

Supplemental Methods S1. Systematic review of literature.

We performed a systematic review and meta-analysis to determine the impact of malignant peritoneal cytology on prognosis in patients with early endometrial cancer. The meta-analysis aimed to investigate survival outcome (OS), cause-specific survival (CSS), and disease-free survival (DFS), with comparison of malignant and negative peritoneal cytology results.

1. Article retrieval

We conducted a systematic search of articles published through September 30, 2019, using PubMed, Scopus, and Cochrane Central Register of Controlled Trials (CENTRAL), as performed in our previous study (1, 2). We reviewed articles according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (3). Studies were identified by screening the titles, abstracts, and full texts of relevant articles, as previously described. All abstracts were screened by two authors (SM and YN).

Initially, various patterns of keywords listed below were used to identify studies on endometrial cancer. We used the International Federation of Obstetrics and Gynecology (FIGO) 1988 or 2009 system to identify FIGO stage I and II endometrial cancer. The keywords were as follows: "corpus neoplasm" OR "corpus cancer" OR "corpus carcinoma" OR "corpus malignancy", "endometrial neoplasm" OR "endometrial cancer" OR "endometrial carcinoma" OR "endometrial malignancy", "carcinoma of the corpus" OR "carcinoma of the uterine corpus", "carcinoma of the endometrium" OR "carcinoma of the endometrium", "invasive carcinoma of the corpus" OR "invasive carcinoma of the uterine corpus", "invasive carcinoma of the endometrium" OR "invasive carcinoma of the uterine endometrium", and "endometrial adenocarcinoma" OR "endometrioid adenocarcinoma", and "adenocarcinoma of the endometrium" OR "adenocarcinoma of the endometrium"

Thereafter, the selected studies were screened to identify studies that investigated the impact of malignant peritoneal cytology on endometrial cancer, using the following keywords: "peritoneal cytology or peritoneal washing cytology or pelvic cytology or abnormal cytology or malignant cytology" and "stage IIIA". The references of the identified articles were also reviewed, and articles that met the inclusion criteria were included (Figure S3).

2. Inclusion criteria

Studies were included if they met the following inclusion criteria: (i) patients with early endometrial cancer (tumour confined to the uterus); (ii) intraoperative peritoneal cytology at laparotomy; (iii) sufficient information to investigate relevant outcomes; (iv) effect sizes for outcomes with hazard ratio; and (v) original articles involving studies, such as retrospective or prospective cohort studies, population-based case-control studies, and randomised controlled trials.

The exclusion criteria were as follows: (i) insufficient information to clearly identify malignant peritoneal cytology cases; (ii) insufficient survival or recurrence information; (iii) not in the field of interest; (iv) inclusion of advanced stage or recurrent cases; (v) lack of a negative peritoneal cytology group; (vi) articles involving case reports, case series, and systematic reviews; (vii) articles not in English; and (viii) conference abstracts.

3. Data extraction

Data were extracted by two authors (S.M. and Y.N.), and the following variables were recorded: histology type, year of study, first author's name, number of included cases, rate of malignant peritoneal cytology cases, and outcomes of interest (OS, CSS, and DFS).

4. Meta-analysis plan

From the eligible study data (4-17), survival outcome estimates for malignant versus negative peritoneal cytology were computed by using the 95% confidence intervals of the reported values to estimate the hazard ratios for OS and DFS. If the comparison of outcome between malignant peritoneal cytology group and negative peritoneal cytology group was not investigated under the same stage of endometrial cancer, we excluded the studies from meta-analysis. Heterogeneity across studies was examined using I^2 , which measures the percentage of total variation across studies. The meta-analysis and the production of all graphics were performed using RevMan 5.3 software (Cochrane Collaboration, Copenhagen, Denmark). For consistency, data from all outcomes (continuous and bivariate) were entered into RevMan 5.3 in such a way that negative effect sizes or relative risks less than one favored active intervention.

5. References

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Supplemental Table S1. Patient demographics per peritoneal cytology status (N=24800).

