, Meza R, Jeon J. Trends of ovarian cancer incidence by histotype and race/ethnicity in the United States 1992-2019. *Cancer Res Commun*. 2023;3(1):1–8.
4 Cabasag CJ, Arnold M, Butler J, et al. The influence of birth cohort and calendar period on global trends in ovarian cancer incidence. *Int J Cancer*. 2020;146(3):749–758.
5 Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet*. 2018;391(10125):1023–1075.
6 Matulonis UA, Sood AK, Fallowfield L, Howitt BE, Sehouli J, Karlan BY. Ovarian cancer. *Nat Rev Dis Prim*. 2016;2:16061.
7 The WHO Classification of Tumours Editorial Board. *Female genital tumours. WHO classification of tumours*. 5th ed. 2020.
8 Low JJ, Ilancheran A, Ng JS. Malignant ovarian germ-cell tumours. *Best Pract Res Clin Obstet Gynaecol*. 2012;26(3):347–355.
9 Prat J, D'Angelo E, Espinosa I. Ovarian carcinomas: at least five different diseases with distinct histological features and molecular genetics. *Hum Pathol*. 2018;80:11–27.

10 Ray-Coquard I, Morice P, Lorusso D, et al. Non-epithelial ovarian cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2018;29(Suppl 4):iv1–iv18.
11 Lee AW, Ness RB, Roman LD, et al. Association between menopausal estrogen-only therapy and ovarian carcinoma risk. *Obstet Gynecol*. 2016;127(5):828–836.
12 Wentzensen N, Poole EM, Trabert B, et al. Ovarian cancer risk factors by histologic subtype: an analysis from the ovarian cancer cohort consortium. *J Clin Oncol*. 2016;34(24):2888–2898.
13 Yachida N, Yoshihara K, Yamaguchi M, Suda K, Tamura R, Enomoto T. How does endometriosis lead to ovarian cancer? The molecular mechanism of endometriosis-associated ovarian cancer development. *Cancers*. 2021;13(6).
14 Cabasag CJ, Arnold M, Rutherford M, et al. Shifting incidence and survival of epithelial ovarian cancer (1995-2014): a SurvMark-2 study. *Int J Cancer*. 2023;152(9):1763–1777.
15 Coburn SB, Bray F, Sherman ME, Trabert B. International patterns and trends in ovarian cancer incidence, overall and by histologic subtype. *Int J Cancer*. 2017;140(11):2451–2460.
16 Hao W, Zhang Y, Li Z, et al. International trends in ovarian cancer incidence from 1973 to 2012. *Arch Gynecol Obstet*. 2021;303(6):1589–1597.
17 Bray F, Colombet M, Aitken JF, et al. *Cancer incidence in five continents, vol. XII (IARC CancerBase No. 19)*. Lyon: International Agency for Research on Cancer; 2023. Available from: https://ci5.iarc.who.int/ci5-xii/.
18 Ferlay J, Colombet M, Bray F. Cancer incidence in five continents, CI5plus: IARC CancerBase No. 9. Lyon: International Agency for Research on Cancer. Available from: https://ci5.iarc.who.int/ci5plus/.
19 United Nations Development Programme. Human development index (HDI). Available from: https://hdr.undp.org/data-center/human-development-index#/indicies/HDI.
20 Doll R, Payne P, Waterhouse J. *Cancer incidence in five continents: a technical report*. Berlin: Springer-Verlag; 1966.
21 Bray F, Guilloux A, Sankila R, Parkin DM. Practical implications of imposing a new world standard population. *Cancer Causes Control*. 2002;13(2):175–182.
22 National Cancer Institute. The division of cancer control and population sciences (DCCPS). Available from: https://surveillance.cancer.gov/help/joinpoint/setting-parameters/method-and-parameters-tab/number-of-joinpoints.
23 Devesa SS, Donaldson J, Fears T. Graphical presentation of trends in rates. *Am J Epidemiol*. 1995;141(4):300–304.
24 Fidler MM, Soerjomataram I, Bray F. A global view on cancer incidence and national levels of the human development index. *Int J Cancer*. 2016;139(11):2436–2446.
