

Original Research

Global Burden of Endometriosis in 204 Countries and Territories from 1990 to 2019

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Abstract

Background: To our knowledge, no systematic update on the descriptive epidemiology of endometriosis and its trends has been published based on the Global Burden of Disease (GBD) datasets. To investigate the burden of endometriosis in 204 countries and territories from 1990 to 2019. **Methods:** Data were extracted from the Global Burden of Disease (GBD) 2019 datasets. Estimated annual percentage changes (EAPCs) were calculated to assess trends in the incidence and disability-adjusted life-years (DALYs) of endometriosis. Measures were stratified by region, country, age, and socio-demographic index (SDI). **Results:** From 1990 to 2019, the global incidence and DALYs of endometriosis increased by 10.37% and 16.36%, respectively. However, both the age-standardized incidence rate (ASIR) and age-standardized DALY rate of endometriosis showed downward trends (EAPC = -0.81 and -0.80, respectively). The ASIR decreased in all SDI regions, with the largest decrease observed in low-middle SDI regions [EAPC = -1.19, 95% Confidence Interval (CI): -1.21 to -1.16] except Eastern Europe, the only region where the ASIR increased (EAPC = 0.15, 95% CI: 0.01 to 0.29). The largest decreases in the ASIR and age-standardized DALY rate of endometriosis were observed in Qatar and Oman, respectively. **Conclusions:** The global incidence and DALYs of endometriosis continued to increase during 1990–2019. However, the ASIR and age-standardized DALY rate have shown decreasing trends worldwide, with increasing trends detected only in Eastern Europe.

Keywords: endometriosis; incidence; disability-adjusted life-year (DALY); Global Burden of Disease

1. Introduction

Endometriosis, as a common gynecological disease, occurs in women of childbearing age, and refers to the site where endometrial glands and stroma are implanted outside the uterine mucosa, mainly manifested as chronic pelvic pain, pelvic cyst. The incidence rate of endometriosis is about 5%–15% [1]. The pathogenesis of endometriosis is complex, showing benign morphological manifestations in pathology, but with implantation, invasion and distant metastasis, such as relapse and relapse, which affect women's reproductive health and quality of life seriously [2].

To our knowledge, no systematic update on the descriptive epidemiology of endometriosis and its trends has been published based on the Global Burden of Disease (GBD) datasets. In this study, we extracted detailed data of the incidence and disability-adjusted life-years (DALY) of endometriosis from the GBD 2019 dataset to assess temporal trends in the incidence and DALYs of endometriosis at the global, regional, and national levels from 1990 to 2019 in terms of age and social development index (SDI).

2. Methods

2.1 Overview

The GBD 2019 estimates the incidence of 369 diseases and injuries among both men and women in 204 countries and regions, which are divided into 21 regions and 7 super regions [3]. This study used data on the annual inci-

dence, age-standardized incidence rates (ASIRs), DALYs, and age-standardized DALY rates of endometriosis from 1990 to 2019 collected from the Global Health Data Exchange (GHDx) query tool (<http://ghdx.healthdata.org/gbd-results-tool>).

The SDI is a comprehensive index of the per capita lagging distributive income of women of childbearing age, the average number of years of education, and the fertility rate in a country [4]. According to SDI values in 2019, the 204 countries and territories were divided into five regions, namely, low, low-middle, middle, high-middle, and high SDI regions. This study followed the Guidelines for Accurate and Transparent Health Estimates Reporting. The Ningbo Women and Children's Hospital approved the study.

2.2 Estimation Framework

The incidence of endometriosis was estimated using the Bayesian element regression disease modeling tool Dismod-MR [3]. Nonspecific codes for all available morbidity data were corrected and used to estimate the incidence of the causes, including endometriosis, listed in the GBD datasets. Etiology models were used to estimate incidence by age, year, and country. The number of DALYs due to endometriosis was calculated as the sum of years of life lived with a disability (YLDs) and years of life lost due to premature death (YLLs).



Table 1. The incident cases and ASIR of endometriosis in 1990 and 2019 and its trends.