Characteristics	Negative	Malignant
No.	n=23719	n=1081
Age (yr)		
<40	800 (96.5%)	29 (3.5%)
40-49	2176 (96.1%)	88 (3.9%)
50-59	7570 (95.2%)	382 (4.8%)
60-69	8512 (95.6%)	388 (4.4%)
70-79	3584 (96.4%)	135 (3.6%)
≥80	1077 (94.8%)	59 (5.2%)
Year		
2010	3265 (96.2%)	130 (3.8%)
2011	3231 (95.9%)	137 (4.1%)
2012	3346 (95.9%)	144 (4.1%)
2013	3248 (95.4%)	158 (4.6%)
2014	3525 (95.3%)	175 (4.7%)
2015	3631 (95.5%)	173 (4.5%)
2016	3473 (95.5%)	164 (4.5%)
Race/ethnicity		
White	16846 (95.5%)	801 (4.5%)
Black	1529 (97.5%)	35 (2.5%)
Hispanic	2674 (96.0%)	111 (4.0%)
Asian	2250 (95.0%)	119 (5.0%)
Others	203 (99.0%)	2 (1.0%)
Unknown	217 (94.3%)	13 (5.7%)
Marital status		
Single	4486 (95.0%)	234 (5.0%)
Married	12847 (95.8%)	561 (95.8%)
Divorced	2453 (95.9%)	105 (95.9%)
Separated	209 (96.8%)	7 (96.8%)
Widowed	2504 (95.7%)	112 (95.7%)
Unmarried/domestic	79 (94.0%)	5 (94.0%)
Unknown	1141 (95.2%)	57 (95.2%)
Insurance		
Yes	22883 (95.6%)	1047 (4.4%)
No	553 (96.2%)	22 (3.8%)
Unknown	283 (95.9%)	12 (4.1%)
Registry area		
West	12681 (53.5%)	617 (57.1%)
Central	4521 (19.1%)	125 (11.6%)
East	6517 (27.5%)	339 (31.4%)
Tumour differentiation		
Well	10488 (96.4%)	394 (3.6%)
Moderate	5280 (95.0%)	275 (5.0%)
Poor	1826 (93.2%)	133 (6.8%)
Unknown	6125 (95.6%)	279 (4.4%)
T stage		
IA	18870 (96.2%)	738 (3.8%)
IB	4246 (93.0%)	320 (7.0%)
I NOS	603 (96.3%)	23 (3.7%)
Pelvic lymphadenectomy		
No	14 (IQR 9-20)	14 (IQR 9-20)
No	8405 (35.4%)	264 (24.4%)
Yes	15218 (64.2%)	814 (75.3%)
Unknown	96 (0.4%)	3 (0.3%)
Para-aortic lymphadenectomy		
No	5 (IQR 3-9)	5 (IQR 9-20)
No	16755 (70.6%)	659 (61.0%)
Yes	6819 (28.7%)	416 (38.5%)

Unknown	145 (0.6%)	6 (0.6%)
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Tumour size (cm)		
≤2.0	5662 (96.6%)	201 (3.4%)
2.1-4.0	7528 (95.0%)	398 (5.0%)
4.1-6.0	3825 (94.9%)	207 (5.1%)
6.1-8.0	1179 (95.9%)	51 (4.1%)
>8.0	540 (94.2%)	33 (5.8%)
Unknown	4985 (96.3%)	191 (3.7%)
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Hysterectomy type		
Simple	22114 (95.7%)	1004 (4.3%)
Modified / radical	755 (95.6%)	35 (4.4%)
Supracervical	213 (97.3%)	6 (2.7%)
NOS	637 (94.7%)	36 (5.3%)
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Postop therapy		
None	19263 (96.6%)	668 (3.4%)
VBT	2887 (94.3%)	173 (5.7%)
WPRT	949 (92.3%)	79 (7.7%)
VBT / chemo	239 (78.9%)	64 (21.1%)
Chemo	205 (76.2%)	64 (23.8%)
WPRT / chemo	140 (81.9%)	31 (18.1%)
RT NOS	31 (96.9%)	1 (3.1%)
RT NOS / chemo	5 (83.3%)	1 (16.7%)

Number (% per row) or median (IQR) is shown. Abbreviations: NOS, not otherwise significant; VBT, vaginal brachytherapy; WPRT, whole pelvic radiotherapy; RT, radiotherapy; and chemo, chemotherapy.

