



## Review Article

# Incidence and impact on survival outcomes of postoperative radiological evidence of residual disease in women with advanced stage ovarian cancer undergoing debulking surgery: a meta-analysis



Vasilios Pergialiotis<sup>a,\*</sup>, Nikolaos Thomakos<sup>a</sup>, Maria Fanaki<sup>a</sup>, Vasilios Lygizos<sup>a</sup>, Pantelis Antonakis<sup>b</sup>, Konstantinos Bramis<sup>b</sup>, Nikolaos Alexakis<sup>c</sup>, Dimitrios Haidopoulos<sup>a</sup>

<sup>a</sup> First Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, "Alexandra" General Hospital, National and Kapodistrian University of Athens, Athens, Greece

<sup>b</sup> 2nd Department of Surgery, Medical School, National and Kapodistrian University of Athens, Athens, Greece

<sup>c</sup> First Department of Propedeutic Surgery, National Kapodistrian University of Athens, Hippocraton Hospital, 11528, Athens, Greece

## ARTICLE INFO

## Keywords:

Ovarian cancer  
Debulking surgery  
Residual disease  
Survival outcomes  
Meta-analysis

## ABSTRACT

**Objective:** The present systematic review and meta-analysis aims to assess the proportion of patients with radiological findings of residual disease following debulking surgery and determine its impact on survival outcomes.

**Methods:** We systematically searched the international literature using the Medline, Scopus, [Clinicaltrials.gov](http://Clinicaltrials.gov), Cochrane Central Register of Controlled Trials CENTRAL and Google Scholar until July 2025 for studies that evaluated the proportion of patients with radiological evidence of residual disease following debulking surgery. The review was registered in PROSPERO prior to its conduct (CRD420251065596).

**Results:** Eleven studies were found eligible for inclusion in the present systematic review. Proportion meta-analysis indicated that 40% of patients had radiologic evidence of residual disease postoperatively (Generalized Mixed Linear Model 40%, 95% CI 33%, 48%). Differences in progression free survival were significantly worse among patients with residual disease (HR 2.08, 95% CI 1.42, 3.05). Similar findings were observed in the overall survival of patients (HR 1.93, 95% CI 1.49, 2.52).

**Conclusion:** The proportion of patients with radiological criteria of residual disease following debulking surgery appears to be significant. There seem to be evidence that indicate a negative impact on survival outcomes of patients with epithelial ovarian cancer, although these should be interpreted cautiously given the heterogeneity and limitations of the available evidence, but may be relevant during preoperative patient counseling to help establish realistic expectations.

## 1. Introduction

Ovarian cancer is the eighth most common malignancy in women accounting for 3.7 cancer cases and 4.7 of cancer related deaths and with a lifetime risk of approximately 1 in 91 [1]. Current treatment of epithelial ovarian cancer is multidisciplinary comprising of systemic chemotherapy, surgery and targeted therapy that is directed by molecular testing. Cytoreductive surgery is considered a cornerstone of treatment as appropriate tumor reduction offers considerable advantages in terms of survival outcomes. On the other hand, suboptimal tumor debulking has is associated with poorer survival outcomes of

ovarian cancer patients and only complete tumor resection offers a significant benefit compared to that of patients that were not offered surgery [2,3]. Despite the advances in surgical expertise the rates of optimal resection (<1 cm of residual disease) seem to be modest even among the largest randomized clinical trials published to date [4–6].

Evidence from radiological studies supports that the rates of complete debulking may significantly differ compared to those that are confirmed by surgeons [7] and these may partly explain observed differences in survival outcomes [8]. In the present we sought to identify the actual proportion of patients that have radiological findings of residual disease following debulking surgery, determine the extent of

\* Corresponding author. 2, Lourou str. Athens, 11528, Greece.

E-mail address: [pergialiotis@yahoo.com](mailto:pergialiotis@yahoo.com) (V. Pergialiotis).

<https://doi.org/10.1016/j.ejso.2026.111462>

Received 22 October 2025; Received in revised form 29 January 2026; Accepted 4 February 2026

Available online 5 February 2026

0748-7983/© 2026 Elsevier Ltd, BASO The Association for Cancer Surgery, and the European Society of Surgical Oncology. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

disease as well as its impact on survival outcomes.

## 2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed in conducting the systematic review, which was pre-registered in PROSPERO (International Prospective Register of Systematic Reviews) with registration number CRD420251065596 [9]. Since all of the data came from research that was published in global literature, institutional review board permission and patient consent were not required.

### 2.1. Eligibility criteria, information sources, search strategy

Studies were included based on predefined qualifying requirements. All studies that presented radiological evidence of postoperative residual disease following debulking surgery for ovarian cancer were thought to be possibly eligible for inclusion. In the present review all histology groups were considered as well as patients submitted to either primary debulking surgery (PDS) or interval debulking surgery (IDS). Postoperative radiological residual disease was analyzed as a binary variable (presence vs absence), as granular reporting of residual tumor burden (residual tumor size, volume, or metrics comparable to the peritoneal cancer index) was inconsistent or unavailable across primary studies. This precluded a burden-based quantitative synthesis, rendering binary

classification the only methodologically feasible approach for meta-analysis. In light of available data, we considered the possibility of subgroup analysis considering these variables. The current meta-analysis did not include case reports or research on preclinical models.

In our primary search, we looked for articles published in the Latin alphabet, regardless of the language used, using the Medline (1966–2024), Scopus (2004–2024), [Clinicaltrials.gov](https://www.clinicaltrials.gov) (2008–2024), Cochrane Central Register of Controlled Trials CENTRAL (1999–2024), and Google Scholar (2004–2024) databases in addition to the reference lists of electronically retrieved full-text papers. Before the search began, the decision was made to use internet translation tools to translate languages other than English, French, German, Italian, and Spanish. Our most recent search was scheduled for June 30, 2025. Fig. 1 provides a quick overview of our search approach, which includes the text phrases "Ovarian cancer; Residual disease; Residual tumour; Postoperative imaging; Postoperative CT; Postoperative PET-CT; Postoperative MRI; Overall survival; Disease-free survival."

