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Review article

Increased risk of cardiovascular disease in women with endometriosis: A systematic review and meta-analysis

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ABSTRACT

Background: The association between endometriosis and cardiovascular disease remains poorly understood. This study conducted a meta-analysis to evaluate the risk of adverse cardiovascular outcomes in women with endometriosis compared to those without the condition.

Methods: A comprehensive search of online databases was performed up to November 2024 to identify studies comparing adverse cardiovascular outcomes in women with and without endometriosis. A random-effects model was employed for the meta-analysis to calculate hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: The meta-analysis included seven studies encompassing a total of 1,407,875 participants. Women with endometriosis demonstrated a significantly increased risk of cerebrovascular disease (HR: 1.19, 95 % CI: 1.13–1.24, $p < 0.00001$) and ischemic heart disease (HR: 1.35, 95 % CI: 1.32–1.39, $p < 0.00001$). Additionally, the risk of major adverse cardiovascular events (HR: 1.15, 95 % CI: 1.13–1.19, $p < 0.00001$) and arrhythmias (HR: 1.21, 95 % CI: 1.17–1.25, $p < 0.00001$) was significantly elevated. However, no significant associations were observed for heart failure or all-cause mortality.

Conclusion: This meta-analysis indicates that women with endometriosis are at heightened risk for several cardiovascular conditions. These findings underscore the need for robust prospective studies to validate these associations and to explore underlying mechanisms.

Introduction

Cardiovascular disease (CVD) remains the leading global cause of death among women, accounting for approximately one-third of all deaths [1]. Notably, middle-aged women (45–64 years) are experiencing the most rapid relative increase in atherosclerotic cardiovascular disease (ASCVD) mortality, highlighting this demographic as a critical high-risk group requiring focused attention [1,2]. While traditional risk factors such as smoking and diabetes are shared between men and women, emerging research highlights unique, sex-specific contributors to CVD in women, including polycystic ovary syndrome (PCOS) [3], hypertensive disorders of pregnancy [4–6], and primary ovarian insufficiency [7,8]. These conditions collectively heighten the risk of CVD, specifically ASCVD, in women.

Endometriosis, a condition characterized by the presence of endometrial glands and stroma outside the uterine cavity [9], affects approximately 10 % of women of reproductive age [10]. This disorder shares several pathophysiological features with CVD, including systemic inflammation, oxidative stress, endothelial dysfunction, and dysregulated lipid metabolism [11–13]. Endometriosis often manifests with debilitating symptoms, including chronic pelvic pain and dyspareunia, which significantly impair quality of life [9]. Its diagnosis typically relies on imaging or surgical visualization, although histopathological confirmation remains the gold standard [11]. Management involves hormonal therapies or surgical excision of lesions [14].

Recent studies have highlighted a potential link between endometriosis and heightened risk of adverse cardiovascular outcomes, including coronary artery disease and stroke [15–21]. However, significant gaps persist in the understanding of the relationship between endometriosis and CVD. Recent expert commentary has underscored the

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need for comprehensive investigations [12,13]. Previous meta-analyses on this topic were limited to a narrow range of outcomes [22,23]. Since then, large-scale observational studies have emerged that demand a more comprehensive analysis.

This systematic review and meta-analysis aim to consolidate the existing body of evidence by examining the association between endometriosis and cardiovascular disease comprehensively. By synthesizing all available data, this review seeks to provide a more nuanced understanding of the relationship and guide future research efforts in this critical area of women's health.

Methods

This systematic review and meta-analysis followed the methodological standards set by the Cochrane Handbook for Systematic Reviews of Interventions. The findings were reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [24,25].

Eligibility criteria and outcomes

The inclusion criteria were as follows: (i) all prospective and retrospective cohort studies; (ii) patients with endometriosis, regardless of age, duration, or severity of the disease; (iii) studies reporting cardiovascular outcomes, including cerebrovascular disease, ischemic heart disease, major adverse cardiovascular events (MACE), arrhythmias, heart failure, and mortality; (iv) studies that included one group of patients with endometriosis and a comparison group without endometriosis; and (v) studies reporting cardiovascular outcomes using adjusted hazard ratios. The exclusion criteria were: (i) cross-sectional studies, reviews, case series, and case reports; and (ii) studies that reported effect estimates other than adjusted hazard ratios.

