

# A Systematic Review of the Global Burden of Endometriosis

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## Introduction

- Endometriosis is a chronic gynecological condition characterized by the presence of tissue resembling endometrium (the lining of the uterus) outside the uterus. This causes a chronic inflammatory reaction that can lead to the formation of scar tissue within the pelvis and other areas of the body.
- The symptoms of endometriosis include: chronic pelvic pain (CPP); pain during periods, sexual intercourse, bowel movements and urination; fatigue; depression/anxiety; abdominal bloating; nausea. Endometriosis can also cause infertility.
- These symptoms can have a negative influence on many aspects of a woman's daily life, including their emotional well-being, social and family relations, sexual function and work productivity (Culley 2013, Moradi 2014).
- The prevalence of endometriosis is approximately 10% in women of reproductive age, 25–40% in women with infertility, and >50% in women with CPP (Ozkan 2008, Triolo 2013). Currently, there is no cure for endometriosis, and the goal of therapy and surgery is to alleviate symptoms.
- In addition to medical costs, the economic burden of endometriosis is exacerbated by absences and reduced productivity at work, which are proportional to disease severity (Facchin 2018, Soliman 2017a, Soliman 2018).
- This review explores the economic burden of moderate-to-severe endometriosis from a global and societal perspective.

## Methods

- A literature search was conducted using Embase.com (Medline + EMBASE) on 16 April 2023. The search and screening of evidence was structured according to the following PICOS framework: Population (women with moderate-to-severe endometriosis), Intervention/Comparators (not relevant), Outcomes (burden-of-illness [BOI] reported in monetary terms, health care resource use [HCRU] quantities, or lost time [total per population or average per patient]), Study Type (original BOI study). Studies only reporting numbers or proportions of women accessing specific treatments/services were excluded.
- An initial scoping search found few studies reporting the BOI from endometriosis at the population level. Therefore, the review also included studies reporting the average BOI per patient.
- The search was restricted to English language studies published since 2017 to identify BOI estimates that best reflect current epidemiology and treatment practice. In total, 436 citations were identified.
- Screening was conducted in line with the PICOS criteria. Studies where women with endometriosis were a subgroup (e.g., of women with CPP) were included if subgroup results were reported. To maximize the relevant information, conference abstracts were eligible for inclusion.
- Following two rounds of independent screening by two researchers, 27 studies (17 full papers and 10 conference abstracts) were retained. Study data were extracted into a Microsoft Excel data collection form by one researcher and audited by another researcher. Reported costs were not converted to other currencies or inflated to current prices.

## Results

- Twenty-seven studies were identified, including: 20 retrospective analyses of United States (US), Hungarian and Brazilian databases; five patient surveys conducted in Australia, Canada, Sweden, and an international trial; and two prospective hospital cost studies in Canada and Finland.
- Generally, studies used primary/secondary diagnosis codes to identify endometriosis-related healthcare claims and hospital admissions. Two studies instead compared total costs in women with or without endometriosis.
- Only six studies reported a total population BOI: others reported the mean cost per patient or hospital admission.
- The highest costs were reported in US hospital studies, which are less generalizable since many patients require no inpatient care. In other studies, the relative contribution of outpatient to total costs varied, although pharmaceutical costs were consistently minor. Direct costs increased with disease/pain severity, symptoms, diagnostic delay, opioid use, and surgical complexity.
- Seven studies reported indirect costs, suggesting these comprise at least half of the total BOI (although most only considered absenteeism). One study also accounted for informal caregiver time.
- Only six studies estimated the total national burden of endometriosis, including three in Hungary, and others in Australia, Brazil and Canada.
- Study limitations were common to retrospective studies (biases) and hospital studies (narrow perspective/generalizability, use of charges). Most studies did not consider costs beyond the first year after diagnosis.

## Conclusions

- Published studies of the burden from endometriosis vary considerably by setting, scope, and methodology, which contributes to the large variations in reported costs.
- However, the overall findings suggest a substantial economic burden is associated with endometriosis with respect to both direct healthcare costs and indirect costs of lost productivity.

