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Systematic Review

Prognostic Factors for Survival Outcomes Following Pelvic Exenteration for Recurrent Gynaecological Malignancies: A Systematic Review and Meta-Analysis

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Simple Summary

Pelvic exenteration, the removal of several pelvic organs, can cure some women whose gynaecological cancer has returned in the pelvis, but it is major surgery with a long recovery, so choosing who will benefit matters. We combined 40 reports of 37 studies (about 3160 patients) to identify features linked to survival after this operation. Cancer left at the edges of the removed tissue was linked to about twice the risk of death or recurrence, and cancer found in small blood or lymph vessels was also linked to worse outcomes, as was cancer in lymph nodes, although this was less certain. Tumours reaching the pelvic side wall, bladder, or bowel, and cancers returning soon after earlier treatment, tended to do worse. These findings may help doctors and patients weigh the likely benefit of surgery, but most studies were small and of limited quality, so larger, better-reported studies are needed.

Abstract

Background/Objectives: Pelvic exenteration can cure selected patients with recurrent gynaecological cancer, but evidence to guide patient selection is fragmented. We systematically reviewed prognostic factors for survival after this procedure. **Methods:** Medline and Embase were searched to 20 November 2026, with a supplementary Google Scholar search. Risk of bias was assessed with the Quality in Prognosis Studies (QUIPS) tool and certainty with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. Adjusted hazard ratios (HRs) were pooled by random-effects meta-analysis; other results were synthesised by direction of effect. **Results:** Thirty-seven studies (approximately 3160 patients, predominantly with cervical cancer) were included; 30 of 39 reports were at high risk of bias. Of 58 factors assessed, positive margins (overall survival HR 1.96, 95% confidence interval [CI] 1.44–2.68; 6 cohorts, 1241 patients), lymphovascular space invasion (LVSI; recurrence-based survival HR 1.68, 95% CI 1.32–2.14; 6 cohorts, 1139 patients), and nodal involvement (overall survival HR 2.43, 95% CI 1.18–5.00; 5 cohorts, 548 patients) were associated with poorer survival, with low to very low certainty. Pelvic side-wall, bladder or rectal invasion, and a shorter time interval before exenteration were associated with poorer survival in most cohorts. **Conclusions:** This is the first systematic review to apply established prognostic factor methods to survival after pelvic exenteration. Side-wall, organ

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invasion, and a short interval before exenteration may help inform selection; and positive margins, LVSI, and, less certainly, nodal involvement may identify patients at higher risk of relapse or death.

Keywords: pelvic exenteration; recurrence; gynaecological cancer; prognostic factor; survival; meta-analysis

1. Introduction

Pelvic exenteration is an extensive procedure with higher morbidity and mortality than most gynaecological oncology procedures, which has historically led to hesitancy among oncology units to offer it as a curative option for recurrent gynaecological cancers. Severe complications following surgery are still reported and the procedure has lasting effects on quality of life [1,2]. However, outcomes have improved with a 2-year and 5-year overall survival of 51.1% and 30.8% reported in a recent systematic review, and a recent series reporting no deaths within 30 days [3,4]. As a result, tertiary centres worldwide now undertake pelvic exenteration as a potentially curative treatment for selected patients with recurrent gynaecological malignancies.

Careful patient assessment and selection are therefore fundamental in planning pelvic exenteration with curative intent. However, evidence on the clinical, pathological and radiological factors influencing survival following treatment is fragmented and derived largely from small retrospective series with conflicting findings, particularly for factors such as age, tumour size, and interval to recurrence [4–6]. Previous syntheses have been narrative or have related study-level characteristics to survival across cohorts, an approach that can miss associations evident when patients are compared within studies [4,6,7]. To our knowledge, no review has synthesised prognostic effect estimates using established methods for prognostic factor research, with formal assessment of risk of bias and certainty of evidence.

In this systematic review, we aimed to identify and appraise studies investigating prognostic factors for survival after pelvic exenteration for recurrent or persistent gynaecological malignancies, to synthesise their findings by meta-analysis where possible and by structured narrative synthesis otherwise, and to identify gaps in the existing evidence.

2. Materials and Methods

2.1. Standards

This review was conducted and reported in line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) and Cochrane Prognosis Group guidance for prognostic factor reviews [8–10]. The completed PRISMA 2020 and PRISMA 2020 for Abstracts checklists are provided in Supplementary Materials S2. The review was registered retrospectively on the Open Science Framework (OSF; https://doi.org/10.17605/OSF.IO/2NDRT); methodological decisions made during screening and after data extraction are listed in the Supplementary Table S11, together with whether each could have affected the main findings and how this was tested. Risk of bias was independently assessed by S.S. and R.C. using the Quality In Prognosis Studies (QUIPS) tool, and disagreements were resolved by discussion with two senior authors (A.T. and D.P.J.B.) [11]. Six domains were rated for each report as low, moderate, or high using review-specific criteria. Prognostic factor measurement was rated low risk when the factor was defined and measured on the pathology specimen; confounding was rated high when no multivariable analysis was reported and moderate when adjustment covariates were data-driven; statistical analysis and reporting was rated high when effect estimates were missing or events were few.

The overall rating was high if any domain was rated high. Certainty of evidence was determined according to Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Guidelines 28 [12]. Selective reporting was considered under risk of bias assessment. Results synthesised narratively were rated following Murad et al. [13]. Narrative synthesis followed the Synthesis Without Meta-analysis (SWiM) guideline and Cochrane handbook [14,15]. In this review, a report was a single publication, a study was one or more reports of the same patients, and a cohort was the group of patients analysed for a given factor. Linked reports of the same dataset were combined under one study.

2.2. Eligibility Criteria, Search, and Study Selection

Medline (via PubMed) and Embase (via Ovid) were searched from inception to 20 November 2026. A supplementary Google Scholar search was also run and the first 100 results were screened. Full search strategies are given in Supplementary Materials S1.

Title/abstract and full text screening was conducted independently by two authors (S.S./A.T.) with two additional co-authors consulted for disagreements (A.S./D.P.J.B.). All studies reporting prognostic factors affecting survival outcomes following pelvic exenteration for recurrent gynaecological malignancies were included with no time limit and regardless of observational design. Reports not in English were excluded at screening ($n = 61$). Previous studies have suggested that limiting systematic reviews to English-language reports rarely changes their conclusions [16,17]. To account for heterogeneity in disease definitions and the scarcity of studies restricted to recurrent disease, a threshold of at least 80% of each cohort, set during screening, had to meet all three inclusion criteria: (1) recurrent or persistent disease, (2) gynaecological malignancy, and (3) curative-intent pelvic exenteration. Studies in which more than 20% of patients had primary disease, a non-gynaecological cancer, or palliative-intent surgery, or in which surgical intent could not be determined, were excluded. The make-up of each pooled cohort is shown in Supplementary Table S10, demonstrating that a stricter threshold would have left too few cohorts to pool. Case reports, conference abstracts, and review articles were excluded.

Data extraction was performed by S.S. and checked independently by R.C., following the checklist for critical appraisal and data extraction for systematic reviews of prognostic factor studies (i.e., study design, population, n, events, outcomes, follow-up, analysis, adjustment) as well as every factor-outcome estimate (HR with 95% CI, p-value, direction, univariable or multivariable) [10].

2.3. Analysis

Survival outcomes including overall survival (OS), recurrence-based survival (RBS) including disease-free survival (DFS), progression-free survival (PFS), recurrence-free survival (RFS), time-to-recurrence (TTR), and disease- or cancer-specific survival (DSS and CSS) were included. Authors' outcome labels are retained. Recurrence-based outcomes were grouped because labels were often not defined or were used interchangeably, and the same label described different events in different studies (Supplementary Table S9).

Multivariable estimates were preferred where available and whole cohort estimates were preferred over subgroups. Each cohort was counted once per factor. Where reports from the same cohort overlapped, the report giving an adjusted estimate for that factor was used. If both or neither reported an adjusted estimate, the larger report was used. Where overlap was probable but partial (different time periods or additional centres), both reports were kept and the effect of excluding one was tested in sensitivity analyses. In interobserver imaging studies, a result was considered significant only if it was significant for both readers on the study's main imaging modality. Factors assessed in five or more independent

cohorts are presented in the main text and the remaining factors are summarised in the Supplementary Materials.

