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Review Article

Risk, Prevalence and Survival Outcomes of Ovarian Cancer in Women with Endometriosis: The ENDOCANCER Systematic Review and Meta-Analysis

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ABSTRACT **Objective:** Endometriosis is linked to an increased risk of epithelial ovarian cancer (EOC), especially clear cell and endometrioid subtypes. The extent and prognostic significance of this link are still not fully understood. This systematic review and meta-analysis compiles existing evidence on ovarian cancer risk, histotype distribution, and survival outcomes in women with endometriosis.

Data Sources: Systematic search up to August 2025.

Methods of Study Selection: A systematic search of PubMed and Google Scholar was performed up to August 2025. Studies reporting ovarian cancer risk estimates or survival outcomes in endometriosis-associated ovarian cancer (EAOC) were included. Random-effects models generated pooled odds ratios (OR), hazard ratios (HR), and standardized incidence ratios (SIR). Risk analyses included >500 000 women; survival analyses >10 000.

Tabulation, Integration, and Results: Sixty-seven studies met inclusion criteria. Endometriosis increased ovarian cancer risk (OR: 1.82, HR: 3.03, SIR: 1.62). EAOC patients were younger, more often premenopausal, and more frequently diagnosed with early-stage (OR: 0.29) and low-grade tumors (OR: 1.71). Clear cell and endometrioid histotypes predominated. Overall survival was significantly better in EAOC (HR: 0.48); recurrence and mortality were lower, while platinum resistance was similar.

Conclusion: Endometriosis confers an increased relative but still low absolute risk of ovarian cancer. EAOC exhibits distinct clinicopathologic features and improved survival compared with non-EAOC. These findings support personalized counseling and emphasize the need for phenotype-based risk stratification and molecular markers of malignancy transformation. Journal of Minimally Invasive Gynecology (2026) 00, 1−12. © 2026 The Authors. Published by Elsevier Inc. on behalf of AAGL. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

Keywords: Endometriosis; Ovarian cancer; Risk; Prevalence; Survival outcomes; Meta-analysis

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The authors declare that they have no conflict of interest.

IRB statement: This study is a systematic review and meta-analysis of previously published data. No new data were collected, and no human participants were directly involved. Therefore, Institutional Review Board (IRB) approval was not required.

PROSPERO study registration: CRD420251154935—registered on September 29st, 2025.

Data availability statement: Data will be made available to the editors for review or query upon request. The data included in this article were extracted as published in the available original articles. No new data were generated to support this paper.

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Endometriosis affects roughly 10% of women of reproductive age and is characterized by ectopic endometrial-like tissue associated with chronic inflammation, estrogen responsiveness, and progressive symptoms [1−4]. The ovaries are the most commonly involved site [2], and ovarian endometriomas have long raised clinical interest due to their potential malignant transformation. The link between endometriosis and epithelial ovarian cancer (EOC) was first described by Sampson [5] and later expanded by Scott [6]. Epidemiologic studies [7,8], along with the 2022 ESHRE guidelines [9], confirmed an increased relative risk of EOC in women with endometriosis, especially for clear cell and endometrioid histotypes. Atypical endometriosis is increasingly seen as a potential precursor lesion and molecular evidence—including ARID1A mutations—supports a plausible biological continuum between endometriosis and EOC [10−14]. Previous meta-analysis [15−17] are available on this topic, showing a correlation between endometriosis and ovarian cancer risk and prognosis. However, evidence are now dated and limited by methodological heterogeneity, particularly regarding the different risk estimates used across studies, which may affect the accuracy and interpretability of pooled results. Therefore, we conducted an updated and comprehensive meta-analysis incorporating a larger number of studies and stratifying results according to the specific risk measures reported and complemented by sensitivity analyses, allowing a more precise evaluation of the relationship between endometriosis, ovarian cancer risk, and prognosis.

Materials and Methods

Search Strategy

A systematic search of PubMed and Google Scholar databases was conducted using the following terms: "endometriosis," "ovarian cancer." The full search string is available in Supplemental materials. The literature review covered the period from inception up to August 2025. References from pertinent articles were also manually checked. This systematic review and meta-analysis protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (Registration number: CRD420251154935).

Eligibility Criteria and Study Selection

Study inclusion was determined according to the following criteria: [1] studies reporting data about prevalence and risk of ovarian cancer in adult women diagnosed with endometriosis, with possible specification of its association with ovarian cancer histotypes; [2] studies reporting survival measures and outcomes of adult women diagnosed with ovarian cancer and endometriosis. We included studies reporting at least 1 risk estimate measure (Relative Risk [RR], Incidence Rate Ratio [IRR], Hazard ratio [HR], Standardized Incidence Ratio [SIR], Odds Ratio [OR], adjusted Risk Difference [aRD] or 1 primary survival outcome (overall survival [OS], disease free survival [DFS], progression free survival [PFS].

No restriction was applied regarding endometriosis diagnostic criteria as, considering the variability in clinical practice across countries and guidelines, diagnosis may be anamnestic, clinical, ultrasound-based, or histological/laparoscopic. Similarly, no restrictions were applied to the diagnostic approaches used by the included studies to define the temporal or causal relationship between endometriosis and ovarian cancer, therefore both endometriosis associated ovarian cancer and ovarian cancer arising from endometriosis cases were included. We excluded studies examining the association between endometriosis and others gynecological cancers. Case reports, conference proceedings, meta-analysis, book chapters were excluded. No restrictions on language, date, or location. Three reviewers (VT, IP, BG) independently screened titles, abstracts and full texts. Any discordance was discussed until agreement.