Characteristics	1990	2019	1990–2019	
	ASIR (per 100,000)	ASIR (per 100,000)	Change in Number No. (%)	EAPC
	No. (95% UI)	No. (95% UI)		No. (95% CI)
Global	60.40 (43.44, 85.62)	48.31 (35.21, 68.15)	0.10 (0.07, 0.14)	–0.81 (–0.86, –0.77)
Sociodemographic index	-	-	-	-
Low SDI	74.28 (52.71, 104.55)	54.55 (38.54, 78.00)	0.70 (0.65, 0.75)	–1.09 (–1.13, –1.05)
Low-middle SDI	70.28 (50.26, 99.25)	50.47 (36.50, 71.14)	0.20 (0.16, 0.24)	–1.19 (–1.21, –1.16)
Middle SDI	59.54 (42.55, 83.65)	47.55 (34.36, 66.49)	0.04 (–0.02, 0.10)	–0.78 (–0.84, –0.73)
High-middle SDI	53.80 (38.42, 76.06)	44.36 (32.36, 61.84)	–0.08 (–0.14, –0.01)	–0.67 (–0.72, –0.61)
High SDI	49.98 (36.18, 70.09)	40.81 (29.82, 56.83)	–0.14 (–0.19, –0.08)	–0.87 (–0.93, –0.81)
Region	71.01 (50.71, 99.62)	51.09 (36.73, 71.71)	0.21 (0.11, 0.33)	–1.08 (–1.13, –1.04)
Andean Latin America	64.88 (45.37, 93.42)	57.20 (40.87, 81.22)	0.05 (–0.05, 0.15)	–0.33 (–0.44, –0.22)
Australasia	61.53 (44.01, 87.49)	48.60 (35.24, 68.56)	–0.02 (–0.09, 0.05)	–0.81 (–0.83, –0.80)
Caribbean	69.72 (50.10, 97.74)	60.87 (43.46, 86.37)	0.21 (0.12, 0.29)	–0.30 (–0.43, –0.16)
Central Asia	42.08 (30.23, 58.35)	38.03 (27.23, 53.31)	–0.27 (–0.31, –0.23)	–0.35 (–0.46, –0.24)
Central Europe	63.57 (44.80, 89.85)	40.15 (28.08, 56.56)	–0.04 (–0.15, 0.06)	–1.69 (–1.74, –1.64)
Central Latin America	68.29 (48.40, 97.21)	49.43 (35.17, 70.80)	0.82 (0.66, 1.01)	–1.03 (–1.13, –0.94)
Central sub-Saharan Africa	50.97 (35.82, 70.57)	36.41 (26.13, 49.36)	–0.26 (–0.34, –0.17)	–1.14 (–1.30, –0.98)
East Asia	67.05 (48.42, 93.34)	65.48 (47.27, 90.62)	–0.18 (–0.23, –0.13)	0.15 (0.01, 0.29)
Eastern Europe	67.37 (47.99, 94.47)	48.93 (34.65, 69.94)	0.72 (0.66, 0.78)	–1.11 (–1.14, –1.07)
Eastern sub-Saharan Africa	60.48 (43.24, 85.79)	52.94 (38.73, 73.01)	–0.26 (–0.33, –0.18)	–0.70 (–0.79, –0.60)
High-income Asia Pacific	46.17 (32.00, 65.47)	31.23 (23.18, 42.66)	–0.27 (–0.38, –0.15)	–1.83 (–1.98, –1.68)
High-income North America	82.18 (58.35, 114.87)	60.28 (43.01, 85.00)	0.37 (0.27, 0.49)	–1.39 (–1.46, –1.31)
North Africa and middle East	74.83 (52.93, 103.53)	67.94 (47.69, 95.73)	0.91 (0.77, 1.07)	–0.33 (–0.35, –0.30)
Oceania	70.98 (50.83, 100.61)	51.01 (36.71, 72.27)	0.28 (0.25, 0.32)	–1.10 (–1.14, –1.05)
South Asia	66.43 (48.17, 91.66)	55.06 (39.41, 76.17)	0.20 (0.13, 0.28)	–0.61 (–0.65, –0.58)
Southeast Asia	50.66 (36.37, 73.10)	43.04 (30.74, 60.21)	0.15 (0.06, 0.25)	–0.49 (–0.54, –0.44)
Southern Latin America	58.80 (41.79, 82.62)	42.99 (30.93, 60.97)	0.11 (0.03, 0.20)	–1.04 (–1.07, –1.02)
Southern sub-Saharan Africa	58.14 (40.38, 83.83)	45.51 (32.29, 64.28)	0.11 (0.01, 0.22)	–0.87 (–0.91, –0.83)
Tropical Latin America	40.45 (28.80, 59.20)	38.92 (27.58, 56.29)	–0.12 (–0.17, –0.06)	–0.11 (–0.13, –0.08)
Western Europe	65.56 (46.68, 92.35)	50.04 (35.71, 71.33)	0.91 (0.84, 0.97)	–0.94 (–0.99, –0.89)
Western sub-Saharan Africa				

ASIR, age-standardized incidence rate; EAPC, estimated annual percentage change; NA, not available; UI, uncertainty interval.

2.3 Case Definition of Endometriosis

For GBD 2019, endometriosis cases was defined according to the American College of Obstetricians and Gynecologists (ACOG) guidelines as cases diagnosed by pelvic exam confirmed by laparoscopy or pathology [5]. Determination of endometriosis in the GBD study is based on the International Classification of Diseases (ICD)-10 codes N80–N80.9.