Meta-analysis was performed for positive margins, lymph node involvement, and lymphovascular space invasion (LVSI). Adjusted hazard ratios were pooled on the log scale using random-effects meta-analysis with the between-study variance ($\tau 2$) estimated by restricted maximum likelihood (REML). The 95% CIs were calculated using the Hartung–Knapp–Sidik–Jonkman method with ad hoc variance correction to ensure that the intervals were no narrower than those of the standard random-effects model, and approximate 95% prediction intervals were reported. Heterogeneity was quantified using $\tau 2$ and I2 [10,14,18–20]. Only adjusted estimates were pooled in the main analysis. Because factors are often left out of multivariable models through data-driven selection, which can overestimate pooled associations, a sensitivity analysis added univariable estimates from cohorts in which the factor was tested but not entered or retained in the model. The adjustment variables for each pooled estimate are listed in Supplementary Table S8. Pooling required adjusted HRs for the same outcome group from 3 or more cohorts and prediction intervals used a t distribution with $k-2$ df. Subgroup analysis or meta-regression was not undertaken given the small number of studies.

Sensitivity analyses examined the effect of (i) substituting the alternative report where cohorts overlapped, (ii) excluding the likely overlapping cohort from the same institution, (iii) excluding the largest cohort, (iv) excluding a study that reported relative risks rather than hazard ratios, and (v) adding univariable estimates as described above (Supplementary Materials S7).

Results that could not be pooled were synthesised narratively. For each of the main prognostic factors, one result per cohort was selected and its direction was harmonised to a single standard comparison per factor, defined as the category expected to carry the higher risk versus the reference. Where no a priori direction could be defined, only statistical significance was displayed. Statistical significance was defined as $p < 0.05$ or a 95% CI excluding one [14,15,21].

Results were summarised in an effect direction plot showing the direction of each result, its statistical significance, and cohort size. Cohort-size categories were re-defined by the review authors because most cohorts were smaller than the original categories [22,23]. For factors with a hypothesised direction, albatross plots displayed each result's two-sided p-value, signed by the harmonised direction against cohort size [24]. Where p-values were not reported, they were derived from the HR and its 95% CI [14]. Analysis was conducted in R version 4.5.2, using metafor, ggplot2, and ragg. The risk of bias figure was produced with robvis [25–28].

3. Results

3.1. Study Selection

Forty reports describing thirty-seven studies were included (Figure 1 and Table 1). Three reports from the same institution and period described the same dataset and were treated as a single study, with results extracted from Westin et al. where the same factor was reported and from other reports for the factors only analysed in that report [29–31]. A multicentre series, which included patients from two other included cohorts from the same centres, reported survival results identical to those publications and focused primarily on morbidity. It was therefore linked to these cohorts and excluded from the analysis and risk-of-bias assessment as it contributed no independent prognostic data [32–34]. Two further reports from the same centre overlapped partially. For each factor, the report with an adjusted estimate was used, and when neither or both reported one, the larger report was used. The other report was substituted in a sensitivity analysis [35,36]. Probable partial overlap, suggested by the same institution and overlapping study periods, is indicated in Table 1.

Table 1. Characteristics of the included studies.

Study, Year	Country	Type of Study	Setting; Period	Diagnoses	%Recurrent and Persistent	*n*	Events	Outcomes (as Reported)	Median Follow-Up (Months)	Analysis
Valstad et al. 2026 [37]	Norway	Retrospective cohort	Single centre; 1995–2020	Cervix 55	100	55	28 recurrences; 36 deaths	OS, RFS, CSS	168	UV + MV
Peacock et al. 2026 [38]	Australia	Retrospective cohort (prospectively collected data)	Single centre; 1994–2024	Cervix 24	88	24	11 deaths	OS	37.6	UV
Bizzarri et al. 2025 § [39]	Italy (European multicentre)	Retrospective cohort	Multicentre; 2005–2023	Cervix 572, vagina 70, vulva 79, endometrium 140, other 1	92	725	NR	OS, DFS, CSS	47	UV + MV
Tammik et al. 2024 [40]	Estonia	Retrospective cohort	Single centre; 2001–2021	Cervix 22, vagina 3	100	25	18 deaths	OS	92	UV/MV
Gomes et al. 2024 ‡ [41]	United Kingdom	Retrospective cohort	Single centre; 1993–2018	Cervix 46, vagina 16, vulva 20, endometrium 18, ovary 1	100	101	61 recurrences	OS, PFS	49	UV
Classen-von Spee et al. 2024 [42]	Germany	Retrospective cohort	Single centre; 2007–2022	Vulva 17	100	17	10 deaths	OS	NR	UV
Moolenaar et al. 2023 [43]	Netherlands	Retrospective cohort	Multicentre; 2000–2020	Cervix 39, vagina 16, vulva 20, endometrium 15	87	90	NR	OS, PFS	19	UV + MV
Bizzarri et al. 2023 § [44]	Italy	Retrospective matched cohort	Multicentre; 2010–2021	Cervix 78, vagina 9, vulva 3, uterus 26, ovary 1	96	117	NR	DFS, CSS	37	UV
Seebacher et al. 2022 ‡ [3]	United Kingdom	Retrospective cohort	Single centre; 2000–2015	Cervix 31, vagina/vulva 25, uterus 9	100	65	40 deaths; 40 recurrences	OS, PFS	40 (survivors)	UV + MV

Table 1. *Cont.*

Study, Year	Country	Type of Study	Setting; Period	Diagnoses	%Recurrent and Persistent	*n*	Events	Outcomes (as Reported)	Median Follow-Up (Months)	Analysis
Martin et al. 2022 [45]	United States	Retrospective cohort	Single centre; 2000–2019	Cervix 58, vagina 14, vulva 18, endometrium 9, uterus 6, ovary 12, colorectal 15, other 7	86	139	80 deaths; 61 recurrences	OS, PFS	43 (mean)	MV
Straubhar et al. 2021 † [46]	United States	Retrospective cohort	Single centre; 2010–2018	Cervix 21, vagina 11, vulva 23, uterus 16	100	71	31 deaths; 34 recurrences or deaths	OS, PFS	41 (survivors)	UV + MV
Lewandowska et al. 2020 [47]	Poland	Retrospective cohort	Single centre; 2010–2018	Cervix 32	100	32	NR	OS	NR	UV + MV
Li et al. 2018 [48]	China	Cohort (design not stated)	Single centre; 2009–2016	Cervix 38	100	38	21 deaths; 21 recurrences	OS, DFS	29	UV + MV
Westin et al. 2014 [31]; Huang et al. 2014 [29]; Iglesias et al. 2012 [30]	United States	Retrospective cohort	Single centre; 1993–2010	Cervix 86, vagina 38, vulva 20, uterus 15, other 1	89	160	85 recurrences	OS, RFS, TTR	27	UV + MV
Tanaka et al. 2014 [49]	Japan	Retrospective cohort	Single centre; 2002–2011	Cervix 12	92	12	6 deaths	OS, PFS	22	UV
Sardain et al. 2014 [50]	France	Retrospective cohort	Single centre; 1997–2014	Cervix 13, vagina 3	100	16	10 deaths; 11 recurrences	DFS	12	UV + MV
Chiantera et al. 2014 § [34]	Germany, Italy	Retrospective cohort	Multicentre; 1998–2011	Cervix 167	84	167	99 deaths; 41 recurrences	OS	68	UV + MV
Chiantera et al. 2014 § [33]	Germany, Italy	Retrospective cohort	Multicentre; 2000–2011	Endometrium 21	100	21	10 deaths; 8 recurrences	OS	19	UV
Vargas et al. 2013 † [51]	United States	Retrospective cohort	Single centre; 2002–2011	Cervix 16, vagina/vulva 7, endometrium 8	100	31	11 deaths	OS, PFS	26 (mean)	UV

