

## INPLASY

## Microbiome measurement and microbiome-directed intervention in the treatment of gynecologic cancer: a scoping review

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**ADMINISTRATIVE INFORMATION****Support** - No specific funding.

**Review Stage at time of this submission** - Completed but not published. Searches, study selection, data charting and descriptive synthesis were completed before registration. The manuscript is being prepared for journal submission.

**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2026100047

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 October 2026 and was last updated on 10 October 2026.

**INTRODUCTION**

**Review question / Objective** What microbial measurements and microbiome-directed interventions have been investigated in patients with invasive gynecologic cancer, and how do their reported findings relate to cancer treatment, treatment-related toxicity and survivorship?

The population comprises patients with cervical, endometrial or uterine, ovarian, fallopian tube, primary peritoneal, vulvar or vaginal cancer, including eligible patients within mixed-cancer cohorts. The concept comprises bacterial or fungal measurements in human samples and interventions directed at the microbiota. The context extends from diagnosis through treatment and survivorship.

The objectives are to map the available and planned research; describe specimen compartments, assays, sampling times, interventions and clinical endpoints; examine recurring and divergent clinical findings; and distinguish discovery associations, validation studies, microbial changes and demonstrated clinical effects.

**Background** Gynecologic cancer treatment exposes the gut, lower genital tract and tumour microenvironment to different effects of surgery, radiotherapy and systemic therapy. Microbial communities may change during treatment, and studies have investigated their associations with toxicity, treatment response and survival. A parallel literature evaluates probiotics and other interventions intended to modify the microbiota.

These approaches address related but distinct clinical questions. A microbial association does not

establish treatment benefit, and a change in microbial composition does not necessarily improve a patient-relevant outcome. Findings may also depend on the sampled compartment, measurement timing, treatment regimen and endpoint.

Existing reviews have addressed narrower topics, including probiotics, treatment-related diarrhoea and microbial changes during pelvic radiotherapy. A scoping review can bring measurement and intervention studies together across gynecologic cancer sites while retaining the clinical and methodological differences that affect interpretation.

**Rationale** The literature contains observational measurements, microbial-marker development studies, intervention trials and registrations without reported results. Considering these sources together can clarify which clinical questions have been studied, which measurements have actually been reported and where research remains planned.

The review connects microbial measurement with microbiome-directed intervention across the gynecologic cancer treatment pathway. It distinguishes specimen compartments and sampling times, primary and secondary outcomes, microbial and clinical effects, and discovery findings from external validation. This approach supports a clinically interpretable account of the evidence without assuming that heterogeneous microbial signatures or intervention products are interchangeable.

A scoping design was selected to map this breadth of evidence and identify gaps in measurement, validation and clinical evaluation. The review was not designed to estimate a pooled treatment effect.

## METHODS

**Strategy of data synthesis** Six sources were searched on 8 October 2026: PubMed, Europe PMC, Scopus, Web of Science Core Collection, the Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov. Searches had no date, language or publication-type restrictions.

The bibliographic strategies combined three concept blocks with AND: gynecologic malignancy; microbial measurement or microbiome-directed intervention; and cancer treatment or treatment-related clinical outcomes. Synonyms within each block were combined with

OR. Controlled vocabulary and free-text terms were adapted to each source.

Population terms covered cervical, endometrial, uterine, ovarian, fallopian tube, primary peritoneal, vulvar, vaginal and gynecologic malignancies, together with pelvic cancer and pelvic radiotherapy. Microbial terms included microbiome, microbiota, microflora, mycobiome, dysbiosis, metagenomics, probiotics, prebiotics, synbiotics, *Lactobacillus*, *Bifidobacterium*, *Fusobacterium*, 16S, microbial communities, faecal microbiota transplantation and relevant dietary products. Treatment and outcome terms covered radiotherapy, chemoradiotherapy, brachytherapy, chemotherapy, immunotherapy, treatment response, resistance, recurrence, survival, toxicity, gastrointestinal symptoms and quality of life.

CENTRAL and ClinicalTrials.gov used the population and microbial concept blocks without requiring a treatment-outcome block. The PubMed strategy excluded animal-only records. Complete source-specific Boolean strategies, search dates and yields are retained in the search documentation.

Reference lists of nine earlier reviews were screened as an additional identification route. Synthesis used linked studies as the unit of analysis and combined descriptive counts and proportions with narrative comparison of source-reported clinical findings. Reports without results were presented separately from studies reporting findings. No pooled efficacy estimate was calculated.

**Eligibility criteria** Population: Patients with invasive cancer of the cervix, endometrium or uterine corpus, including uterine sarcoma; ovary, fallopian tube or primary peritoneum; vulva; or vagina. Patients could be at any point from diagnosis to survivorship. Mixed-cancer cohorts were eligible when they included patients with gynecologic cancer.

Concept: Bacterial or fungal measurements in human samples from any anatomical compartment, including culture, 16S rRNA sequencing, shotgun metagenomics, metatranscriptomics, quantitative polymerase chain reaction, fluorescence in situ hybridisation, immunohistochemistry, Gram stain or Nugent scoring. A microbiome-directed intervention qualified independently of whether microbial measurements were reported. Other interventions qualified when they measured the microbiome as an outcome.

Eligible intervention classes included probiotics, prebiotics, synbiotics, postbiotics, fermented products, faecal microbiota transplantation, vaginal lactobacilli and microbiota-directed dietary interventions. Purified microbial metabolites and bacterial agents directed at targets other than the microbiota, such as bacterial-vector vaccines, heat-killed bacterial immunotherapy, bacterial toxins or engineered drug carriers, were excluded.

