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Patterns of residual parametrial involvement and pelvic nodal metastasis at completion surgery after simple hysterectomy for occult cervical cancer: protocol for a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 July 2026 and was last updated on 31 July 2026.

INTRODUCTION

Review question / Objective Among women with invasive cervical carcinoma discovered incidentally in a simple or extrafascial hysterectomy specimen (P), in whom completion radical parametrectomy with or without pelvic lymphadenectomy is performed (I), with no external comparator arm (C), what is the pooled proportion of histologically confirmed parametrial soft-tissue involvement and the pooled proportion of pelvic nodal metastasis, and how are these two findings distributed jointly within the same individual patients (O)? Observational studies (S).

The principal objective is not merely to estimate two pathological event rates, but to determine whether residual parametrial disease and pelvic nodal metastasis follow different pathological patterns and are therefore better treated as complementary pathological questions than as a single composite residual-disease endpoint. A secondary objective is to place those estimates within current surgical de-escalation, staging, imaging, and nodal-assessment practice.

Rationale Occult invasive cervical cancer diagnosed after simple hysterectomy creates a management problem after the primary tumour has already been removed. Current options include observation, radiotherapy-based treatment, nodal assessment, and completion radical parametrectomy. The value of each option depends on which disease process is still likely to be present.

Completion surgery is not a single pathological test. Parametrectomy evaluates residual parametrial involvement; nodal surgery evaluates regional metastatic spread. Although related, the two components arise through different anatomical pathways, carry different staging consequences, and may not decline in parallel as patient selection improves. Contemporary classification already reflects this separation: FIGO 2018 assigns nodal metastasis an independent stage-defining role, and the ICCR cervical dataset records parametrial and regional nodal status as separate core elements. Post-hysterectomy series, however, have often been interpreted through overall

residual-disease or treatment-yield endpoints, which can conceal the frequency and clinical meaning of each pathological finding.
Surgical de-escalation trials (SHAPE, ConCerv) have shown that less-radical local surgery can be used in prospectively selected low-risk disease, but they did not include women whose diagnosis was made only after hysterectomy. In this population, risk must be reconstructed from the hysterectomy specimen, previous cervical pathology, conisation findings, expert pathological review, and postoperative imaging.
The available evidence also spans several decades during which imaging, pathological review, nodal assessment, surgical technique, and patient selection changed substantially, so historical pooled estimates require calibration rather than direct transfer to contemporary practice. A synthesis that keeps the two pathological components separate, and that additionally reconstructs their joint within-patient distribution, is therefore needed.

Condition being studied Occult (inadvertently diagnosed) invasive carcinoma of the uterine cervix: invasive cervical cancer identified only on histopathological examination of a simple or extrafascial hysterectomy specimen removed for a benign or presumed pre-invasive indication. Because the operation was not planned as an oncological procedure, the parametria, the pelvic lymph nodes, and the upper vagina are not assessed, and preoperative staging is incomplete by definition. The clinical problem is the residual risk in two anatomically and biologically separate compartments after the primary tumour has already been removed: residual parametrial soft-tissue extension, and pelvic lymph node metastasis. Management options range from observation, through surgical nodal assessment and completion radical parametrectomy, to radiotherapy-based treatment.

METHODS

Search strategy Occult (inadvertently diagnosed) invasive carcinoma of the uterine cervix: invasive cervical cancer identified only on histopathological examination of a simple or extrafascial hysterectomy specimen removed for a benign or presumed pre-invasive indication. Because the operation was not planned as an oncological procedure, the parametria, the pelvic lymph nodes, and the upper vagina are not assessed, and preoperative staging is incomplete by definition. The clinical problem is the residual risk in two anatomically and biologically separate compartments after the primary tumour has already been removed: residual parametrial soft-tissue extension, and pelvic lymph node metastasis. Management options range from observation, through surgical nodal assessment and completion radical parametrectomy, to radiotherapy-based treatment.

Participant or population Women of any age with histologically confirmed invasive carcinoma of the uterine cervix discovered incidentally in a simple or extrafascial hysterectomy specimen removed for a benign or presumed pre-invasive indication. Studies of planned simple hysterectomy for micro-invasive disease, cervical stump carcinoma, and endometrial or ovarian primaries are not eligible.

Intervention Completion radical parametrectomy, with or without upper vaginectomy and with or without pelvic and/or para-aortic lymphadenectomy, performed after the index simple or extrafascial hysterectomy. At least one patient in the study must have undergone completion radical parametrectomy.

Comparator No external comparator arm. The included studies are non-randomised single-arm surgical series, and the synthesis is a meta-analysis of proportions. The planned internal comparison is the paired within-patient contrast between the two pathological outcomes: parametrial involvement versus pelvic nodal metastasis in the same patients. Non-surgical, observation-only, and mixed cohorts without separable post-hysterectomy data are retained as contextual data only and are not pooled.