Supplemental Table S2. Metadata for the results of systematic review.

Author	Year	No.	Histology	Stage	The rate of MPC	Survival	Recurrence	Adjuvant chemo
Matsuo current	2020	24800	EM	Stage I	1081 (4.4%)	↓ OS, CSS	NA	NA
		4346		Stage I, HIR	277 (6.4%)	↓ OS, CSS	NA	↓ death
		12761		Stage I, low risk	459 (3.5%)	↓ CSS	NA	
Takahashi ⁴	2019	251	EM, non-EM	Stage I, II	30 (12.0%)	NA	↓ DFS	NA
Matsuo ⁵	2018	1668	EM	Stage I, II	125 (7.5%)	↓ CSS	↓ DFS	↓ recurrence
				Stage I Low risk [*]	NA	NA	↓ DFS	NA
				Stage I High risk [#]	NA	NA	No association	NA
Tate ⁶	2018	68	SC	Stage I, II	14 (20.6%)	↓ OS	↓ DFS	NA
Seagle ⁷	2018	16851	EM, CS, CCC, other	Stage I, II	953 (5.7%)	↓ OS	NA	↓ death
		9550	Low-grade EM	Stage I, II	NA	↓ OS	NA	NA
Scott ⁸	2017	668	EM	Stage I ^{\$}	15 (2.2%)	No association	↓ DFS	NA
Shiozaki ⁹	2014	265	EM, CS, SC	Stage I	27 (10.2%)	NA	↓ DFS	NA
Haltia ¹⁰	2014	685	EM	Stage I, II	11 (1.6%)	↓ CSS		NA
Garg ¹¹	2013	14704	EM, Mu, CS, CCC	Stage I, II	485 (3.3%)	↓ CSS [‡]	NA	NA
Bansal ¹²	2009	17945	EM	Stage I ^{**}	485 (2.7%)	↓ OS ^{‡‡}	NA	NA
Metindir ¹³	2008	46	EM	Stage I, II	4 (9.5%)	NA	↓ DFS	NA
Havrilesky ¹⁴	2007	524	EM, Mu, SC, CCC	Stage I, II	37 (7.1%)	↓ OS	NA	NA
Saga ¹⁵	2006	307	EM	Stage I, II	32 (10.4%)	↓ CSS	NA	NA
Tebeu ¹⁶	2004	331	NA	Stage I	33 (10.0%)	No association	NA	NA
Kasamatsu ¹⁷	2003	280	EM	Stage I, II	48 (17.1%)	No association	No association	NA

^{*}ESMO-ESGO-ESTRO criteria: low risk, stage IA grade 1–2 endometrioid tumours without LVSI

[#]Analyzed stage cases for GOG-099 high-intermediate risk group (modified)

^{\$}Stage IA grade 1 to 3 tumours, and Stage IB grade 1 or 2 tumours.