2.4 Statistical Analyses

We calculated the estimated annual percentage changes (EAPCs) in the age-standardized rates (ASRs) of endometriosis. The EAPCs describe ASR trends within a specified time interval and were determined by the formula: $Y = \alpha + \beta X + \varepsilon$, where Y means $\ln(\text{ASR})$, X is the calendar year, ε is the error term, and β refers to the positive or negative ASR trend. Assuming that the natural logarithm of the ASR is linear with time, then $\text{EAPC} = 100 \times [\exp(\beta) - 1]$. The 95% confidence interval (CI) of

an EAPC was calculated from the linear model. When the EAPC and its 95% CI lower limit are both positive, its corresponding ASR shows an upward trend; in contrast, when the EAPC and its 95% CI upper limit are both negative, its corresponding ASR shows a downward trend. Otherwise, the ASR is regarded as stable [6].

The correlations between the EAPCs and ASRs and between the SDIs and EAPCs were calculated using Gaussian process regression and Pearson's correlation coefficient (ρ). All calculations were performed using R software (version 3.5.1, R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1 Changes in the Incidence of Endometriosis

At the global level, the incidence of endometriosis was 3,430,094 (95% UI (uncertainty interval), 2,747,346–5,326,824) in 1990 and 3,785,955 (95% UI, 2,434,876–4,932,100) in 2019 (Table 1), indicating a 10.37% increase

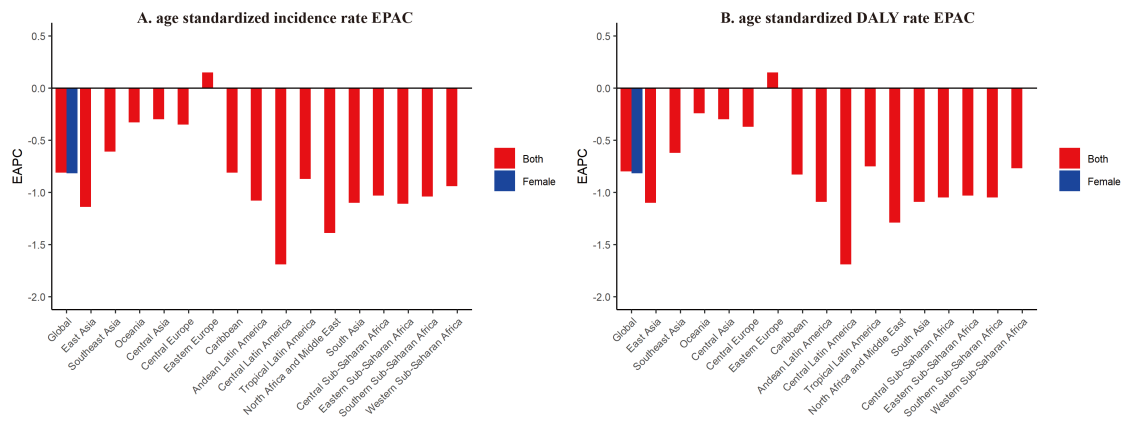


Fig. 1. The EAPC of endometriosis ASRs from 1990 to 2019, by sex and region. (A) The EAPC of ASIR. (B) The EAPC of age-standardized DALY rate. EAPC, estimated annual percentage change; ASRs, age-standardized rates; ASIR, age standardized incidence rate; DALY, disability adjusted life-year.

in incidence during this period. In contrast, the ASIR declined from 60.40/100,000 persons (95% UI, 43.44–85.62) in 1990 to 48.31/100,000 persons (95% UI, 35.21–68.15) in 2019 (Table 1, Fig. 1A, Supplementary Fig. 1A).

At the SDI level, as shown in Table 1, the ASIR in the five SDI regions showed declining trends from 1990 to 2019 with EAPCs as follows: -1.09 (95% CI: -1.13 to -1.05) in low SDI regions; -1.19 (95% CI: -1.21 to -1.16) in low-middle SDI regions; -0.78 (95% CI: -0.84 to -0.73) in middle SDI regions; -0.67 (95% CI: -0.72 to -0.61) in high-middle SDI regions; and -0.87 (95% CI: -0.93 to -0.81) in high SDI regions. The highest incidence both globally and in all SDI regions was reported in the 20–24-year age group (Supplementary Fig. 2).

At the country level, in 2019, the highest ASIR of endometriosis was observed in New Zealand (86.42 per 100,000 population), followed by Afghanistan (71.83 per 100,000 population) and Solomon Islands (71.01 per 100,000 population), whereas the lowest ASIR was observed in Iceland (21.47 per 100,000 population), followed by Qatar (27.89 per 100,000 population) and Malta (29.42 per 100,000 population) (Supplementary Tables 1,2, Fig. 2A). From 1990 to 2019, the largest decrease in the ASIR of endometriosis was found in Qatar (EAPC, -2.67), whereas the largest increase was found in Iceland (EAPC, 1.78) (Supplementary Tables 1,2, Fig. 3A). The three countries with the highest EAPC were Iceland, Sweden, and the United Kingdom, whereas the three countries with the lowest EAPC were Qatar, Equatorial Guinea, and Oman (Supplementary Table 1).