25 Khazaei Z, Namayandeh SM, Beiranvand R, Naemi H, Bechashk SM, Goodarzi E. Worldwide incidence and mortality of ovarian cancer and Human Development Index (HDI): GLOBOCAN sources and methods 2018. *J Prevent Med Hyg*. 2021;62(1):E174–E184.
26 Bohsas H, Alibrahim H, Swed S, et al. Knowledge toward ovarian cancer symptoms among women in Syria: cross-sectional study. *Heliyon*. 2023;9(8):e19076.
27 Okunowo AA, Adaramoye VO. Women's knowledge on ovarian cancer symptoms and risk factors in Nigeria: an institutional-based study. *J Epidemiol Glob Health*. 2018;8(1–2):34–41.
28 Mei S, Chelmow D, Gecsi K, et al. Health disparities in ovarian cancer: report from the ovarian cancer evidence review conference. *Obstet Gynecol*. 2023;142(1):196–210.
29 Pezzulo C, Nilsen K, Carioli A, et al. Geographical distribution of fertility rates in 70 low-income, lower-middle-income, and upper-middle-income countries, 2010-16: a subnational analysis of cross-sectional surveys. *Lancet Glob Health*. 2021;9(6):e802–e812.
30 Qiu W, Lu H, Qi Y, Wang X. Dietary fat intake and ovarian cancer risk: a meta-analysis of epidemiological studies. *Oncotarget*. 2016;7(24):37390–37406.
31 Chornokur G, Lin HY, Tyrer JP, et al. Common genetic variation in cellular transport genes and epithelial ovarian cancer (EOC) risk. *PLoS One*. 2015;10(6):e0128106.
32 dos Santos Silva I, Swerdlow AJ. Recent trends in incidence of and mortality from breast, ovarian and endometrial cancers in England and Wales and their relation to changing fertility and oral contraceptive use. *Br J Cancer*. 1995;72(2):485–492.
33 Beral V, Doll R, Hermon C, Peto R, Reeves G. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. *Lancet*. 2008;371(9609):303–314.
34 Sung HK, Ma SH, Choi JY, et al. The effect of breastfeeding duration and parity on the risk of epithelial ovarian cancer: a systematic review and meta-analysis. *J Prevent Med Public Health*. 2016;49(6):349–366.
35 United Nations. *Department of economic and social affairs, population division*. World Population Prospects; 2024. Available from: https://population.un.org/wpp/.
36 Bristow RE, Karlan BY. Ovulation induction, infertility, and ovarian cancer risk. *Fertil Steril*. 1996;66(4):499–507.
37 Lundberg FE, Johansson ALV, Rodriguez-Wallberg K, Gemzell-Danielsson K, Iliadou AN. Assisted reproductive technology and risk of ovarian cancer and borderline tumors in parous women: a population-based cohort study. *Eur J Epidemiol*. 2019;34(11):1093–1101.
38 Global fertility in 204 countries and territories, 1950-2021, with forecasts to 2100: a comprehensive demographic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403(10440):2057–2099.
39 Beral V, Gaitskell K, Hermon C, Moser K, Reeves G, Peto R. Menopausal hormone use and ovarian cancer risk: individual participant meta-analysis of 52 epidemiological studies. *Lancet*. 2015;385(9980):1835–1842.
40 Yang HP, Anderson WF, Rosenberg PS, et al. Ovarian cancer incidence trends in relation to changing patterns of menopausal hormone therapy use in the United States. *J Clin Oncol*. 2013;31(17):2146–2151.
41 Kahn RM, Gordhandas S, Godwin K, et al. Salpingectomy for the primary prevention of ovarian cancer: a systematic review. *JAMA surgery*. 2023;158(11):1204–1211.
42 Kauff ND, Satagopan JM, Robson ME, et al. Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med*. 2002;346(21):1609–1615.
43 Harmsen MG, Arts-de Jong M, Horstik K, et al. Very high uptake of risk-reducing salpingo-oophorectomy in BRCA1/2 mutation carriers: a single-center experience. *Gynecol Oncol*. 2016;143(1):113–119.
44 Mikhail E, Salemi JL, Mogos MF, Hart S, Salihu HM, Imudia AN. National trends of adnexal surgeries at the time of hysterectomy for benign indication, United States, 1998-2011. *Am J Obstet Gynecol*. 2015;213(5):713.e1–713.e13.
