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Global and regional trends in the burden of surgically confirmed endometriosis from 1990 to 2021

Ruijie Li¹, Ling Zhang^{1*} and Yi Liu^{1*}

Abstract

Background endometriosis as a common gynecologic finding significantly affects the quality of life of many women. An accurate understanding of the epidemiological characteristics of endometriosis is essential for disease control and prevention. We aimed to use the latest data from the Global Burden of Disease (GBD) 2021 to comprehensively analyze the various epidemiological indicators of surgically confirmed endometriosis and their changing trends to better measure the disease burden and help improve health management.

Methods We delineated incidence, prevalence, and years lived with disability (YLDs) of surgically confirmed endometriosis at the global, regional, and national levels. The estimated annual percentage change (EAPC) was calculated to assess temporal trends in the age-standardized rate (ASR). In addition, we used joinpoint regression models to describe local trends in these indicators, assessed the correlation between disease burden and Socio-demographic index (SDI) levels, and used decomposition analysis to quantitatively analyze the driving factors leading to changes in disease burden.

Results Globally, the age-standardized rate of incidence, prevalence, and YLDs of surgically confirmed endometriosis all showed a decreasing trend from 1990 to 2021. The burden of surgically confirmed endometriosis is mainly concentrated in women aged 20–30 years and declines with increasing SDI levels. The results of the decomposition analysis indicated that population growth is the main driving factor for the upward in the number of incidence, prevalence, and YLDs cases of endometriosis worldwide.

Conclusions The overall burden of endometriosis has decreased globally from 1990 to 2021, but there are regional disparities. Managing this condition remains a major challenge, and more refined policies and interventions are needed to effectively address the burden of endometriosis.

Keywords Endometriosis, Disease burden, Estimated annual percentage change, Incidence, Prevalence

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Introduction

Endometriosis is a prevalent gynecological finding defined by the presence of endometrium-like epithelium and/or stroma (lesions) outside the endometrium and myometrium, usually with an associated inflammatory process [1]. According to surveys, over 176 million women worldwide suffer from this condition, constituting 5–10% of women of reproductive age [2]. Although endometriosis is considered benign, it exhibits malignant behaviors such as invasion, implantation, and recurrence [3]. This chronic and refractory trait consumes a large amount of social resources and causes a serious economic burden [4]. Endometriosis often leads to infertility and chronic pelvic discomfort [5], and patients are prone to experience depression and anxiety [6], which severely affect the physical health, mental health, and quality of life of many women [7].

Although the impact of endometriosis on women's health urgently needs attention, global research data on the burden of this disease are currently very limited. Given the diagnostic barrier and delay, the exact prevalence of endometriosis is unknown. This is due to the fact that although laparoscopy is the gold standard for diagnosis, it is an invasive examination that is not routinely used in women with a suspicion of endometriosis. Sometimes doctors tend to give a “working diagnosis” of probable endometriosis and prompt early drug treatment without waiting for a more definitive diagnosis, which makes accurate assessment difficult [8–10]. Similarly, there are no established criteria for the exact time of onset of endometriosis, as symptoms must be present and sufficiently disruptive to obtain a referral for a definitive diagnosis. Different nonspecific symptoms, clinician awareness of endometriosis, and economic and geographic access to care all contribute to an average delay of 7 years from symptom onset to surgical diagnosis [11].

Therefore, it should be recognised that when attempting to conduct epidemiological studies on endometriosis, we need to take into account that it varies across populations and across time and space. This requires a large amount of well-documented longitudinal data. To address this issue, the study utilized the latest data from the Global Burden of Disease (GBD) to conduct a comprehensive and updated analysis of various epidemiological indicators of surgically confirmed endometriosis. In this study, we described the long-term and partial spatio-temporal trends of the incidence, prevalence, and YLDs of endometriosis at global and regional levels, and analyzed the contributions of different factors to changes in the epidemiological indicators of endometriosis from multiple perspectives. The aim is to better measure the current burden of endometriosis to enhance women's health awareness, help improve health management,

and develop timely and effective prevention and control strategies.

Methods

Overview

The GBD 2021 database (<https://ghdx.healthdata.org/gbd-2021>), led by the Institute for Health Metrics and Evaluation (IHME), provides the most comprehensive and up-to-date data assessment of the descriptive epidemiology of diseases in 21 regions and 204 countries and territories from 1990 to 2021, using all available data. All data is calculated by direct query and downloaded from the GBD results tool. A detailed description of the method can be found on the help page of the database and other publications [12]. The GBD collects health data from life records, censuses, registers, health surveys, population surveillance, administrative reports, scientific research, discharge records, records of outpatient visits, and health insurance claims, as well as many other sources. These are then input into an algorithm to generate an estimate of the burden of disease. In the GBD study, disease estimates were generated by age, year, and location using the Bayesian meta-regression tool DisMod-MR 2.1 to ensure consistent epidemiological parameters for the conditions under study.

Data source

Data on the global burden of surgically confirmed endometriosis were obtained from published sources using the Global Health Data Exchange Query Tool. GBD 2021 defines endometriosis cases according to the ACOG guidelines as cases diagnosed by pelvic exam confirmed by laparoscopy or laparotomy. This study obtained global, regional, territorial, and socio-demographic index (SDI) quintile data on incidence, prevalence, and years lived with disability (YLDs) of endometriosis from 1990 to 2021 from the GBD 2021. Incidence is the frequency of new cases of a disease in a population over a certain period of time. Prevalence is the ratio of new and old cases of a disease in the entire population over a certain period of time. YLDs are years of life lost due to disability caused by the disease, estimated as the product of prevalence estimate and disability weight for health states of each mutually exclusive sequela adjusted for comorbidity. The age range is limited to between 15 and 54 years old, divided into eight 5-year-old age groups. GBD divides the SDI of 21 regions and 204 countries and territories into five components (high, high-middle, middle, low-middle, and low) based on the lag-distributed income per capita, average years of schooling, and the fertility rate in females younger than 25 years for a given location. SDI ranges from 0 to 1, with higher values indicating higher income and years of schooling, and lower fertility. In

addition, GBD regions are not actual geopolitical units, but groupings of countries created for analysis.

Statistical analyses

Calculation of the estimated annual percentage change

Age-standardized rates of incidence, prevalence, and YLDs from 1990 to 2021 were used to assess the burden of endometriosis. Temporal trends of burden over thirty years are reflected by the estimated annual percentage change (EAPC). The EAPC is a widely used measure of the age-standardized rate trend over a specified time interval [13]. We fitted a regression line to the natural logarithm of the age-standardized rate to calculate the EAPC:

$$y = \alpha + \beta x + \varepsilon$$

where $y = \ln$ (age-standardized rate), x = calendar year, β is the regression coefficient, and ε is the error term in the regression model (also known as residual). This was then expressed as a percentage: $EAPC = 100 * (\exp(\beta) - 1)$. The 95% confidence interval (CI) of the EAPC was calculated to reflect the temporal trend in the age-standardized rate (ASR). An upward trend in the age-standardized rate was indicated when the EAPC and the lower boundary of the 95% CI were positive, whereas a downward trend was indicated when the EAPC and the upper boundary of the 95% CI were negative.

Joinpoint regression analysis

In order to detect changes in parameter trends of endometriosis health metrics, the joinpoint regression model was utilized. Joinpoint regression model partitions a long-term trend line into several segments through model-fitting, using permutation tests to identify points (joinpoints) where linear trends change significantly in direction or magnitude (e.g., zero joinpoints indicate a straight line). This model's calculating approach is to estimate the changing rule of illness rates using the least square method, avoiding the non-objectivity of typical trend analyses based on linear trends [14]. Therefore, we analyzed the age-standardized rate of endometriosis incidence, prevalence and, YLDs by different SDI regions, calculated the number of junction points and the position of each junction point by Monte Carlo permutation test, and the corresponding test statistic P value ($\alpha = 0.05$). For convenience of understanding, slopes are often converted to annual percentage changes (APCs) and average annual percent change (AAPC); that is, the estimated annual percentage change from one connection point to the next [15].

Socio-demographic index

The association between the burden of surgically confirmed endometriosis and SDI, for global and the 21 GBD regions from 1990 to 2021, were assessed using smoothing splines models. The SDI ranges from 0 (less developed) to 1 (most developed) and is comprised of the: (1) lag-distributed income per capita, which is the gross domestic product per capita smoothed over the preceding decade; (2) average years of schooling for the population older than 15 years of age; and (3) the fertility rate in females younger than 25 years for a given location. The statistical analyses were conducted using R software, version 4.3.2.