At the country level, the ASIR showed an upward trend in 8 countries (Austria, Belarus, Iceland, Kazakhstan, Kyrgyzstan, the Russian Federation, Sweden, and the United Kingdom) but a downward trend in the remaining 196 countries. The ASIR showed an upward trend in 9 countries (Austria, Belarus, Estonia, Georgia, Iceland, Kyrgyzstan, the Russian Federation, Sweden, and the United Kingdom) but a downward trend in the remaining 195 countries (Supplementary Table 2, Fig. 3A).

At the region level, in 2019, the highest ASIR of endometriosis was observed in Oceania (67.94 per 100,000 population), followed by Eastern Europe (65.48 per 100,000 population) and Central Asia (60.87 per 100,000 population), whereas the lowest ASIR was observed in High-income North America (31.23 per 100,000 population), followed by East Asia (36.41 per 100,000 population) and Central Europe (38.03 per 100,000 population) (Supplementary Table 3). From 1990 to 2019, the largest decrease in the ASIR of endometriosis was observed in High-income North America (EAPC, -1.83) (Supplementary Table 3). At the region level, the ASIR showed an upward trend in only one region, namely Eastern Europe, but a downward trend in the remaining 20 regions (Table 1).

The three regions with the highest ASIR of endometriosis were Central Asia, Eastern Europe, and Oceania; the three regions with the lowest ASIR were High-income North America, East Asia, and Central Europe. The three regions with the highest EAPC were Central Asia, Western Europe, and Eastern Europe, whereas the three regions with the lowest EAPC were High-income North America, Central Latin America, and North Africa and Middle East (Supplementary Table 3).

3.2 Change in the DALYs due to Endometriosis

At the global level, the DALYs due to endometriosis were 1,882,003 (95% UI, 55,801–79,370) in 1990 and 2,250,033 (95% UI, 87,968–118,746) in 2019 (Table 1, Supplementary Fig. 1A), indicating a 16.36% increase in DALYs during the study period. In contrast, the age-standardized DALY rate decreased significantly from 35.08/100,000 persons (95% UI, 20.98–55.56) in 1990 to

