The Cost-effectiveness of Immunotherapies for Advanced or Recurrent Endometrial Cancer: A Systematic Review

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SUMMARY

OBJECTIVES

- Endometrial cancer is the sixth most common cancer in women worldwide. Limited healthcare resources and high cost of immunotherapies warrant cost-effectiveness evidence for coverage.
- This study aimed to review published literature on the economic impact of immunotherapies and to identify key drivers that impact cost-effectiveness.

METHODS

- A comprehensive systematic literature review involving electronic databases and grey literature was conducted.
- Studies that assessed the cost-effectiveness of immunotherapies for advanced or first recurrent endometrial cancer and were published before May 2024, were included.
- Cochrane collaboration methods and PRISMA guidelines for SLRs were followed.

FINDINGS

- 18 CEAs investigating the use of pembrolizumab, bevacizumab, atezolizumab, trastuzumab and dostarlimab were retrieved (**Figure 1**).
- Immunotherapy options for A/R EC are limited, and that their cost-effectiveness when compared to SoC is dependent on the patient subgroup, treatment cost, and the country's willingness-to-pay threshold.

BACKGROUND & AIMS

- Endometrial cancer (EC) is the sixth most common gynaecologic malignancy in women, accounting for 4.5% of all cancer cases.[1]
- Due to limited healthcare resources and the recent availability of new interventions including combinations of immunotherapy with chemotherapy for advanced or recurrent (A/R) EC, economic evaluations of A/R EC therapies are becoming increasingly important.
- This study aimed to systematically identify evidence describing the cost-effectiveness of immunotherapies alone or in combination, compared with standard of care (SoC) chemotherapy in patients with advanced stage III/IV, or first recurrent EC.

METHODS

- A PRISMA-adherent systematic literature review was undertaken to identify relevant cost-effectiveness analyses (CEAs) published in the English language before 30th May 2024.[2]
- Electronic database searches were conducted in Embase, MEDLINE(R) ALL, and the Cochrane Library via Ovid with supplementary searches undertaken in Gynecologic Oncology and the Cost-Effectiveness Analysis registry, and forward tracking via Google Scholar.
- The peer-reviewed search strategies used a combination of sophisticated subject headings, text words, synonyms and Boolean combination techniques.
- Two reviewers independently screened the literature, extracted data from full publications, and assessed methodological quality using the Drummond 10-item rated checklist.[3]
- The eligibility criteria for screening in the review are shown in **Table 1**.

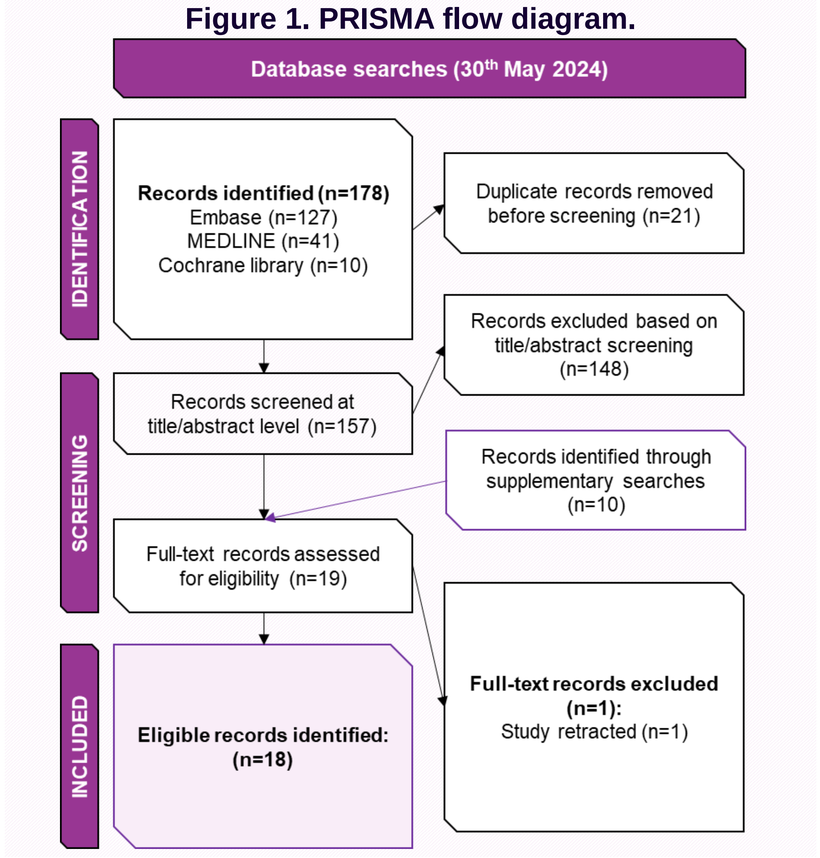
Table 1. Inclusion/exclusion criteria.