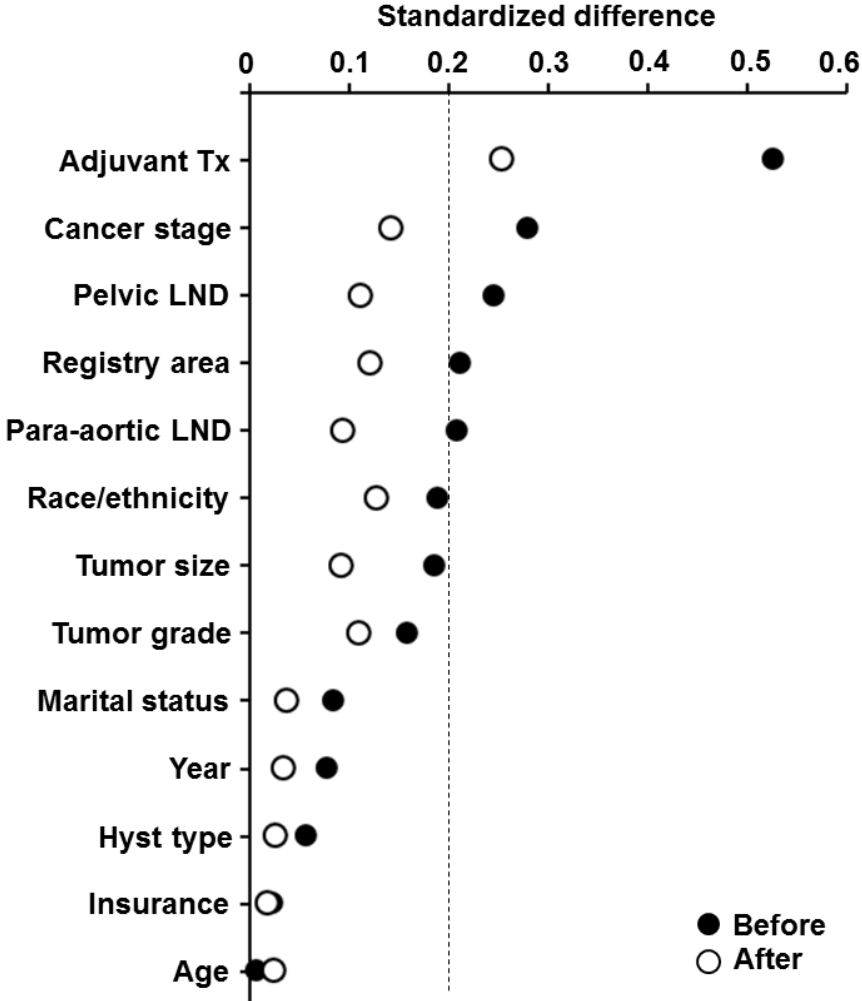
[‡]Malignant peritoneal cytology (Stage I and II) and negative peritoneal cytology (stage IA) was compared

^{**} FIGO 1988 stage IB and IC

^{‡‡} Positive peritoneal cytology and negative peritoneal cytology (FIGO 1988 stage IB and IC) was compared

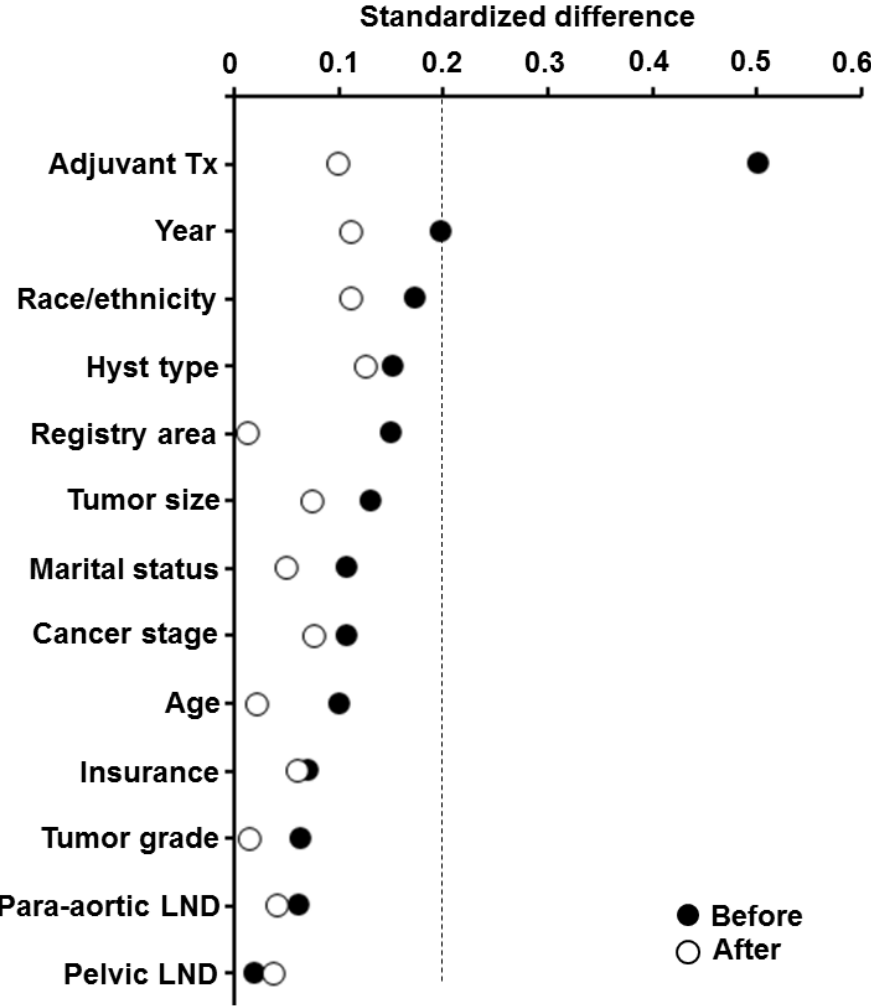
Abbreviations: CCC, clear cell carcinoma, CS, carcinosarcoma; CSS, cause-specific survival; DFS, disease-free survival; EM, endometrioid adenocarcinoma; ESMO, European Society for Medical Oncology; ESGO, European Society of Gynaecological Oncology; ESTRO, European Society for Radiotherapy and Oncology; HIR, high-intermediate; GOG, Gynecologic Oncology Group; Mu, mucinous carcinoma; NA, not available; OS, overall survival; PPC, positive peritoneal cytology; SC, serous carcinoma.

