



Global, regional, and national prevalence and disability-adjusted life-years for endometriosis in 204 countries and territories, 1990–2019: Findings from a global burden of disease study

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ABSTRACT

Introduction: This study aimed to analyze the worldwide, regional burden of endometriosis and its trends from 1990 to 2019, utilizing the latest data from Global Burden of Disease (GBD) 2019. GBD 2019 is a global database tool for comprehensive analysis and an important result of long-term collaboration among governments worldwide.

Methods: We utilized the Global Health Data Exchange Query tool to analyze endometriosis in prevalence numbers, age-standardized prevalence rates (ASPR), and disability-adjusted life-years (DALYs) from 1990 to 2019 in 204 countries and regions. Additionally, this study investigated the impacts of period, age, and cohort on the prevalence and DALYs of endometriosis from the global perspective and in the five sociodemographic index (SDI) regions.

Results: Among the 21 regions, the most significant reduction in the prevalence of endometriosis between 1990 and 2019 occurred in Central Latin America. In 204 countries, the most pronounced decline was observed in Guatemala. At the SDI level, with the increase of SDI, the ASPR of endometriosis in all regions worldwide showed an overall decreasing trend. The prevalence of endometriosis peaked between the ages of 25 and 29.

Discussion: The findings of this study reflect the temporal and spatial tendency of the burden of endometriosis during the study period, and provide a reference for health agencies around the world to formulate policies on endometriosis, so as to reduce the harm of endometriosis to women worldwide.

1. Introduction

Endometriosis is a common, chronic, non-fatal gynecological condition that affects approximately 5–10 % of women of reproductive age worldwide, with clinical symptoms including infertility, dysmenorrhea, and non-menstrual pelvic pain [1,2]. Pelvic pain is prevalent in 50–80 % of women with endometriosis, and female infertility is present in 50 % of affected women. Endometriosis affects more than 176 million women globally [3]. Despite the high prevalence of endometriosis, diagnosing the condition remains challenging, with 65 % of women being initially misdiagnosed [4].

Endometriosis is now recognized not only as a pelvic disease but also considered a systemic condition. The constant inflammation caused by

endometriosis affects the nervous system, leading to central pain sensitization [1]. Researchers have also studied the association between endometriosis and mental illness, and approximately 87 % of women with endometriosis reported some type of mental illness [5,6]. Additionally, despite endometriosis being a non-malignant disease, there is substantial evidence that endometriosis is associated with an elevated risk of cancer, especially ovarian and breast cancer [7,8].

The Global Burden of Disease (GBD) 2019 provides an opportunity to explore the global burden of endo diseases by systematically assessing and updating disease burdens and influencing factors in 204 territories and countries. Previous researchers have employed GBD tools to analyze the burden of endometriosis [9–12], each of these studies has its own advantages and limitations. This study aimed to analyze the worldwide,

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regional, and intra-country burden of endometriosis and its trends from 1990 to 2019, utilizing the latest data and improved methodologies from GBD 2019.

2. Materials and methods

2.1. Data sources

This study used data on the annual prevalence numbers, age-standardized prevalence rates (ASPR), and DALYs of endometriosis in 204 countries and regions from 1990 to 2019 collected from the Global Health Data Exchange Query tool (<http://ghdx.healthdata.org/gbd-results-tool>) and SDI data (<http://ghdx.healthdata.org/data-type/estimate>). The GBD 2019 database encompasses population health and demographic data worldwide, sourced from census data, surveys, registries, indicators and estimates, administrative health data, and health-related financial data. Previous studies have detailed methods of data selection and entry [13,14].

2.2. Data definition

The GBD 2019 study utilizes the SDI as a composite indicator to summarize the sociodemographic development of an area [15]. The SDI, with a scale of 0–1, provides a comprehensive indicator of geographical development based on national per capita income, total fertility, and average educational attainment [16].

2.3. Statistical analysis

GBD was determined utilizing the Bayesian meta-regression tool to model the burden of non-fatal diseases [17]. Age-standardized rate (ASR), as a weighted average of a specific age ratio, was calculated by aggregating measures of the ratio that a population would have if it had a standard age structure. The assignment of weights was derived from the distribution of the standard population using the following equation:

$$ASR = \frac{\sum_{i=1}^A aiwi}{\sum_{i=1}^A wi} \times 100,000$$

, *ai* is a specific age ratio. The number (or weight) of the chosen standard population was 100,000 (per 100,000 people).

The estimated annual percentage change (EAPC) was derived by fitting the linear regression line to the natural logarithm of the ASR: $EAPC = \ln(ASR) = \alpha + \beta x + \varepsilon$, the *x* denotes the calendar year, and the ε denotes the error term, whose 95 % confidence interval (CI) is established utilizing the formula $100 \times (\exp(\beta) - 1)$ [18]. A positive value of EAPC, alongside a 95 % CI, denotes an upward trend. Conversely, a negative value for both suggests a downward trend.