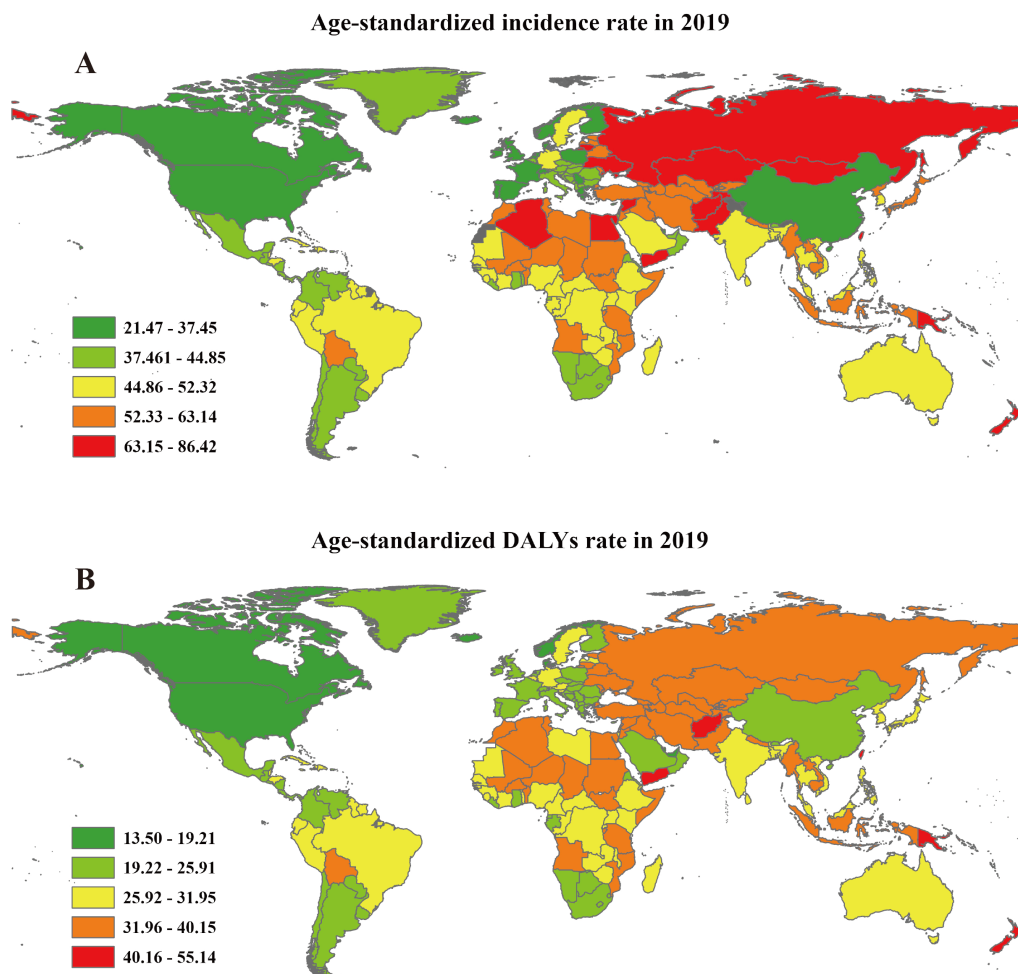


Fig. 2. The global ASRs of endometriosis in 204 countries in 2019, by countries. (A) The ASIR. (B) The age-standardized DALY rate. ASIR, age standardized incidence rate; DALY, disability adjusted life-year.

28.05/100,000 persons (95% UI, 16.87–44.42) in 2019, with an EAPC of -0.80 (95% CI: -0.83 to -0.76) (Table 2, Fig. 1B, Supplementary Fig. 1B).

At the SDI level, the age-standardized DALY rate in all SDI regions showed a declining trend (Table 2). The highest DALYs both globally and in all SDI regions were reported in the 25–29-year age group (Supplementary Fig. 3).

At the country level, in 2019, the highest age-standardized DALY rate of endometriosis was observed in New Zealand (55.14 per 100,000 population), followed by Taiwan (Province of China) (47.76 per 100,000 population) and Afghanistan (44.68 per 100,000 population), whereas the lowest age-standardized DALY rate was observed in Iceland (13.50 per 100,000 population), followed by Qatar (14.44 per 100,000 population) and the United States of America (17.04 per 100,000 population) (Supplementary Table 1, Fig. 2A). From 1990 to 2019, the largest decreased in the age-standardized DALY rate of endometriosis was observed in Oman (EAPC, -2.81), whereas the

largest increase was observed in Sweden (EAPC, 1.54). (Supplementary Table 1, Fig. 3B).

4. Discussion

Based on the GBD 2019, this study reported the global ASIR and age-standardized DALY rate of endometriosis and the temporal trends and geographic patterns in them from 1990 to 2019 at the global, regional, and national levels. Given the increase in the global population, the incidence and DALYs were found to increase during the study period, but the ASIR and age-standardized DALY rate showed decreasing trends worldwide, with increasing trends observed only in Eastern Europe. Moreover, after stratification by SDI quintiles, the largest decline in the disease burden of endometriosis was detected in the low-middle SDI regions, followed by the low SDI, high SDI, middle SDI, and high-middle SDI regions. Our results demonstrate substantial improvement in endometriosis management worldwide and highlight the importance of