Data Extraction

Data extraction was performed independently by 3 authors (VT, IP, BG). The following information were extracted for each study, where available: first author, publication year, country of origin, study design and population type and sample size (number of endometriosis and cancer cases, number of controls and source population). In the endometriosis cohort, risk estimate, 95% confidence intervals (CIs) and variables adjusted for the analysis were collected, where available. In the ovarian cancer cohort, general and clinical characteristics of patients were extracted as follows: age, menopausal state, FIGO stage and grading and CA125 level at diagnosis. Survival data, recurrence rate and mortality were also recorded.

Risk of Bias Assessment

Risk of bias of included studies was assessed independently by 3 authors (VT, IP, BG) using Risk of Bias in Non-randomized Studies—of Exposure (ROBINS-E) scale for observational studies [18]. Any discordance was discussed until agreement.

Statistical Analysis

Each meta-analysis was conducted with a random effect using Review Manager Web v7.9.0, with $p < .05$ as significant. The mean difference and 95% CI were calculated for continuous variables and OR 95% CIs for dichotomous variables, using the inverse variance method and the Mantel-Haenszel method respectively. DerSimonian-Laird heterogeneity estimator was employed. Time-to-event data were analyzed with a generic inverse variance method, reporting summary risk estimate measure and 95% CIs. The

statistical analysis of risk estimates was conducted by grouping and analyzing data according to studies reporting the same risk measure, to provide homogeneous and comparable results. Variability due to heterogeneity was assessed using the I-squared (I^2) statistic, with an I^2 value greater than 75% indicating high heterogeneity. Sensitivity analyses were conducted to evaluate the impact of each individual dataset on the overall results by sequentially omitting 1 trial at a time.

Results

Study Selection and Characteristics

The search strategy identified 4302 articles. After removing duplicates (195 articles), articles were screened to identify those that met the inclusion criteria. Final analysis comprised 67 articles: 42 studies [8,19−59] exploring the association between endometriosis and risk of ovarian cancer and 25 studies [60−84] presenting survival data in women diagnosed with ovarian cancer and endometriosis. All included studies had an observational design and have been published between 1997 and 2025. Table 1 summarizes general characteristics of included studies and the reference populations considered in each study. When more than 1 article was published using the same study population (i.e., women listed in the National Swedish Inpatient Register and linked to the National Swedish Cancer Register; women diagnosed with ovarian cancer at Division of Gynecological Oncology of the Department of Obstetrics and Gynecology in Peking Union Medical College Hospital; Dutch nationwide registry of histopathology and cytopathology) we selected the most recent published one and that included the largest number of cases [51,61,65]. PRISMA flowchart shows the study inclusion process (Fig. S1).

Quality Assessment

The overall risk of bias of included studies was judged "moderate." The most relevant sources of bias were related to inadequate control for known risk factors independently associated with EOC (e.g., age, body mass index, comorbidities, prior hormonal treatments, and menopausal status) and, consequently, to selection bias in the recruitment of participants. Furthermore, bias in the measurement of exposure was frequently observed, due to heterogeneity in the diagnostic ascertainment of endometriosis (e.g., self-reported diagnosis vs medical records vs histological confirmation or laparoscopy). Bias due to missing data was judged as moderate to high, given that several studies failed to report complete data for the entire study population and did not justify the missing information. In contrast, bias in measurement of outcomes and selection of reported results were mainly judged low, as ovarian cancer diagnoses and prognostic outcomes were ascertained using registry-based or standardized clinical criteria and all relevant predefined endpoints were consistently reported. No other sources of bias were identified. Further details on assessment of risk of bias are provided in Fig. S2 and Fig. 1.

Ovarian Cancer Risk

Table 2 presents the risk estimates of EOC in women with endometriosis, stratified by the type of risk measure used. The meta-analysis conducted according to this predefined classification revealed a significantly increased risk: OR: 1.82 [95% CI: 1.33−2.50; p = .0002; I^2 = 98%], HR: 3.03 [95% CI: 2.16−4.25; p <.00001; I^2 = 82%], SIR: 1.62 [95% CI: 1.03−2.22; p <.00001; I^2 = 83%] (Fig. S3). Substantial heterogeneity was observed across studies for all risk measures. Sensitivity analyses did not significantly reduce heterogeneity, indicating persistent inconsistency. Egger's test did not demonstrate significant evidence of small-study effects for OR estimates (p = .18), while a borderline result was observed for HRs (p = .07). However, the interpretation of these findings is limited by the small number of included studies (<10) and the substantial between-study heterogeneity, which may contribute to funnel plot asymmetry independently of publication bias. Egger's test was not performed for SIR and IRR estimates due to the very limited number of studies.