This study employed the R language-based network APC analysis tool developed by the National Cancer Institute of the United States to ascertain the independent estimates of the impacts of period, age, and birth cohort on the burden of endometriosis globally and in five SDI-level regions. Period factors pertain to alterations in the load of anthropogenic factors in a particular epoch. Age factors contribute to the establishment of the aging factor. The changes in the cohort factor were associated with the various population exposure conditions at distinct birth periods.

In this study, each step utilized to analyze the GBD database adhered to the cross-sectional study guidelines described in the Guidelines for Accurate and Transparent Health Estimates Reporting [19]. R version 4.3.1 (R Foundation, Vienna, Austria, <https://www.r-project.org/>) was used in this study.

3. Results

3.1. The endometriosis burden at the global level

Globally, the prevalence change (PC) in ASR of endometriosis prevalence declined by 20.47 % (95 % CI: –22.82 % to –18.32 %) from 1990 to 2019 (Tables S1; Fig. 1A). The ASPR of endometriosis changed from 767.75 (95 % uncertainty interval [UI]: 540.26–1060.37 per 100,000 population) in 1990–610.57 (95 % UI: 436.15–842.30) per 100,000 population in 2019 (Tables S1; Fig. 2A). The ASR in DALYs due to endometriosis was 71.08 (95 % UI: 42.52–112.47) worldwide in 1990, decreasing to 56.61 (95 % UI: 34.05–89.66) per 100,000 population in 2019 (Tables S1; Fig. 3A).

3.2. Endometriosis burden at the SDI quintile level

When stratified by SDI levels, a downward trend was observed for ASPR in endometriosis in all SDI quintiles from 1990 to 2019 (Tables S1; Fig. 1A). The most substantial downward trend was consistently observed in the low-middle SDI quintiles, accounting for –31.03 % (95 % CI: –33.14 % to –28.77 %) of the overall downward trend for PC in ASPR during this period (Tables S1; Fig. 1A).

In 2019, the highest ASPR of endometriosis among SDI levels was observed in low SDI countries (718.35 (95 % UI: 502.46–1001.61) per 100,000 population), while the lowest ASPR was in high SDI countries (538.61 (95 % UI: 394.87–719.64) per 100,000 population) (Tables S1; Fig. 2 A). Similarly, low SDI countries exhibited the highest age-standardized DALYs rate (66.22 (95 % UI: 39.35–106.15) per 100,000 population) in 2019, whereas high SDI countries (49.72 (95 % UI: 30.46–76.75) per 100,000 population) had the lowest rate (Tables S1; Fig. 3 A).

3.3. Endometriosis burden at the regional level

From 1990 to 2019, all 21 regional levels demonstrated a decline in PC for ASPR of endometriosis (Table S2). Three areas where the decline was most pronounced were Central Latin America (–36.44 % (95 % CI: –41.75 to –31.04 %)), South Asia (–31.56 % (95 % CI: –33.97 to –28.91 %)), and high-income North America (–29.58 % (95 % CI: –42.23 to –15.47 %)) from 1990 to 2019 (Table S2). Eastern Europe (–2.06 % (95 % CI: –4.50–0.26 %)), Western Europe (–5.41 % (95 % CI: –8.94 to –1.30 %)), and Central Europe (–8.18 % (95 % CI: –10.69 to –5.36 %)) showed the least decline in PC for ASPR of endometriosis from 1990 to 2019 (Table S1).

The three regions with the highest ASPR in 2019 for endometriosis were Oceania (915.28 (95 % UI: 644.53–1266.00) per 100,000 population), Eastern Europe (833.83 (95 % UI: 589.84–1143.83) per 100,000 population), and North Africa and Middle East (798.85 (95 % UI: 568.90–1104.77) per 100,000 population) (Table S1; Fig. 2B). Moreover, three regions with the lowest ASPR were high-income North America (377.99 (95 % UI: 282.88–497.81) per 100,000 population), East Asia (459.19 (95 % UI: 327.72–614.23) per 100,000 population), and Central Europe (483.31 (95 % UI: 340.10–675.63) per 100,000 population) in 2019 (Table S1; Fig. 2B).

The three regions with the highest age-standardized DALYs rate in endometriosis were Oceania (84.48 (95 % UI: 49.95–134.33) per 100,000 population), Eastern Europe (77.74 (95 % UI: 46.30–122.85) per 100,000 population), and North Africa and Middle East (73.71 (95 % UI: 44.14–117.62) per 100,000 population) in 2019 (Table S1; Fig. 3B). Additionally, the three regions with the lowest age-standardized DALYs rate were high-income North America (34.56 (95 % UI: 21.57–53.12) per 100,000 population), East Asia (43.03 (95 % UI: 26.03–67.67) per 100,000 population), and Central Europe (45.07 (95 % UI: 26.70–72.05) per 100,000 population) in 2019 (Table S1; Fig. 3B).