Data sources and search strategy

A thorough electronic search was performed in PubMed, Scopus, and the Cochrane Central Register of Controlled Trials from inception until November 2024. The detailed search strategy is presented in (Online Supplementary Table S1). Articles identified through this systematic search were imported into rayyan.ai for the removal of duplicates. The selection process occurred in two stages: an initial screening based on titles and abstracts, followed by a full-text review using predefined eligibility criteria. Both stages were conducted independently by two reviewers (SIA and IA), with any discrepancies resolved through discussion between them.

Data extraction and quality assessment

Two independent reviewers (IA and SIA) conducted data extraction and quality assessment of the included studies, resolving any disagreements through discussion. The extracted data encompassed baseline characteristics, trial demographics, and outcome measures, which were recorded in an Excel spreadsheet. The risk of bias in the included studies was assessed using the Newcastle-Ottawa tool. To ensure the accuracy and reliability of the extracted data, all authors collectively reviewed the information.

Statistical analysis

The primary effect measure used in this meta-analysis was the adjusted hazard ratio (HR) with corresponding 95 % confidence intervals (CIs). Adjusted HRs were extracted from each study to account for potential confounding variables. The Higgins I^2 statistic was used to assess heterogeneity across studies, with I^2 values of 25 %, 50 %, and 75 % serving as benchmarks for low, medium, and high heterogeneity, respectively. Statistical significance was defined as a p-value of < 0.05. Forest plots were generated for visual representation, and funnel plots were utilized to evaluate potential publication bias. Sensitivity analyses were planned to evaluate the robustness of the results by excluding individual studies to assess their impact on the overall findings. All statistical analyses were conducted using Review Manager (Version 5.4, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020).

Results

Literature search and selection

The PRISMA flowchart (Online Supplementary Fig. S1) summarizes the search and selection process. After screening 692 titles and abstracts, 26 studies were selected for full-text review. Of these, seven observational studies examining the relationship between endometriosis and CVD, with a combined sample size of 1,407,875 participants, met the inclusion criteria and were included in the final analysis [16–21,26].

Study characteristics

All seven studies were cohort studies, with six retrospective [16,18–21,26] and one prospective [17]. The studies were conducted in diverse locations, including Canada [20], Denmark [21], Taiwan [18,19,26], the United States [17], and the United Kingdom [16].

The sample sizes varied significantly, ranging from 5,244 endometriosis patients vs. 106,812 controls to 166,853 endometriosis patients vs. 333,706 controls. The mean ages of endometriosis patients across studies were comparable, generally between 36 and 38 years, with standard deviations reflecting slight variations. The median follow-up duration ranged from 7.02 years [26] to 28 years [17].

The diagnosis of endometriosis was predominantly based on ICD codes, including ICD-9 and ICD-10, with some studies requiring surgical confirmation [16,20], while others accepted clinical or self-reported diagnoses [17,18]. (Table 1).

Adjustments for confounders varied among studies. Commonly adjusted variables included age, hypertension, diabetes, hyperlipidemia, obesity, and hormone use. Other specific factors, such as socioeconomic status, smoking, and parity, were also accounted for in certain studies. Based on the Newcastle-Ottawa Scale (NOS) assessment, the majority of the observational studies included in this analysis were of high to fair quality, with only one study categorized as low quality. Three studies received a perfect NOS score of 9/9 [19–20]. Two studies demonstrated high quality with scores of 8/9 [16,18]. One study received a fair-quality score of 7/9 [17]. However, Li et al., scoring 6/9, was the only study classified as low quality [26]. The quality assessment for included studies is summarized in (Online Supplementary Table S2).

Results of meta-analysis

Cerebrovascular disease

Four studies reported the risk of cerebrovascular disease in women with endometriosis compared to those without. The pooled analysis showed that endometriosis was associated with an increased risk of cerebrovascular disease (HR: 1.19 [1.13–1.24]; $p < 0.00001$; $I^2 = 0$ %). (Fig. 1).

Ischemic heart disease (IHD)

The association between endometriosis and IHD was examined in four studies. The meta-analysis indicated a significantly elevated risk of ischemic heart disease in women with endometriosis (HR: 1.35 [1.32–1.39]; $p < 0.00001$; $I^2 = 0$ %) (Fig. 2).