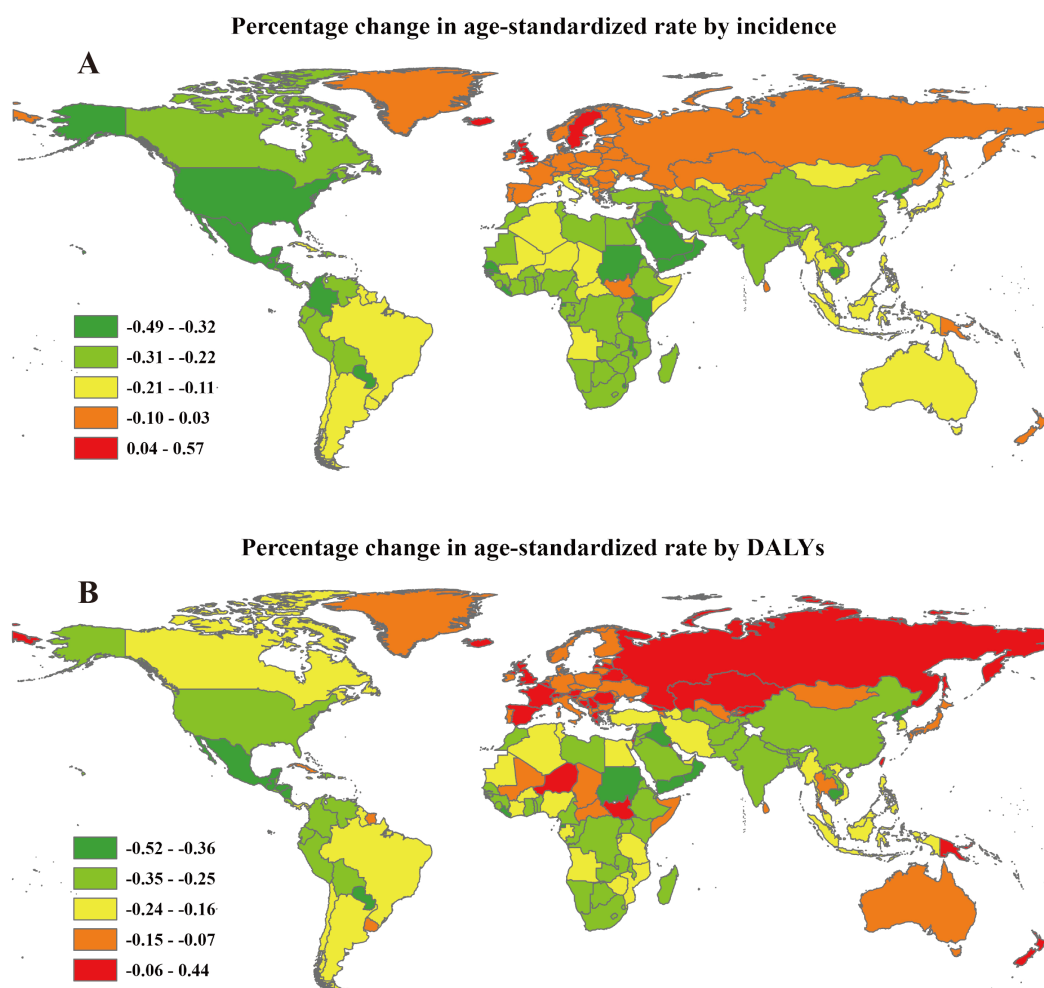


Fig. 3. The global EAPC of endometriosis ASRs from 1990 to 2019, by countries. (A) The EAPC of ASIR. (B) The EAPC of age-standardized DALY rate. EAPC, estimated annual percentage change; ASRs, age-standardized rates; ASIR, age standardized incidence rate; DALY, disability adjusted life-year.

endometriosis monitoring and treatment in countries with a high burden of this disease, especially among women aged 20–29 years.

Endometriosis is a common disease in women of reproductive age, and it is a “modern disease”, frequently-occurring disease, affecting about 6% to 10% of women of reproductive age [7,8], and 20% to 50% of women with Infertility [9], and Leiserowitz *et al.* [10] believe that the incidence of endometriosis is increasing year by year. The time of diagnosis of endometriosis usually lags behind that of the disease. Therefore, attention should be paid to women in puberty and early reproductive period, and extensive epidemiological research should be carried out. The clinical diagnosis of endometriosis (referring to non-surgical diagnosis) has certain value, but the “gold standard” for diagnosis is surgery and postoperative pathological examination. The current gold standard for diagnosing endometriosis is laparoscopy [11]. However, it is often impossible to diag-

nose endometriosis in the first place, resulting in delayed diagnosis.

Given the inconsistencies in the level of health care among countries, women with a higher socioeconomic status (SES) in developed countries may have better access to health care and therefore would be more likely to be diagnosed with endometriosis [12]. In contrast, due to limited medical resources, the burden of endometriosis would likely have been underestimated in developing countries. Consistently, our results showed that the highest ASIRs and age-standardized DALY rates from 1990 to 2019 were observed in high SDI regions, where women have better access to health care services. Therefore, given the limited availability of burden estimates in developing countries/territories, more studies should focus on the development of screening tools for endometriosis in such countries to enable accurate estimation of the number of affected women.

Table 2. The DALY cases and age-standardized DALY rate of endometriosis in 1990 and 2019 and its trends.