Decomposition analysis

Decomposition analysis refers to the breakdown of a composite indicator (e.g., incidence, prevalence, etc.) into multiple components in order to gain a clearer understanding of the contribution of each factor to the overall outcome. Specifically, the disease burden can be decomposed into different influencing factors, such as age, population, and epidemiological changes, to quantify the impact of each factor on the total change. We employed the decomposition analysis proposed by Das Gupta combined with an improved method proposed by Cheng and colleagues in 2020 to disentangle alterations in the burden of endometriosis into three group-level determinants: population aging, population growth, and epidemiological change [16, 17]. The approaches can be briefly summarized as follows.

The number of disease burden indicators(X) at each location was obtained from the following formula:

$$X_{ay, py, ey} = \sum_{(i=1)}^{17} (a_{i, y} * p_y * e_{i, y})$$

Where $X_{ay, py, ey}$ represented disease burden indicators based on the factors of age structure, population, and ASR for specific year y ; $a_{i, y}$ represents the proportion of population for the age category i in given year y ; p_y represents the total population in given year y ; and $e_{i, y}$ represents ASR given age category i in year y . The contribution of each factor to the change of disease burden from 1990 to 2021 was defined by the effect of one factor changing while the other factors were held constant. And the sum of the effects of each driving factor should exactly equal the total change in the disease burden indicator.

Results

The overall burden of surgically confirmed endometriosis from 1990 to 2021

From 1990 to 2021, there was a downward trend in the global age-standardized incidence, prevalence and YLDs rates of surgically confirmed endometriosis. The number

of incidence, prevalence and YLDs cases rose during this timeframe. In 2021, the incident cases of surgically confirmed endometriosis worldwide were 3.45 million, the prevalent cases arrived at 22.28 million, and the YLDs cases increased to 2.05 million (Table 1, S1, S2) (Fig. 1).

As far as SDI regions are concerned, the most significant annual decrease in age-standardized incidence, prevalence and YLDs rates from 1990 to 2021 occurred in low-middle SDI regions (EAPC of ASIR: -1.5, 95%UI: -1.52 to -1.47; EAPC of ASPR: -1.67, 95%UI: -1.7 to -1.64; EAPC of YLDs: -1.65, 95%UI: -1.68 to -1.62), while the smallest decrease was seen in high-middle SDI regions (EAPC of ASIR: -0.72, 95%UI: -0.82 to -0.62; EAPC of ASPR: -0.71, 95%UI: -0.81 to -0.62; EAPC of YLDs: -0.71, 95%UI: -0.8 to -0.61) (Table 1, S1, S2) (Fig. 1).

The burden due to surgically confirmed endometriosis varied significantly across different regions. In 2021, the age-standardized incidence, prevalence and YLDs

rates were highest in Oceania, Eastern Europe, Western Sub-Saharan Africa, and North Africa and Middle East. High-income North America, Central Latin America, East Asia, and Southern Latin America observed the lowest rates (Fig. 2, S1, S2). The annual percentage change in age-standardized rates varied from 1990 to 2021, with the highest decrease observed in High-income North America (EAPC of ASIR: -2.07, 95%UI: -2.24 to -1.9; EAPC of ASPR: -1.91, 95%UI: -2.08 to -1.75; EAPC of YLDs: -1.92, 95%UI: -2.09 to -1.76) and the most significant increase found in Eastern Europe (EAPC of ASIR: 0.32, 95%UI: 0.15 to 0.5; EAPC of ASPR: 0.32, 95%UI: 0.15 to 0.5; EAPC of YLDs: 0.33, 95%UI: 0.15 to 0.51) (Table 1, S1, S2) (Fig. 1).

Table 1 The incidence of endometriosis in 1990 and 2021 and Temporal trends between 1990 and 2021

Location	1990		2021		1990–2021 (%)
	Incidence_Num- ber_1000 (95%UI)	ASIR per 100,000 (95%UI)	Incidence_Num- ber_1000 (95%UI)	ASIR per 100,000 (95%UI)	
Global	3330.2 (2308.6 to 4507)	119.6 (83.5 to 160.5)	3447.1 (2436.3 to 4611.5)	88.5 (62.5 to 119.5)	-1(-1.05 to -0.96)
SDI region					
High SDI	437.9 (305.8 to 594.9)	96.3 (67.2 to 130.6)	358 (260.6 to 467.1)	75.4 (54.1 to 99.2)	-0.92(-0.99 to -0.85)
High-middle SDI	593.6 (412.1 to 799.1)	103.9 (72.5 to 141.1)	488.9 (353.4 to 647.9)	83.1 (59.4 to 110.5)	-0.72(-0.82 to -0.62)
Middle SDI	1049.8 (715 to 1440.1)	112.3 (77.5 to 151.1)	1008.1 (709 to 1348.9)	82.4 (58.1 to 111.2)	-1.04(-1.12 to -0.97)
Low-middle SDI	863 (597 to 1197.1)	149.5 (105.2 to 200.1)	981.6 (680.6 to 1336.9)	94.1 (65.8 to 127.3)	-1.5(-1.52 to -1.47)
Low SDI	383.2 (264.5 to 531.7)	160.3 (112.7 to 215.3)	607.9 (420.3 to 848.8)	103.6 (72 to 141.1)	-1.41(-1.46 to -1.36)
GBD region					
Andean Latin America	20.9 (14.2 to 29.3)	104.3 (72.5 to 140.7)	25 (17.3 to 34.5)	70.9 (49.1 to 97.5)	-1.19(-1.26 to -1.12)
Australasia	10.7 (7.5 to 14.7)	100.7 (70.1 to 137.7)	12 (8.3 to 16)	88.4 (61.3 to 119.6)	-0.25(-0.33 to -0.18)
Caribbean	18.4 (12.7 to 25.9)	94.3 (65.4 to 128.5)	17.1 (11.8 to 23.4)	70.8 (48.8 to 97.5)	-0.88(-0.91 to -0.86)
Central Asia	39.4 (27 to 55)	111.1 (77.3 to 150.1)	42.3 (29.5 to 56.3)	89 (61.8 to 119)	-0.39(-0.57 to -0.21)
Central Europe	50.9 (35.8 to 68.9)	84.5 (59.4 to 113.9)	36.1 (25.6 to 48.8)	76.3 (53.7 to 103)	-0.23(-0.37 to -0.09)
Central Latin America	88.2 (60.2 to 124)	99 (68.5 to 133.5)	89.8 (62.5 to 121.7)	65.3 (45.3 to 88.8)	-1.3(-1.39 to -1.21)
Central Sub-Saharan Africa	41.9 (28.6 to 58.5)	157.4 (109.2 to 212.8)	68.8 (46.6 to 96.8)	99 (67.6 to 135.7)	-1.42(-1.54 to -1.31)
East Asia	704.5 (477.8 to 971.7)	102.9 (70.7 to 142.1)	444.7 (320.3 to 592.9)	67 (47.9 to 89.3)	-1.51(-1.68 to -1.34)
Eastern Europe	148.3 (102.9 to 200.5)	136.4 (96.5 to 184)	117.9 (83.5 to 157)	133.6 (93.2 to 180.3)	0.32(0.15 to 0.5)
Eastern Sub-Saharan Africa	130.3 (89.7 to 181.6)	139.6 (96.6 to 189.4)	195.6 (135.2 to 273.4)	85.2 (58.6 to 117)	-1.59(-1.64 to -1.54)
High-income Asia Pacific	110.5 (75.5 to 148.2)	120.2 (82 to 161.4)	77.2 (54.7 to 103.2)	104.4 (73.4 to 137.1)	-0.53(-0.63 to -0.42)
High-income North America	133.5 (88.4 to 188.2)	86.8 (58.3 to 122.9)	91.2 (65.3 to 118.7)	54.1 (38.6 to 71.1)	-2.07(-2.24 to -1.9)
North Africa and Middle East	260 (178.5 to 368.6)	154.1 (107.8 to 210.2)	341.4 (238.6 to 462.3)	106.7 (74.7 to 144.4)	-1.19(-1.29 to -1.09)
Oceania	5.9 (4.1 to 8.1)	181.5 (127.8 to 243.9)	10.5 (7.4 to 14.6)	148.3 (104.5 to 204.3)	-0.63(-0.65 to -0.61)
South Asia	801.1 (554.3 to 1098.6)	149.1 (104.3 to 200.6)	936.8 (643.3 to 1268.5)	92.2 (63.8 to 124.6)	-1.57(-1.6 to -1.55)
Southeast Asia	341.5 (236.6 to 465.5)	136.1 (95.6 to 182.7)	386.1 (271.9 to 518.4)	105 (73.7 to 141.2)	-0.79(-0.82 to -0.76)
Southern Latin America	21.1 (14.6 to 28.3)	84.1 (58.1 to 113)	24.6 (17.4 to 32.1)	69.9 (49.4 to 91.5)	-0.47(-0.56 to -0.38)
Southern Sub-Saharan Africa	33.5 (22.9 to 46.1)	117.2 (80.8 to 157.7)	40.5 (27.6 to 55.2)	92.1 (63.3 to 125.3)	-0.75(-0.77 to -0.72)
Tropical Latin America	82.4 (55.4 to 114.8)	99.5 (67.9 to 137.4)	90.7 (63.4 to 120.4)	76 (52.6 to 102)	-1.2(-1.36 to -1.04)
Western Europe	140.9 (96.9 to 191.9)	74.7 (51.7 to 102.2)	126.3 (89.6 to 167.3)	72.4 (50.5 to 98)	0.02(-0.02 to 0.07)
Western Sub-Saharan Africa	146.2 (100.5 to 203.8)	154.9 (107.6 to 209.1)	272.5 (186.8 to 380.7)	105.4 (72.7 to 142.5)	-1.22(-1.28 to -1.16)