Patients' General and Clinical Characteristics

Patients diagnosed with endometriosis-associated ovarian cancer (EAOC) were significantly less likely to be in a menopausal state at the time of diagnosis compared to those with non-endometriosis-associated ovarian cancer (p <.0001). Additionally, the average age was lower in the endometriosis group than in the comparison group across all included studies except one [58]. Clinical characteristics of the disease, including histological subtype, tumor grade, and stage at diagnosis, were analyzed (Table S3). For the assessment and comparison of histological subtypes, only studies that included multiple histotypes were considered; studies limited to a single subtype were excluded for this analysis. Meta-analyses showed that the serous subtype—including both low-grade serous ovarian cancer and high-grade serous ovarian cancer— and the mucinous subtype were more frequently observed in the non-endometriosis group compared to the endometriosis group (54.9% vs 24.5%, p <.00001; 13.2% versus 8.3%, p = .03) (Fig. S4). Conversely, clear cell (29.5% versus 11.8%, p <.00001) and endometrioid histotype (35.7% versus 18.9%, p = .001) was more represented in the endometriosis group (Fig. S5 and S6). Low to moderate grade (G1−G2) and high-grade (G3) ovarian cancers were diagnosed in 48.3% and 47.7% of patients in the endometriosis group, compared to 27.4% and 72.6% in the non-endometriosis group. These distributions corresponded to a meta-analytic OR: 1.71 [95% CI: 1.30−2.26; p = .0002; I^2 = 32%] for low-moderate grade

Table 1

General characteristics of included studies

Authors	Year of publication	Country	Study design	Study population
Jimbo	1997	Japan	OBS	25 EAOC; 147 non-EAOC
Komiyama	1999	Japan	OBS	20 EAOC; 33 non-EAOC
Erzen	2001	Slovenia/Italy	OBS	58 EAOC; 232 non-EAOC
Oral	2003	Turkey	OBS	183 with OC, 14 of which with endometriosis
Modugno	2004	America	OBS	2098 OC; 2953 healthy controls
Kobayashi	2007	Japan	OBS	6398 with endometriosis, 46 of which with OC
Kontoravdis	2007	Greece	OBS	667 with endometriosis, 13 of which with OC
Aris	2010	America	OBS	2521 with endometriosis; 292 non EAOC; 41 EAOC
Melin A	2010	Sweden	OBS	4278 with endometriosis, 750 EAOC
Kumar	2011	USA	OBS	42 EAOC; 184 non-EAOC
Noli	2011	Italy	OBS	36 EAOC; 77 non-EAOC
Pearce	2012	USA	OBS	7911 OC (738 with endometriosis); 13 226 healthy controls (818 with endometriosis)
Boyraz	2013	Turkey	OBS	45 EAOC; 1041 non-EAOC
Buis	2013	The Netherlands	OBS	3657 with endometriosis; 5247 without endometriosis; 17 total OC
Dzatic-Smiljkovic O	2013	Serbia	OBS	210 with OC, 23 of which with endometriosis
Machado-Linde	2013	Spain	OBS	27 EAOC; 469 non-EAOC
Wang Shu	2013	China	OBS	188 with OC, 32 of which with endometriosis
Chang	2014	Taiwan	OBS	7537 with endometriosis; 15 074 without endometriosis; 24 total OC
Wang Kuan Chin	2014	Taiwan	OBS	5945 with endometriosis; 23 780 without endometriosis; 75 total OC
Ye	2014	China	OBS	79 EAOC; 131 non-EAOC
Acien	2015	Spain	OBS	20 EAOC; 172 non-EAOC
Akbarzadeh-Jahromi	2015	Iran	OBS	28 EAOC; 82 non-EAOC
Kadan	2015	USA	OBS	42 EAOC; 96 with endometriosis
Kok	2015	Taiwan	OBS	2266 with endometriosis; 9064 without endometriosis
Bounous	2016	Italy	OBS	45 EAOC; 158 non-EAOC
Dinkelspiel	2016	USA	OBS	49 EAOC; 90 non-EAOC
Haraguchi	2016	Japan	OBS	485 with endometriosis (endometrioma), 4 of which with OC
Lu Jiaqi	2016	China	OBS	58 EAOC, 138 non-EAOC
Mogensen	2016	Denmark	OBS	45 790 with endometriosis; 133 OC
Kuo	2017	Taiwan	OBS	7629 with endometriosis, 7 of which with OC
Park	2017	Korea	OBS	78 EAOC; 77 non-EAOC
Ren	2017	China	OBS	68 EAOC; 236 non-EAOC
Saavalainen	2017	Finland	OBS	49 933 with endometriosis; 129 OC
Saraswat	2017	England	OBS	17 834 endom (44 EAOC)—83 303 controls (229 non-EAOC)
Schnack	2017	Denmark	OBS	80 EAOC; 95 non-EAOC
Sun Paik	2017	Korea	OBS	41 EAOC;183 non-EAOC
Barreta	2018	Brazil	OBS	40 EAOC; 10 non-EAOC
Bassiouny	2018	USA, Egypt, Canada	OBS	168 EAOC; 534 non-EAOC
Matalliotakis	2018	Greece	OBS	550 with endometriosis, 20 of which with OC
Muangtan	2018	Thailand	OBS	31 EAOC; 141 non- EAOC
Park HK	2018	America	OBS	600 OC (49 EAOC—551 non-EAOC); 752 healthy controls
Sahin	2018	Turkey	OBS	48 EAOC, 43 non-EAOC
Ayhan	2019	Turkey	OBS	52 EAOC, 26 non-EAOC
Bas-esteve	2019	Spain	OBS	36 EAOC; 305 non-EAOC
Cai	2019	China	OBS	40 EAOC; 54 non-EAOC
Ju	2019	Corea	OBS	30 EAOC; 89 non-EAOC
Li	2019	China	OBS	34 EAOC; 94 non-EAOC
Oral	2020	Turkey	OBS	33 EAOC; 243 non-EAOC
Shen	2020	China	OBS	108 OC (5 EAOC-103 non-EAOC); 500 healthy controls
Capmas	2021	USA	OBS	271 444 with endometriosis, 1861 of which with OC
Charatsingha	2021	Thailand	OBS	167 EAOC (96 coexisting with endometriosis, 71 arising from endometriosis); 82 non-EAOC
Eoh	2021	Corea	OBS	179 865 with endometriosis; 87 408 healthy controls; 607 total OC
Hermens	2021	The Netherlands	OBS	51 544 with endometriosis; 132 654 without endometriosis; 2772 total OC
Huang	2021	Taiwan	OBS	20 510 with endometriosis; 135 236 without endometriosis; 55 total OC
Zhou	2021	China	OBS	211 cancer (114 EAOC—97 nonEAOC)
Sarria-Santamera	2022	Kazakistan	OBS	4505 OC (100 EAOC; 4405 non-EAOC); 604 475 healthy controls
Tranoulis	2022	England	OBS	48 EAOC; 46 non-EAOC)
Bergamini	2023	Italy	OBS	48 EAOC
Kundur	2023	India	OBS	37 EAOC; 40 non-EAOC
Sun	2023	China	OBS	70 EAOC; 55 non-EAOC
Wang H	2023	China	OBS	74 EAOC; 100 non-EOAC
Wang L	2023	China	OBS	17 045 with endometriosis; 191 596 without endometriosis
Al-Badawi	2024	Saudi Arabia	OBS	542 EAOC; 45 705 non-EAOC