Supplemental Figure S1. Standardised differences before and after PS-IPTW (whole cohort).



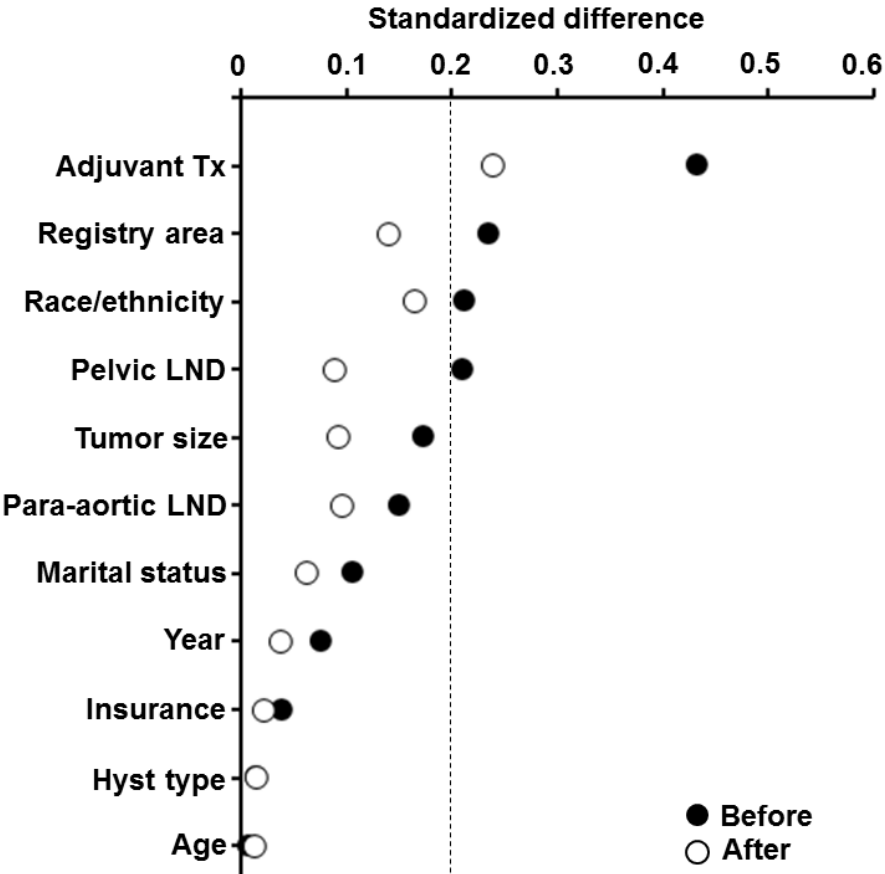
Standardised difference of 0.2, 0.5, and 0.8 were used for the cutoff of small, medium, and large effect size. Abbreviations: PS-IPTW, propensity score inverse probability of treatment weighting; hyst, hysterectomy; LND, lymphadenectomy; and Tx, therapy.

Supplemental Figure S2. Standardised differences before and after PS-IPTW (high-intermediate risk group).