EAPC, estimated annual percentage change; ASIR, age-standardized incidence rate; SDI, socio-demographic index

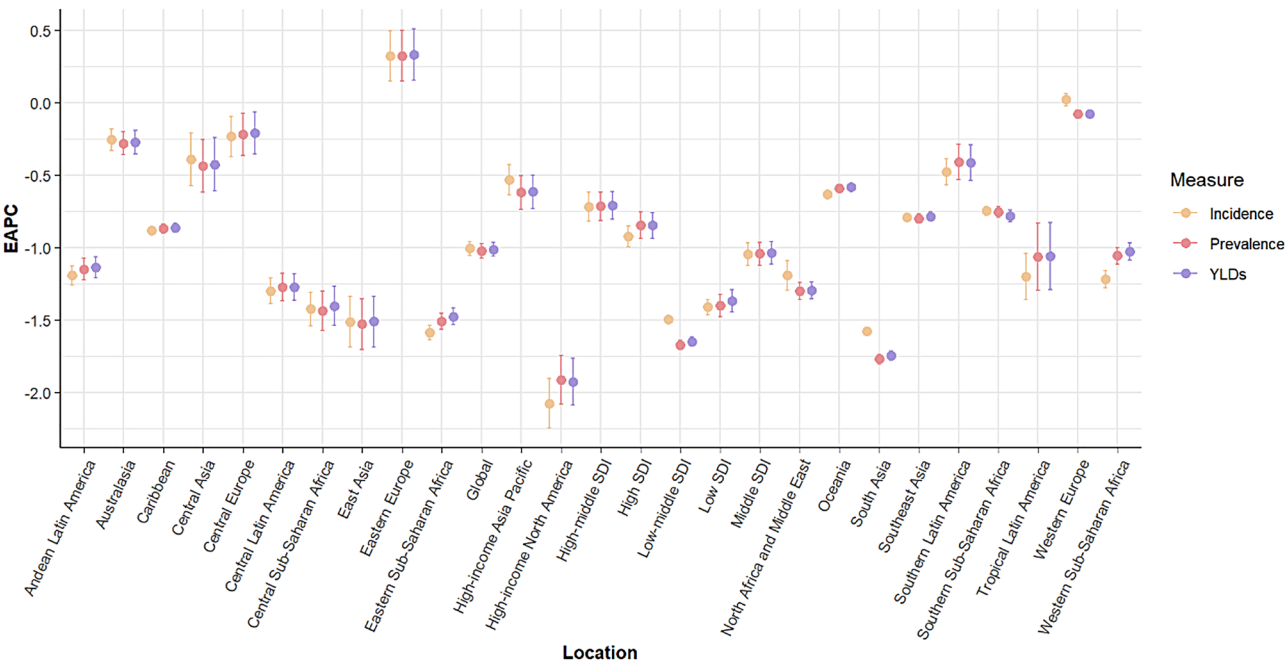


Fig. 1 The EAPC for ASIR, ASPR, and Age Standardized YLDs Rate at the regional level. EAPC, estimated annual percentage change; ASIR, age-standardized incidence rate; ASPR, age-standardized prevalence rate; YLDs, years lived with disability

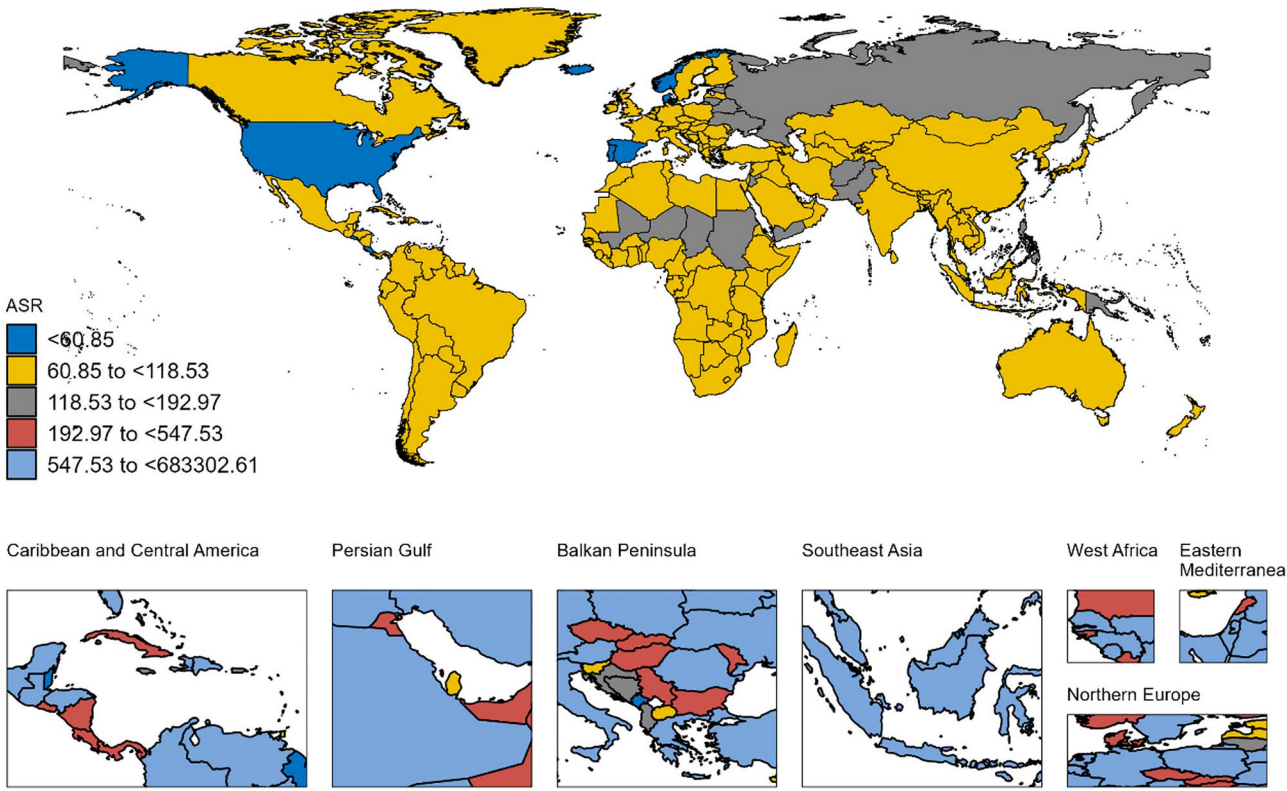


Fig. 2 The ASIR of endometriosis in 204 countries and territories in 2021. ASIR, age-standardized incidence rate

Joinpoint regression analysis of surgically confirmed endometriosis burden

Age-standardized incidence, prevalence and YLDs rates showed a year-by-year decline in global and most SDI regions (Table 2). However, the change trend in high-middle SDI and middle SDI was relatively more complex. The tendency of ASIR and ASPR in high-middle SDI and middle SDI decreased from 1990 to 2010 and 2015 to 2021, but increased from 2010 to 2015 (Fig. 3, S3). The age-standardized YLDs rate in high-middle SDI showed

an upward trend from 2010 to 2015 and a downward trend for the rest of the years (Fig. S4).