Barnard	2024	USA	OBS	78 476 with endometriosis; 372 430 without endometriosis; 597 total OC
Leone Roberti Maggiore	2024	Italy	OBS	83 EAOC; 144 non-EAOC
Liu D	2025	China	OBS	326 with endometriosis; 3766 without endometriosis; 12 total OC
Zhang	2025	China	OBS	25 509 OC; 40 941 healthy controls

OBS = observational study; USA = United States of America; OC = ovarian cancer; EAOC = endometriosis-associated ovarian cancer;

Fig. 1

Risk of bias of included studies (summary plot).

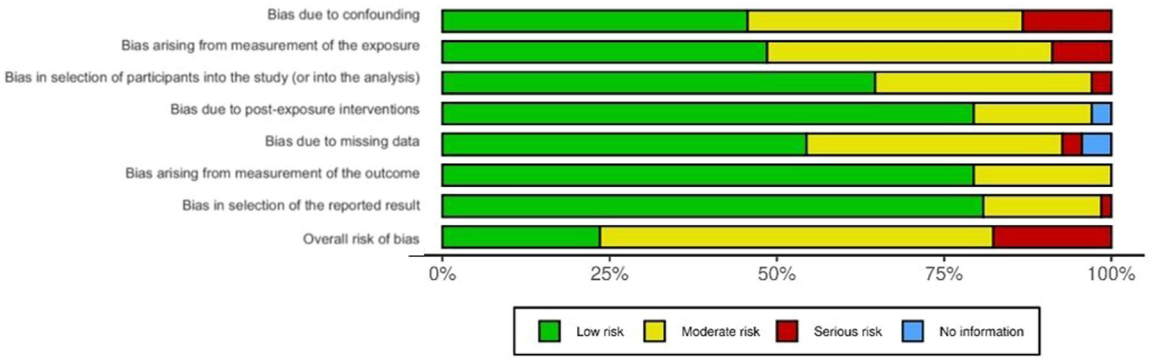


Table 2

Risk estimates of ovarian cancer in women diagnosed with endometriosis

Odds ratio (OR)	
Modugno	OR: 1.32 (CI 95% 1.06−1.65)
Pearce	OR: 1.46 (CI 95% 1.31−1.63)
Park HK	OR: 1.78 (CI 95% 1.23−3.05)
Capmas	OR: 2.39 (CI 95% 2.26−2.52)
Tranoulis	OR: 3.34 (CI 95% 2.97−3.75)
Wang L	OR: 1.23 (CI 95% 1.11−1.36).
Liu D	OR: 10.75 (CI 95% 2.74−42.22)
Zhang	OR: 1.182 (CI 95% 1.095−1.276)
Hazard ratio (HR)	
Kumar	HR: 1.3 (CI 95% 0.7−2.3)
Buis	HR: 12.7 (CI 95% 2.9−55.5)
Chang	HR: 3.28 (CI 95% 1.37−7.85)
Wang Kuan Chin	HR: 5.62 (CI 95% 3.46−9.14)
Kok	HR: 4.56 (CI 95% 1.72−12.11)
Schnack	HR: 1.30 (CI 95% 0.79−2.14)
Eoh	HR: 2.51 (CI 95% 1.99−3.16)
Huang	HR: 3.12 (CI 95% 2.15−4.52)
Barnard	HR: 4.20 (CI 95% 3.59−4.91)
Standardized incidence ratio (SIR)	
Kobayashi	SIR: 8.95 (CI 95% 4.12−15.3)
Mogensen	SIR: 1.34 (CI 95% 1.16−1.55)
Saavalainen	SIR: 1.76 (CI 95% 1.47−2.08)
Incidence rate ratio (IRR)	
Eoh	IRR: 2.15 (CI 95% 1.75−2.63)
Hermens	IRR: 19.75 (CI 95% 16.70−23.35)

OR = odds ratio; HR = hazard ratio; SIR = standardized incidence ratio; IRR = incidence rate ratio; CI = interval of confidence.