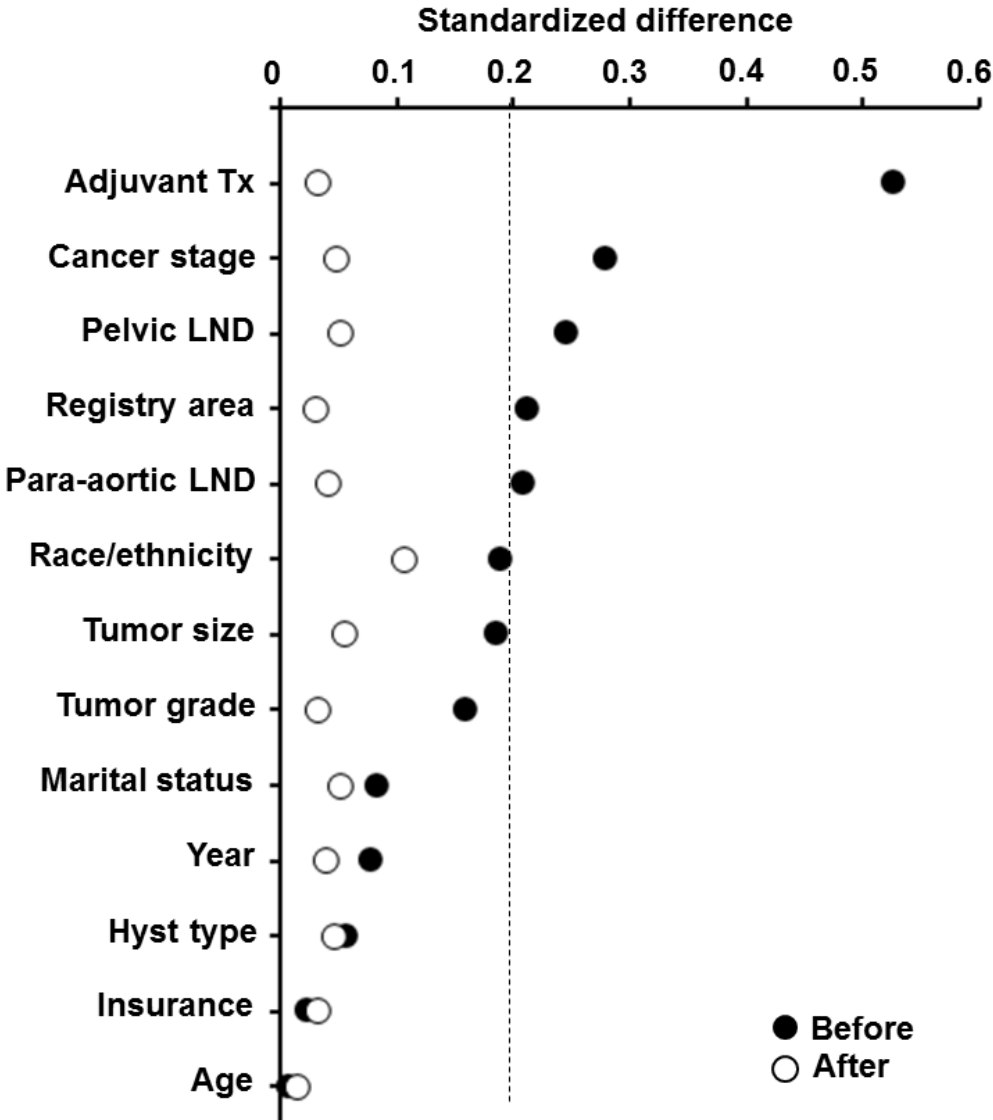
Standardised difference of 0.2, 0.5, and 0.8 were used for the cutoff of small, medium, and large effect size. Abbreviations: PS-IPTW, propensity score inverse probability of treatment weighting; hyst, hysterectomy; LND, lymphadenectomy; and Tx, therapy.

Supplemental Figure S3. Standardised differences before and after PS-IPTW (low-risk group).