### 2.2. Study selection

Three steps were taken in order to retrieve the relevant studies. First, the Rayyan program was used to deduplicate the articles that were retrieved. Two authors (VL and MF) then manually screened the titles and abstracts of all remaining electronic papers to determine their eligibility. Studies deemed possibly eligible were chosen for full-text

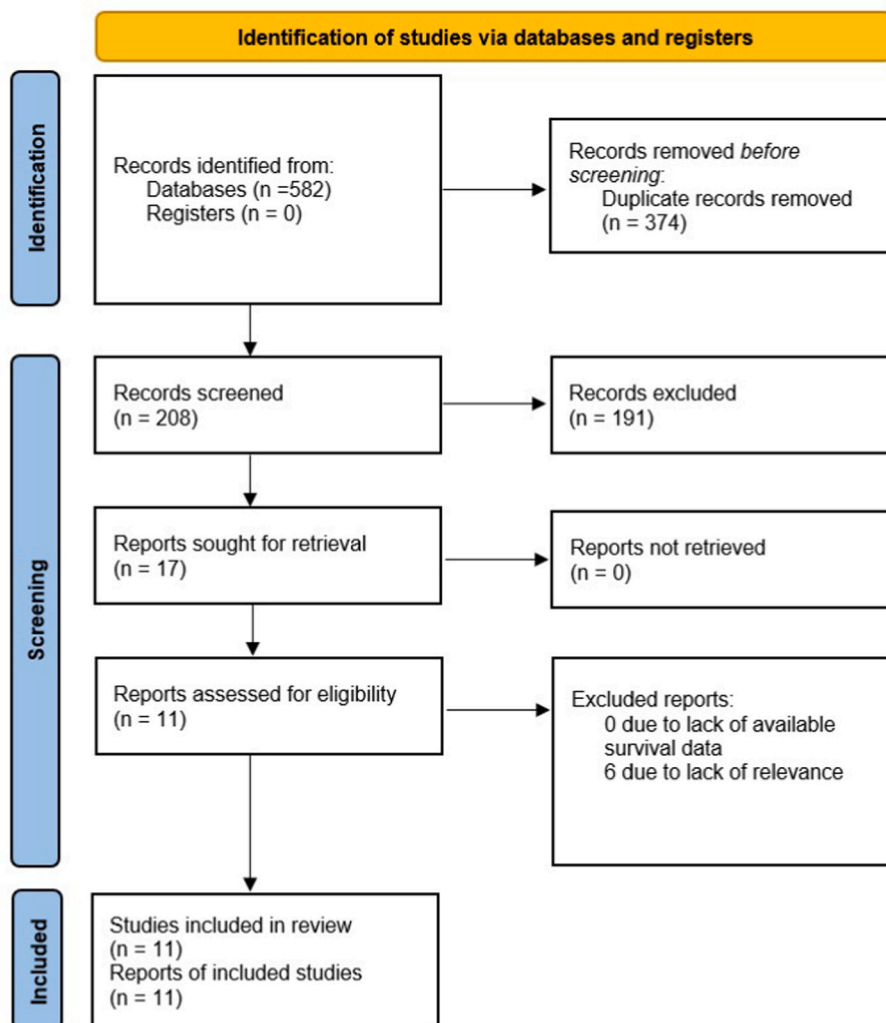


Fig. 1. Flowchart of study selection.

assessment in the last stage of the research selection procedure. Any disagreements that surfaced beyond this point were settled by agreement among all authors.

### 2.3. Data extraction

During the current systematic review's design, outcome measures were predetermined. A modified data form based on Cochrane's data collection form for intervention reviews for randomized controlled trials (RCTs) and non-RCTs was used to extract data. The main goal of the present systematic review was to assess the actual proportion of patients with radiological criteria of residual disease following procedures that were clinically considered complete. Differences in survival outcomes (progression free and overall survival) among those with evidence of residual disease compared to those that had no evidence of residual disease were also considered as a secondary outcome. Differences in histology, as well as patient performance status and surgical complexity of performed procedures were expected among included studies. These were recorded with the aim of performing subgroup analysis if such evidence existed. We also noted the interval between surgery and radiological evaluation.

### 2.4. Assessment of risk of bias

Two authors (MF and VP) evaluated the methodological quality of the included observational studies using the QUIPS (Quality in Prognostic Studies) score, which evaluates the risk of bias by taking into account the population and attrition characteristics, the definition and measurement of the outcome (which in the present systematic review was considered as 1) low risk of bias if both the proportion of patients with residual disease and their corresponding survival was mentioned and compared to that of patients with no residual disease and 2) high risk of bias if only the proportion was mentioned), the potential confounders (we considered differentiation of patients to primary debulking surgery/interval debulking surgery (PDS/IDS) as an essential subgrouping to include studies as low risk of bias) and the statistical reporting [10].

### 2.5. Data synthesis

The meta function in RStudio was used to conduct a statistical meta-analysis (RStudio Team, 2015). <http://www.rstudio.com/RStudio>: Integrated Development for R. RStudio, Inc., Boston, MA. Since the significant methodological heterogeneity of observational studies precludes the assumption of comparable effect sizes among studies included in meta-analyses, statistical heterogeneity was not taken into account when evaluating the appropriate model (fixed effects or random effects) of statistical analysis [11]. Multivariate models were favored over aggregated data from univariate analyses in order to decrease the impact of potential confounders, such as disease stage, differentiation grade, and other factors, such as lymphovascular space involvement and tumor molecular profile. 95% confidence intervals were used. Instead of using the conventional Dersimonian-Laird Random Effects Model analysis (REM), we used the Hartung-Knapp-Sidik-Jonkman to compute the pooled hazards ratio (HR) of survival and 95% confidence intervals (CI). We chose to employ this model because recent studies show that it is more effective than the Dersimonian-Laird model at explaining the heterogeneity of the included observational studies, which are likely to have quite different methodologies [12].