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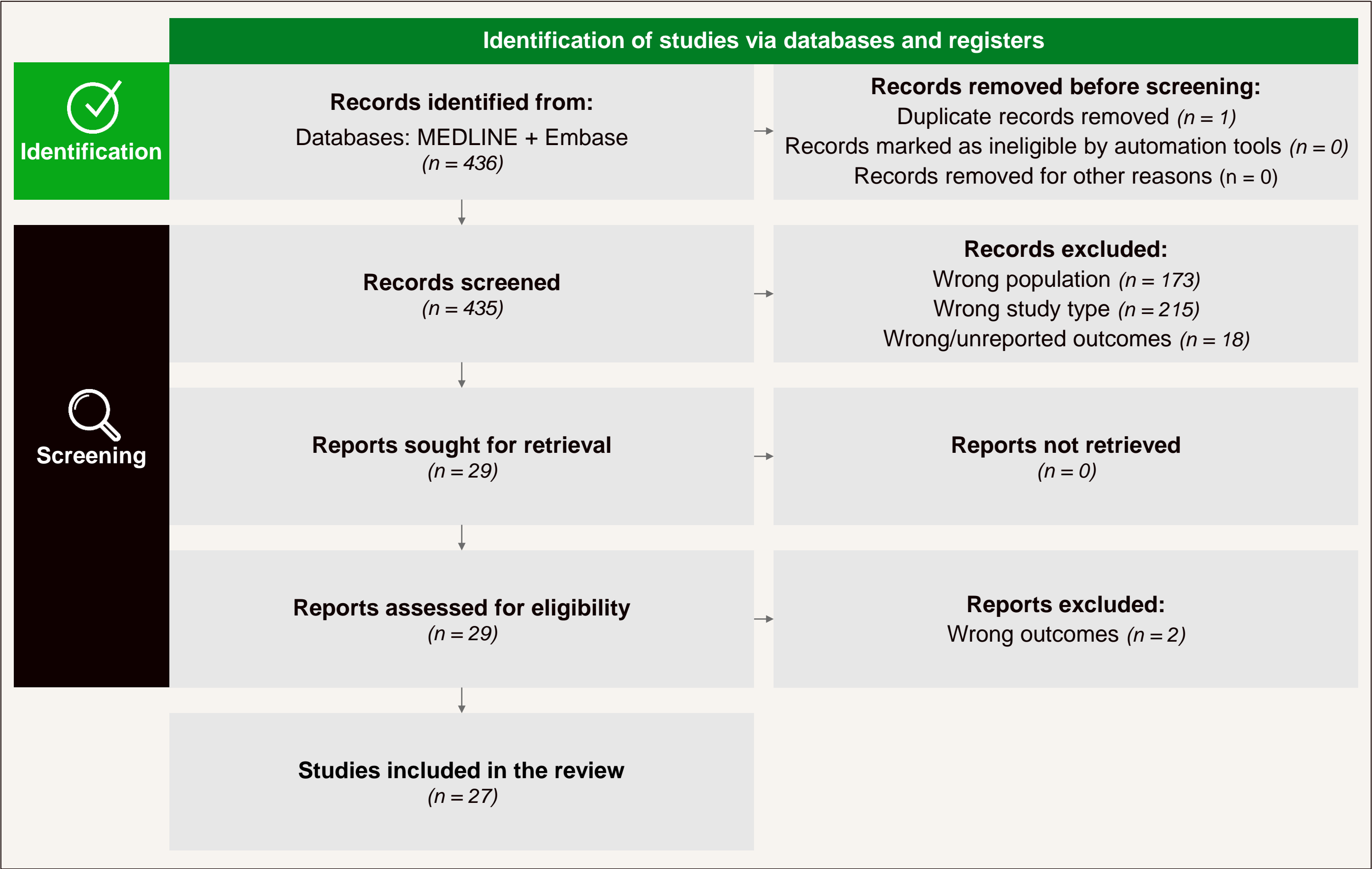