Table 1. *Cont.*

Study, Year	Country	Type of Study	Setting; Period	Diagnoses	%Recurrent and Persistent	*n*	Events	Outcomes (as Reported)	Median Follow-Up (Months)	Analysis
Jäger et al. 2013 [52]	Sweden	Retrospective cohort	Single centre; 2002–2011	Cervix 10, vagina 5, vulva 2, uterus 4, ovary/tube 7	100	28	7 deaths; 13 recurrences	OS, DFS	27	UV
Donati et al. 2013 † [53]	United States	Retrospective cohort	Single centre; 1999–2011	Cervix 28, vagina 6, vulva 3, uterus 12, other 1	100	50	20 deaths; 17 recurrences	OS, RFS	22	UV
Burger et al. 2013 † [54]	United States	Retrospective cohort	Single centre; 2002–2011	Cervix 18, vagina/vulva 7, uterus 8	100	33	12 deaths	OS, PFS	27 (mean)	UV
Yoo et al. 2012 ¶ [36]	South Korea	Retrospective cohort	Single centre; 2001–2011	Cervix 61	100	61	18 deaths; 28 recurrences	OS, DFS	22	UV + MV
Baiocchi et al. 2012 [55]	Brazil	Retrospective cohort	Single centre; 1982–2010	Cervix 73, vagina 10, vulva 7, endometrium 14, uterine sarcoma 3	91	107	48 recurrences	OS, PFS, CSS	26	UV + MV
McLean et al. 2011 [56]	United States	Retrospective cohort	Single centre; 1990–2008	Cervix 29, vagina 5, vulva 4, uterus 6	86	44	21 recurrences	OS	NR	UV
Benn et al. 2011 [57]	United States	Retrospective cohort	Single centre; 1990–2009	Cervix 40, vagina 5, vulva 9	93	54	NR	OS, DFS, DSS	13	UV
Spahn et al. 2010 [58]	Germany, Switzerland	Retrospective cohort	Multicentre; 1992–2006	Cervix 41, endometrium 2	100	43	27 deaths; 29 recurrences	DSS	31	UV + MV
Maggioni et al. 2009 [59]	Italy	Retrospective cohort	Single centre; 1996–2007	Cervix 62, vagina 21, vulva 9, endometrium 9, ovary 4, sarcoma 1	97	106	50 deaths; 47 recurrences	OS	22	UV

Table 1. *Cont.*

Study, Year	Country	Type of Study	Setting; Period	Diagnoses	%Recurrent and Persistent	*n*	Events	Outcomes (as Reported)	Median Follow-Up (Months)	Analysis
Park et al. 2007 ¶ [35]	South Korea	Prospective cohort	Single centre; 2001–2006	Cervix 33, vagina 2, vulva 4, endometrium 1, ovary 1, sarcoma 3	86	44	18 deaths; 21 recurrences	OS, DFS	24	UV + MV
Terán-Porcayo et al. 2006 [60]	Mexico	Retrospective cohort	Single centre; 1984–1989	Cervix 42	100	42	NR	OS	56 (mean)	UV
Mourton et al. 2006 † [61]	United States	Retrospective cohort	Single centre; 1992–2003	Cervix 19, vagina 4, vulva 2, uterus 5	100	30	21 recurrences	TTR	NR	UV
Goldberg et al. 2006 [62]	United States	Retrospective cohort	Single centre; 1987–2003	Cervix 95, vulva 1, endometrium 2, rectosigmoid 5	100	103	59 deaths	OS	NR	UV
Berek et al. 2005 [63]	United States	Retrospective cohort	Single centre; 1956–2001	Cervix 53, vagina 14, uterus 8	100	75	35 deaths	OS	50	UV
Goldberg et al. 1998 [64]	United States	Retrospective cohort	Single centre; 1954–1994	Cervix 109, vagina 15, other 30	82	154	NR	OS	NR	UV
Crozier et al. 1995 [65]	United States	Retrospective matched cohort	Single centre; 1955–1989	Cervix 105	100	105	55 recurrences	OS, PFS	NR	UV + MV
Hatch et al. 1990 # [66]	United States	Retrospective cohort	Single centre; 1979–1989	Cervix 31	90	31	9 recurrences	OS	NR	UV
Shingleton et al. 1989 # [67]	United States	Retrospective cohort	Single centre; 1969–1986	Cervix 143	100	143	69 recurrences	OS	NR	UV + MV

Probable or partial cohort overlap (same institution and overlapping period): † Memorial Sloan Kettering Cancer Center (MSKCC); ‡ Royal Marsden; § Gemelli; ¶ National Cancer Center (NCC) Korea; # University of Alabama. Each cohort counted once per factor in the synthesis. Outcomes as labelled by study authors. For synthesis, DFS, PFS, RFS, and TTR were grouped as recurrence-based survival. OS = overall survival; DFS = disease-free; PFS = progression-free; RFS = recurrence-free survival; TTR = time to recurrence; CSS/DSS = cancer-/disease-specific survival.

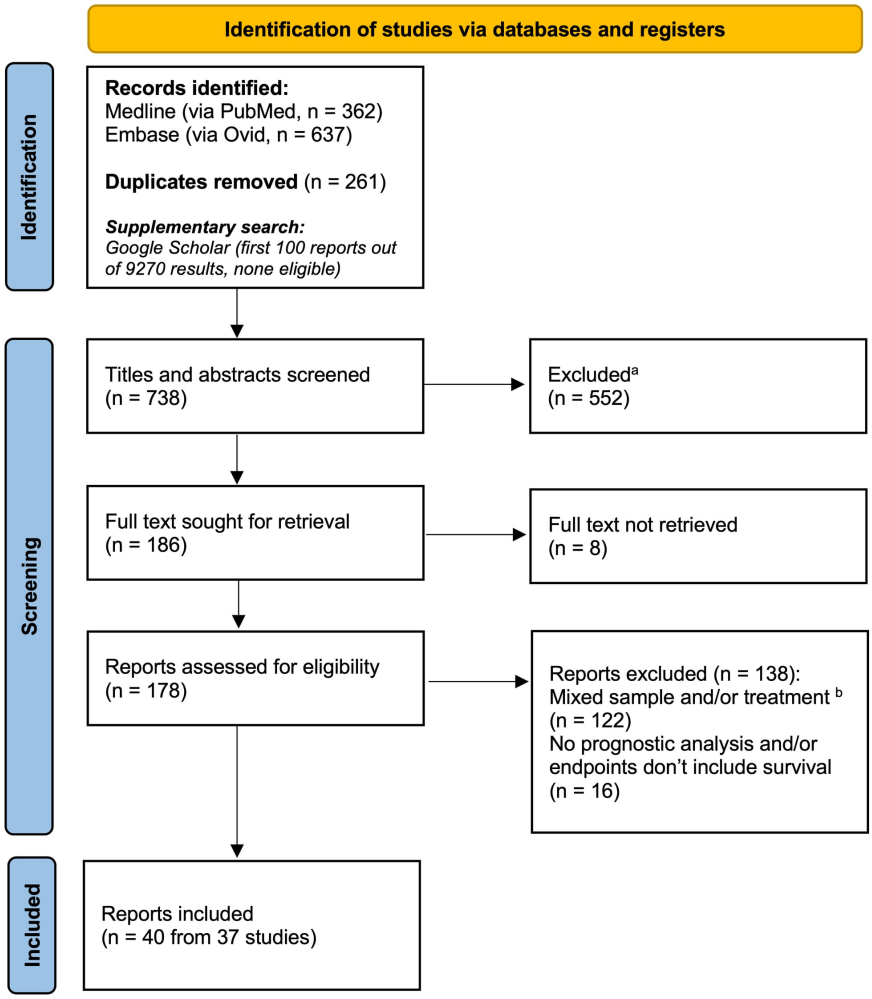


Figure 1. PRISMA flow diagram. [a] No automation tools were used. Abstracts and keywords were manually reviewed by the authors. [b] <80% of the sample consisted of the target population (exenteration for recurrent or persistent gynaecological malignancies).

3.2. Study Characteristics

Thirty-one single-centre and six multicentre studies were published between 1989 and 2026 (Table 1). Thirteen studies were published in the last decade. Thirty-three studies were retrospective cohorts, two were retrospective matched cohorts, one was reported to be a prospective cohort, and one study design was not stated in the report. Cohort sizes ranged from 12 to 725 (median: 54), comprising approximately 3160 patients in total; however, this figure may be overestimated due to the probable partial overlap between some cohorts. One multicentre study was much larger than the rest and contributed almost a quarter of all patients. Most studies included several primary sites, with cervical cancer the most common. Median or mean follow-up was reported in twenty-nine studies, ranging from 12 to 168 months.