Age-based description of the burden of surgically confirmed endometriosis

We analyzed the burden of surgically confirmed endometriosis according to age groups in 2021 (Fig. 4). The global age-specific incidence rate and the number of incident cases peaked in the 20–24 age group (Fig. 4 A). The global prevalence rate and number of prevalent cases

Table 2 The trends in endometriosis burden by joinpoint regression

SDI factor	Index	Incidence		Prevalence		YLDs	
		Period	Estimate(%) (95%UI)	Period	Estimate(%) (95%UI)	Period	Estimate(%) (95%UI)
Global	APC	1990–1992	-1.27(-1.51 to -1.03)	1990–1994	-1.3(-1.4 to -1.19)	1990–1994	-1.27(-1.37 to -1.17)
		1992–2003	-0.99(-1 to -0.97)	1994–2006	-1(-1.02 to -0.97)	1994–2006	-0.98(-1 to -0.96)
		2003–2006	-1.12(-1.36 to -0.89)	2006–2009	-2.14(-2.45 to -1.83)	2006–2009	-2.13(-2.43 to -1.84)
		2006–2009	-2.09(-2.32 to -1.85)	2009–2012	-0.67(-0.98 to -0.35)	2012–2019	-0.64(-0.93 to -0.34)
		2009–2018	-0.48(-0.5 to -0.45)	2012–2018	-0.43(-0.5 to -0.36)	2019–2021	-0.45(-0.5 to -0.4)
		2018–2021	-0.87(-0.99 to -0.76)	2018–2021	-0.77(-0.93 to -0.61)		
High SDI	AAPC	1990–2021	-0.97 (-1.01 to -0.93)	1990–2021	-0.98 (-1.03 to -0.94)	1990–2021	-0.98 (-1.03 to -0.94)
		1990–1996	-0.24(-0.33 to -0.15)	1990–1996	-0.29(-0.36 to -0.22)	1990–1996	-0.28(-0.32 to -0.24)
		1996–2004	-1.63(-1.69 to -1.56)	1996–2001	-1.36(-1.47 to -1.25)	1996–2001	-1.37(-1.44 to -1.29)
		2004–2008	-0.99(-1.21 to -0.76)	2001–2004	-2.06(-2.38 to -1.73)	2001–2004	-2.05(-2.27 to -1.83)
		2008–2021	-0.48(-0.51 to -0.46)	2004–2009	-0.95(-1.04 to -0.85)	2004–2009	-0.93(-1 to -0.87)
				2009–2014	-0.12(-0.21 to -0.03)	2009–2015	-0.12(-0.17 to -0.08)
High-middle SDI	AAPC	1990–2021	-0.8 (-0.83 to -0.76)	1990–2021	-0.71 (-0.75 to -0.66)	1990–2021	-0.71 (-0.74 to -0.68)
		1990–1995	-1.61(-1.74 to -1.49)	1990–1994	-1.93(-2.03 to -1.83)	1990–1994	-1.89(-2.02 to -1.77)
		1995–2005	-0.62(-0.67 to -0.57)	1994–1999	-0.96(-1.06 to -0.86)	1994–1999	-0.95(-1.07 to -0.82)
		2005–2010	-2.04(-2.21 to -1.87)	1999–2005	-0.41(-0.48 to -0.34)	1999–2005	-0.41(-0.49 to -0.32)
		2010–2015	0.81(0.64 to 0.98)	2005–2010	-1.95(-2.05 to -1.86)	2005–2010	-1.95(-2.06 to -1.83)
		2015–2021	-0.22(-0.31 to -0.13)	2010–2015	0.66(0.57 to 0.76)	2010–2015	0.69(0.57 to 0.8)
Middle SDI	AAPC	1990–2021	-0.7 (-0.75 to -0.66)	1990–2021	-0.74 (-0.77 to -0.71)	1990–2021	-0.74 (-0.77 to -0.7)
		1990–1993	-1.6(-1.74 to -1.45)	1990–1995	-1.52(-1.62 to -1.42)	1990–1995	-1.49(-1.6 to -1.39)
		1993–2005	-0.96(-0.98 to -0.94)	1995–2005	-0.88(-0.92 to -0.84)	1995–2005	-0.87(-0.91 to -0.83)
		2005–2010	-2.3(-2.39 to -2.21)	2005–2010	-2.3(-2.44 to -2.17)	2005–2010	-2.29(-2.43 to -2.14)
		2010–2015	0.1(0.01 to 0.19)	2010–2015	0.01(-0.12 to 0.15)	2010–2016	-0.03(-0.13 to 0.08)
		2015–2021	-0.52(-0.57 to -0.47)	2015–2021	-0.42(-0.49 to -0.34)	2016–2021	-0.52(-0.62 to -0.43)
Low-middle SDI	AAPC	1990–2021	-0.98 (-1.01 to -0.96)	1990–2021	-0.98 (-1.02 to -0.94)	1990–2021	-0.98 (-1.02 to -0.94)
		1990–1998	-1.63(-1.66 to -1.61)	1990–1999	-1.75(-1.76 to -1.73)	1990–1999	-1.71(-1.74 to -1.69)
		1998–2006	-1.45(-1.48 to -1.42)	1999–2006	-1.61(-1.65 to -1.58)	1999–2006	-1.58(-1.62 to -1.55)
		2006–2009	-1.84(-2.07 to -1.61)	2006–2009	-2.2(-2.4 to -1.99)	2006–2009	-2.17(-2.39 to -1.96)
		2009–2014	-1.46(-1.53 to -1.38)	2009–2014	-1.68(-1.75 to -1.62)	2009–2014	-1.67(-1.74 to -1.6)
		2014–2019	-1.12(-1.19 to -1.04)	2014–2019	-1.1(-1.17 to -1.04)	2014–2019	-1.08(-1.15 to -1.01)
Low SDI	AAPC	1990–2021	-1.4 (-1.51 to -1.45)	1990–2021	-1.63 (-1.66 to -1.6)	1990–2021	-1.61 (-1.64 to -1.59)
		1990–1995	-0.89(-0.93 to -0.85)	1990–1995	-0.7(-0.76 to -0.65)	1990–1996	-0.73(-0.77 to -0.68)
		1995–2006	-1.2(-1.22 to -1.19)	1995–2003	-1.05(-1.09 to -1.02)	1996–2006	-1.06(-1.09 to -1.04)
		2006–2014	-1.67(-1.68 to -1.66)	2003–2006	-1.18(-1.44 to -0.92)	2006–2019	-1.76(-1.78 to -1.74)
		2014–2019	-2(-2.18 to -1.82)	2006–2019	-1.79(-1.8 to -1.77)	2019–2021	-2.22(-2.49 to -1.95)
		2019–2021	-0.89(-0.93 to -0.85)	2019–2021	-2.11(-2.36 to -1.85)		
	AAPC	1990–2021	-1.4 (-1.42 to -1.39)	1990–2021	-1.39 (-1.42 to -1.35)	1990–2021	-1.37 (-1.39 to -1.34)

YLDs, years lived with disability; SDI, socio-demographic index; APC, annual percentage changes; AAPC, average annual percent change