Major adverse cardiovascular events (MACE)

Four studies explored the relationship between endometriosis and MACE. The meta-analysis revealed that endometriosis was significantly

Table 1
Baseline characteristics of the included studies.

Study, year	Design	Location	Data source	No. of endometriosis patient's vs women without endometriosis	Age, year, mean ± SD	Median Follow up (years)	Diagnosis of endometriosis	Outcome assessment	Outcome adjustment	Outcome
Blom 2023	Retrospective Cohort	Canada	Institute for Clinical Evaluative Sciences	166,853 EM vs 333,706 Non-EM	36.4 ± 8.0 EM vs 36.4 ± 8.0 Non-EM	24	ICD9 Diagnostic codes including surgical confirmation	Cardiovascular Health in Ambulatory Care Research Team (CANHEART) study and Discharge Abstracts Data base (DAD), National Ambulatory Care Reporting System database (NACRS), Same Day Surgery Database (SDS) and Ontario Health Insurance Plan (OHIP), using ICD9 and ICD10 codes	Age, parity, hypertension, diabetes, obesity and immigration status, diagnosis of premature ovarian insufficiency	Primary outcome: CVD (acute myocardial infarction, stroke, congestive heart failure, percutaneous coronary intervention, coronary artery bypass graft surgery, ischemic heart disease and cerebrovascular disease) Secondary outcomes: cardiac catheterization, unstable angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, atrial fibrillation, abdominal aortic aneurysm, peripheral artery disease and cardiac stent), emergency department visits for CVD
Havers-Borgerson 2024	Retrospective Cohort	Denmark	Danish National Patient Registry	60,508 EM vs 242,032 Non-EM	37.3 ± 3.7 Overall	16.1	ICD8 and 10 codes	ICD8 and 10 codes	pre-existing CVD (acute myocardial infarction or ischaemic stroke), congenital heart disease, cardiomyopathy, thyroid dysfunction, diabetes, gestational diabetes, hypertension, chronic kidney disease, rheumatological disease, pre-eclampsia, and polycystic ovarian syndrome	Primary outcome: Composite of Acute myocardial infarction and ischemic stroke Secondary outcomes: Acute myocardial infarction, Ischemic stroke, arrhythmias (i.e. sinoatrial dysfunction, atrial flutter/ fibrillation, advanced atrioventricular block, ventricular arrhythmias, cardiac arrest, and implantation of cardiac electronic devices), heart failure, and all-cause mortality
Wei 2021	Retrospective Cohort	Taiwan	Taiwan National Health Insurance Research Database (NHIRD)	13,988 EM vs 13,988 Non-EM	37.8 ± 8.4 EM vs 37.9 ± 8.5 Non-EM	13	ICD9-CM codes	Clinical codes (ICD9-CM code 410–414 and emergency or inpatient diagnosis of CAD)	Age, hypertension, hyperlipidemia, diabetes, cancer, COPD (Chronic Obstructive Pulmonary Disease), autoimmune diseases, stroke, hysterectomy/ oophorectomy, frequency of outpatient visits, corticosteroids, NSAIDs, aspirin and statin.	Coronary heart disease

(*continued on next page*)

Table 1 (*continued*)