Thirty-three studies reported overall survival, twenty-two reported recurrence-based survival, and six studies reported disease- or cancer-specific survival. Nineteen studies used univariable analyses only, one study did not transparently report the analysis method, and seventeen studies used multivariable analysis.

Twelve studies were restricted to recurrent disease [33,36,37,42,50,52,56,61,62,65–67], and of the remaining studies, only five defined persistent disease [34,38–40,48].

3.3. Risk of Bias

Of thirty-nine reports assessed (all except the linked multicentre series which contributed no independent data), thirty were at high and nine were at moderate risk of bias, with none qualifying for low risk (Figure 2). The main contributors were statistical analysis and reporting, mostly because *p*-values were reported without effect estimates, event numbers were small, or results were reported inconsistently. Confounding was the second largest contributor. Outcome measurement was at low risk in twenty-eight reports, reflecting the use of all-cause overall survival.

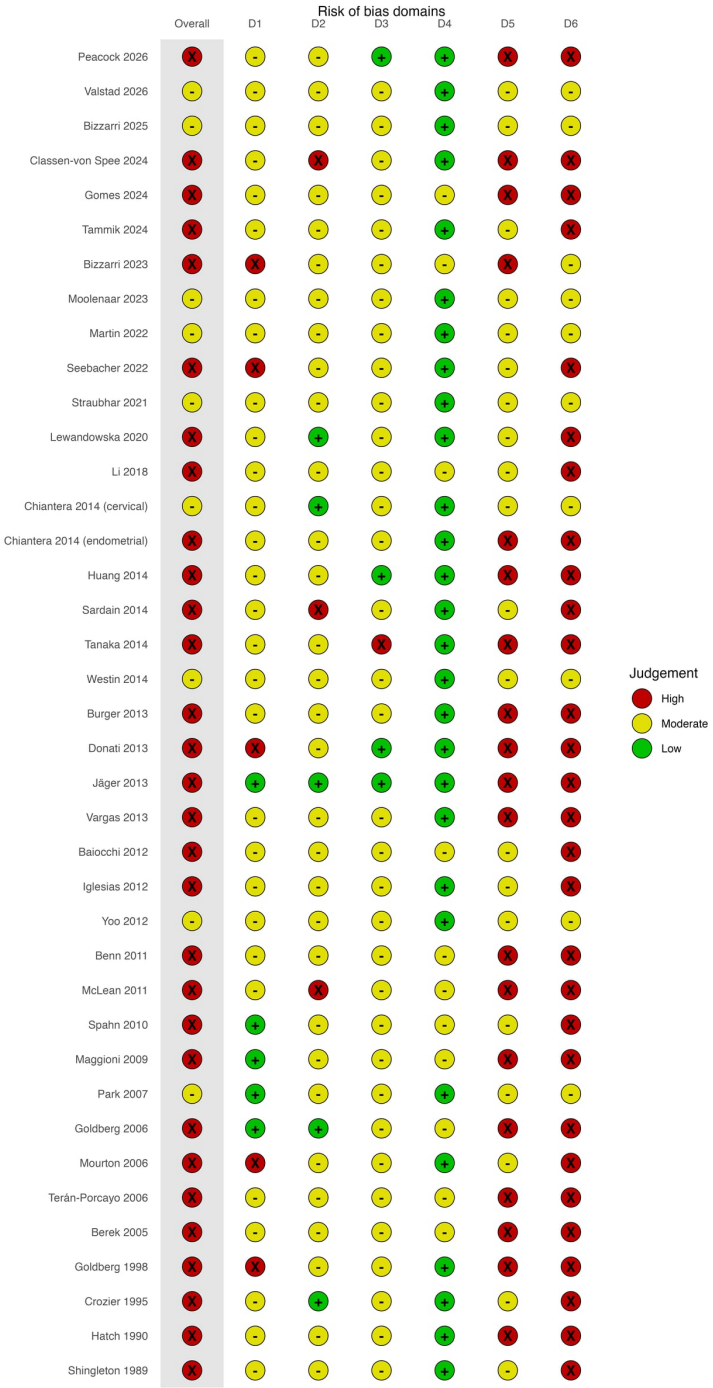


Figure 2. Risk of bias of included reports (QUIPS) [3,29–31,33–67]. D1, study participation; D2, study attrition; D3, prognostic factor measurement; D4, outcome measurement; D5, confounding; D6, statistical analysis and reporting.

3.4. Prognostic Factors Assessed

Fifty-eight factors were assessed in total. Each prognostic factor was analysed separately but, for presentation, factors were grouped into seven categories (patient, nutritional, disease history, tumour and pathological, imaging, surgical and treatment, and perioperative factors). Sixteen factors were assessed in at least five independent cohorts and are presented in the main text (Figure 3 and Supplementary Materials S3) and the remaining forty-two were each assessed in one to four cohorts (Supplementary Materials S4). The most frequently assessed factors were lymph node involvement and margin status (25 cohorts each), age (20 cohorts), tumour size (16 cohorts), and progression-free interval (15 cohorts).

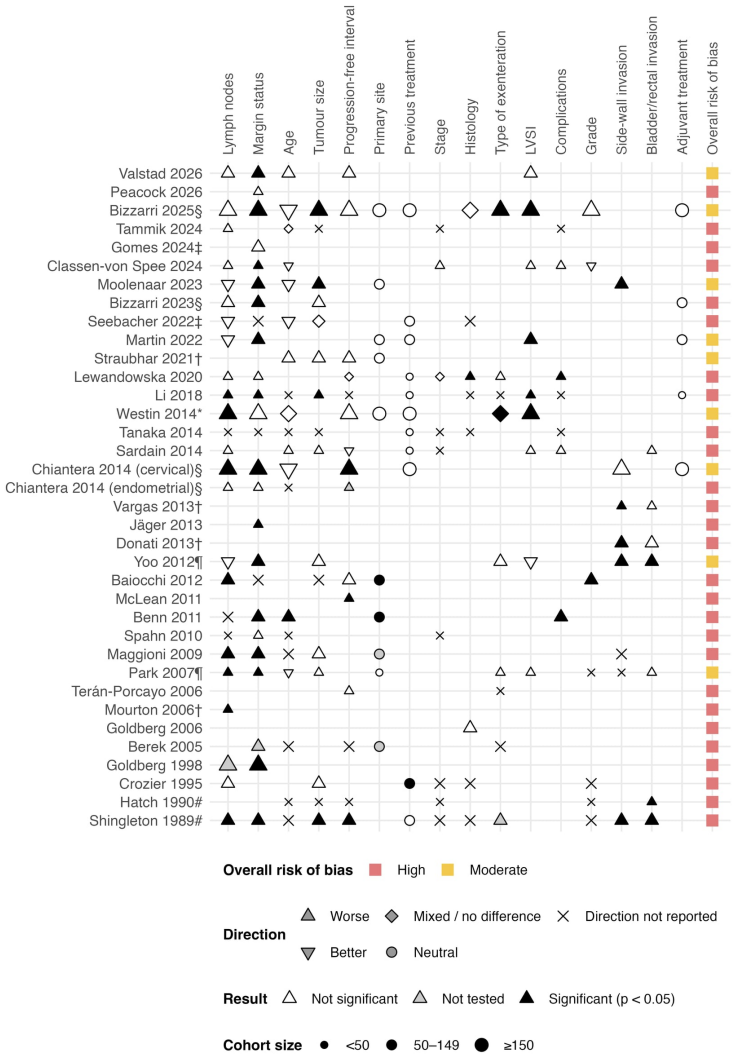


Figure 3. Effect direction plot for the 16 main prognostic factors [3,29–31,33–67]. Worse/better = survival in the expected high-risk category versus the reference: lymph nodes and margin status, positive vs. negative; age, older vs. younger; tumour size, larger vs. smaller; progression-free interval, shorter vs. longer; stage, higher vs. lower; histology, non-squamous vs. squamous; type of exenteration, total vs. partial; LVSI, present vs. absent; complications, present or severe vs. none; grade, high vs. low; side-wall and bladder or rectal invasion, involved vs. not. For primary site, previous treatment, and adjuvant treatment, no direction was hypothesised and only statistical significance is shown (circles). One result per cohort: overall survival where reported with a direction, otherwise recurrence-based survival, then cancer- or disease-specific survival; multivariable estimates preferred. Cohort-size categories were defined by the review authors. Adapted from the effect direction plot [23]. * Westin, Huang, and Iglesias (one dataset). Probable cohort overlap: † MSKCC; ‡ Royal Marsden; § Gemelli; ¶ NCC Korea; # University of Alabama.