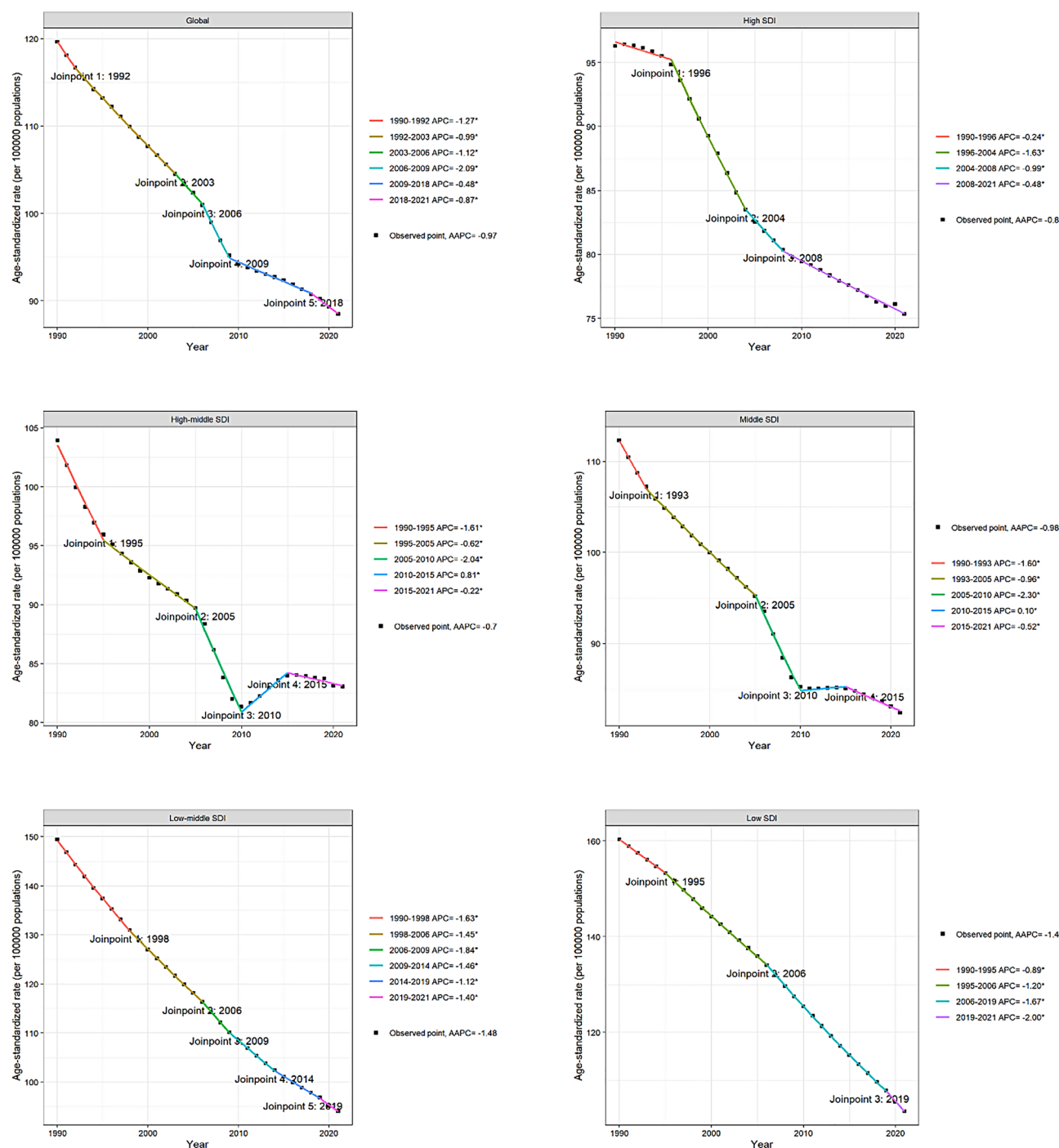


Fig. 3 Joinpoint regression analysis in ASIR of endometriosis from 1990 to 2021 by SDI region. ASIR, age-standardized incidence rate; SDI, socio-demographic index; APC, annual percentage change; * $P < 0.05$

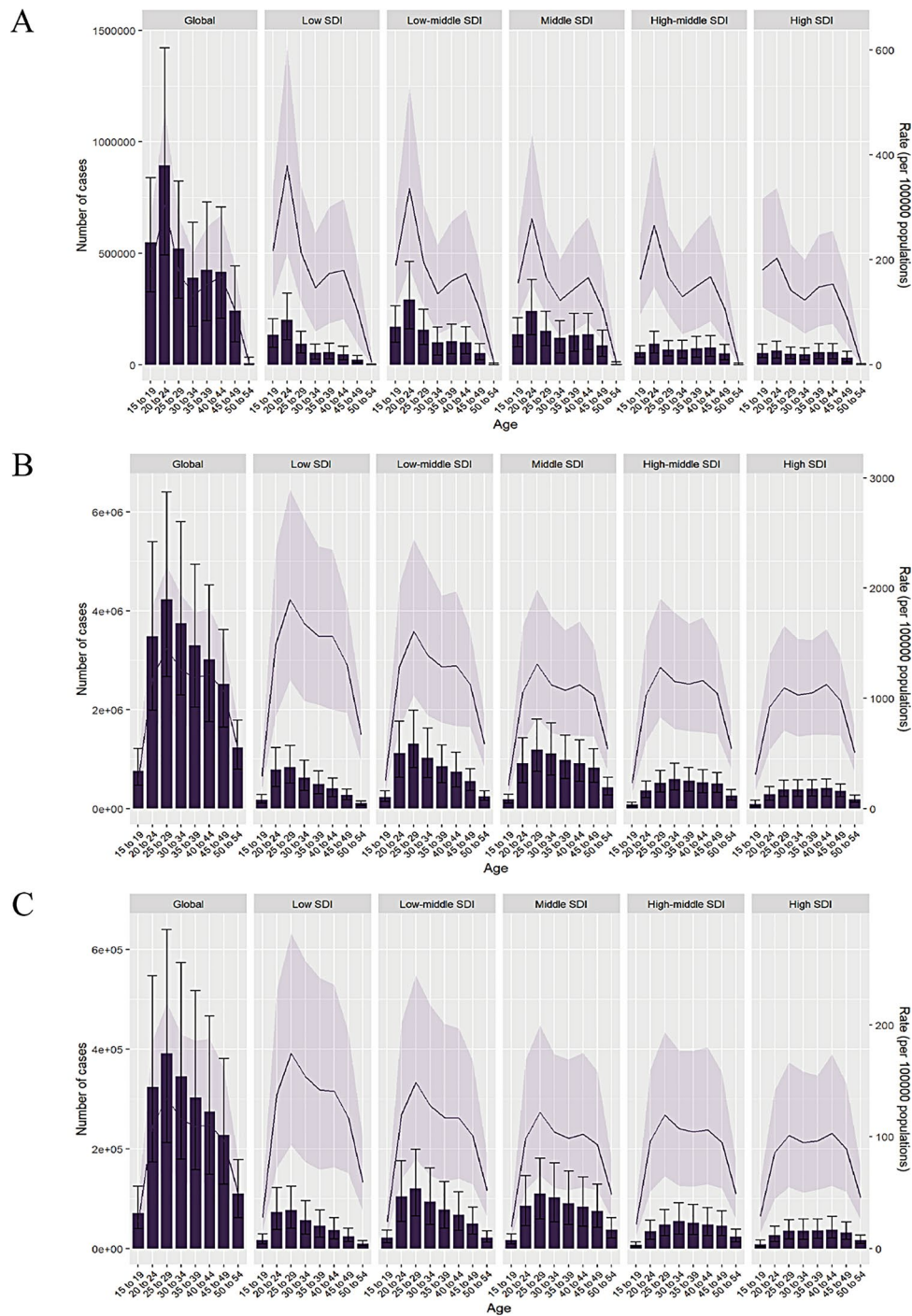


Fig. 4 Age-specific burdens on incidence (A), prevalence (B), and YLDs (C) of endometriosis in 2021. YLDs, years lived with disability. The y-axis of Fig. 4B and C: “e” represents “multiply by a power of 10”. For example, in $2e+05$, 2 is the base (valid numeric part), and $e+05$ means “multiply by 5 powers of 10”, i.e. $2e+05 = 2 \times 100,000 = 200,000$

peaked in the 25–29 age group (Fig. 4B), while the global YLDs rate and the number of YLDs similarly peaked in the 25–29 years age group (Fig. 4 C). In all SDI regions, the highest incidence rate was concentrated in the 20–24 age group (Fig. 4 A). In low SDI, low-middle SDI, middle SDI, and high-middle SDI regions, high prevalence rate

and high YLD rate were concentrated in the 25-29-year-olds. But in the high SDI region, the highest prevalence rate and YLD rate were concentrated in the 40–44 age group (Fig. 4B, C).

Burden of surgically confirmed endometriosis and SDI level estimates

Fig. 5 showed the relationship between the SDI levels and the estimated burden of surgically confirmed endometriosis globally and in 21 GBD regions from 1990 to 2021. Age-standardized rates of incidence, prevalence, and YLDs of endometriosis all illustrated a broadly negative correlation with SDI levels. Overall, the average expected values of the estimated burden rates of endometriosis decreased with increasing SDI levels. The global endometriosis burden consistently remained higher than expected between 1990 and 2021 (Fig. 5, S5, S6).

Decomposition analysis of the changes in the number of surgically confirmed endometriosis incidence, prevalence and YLDs between 1990 and 2021

Table 3 presented the decomposition analysis results concerning changes in the number of incidence, prevalence, and YLDs cases, influenced by three population-levels determinants: population aging, population growth, and epidemiological changes at the global level, five SDI strata and GBD regions (Table 3). Globally, from 1990 to 2021, population growth resulted in a 1,211.68% increase of incident cases, epidemiological changes accounted for an 892.28% reduction, and population aging led to a 219.4% decrease. The increase in prevalence and YLDs was also mainly attributed to population growth, while epidemiological changes were an important reason for

limiting the increase. Among the five SDI regions, the incidence, prevalence and YLDs cases decreased in high and high-middle SDI regions, mainly due to epidemiological changes. While the numbers increased in low and low-middle SDI regions, and population growth played the most important role in it. At the regional level, South Asia saw the most significant increase in all incidence (135,743.42 cases), prevalence (936,710.51 cases), and YLDs (87,635.03 cases), followed by Western Sub-Saharan Africa and North Africa and Middle East, primarily driven by population growth. The most notable decrease occurred in East Asia, followed by High-income North America, mainly due to epidemiological changes (Fig. 6, S7, S8).