Study, year	Design	Location	Data source	No. of endometriosis patient's vs women without endometriosis	Age, year, mean ± SD	Median Follow up (years)	Diagnosis of endometriosis	Outcome assessment	Outcome adjustment	Outcome
Li 2021	Retrospective Cohort	Taiwan	Taiwan National Health Insurance Research Database (NHIRD)	19,454 EM vs 77,816 Non-EM	37.37 ± 8.95 EM vs 37.34 ± 9.13 Non-EM	7.36 EM vs 7.02 Non-EM	ICD9-CM codes	ICD9-CM codes	Obesity, CKD, Hypertension, Hyperlipidemia, diabetes mellitus, hysterectomy and oophorectomy, hormone, statin, aspirin, antihypertensives, diabetes medication, insulin therapy	Coronary artery disease
Farland 2022	Prospective Cohort	United States	Nurses' Health Study II	5244 EM vs 106,812 Non-EM	36 ± 4.2 EM vs 34.7 ± 4.7 Non-EM	28	Self-reported laparoscopic confirmation	Self-reported	Hypertension, hypercholesterolemia, age at menopause, hysterectomy of oophorectomy and hormone therapy use	Stroke
Okoth 2021	Retrospective Cohort	United Kingdom	The Health Improvement Network database (THIN)	56,090 EM vs 223,669 Non-EM	36.7 ± 2.9 EM vs 36.7 ± 2.9 Non-EM	20	Diagnostic codes including surgically confirmed and coded endometriosis cases, and physician assigned codes based on clinical suspicion	Clinical codes	Age, smoking status, hormonal contraceptive use, lipid-lowering medication, BMI (Body Mass Index), alcohol use, polycystic ovary syndrome, migraine and connective tissue disorders.	Primary outcome: cardiovascular disease including ischemic heart disease, heart failure and cerebrovascular disease. Secondary outcome: all-cause mortality.
Chiang 2021	Retrospective Cohort	Taiwan	Taiwan National Health Insurance Research Database (NHIRD)	17,543 EM vs 70,172 Non-EM	38 ± 3.3 Overall	9.3	Clinically diagnosed (ICD9CM code: 617) and with image or procedure-proven evidence	Identified with ICD9-CM codes and confirmed by 3 consecutive records of outpatient visits or a one-time diagnosis on admission with the corresponding standard treatment during the whole study period.	Age, socioeconomic background, hypertension, diabetes mellitus, dyslipidemia, gout and amenorrhea	Major cardiovascular disease (including acute myocardial infarction or heart failure) and cerebrovascular accident (including acute ischemic or hemorrhagic stroke).

EM = Endometriosis, Non-EM= Non-Endometriosis, CKD= Chronic Kidney Disease, CVD= Cardiovascular Disease, NSAIDs= Non-Steroidal Anti-Inflammatory Drug.

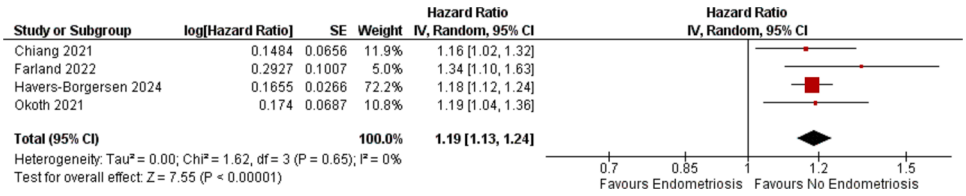

Fig. 1. Risk of cerebrovascular disease in women with endometriosis compared to those without.

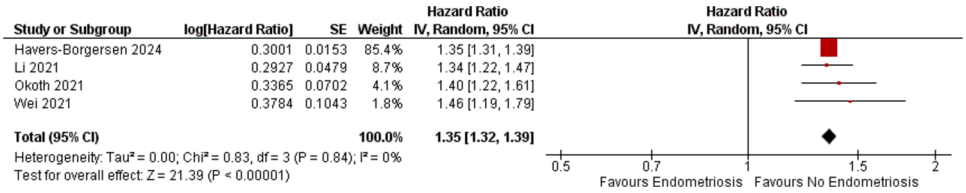

Fig. 2. Risk of ischemic heart disease in women with endometriosis compared to those without.

associated with a higher risk of MACE (HR: 1.15 [1.13–1.19]; $p < 0.00001$; $I^2 = 11$ %) (Fig. 3).

Arrhythmia

Two studies assessed the risk of arrhythmia in women with endometriosis. The pooled analysis showed a significant association, with women with endometriosis exhibiting a higher likelihood of arrhythmias (HR: 1.21 [1.17–1.25]; $p < 0.00001$; $I^2 = 0$ %) (Fig. 4).

Heart failure

Two studies investigated the incidence of heart failure among women with and without endometriosis. The meta-analysis showed that heart failure risk was comparable between the two groups (HR: 0.96 [0.66–1.37]; $p = 0.80$; $I^2 = 78$ %) (Fig. 5). Due to the limited number of studies available, sensitivity analysis could not be conducted for this outcome.