3.5. Meta-Analyses

Adjusted estimates could be pooled for three factors (Figures 4–6). Positive surgical margins were associated with worse overall survival with six cohorts including 1241 patients (HR 1.96, 95% CI 1.44–2.68) and worse recurrence-based survival with six cohorts including 1129 patients (HR 2.15, 95% CI 1.40–3.31). Lymph node involvement was associated with worse overall survival (HR 2.43, 95% CI 1.18–5.00; PI 0.66–8.98, I^2 36%) and with worse recurrence-based survival (HR 2.75, 95% CI 1.07–7.09; PI 0.41–18.57), but both prediction intervals included no effect. LVSI was associated with worse recurrence-based survival (HR 1.68, 95% CI 1.32–2.14) whereas the estimate for overall survival, based on three cohorts, was imprecise (HR 1.75, 95% CI 0.99–3.09).

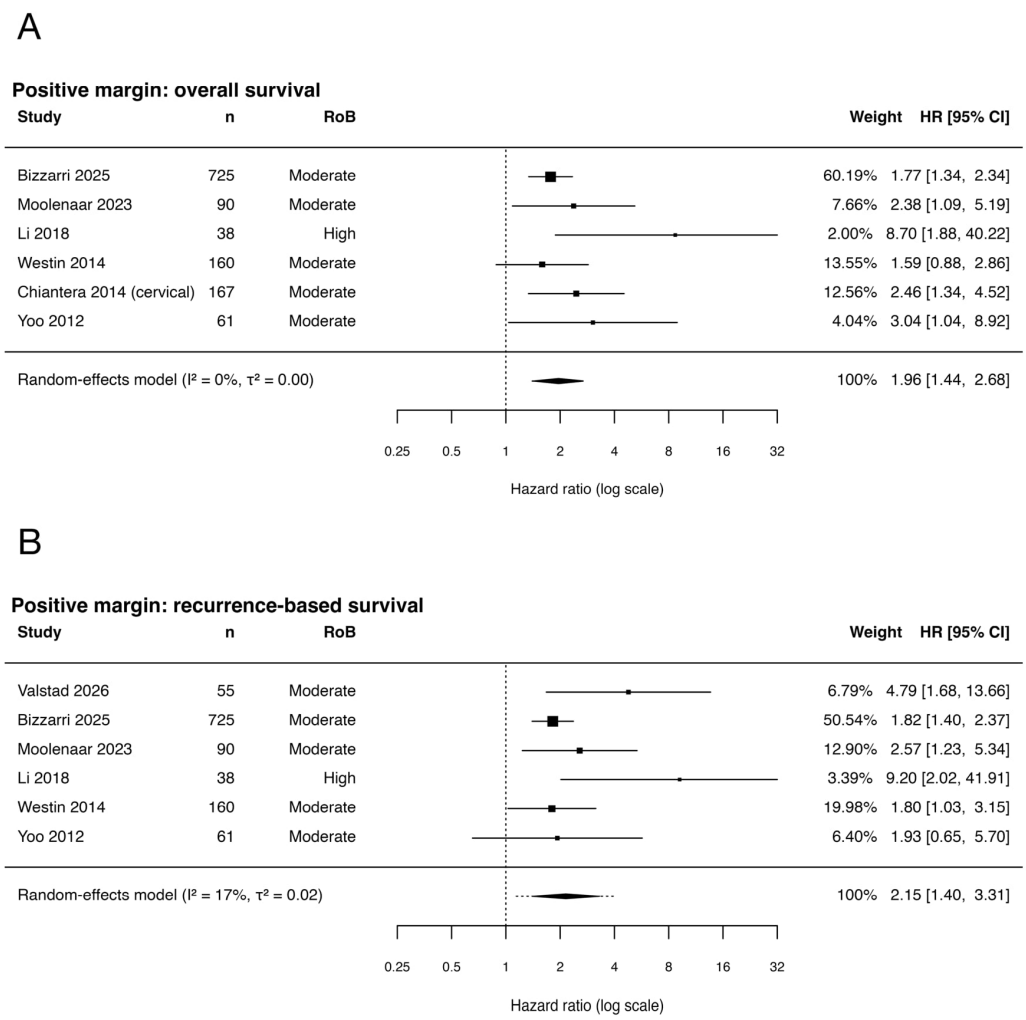


Figure 4. Positive surgical margins: pooled adjusted hazard ratios for (**A**) overall survival and (**B**) recurrence-based survival [31,34,36,37,39,43,48]. Random-effects meta-analysis (REML; Hartung–Knapp–Sidik–Jonkman 95% CI with ad hoc correction). Squares show study estimates sized by weight; diamonds show pooled estimates; dotted lines show 95% prediction intervals. *n*, cohort size; RoB, overall risk of bias (QUIPS); HR, hazard ratio; CI, confidence interval; τ^2, between-study variance.

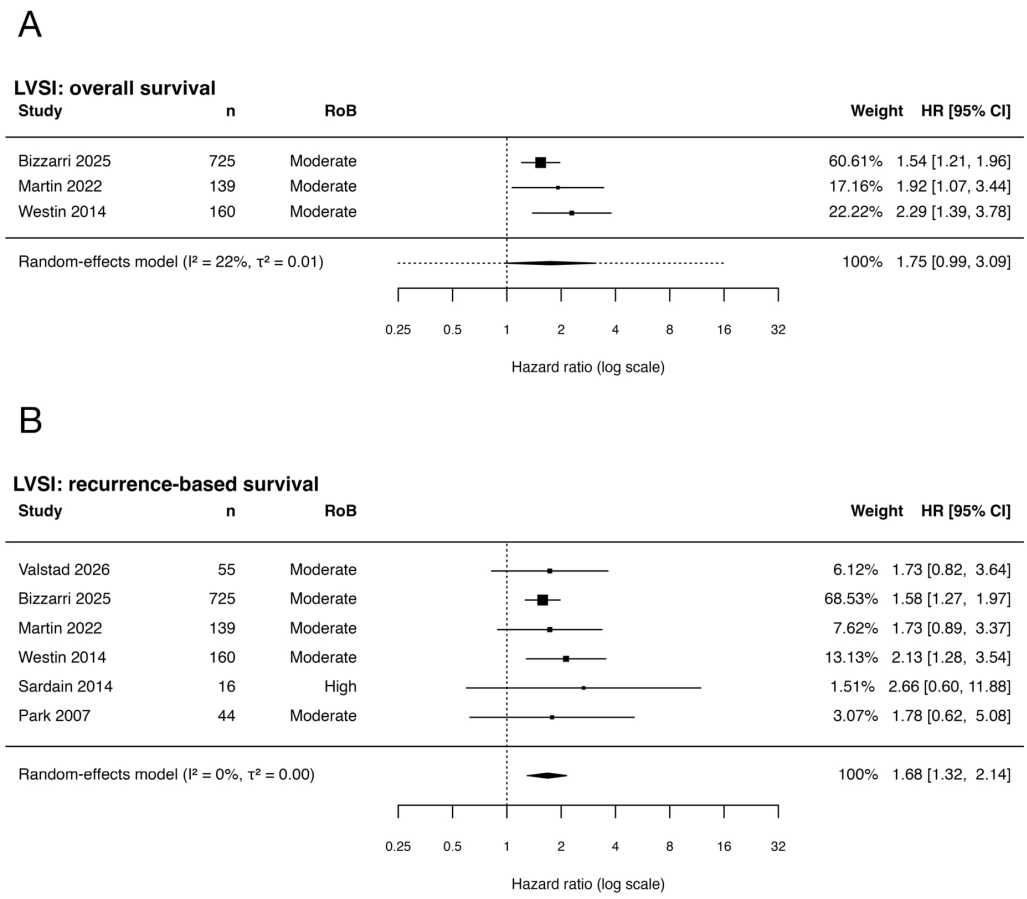


Figure 5. Lymphovascular space invasion (LVSI): pooled adjusted hazard ratios for (**A**) overall survival and (**B**) recurrence-based survival [31,35,37,39,45,50]. Random-effects meta-analysis (REML; Hartung–Knapp–Sidik–Jonkman 95% CI with ad hoc correction). Squares show study estimates sized by weight; diamonds show pooled estimates; dotted lines show 95% prediction intervals. *n*, cohort size; RoB, overall risk of bias (QUIPS); HR, hazard ratio; CI, confidence interval; τ^2, between-study variance.