Discussion

This study provides a comprehensive analysis of the global burden of endometriosis from 1990 to 2021 using data from GBD. Our study indicated that during the period of 1990–2021, the global ASIR, ASPR, and age-standardized YLDs rate for endometriosis showed a widely decreasing trend, but EAPC varied across different SDI regions and GBD regions. The burden of surgically confirmed endometriosis is mainly concentrated in women aged 20–30 years, and declines with increasing SDI levels. The result of decomposition analysis reveals the global numbers of incidence, prevalence, and YLDs of endometriosis significantly increased over the past 30

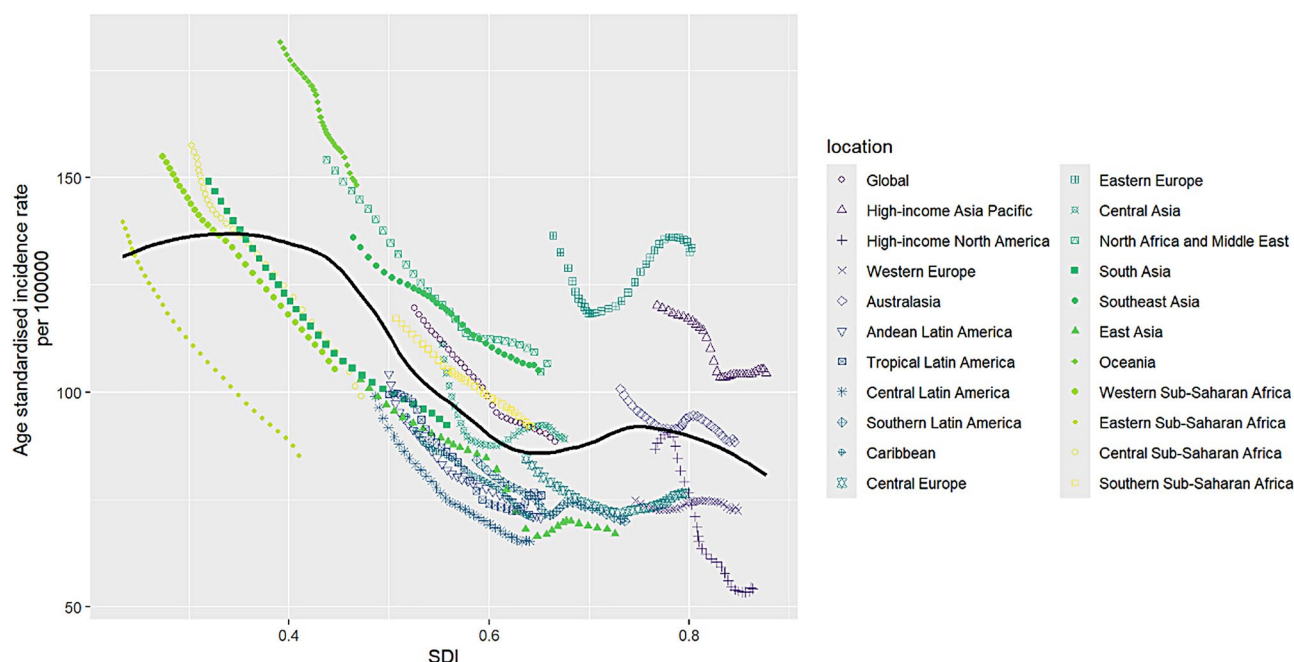


Fig. 5 Coevolution of ASIR with SDI globally and for GBD regions of endometriosis, 1990–2021. Colored lines show global and regional values for age-standardized burden estimate rates. Each point in a line represents 1 year starting in 1990 and ending in 2021. The black line represents the average expected relationship between SDI and burden estimate rates for endometriosis based on values from each region. Regions above the solid line have higher than expected burdens, while those below the line have lower than expected burdens

Location	Incidence		Prevalence				YLDs		Epidemiological change (Percent %)			
	Overall difference	Aging (Percent %)	Population (Percent %)	Epidemiological change (Percent %)	Overall difference	Aging (Percent %)	Population (Percent %)					
Global	116925.82	-256537.99 (-219.4%)	1416764.98 (1211.68%)	-1043301.16 (-892.28%)	2405819.57	236055.64 (9.81%)	8777925.95 (364.86%)	-6608162.02 (-274.67%)	218757.57	17529.95 (8.01%)	807097.8 (368.95%)	-605870.17 (-276.96%)
SDI region												
High SDI	-79889.08	-26852.49 (33.61%)	45157.9 (-56.53%)	-98194.49 (122.91%)	-289065.55	-11146.77 (3.86%)	299551.78 (-103.63%)	-577470.55 (199.77%)	-27631.81	-1404.11 (5.08%)	27570.99 (-99.78%)	-53798.69 (194.7%)
High-middle SDI	-104723.65	-63865.95 (60.99%)	81469.2 (-77.79%)	-122326.9 (116.81%)	-216141.17	78286.99 (-36.22%)	529932.53 (-245.18%)	-824360.69 (381.4%)	-21170.94	6033.07 (-28.5%)	48974.05 (-231.33%)	-76178.06 (359.82%)
Middle SDI	-41768.87	-118430.37 (283.54%)	400751.22 (-959.45%)	-324089.72 (775.91%)	657080.81	213368.95 (32.47%)	2407440.02 (366.38%)	-1963728.17 (-298.86%)	58349.92	17615.19 (30.19%)	22240.64 (380.88%)	-181505.9 (-311.06%)
Low-middle SDI	118524.52	-42078.69 (-35.5%)	610259.79 (514.88%)	-449656.57 (-379.38%)	866487.36	145185.82 (16.76%)	3751133.49 (432.91%)	-3029831.95 (-349.67%)	80703.72	12445.7 (15.42%)	343166.82 (425.22%)	-274908.81 (-340.64%)
Low SDI	224730.03	-511.24 (-0.23%)	457893.76 (203.75%)	-232652.48 (-103.53%)	1385798.85	-468.78 (-0.03%)	2784468.73 (200.93%)	-1398201.11 (-100.89%)	128358.07	-97.12 (-0.08%)	253975.67 (197.86%)	-125520.48 (-97.79%)
GBD region												
Andean Latin America	4143.7	-1752.74 (-42.3%)	15189.97 (366.58%)	-9293.53 (-224.28%)	39761.37	5065.26 (12.74%)	88516.64 (222.62%)	-53820.53 (-135.36%)	3637.8	439.31 (12.08%)	8154.74 (224.17%)	-4956.26 (-136.24%)
Australasia	1267.38	-1114.7 (-87.95%)	3922.55 (309.5%)	-1540.47 (-121.55%)	13452.44	-1389.4 (-10.33%)	25431.33 (189.05%)	-10589.5 (-78.72%)	1256.02	-133.5 (-10.63%)	2325.82 (185.17%)	-936.31 (-74.55%)
Caribbean	-1349.18	-1562.38 (115.8%)	5351.71 (-396.66%)	-5138.51 (380.86%)	2132.86	1041.3 (48.82%)	33405.64 (1566.24%)	-32314.07 (-1515.06%)	156.82	71.39 (45.52%)	3063.26 (1953.34%)	-2977.82 (-1898.87%)
Central Asia	2873.81	-3620.45 (-125.98%)	15727.6 (547.27%)	-9233.35 (-321.29%)	39964.28	2658.79 (6.65%)	99194.34 (248.21%)	-61888.85 (-154.86%)	3630.44	189.65 (5.22%)	9188.07 (253.08%)	-5747.28 (-158.31%)
Central Europe	-14819.64	-4163.73 (28.1%)	-6277.71 (42.36%)	-4378.2 (29.54%)	-69770.89	-889.11 (1.27%)	-42768.23 (61.3%)	-26113.55 (37.43%)	-6524.41	-150.42 (2.31%)	-3953.38 (60.59%)	-2420.6 (37.1%)
Central Latin America	1548.96	-9049.13 (-584.21%)	48965.33 (3161.18%)	-38367.24 (-2476.97%)	77108.97	12598.99 (16.34%)	293150.27 (380.18%)	-228640.29 (-296.52%)	6901.97	990.49 (14.35%)	27003.9 (391.25%)	-21092.42 (-305.6%)
Central Sub-Saharan Africa	26915.85	-418.36 (-1.55%)	55564.8 (206.44%)	-28230.59 (-104.88%)	158618.07	260.8 (0.16%)	327707.23 (206.6%)	-169349.96 (-106.77%)	14656.26	11.6 (0.08%)	29750.28 (202.99%)	-15105.62 (-103.07%)
East Asia	-259803.1	-73729.5 (28.38%)	54827.8 (-21.1%)	-240901.4 (92.72%)	-886838.3	298450.19 (-33.65%)	343417.25 (-38.72%)	-1528705.74 (172.38%)	-82995.71	26017.94 (-31.35%)	31951.92 (-38.5%)	-140965.57 (169.85%)
Eastern Europe	-30429.52	-8105.03 (26.64%)	-19265.52 (63.31%)	-3058.97 (10.05%)	-155473.58	5268.56 (-3.39%)	-139412.01 (89.67%)	-21330.12 (13.72%)	-14637.08	227.97 (-1.56%)	-12809.25 (87.51%)	-2055.8 (14.05%)
Eastern Sub-Saharan Africa	65294.56	-1086.29 (-1.66%)	154463.89 (236.56%)	-88083.05 (-134.9%)	410760.63	7767.14 (1.89%)	888345.13 (216.27%)	-485351.63 (-118.16%)	38048.21	668.96 (1.76%)	81220.16 (13.47%)	-43840.91 (-115.22%)
High-income Asia Pacific	-33235.49	-9633.04 (28.98%)	-11335.09 (34.11%)	-1267.36 (6.91%)	-153915.47	11272.06 (-7.32%)	-75590.18 (49.11%)	-8				