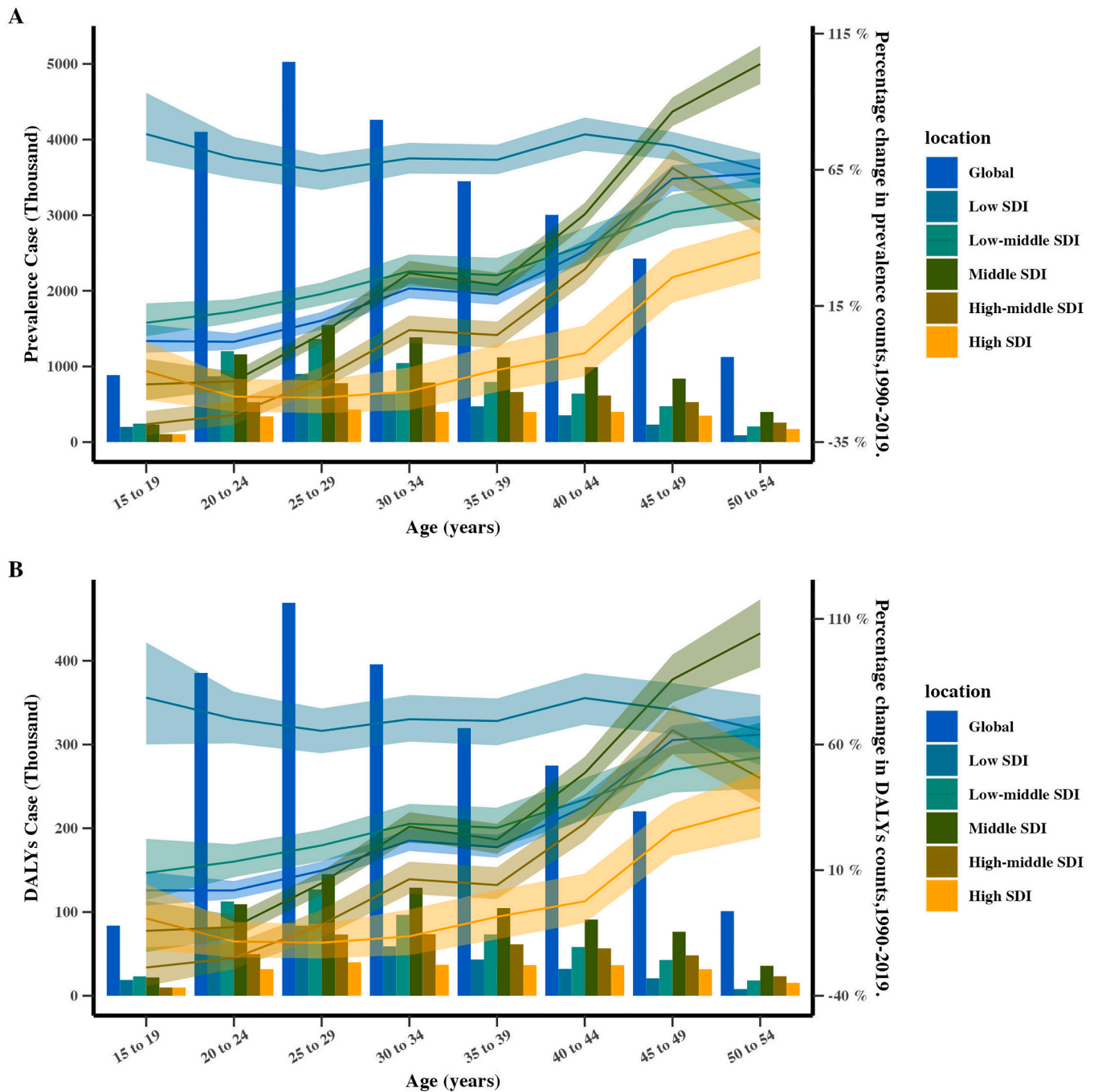


Fig. 1. SDI-specific counts in 2019 and percentage change counts of endometriosis, 1990–2019 of prevalence and DALYs across various age groups ranging from 15 years to more than 54 years old. (A) Age-SDI-specific prevalence counts in 2019 and their percentage change counts of endometriosis during 1990–2019. (B) Age-SDI-specific DALYs count in 2019 and their percentage change counts of endometriosis during 1990–2019.

3.4. Endometriosis burden at countries' level

Except for the Russian Federation, Austria, Iceland, and Sweden, the PC of ASPR in endometriosis showed a downward trend in the other 200 countries included in the GBD database from 1990 to 2019. The three countries with the greatest decline in the PC of ASPR in this period were Guatemala (-48.81 % (95 % CI: -55.31 to -41.49 %)), Oman (-46.89 % (95 % CI: -53.34 to -38.39 %)), and Equatorial Guinea (-41.80 % (95 % CI: -48.44 to -33.57 %))(Table S2). Only Sweden (45.14 % (95 % CI: 13.26–84.01 %)), Iceland (12.30 % (95 % CI: -19.62–59.06 %)), Austria (7.33 % (95 % CI: -9.14–24.19 %)), and Russian Federation (0.22 % (95 % CI: -1.51–1.66 %)) experienced an

increase in PC of ASPR in endometriosis(Table S2).

