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Original Article

A Prospective Cost-Utility Analysis of Bevacizumab-Based Combination Therapy Versus Chemotherapy Alone in Ovarian Cancer

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ABSTRACT

Background: Ovarian cancer remains a leading cause of gynaecologic cancer mortality globally. While chemotherapy is the standard treatment, the addition of targeted therapies such as bevacizumab may improve clinical outcomes. However, the economic burden and quality-of-life impact of these regimens remain insufficiently explored. This study compared the cost-utility and Quality-Adjusted Life Years (QALYs) of chemotherapy alone versus bevacizumab-based combination therapy in ovarian cancer patients. **Materials and Methods:** This prospective pharmacoeconomic study was conducted over six months at a tertiary care hospital and included 110 ovarian cancer patients. Participants received either chemotherapy alone (*n*=61) or combination therapy (*n*=49). Data were obtained from patient case records and quality-of-life questionnaires; QALYs were calculated using utility scores. Direct medical costs were used for cost-utility analysis. **Results:** Mean total treatment cost was INR 87,365.17±35,460.39 for chemotherapy and INR 5,44,413.11±1,43,754.25 for combination therapy. QALYs were 2.47 (chemotherapy) and 2.68 (combination therapy). The Incremental Cost-Utility Ratio (ICUR) for combination therapy was INR 21,88,200.99 per QALY, exceeding the Willingness-To-Pay (WTP) threshold of INR 2,00,000 per QALY. **Conclusion:** Although combination therapy yielded marginally higher QALYs and better quality-of-life outcomes, its substantially higher cost limits cost-effectiveness within the current Indian healthcare context. Chemotherapy alone remained cost-effective at the defined WTP threshold.

Keywords: Cost-utility Analysis, Ovarian Cancer, Pharmacoeconomics, Quality of Life, Quality-Adjusted Life Years.

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INTRODUCTION

Cancer is a disease with one of the highest incidences globally (Sung *et al*., 2021), placing significant pressure on healthcare systems to ensure the availability of essential resources for its management and treatment. Resources such as time, expertise, equipment, and funding are limited, making it crucial to make strategic decisions to allocate them sustainably (Drummond, 2015). With the growing global emphasis on evidence-based therapy and personalized patient care, there is a growing demand to comprehend how to distribute these finite resources effectively.

It is essential to evaluate both the economic and clinical impacts of different approaches for cancer patient therapy. The financial burden of cancer treatment is considerable, due to high treatment costs, supportive care, and extended hospital stays. Understanding this burden is crucial for optimizing treatment decisions and ensuring that both therapeutic and financial aspects of care are addressed.

Pharmacoeconomic analysis enables the assessment of the monetary value of the treatment on the Quality of Life (QOL) of the patient to assess the overall burden of the disease and the therapeutic efficacy of the intervention (Drummond, 2015). Quality of life refers to an individual's perception of their physical, psychological, and social-wellbeing. The reporting and interpretation of QOL can be affected by patient-related factors, cancer type, and treatment received (Bhat *et al*., 2020).

Patients undergoing systemic treatment for progressive ovarian cancer commonly experience disease recurrence, which negatively impacts utility values through increased symptoms and adverse

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effects (Bhat *et al.*, 2020). Chemotherapy-induced adverse effects are known to impair QOL (Sfakianos and Havrilesky, 2011).

As oncology treatment evolves, pharmacoeconomic analyses are increasingly used to assess the financial feasibility of different treatment options. By combining quality and quantity of life into a single unit, the Quality-Adjusted Life Year (QALY) comparisons across diverse health interventions are facilitated (Prieto and Sacristán, 2003). This framework ensures healthcare spending is directed towards treatments with meaningful clinical benefit relative to their costs (Whitehead and Ali, 2010).

Despite the growing use of pharmacoeconomic tools in oncology, limited prospective studies have evaluated the cost-utility of bevacizumab-based combination therapy versus chemotherapy alone in Indian ovarian cancer patients. Therefore, this study aimed to compare the cost-utility and QALY of these two treatment approaches. We hypothesised that while combination therapy may yield higher QALYs, its incremental cost would exceed WTP thresholds, rendering it less cost-effective in a resource-limited setting.

MATERIALS AND METHODS

This observational, prospective pharmacoeconomic study was conducted at a tertiary care hospital in India over a six-month period among patients receiving treatment for ovarian cancer. The study compared economic and QOL outcomes of conventional Chemotherapy (CT) and bevacizumab-based Combination Therapy (CT+TT) in routine clinical practice.

Following screening based on predefined inclusion and exclusion criteria, 110 patients diagnosed with ovarian cancer were enrolled and assigned to two groups: CT alone (n=61) and CT+TT (n=49). Group allocation was based on the treating physician's clinical decision; investigators did not influence treatment assignment. Of 200 diagnosed ovarian cancer patients screened, 110 were selected based on predefined inclusion and exclusion criteria. Sample size was determined using the Finite Population Correction (FPC) formula, assuming a 95% confidence interval and a 5% margin of error.