We considered the Egger's test as a statistical technique to assess the potential for publication bias when designing this systematic review. The intervention effect estimates and their standard errors, which are weighted by their inverse variance, are considered in this method's linear regression analysis [13]. It is only deemed significant when there is strong evidence, and in order to guarantee the proper trustworthiness of the results returned, a minimum cut-off of 10 studies was established

for each analyzed outcome [14].

We used Rucker's Limit Meta-Analysis, which allows the examination of small study effects in the meta-analytic pooled effect, to investigate the possible impact of aggregate results from smaller research. P-curve analysis was also used to rule out the possibility of data tampering (p-hacking) and examine the veracity of the combined findings of the included research.

## 3. Results

Overall, 17 studies were retrieved of which 11 studies were found eligible for inclusion in the present systematic review [7,8,15–24]. Six studies were excluded due to lack of relevance (Appendix). The methodological characteristics of included studies are summarized in Table 1. Briefly 7 retrospective studies were identified along with two prospective studies and two studies that were based on post-hoc analysis of data retrieved from a randomized controlled trial [16] and a retrospective study respectively [19]. Patient and tumor characteristics are presented in Table 2. Most of the studies reported findings following cytoreduction of advanced stage disease. Only two studies included a small number of patients that had early-stage disease [7,22]. The predominant histological type was high grade serous carcinoma. The extent of the procedure in terms of surgical complexity was not reported in the majority of included studies, despite the fact that some studies reported data on the actual visceral excisions that were performed<sup>15, 24</sup>. The median interval of surgery and postoperative radiology ranged between 9 and 40 days among the studies included. The QUIPS analysis revealed bias mainly arising from the absence of reporting of survival outcome differences among patients that had radiological findings of residual disease compared to those that did not have (Table 3).

The meta-analysis of included data indicated that 40% of patients that were considered optimally debulked had radiologic evidence of residual disease postoperatively (Generalized Mixel Linear Model 40%, 95% CI 33%, 48%, Fig. 2). Significant statistical heterogeneity was noted among included studies (I-square test = 92%) which is reflected in the wide variance of prediction intervals (16%, 70%).

Six articles reported data focusing on differences in survival outcomes among women with radiological evidence of persistent disease and those with no residual tumor [15,16,19–22]. Differences in progression free survival were significantly worse among patients with residual disease (HR 2.08, 95% CI 1.42, 3.05 Fig. 2). Considerable statistical heterogeneity was noted (I-square = 76%). Prediction intervals were extremely large and indicated the possibility of non-statistical results in future studies. Considering these two latter findings we performed adjustment of the aggregate effect estimate using Rucker's analysis that considers the sample size of included studies and observed the presence of considerable small study effects on the final results ( $p < .001$ ). However, even after adjustment the overall effect estimate remained significant (HR 1.31, 95% CI 1.01, 1.71,  $p = .043$ ). P-curve analysis indicated that there was no evidence of data manipulation in terms of p-hacking.

Differences in overall survival were also statistically significant showing improved survival among patients that did not have radiologic evidence of residual disease (HR 1.93, 95% CI 1.49, 2.52) (Fig. 2). There was no statistical heterogeneity (I-square = 0%); hence, prediction intervals continued to indicate significant results. Small study effects analysis indicated that studies with small sample size seem to influence the adjusted effect estimate ( $p = .049$ ) as this was not statistically significant following adjustment with Rucker's analysis (HR 1.23, 95% CI 0.61, 2.44,  $p = .056$ ). Nevertheless, p-curve analysis indicated that p-hacking was absent.