The three countries with the highest ASPR of endometriosis in 2019 were New Zealand (1172.91 (95 % UI:866.04–1566.59) per 100,000 population), Afghanistan (1017.18 (95 % UI: 705.67–1448.47) per 100,000 population), and Solomon Islands (953.85 (95 % UI:670.81–1315.52) per 100,000 population). Conversely, Iceland (301.96 (95 % UI:207.63–445.17) per 100,000 population), United States of America (374.15 (95 % UI: 282.40–491.91) per 100,000 population), and Denmark (378.56 (95 % UI:261.33–541.77) per 100,000 population) had the lowest ASPR in 2019 (Table S2; Fig. 4A).

The three countries with the highest age-standardized DALYs rates of endometriosis per 100,000 population in 2019 were New Zealand

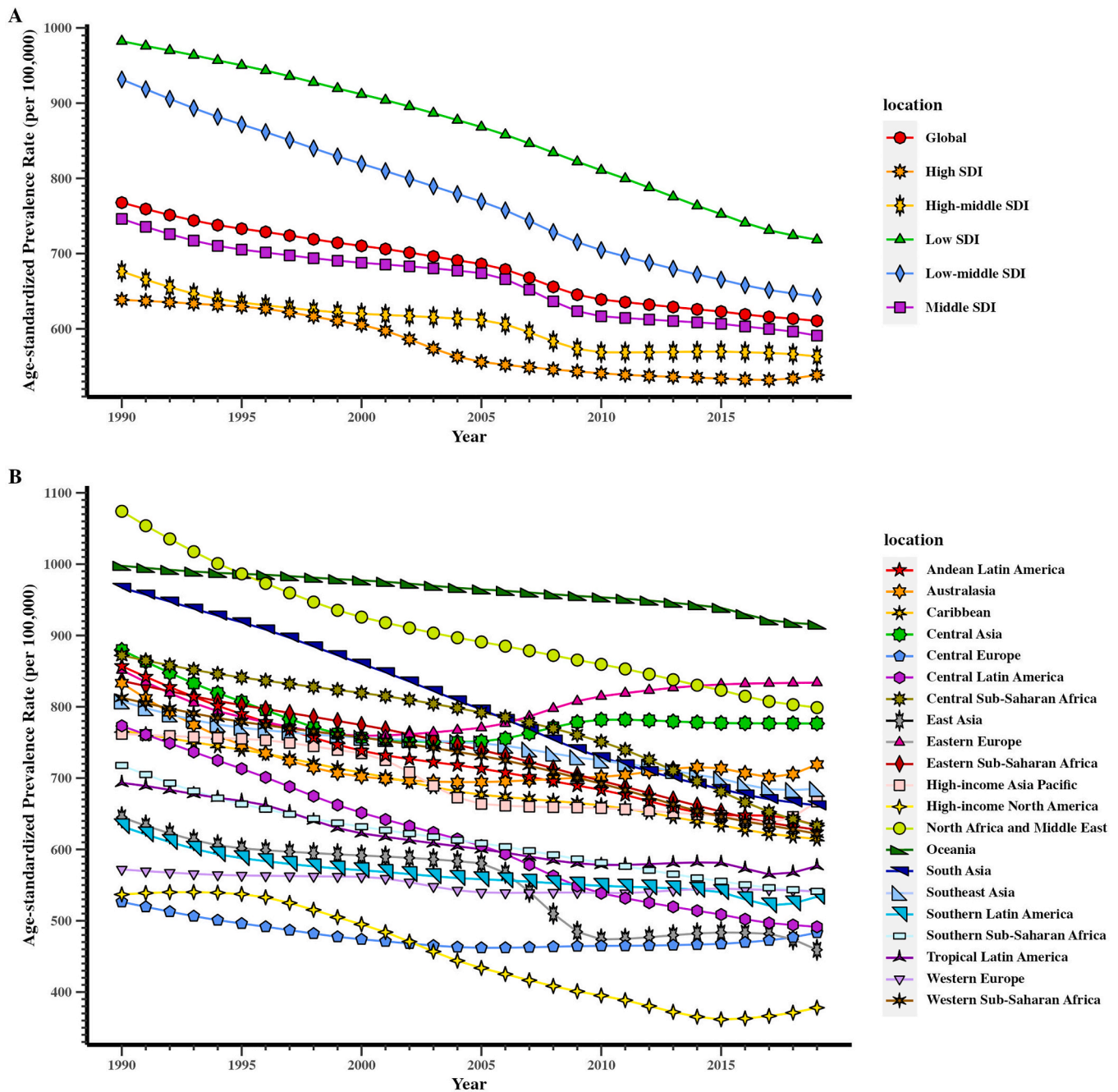


Fig. 2. Trends in global disease burden of endometriosis prevalence from 1990 to 2019. (A) Trends in global disease burden of endometriosis prevalence based on sociodemographic index from 1990 to 2019; (B) Trends in global disease burden of endometriosis prevalence by region from 1990 to 2019.