All-cause mortality

Two studies examined the association between endometriosis and all-cause mortality. The meta-analysis found no statistically significant link between endometriosis and all-cause mortality (HR: 0.79 [0.56–1.10]; $p = 0.16$; $I^2 = 97$ %). (Fig. 6) Due to the limited number of studies available, sensitivity analysis could not be conducted for this outcome.

Discussion

In our meta-analysis assessing cardiovascular risk in women with endometriosis compared to those without, we identified several key findings. Endometriosis was significantly associated with an elevated risk of cerebrovascular disease, IHD, MACE, and arrhythmia. Conversely, heart failure and mortality rates were comparable between women with and without endometriosis. These results underscore the critical intersection between endometriosis and cardiovascular risk, particularly pertinent given the rising prevalence of CVD in middle-aged women [1]. Our findings contribute valuable insights to a growing body of literature that calls for moving beyond traditional risk factors and adopting a more comprehensive approach—integrating cardiovascular health with gynecological profiles and addressing sex-specific determinants [21] (Graphical Abstract, Fig. 7).

Our results are consistent with previous studies, including a meta-analysis by Poeta do Couto et al, which reported an increased risk of cerebrovascular disease and IHD associated with endometriosis [23]. While these studies have highlighted significant knowledge gaps in endometriosis research, prior analyses are limited by poor-quality studies, inadequate adjustments for confounders, and a limited range of cardiovascular outcomes, diminishing their reliability and scope. By incorporating two recent studies [20,21], including the rigorously matched and high-quality analysis by Havers-Borgensen et al. [21], our meta-analysis doubles the sample size, thereby enhancing statistical power and delivering more robust quantitative conclusions. Additionally, our exploration of previously underreported cardiovascular outcomes—including MACE, arrhythmias, heart failure, and mortality—provides a more comprehensive risk profile for women with endometriosis.

The pathophysiology of endometriosis is complex and multifaceted, involving several interconnected mechanisms that may explain its association with an elevated cardiovascular risk. Chief among these are chronic inflammation, oxidative stress, and immune dysregulation, which collectively create a systemic environment conducive to cardiovascular dysfunction. Inflammation, a pivotal driver, primarily arises in endometriosis from hormonal imbalances, specifically elevated estrogen levels and progesterone resistance [9]. Elevated estrogen promotes the growth of ectopic endometrial tissue, leading to chronic inflammation, scarring, and adhesions [27,28]. This cascade triggers the release of pro-inflammatory cytokines and growth factors, which exert widespread systemic effects, including those on the cardiovascular system [12,29]. Conversely, progesterone resistance diminishes the anti-inflammatory and antiproliferative effects of progesterone [27,28], creating a positive feedback loop that sustains and amplifies chronic inflammation over time [30]. This heightened inflammatory state is evidenced by elevated levels of inflammatory biomarkers found in both the serum and

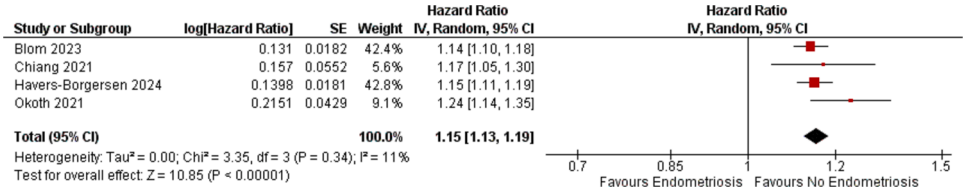

Fig. 3. Risk of major adverse cardiovascular events in women with endometriosis compared to those without.

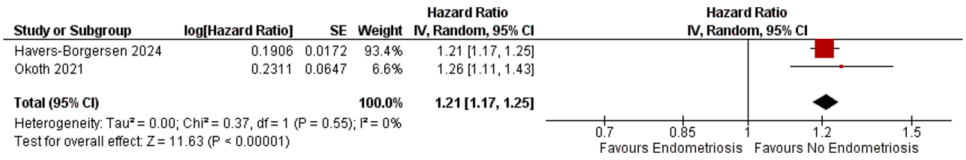

Fig. 4. Risk of arrhythmias in women with endometriosis compared to those without.