**Table 1**  
Methodological characteristics of included studies.

Study; Year	Country	Study population	Study	Inclusion criteria	Exclusion criteria
Trelis Blanes; 2023, 2025	Spain	117	Retrospective	Patients with stage III or IV ovarian cancer who underwent a primary or interval cytoreductive surgery with complete tumor resection (R0) or with residual disease <1 cm (R1)	Patients who did not undergo postoperative CT scan between the third- and eighth week following surgery and prior to the start of chemotherapy were excluded.
Lim; 2022	<u>Korea</u>	<u>266</u>	Retrospective	Patients with stage III high grade serous ovarian carcinoma who underwent primary debulking surgery with no gross residual or gross residual <1 cm resection and a postoperative CT before initiation of adjuvant chemotherapy.	Patients who received neoadjuvant chemotherapy followed by interval debulking surgery, or had non-HGSC, or did not undergo either preoperative or postoperative CT scan before adjuvant chemotherapy, and/or had lung parenchymal metastasis were excluded.
Eskander; 2020	USA	627	Post-trial ad hoc analysis	Patients with newly diagnosed with stage III and IV ovarian, fallopian tube or primary peritoneal cancer who underwent maximal effort cytoreductive surgery.	Patients with stage III disease, and residual lesions less than 1 cm were excluded.
Joo-Hyuk Son; 2018	Korea	68	Retrospective	Patients aged over 70, with poor performance status or comorbidities, unresectable disease on CT scan, laparoscopy or laparotomy, and histologically confirmed ovarian cancer who received neoadjuvant chemotherapy followed by interval debulking surgery	Older patients or patients with comorbidities who received only NAC and did not undergo IDS were excluded.
Suidan; 2017	USA	350	Secondary post-hoc analysis	Patients aged $\geq 18$ years with histologically confirmed advanced epithelial ovarian, fallopian tube, or peritoneal cancer, who underwent a serum CA-125 within 14 days and CT scan within 35 days prior to surgery.	Patients who did not have ovarian, fallopian tube, or peritoneal cancer, or patients with carcinosarcoma, mesothelioma, mucinous, germ cell, sex-cord stromal cell carcinoma, low- malignant potential, and benign tumors, or advanced disease, or if they received neoadjuvant chemotherapy, or if there was significant delay in surgery after CT scan (>35 days) or serum CA-125 (>14 days), or if the CT scan was of poor quality, lacking contrast, or not assessed by a protocol radiologist were excluded.
Burger; 2015	USA	212	Retrospective	Patients with complete clinical data who underwent primary cytoreductive surgery for stage III or IV ovarian cancer and had a postoperative CT scan within 1 to 7 weeks following surgery and prior to the initiation of chemotherapy.	NA
Lorusso; 2014	Italy	64	Retrospective	Patients with newly diagnosed stage III–IV ovarian, tubal, or primary peritoneal cancer, who underwent optimal (<1 cm residual disease) debulking surgery, a postoperative CT scan, and standard adjuvant chemotherapy.	Patients receiving experimental adjuvant treatment.
Lakhman; 2012	USA	63	Retrospective	Patients aged 18 years or older with histologically confirmed stage III or IV ovarian, tubal, or primary peritoneal cancer, who underwent a preoperative CT performed 2–25 days before surgery, optimal cytoreduction (i.e., residual disease $\leq 1$ cm), and a postoperative CT 7–49 days following surgery and before initiation of chemotherapy.	NA
Sala; 2011	UK	51	Retrospective	Patients who underwent debulking surgery (<1 cm residual disease), and a postoperative CT within 60 days after surgery were included.	NA
Chi; 2010	USA	67	Prospective	Patients with histologically confirmed stage III or IV ovarian, fallopian tube, or primary peritoneal cancer with residual disease less than 1 cm and underwent postoperative CT scan 7 to 35 days following surgery and before the initiation of postoperative chemotherapy.	Patients who did not undergo postoperative CT scan.
Chi; 2007	USA	78	Prospective	Patients aged 18 years or older who underwent surgery for histologically confirmed, stage III or IV ovarian, fallopian tube, or primary peritoneal carcinoma with residual disease less than 1 cm.	Patients who did not undergo postoperative CT scan.

## 4. Discussion

### 4.1. Principal findings

The findings of this systematic review suggest that postoperative evidence of residual disease exists in a substantial proportion of patients undergoing debulking surgery that was clinically considered optimally cytoreduced. Despite differences in terms of population characteristics these findings are observed unanimously among included studies which report a median proportion of residual disease among surgically treated patients that ranges between 40 and 50%. While the available evidence concerning the impact of this observation on survival outcomes is

scarce, evidence presented in the present meta-analysis suggests that radiological findings of residual disease were associated with reduced disease free as well as the overall survival of patients when these are compared to patients with no radiological evidence of residual disease. These findings suggest that radiological residual disease should be interpreted primarily as a prognostic marker, reflecting disease biology, extent, and imaging detectability, rather than as a direct measure of surgical failure. It should be noted, however, that prediction intervals indicated that future studies may observe null or smaller effects, highlighting the variability of associations across different clinical and methodological settings.

**Table 2**

Patient and tumor characteristics. NA: data were not available, ASA: American Society of Anesthesiologists, ECOG: Eastern Cooperative Oncology Group, BMI: Body Mass Index, CT: Computed Tomography.