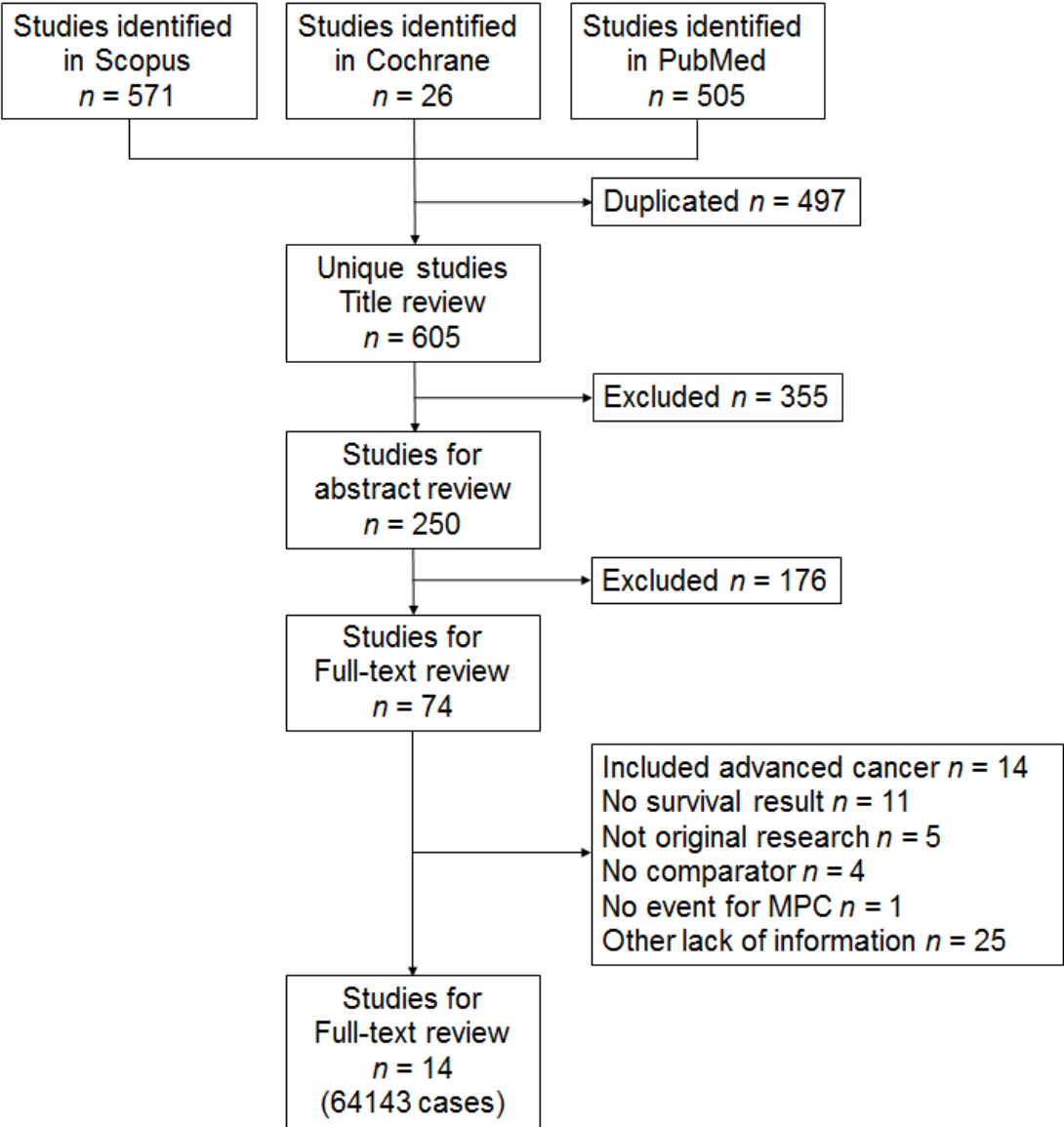
Standardised difference of 0.2, 0.5, and 0.8 were used for the cutoff of small, medium, and large effect size. Abbreviations: PS-IPTW, propensity score inverse probability of treatment weighting; hyst, hysterectomy; LND, lymphadenectomy; and Tx, therapy.

Supplemental Figure S4. Standardised differences before and after generalized boost modeling (whole cohort).



Standardised difference of 0.2, 0.5, and 0.8 were used for the cutoff of small, medium, and large effect size. Abbreviations: PS-IPTW, propensity score inverse probability of treatment weighting; hyst, hysterectomy; LND, lymphadenectomy; and Tx, therapy.