45 Pal T, Permuth-Wey J, Betts JA, et al. BRCA1 and BRCA2 mutations account for a large proportion of ovarian carcinoma cases. *Cancer*. 2005;104(12):2807–2816.
46 Risch HA, McLaughlin JR, Cole DE, et al. Prevalence and penetrance of germline BRCA1 and BRCA2 mutations in a population series of 649 women with ovarian cancer. *Am J Hum Genet*. 2001;68(3):700–710.
47 Zwimpfer TA, Tal O, Geissler F, et al. Low grade serous ovarian cancer - a rare disease with increasing therapeutic options. *Cancer Treat Rev*. 2023;112:102497.
48 Oddoux C, Struewing JP, Clayton CM, et al. The carrier frequency of the BRCA2 6174delT mutation among Ashkenazi Jewish individuals is approximately 1. *Nat Genet*. 1996;14(2):188–190.
49 Struewing JP, Abeliovich D, Peretz T, et al. The carrier frequency of the BRCA1 185delAG mutation is approximately 1 percent in Ashkenazi Jewish individuals. *Nat Genet*. 1995;11(2):198–200.
50 Zlotogora J. Genetics and genomic medicine in Israel. *Mol Genet Genom Med*. 2014;2(2):85–94.
51 Ovarian cancer and body size: individual participant meta-analysis including 25,157 women with ovarian cancer from 47 epidemiological studies. *PLoS Med*. 2012;9(4):e1001200.
52 Faber MT, Kjær SK, Dehlendorff C, et al. Cigarette smoking and risk of ovarian cancer: a pooled analysis of 21 case-control studies. *Cancer Causes Control*. 2013;24(5):989–1004.
53 Modugno F, Ness RB, Allen GO. Alcohol consumption and the risk of mucinous and nonmucinous epithelial ovarian cancer. *Obstet Gynecol*. 2003;102(6):1336–1343.
54 Sreeramareddy CT, Pradhan PM, Mir IA, Sin S. Smoking and smokeless tobacco use in nine South and Southeast Asian countries: prevalence estimates and social determinants from Demographic and Health Surveys. *Popul Health Metrics*. 2014;12:22.
55 Cheasley D, Wakefield MJ, Ryland GL, et al. The molecular origin and taxonomy of mucinous ovarian carcinoma. *Nat Commun*. 2019;10(1):3935.

56 Kurman RJ, Shih Ie M. Molecular pathogenesis and extraovarian origin of epithelial ovarian cancer–shifting the paradigm. *Hum Pathol*. 2011;42(7):918–931.
57 McCluggage WG. Immunohistochemistry in the distinction between primary and metastatic ovarian mucinous neoplasms. *J Clin Pathol*. 2012;65(7):596–600.
58 Arumugam K, Templeton AA. Endometriosis and race. *Aust N Z J Obstet Gynaecol*. 1992;32(2):164–165.
59 Van Nieuwenhuysen E, Lambrechts S, Lambrechts D, Leunen K, Amant F, Vergote I. Genetic changes in nonepithelial ovarian cancer. *Expet Rev Anticancer Ther*. 2013;13(7):871–882.
60 Shirvani Shiri M, Emamgholipour S, Heydari H, Fekri N, Karami H. The effect of human development index on obesity prevalence at the global level: a spatial analysis. *Iranian J Public Health*. 2023;52(4):829–839.
61 Riahi M, Mohammadi AA, Rohani H, Bidkhori M. Dataset on the prevalence of tobacco smoking in men and women of selected countries whit difference human development. *Data Brief*. 2018;18:506–511.
62 Gelman A, Carlin JB, Stern HS, Dunson DB, Vehtari A, Rubin DB. *Bayesian data analysis*. 3rd ed. New York: Chapman and Hall/CRC; 2013. https://doi.org/10.1201/b16018.
63 Martinez-Beneito MA, García-Donato G, Salmerón D. A bayesian joinpoint regression model with an unknown number of break-points. *Ann Appl Stat*. 2011;5(3):2150–2168.
64 González-Martín A, Harter P, Leary A, et al. Newly diagnosed and relapsed epithelial ovarian cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2023;34(10):833–848.