Study; Year	Age	ASA score	ECOG status	BMI (kg/m2)	Primary disease site	Ascites	Histology	Stage	Grade	Surgical debulking	Days between surgery and CT
Burger; 2015	<b>Median:</b> 60 (23.1-81.6)	<b>I:</b> 7/212 <b>II:</b> 118/212 <b>III:</b> 2/212 <b>IV:</b> 19/212	NA	NA	NA	NA	<b>Serous:</b> 202/212 <b>Endometrioid:</b> 2/212 <b>Clear cell:</b> 3/212 <b>Mixed:</b> 5/212	<b>III:</b> 123/212 <b>IV:</b> 89/212	NA	<ul style="list-style-type: none"> <li>• <b>No gross residual disease:</b> 104/212</li> <li>• <b>&lt;1 cm:</b> 83/212</li> <li>• <b>&gt;1 cm:</b> 25/212</li> </ul>	<b>Median:</b> 19 (6-49)
Chi; 2007	<b>Median:</b> 60 (39-81)	NA	NA	<b>Median:</b> 25 (17-42)	<b>Ovary:</b> 66/78 <b>Peritoneum:</b> 8/78 <b>Fallopian tube:</b> 4/78	<b>Yes:</b> 65/78 <b>No:</b> 13/78	<b>Serous:</b> 68/78 <b>Clear cell:</b> 2/78 <b>Mixed:</b> 8/78	<b>IIIA:</b> 1/78 <b>IIIB:</b> 0/78 <b>IIIC:</b> 62/78 <b>IV:</b> 15/78	<b>1:</b> 2/78 <b>2:</b> 5/78 <b>3:</b> 71/78	<ul style="list-style-type: none"> <li>• <b>Microscopic/No gross residual disease:</b> 31/78</li> <li>• <b>0.1-0.5 cm:</b> 24/78</li> <li>• <b>0.6-1.0 cm:</b> 23/78</li> </ul>	<b>Median:</b> 14
Chi; 2010	<b>Median:</b> 60 (42-81)	NA	NA	NA	<b>Ovary:</b> 51/67 <b>Peritoneum:</b> 10/63 <b>Fallopian tube:</b> 6/63	<b>Yes:</b> 53/67 <b>No:</b> 14/63	<b>Serous:</b> 63/67 <b>Clear cell:</b> 0/67 <b>Mixed:</b> 4/67	<b>IIIC:</b> 49/67 <b>IV:</b> 18/67	<b>1:</b> 5/67 <b>2:</b> 7/67 <b>3:</b> 55/67	<ul style="list-style-type: none"> <li>• <b>No gross residual disease:</b> 25/67</li> <li>• <b>≤5 mm:</b> 21/67</li> <li>• <b>6-10 mm:</b> 21/67</li> </ul>	7-35
Eskander; 2020	<b>20-29:</b> 5/627 <b>30-39:</b> 20/627 <b>40-49:</b> 98/627 <b>50-59:</b> 194/627 <b>60-69:</b> 197/627 <b>70-79:</b> 103/627 <b>80-89:</b> 10/627	NA	<b>0:</b> 354/627 <b>1:</b> 248/627 <b>2:</b> 25/627	<b>&lt;30:</b> 469/627 <b>&gt;30:</b> 158/627	NA	NA	<b>Serous:</b> 627 <b>Clear cell:</b> 0/67 <b>Mixed:</b> 4/67	<b>IIIA:</b> 15/627 <b>IIIB:</b> 45/627 <b>IIIC:</b> 557/627 <b>III not otherwise specified:</b> 10/627	<b>1:</b> 31/627 <b>2:</b> 90/627 <b>3:</b> 448/627 <b>Not reported:</b> 58/627	<ul style="list-style-type: none"> <li>• <b>≤1 cm:</b> 376/627</li> <li>• <b>&gt;1 cm:</b> 251/627</li> </ul>	<b>Mean:</b> 26 (1-109)
Joo-Hyuk Son; 2018	<b>Median:</b> 57 (38-80)	NA	NA	NA	NA	NA	<b>High grade serous:</b> 65/68 <b>Endometrioid:</b> 1/68 <b>Clear cell:</b> 1/68 <b>Mixed:</b> 1/68	<b>IIIC:</b> 47/68 <b>IVA:</b> 16/68 <b>IVB:</b> 5/68	NA	<ul style="list-style-type: none"> <li>• <b>No gross residual disease:</b> 46/68</li> <li>• <b>Near optimal:</b> 16/68</li> <li>• <b>Suboptimal:</b> 6/68</li> </ul>	NA
Lakhman; 2012	<b>Median:</b> 60 (39-81)	NA	NA	NA	<b>Ovary:</b> 50/63 <b>Peritoneum:</b> 8/63 <b>Fallopian tube:</b> 5/63	<b>Yes:</b> 54/63 <b>No:</b> 9/63	<b>Serous:</b> 58/63 <b>Clear cell:</b> 1/63 <b>Mixed:</b> 4/63	<b>IIIA:</b> 1/63 <b>IIIC:</b> 47/63 <b>IV:</b> 15/63	<b>1:</b> 4/63 <b>2:</b> 4/63 <b>3:</b> 52/63 <b>Unknown:</b> 3/63	<ul style="list-style-type: none"> <li>• <b>Microscopic/No gross residual disease:</b> 27/63</li> <li>• <b>0.1-0.5 cm:</b> 22/63</li> <li>• <b>0.6-1.0 cm:</b> 14/63</li> <li>• <b>&gt;1 cm:</b> 0/63</li> </ul>	<b>Median:</b> 15 (4-49)
Lim; 2022	<b>RO Median:</b> 53 (22-86) <b>RI Median:</b> 56 (29-79)	<b>RO I:</b> 158/266 <b>RI:</b> 103/266	NA	<b>RO &lt;30:</b> 259/266 <b>RO &gt;30:</b> 7/266 <b>RI &lt;30:</b> 166/170 <b>RI &gt;30:</b> 4/170	NA	<b>RO Yes:</b> 118/266 <b>RO No:</b> 148/266 <b>RI Yes:</b> 103/170	<b>High grade serous:</b> 436/436	<b>III:</b> 436/436	NA	<ul style="list-style-type: none"> <li>• <b>No gross residual disease:</b> 266/436</li> <li>• <b>1 cm:</b> 170/436</li> </ul>	<b>RO Median:</b> 9 (0-36) <b>RI Median:</b> 8 (0-23)

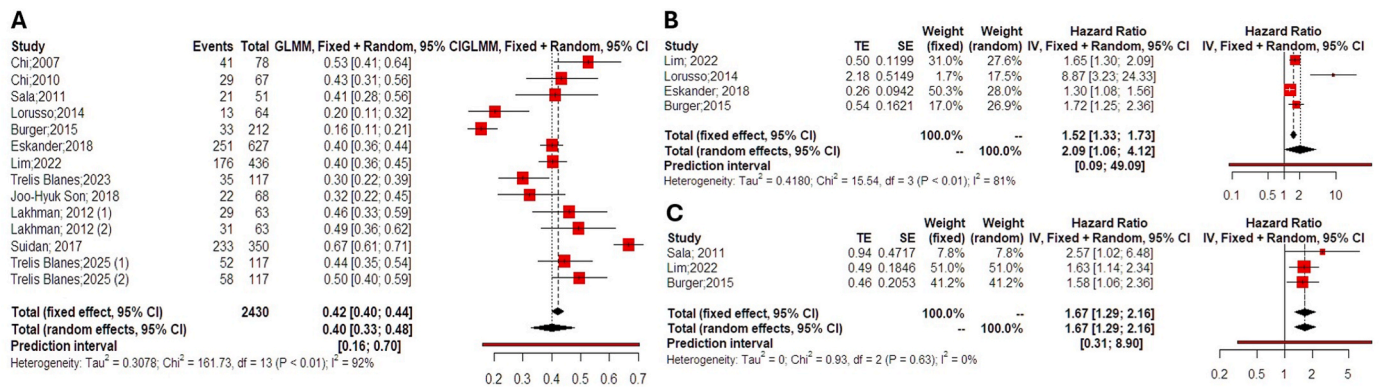
(continued on next page)

Table 2 (continued)