Direct medical costs were recorded for pharmacoeconomic evaluation. Patient demographic information was obtained from case records; drug costs were extracted from hospital billing records. Cost data were collected over the entire study period and analysed in Indian Rupees (INR). The economic evaluation included direct drug acquisition costs only. Costs related to adverse event management, supportive care and indirect patient costs were not included.

QOL was assessed in consenting patients using a composite questionnaire based on the EORTC QLQ-OV28 (Greimel *et al.*, 2003) and the City of Hope QOL instrument for ovarian cancer patients (Ferrell *et al.*, 2003). Assessments were conducted at baseline (before treatment initiation) and at the end of the six-month study period.

Key parameters included disease status, treatment dates, regimen details (drug, dose, cycle, and cost), and QOL scores. Utility values derived from QOL data were used to calculate QALYs. Cost-utility analysis was performed by comparing costs and QALYs between treatment groups, and the ICUR was calculated. Within-group QOL changes were compared using a paired t-test; between-group differences were assessed with an independent-samples t-test. Pearson correlation coefficients and simple linear regression were used to examine cost-QOL relationships. All analyses were performed using Microsoft Excel 2021 (Microsoft Corporation, Redmond, WA, USA), with statistical significance set at α=0.05. Baseline comparability was assessed using QOL scores, which did not differ significantly between groups (p=0.281).

Ethical approval for the study was obtained from an Institutional Ethics Committee. Informed consent was obtained from all participants before data collection. Patient confidentiality was strictly maintained, and all data were anonymized prior to analysis.

RESULTS

A total of 110 patients aged 18-75 years were enrolled. The largest age group was 51-60 years (n=37; 33.46%), followed by 41-50 years (n=30; 27.27%) and 61-70 years (n=24; 21.82%). The remaining patients were distributed across the 18-40 years (n=7; 6.36%) and 71-75 years (n=12; 10.91%) age groups.

Among the 76 patients with documented metastatic disease, peritoneal metastasis was the most common (26.32%), followed by liver metastasis (23.68%). Lymph node and lung metastases each accounted for 13.16% of cases. Stomach and bladder/rectum metastases were each present in 7.89% of patients, while bone and spleen metastases were observed in 5.26% and 2.63% of patients, respectively.

Of 110 patients, 103 (93.64%) underwent cytoreductive surgery; 7 (6.36%) received no surgical intervention. The most common procedure was Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy (TAH+BSO), Bilateral Pelvic Lymph Node Dissection (BLPLND), and total omentectomy (n=43; 41.75%), followed by BSO with BLPLND and omentectomy (n=8; 7.77%).

Conventional Chemotherapy alone (CT) was administered to 61 patients (55%), and bevacizumab-based Combination Therapy (CT+TT) to 49 patients (45%). The mean age of patients receiving CT alone was 53.87 years, compared with 57.27 years in CT+TT group.

Table 1 presents QOL and QALY outcomes for both treatment groups. Baseline QOL scores were comparable between groups (p=0.281), confirming similarity at enrolment. Following

treatment, both groups demonstrated significant within-group QOL improvement; however, the CT+TT group showed a significantly greater change in QOL (0.1097 ± 0.1815 vs. 0.0502 ± 0.1901; p=0.005) and a significantly higher post-treatment QOL score (0.7239 ± 0.1783 vs. 0.6420 ± 0.2013; p=0.028). QALY gains were also significantly higher in the CT+TT group (2.676 ± 0.482 vs. 2.468 ± 0.509; p=0.025).

Table 2 details the direct medical costs of individual CT regimens over the six-month study period. Gemcitabine + Oxaliplatin had the highest total cost per patient (INR 1,37,892), followed by Topotecan (INR 1,36,000) and Nab-Paclitaxel + Carboplatin (INR 83,016). The elevated costs for Gemcitabine + Oxaliplatin and Irinotecan + Cisplatin reflect their more frequent bi-weekly dosing schedules. The mean total cost for CT was INR 87,365.17 ± 35,460.39 per patient.

The addition of Bevacizumab (BEV) to conventional chemotherapy resulted in substantially higher treatment costs, as shown in Table 3. Topotecan + Cisplatin + BEV was the most expensive regimen (INR 7,50,016), followed by Gemcitabine + Oxaliplatin + BEV (INR 6,97,577) and Nab-Paclitaxel + Carboplatin + BEV (INR 6,40,211). The mean total cost for CT+TT was INR 5,44,413.11 ± 1,43,754.25 per patient, representing a 6.23-fold increase compared to CT alone.

Pearson correlation analyses examining the relationship between treatment cost and QOL outcomes are presented in Table 4, Section A. A weak-to-moderate positive correlation was observed between cost and change in QOL for CT (r=0.278; R^2=0.077) and a moderate positive correlation for CT+TT (r=0.492; R^2=0.242). The correlation between cost and baseline QOL was negligible in both groups, indicating that initial QOL was independent of treatment cost. Linear regression confirmed that costlier CT+TT regimens were associated with greater QOL improvement, though cost alone accounted for only 24.2% of the variance in QOL change, suggesting that clinical and disease-related factors also contribute substantially.