Figure 1. PRISMA diagram of the study selection process

Reference	Country	Study period	Study design	Subjects evaluated	Key results
Armour 2019	Australia	Feb–Apr 2017	RS	407	Mean total (direct + indirect) annual cost per patient = US\$20,898 (95% CI: US\$18,999, US\$23,213). Total economic burden per year = US\$6.50bn. 2017 prices.
As-Sanie 2020	US	Jan 2011–Dec 2016	RCD	43,516	Mean 12-month endometriosis-related direct costs per patient = US\$6162 (opioid group), US\$4119 (non-opioid group). 2015 prices.
Chen 2020	Canada	Apr 2008–Mar 2013	RHD	47,021	Total hospital costs over study period = Ca\$152m, Mean hospital cost = Ca\$30m per year, Ca\$3237 per case. Prices as per study year.
Darba 2022a	Spain	Jan 2009–Dec 2018	RHD	41,118	Mean admission cost per patient over study period = €3566. Prices as per study year.
Epstein 2017	US	Jan 2006–Sep 2015	RCD	180,278	Mean cumulative total spending per patient since endometriosis diagnosis ranged from US\$20,171 (year 1) to US\$58,191 (year 5). 2015 prices.
Estes 2019	US	2006–2015	RHD	189,443	Mean total hospital charge per stay = US\$22,642 (2006-07), US\$30,977 (2010-11), US\$39,662 (2014-15). 2015 prices.
Estes 2020a	US	Jan 2009–Sep 2018	RHD	24,235	Mean endometriosis-related costs per patient in 24 months post-index by opioid use = US\$8629 (opioid users), US\$5792 (non-opioid users). 2018 prices.
Estes 2020b	US	Jan 2009–Sep 2018	RHD	24,235	Mean endometriosis-related costs per patient in 12 months post-index by opioid use = US\$525 (high-risk users), US\$ 420 (low-risk users), US\$656 (chronic users), US\$380 (non-chronic users). 2018 prices.
Grundstrom 2020	Sweden	Jan–Dec 2010	RS	431	Mean total (direct + indirect) annual cost per patient = €8768 (2019 prices).
Malik 2022	Australia	Feb–Apr 2017	RS	340	Women on average spent A\$460.04 on complementary therapy and allied health services. Total direct costs in the past two months for all endometriosis patients were A\$10,525 (physiotherapists), A\$7555 (mental health workers), A\$7320 (naturopaths), A\$6587 (acupuncturists). Prices as per study year.
Pokrzywinski 2019	US	Jul 2012–Jul 2015	RCD	1298	Mean annual work lost per patient due to endometriosis-associated pain = 792 hours (EM-I), 730 hours (EM-II).
Pynna 2021	Finland	Jun 2012–Aug 2015	PS	389	Direct hospital costs: at six months = €808 (university hospitals), €190 (community hospitals); at two years = €3958 (university hospitals), €2421 (community hospitals). Mean productivity cost = €424 (baseline), €804 (two years). Prices according to study year.
Soliman 2017b	US	Jan 2006–Jun 2014	RCD	161,636	Mean endometriosis-related healthcare costs per patient 12 months post-index = US\$8417 (surgery cohort), US\$275 (non-surgery cohort). 2014 prices.
Soliman 2018	US	Jan 2009–Jun 2015	RCD	113,506	Mean endometriosis-related healthcare cost per patient 12 months post-index = US\$6498. 2014 prices. Results also report endometriosis-related HCRU as per Soliman (19), and mean costs by age group and pharmacy component. Total (all-cause) costs for endometriosis patients statistically significantly higher than controls.
Soliman 2019	US	Jan 2007–Dec 2015	RCD	15,615	Mean endometriosis-related healthcare costs per patient 12 months post-index = US\$3069. 2015 prices.
Soliman 2021	Canada	Dec 2018–Jan 2019	RS	2004	Hours worked/missed in the week prior to survey completion: women employed full/part-time = 25.4/3.8, women with ≥1 hallmark symptom = 26.6/4.1, women with no hallmark symptoms = 22.7/3.1.
Surrey 2020	US	Jan 1999–Jul 2017	RCD	11,793	Mean endometriosis-related HCRU per woman in 60-month pre-diagnosis period = 4.6 ambulatory visits, 0.2 ED visits, 0.03 inpatient stays. Mean endometriosis-related healthcare cost per woman in 60-month pre-diagnosis period = US\$3553. 2016 prices.