(107.65 (95 % UI: 65.60–169.33)), Afghanistan (92.50 (95 % UI: 54.13–149.79)), and Solomon Islands (88.45 (95 % UI: 51.75–140.54)). Contrastingly, the lowest age-standardized DALYs rates per 100,000 population were recorded for Iceland (27.89 (95 % UI: 16.02–45.88)), United States of America (34.15 (95 % UI: 21.56–52.09)), and Denmark (34.80 (95 % UI: 19.88–55.20))(Table S2).

The three countries with the highest EAPC in endometriosis ASPR from 1990 to 2019 value were Sweden (154.02 % (95 % UI: 118.46–189.69 %)), Iceland (59.07 % (95 % UI: 39.27–78.90 %)), and Austria (49.54 % (95 % UI: 36.43–62.67 %)). Conversely, the three countries with the lowest EAPC values were Guatemala (-243.71 % (95 % UI: -260.76 % to -226.64 %)), Oman (-225.05 % (95 % UI: -247.14 % to -202.92 %)), and Equatorial Guinea (-196.36 % (95 % UI: -202.97 % to -189.74 %)). (Table S3; Fig. 4B).

3.5. Effect of sociodemographic transition on the burden of endometriosis

We observed an overall downward trend in endometriosis ASPR in all regions of the world as SDI increased, as shown in Fig. 5A. In regions where $0.4 < SDI < 0.6$, ASPR showed a significant decrease. When SDI was between 0.65 and 0.8, the decline trend tended to be flat, and when $SDI > 0.8$, ASPR declined significantly again. There was a U-shaped correlation between ASPR and SDI levels in Central Asia, Australasia, and Eastern Europe. ASPR in high-income North America decreased significantly with SDI. When SDI exceeded 0.8, its ASPR showed a small increase (Table S4; Fig. 5A).

Fig. 5B illustrates the association between endometriosis and SDI levels in 204 countries worldwide for the year 2019. As SDI increased, the ASPR of endometriosis in all countries in the world exhibited a