Table 3 (continued)

Location	Incidence		Prevalence				YLDs			
	Overall difference	Aging (Percent %)	Population (Percent %)	Epidemiological change (Percent %)	Overall difference	Aging (Percent %)	Population (Percent %)	Epidemiological change (Percent %)	Overall difference	Aging (Percent %)
North Africa and Middle East	81390.06	-28897.69 (-35.51%)	228090.84 (280.24%)	-117803.08 (-144.74%)	696104.36	61262.06 (8.8%)	1389352.8 (199.59%)	-754510.5 (-108.39%)	62972.61	5016 (7.97%)
Oceania	4643.25	-244.91 (-5.27%)	6644.45 (143.1%)	-1756.29 (-37.82%)	32789.81	1753.34 (5.35%)	41208.17 (125.67%)	-10171.7 (-31.02%)	3020.72	153.69 (5.09%)
South Asia	135743.42	-40917.33 (-30.14%)	618570.69 (455.69%)	-441909.94 (-325.55%)	936710.51	119008.42 (12.7%)	3853516.61 (411.39%)	-3035814.52 (-324.09%)	87635.03	10048.38 (11.47%)
Southeast Asia	44672.55	-29112.38 (-65.17%)	170824.49 (382.39%)	-97039.57 (-217.22%)	488059.78	64870.98 (13.29%)	1015017.25 (207.97%)	-591828.45 (-121.26%)	45101.2	5470.57 (12.13%)
Southern Latin America	3461.2	-554.81 (-16.03%)	8278.13 (239.17%)	-4262.12 (-123.14%)	31537.37	4869.99 (15.44%)	51669.95 (163.84%)	-25002.57 (-79.28%)	2829.94	429.49 (15.18%)
Southern Sub-Saharan Africa	7004.47	-2915.59 (-41.62%)	19129.7 (273.11%)	-9209.64 (-131.48%)	66252.34	8294.31 (12.52%)	115780.21 (174.76%)	-57822.18 (-87.28%)	5803.79	690.38 (11.9%)
Tropical Latin America	8246.96	-8424.02 (-102.15%)	40779 (494.47%)	-24108.02 (-292.33%)	150810.21	11238 (7.45%)	253965.95 (168.4%)	-114393.75 (-75.85%)	13563.06	855.27 (6.31%)
Western Europe	-14597.53	-12318.95 (84.39%)	2532.94 (-17.35%)	-4811.52 (32.96%)	-60966.04	-28304.25 (46.43%)	17662.72 (-28.97%)	-50324.51 (82.55%)	-5781.27	-2742.36 (47.44%)
Western Sub-Saharan Africa	126274.28	-3675.81 (-2.91%)	215682.9 (170.81%)	-85732.81 (-67.89%)	792120.98	-2834.02 (-0.36%)	1247366.32 (157.47%)	-452411.32 (-57.11%)	73105.26	-332.99 (-0.46%)

YLDs, years lived with disability; SDI, socio-demographic index

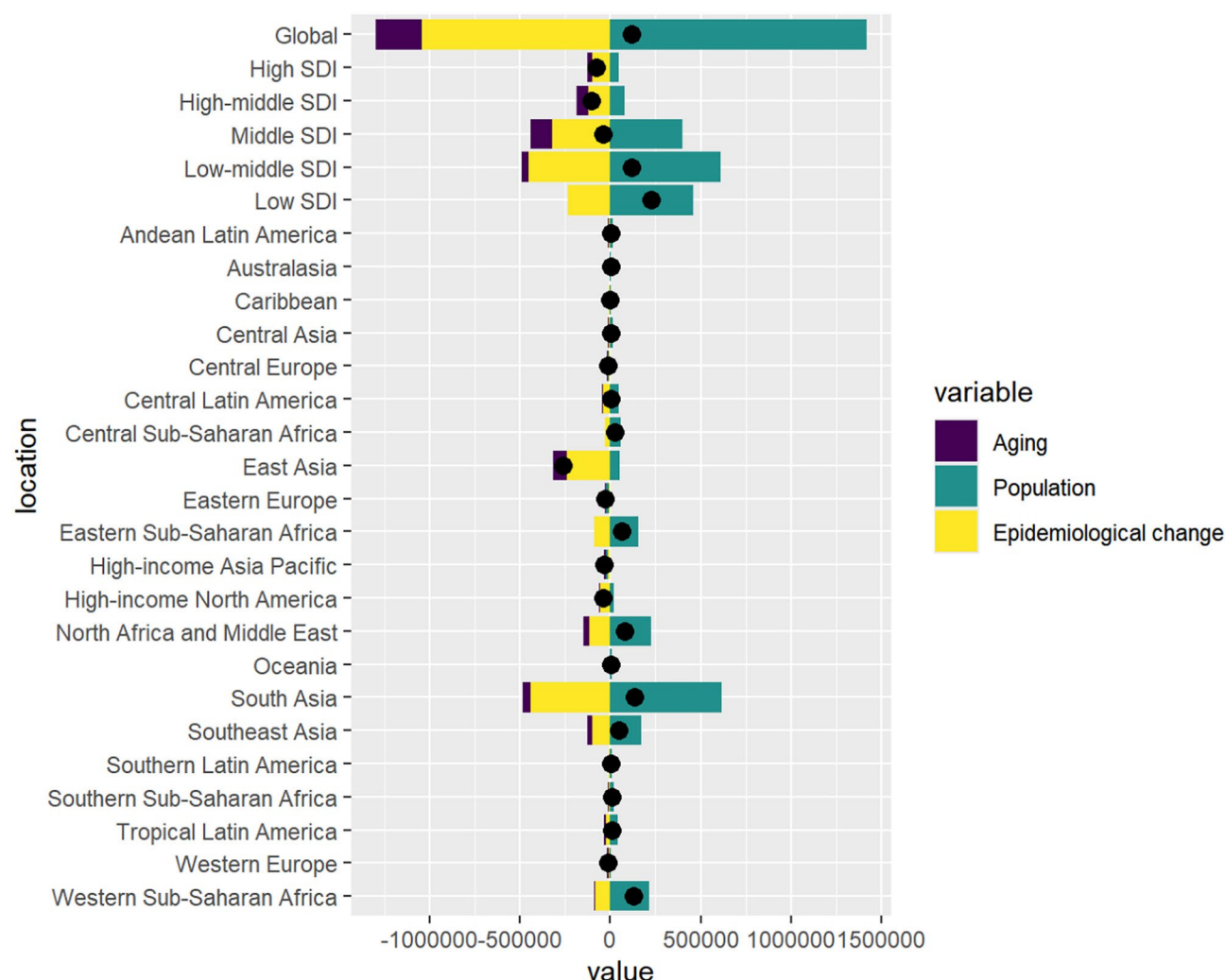


Fig. 6 Changes in endometriosis incidence, decomposed by three population-level determinants: aging, population and epidemiological change

years, and these upwards are primarily driven by population growth. Conversely, epidemiological changes, reflecting reductions in incidence, prevalence, and YLDs, mitigated these increases.

The joinpoint regression analysis shows that from 1990 to 2021, the burden of endometriosis has decreased year by year in most SDI regions. However, high-middle and middle SDI regions experienced fluctuating trends: declines from 1990 to 2010 and 2015 to 2021, but an increase from 2010 to 2015. This fluctuation may be due to changes in medical therapeutic patterns or therapy guidelines. For example, a German study indicated that the proportion of endometriosis patients treated with dienogest significantly increased between 2010 and 2019, and during the same period, the prevalence of endometriosis also significantly increased [18].

The analysis of the burden of surgically confirmed endometriosis by age groups in 2021 reveals critical insights into the demographic distribution of the disease.