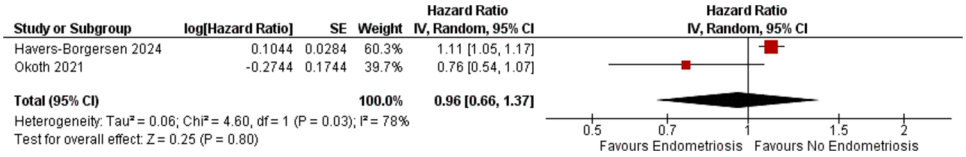

Fig. 5. Risk of heart failure in women with endometriosis compared to those without.

peritoneal fluid of women with endometriosis [13], many of which have been directly linked to endothelial dysfunction—a recognized surrogate marker for cardiovascular risk [9,13]. Oxidative stress represents another critical pathway, as increased exposure to reactive oxygen species in endometriosis has been linked to vascular dysfunction and arrhythmias [31,32]. Moreover, the aberrant immune-endocrine environment characteristic of endometriosis also amplifies its association with CVD. Key features of this immune dysregulation include the reduced apoptotic activity of natural killer cells and angiogenesis-promoting M2 macrophages in the peritoneal fluid [33]. These immune alterations further drive the growth of ectopic endometrial tissue, perpetuate chronic inflammation, and promote endothelial dysfunction, reinforcing the connection between endometriosis and cardiovascular pathology [9,13]. Lastly, women with endometriosis often exhibit a more atherogenic lipid profile, with elevated high-density lipoprotein and low-density lipoprotein cholesterol levels, providing additional evidence for the link between endometriosis and CVD [34]. Together, these interconnected mechanisms illustrate the complex relationship between endometriosis and cardiovascular dysfunction, emphasizing the need for more targeted research to elucidate these links fully.

A significant confounder in studies examining the relationship between endometriosis and CVD is the impact of endometriosis treatments on cardiovascular risk. Surgical interventions, including hysterectomy and oophorectomy, are associated with an increased risk of coronary artery disease (CAD) [15] and stroke [17] in women with endometriosis compared to those without. While hysterectomy alone is a well-established CVD risk factor, the addition of oophorectomy may exacerbate this effect due to the abrupt decline in estrogen levels [35]. Similarly, hormonal treatments, including combined oral contraceptives and gonadotropin-releasing hormone analogs can worsen lipid profiles, increasing CVD risk [13]. These treatment-related factors may act as potential confounders in our meta-analysis, as the included studies lacked relevant data to adjust for these treatment strategies. However, the most recent analysis conducted by Havers-Borgensen et al revealed

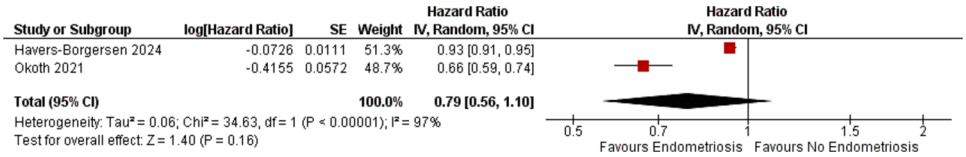

Fig. 6. Risk of all-cause mortality in women with endometriosis compared to those without.