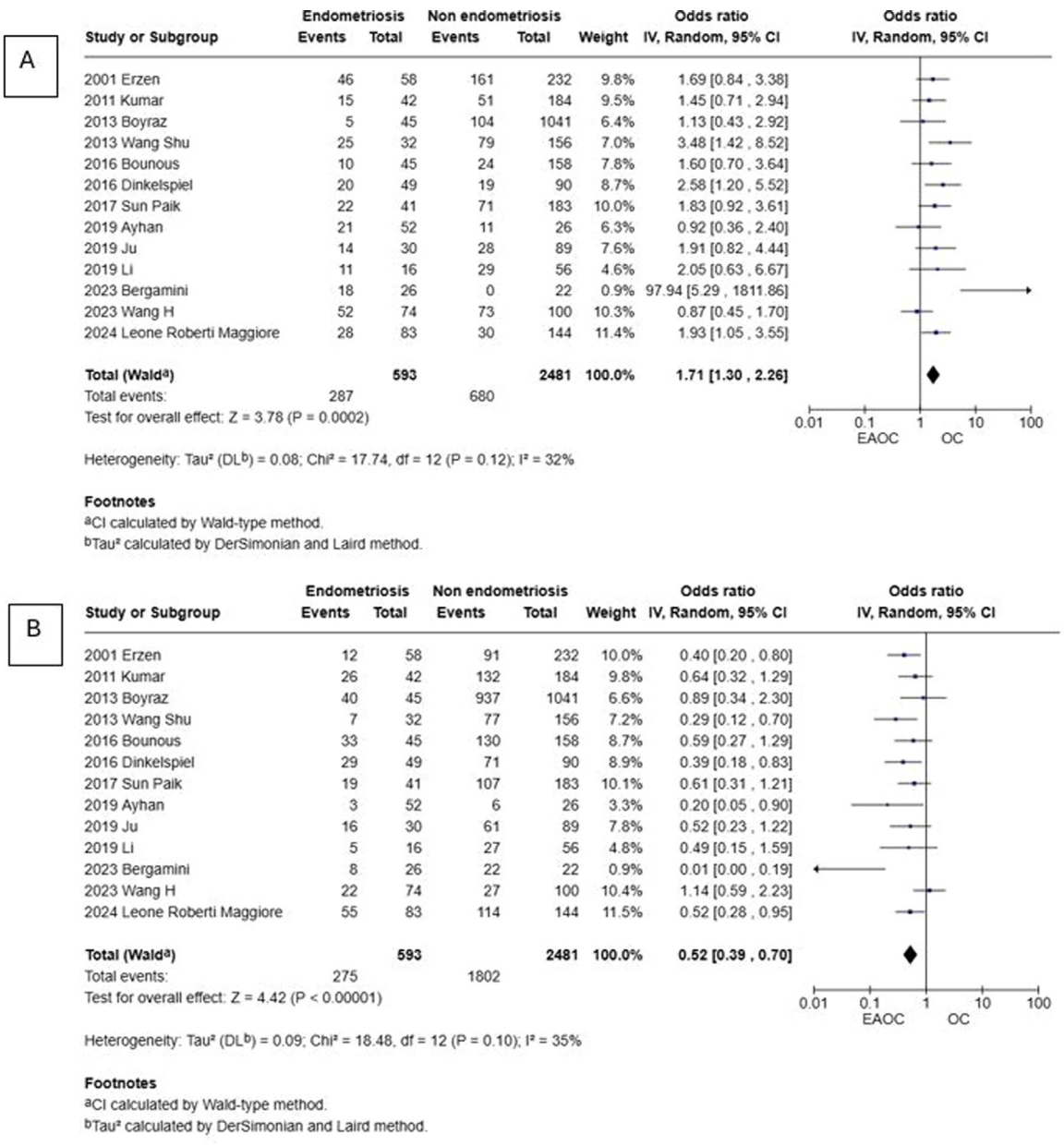
tumors, and an OR: 0.52 [95% CI: 0.39−0.70; p <.00001; I^2 = 35%] for high-grade tumors, indicating a significantly higher rates of aggressive disease in the non-endometriosis group (Fig. 2). Similarly, advanced-stage ovarian cancer (III-IV FIGO stage) was less frequent in patients with endometriosis, with a pooled OR: 0.29 [95% CI: 0.23−0.37; p <.00001; I^2 = 57%] (Fig. 3). Preoperative CA125 was significantly lower in the endometriosis group with a pooled mean difference −358.83 [95% CI: −495.51, −222.15; p <.00001; I^2 = 43%] (Fig. S7).