Characteristics	1990	2019	1990-2019	
	age-standardized DALY rate (per 100,000)	age-standardized DALY rate (per 100,000)	Change in Number No. (%)	EAPC
	No. (95% UI)	No. (95% UI)		No. (95% CI)
Global	35.08 (20.98, 55.56)	28.05 (16.87, 44.42)	0.20 (0.15, 0.24)	-0.80 (-0.83, -0.76)
Sociodemographic index	-	-	-	-
Low SDI	45.56 (26.90, 72.24)	33.48 (19.88, 53.74)	0.70 (0.65, 0.76)	-1.09 (-1.14, -1.04)
Low-middle SDI	42.22 (25.11, 67.28)	29.68 (17.70, 47.46)	0.25 (0.20, 0.30)	-1.26 (-1.29, -1.23)
Middle SDI	34.08 (20.36, 53.90)	27.37 (16.45, 43.13)	0.20 (0.13, 0.27)	-0.74 (-0.79, -0.68)
High-middle SDI	31.03 (18.54, 49.24)	25.52 (15.31, 40.09)	0.04 (-0.03, 0.11)	-0.65 (-0.70, -0.59)
High SDI	29.08 (17.29, 45.57)	24.08 (14.76, 37.14)	-0.07 (-0.14, 0.00)	-0.84 (-0.92, -0.75)
Region	-	-	-	-
Andean Latin America	41.64 (24.69, 65.95)	29.61 (17.97, 47.11)	0.32 (0.18, 0.46)	-1.09 (-1.16, -1.01)
Australasia	38.11 (22.28, 61.24)	33.20 (19.87, 53.43)	0.11 (-0.01, 0.25)	-0.34 (-0.49, -0.19)
Caribbean	36.52 (21.84, 58.66)	28.78 (16.93, 46.25)	0.07 (-0.01, 0.17)	-0.83 (-0.85, -0.80)
Central Asia	41.33 (24.58, 65.56)	36.09 (21.35, 57.19)	0.31 (0.21, 0.42)	-0.30 (-0.44, -0.16)
Central Europe	24.45 (14.60, 38.50)	22.08 (13.09, 35.29)	-0.20 (-0.24, -0.15)	-0.37 (-0.49, -0.26)
Central Latin America	37.24 (22.26, 59.57)	23.46 (13.88, 37.10)	0.06 (-0.04, 0.18)	-1.69 (-1.75, -1.64)
Central sub-Saharan Africa	40.83 (23.86, 65.42)	29.37 (17.37, 47.47)	0.83 (0.65, 1.02)	-1.05 (-1.15, -0.95)
East Asia	28.91 (17.07, 46.01)	21.04 (12.73, 33.12)	-0.08 (-0.17, 0.03)	-1.10 (-1.26, -0.93)
Eastern Europe	39.97 (24.12, 62.95)	39.03 (23.33, 61.47)	-0.12 (-0.17, -0.07)	0.15 (0.01, 0.29)
Eastern sub-Saharan Africa	40.10 (23.80, 63.86)	29.81 (17.68, 47.75)	0.78 (0.69, 0.87)	-1.03 (-1.06, -1.00)
High-income Asia Pacific	34.88 (20.55, 56.34)	30.12 (18.37, 46.33)	-0.18 (-0.26, -0.09)	-0.76 (-0.85, -0.66)
High-income North America	24.69 (14.12, 40.24)	17.25 (10.77, 26.46)	-0.21 (-0.36, -0.05)	-1.69 (-1.83, -1.55)
North Africa and middle East	48.18 (28.68, 77.01)	35.08 (21.01, 56.00)	0.54 (0.44, 0.66)	-1.29 (-1.37, -1.22)
Oceania	44.96 (26.52, 70.81)	41.71 (24.62, 66.48)	1.05 (0.87, 1.29)	-0.24 (-0.27, -0.21)
South Asia	42.49 (25.30, 67.77)	29.93 (17.89, 48.14)	0.32 (0.27, 0.37)	-1.09 (-1.13, -1.06)
Southeast Asia	38.70 (23.44, 60.78)	31.90 (19.02, 50.08)	0.33 (0.24, 0.42)	-0.62 (-0.65, -0.58)
Southern Latin America	29.76 (17.36, 48.24)	24.95 (14.56, 40.43)	0.20 (0.09, 0.33)	-0.54 (-0.60, -0.48)
Tropical Latin America	32.93 (19.45, 54.07)	27.15 (16.23, 43.66)	0.30 (0.19, 0.44)	-0.75 (-0.85, -0.65)
Western Europe	26.17 (15.52, 41.64)	24.57 (14.72, 39.98)	-0.08 (-0.14, -0.02)	-0.22 (-0.26, -0.18)
Western sub-Saharan Africa	37.95 (22.29, 60.77)	30.18 (17.85, 47.67)	0.97 (0.89, 1.05)	-0.77 (-0.82, -0.73)

DALY, disability adjusted life-years; NA, not available; UI, uncertainty interval.

From 1990 to 2019, the global incidence and DALYs of endometriosis were found to increase, but the ASIR and age-standardized DALY rate showed decreasing trends worldwide. Increasing trends in these ASRs were only observed in Eastern Europe, which emphasizes the need for improving prevention and treatment strategies for endometriosis in these regions. Globally, the ASIR of endometriosis was highest in women aged 20–24 years, and the age-standardized DALY rate was highest in women aged 25–29 years. The age of onset of endometriosis is mainly in the reproductive age. In order to avoid delaying the patient's condition and reduce the misdiagnosis rate, the diagnostic level of endometriosis needs to be further improved. Laparoscopy is currently an important method for the diagnosis and treatment of endometriosis, but considering the invasiveness of the operation, the limitations of medical technology and the economic conditions of patients, laparoscopy is still not the preferred method for the diagnosis and treatment of endometriosis [1,2]. Future studies are warranted recommended the convenient prevention, diagnostic, and treatment policies for endometriosis.

To the best of our knowledge, the current study is the first to comprehensively analyze the burden of endometriosis from 1990 to 2019 at global, regional, and national levels and further explore the relationship between endometriosis burden estimates and SES. Compared with earlier GBD studies, the GBD 2019 used more sophisticated up-to-date statistical approaches, in addition to a unified and standardized approach, to obtain globally comparable estimates of the temporal trends and geographic patterns in the ASIRs and DALY rates of 369 diseases [12,13]. This makes the GBD datasets an ideal source of empirical data on preferred case definitions and study methods for epidemiologists [12,13].