Study; Year	Age	ASA score	ECOG status	BMI (kg/m2)	Primary disease site	Ascites	Histology	Stage	Grade	Surgical debulking	Days between surgery and CT
		<b>I:</b> 89/ 170				<b>No:</b> 63/ 170					
		<b>II:</b> 74/ 170									
		<b>III:</b> 7/ 170									
Lorusso; 2014	<b>Median:</b> 66.5 (38-77)	NA	NA	NA	NA	NA	<b>Serous:</b> 51/64 <b>Clear cell:</b> 5/64 <b>Mixed:</b> 8/64	<b>IIIA:</b> 2/64 <b>IIIB:</b> 2/64 <b>IIIC:</b> 45/64 <b>IV:</b> 15/64	<b>I:</b> 3/64 <b>2:</b> 1/64 <b>3:</b> 52/64 <b>Unknown:</b> 8/64	<ul style="list-style-type: none"> <li>• <b>No gross residual disease:</b> 53/64</li> <li>• <b>0.1–1 cm:</b> 11/64</li> </ul>	<b>Median:</b> 23 (9-30)
Sala; 2011	<b>Mean:</b> 63.2 (34-80)	NA	NA	NA	NA	NA	<b>Serous:</b> 33/51 <b>Endometrioid:</b> 7/51 <b>Clear cell:</b> 1/51 <b>Mucinous:</b> 2/51 <b>Malignant mixed mullerian tumor:</b> 2/51 <b>Mixed:</b> 6/51	<b>I:</b> 11/51 <b>II:</b> 5/51 <b>III:</b> 35/51	<b>I:</b> 2/51 <b>2:</b> 19/51 <b>3:</b> 30/51	NA	<b>Median:</b> 40.5 (4-60)
Suidan; 2017	<b>Median:</b> 61 (34-86)	<b>I:</b> 10/ 350	NA	NA	<b>Ovary:</b> 264/ 350 <b>Peritoneum:</b> 44/350 <b>Fallopian tube:</b> 42/350	NA	<b>Serous:</b> 314/ 350 <b>Endometrioid/</b> <b>Clear cell:</b> 2/ 350 <b>Mixed/Other:</b> 34/350	<b>IIIA/B:</b> 8/ 350 <b>IIIC:</b> 248/ 350 <b>IV:</b> 94/350	<b>I + 2:</b> 19/ 350 <b>3:</b> 328/350	NA	NA
Trelis Blanes; 2023, 2025	<b>Mean:</b> 55.4 ± 12.3	NA	<b>0-I:</b> 112/ 117 <b>2:</b> 5/ 117	<b>Mean:</b> 25.5 ± 5.2.	NA	NA	<b>Serous:</b> 92/117 <b>Endometrioid:</b> 6/117 <b>Mucinous:</b> 2/ 117 <b>Clear cell:</b> 4/ 117 <b>Other:</b> 12/117	<b>II:</b> 7/117 <b>III:</b> 87/117 <b>IV:</b> 22/117	NA	<ul style="list-style-type: none"> <li>• <b>No gross residual disease:</b> 79/117</li> <li>• <b>&gt;1 cm:</b> 38/117</li> </ul>	<b>Mean:</b> 40

Table 3  
QUIPS (Quality In Prognosis Studies) assessment of included studies.

Table 3. Quality In Prognosis Studies assessment					
	Participation	Attrition	Prognostic factors	Outcome measurement	Confounding
Burger;2015					
Chi;2007					
Chi;2010					
Eskander;2020					
Joo-Hyuk Son;2018					
Lakhman; 2012					
Lim; 2022					
Lorusso; 2014					
Sala;2011					
Suidan; 2017					
Trelis Blanes; 2023					
Trelis Blanes; 2025					



**Fig. 2.** Meta-analytic outcomes of included studies. **A)** Meta-analysis of proportion of patients with radiological data of residual disease following debulking surgery, **B)** Progression free survival differences. **C)** Overall survival differences. Hazard ratios of 5-year overall survival (lower forest plot). Forest plot analysis: Vertical line = "no difference" point between the two groups. Red squares = hazard ratios of overall survival of included studies; Horizontal black lines = 95% CI of included studies; Diamond = pooled hazard ratios retrieved from the outcomes of the meta-analysis and 95% CI for all studies; Horizontal red line = prediction intervals. The weight of included studies is depicted for fixed and random effects model separately.

#### 4.2. Comparison with existing literature

It should be noted that the majority of studies included in the present systematic review presented data from tertiary centers, most of which are considered centers of excellence in the treatment of ovarian cancer. Therefore, both the clinical estimation of debulking status as well as the radiological evidence that is provided refer to optimal conditions that may significantly deviate from real world data that refer to clinical practice outside these prerequisites. Rates of optimal debulking significantly differ among studies published in the international literature and these are related to the actual extent of the disease as well as patients' performance status and surgical expertise [25,26].

Several factors affect the survival of ovarian cancer patients, including frailty, tumor biology, extent of disease and timing of cytoreductive surgery and these factors are affect the ability of complete surgical tumor resection, thus, every effort must be made to identify patients at risk of residual disease as the latter seems to offer no benefit compared to no surgery [27].

It should be noted that that the latest data from large randomized controlled trials such as the TRUST trial that was presented at the 2025 ASCO (American Society of Clinical Oncology) Annual Meeting do not suggest better results denoting the extent of this problem [28].