Survival Outcomes in Women Diagnosed with Ovarian Cancer and Endometriosis

Data are presented in Table S4. As shown in Fig. 4, meta-analysis found a significant difference in overall survival between groups with HR: 0.48 [CI 95% (0.32, 0.74); I^2= 62%; p = .0008] indicating a survival benefit for patients diagnosed with EAOC; pooled HR of progression free survival also favors EAOC group, although not reaching statistical significance with HR: 0.58 [CI 95% (0.27, 1.22); I^2= 81%; p = .15]. Heterogeneity among groups regarding PFS remained high after sensitivity analysis. Publication bias was assessed for OS using Egger's test. The results indicated significant funnel plot asymmetry (p = .040), suggesting a potential risk of publication bias. Visual inspection of the forest plot confirmed that smaller studies reported more pronounced protective effects compared to larger ones. Regarding PFS, Egger's test was not performed due to the limited number of studies reporting HRs with sufficient data. Visual inspection of the PFS forest plot highlights a lack of overlap between the confidence intervals of the included studies which accounts for the high I^2 value and suggests clinical

Fig. 2

Forest plot of grading of ovarian cancer: (A) low-moderate grade (G1-G2) (B) high grade (G3).



or methodological diversity among the trials. A meta-analysis of disease-free survival data was not conducted due to substantial differences in data presentation. Nonetheless, an advantage in 5-year DFS was observed, with a higher proportion of patients diagnosed with EAOC demonstrating prolonged DFS and achieving 5-year disease-free survival compared to the other group. Recurrence of disease and mortality were significantly lower in the EAOC group showing an OR: 0.48 [CI 95% (0.38, 0.60); I^2 = 14%; p <.00001] and OR: 0.62 [CI 95% (0.42, 0.91); I^2= 27%; p = .02], respectively (Fig. S8). Rate of platinum resistant patients was similar [OR: 0.72, CI 95% (0.33, 1.56); I^2= 43%; p = .41] (Fig. S8). Average follow up was more than 24 months in all included studies.

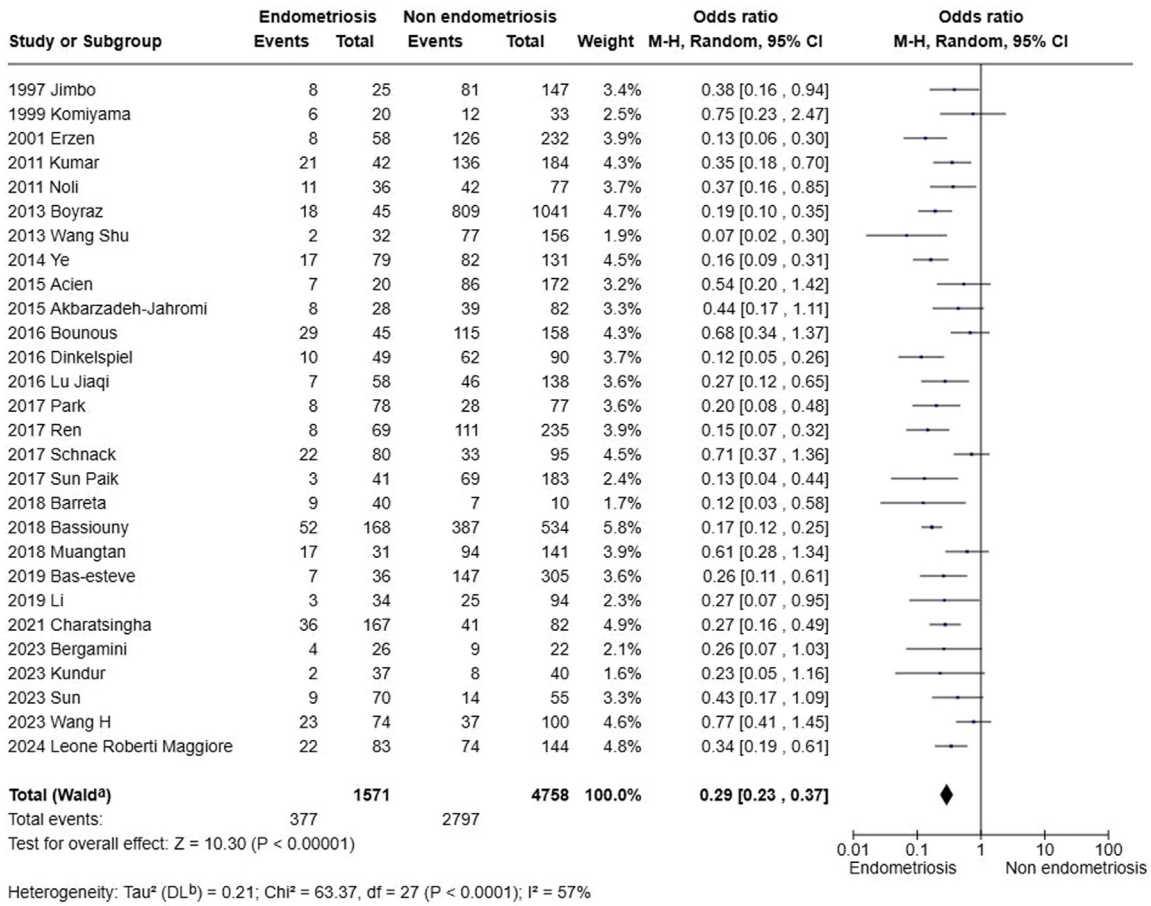
Discussion

Principal Findings

This systematic review and meta-analysis confirm that women with endometriosis have an increased relative risk

Fig. 3

Forest plot of advanced stages.



of EOC. Nevertheless, the absolute incidences across groups remained low (≈0.7−1.5%) and ovarian cancer continues to represent a rare outcome in this population. EAOC exhibits specific characteristics: younger age at diagnosis, higher likelihood of premenopausal status, earlier FIGO stage, lower tumor grade, and predominance of clear cell and endometrioid histotypes. These features contribute to the significantly improved overall survival and lower recurrence and mortality observed in EAOC compared with non-EAOC. The observed survival benefit in our analysis may be partially attributed to distinctive tumor biology and favorable stage at diagnosis. Despite variability in PFS, the overall trend supports the prognostic importance of coexisting endometriosis. Indeed, endometriosis-associated ovarian cancer is characteristically linked to less aggressive histotypes and lower histological grades. This is likely a result of earlier detection facilitated by the frequent clinical surveillance of these patients, which further corroborates our findings. Taken together, our results support the classification of EAOC as a rare distinct clinicopathologic and prognostic entity and emphasize the importance of phenotype-specific clinical assessment.