Figure 2. Summary of full papers on the BOI for endometriosis published since 2017

Reference	Country	Study period	Study design	Subjects evaluated	Key results
Aggarwal 2018	US	Jan–Dec 2015	RHD	NR	4492 admissions. Overall mean (SD) charge per admission by payer: all = US\$40,325 (US\$34,894), Medicare = US\$51,295 (US\$76,692), Medicaid = US\$39,566 (US\$37,589), private = US\$39,985 (US\$27,766)
Boncz 2019	Hungary	Jan–Dec 2017	RCD	NR	Total cost in 2017 = 1.68bn HUF
Csakvari 2022	Hungary	Jan – Dec 2019	RCD	NR	Total cost in 2019 = 133m HUF. Annual health care treatment cost per patient was 82,786 HUF according to patients receiving outpatient care.
Darba 2022b	Spain	Jan 2009–Dec 2018	RHD	41,118	Mean admission cost per patient over study period = €3566. Prices as per study year.
Estes 2020b	US	Jan 2009–Dec 2018	RCD	61,019	Mean annual results by opioid use (high-risk/low-risk/chronic/non-chronic): outpatient visits = 18.6/14.9/19.2/14.7; inpatient visits = 0.2/0.1/0.3/0.1; ED visits = 0.8/0.5/0.9/0.5; prescriptions = 21.3/16.9/23.3/16.5; inpatient days = 1.1/0.6/1.2/0.6; mean total cost per patient = US\$17,993/12,213/20,240/11,770 (price year not reported). All differences for high-risk vs low-risk and chronic vs non-chronic were significant (p<0.0001)
Guilhon 2020	Brazil	Jan 2008–Aug 2019	RCD	NR	Overall cost for study period = 93,081,503 BRL (2019 prices). Goserelin was the most dispensed drug (27,115 patients) and hysterectomy with unilateral / bilateral adnexectomy was the most applied procedure (26,601 patients). Total drug costs were 37,263,506 BRL (goserelin), 225,018 BRL (triptorelin), 1,514,510 BRL (leuporelin) and 211,995 BRL (danazol). Hospitalizations/costs decreased from 7,136/4m BRL in 2008 to 3,793/2m BRL in 2019.
Kajos 2022	Hungary	Jan – Dec 2019	RCD	NR	Total cost in 2019 = 416m HUF. Annual health care treatment cost per patient = 128,446 HUF.
Kelly 2020	US	Jan 2015–Mar 2018	RCD	72,840	Mean (SD) total costs per patient by method of annualizing costs: method A = US\$20,950 (US\$31,352); method B = US\$22,868; method C = US\$32,379 (US\$171,563)
Nometh 2020	Hungary	Jan–Dec 2018	RCD	NR	Total cost in 2018 = 725m HUF. Mean annual cost per woman = 96,932 HUF.
Yeung 2017	Canada	NR	PS	NR	Costs at 5/10 years for ≤10 cases/month = HGPE \$429,760, laser \$791,385/HGPE \$786,660, laser \$1,358,065. Costs at 5 years for 21 cases/month = HGPE \$822,350, laser \$791,385. Costs at 10 years for 19 cases/month = HGPE \$1,429,080/laser \$1,358,065. HGPE less expensive than laser at 5 and 10 years when monthly cases <20.

Figure 3. Summary of conference abstracts on the BOI for endometriosis published since 2017

## Abbreviations

A\$=Australian dollars; BOI=burden of illness; BRL=Brazilian Real; Ca\$=Canadian dollars; CI=confidence interval; CPP=chronic pelvic pain; AE=emergency department; HCRU=healthcare resource utilization; HGPE=helium gas plasma energy; HUF=Hungarian forint; NR=not reported; PRISMA=Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PS=prospective study; RCD=retrospective claims database; RHD=retrospective hospital database; RS=retrospective survey; SD=standard deviation; US=United States; US\$=United States dollars