#### 4.3. Implications for current clinical practice and future research

Considering this information, it seems important to address the issue of residual disease in patient counseling prior to surgery and to inform about the negative impact of radiologically confirmed disease on the actual course of the disease. However, radiological evidence of residual disease should not be considered as a determinant of treatment adequacy but rather assist in postoperative risk stratification. Future research should focus on differences in postoperative residual disease among primary debulking surgery (PDS) and interval debulking surgery (IDS) and sub-stratify patients to those with clinical criteria of residual disease following debulking surgery and those with radiological criteria only. This will permit accurate determination of the actual incidence of residual disease as well as to evaluate the presence of potential differences in survival rates among these two distinct groups. In addition, it should be emphasized that radiological evidence of residual disease following debulking surgery represents a complex postoperative finding that may be influenced by several factors beyond true viable tumor persistence. Differences in imaging modality, timing of postoperative evaluation, and interpretation criteria may affect the detection and characterization of residual disease. The absence of standardized postoperative imaging protocols and reporting systems limits the translation

of radiological findings into uniform clinical decision-making. This underlines the need for evidence that incorporates quantitative or semi-quantitative measures of residual disease burden, such as lesion size, volumetric assessment, or radiology-adapted peritoneal cancer scores, to allow evaluation of potential dose-response relationships between residual disease extent and survival outcomes. Future prospective studies should aim to incorporate predefined imaging timepoints, structured radiological assessment frameworks, and, where feasible, centralized or blinded image review, in order to better distinguish postoperative changes from true residual disease and to allow more accurate prognostic stratification.

#### 4.4. Strengths and limitations

The present meta-analysis was based on abundant information about the actual incidence of residual disease following debulking surgery in epithelial ovarian cancer. Moreover, the introduction of thorough sensitivity analysis permitted a more accurate interpretation of the meta-analytic findings. Specifically, prediction intervals illustrate the expected variability of postoperative radiological residual disease across different clinical settings and emphasize that the pooled estimates reflect an average effect rather than a uniform outcome. Similarly, the attenuation of survival estimates following adjustment for small-study effects indicates that the magnitude of the observed associations may vary according to study size and design, underscoring the need for careful translation of statistical significance into clinical relevance.

Several limitations should be acknowledged that relate to the nature and quality of the available evidence, including heterogeneity in study design, patient populations, surgical strategies, definitions of optimal debulking, and postoperative imaging assessment. The results of the QUIPS tool indicate the presence of significant selective outcome reporting, as survival outcomes were not consistently reported for patients with and without radiological evidence of residual disease, while adjustment for key confounding variables such as surgical complexity, disease burden, and patient performance status was frequently limited or absent. These issues may have influenced the magnitude of the observed associations and likely contributed to the heterogeneity noted across analyses, reinforcing the need for cautious interpretation of the pooled estimates. Additional constraints arise from the limited amount of prospective data, potential inter-observer variability in radiological interpretation, the predominance of high-volume tertiary centers and the lack of comparative data between radiological and clinically evident residual disease which may affect the generalizability and interpretation of the findings. These key issues are presented in detail in the **Appendix**.

## 5. Conclusion

The proportion of patients with radiological criteria of residual disease following debulking surgery appears to be considerable and is associated with less favorable survival outcomes in patients with epithelial ovarian cancer. Considering this observation physicians should regard positive radiological findings following debulking surgery as a prognostic marker that should be taken into account during decision making for patient handling. Given the heterogeneity of the included studies, the limited prospective evidence, and the methodological constraints of postoperative imaging assessment, these findings should be interpreted cautiously. To date it is not known if the incidence of residual disease differs among patients subjected to primary debulking surgery (PDS) compared to those receiving neoadjuvant chemotherapy or how radiological residual disease compares prognostically with clinically evident residual disease. Nevertheless, consideration of postoperative radiological findings may be informative during preoperative patient counseling, while further prospective studies are needed to better define their clinical relevance.

## Informed consent statement

The review is based on aggregated data that have been already published in international literature. Patient consent and institutional review board approval were, therefore, waived.

## Data availability statement

Data available upon reasonable request.

## Author contributions

Conceptualization: V. Pergialiotis & D. Haidopoulos, Data curation: N. Thomakos & M. Fanaki, Methodology: V. Pergialiotis, K. Bramis & P. Antonakis, Formal analysis: V. Pergialiotis & V. Lygizos, Supervision: D. Haidopoulos, Writing original Draft: V. Pergialiotis, N. Thomakos, M. Fanaki, V. Lygizos, K. Bramis, P. Antonakis, Writing – review and editing: V. Pergialiotis & D. Haidopoulos

## Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

## Declaration of competing interests

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.

## Acknowledgments

No acknowledgments.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2026.111462>.