The global age-specific incidence rate and the number of incident cases peaked in the 20–24 age group. The global prevalence rate and the number of prevalent cases, as well as the YLDs rate and the number of YLDs, peaked in the 25–29 age group in most SDI regions. The peak burden in women aged 20–30 highlights its impact on quality of life and reproductive health. Thus, this period is a critical time for intervention. We should focus on the prevention and comprehensive management of the 20–30 age group, and improve the ability of early diagnosis and treatment. However, in the high SDI region, the highest prevalence and YLDs rates were concentrated in the 40–44 age group. Previous studies have shown that cesarean section and induced abortion are important risk factors that cannot be ignored for developing endometriosis [19, 20]. The average childbearing age in developed countries is higher than in less developed countries, and the prevalence of cesarean and abortion procedures is

very high. This may be an important reason why the age of onset in high SDI regions is later than in other regions.

By analyzing the relationship between SDI levels and endometriosis burden, we found that the average expected values of the burden of endometriosis decreased with increasing SDI levels. This contrasts with some previous studies [21, 22], but also shows the same trend as the conclusions of others [23, 24]. In fact, the true incidence of endometriosis is difficult to determine, because the gold standard for the diagnosis of endometriosis is the combination of laparoscopy visualization and histologic confirmation of the presence of endometrial glands and/or stroma [25, 26]. However, laparoscopy is an invasive procedure, and clinicians in some regions typically prefer other non-invasive techniques, such as ultrasound and magnetic resonance imaging (MRI), to identify endometriosis, but their accuracy is limited [27]. Furthermore, the nonspecific nature of endometriosis symptoms and the tendency to normalise them may contribute to the delay in diagnosis. For example, non-specific symptoms such as dysmenorrhea have often been treated with hormonal drugs without consideration of endometriosis [28]. Thus, clinicians' skills, awareness of endometriosis, and economic and geographic access to care will all affect diagnostic outcomes [29, 30]. In high-level SDI regions, the increased medical management of endometriosis reduce the need for surgical treatment, thereby decreasing the incidence of surgically confirmed diagnoses. Moreover, the operative treatment and diagnostic procedures concerning fibroids in particular, and also female sterilization and infertility, have decreased during the years, decreasing the possibility to diagnose endometriosis as an incidental finding. These changing treatment trends may reduce the incidence of surgically validated endometriosis [23]. Additionally, oral contraceptives have been proven to significantly reduce menstrual flow and may prevent the occurrence of endometriosis by interfering with the implantation of retrograde endometrial cells [31, 32]. The use of the pill is more widespread in developed regions, which reduces the incidence of endometriosis to some extent [33–35]. Meanwhile, multiple studies have shown that environmental toxicants such as dioxins, phthalates, bisphenol A, or organochlorinated pollutants play a significant role in the development of endometriosis [36–38]. Compared to high-level SDI regions, low-level SDI regions generally have poorer environmental governance. Activities such as waste incineration or metal smelting release large amounts of dioxins, increasing the likelihood of exposure to harmful chemicals. These warn us that regions with lower SDI may face more severe challenges. Addressing these disparities requires multifaceted approaches, including promoting access to healthcare, enhancing

health education, improving living environments, and implementing targeted public health strategies.

Furthermore, we employed decomposition analysis to disentangle the contributions of population aging, population growth, and epidemiological changes to the disease burden. High SDI and High-middle SDI regions experienced declines in numbers of incidence, prevalence, and YLDs, primarily driven by favorable epidemiological changes. This indicates that disease prevention and health promotion can effectively mitigate the challenges posed by demographic changes (population growth and population aging) to endometriosis. Low SDI and Low-middle SDI regions saw increases in incident cases, prevalent cases, and YLDs cases, with population growth being the dominant factor. Statistically, the 47 least developed countries are among the fastest growing countries in the world, and many of them are expected to double their populations from 2019 to 2050 [34]. Overall, in the coming decades, population growth will have a greater impact on some low SDI and lower-middle SDI regions, leading to a continued increase in the burden of endometriosis, while the impact on high-level SDI regions will stabilize. Therefore, when formulating or adjusting health prevention measures, international organizations or national governments should consider the potential impact of population growth on health in different regions.

To the best of our knowledge, this study is the first to comprehensively analyze the global burden of surgically confirmed endometriosis from 1990 to 2021, using robust statistical methods to assess trends and correlations. With each iteration of the GBD, the disease classification methods have become more standardized, and more in-depth systematic evaluation methods have been used to obtain country-specific information, providing reliable data sources for this study. Methodological advancements have enabled GBD 2021 to produce estimates more easily than in previous iterations; however, as with any study of this scope, there are several important limitations to acknowledge. First of all, inconsistencies in the availability of primary epidemiological data remain a limitation and source of instability within GBD analyses. The estimates of disease burden depend on the out-of-sample predictive validity of modelling processes in cases where data are insufficient to produce burden estimates for all 204 countries and territories (by year, sex, and age). Although this approach cannot fully replace high quality primary data, it ensures that populations or causes with no or little data are not excluded from important benchmarking exercises intended for burden estimation. In addition, with any given GBD release, there might be extant data not identified or incorporated, which is a key part of the rationale for ongoing cycles of releases, rather than a single update. For the primary

data available, the data processing methods account for known sources of variation wherever possible, but fully disentangling variation in estimates is not always possible due to measurement error and reporting inaccuracies. There are problems with the quality and collection of primary data, such as flawed methodologies and potential under-reporting of illnesses, which is a recurring limitation for GBD that can be continually improved on by strengthening data-collection systems [39]. This study also has some limitations. First, sparsity of data or unreliability of data from specific regions, time periods, or age groups can influence the accuracy of the endometriosis burden estimates, particularly poor data quality and coverage from western, eastern, southern, and central sub-Saharan Africa and south Asia [40]. Second, the disease burden may be underestimated in some low- and middle-income regions due to limited data or lack of gold-standard diagnostics like laparoscopy. Third, as our study spans three decades, changes in the diagnostic criteria for the disease may impact the temporal trend analysis. Finally, in the decomposition analysis, the selection of driving factors may not be comprehensive enough, attributing only to population aging, population growth, and epidemiological changes. Due to the lack of relevant data, other influencing factors such as environment, diet, lifestyle, or genetic susceptibility were not included temporarily, future research may focus on this issue.

Conclusions

Despite the global age-standardized rates of incidence, prevalence, and YLDs have shown a decreasing trend in the past 30 years, endometriosis will continue to be a major public health burden due to the increasing number of cases worldwide. Managing this condition remains a significant challenge and requires better allocation of healthcare resources and more targeted interventions. Our study has comprehensively assessed the burden of surgically confirmed endometriosis and offered epidemiological evidence, which will provide valuable solutions for relevant policymakers to improve health management.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12958-025-01421-z>.

Supplementary Material 1: Table S1. The prevalence of endometriosis in 1990 and 2021 and temporal trends between 1990 and 2021.

Supplementary Material 2: Table S2. The YLDs of endometriosis in 1990 and 2021 and temporal trends between 1990 and 2021.

Supplementary Material 3: Figure S1. The ASPR of endometriosis in 204 countries and territories in 2021. ASPR, age-standardized prevalence rate.

Supplementary Material 4: Figure S2. The age-standardized YLDs rate of endometriosis in 204 countries and territories in 2021. YLDs, years lived with disability.

Supplementary Material 5: Figure S3. Joinpoint regression analysis in ASPR from 1990 to 2021 by SDI region, * $P < 0.05$. ASPR, age-standardized prevalence rate; SDI, socio-demographic index.

Supplementary Material 6: Figure S4. Joinpoint regression analysis in age-standardized YLDs rate from 1990 to 2021 by SDI region, * $P < 0.05$. YLDs, years lived with disability; SDI, socio-demographic index.

Supplementary Material 7: Figure S5. Coevolution of ASPR with SDI globally and for GBD regions of endometriosis, 1990–2021. ASPR, age-standardized prevalence rate; SDI, socio-demographic index.

Supplementary Material 8: Figure S6. Coevolution of age-standardized YLDs rate with SDI globally and for GBD regions, 1990–2021. YLDs, years lived with disability; SDI, socio-demographic index.

Supplementary Material 9: Figure S7. Changes in endometriosis prevalence, decomposed by three population-level determinants: aging, population, and epidemiological change.

Supplementary Material 10: Figure S8. Changes in endometriosis YLDs, decomposed by three population-level determinants: aging, population, and epidemiological change. YLDs, years lived with disability.

Author contributions

Ruijie Li: Methodology, Data curation, Formal analysis, Writing—original draft. Ling Zhang: Writing—review & editing. Yi Liu: Conceptualization, Project administration, Writing—review & editing.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

The requirement for ethical approval and informed consent was not applicable because the data in this study were secondary data and did not contain any data which could identify individuals.

Competing interests

The authors declare no competing interests.

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