Criteria	Inclusion	Exclusion
Population	Adults with advanced (III/IV) or first recurrent endometrial cancer (EC)	Patients aged <18 years Patients with a condition other than EC
Intervention	Any immunotherapy alone or in combination	Interventions not recommended, marketed or used for the treatment of EC
Comparator	Any chemotherapy alone or in combination	Hormonal therapy Radiotherapy Alternative medicine
Outcomes	Cost effectiveness estimates Cost drivers and modelling assumptions Study design or model structure Treatment costs (unit and average) and health outcomes	Studies not reporting any outcomes of interest
Study design	Economic evaluations including cost-effectiveness analyses	Non-economic assessments
Limitation(s)	English language publications	Non-English language publications

RESULTS

- Of the 167 individual articles identified, 18 CEAs met the eligibility criteria. Overall, the reporting quality was assessed as high with 89% of these studies scoring ≥8 points on the Drummond 10-item checklist.
- The cost-effectiveness of immunotherapy in EC was investigated using the United States (US) (n=16 analyses), China (n=3) and Sweden (n=2) payer/ societal perspectives.

Figure 1. PRISMA flow diagram.



- **Immunotherapies investigated:** Analyses considered pembrolizumab in mono or combination-therapy (n=16), bevacizumab (n=2), atezolizumab (n=1), trastuzumab (n=1), or dostarlimab (n=1).
- **Model structures**: Analyses favoured using a partitioned survival (PS) model or Markov model with three mutually exclusive health states (progression free [PFS], progressed disease [PD], and death).
- **Sources of model inputs**: efficacy and safety data were derived from published literature and KEYNOTE-146, KEYNOTE-158, KEYNOTE-775, NRG-GY018, ENGOT-en7, MaNGO, AtTEnd, GOG0209, and RUBY trials.
- **Cost-effectiveness threshold**: Studies used willingness-to-pay (WTP) thresholds of $100,000 per year (of overall survival or per quality-adjusted life year [QALY]), $150,000/QALY, $200,000/QALY, 1-million SEK/QALY, or 3x the Chinese gross domestic product (GDP) (in 2021 or 2023).
- **Subgroups:** Stratifications by microsatellite stable /instable (MSS/ MSI) and mismatch repair proficient/ deficient (pMMR/ dMMR) tumour subgroups were made.
- **Incremental cost-effectiveness ratio (ICER):** The ICERs for immunotherapies compared to SoC varied significantly between the studies and ranged from $41,305.09 in the dMMR subgroup to $2,849,882 in the MSI-high cohort.
- Pembrolizumab or trastuzumab + carboplatin + paclitaxel combination therapies were considered **cost-effective** compared to carboplatin + paclitaxel in the pMMR and dMMR subgroup (pebrolizumab) or Her2/neu-positive subgroup (trastuzumab). Pembrolizumab + lenvatinib was also considered **cost-effective** compared to doxorubicin or paclitaxel dependent on the country's WTP threshold.

CONCLUSIONS

- We identified 18 CEAs which assessed 5 immunotherapies that were mainly compared with doxorubicin, pegylated liposomal doxorubicin, paclitaxel or carboplatin chemotherapy in mono or combination-therapies.
- Several chemotherapies were considered cost-effective in one country but not the other (China vs. US) and in one subgroup but not the other (dMMR vs. pMMR). Considerable drug price discounts were important strategies to achieve cost-effectiveness.
- **Key drivers of cost-effectiveness** included cost of treatment, utility of PD, utility of PFS state and adjustments for subsequent therapies.
- There are new therapeutic approaches to A/R/EC on the horizon e.g., niraparib plus dostarlimab, the HER-2 antibody drug conjugate BNT323/ DB-1303, etc.
- Evidence-based pricing strategy is required to ensure successful outcomes for pharmaceutical companies, healthcare stakeholders, and patients alike.

References

1. *World Cancer Research Fund International (2020). Endometrial cancer statistics.*
2. *Page et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. bmj, 372.*
3. *Doran (2008). Economic evaluation of interventions to treat opiate dependence: a review of the evidence. Pharmacoeconomics, 26, pp.371-393.)*

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