In sensitivity analyses, the association of positive margins with survival was unchanged when the alternative overlapping report was substituted (overall survival HR 2.01, 95% CI 1.41–2.86; recurrence-based survival HR 2.34, 95% CI 1.44–3.79) and when the study reporting relative risks was excluded (HR 1.90, 95% CI 1.40–2.59 and HR 1.96, 95% CI 1.44–2.66, respectively). It was also unchanged when the largest cohort (overall survival HR 2.29, 95% CI 1.35–3.89; recurrence-based survival HR 2.63, 95% CI 1.32–5.24) or the likely overlapping cohort from the same institution (overall survival HR 1.90, 95% CI 1.30–2.78) was excluded. Similarly, the LVSI results did not change when the largest cohort was excluded (recurrence-based survival HR 1.93, 95% CI 1.21–3.07) or when univariable estimates were added (overall survival HR 1.65, 95% CI 1.01–2.69). In contrast, the association of lymph node involvement with survival was not robust to exclusion of the study reporting relative risks (overall survival HR 2.29, 95% CI 0.85–6.16; recurrence-based survival HR 2.55, 95% CI 0.66–9.89), exclusion of the likely overlapping cohort (overall survival HR 2.66, 95% CI 0.81–8.77), or the addition of univariable estimates (overall survival HR 1.70, 95% CI 1.00–2.88; recurrence-based survival HR 1.61, 95% CI 0.89–2.93). All sensitivity analyses are reported in Supplementary Materials S7.

Effect size contours were not drawn because most studies did not report the event counts and group sizes required. Small study effects could not be assessed as there were fewer than 10 studies per analysis.

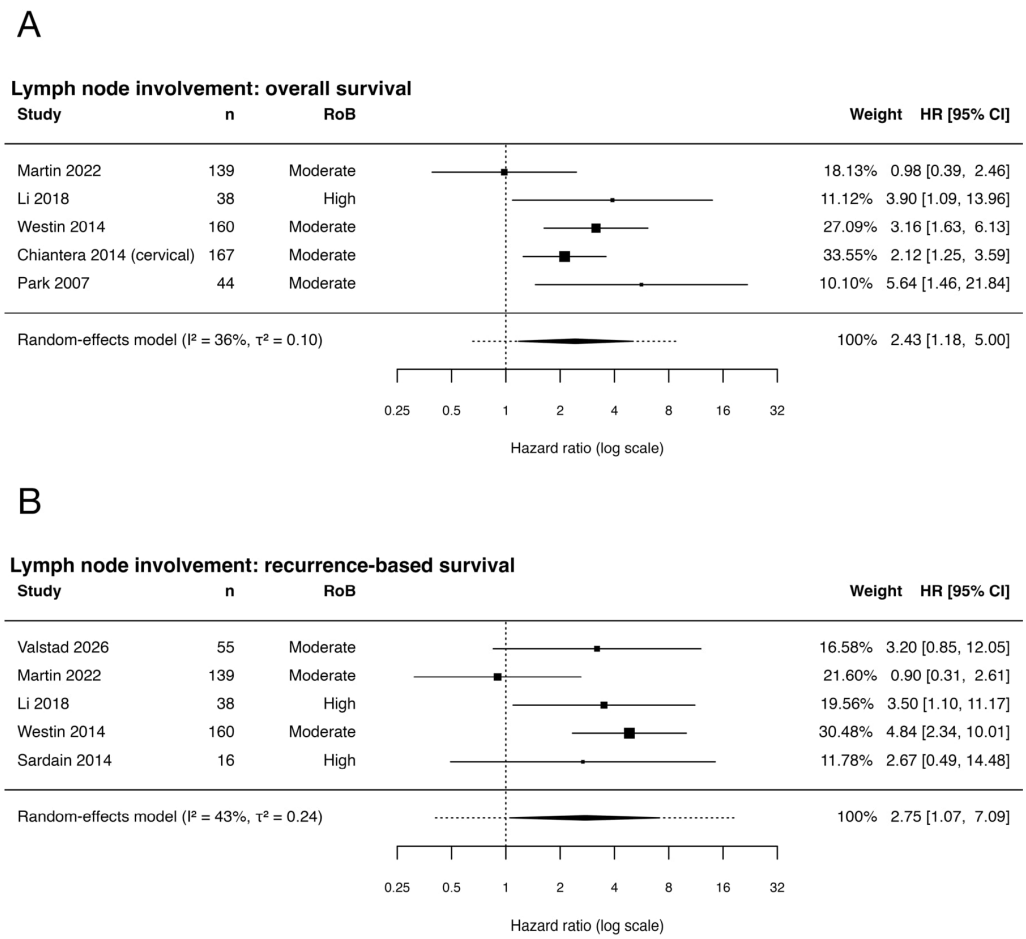


Figure 6. Lymph node involvement: pooled adjusted hazard ratios for (**A**) overall survival and (**B**) recurrence-based survival [31,34,35,37,45,48,50]. Random-effects meta-analysis (REML; Hartung–Knapp–Sidik–Jonkman 95% CI with ad hoc correction). Squares show study estimates sized by weight; diamonds show pooled estimates; dotted lines show 95% prediction intervals. *n*, cohort size; RoB, overall risk of bias (QUIPS); HR, hazard ratio; CI, confidence interval; τ^2, between-study variance.

3.6. Narrative Synthesis

Across all cohorts assessing the main factors, directions of effect were most consistent for margin status and local tumour extent. All twenty-two cohorts reporting a direction for margin status showed worse survival with positive margins, as did eighteen of twenty-two cohorts for lymph node involvement, and eight out of nine cohorts for LVSI (Figure 3). All cohorts reporting a direction showed worse survival with side-wall involvement and bladder or rectal invasion, although involvement was assessed clinically, radiologically, or pathologically in different studies. Larger tumour size was associated with worse survival in eleven out of twelve cohorts reporting a direction, with cut-offs ranging from 3 to 5 cm, and a shorter interval prior to exenteration in ten out of twelve cohorts, with varying definitions of this interval. Total exenteration was associated with worse survival in five of six cohorts while in one cohort posterior exenteration had the poorest outcome.

Distance for margin involvement was defined in five out of twenty-five cohorts [31,34,41,45,48], whilst the remaining studies did not specify a margin distance. Of the twenty-five cohorts that studied nodal involvement, twelve did not state which nodal site was analysed [3,31,35,37,40,42,43,45,47,49,58,59]. Only one study separated nodal involvement at primary presentation from nodal involvement at exenteration [50]. No study tested nodal involvement against side-wall involvement.

No consistent association was observed for age. Older age was associated with better survival in six cohorts and worse survival in four, with almost all estimates non-significant. Of the twenty reports that investigated age as a prognostic factor, eight of them did not specify whether the age at diagnosis or age at the time of surgery was used [33–35,40,43,58,66,67]. Albatross plots showed results for margin status and lymph node involvement clustering on the side of worse survival, while results for age were distributed around the null (Supplementary Materials S6).

Tumour size cut-offs varied with 3 cm in four studies [43,46,66,67], 4 cm in two studies [35,36], 5 cm in five studies [39,44,48,50,55], several cut-offs in Maggioni et al. [59], a continuous measure in Seebacher et al. [3], and the remaining three studies did not state a cut-off [40,49,65]. Measurement was based on the pathology specimen in six cohorts [3,39,43,44,46,48], and clinically in three studies [65–67]. The method was not reported in the remaining seven.