Study designs to be included Observational studies of any design reporting completion radical parametrectomy after simple or extrafascial hysterectomy for occult invasive cervical carcinoma: retrospective or prospective case series and cohort studies with extractable patient-level counts. Randomised trials were eligible but none were identified. Excluded: narrative reviews, editorials, abstracts without extractable denominators, non-surgical or observation-only cohorts, and mixed cohorts in which the occult post-hysterectomy subgroup could not be separated with outcome denominators.

Eligibility criteria Include: original observational studies reporting completion radical parametrectomy for occult invasive cervical carcinoma discovered in a simple or extrafascial hysterectomy specimen; at least one patient undergoing completion radical parametrectomy; an extractable pathological denominator for

parametrial involvement, pelvic nodal metastasis, or both.
Exclude: studies without any completion radical parametrectomy; cohorts managed non-surgically or by observation only (retained as context); mixed cohorts in which the occult cervical subgroup cannot be isolated with outcome denominators; secondary or pooled tables reproduced within review articles, since extraction is from primary full texts only; duplicate publications of the same cases.
Overlap handling: when multiple reports cover the same institutional cohort, only the most complete primary record is retained; all overlap adjudications are catalogued in the decision log.
Outcome coding: parametrial involvement is recorded as an event only where the original report contains an explicit parametrial statement or an exhaustive patient-level enumeration of residual findings; otherwise it is coded "not reported", excluded from the parametrial pool, and not counted as negative. Parametrial and nodal pools therefore have independent study eligibility and independent denominators.

Information sources Electronic databases: PubMed/MEDLINE, Embase (Ovid), Scopus, Web of Science Core Collection, searched from inception to 20 July 2026. Grey and supplementary sources: Google Scholar (first 300 relevance-sorted records per focused query); backward and forward citation searching of all included studies; ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform; and conference abstract books of ESGO, IGCS, and SGO for 2016-2026. Non-English full texts were pursued through inter-library loan; those that could not be retrieved are reported in the flow diagram rather than excluded silently. Screening was performed in Rayyan QCRI in blinded mode by two independent reviewers.

Main outcome(s) Pooled proportion of histologically confirmed parametrial soft-tissue involvement in the completion radical parametrectomy specimen, expressed as a specimen-positivity rate in the selected surgical group, not a population prevalence.
Pooled proportion of pelvic lymph node metastasis in the same population, analysed in a separate pool with its own outcome-specific denominator.
The joint within-patient distribution of the two findings across four mutually exclusive states, parametrium only, nodes only, both, neither, reconstructed from source reports, and the resulting paired contrast expressed as a matched odds ratio of nodal-only to parametrial-only discordant pairs.
No timing restriction is applied; all outcomes are pathological findings at the completion procedure.

Additional outcome(s) Organ-specific perioperative morbidity of completion surgery, extracted per organ and per study: bladder injury, ureteric injury, bowel injury, vascular injury, vesicovaginal or ureterovaginal fistula, symptomatic lymphocele, reoperation, and perioperative transfusion. Organ-specific denominators differ across endpoints because numerators are pooled only over series that report that endpoint. Composite any-complication and major-complication pooling is deferred pending independent dual-reviewer re-extraction and endpoint lock.
Descriptive study-level characteristics: recruitment era, FIGO stage, patient-selection criteria, pathology re-review, perioperative imaging protocol, and surgical approach.

Data management Records are de-duplicated and screened independently and in duplicate by two reviewers using Rayyan QCRI in blinded mode, with disagreements resolved by consensus discussion and inter-reviewer agreement reported as observed agreement and Cohen's kappa at both title/abstract and full-text stages. Data are extracted from primary full texts only into a structured extraction workbook; pooled summary tables reproduced within review articles are not used, to avoid double-counting. Organ-specific morbidity is extracted into a separate locked organ-by-study table by both reviewers independently. The dataset is frozen at extraction lock (workbook v1.5, 28 July 2026); no study, outcome definition, or extraction field is added after lock. The extraction-locked workbook, analysis scripts, protocol, search strategies, eligibility framework, statistical and sensitivity analysis plans, PRISMA 2020 checklist, and decision log are deposited as a version-controlled research compendium at Zenodo, doi:10.5281/zenodo.21532732.