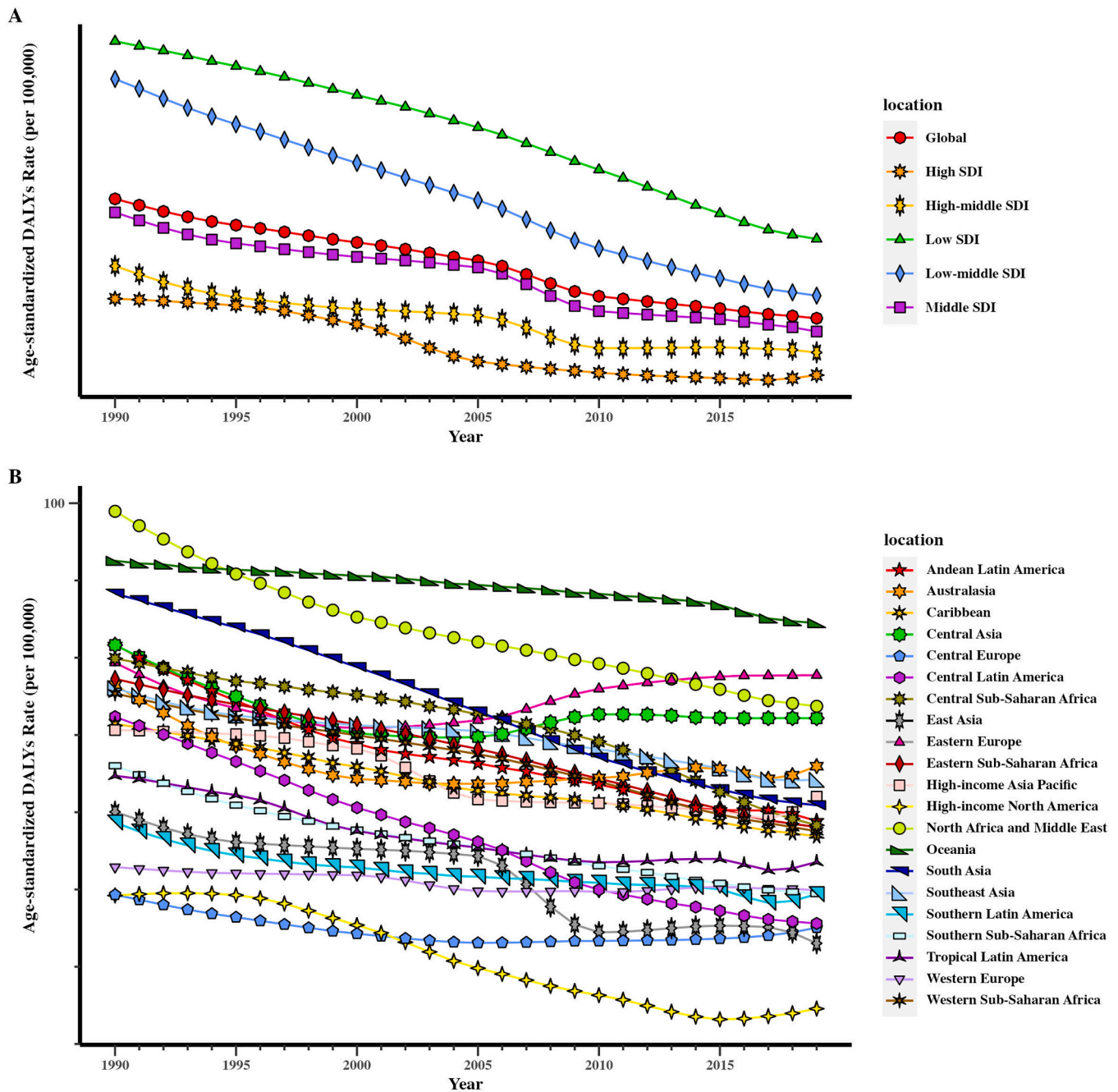


Fig. 3. Trends in global disease burden of endometriosis DALYs from 1990 to 2019. (A) Trends in global disease burden of endometriosis DALYs by sociodemographic index from 1990 to 2019; (B) Trends in global disease burden of endometriosis DALYs by region from 1990 to 2019.

decreasing trend, and the decline was obvious when SDI > 0.8. When 0.3 < SDI < 0.7, the ASPR trend of endometriosis is relatively flat, and when SDI > 0.8, the decreasing trend is significant. Afghanistan, Solomon Islands, Papua New Guinea, Yemen, and New Zealand's ASPR were much higher than expected, while Iceland's ASPR was much lower than expected (Table S5; Fig. 5B).

3.6. Age-period-cohort impact of endometriosis burden

We used an age-period-cohort model to further understand changes in the prevalence burden of endometriosis, and the APC model results showed that for global, middle SDI, low-middle SDI, high-middle SDI, and low SDI categories, NetDrift, all age deviations, 1990–2019 all period deviations, all cohort deviations, all period RR, all cohort RR, all

local drifts demonstrated statistical significance ($P < 0.05$). The Net-Drift, all age deviations, all period deviations, All period RR, and all cohort RR of high SDI had statistical significance ($P < 0.05$). However, all period deviations and all local drifts were not statistically significant (Table S6; Fig. 6A).

After adjusting for period and cohort effects, the prevalence of endometriosis exhibited an inverted V-shaped trend globally and in all five SDI regions, with the peak prevalence of endometriosis observed at 25–29 years and the prevalence decreased after the peak. The global prevalence of endometriosis remained high between the ages of 30 and 39, while the prevalence dropped rapidly when the age exceeded 40 years or between the ages of 15 and 24 years (Table S6, Table S2; Fig. 6B). The time-varying RR values of endometriosis prevalence globally and in any SDI region decreased monotonously throughout the

