Cost-Effectiveness of Poly ADP-Ribose Polymerase (PARP) Inhibitors in Cancer Treatment: A Systematic Review

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Background & Objectives

PARP inhibitors have shown significant improvement in progression-free survival, but their costs cast a considerable financial burden. In line with value-based oncology, it is important to evaluate whether drug prices justify the outcomes.

In this systematic review, we aimed to evaluate PARP inhibitors on: 1) the cost-effectiveness against standard care, 2) impact on cost-effectiveness upon stratification for genetic characteristics, and 3) to elucidate the key factors that determine their cost-effectiveness in the management of breast, ovarian, prostate and pancreatic cancers.

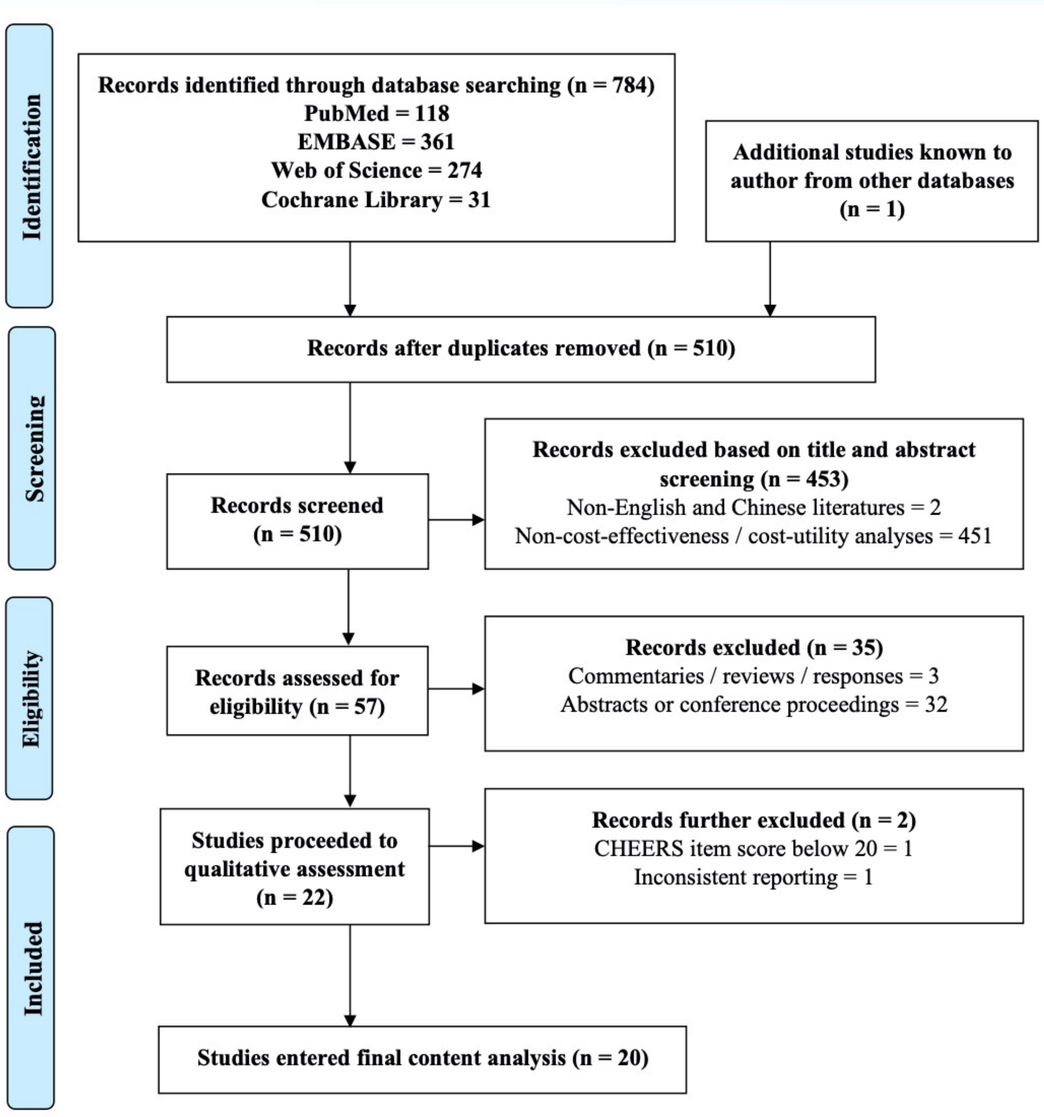
Methods

We systematically searched PubMed, EMBASE, Web of Science, Cochrane Library without language and date restriction, using pre-specified search terms, updated to 31 August 2021. Trial-based or modelling cost-effectiveness analyses of 4 FDA-approved PARP inhibitors (olaparib, niraparib, rucaparib, talazoparib) in Chinese or English language with full text were eligible. Other studies known to authors were included. Reference lists of selected articles were screened.

Literature screening, quality assessment using the Quality of Health Economics Studies (QHES) instrument (for methodological quality) and Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist (for reporting quality), and data extraction were performed by two independent researchers (VKYC & RQY).