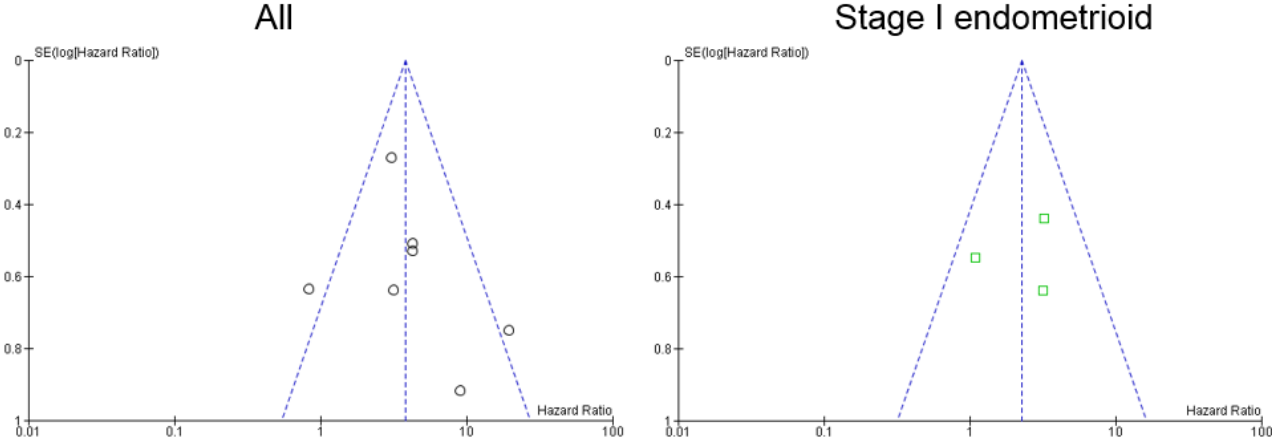
Supplemental Figure S5. Study schema for systematic review of literature.



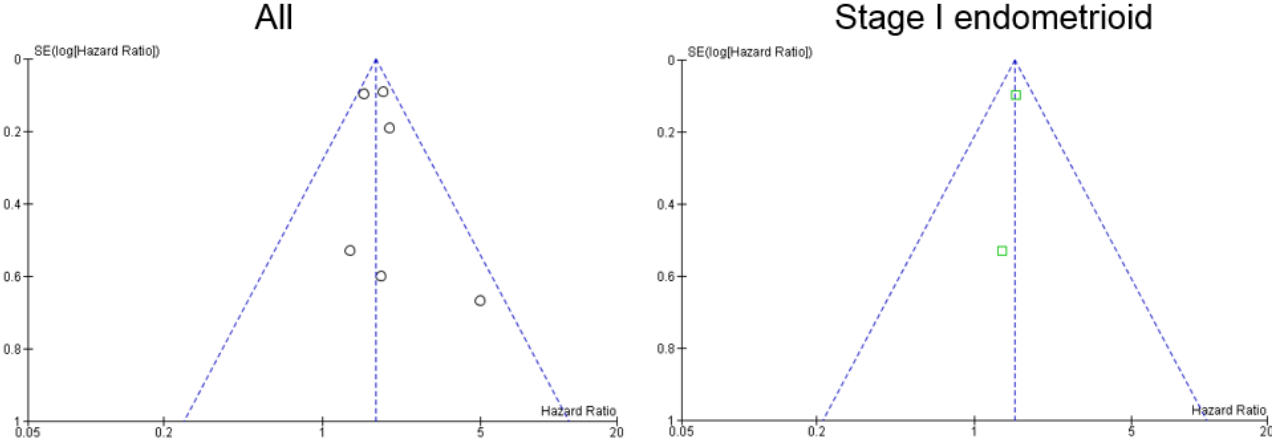
Abbreviation: MPC, malignant peritoneal cytology.

Supplemental Figure S6. Funnel plots for meta-analysis.

Disease-free survival



Overall survival



Funnel plot analysis of studies on disease-free survival and overall survival. The Funnel plots have an almost symmetrical distribution. Publication bias was not found in the meta-analysis.