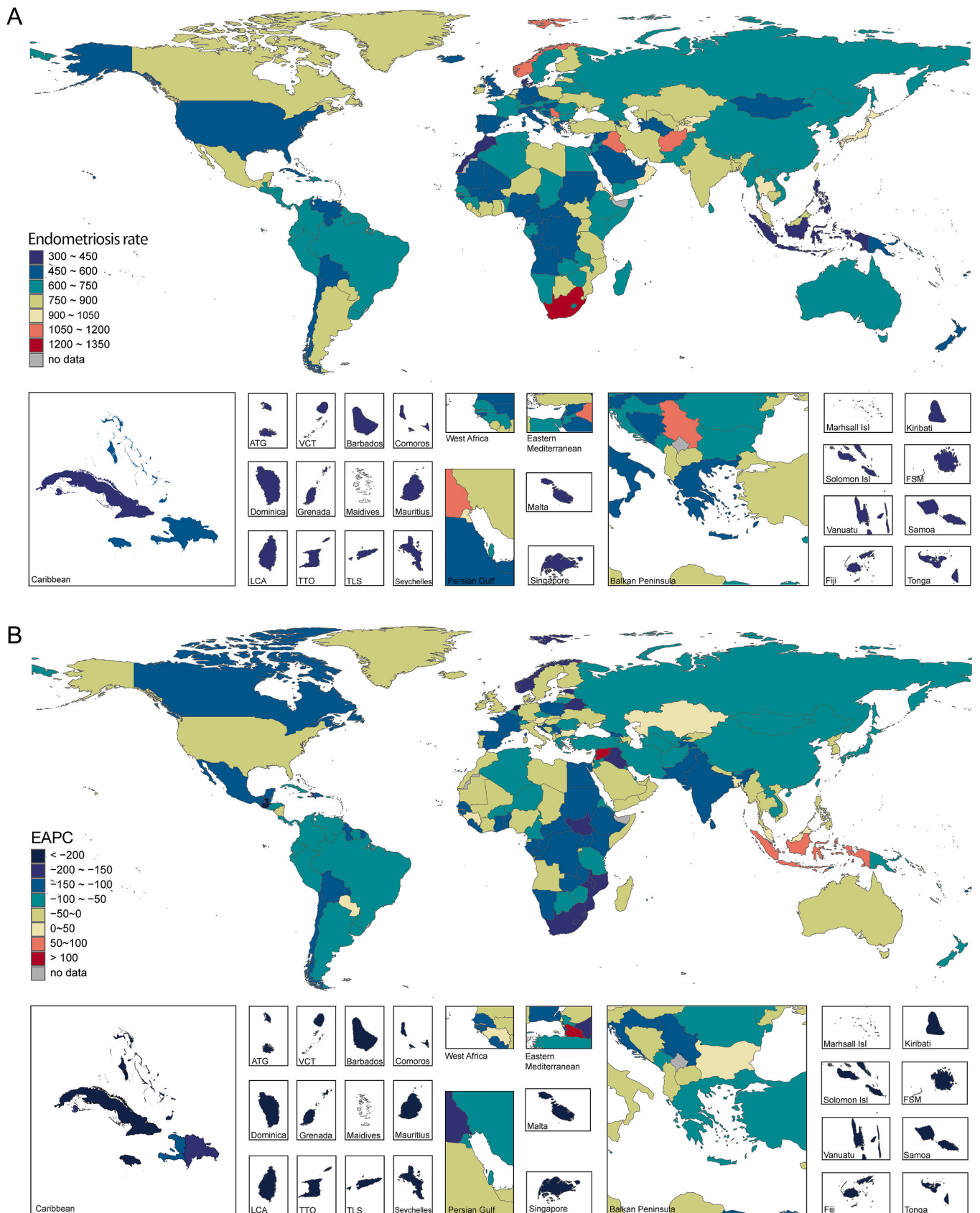


Fig. 4. Global disease burden of endometriosis prevalence in 204 countries and territories. (A) The percent change in age-standardized prevalence of endometriosis between 1990 and 2019; (B) The estimated annual percentage change of endometriosis age-standardized prevalence from 1990 to 2019.