Context: A clinical link to treatment response or resistance, recurrence, progression, survival or prognosis, toxicity, symptoms, quality of life, treatment-induced change or survivorship sequelae was required.

Evidence sources: Original human studies, including randomised trials, observational studies, case reports and secondary analyses of public datasets, were eligible. Trial registrations, protocols, preprints and conference abstracts were also eligible; their reporting status was retained.

Exclusion required a clearly unmet eligibility criterion supported by the available source. Missing information alone was not treated as proof of ineligibility. Unresolved eligibility criteria and limitations of source access were recorded, and a sensitivity analysis was restricted to studies with an eligibility-confirming report.

**Source of evidence screening and selection**  
Serhat Şen and Feyza Gülgel Şen independently screened records, assessed eligibility and charted data. Records advanced when either reviewer recommended inclusion or expressed uncertainty.

Eligibility was assessed against the written population, concept and context criteria. The reviewers compared discordant decisions with the source reports and resolved disagreements by discussion. No third reviewer was involved.

Exclusion reasons and supporting source passages were recorded. Reports with incomplete information were flagged rather than excluded solely because an abstract or truncated source omitted a required detail. Companion reports were considered together when they provided additional information about the same study.

Reference-list screening was recorded as a separate identification route. The selection process is reported using a PRISMA flow diagram, with database and register records, additional sources, reports sought, reports assessed and reasons for exclusion distinguished.

**Data management** Records were organised using stable record and study identifiers. Duplicate assessment used DOI, PubMed or registry identifiers, normalised titles and title similarity. Candidate links involving conflicting DOI or PubMed identifiers were retained for inspection rather than merged.

Data charting used one row per report. Fields included study design, country, cancer site, treatment setting, sample size, specimen compartment, assay, sampling time, clinical question, outcome definition, reported estimates, adjustment variables, intervention details, primary endpoint, trial status and validation stage.

Source-reported values and supporting passages were retained. Unreported and non-applicable items were distinguished. Discordant entries and subsequent corrections were documented with their reasons.

Reports were linked at study level using identifiers, titles, explicit companion-report links and cohort descriptions. A shared registration identifier alone was insufficient to combine distinct recruitment cohorts. Search logs, screening decisions, eligibility records, charting tables and correction records are retained as supporting materials.

**Reporting results / Analysis of the evidence**  
Synthesis was descriptive, using studies as the unit of analysis. Counts and proportions describe cancer sites, treatment settings, specimen compartments, assays, sampling times, clinical questions, intervention classes and reporting status. Studies with results were distinguished from registrations and protocols without results.

Microbial measurement status distinguished reported findings, specified measurement without reported findings, no measurement described and uncertainty. Marker development was described as discovery, internal validation, external validation or prospective clinical utility; these categories were not treated as quality ratings.

Clinical synthesis compared source-reported findings while retaining differences in compartment, timing, comparator, endpoint and analysis population. Primary outcomes were distinguished from secondary analyses, and microbial changes from clinical effects. Effect estimates and uncertainty were presented as reported by the source studies.

No formal risk-of-bias assessment or meta-analysis was performed. Study distributions were

also examined in a sensitivity analysis restricted to studies with an eligibility-confirming report.

**Presentation of the results** Results are presented in a PRISMA flow diagram, an evidence map, three main tables and a narrative clinical synthesis.

Table 1 summarises study characteristics. Table 2 presents selected microbial-measurement studies with their populations, compartments, timing, clinical findings and interpretative limitations. Table 3 presents selected randomised intervention studies, distinguishing comparators, primary and secondary outcomes, favourable findings and null results.

The evidence map displays research coverage across specimen compartments, cancer sites, clinical questions, intervention classes and publication periods. Its counts do not represent effect size or certainty of evidence.

Supplementary materials provide the PRISMA-ScR checklist, definitions, citations for all included reports and full study distributions. Supporting records include Boolean search strategies, search and screening logs, eligibility decisions, report- and study-level charting, sensitivity results and table and figure source data.

**Language restriction** No language limits were applied to searches. Fourteen Chinese-language reports were excluded before retrieval because their full texts could not be obtained.

**Country(ies) involved** Turkey.

**Other relevant information** This is a retrospective registration of a completed, unpublished scoping review. Searches were conducted on 8 October 2026, and screening, eligibility assessment, data charting and descriptive synthesis preceded registration. The review includes 250 reports representing 220 studies.

No protocol was registered or publicly available before the review. This record documents the methods used and the stage reached at registration. The review follows Joanna Briggs Institute guidance and is reported according to PRISMA-ScR, with PRISMA-S search documentation.

**Keywords** Gynecologic cancer; microbiome; microbiota; probiotics; radiotherapy; toxicity; biomarkers; scoping review; evidence map.

**Dissemination plans** The completed review will be submitted to BMC Cancer. Reporting will include the main manuscript, clinical tables, a PRISMA flow diagram, an evidence map and supplementary materials.

Boolean search strategies, screening and eligibility logs, charted datasets and figure source data will be deposited in Zenodo. The registration record and repository identifiers will be linked to the final publication when available.

#### Contributions of each author

Author 1 - serhat sen - Conceived the review, defined its scope and eligibility rules, developed the searches and synthesis approach, independently screened and charted data, resolved discrepancies, interpreted the findings and drafted the manuscript.

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Author 2 - Feyza Gulgel Sen - Contributed to eligibility criteria and charting fields, independently screened and charted data, resolved discrepancies, reviewed the dataset and figures, contributed to interpretation and critically revised the manuscript.

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