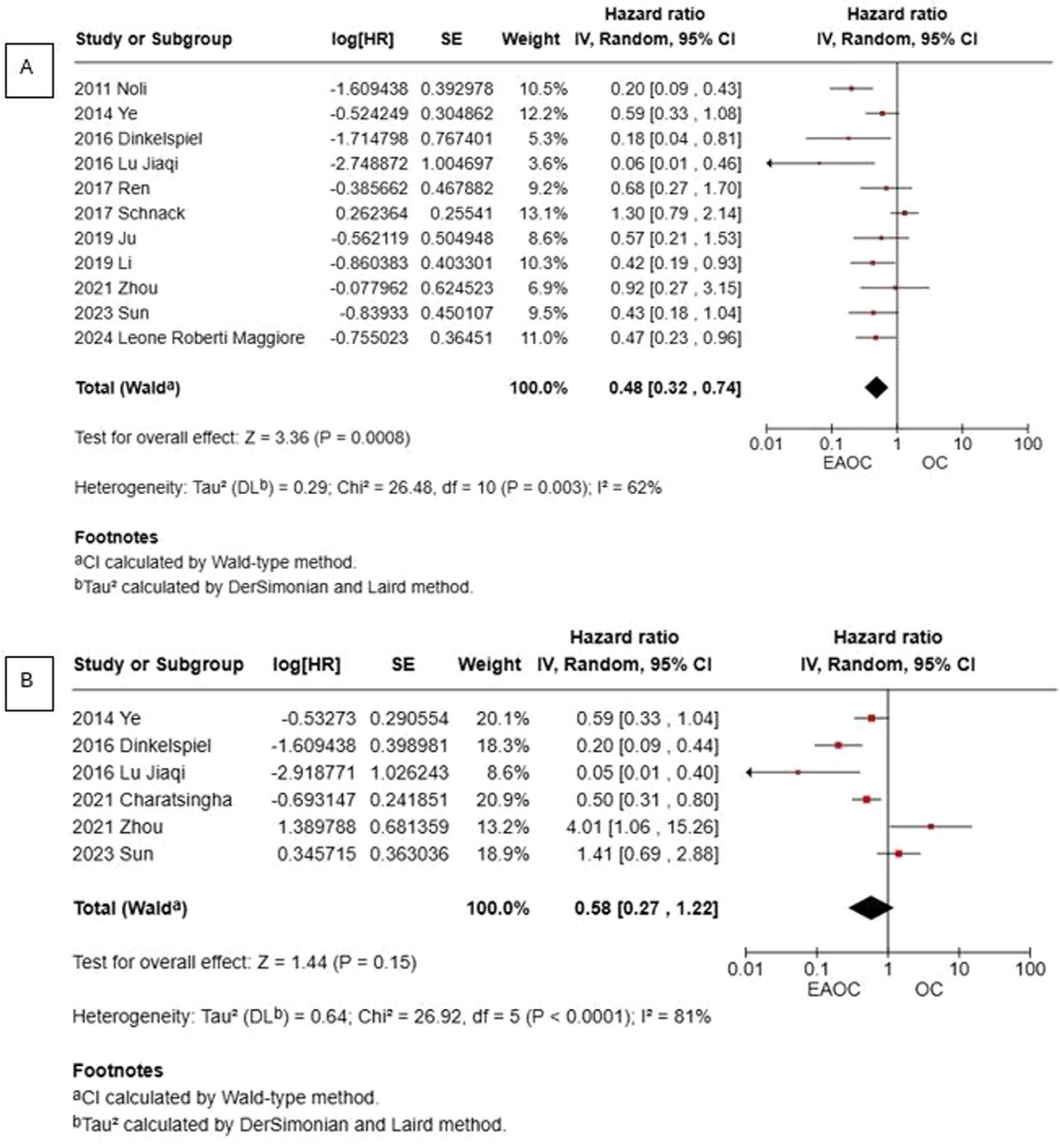
2. Clinical implications

Communicating Risk to Patients

While relative risk estimates are increased, the absolute risk of ovarian cancer remains low. It is therefore essential to avoid generating disproportionate cancer-related anxiety, as highlighted by recent expert commentary [85]. Our findings provide clinicians with a robust evidence base to guide balanced, patient-centered discussions.

Fig. 4

Forest plot of survival outcomes: (A) overall survival (B) progression-free survival.



Surveillance and Follow-up

Current data and the ESHRE 2022 guideline [9] do not support routine oncologic screening solely based on endometriosis. Targeted assessment is more appropriate in selected scenarios:

- Rapid growth of a known endometrioma
- Complex or atypical ultrasound features
- New symptoms in peri/postmenopausal women
- Persistent masses with inconsistent clinical behavior

Earlier diagnosis in EAOC appears related to more frequent imaging rather than dedicated screening programs.