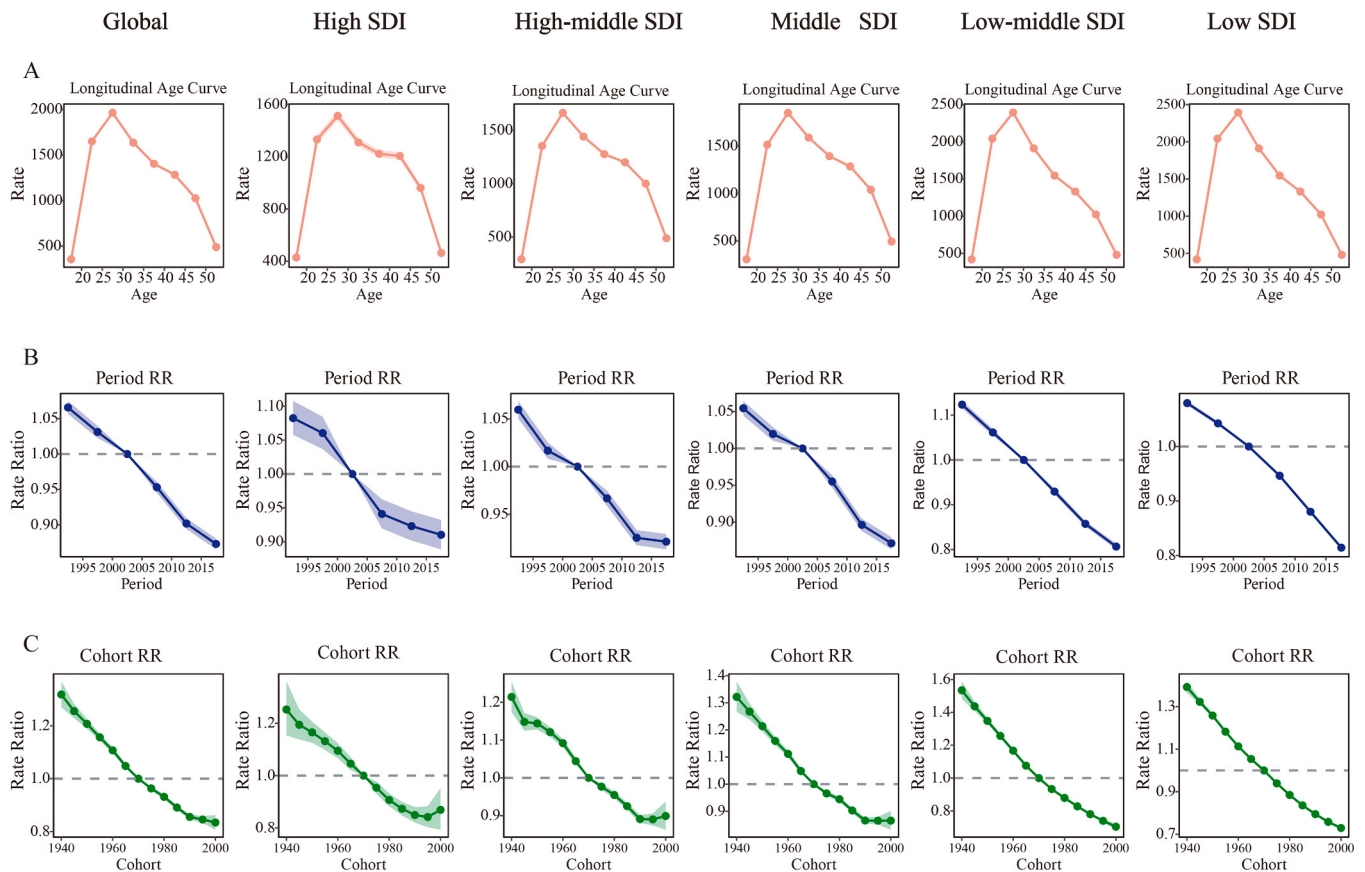


Fig. 6. Age–period–cohort impact of burden for ASPR of endometriosis. Red, blue, and green denotes the age, period, and birth cohort factors, respectively. (A) Longitudinal Age Curve. (B) Period RR. (C) Cohort RR.

study period. Using the 2000–2004 period group as the reference value (RR=1), the risk of endometriosis gradually decreased globally and in all SDI regions since that period. Moreover, we observed that in the low-middle SDI and the low SDI areas, the prevalence decreased rapidly after the 2000–2004 period group, while the high SDI and high-middle SDI started from the 2005–2009 period group and the 2010–2014 period group, respectively, demonstrating a relatively slow downward trend. After considering the influence of the correction period and age factors using the 1970–1974 birth cohort as the reference value (RR=1), the risk of endometriosis in the global and SDI regions basically decreased with the passage of the birth cohort. (Table S6, Table S2; Fig. 6C).

4. Discussion

From 1990 to 2019, this study demonstrated a downward trend in ASPR and DALYs in all regions and countries worldwide. This result indicates some success in the global efforts to combat endometriosis. The endometriosis awareness campaign might have had a huge impact on transforming the knowledge and attitudes of healthcare providers about endometriosis and the importance of early diagnosis of the condition [20].

The prevalence of endometriosis differs among various continents [21]. However, the prevalence rate is not necessarily comparable between countries and regions due to significant structural differences in their respective healthcare systems. The diagnosis and treatment of female endometriosis patients are influenced by various conditions, including views, society, economy, education, medical conditions, and security systems, and there may be delays in the diagnosis of female endometriosis patients in some economically underdeveloped regions. Cultural and social differences may also affect how individuals conceptualize pain [22], and there may be different healthcare

experiences and/or expectations between patients from different regions [23].

Birth cohort effects revealed various risk factors that affect different birth cohorts early in life, encompassing behavioral, environmental, and socioeconomic factors. The prevalence of endometriosis peaked between the ages of 25 and 29, maintained a high global prevalence of endometriosis between the ages of 30 and 39, and dropped rapidly when the age was over 40 or between the ages of 15 and 24, which may also be related to the diagnosis of endometriosis. Normalization of menstrual pain in women acts as an obstacle to the exploration and diagnosis of health issues, and the extensive utilization of hormonal contraceptives suppresses and conceals symptoms associated with endometriosis. However, our findings are inconsistent with those of Christ et al., who suggested that women aged 36–45 had the highest prevalence of endometriosis (2006–2015)[24], this may have something to do with different data sources.

The GBD 2019 study provides a comprehensive and high-quality assessment of the disease burden of endometriosis. However, this study has some limitations. First, the data pertaining to endometriosis from some regions and countries require improvement to generate estimates that are reasonable and relatively more accurate on the disease burden. Second, this study lacked data on factors that impact endometriosis, including diet, environment, and lifestyle. There are differences in social security systems, medical conditions, economies, and cultures in distinct regions and countries, and women have different needs when seeking treatment for endometriosis, which also affects the accuracy of this study. Finally, the 2019 GBD lacks a classification of endometriosis to account for the disease burden of different types of endometriosis separately.

This study presents a comprehensive survey of the global burden of endometriosis among women that can inform decision-makers about

healthcare priorities related to endometriosis, strengthen education, raise public awareness of female endometriosis, safeguard women's legitimate rights, reduce the stigma associated with women's pain visits and reduce delays in endometriosis diagnosis. The findings underscore the importance of maintaining the status and safety of women and implementing necessary preventive and management interventions to reduce the prevalence of female endometriosis and protect women's health.

Abbreviations

GBD, Global Burden of Disease; DALY, Disability-Adjusted Life-Year; SDI, Sociodemographic index; ASPR, Age-Standardized Prevalence Rate; ASR, Age-Standardized Rate; EAPC, Estimated Annual Percentage Change; UI, Uncertainty Interval.

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CRedit authorship contribution statement

Dong Yi Shen: Writing – review & editing, Writing – original draft. **Jing Li:** Writing – review & editing. **PanWei Hu:** Writing – review & editing. **Cong Qi:** Supervision. **Hong Yang:** Supervision.

Declaration of Competing Interest

The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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Declarations

The data in this study were sourced from a publicly available database and do not require ethical review.

This article has been published as a preprint. A preprint has previously been published [<https://doi.org/10.21203/rs.3.rs-3857347/v1>] [25].

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.eurox.2024.100363](https://doi.org/10.1016/j.eurox.2024.100363).

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