Comparisons between the types of exenteration differed between cohorts: four studies compared anterior, posterior, and total exenteration [30,47,48,63], two compared total with partial [35,36], and three compared total with anterior exenteration [39,60,67]. Five studies defined which organs each procedure removed [36,39,47,48,63] and their definitions differed; for example, total exenteration meant removal of the whole bladder and rectosigmoid in some studies but only part of the bladder and bowel in another [48,63]. Total exenteration was associated with poorer survival in the largest cohort [39], whereas posterior exenteration had the shortest time to recurrence in another [30].

For histological subtype, tumour grade, and stage, the direction of effect was reported by three or fewer cohorts each, precluding conclusions. Primary tumour site, previous treatment, and adjuvant treatment, for which no direction was hypothesised, showed no consistent association with survival.

3.7. Certainty of Evidence

Certainty of evidence was rated for thirty factor-outcome combinations across the sixteen main factors (Table 2, Supplementary Materials S5). Certainty was low for the association of positive margins with worse overall survival and recurrence-based survival, and for the association of LVSI with worse recurrence-based survival. It was very low for all other combinations. All ratings were downgraded for risk of bias, reflecting retrospective designs with moderate or high risk of bias and adjustment for data-driven covariates, and for indirectness as most cohorts combined different primary tumour sites and indications. Further downgrading was mainly for imprecision due to small samples, mostly non-significant results or absent effect estimates, and for inconsistency where directions of effect conflicted across cohorts, as for lymph node involvement, age, and type of exenteration. Publication bias could not be assessed formally, as fewer than ten studies contributed to each meta-analysis. No evidence was upgraded.

Table 2. Summary of findings: certainty of evidence (GRADE) for the main prognostic factors. Pooled estimates are from random-effects meta-analysis of adjusted hazard ratios (REML; Hartung–Knapp–Sidik–Jonkman 95% CI with ad hoc correction). HR > 1 indicates worse survival in the first-named category. Direction summaries count the cohorts reporting a direction for overall survival only, so they may differ from the counts in the text, which use one result per cohort across outcomes. Certainty was rated with GRADE for prognostic factors [12]: evidence started at high certainty and was rated down. Publication bias could not be assessed (fewer than 10 studies per analysis). Low certainty: the true association may be substantially different from the estimate. Very low certainty: the true association is likely to be substantially different. All other main factors (histological subtype, tumour grade, stage, complications, type of exenteration, primary site, previous treatment, adjuvant treatment), and the recurrence-based outcomes of the narrative factors, were rated very low (Supplementary Materials S5). OS, overall survival; RBS, recurrence-based survival; HR, hazard ratio; CI, confidence interval; LVSI, lymphovascular space invasion.

Factor	Outcome	Cohorts	Pooled HR (95% CI) or Direction Summary	95% Prediction Interval	Certainty	Reason for Downgrade
Positive vs. negative margin	OS	6 (1241)	1.96 (1.44–2.68)	1.40–2.75	Low	Risk of bias, indirectness
	RBS	6 (1129)	2.15 (1.40–3.31)	1.14–4.04	Low	Risk of bias, indirectness
Positive vs. negative nodes	OS	5 (548)	2.43 (1.18–5.00)	0.66–8.98	Very low	Risk of bias, inconsistency, indirectness, imprecision
	RBS	5 (408)	2.75 (1.07–7.09)	0.41–18.57	Very low	Risk of bias, indirectness, inconsistency, imprecision
LVSI present vs. absent	OS	3 (1024)	1.75 (0.99–3.09)	0.19–16.39	Very low	Risk of bias, indirectness, imprecision
	RBS	6 (1139)	1.68 (1.32–2.14)	1.30–2.18	Low	Risk of bias, indirectness
Side-wall involved vs. not	OS	8 (692)	6/6 worse, 5 significant	–	Very low	Risk of bias, indirectness, imprecision
Bladder/rectal invasion	OS	6 (360)	6/6 worse, 3 significant	–	Very low	Risk of bias, indirectness, imprecision
Shorter vs. longer interval	OS	12 (1496)	8/9 worse, 3 significant	–	Very low	Risk of bias, indirectness, imprecision
Larger vs. smaller tumour	OS	14 (1623)	9/10 worse, 4 significant	–	Very low	Risk of bias, indirectness, imprecision
Older vs. younger age	OS	16 (1800)	5 better, 2 worse, 2 mixed, 1 significant	–	Very low	Risk of bias, inconsistency, indirectness, imprecision

4. Discussion

4.1. Summary of the Main Results

This review synthesised prognostic factors for survival following pelvic exenteration for recurrent gynaecological malignancies from 37 studies.

Margin positivity was associated with about twice the hazard of death and recurrence, and, although certainty was low, this result was unchanged in sensitivity analyses. Margin status was the most consistent factor, but margin distance was poorly characterised. Margin distance could help guide adjuvant treatment as explored with postoperative stereotactic radiotherapy [41], but the optimal threshold could not be derived from the existing studies.

Lymph node involvement was associated with worse overall and recurrence-based survival, but both prediction intervals were wide and the association was not robust in several sensitivity analyses. Nodal disease was analysed as present versus absent or by anatomical site, and no study analysed the number of involved nodes, their size, isolated tumour cells, or extranodal extension. Grouping different nodal sites into one variable may have diluted a true effect and may partly explain the wide prediction intervals.

LVSI was associated with worse survival in eight of nine cohorts and with worse recurrence-based survival in the pooled analysis, consistent with primary cervical and endometrial cancer cohorts [68,69], whereas evidence for perineural invasion was weaker and not consistent across studies. Both factors are known only after surgery, so they are more relevant to counselling after surgery than to selecting patients for exenteration.

Side-wall involvement, bladder or rectal invasion, and larger tumour size were associated with worse survival in all or almost all cohorts that reported a direction, although most estimates were imprecise and definitions and methods of assessment (clinical, radiological, or pathological) varied. Tumour size showed a consistent direction but few significant results, which may reflect inconsistent cut-offs and measurement methods and the limits of a single diameter in recurrent disease. After chemoradiotherapy and previous surgery, the tumour can be hard to separate from the fibrotic tissue on imaging, and recurrence may not form a single measurable mass; therefore, the extent of local spread may matter more than the size alone [53,55].

Despite varying definitions, a longer interval before exenteration was associated with better survival in ten of twelve cohorts that reported a direction, although only three results were statistically significant. This is consistent with the earlier reports and with the view that later recurrences reflect more indolent disease [55,70].

Age, which is prognostic in primary cervical cancer [68], showed no consistent association in this analysis, in line with the recent meta-analysis by Di Donato et al. [4]. One possible explanation is that patient selection for this procedure favours a fitter cohort and weakens any effect of age.

Type of exenteration showed no consistent pattern as a prognostic factor. This may reflect the different categories used and the lack of consistency and transparency of procedure definitions between units. Standardised terminology, such as the lexicon proposed by the UK Pelvic Exenteration Network, would make results comparable across centres [71].

4.2. Results in the Context of Wider Literature

The only previous quantitative synthesis, a meta-regression by Di Donato et al., included 46 studies (4417 patients) and used study-level Poisson regression to relate cohort characteristics to 5-year overall survival and 30-day mortality [4]. Consistent with our findings, that analysis identified pelvic and aortic nodal involvement and pelvic wall involvement as predictors of reduced 5-year survival, although pelvic wall involvement and aortic nodal data were available for eight and five of forty-six included cohorts, respectively. In contrast, the proportion of patients with positive margins was not significantly associated with survival (incidence rate ratio (IRR) 0.971, 95% CI 0.924–1.020, $p = 0.25$), and margin data were missing for over half of the cohorts. This difference probably reflects how the data were analysed. Di Donato et al. compared studies with each other and assessed whether studies with a higher percentage of positive margins had lower overall survival. That approach can miss or blur what happens to individual patients, because each study's patients differ in many other ways too. The present review instead pooled each study's own comparison of patients with and without positive margins, which reflects the effect more directly. Di Donato et al. also found no association between mean or median age and survival, in keeping with our results. Their cohorts combined locally advanced and recurrent disease, and study quality was assessed

with a custom score based on design, sample size, and centre volume rather than a validated risk-of-bias tool, which limits direct comparison.