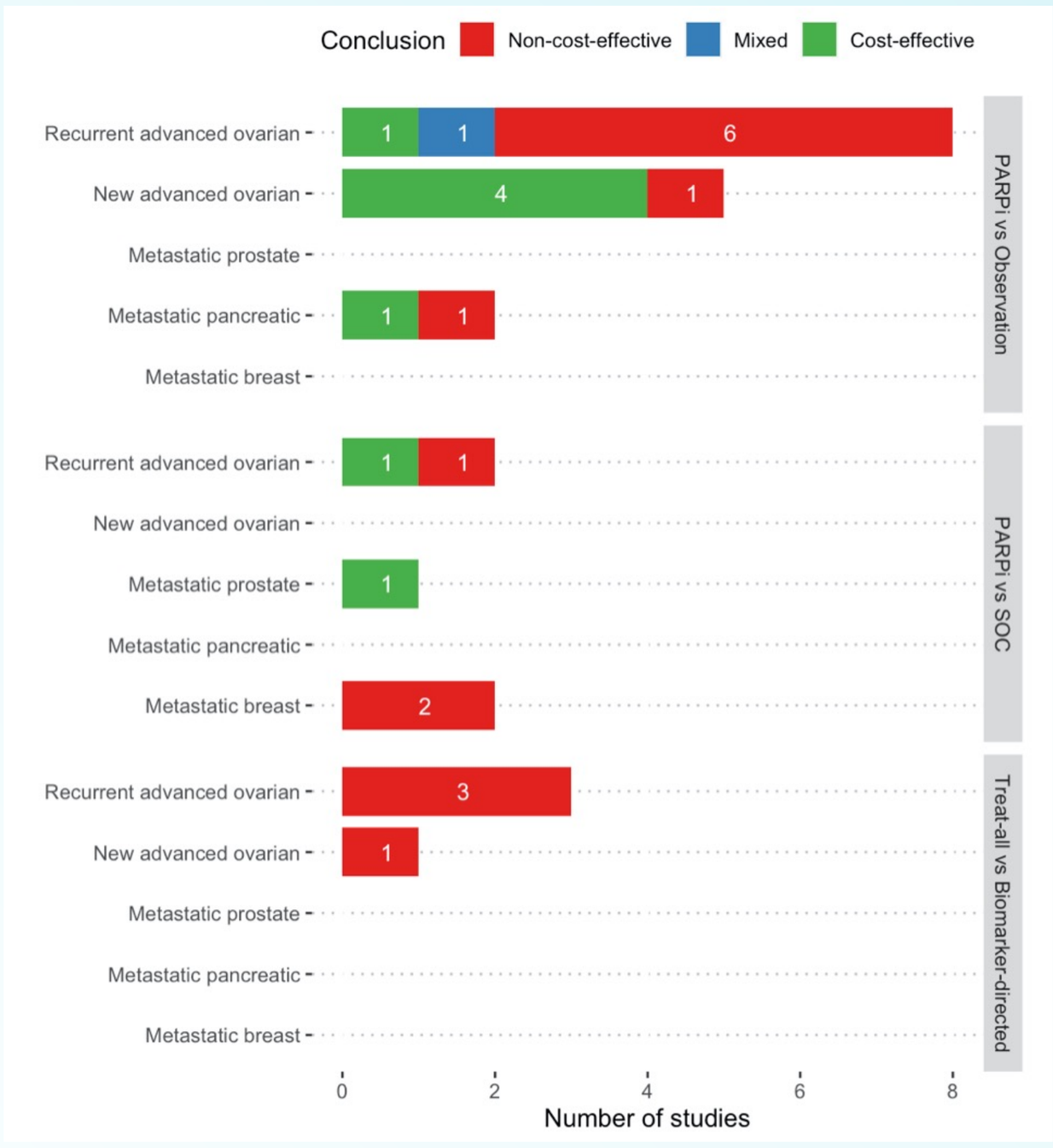
Results

A total of 22 original studies passed the initial screening for eligibility, with 21 achieving good methodological and reporting quality (mean QHES score: 92.5/100, CHEERS score of 22.5/24). One study was excluded further due to inconsistent reporting. Eventually, 20 articles proceeded into final review.



The majority of studies were in the United States (n=13), 5 in Asia and 2 in Europe. Most studies targeted advanced ovarian cancer (n=15), with 9 on recurrence and 6 on new diagnosis setting. The remaining studied metastatic pancreatic (n=2), breast (n=2) and prostate (n=1) cancers. 5 studies examined the role of PARP inhibitors as active treatment, 16 studies as maintenance treatment and 1 covered both categories.

This systematic review depicts several findings. **First, the cost-effectiveness of PARP inhibitors varied with cancer types and lines of treatment**. Regarding **advanced ovarian cancer**, PARP inhibitors were unlikely cost-effective as a maintenance treatment for patients responsive to platinum-based chemotherapy, with 6 studies concluding not cost-effective out of 8 comparing PARP inhibitors against observation, which gave diverse ICER values ranging from US$64,457 per PFS-LY to US$1.9M per QALY. However, when moved to upfront maintenance in a new diagnosis setting, 4 out of 5 studies examining first-line maintenance concluded them cost-effectives. Limited evidence showed that PARP inhibitors were not cost-effective in **metastatic breast cancer**. The conclusions were mixed for **metastatic pancreatic cancer**, whilst olaparib in **metastatic prostate cancer** seemed to be cost-effective.



Next, stratification by tumour genetic characteristics displayed an effect on ICERs. When restricting the use of PARP inhibitors in *BRCA*mut or HRD-positive patients, ICERs generally decreased although still above most pre-defined willingness-to-pay thresholds. ICER values plummeted after confining treatment to *BRCA*mut- and/or HRD-only patients. **Finally, drug cost was consistently highlighted in all models as a strong cost-effectiveness determinant**, followed by hazard ratio of PFS in some models.

Conclusion

In advanced ovarian cancer, the use of PARP inhibitors use should be prioritized for upfront maintenance, and for patients with *BRCA* mutation or *BRCA*ness at recurrence. Additional economic evaluations are warranted for novel indications in other cancer types.

Conflicts of Interest Statement

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