Quality assessment / Risk of bias analysis Methodological quality is appraised independently and in duplicate with the Joanna Briggs Institute critical-appraisal checklist for case series (ten items). In line with current JBI guidance, no composite numerical score is calculated; each item receives a judgement of Yes, No, or Unclear. Each study is then assigned an overall concern band (low, moderate, or high) and an outcome-specific concern reflecting the main limitation affecting parametrial estimation: inadequate denominator, earlier pathology or imaging conventions, or small technique-series size. Disagreements are resolved

by discussion. Item-level appraisal for every included study, with both reviewers' ratings, is reported in the supplementary material.
Certainty of evidence is rated with the GRADE approach, applied separately to pooled parametrial involvement, pooled nodal metastasis, and the paired within-cohort contrast. Each outcome starts at Low certainty because all included studies are observational case series; risk of bias, inconsistency, indirectness, and imprecision are assessed for downgrading. Funnel-plot testing and formal small-study-effect assessment are not performed where pools contain fewer than ten studies, sparse events, or a narrow range of series sizes; publication bias is then reported as unassessed.

Strategy of data synthesis The primary analysis is a random-effects meta-analysis of proportions using a binomial-normal generalised linear mixed model on the logit scale, applied separately to the parametrial and nodal outcomes, each with its own outcome-specific denominator and independent study eligibility. Marginal likelihood is evaluated by adaptive Gauss-Hermite quadrature and profile-likelihood 95% confidence intervals are used. No continuity correction and no Freeman-Tukey transformation is applied. Study-level intervals are exact Clopper-Pearson intervals. Between-study heterogeneity is summarised by tau-squared on the logit scale, and prediction intervals are reported for heterogeneous pools and are not interpreted as treatment thresholds.
Because the two outcomes are paired within study, a Bayesian mixed-effects logistic model with a shared study-level random intercept and a fixed effect for outcome type is fitted as a robustness analysis and interpreted alongside, rather than in place of, the primary frequentist estimates. A separate Bayesian model with weakly informative priors is fitted for the sparse parametrial pool. Posterior distributions are obtained by Markov chain Monte Carlo; convergence requires stable traces, split R-hat below 1.01, and adequate effective sample sizes. Posterior summaries are medians and 95% credible intervals.
Patient-level joint cells are reconstructed only when the source report attributes all parametrial and nodal events to named or mutually exclusive patients, or when a zero marginal count uniquely determines the joint table; treatment indication alone is not sufficient unless the reporting is exhaustive. Unresolved overlap is reported as admissible bounds rather than imputed. From the resulting patient-level table, a matched odds ratio is calculated as the ratio of nodal-only to parametrial-only discordant pairs, with an exact McNemar two-sided p-value and a conditional exact 95% confidence interval. A within-cohort pooled risk difference is not estimated because double-zero series would dominate inverse-variance weighting.

Subgroup analysis Recruitment era. Studies are grouped by recruitment end date with a cut-off at 2005: series whose recruitment ended before 2005 form the pre-2005 recruitment stratum, and those ending in 2005 or later form the 2005-onwards stratum. The boundary is a practical separation of the available evidence, not a claim of a discrete point of clinical change. Given the small number of contributing studies and sparse events, no formal interaction testing across strata is undertaken and the comparison is reported descriptively.

Sensitivity analysis Planned sensitivity analyses: (i) inclusion versus exclusion of the two small technical case series; (ii) alternative classification of a single in-situ parametrial focus; (iii) exclusion of the outlying series identified as influential; and (iv) leave-one-study-out influence analysis with a Baujat plot. Additional analyses: the broadest pool including all eligible series; and a target-population restriction to strictly early-stage series confined to FIGO IA-IB1 by eligibility, adjudicated after extraction lock and reported as post hoc in the decision log, with an intermediate analysis omitting only the single broadest-stage series. For organ-specific morbidity, a sensitivity pool adding the nodal-only and pre-2005 series is examined. Bayesian models are additionally used as robustness analyses for both the sparse parametrial pool and the paired contrast.

Language restriction No language restriction at the electronic search stage. Eligible for synthesis if an English full text or sufficient English-language patient-level data could be obtained.

Country(ies) involved Turkey.

Other relevant information The full protocol, eligibility framework, search strategies, extraction templates, statistical analysis plan, sensitivity analysis plan, PRISMA 2020 checklist, decision log, extraction-locked workbook (v1.5, locked 28 July 2026), and analysis scripts are publicly archived as a version-controlled research compendium at Zenodo, doi:10.5281/zenodo.21532732, enabling independent reproduction of every pooled estimate and figure.
No unpublished individual participant data were obtained; all patient-level data used in matched analyses were reconstructed from published aggregated tables.

The manuscript is being prepared for submission to a peer-reviewed international gynecologic oncology journal.

Keywords cervical cancer; occult cervical cancer; simple hysterectomy; radical parametrectomy; parametrial involvement; lymph node metastasis; risk stratification; meta-analysis.

Dissemination plans Publication as an Original Article in a peer-reviewed international gynecologic oncology journal. Presentation at an international gynecologic oncology congress. Permanent open deposition of the extraction-locked workbook, analysis scripts, and full study documentation as a version-controlled research compendium at Zenodo, doi:10.5281/zenodo.21532732, enabling independent reproduction of every pooled estimate and figure.

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