Hormonal Management

Long-term use of combined oral contraceptives reduces ovarian cancer risk [86]. Progestin-based therapies, including dienogest [87], may also help lower inflammation and ovulation-associated epithelial stress, potentially influencing malignant risk over prolonged exposure, although direct evidence remains limited.

Surgical Considerations

Taking into consideration the results of present meta-analysis, prophylactic bilateral oophorectomy in premenopausal women with endometriosis appears to be not justified. The long-term risks of premature estrogen deprivation—including cardiovascular, skeletal, and cognitive adverse effects [88,89]—outweigh the benefits for most patients. Surgical decisions should be individualized, especially in postmenopausal women with persistent or atypical lesions or in those with hereditary risk factors.

Strengths and Limitations

A major strength lies in the large number of included studies encompassing diverse ethnic and geographic backgrounds. This enhances the external validity and generalizability of the findings across different clinical and demographic contexts. Study inclusion was based on well-defined criteria, focusing specifically on studies reporting risk estimates or survival outcomes in women with both endometriosis and ovarian cancer. This dual inclusion allowed for a broader understanding of both incidence and prognosis. Notably, the analysis differentiated risk estimates according to the type of statistical measure used, rather than pooling them into a single overall estimate. This approach improved the methodological precision and interpretability of the results, particularly in the context of observed heterogeneity. Nevertheless, using Odds Ratio in time-to-event analysis is methodologically suboptimal, although it reflects the measures reported in the original studies. Finally, sensitivity analyses were conducted to test the robustness of findings and to explore potential sources of heterogeneity.

However, this meta-analysis is subject to several methodological limitations inherent to the included studies. Heterogeneity of pooled estimates is likely due to several factors: inter-study differences in methodological quality; varying definitions of endometriosis diagnosis across trials; discrepancies in follow-up periods; diversity in clinical populations. Consequently, Egger's test was performed to assess publication bias for the primary outcomes. While current methodological guidelines generally recommend a minimum of 10 studies, the test was also applied to outcomes involving 8 or 9 studies to provide a preliminary assessment of asymmetry. Conversely, for outcomes with a very small number of trials (fewer than 8), the test was not performed, as the limited sample size would not have allowed for a reliable assessment of funnel plot asymmetry in accordance with standard methodological thresholds. A major concern is the temporal ambiguity between endometriosis and ovarian cancer diagnoses in many studies, which often failed to clearly establish whether endometriosis preceded cancer or was diagnosed concurrently. This lack of clarity highlights the need for analyses that account for time-varying exposure and a reasonable latency window between diagnoses. Another critical issue relates to the definition and ascertainment of endometriosis. Case identification methods varied, ranging from self-reported diagnoses and medical records to surgical or histological confirmation. However, nowadays, the diagnosis of endometriosis has increasingly relied on non-invasive or clinical criteria—such as imaging or symptom-based evaluation—resulting in a reduced frequency of histological confirmation. This diagnostic shift introduces methodological variability and potential misclassification bias in the included studies, potentially weakening the accuracy of the exposure definition. Another limitation is substantial heterogeneity particularly in the risk assessment, which could not be resolved throw sensitivity analysis. Moreover, the absence of detailed information on endometriosis phenotype (i.e., ovarian, peritoneal, deep infiltrating) limited the ability to perform subgroup analyses that could clarify whether specific forms of endometriosis have different prognostic implications. Lastly, reliance primarily on PubMed, without inclusion of other major databases, may have limited the comprehensiveness of the body of evidence.

Future Directions

Future research should aim to:

- Identify biomarkers and molecular signatures predictive of malignant transformation
- Clarify risk differences across endometriosis phenotypes
- Validate standardized imaging criteria for atypical lesions
- Determine the long-term impact of hormonal suppression on EAOC risk.

To improve future research, high-quality prospective studies with standardized diagnostic criteria for both endometriosis and ovarian cancer are needed. These should include clear temporal data and stratified analyses by cancer subtype and endometriosis phenotype. Elucidating the association between endometriosis and ovarian cancer is critical for developing phenotype-driven, molecularly informed risk stratification will be critical for personalized care.

Conclusion

This systematic review and meta-analysis supports the finding that endometriosis is associated with an increased relative, though still low, absolute risk of epithelial ovarian cancer. EAOC exhibits distinctive clinicopathologic features and has better survival rates than non-EAOC. These findings support evidence-based, personalized counseling and do not justify routine oncologic screening or preventive surgery for women at average risk.

Authors' Roles

I.P.: Conceptualization, Investigation, Project administration, Data curation, Formal analysis, Methodology, Software, Visualization, Resources, Writing—original draft. V. T: Conceptualization, Investigation, Project administration, Data curation, Formal analysis, Methodology, Software, Visualization, Resources, Writing—original draft. B.G: Investigation, Validation, Funding acquisition, Writing—review and editing. S.R: Investigation, Data curation, Validation. M.A: Investigation, Data curation, Validation. S.Z: Investigation, Data curation, Validation. A.B: Investigation, Data curation, Validation. F.P: Investigation, Data curation, Validation. D.R: Investigation, Data curation, Validation. L.L: Investigation, Data curation, Validation. A.M., E.Z., R.S., and G.V: Conceptualization, supervision, project administration.

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Supplementary materials

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