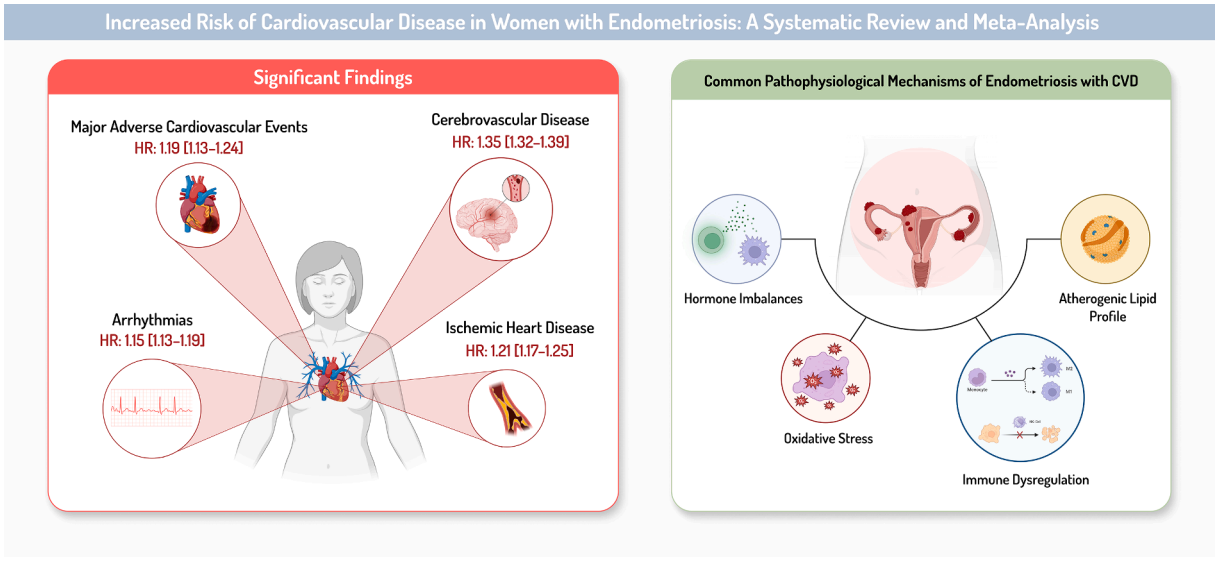

Fig. 7. Graphical Abstract.

that though treatment strategies may partially explain observed differences in CVD risk, they still do not fully account for the association, [21] emphasizing the need for more detailed investigation. Similarly, nonsteroidal anti-inflammatory drugs (NSAIDs), frequently prescribed as first-line therapy for chronic pain in endometriosis, also pose concerns due to their established links to increased cardiovascular and bleeding risks [13,15,36]. Conversely, unmanaged chronic pain exacerbates emotional and physiological stress, depression, and poor quality of life—all recognized CVD risk factors [18,37]. These complexities underscore the need to account for treatment effects in future research, enabling a more accurate and comprehensive evaluation of the endometriosis-CVD relationship.

Interestingly, our analysis revealed that despite the increased risk of cardiovascular events associated with endometriosis, mortality rates showed decreased, albeit non-significant risks. This contrasting finding aligns with previous studies and may be attributed to several factors [16,38]. Endometriosis is often diagnosed after an average delay of seven years [39]. During this time, women may undergo routine monitoring for symptoms, leading to earlier identification of cardiovascular diseases. This surveillance bias likely improves survival outcomes by enabling early detection and closer medical oversight [21,23]. Additionally, women diagnosed with endometriosis often belong to higher socioeconomic groups, benefitting from better access to healthcare, preventive services, and timely medical interventions [38]. Managing a chronic condition may also promote healthier lifestyle choices and greater adherence to treatment regimens after a CVD diagnosis, further reducing risks [23]. Additional research is essential to elucidate the mechanisms driving these observations and to clarify how such factors influence mortality rates in women with endometriosis.

The advent of biotechnological advancements opens new avenues for diagnostics, screening practices, and targeted interventions, making this a pivotal time to establish and consolidate the links between endometriosis and CVD. Such progress can enhance treatment and prevention strategies in women's healthcare. Women with endometriosis have historically faced the challenges of underdiagnosis and misdiagnosis [13]. The development of novel non-invasive diagnostic tools and research into biomarkers—such as lipoprotein(a) and cardiac biomarkers [13,40], which are already linked to CVD but remain understudied in endometriosis [41]—could improve diagnostic accuracy, facilitate CVD prevention and risk stratification, and enable more accurate selection of study populations for future research. Genetic studies have also identified shared susceptibility loci between endometriosis and CVD, including links with atherosclerosis [42]. While further research is required to elucidate specific genetic contributions and advance diagnostic technologies, our meta-analysis underscores the urgent need for these efforts by highlighting the endometriosis-CVD associations that warrant deeper exploration.