A recent meta-analysis of 132 studies (13,434 women) summarised outcomes after pelvic exenteration for gynaecological cancers over six decades [72]. It described outcomes across cohorts, whereas the present review examined which factors were associated with survival within cohorts. Our findings formalise several conclusions of recent narrative reviews. Ubinha et al. argued that age should not be used in isolation to select patients, that the prognostic impact of the disease-free interval is not well established, and that negative margins are one of the main determinants of survival [6]. They also questioned the true impact of tumour size, suggesting that margin status may be the real determinant of outcome. The present review supports these observations with systematically assessed risk of bias and certainty of evidence: margin status had the most robust pooled evidence, whereas the evidence for tumour size and interval to recurrence was consistent in direction but imprecise and heterogeneously defined.

4.3. Clinical Implications

Positive margins had the most consistent association with worse survival. Adjustment sets differed between studies, and not all included local tumour extent, so this association may partly reflect more extensive disease. These results support careful preoperative assessment of local extent, including high-quality imaging, to judge whether complete resection is likely. Side-wall involvement, bladder or rectal invasion, and larger tumour size were also associated with worse survival in most cohorts, and these features are likely to reduce the chance of clear margins. Because the procedure carries substantial morbidity, with complication rates of 30–100% reported, and a lasting impact on quality of life, as summarised in a recent systematic review of 23 studies and 1655 patients, counselling should weigh the limited certainty of the prognostic evidence against the expected burden of surgery [1,2,6,73,74]. Positive margins, nodal involvement, and LVSI may help identify patients at higher risk of relapse, but whether closer follow-up or adjuvant treatment benefits these patients needs to be tested in prospective studies.

4.4. Strengths

This is, to our knowledge, the first review of prognostic factors after pelvic exenteration for recurrent gynaecological cancer to follow established prognostic factor methodology [10,14]. Multiple reports of the same or overlapping cohorts were linked so that each cohort contributed once. Only adjusted estimates were pooled in the main analysis, and meta-analyses used the Hartung–Knapp–Sidik–Jonkman method with an ad hoc correction and prediction intervals, appropriate for few studies. Risk of bias was assessed with QUIPS using explicit criteria, certainty was graded with GRADE for prognostic factors, and results that could not be pooled were synthesised by direction of effect rather than statistical significance, in line with SWiM. Data extraction and risk-of-bias assessment were checked by a second reviewer, and the pooled results were tested in several sensitivity analyses. All factors reported in the included studies were captured, whereas previous syntheses were restricted to a few study-level characteristics.

4.5. Limitations

The findings should be interpreted in light of the underlying evidence. Most included studies were retrospective single-centre series with modest sample sizes, and all were at moderate or high risk of bias, mainly because of unadjusted or data-driven analyses and incomplete reporting of effect estimates. Cohorts frequently combined different primary tumour sites and, in some cases, primary or persistent disease (Supplementary Table S10).

Definitions of key factors such as margin status, nodal involvement, and side-wall involvement varied between studies. Recurrence-based outcomes were not defined in eight of twenty-two studies, and the same label described different events in different studies (Supplementary Table S9). We addressed this by harmonising the direction of effect to a standard comparison, grouping recurrence-based outcomes, and pooling only adjusted estimates, and these sources of heterogeneity were reflected in the certainty ratings.

Comparable adjusted estimates were available for only three factors, each from three to six cohorts, which limits the precision of the pooled estimates and of heterogeneity measures, and precluded formal assessment of small-study effects. The adjusted models included different variables, often selected by statistical significance, so the pooled estimates were not adjusted for the same confounders (Supplementary Table S8). Selective reporting is possible, as several studies reported only statistically significant factors or described non-significant results without data. Overlap between cohorts from the same institutions could not always be confirmed from published reports; overlapping reports were linked and alternative reports substituted in sensitivity analyses. A review protocol was not registered due to the exploratory nature of the review. Decisions made during screening and after data extraction, and whether each could have affected the findings, are listed in Supplementary Table S11. Reports not in English were excluded (61 records), although language restrictions rarely change the conclusions of meta-analyses [16,17]. The included studies span several decades, over which imaging, surgical technique, and perioperative care have changed, and survival was the only outcome considered.

4.6. Future Research

Across included studies, adjunctive therapies including intraoperative and postoperative radiotherapy, chemotherapy, targeted agents, and immunotherapy were applied, though their use reflected institutional practice rather than standardised protocols, limiting the interpretability of survival outcomes attributable to surgery alone [41–44,52,61,75,76]. Notably, only one small study assessed molecular markers (p16 and p53) and found no association between them and survival outcomes [42]. This is an important gap given that contemporary guidelines now recommend biomarker-led pathways in recurrent gynaecological cancer, and immunotherapy has demonstrated meaningful survival gains in molecularly defined subgroups [77,78]. The prognostic landscape described in this review therefore reflects an era in which tumour biology was inferred from histopathology and anatomical extent rather than molecular characterisation. As treatment becomes increasingly personalised and tumour behaviour better characterised at a molecular level, the relative importance of these traditional markers may evolve, underscoring the need for prospective, standardised datasets from high-volume centres that reflect current multimodal practice.

Future studies should adopt standardised definitions and reporting of prognostic factors and outcomes, in line with ongoing efforts to establish core datasets for pelvic exenteration [79]. Multicentre collaborations and prospective registries would allow adequately powered analyses with pre-specified adjustment for key confounders, and all examined factors should be reported with effect estimates and confidence intervals, regardless of statistical significance. Consistent reporting of margin distance, nodal site, and the method of assessing side-wall involvement would be particularly valuable. Individual participant data meta-analysis across existing cohorts could overcome many of the limitations of aggregate data, and prognostic scores derived from recent multicentre cohorts require external validation before routine use. Survival outcomes should be integrated with morbidity and patient-reported quality of life to support shared decision-making. Other factors also need study. Circulating HPV tumour DNA after chemoradiation is associated with recurrence in cervical cancer but has not been studied around exenteration [80,81]. Higher centre volume has been linked with lower perioperative

mortality after exenteration, but its effect on survival is unclear [82,83], and socioeconomic factors were not examined in the included studies.

5. Conclusions

This is the first systematic review and meta-analysis of prognostic factors for survival after pelvic exenteration for recurrent gynaecological malignancies to use established prognostic factor methodology, and the most comprehensive in the range of factors assessed. Positive margins were associated with about twice the hazard of death and recurrence, and LVSI with worse recurrence-based survival, although certainty was low. Lymph node involvement was also associated with worse survival, but this finding was less certain. Side-wall involvement, bladder or rectal invasion, and a shorter interval before exenteration were associated with poorer survival in most cohorts and may help inform case selection. After surgery, positive margins, nodal involvement, and LVSI may help identify patients at higher risk of relapse, in whom follow-up and adjuvant treatment should be studied prospectively. The evidence remains small, retrospective, and inconsistently reported. Standardised definitions across operative, radiology, and pathology reports, and prospective data pooled across high-volume centres, are needed to validate these factors and build prognostic models.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/cancers18233791/s1. S1: Search strategy; S2: PRISMA 2020 and PRISMA 2020 for Abstracts checklists; S3: Results for each cohort for the 16 main prognostic factors; S4: Results for each cohort for the remaining 42 prognostic factors; S5: GRADE evidence profile for the main prognostic factors; S6: Albatross plots for factors with a hypothesised direction; S7: Sensitivity analyses; S8: Adjustment variables for each pooled estimate; S9: Definitions of recurrence-based outcomes; S10: Populations of the pooled cohorts; S11: Methodological decisions and their timing.

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Conflicts of Interest: D.P.J.B., O.M.H. and A.T. are co-authors of one included study (Gomes et al.) and D.P.J.B. of another (Seebacher et al.). Risk of bias for these studies was assessed by S.S., R.C. and A.S. The authors declare no other conflicts of interest. The funders had no role in the design, analysis, or writing of this review.

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