## References

- [1] Webb PM, Jordan SJ. Global epidemiology of epithelial ovarian cancer. *Nat Rev Clin Oncol* 2024;21:389–400.
- [2] Vermeulen CKM, Tadesse W, Timmermans M, Kruitwagen R, Walsh T. Only complete tumour resection after neoadjuvant chemotherapy offers benefit over suboptimal debulking in advanced ovarian cancer. *Eur J Obstet Gynecol Reprod Biol* 2017;219:100–5.
- [3] Gill SE, McGree ME, Weaver AL, Cliby WA, Langstraat CL. Optimizing the treatment of ovarian cancer: neoadjuvant chemotherapy and interval debulking versus primary debulking surgery for epithelial ovarian cancers likely to have suboptimal resection. *Gynecol Oncol* 2017;144:266–73.
- [4] Vergote I, Tropé CG, Amant F, Kristensen GB, Ehlen T, Johnson N, et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med* 2010;363:943–53.
- [5] Kehoe S, Hook J, Nankivell M, Jayson GC, Kitchener H, Lopes T, et al. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. *Lancet* 2015;386:249–57.
- [6] Onda T, Satoh T, Saito T, Kasamatsu T, Nakanishi T, Nakamura K, et al. Comparison of treatment invasiveness between upfront debulking surgery versus interval debulking surgery following neoadjuvant chemotherapy for stage III/IV ovarian, tubal, and peritoneal cancers in a phase III randomised trial: Japan clinical oncology group study JCOG0602. *Eur J Cancer* 2016;64:22–31.
- [7] Trellis Blanes A, Lago Leal V, Padilla Iserte P, Pérez Martínez R, Belloch Ripollés V, Matute L, et al. Optimal cytoreduction: is a CT's picture worth a surgeon's word? *Surg Oncol* 2023;49:101948.
- [8] Trellis Blanes A, Lago V, Pérez Martínez R, Belloch Ripollés V, Montoliu G, Padilla-Iserte P, et al. Residual tumour at CT scan based on radiologic peritoneal carcinomatosis index after optimal cytoreduction in advanced ovarian cancer: a true prognostic factor. *Cancers (Basel)* 2025;17.
- [9] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009;62:e1–34.
- [10] Group CCPM. The cochrane collaboration prognosis methods group. Review tools. 2018.
- [11] Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods* 2010;1:97–111.
- [12] Int'Hout J, Ioannidis JPA, Borm GF. The hartung-knapp-sidik-jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Med Res Methodol* 2014;14:25.
- [13] Souza JP, Pileggi C, Cecatti JG. Assessment of funnel plot asymmetry and publication bias in reproductive health meta-analyses: an analytic survey. *Reprod Health* 2007;4:3.
- [14] Tang JL, Liu JL. Misleading funnel plot for detection of bias in meta-analysis. *J Clin Epidemiol* 2000;53:477–84.
- [15] Lim H, Shim J, Park SJ, Noh J, Kim TM, Lee M, et al. Impact of no residual disease on postoperative computed tomography on survival in patients with optimally debulked advanced high-grade serous ovarian cancer during upfront surgery. *Gynecol Oncol* 2022;165:493–9.
- [16] Eskander RN, Kauderer J, Tewari KS, Mannel RS, Bristow RE, O'Malley DM, et al. Correlation between Surgeon's assessment and radiographic evaluation of residual disease in women with advanced stage ovarian cancer reported to have undergone optimal surgical cytoreduction: an NRG oncology/gynecologic oncology group study. *Gynecol Oncol* 2018;149:525–30.
- [17] Son JH, Chang K, Kong TW, Paek J, Chang SJ, Ryu HS. A study of clinicopathologic factors as indicators for early prediction of suboptimal debulking surgery after neoadjuvant chemotherapy in advanced ovarian cancer. *J Obstet Gynaecol Res* 2018;44:1294–301.
- [18] Suidan RS, Ramirez PT, Sarasohn DM, Teitcher JB, Iyer RB, Zhou Q, et al. A multicenter assessment of the ability of preoperative computed tomography scan and CA-125 to predict gross residual disease at primary debulking for advanced epithelial ovarian cancer. *Gynecol Oncol* 2017;145:27–31.
- [19] Burger IA, Goldman DA, Vargas HA, Kattan MW, Yu C, Kou L, et al. Incorporation of postoperative CT data into clinical models to predict 5-year overall and recurrence free survival after primary cytoreductive surgery for advanced ovarian cancer. *Gynecol Oncol* 2015;138:554–9.
- [20] Lorusso D, Sarno I, Di Donato V, Palazzo A, Torrisi E, Pala L, et al. Is postoperative computed tomography evaluation a prognostic indicator in patients with optimally debulked advanced ovarian cancer? *Oncology* 2014;87:293–9.
- [21] Lakhman Y, Akin O, Sohn MJ, Zheng J, Moskowitz CS, Iyer RB, et al. Early postoperative CT as a prognostic biomarker in patients with advanced ovarian, tubal, and primary peritoneal cancer deemed optimally debulked at primary cytoreductive surgery. *AJR Am J Roentgenol* 2012;198:1453–9.
- [22] Sala E, Mannelli L, Yamamoto K, Griffin M, Griffin N, Grant L, et al. The value of postoperative/preadjuvant chemotherapy computed tomography in the management of patients with ovarian cancer. *Int J Gynecol Cancer* 2011;21:296–301.
- [23] Chi DS, Barlin JN, Ramirez PT, Levenback CF, Mironov S, Sarasohn DM, et al. Follow-up study of the correlation between postoperative computed tomographic scan and primary surgeon assessment in patients with advanced ovarian, tubal, or peritoneal carcinoma reported to have undergone primary surgical cytoreduction to residual disease of 1 Cm or smaller. *Int J Gynecol Cancer* 2010;20:353–7.
- [24] Chi DS, Ramirez PT, Teitcher JB, Mironov S, Sarasohn DM, Iyer RB, et al. Prospective study of the correlation between postoperative computed tomography scan and primary surgeon assessment in patients with advanced ovarian, tubal, and peritoneal carcinoma reported to have undergone primary surgical cytoreduction to residual disease 1 Cm or less. *J Clin Oncol* 2007;25:4946–51.
- [25] Cowan RA, O'Ceirbhail RE, Gardner GJ, Levine DA, Roche KL, Sonoda Y, et al. Is it time to centralize ovarian cancer care in the United States? *Ann Surg Oncol* 2016;23:989–93.

- [26] Nasioudis D, Kahn R, Chapman-Davis E, Frey MK, Caputo TA, Witkin SS, et al. Impact of hospital surgical volume on complete gross resection (CGR) rates following primary debulking surgery for advanced stage epithelial ovarian carcinoma. *Gynecol Oncol* 2019;154:401–4.
- [27] Ledermann JA, Matias-Guiu X, Amant F, Concin N, Davidson B, Fotopoulou C, et al. ESGO-ESMO-ESP consensus conference recommendations on ovarian cancer: pathology and molecular biology and early, advanced and recurrent disease. *Ann Oncol* 2024;35:248–66.
- [28] Mahner S, Heitz F, Salehi S, Reuss A, Guyon F, Du Bois A, et al. TRUST: trial of radical upfront surgical therapy in advanced ovarian cancer (ENGOT ov33/AGO-OVAR OP7). *J Clin Oncol* 2025;43.