A recent "call to action" by Marchandot et al. emphasizes the urgent need to address the intersection between endometriosis and CVD [13]. Our analysis supports this directive, revealing significant risk associations that underscore the importance of future research. Specifically, broader examinations of cardiovascular profiles in women are urgently required, as highlighted by our study, which is the first to comprehensively explore these associations. Additionally, future studies should account for the confounding effects of treatment strategies and gynecological factors like preeclampsia and menopause on CVD risk, as well as the staging and severity of endometriosis [13,43]. Integrating endometriosis history into cardiology trials and conducting well-powered, standardized prospective studies are essential to identify causal links. Epidemiological cardiology initiatives, such as the ongoing FAST-MI program, provide effective models for incorporating endometriosis history screening into cardiology research, establishing a framework for future studies [13,44]. The panel also stressed the need for multidisciplinary collaboration to bridge the gaps between gynecology, cardiology, and research. Our findings further underscore the importance of increasing awareness across specialties about the links between endometriosis and CVD. An integrated approach encompassing proactive care and preventive strategies is essential for improving management and outcomes for women with endometriosis while building a more comprehensive understanding of women's health [13,38,43]. While Marchandot et al deemed current evidence insufficient to recommend routine CVD risk management or additional screening for women with endometriosis [13], our analysis calls for further investigation to better understand the intersection of endometriosis and CVD. Key priorities include enhanced risk stratification, advanced imaging modalities, and the development of novel therapeutic targets to bridge disciplinary gaps and optimize women's healthcare.

Limitations

Our meta-analysis has several limitations that warrant consideration. The observational design of the included studies introduces susceptibility to bias from unmeasured confounders. Key factors—such as surgical management of endometriosis, NSAID use [18,20], family history of CVD [21,26], gynecological risk factors [20,26], and other CVD risk determinants [17–19]—were either inadequately adjusted for or lacked sufficient data. Critical variables like endometrial lesion location, disease severity, histopathological features, and imaging data were also unavailable, limiting comprehensive insights into the observed associations [16,18,20,21]. Additionally, the datasets in some studies predominantly represented women from higher-income quartiles [17,21], limiting generalizability to broader populations. Diagnostic criteria for endometriosis also varied across studies. While most included both surgically or medically confirmed cases, Farland et al. [17] relied solely on laparoscopically confirmed diagnoses. Although laparoscopy is the gold standard, its use is typically reserved for severe or ambiguous cases [38], potentially introducing selection bias by overrepresenting severe disease and skewing results. Variability in the definition of MACE across studies [16,18,20,21] further complicates interpretation. The inherent diagnostic challenges of endometriosis also pose additional complications. Unexposed cohorts may include individuals with undiagnosed or asymptomatic endometriosis, potentially diluting observed associations. Lastly, though our analysis indicated minimal heterogeneity for most outcomes, mortality, and heart failure were the exceptions. However, the limited availability of relevant data from only two studies precluded sensitivity analyses, highlighting the need for further studies. Future research should address these limitations by using diverse populations, standardizing diagnostic criteria, and employing prospective designs to enhance accuracy and generalizability.

Conclusion

Our meta-analysis of 1,407,875 patients identified significantly higher risks of cerebrovascular disease, IHD, MACE, and arrhythmia associated with women with endometriosis. In contrast, heart failure and mortality rates were comparable between those with and without endometriosis. These findings strengthen previously established links, offering robust quantitative evidence across a range of underreported cardiovascular outcomes. While current evidence remains insufficient to warrant routine cardiovascular screening and risk stratification for women with endometriosis, our comprehensive analysis underscores the urgent need for more rigorous prospective studies. Our results advocate for a shift from traditional cardiovascular risk assessments to a sex-specific, holistic approach, highlighting the need for multidisciplinary collaboration, advanced research, and technological innovation to optimize women's healthcare.

Ethical approval

Ethical approval was not required for this meta-analysis.

CRediT authorship contribution statement

Muhammad Saad: Writing – review & editing, Project administration, Formal analysis, Data curation, Conceptualization. **Ifrah Ansari:** Supervision, Investigation, Formal analysis, Data curation, Conceptualization. **Zainab Siddiqua Ibrahim:** Writing – review & editing, Writing – original draft, Formal analysis. **Ruqiat Masooma Batool:** Writing – original draft, Methodology, Investigation. **Syed Ibad Ahsan:** Visualization, Software, Methodology, Investigation. **Muhammad Sameer Arshad:** Writing – review & editing, Software, Investigation. **Peter Collins:** Writing – review & editing, Validation, Supervision. **Raheel Ahmed:** Writing – review & editing, Validation, Supervision.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2025.114081.

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