Despite these strengths, several limitations of the present study should be taken into consideration. First, the true incidence of endometriosis was difficult to determine, Medical history and gynecological examination are the main basis for clinical diagnosis of endometriosis. Due to the often atypical symptoms of patients and the lack of understanding of the clinical characteristics of the disease by some doctors, the rate of misdiagnosis and missed diagnosis is high. Therefore, the diagnosis should be combined with imaging examinations such as ultrasound and MRI, laparoscopy and laboratory examinations [1,2]. Laparoscopy is an effective auxiliary diagnostic method at present, and biopsy is performed when necessary [1,2]. Second, the diagnosis of endometriosis may be influenced by the variation in clinical symptoms not adequately captured, differences in clinical definitions between regions and individual practitioners, or the alternate interpretation of the same symptoms in different healthcare systems [13,14]. Third, population-based prevalence and incidence data on endometriosis were sparse or not available for many countries and regions where the level of health care is low.

Fourth, endometriosis not only causes serious economic losses but also potentially reduces patients' overall well-being, which was not included in the burden estimates in the GBD 2019.

5. Conclusions

In conclusion, the burden estimates of endometriosis have been decreasing globally over the past few decades. However, the ASIRs and age-standardized DALY rates of endometriosis have shown increasing trends in Eastern Europe and some countries in this period. These results are based on limited data, indicating that the burden of endometriosis may be underestimated. Therefore, future studies are required to collect more data on the epidemiological characteristics of endometriosis to enable more accurate estimates of the disease burden.

Author Contributions

JF took part in the collection and analysis of data, and wrote and revised the manuscript. SZ and JC participated in data collection and results interpretation. JZ checked and revised the manuscript. JY managed and developed the project. All authors have read and approved the final manuscript.

Ethics Approval and Consent to Participate

The Ningbo Women & Children's Hospital approved this study (20220205).

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.31083/j.ceog4910235>.

References

- [1] Koninckx PR, Fernandes R, Ussia A, Schindler L, Wattiez A, Al-Suwaidei S, *et al.* Pathogenesis Based Diagnosis and Treatment of Endometriosis. *Frontiers in Endocrinology*. 2021; 12: 745548.
- [2] Arezzo F, Cormio G, La Forgia D, Kawosha AA, Mongelli M, Putino C, *et al.* The Application of Sonovaginography for Implementing Ultrasound Assessment of Endometriosis and Other Gynaecological Diseases. *Diagnostics*. 2022; 12: 820.

- [3] GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020; 396: 1204–1222.
- [4] GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018; 392: 1789–1858.
- [5] Sinaii N, Cleary SD, Ballweg ML, Nieman LK, Stratton P. High rates of autoimmune and endocrine disorders, fibromyalgia, chronic fatigue syndrome and atopic diseases among women with endometriosis: a survey analysis. *Human Reproduction*. 2002; 17: 2715–2724.
- [6] Liu X, Jiang J, Yu C, Wang Y, Sun Y, Tang J, *et al*. Secular trends in incidence and mortality of bladder cancer in China, 1990–2017: a joinpoint and age-period-cohort analysis. *Cancer Epidemiology*. 2019; 61: 95–103.
- [7] Giudice LC, Kao LC. Endometriosis. *The Lancet*. 2004; 364: 1789–1799.
- [8] Treloar SA, O'Connor DT, O'Connor VM, Martin NG. Genetic influences on endometriosis in an Australian twin sample. *Fertility and Sterility*. 1999; 71: 701–710.
- [9] Gao X, Outley J, Botteman M, Spalding J, Simon JA, Pashos CL. Economic burden of endometriosis. *Fertility and Sterility*. 2006; 86: 1561–1572.
- [10] Leiserowitz GS, Gumbs JL, Oi R, Dalrymple JL, Smith LH, Ryu J, *et al*. Endometriosis-related malignancies. *International Journal of Gynecological Cancer*. 2003; 13: 466–471.
- [11] Pascoal E, Wessels JM, Aas-Eng MK, Abrao MS, Condous G, Jurkovic D, *et al*. Strengths and limitations of diagnostic tools for endometriosis and relevance in diagnostic test accuracy research. *Ultrasound in Obstetrics & Gynecology*. 2022. (in press)
- [12] Zhang S, Gong T, Wang H, Zhao Y, Wu Q. Global, regional, and national endometriosis trends from 1990 to 2017. *Annals of the New York Academy of Sciences*. 2021; 1484: 90–101.
- [13] Han L, Liu J, Yin P, Cai T, Zhou M. Burden of maternal disorders in China from 1990 to 2019: Analysis of the Global Burden of Disease Study 2019. *The Lancet Regional Health - Western Pacific*. 2021; 11: 100141.
- [14] Bougie O, Yap MI, Sikora L, Flaxman T, Singh S. Influence of race/ethnicity on prevalence and presentation of endometriosis: a systematic review and meta-analysis. *BJOG*. 2019; 126: 1104–1115.