The cost-utility analysis (Table 4, Section B) demonstrated that CT alone had a Cost-Utility Ratio (CUR) of INR 35,406.11/QALY, well within the Willingness-To-Pay (WTP) threshold of INR 2,00,000/QALY (based on India's 2025 GDP per capita), confirming it as cost-effective. CT+TT had a CUR of INR 2,03,413.51/QALY. The incremental Cost-Utility Ratio (ICUR) for CT+TT versus CT was INR 21,88,200.99/QALY, calculated as follows: ICUR = (INR 5,44,413.11 - INR 87,365.17) ÷ (2.676 - 2.468) = INR 21,88,200.99/QALY. This value substantially exceeds the WTP threshold, indicating that CT+TT is not cost-effective under current Indian economic conditions. Figure 1 illustrates the cost-effectiveness plane, with CT plotted within and CT+TT plotted above the WTP threshold.

DISCUSSION

Ovarian cancer is a leading cause of gynaecological cancer mortality, predominantly affecting post-menopausal women; the lifetime risk in females is approximately 1 in 91 (American Cancer Society, 2025). This prospective study evaluated the cost-utility of bevacizumab-based combination therapy versus chemotherapy alone over a six-month treatment period in an Indian tertiary care setting.

The predominance of peritoneal metastasis (26.32%) in this cohort is consistent with the known pathophysiology of ovarian cancer, wherein transcelomic spread is the principal dissemination route (Bhat *et al.*, 2020). The high rate of cytoreductive surgery (93.6%) reflects current guideline-concordant management, with TAH+BSO, BLPLND, and omentectomy being the most performed procedure (Sfakianos and Havrilesky, 2011).

Both treatment groups demonstrated significant post-treatment QOL improvement, consistent with the expected disease response to active therapy. Patients receiving CT+TT achieved significantly higher post-treatment QOL scores and greater QALY gains, suggesting that the addition of bevacizumab confers measurable clinical benefit. These findings align with phase III trial data from GOG-0218 and ICON7, which reported improved

Table 1: Quality of Life (QOL) scores and Quality-Adjusted Life Years (QALYs) by treatment group (n=110).

Treatment Group (n=110)	Baseline QOL (Mean ± SD)	Post-treatment QOL (Mean ± SD)	Change in QOL (Mean ± SD)	p-value	QALY (Mean ± SD)
Chemotherapy alone (CT) (n=61)	0.5918 ± 0.1001	0.6420 ± 0.2013	0.0502 ± 0.1901	0.044	2.468 ± 0.509
Bevacizumab-based combination therapy (CT+TT) (n=49)	0.6143 ± 0.1172	0.7239 ± 0.1783	0.1097 ± 0.1815	< 0.001	2.676 ± 0.482
p-value (between groups)	0.281	0.028*	0.005*	-	0.025*

QOL = Quality of Life; QALY = Quality-Adjusted Life Year; CT = Chemotherapy alone; CT+TT = bevacizumab-based combination therapy; Within-group p-value (paired t-test comparing baseline vs. post-treatment QOL); Between-group p-value (independent-samples t-test). *p≤0.05, statistically significant. All values reported as Mean ± SD unless otherwise stated.

Table 2: Direct medical costs of conventional Chemotherapy (CT) regimens over a six-month treatment period (*n*=61).

Treatment Regimen	Cost Per Cycle (INR)	Dosing Frequency	No. of Cycles (6 months)	Total Cost Per Patient (INR)
Nab-Paclitaxel + Carboplatin	10,377.00	Once every 3 weeks	8	83,016.00
Paclitaxel + Carboplatin	11,804.60	Once every 3 weeks	8	94,437.33
Docetaxel	11,087.00	Once every 3 weeks	8	88,696.00
Gemcitabine + Carboplatin	3,179.90	Once every 3 weeks	8	25,439.20
Gemcitabine + Oxaliplatin	11,491.00	Once every 2 weeks	12	1,37,892.00
Lipodox (Liposomal Doxorubicin)	15,771.00	Once every 4 weeks	6	94,626.00
Lipodox + Carboplatin	10,762.00	Once every 4 weeks	6	64,572.00
Topotecan	17,000.00	Once every 3 weeks	8	1,36,000.00
Irinotecan + Cisplatin	5,134.00	Once every 2 weeks	12	61,608.00
Mean ± SD	10,734.06 ± 4,402.14	-	-	87,365.17 ± 35,460.39

CT = Conventional Chemotherapy; INR = Indian Rupees (2024-2025 prices, exchange rate: 1 USD ≈ INR 83). Costs represent drug acquisition costs extracted from hospital billing records; supportive care and hospitalisation costs were not included. All values reported as Mean ± SD for the average row.

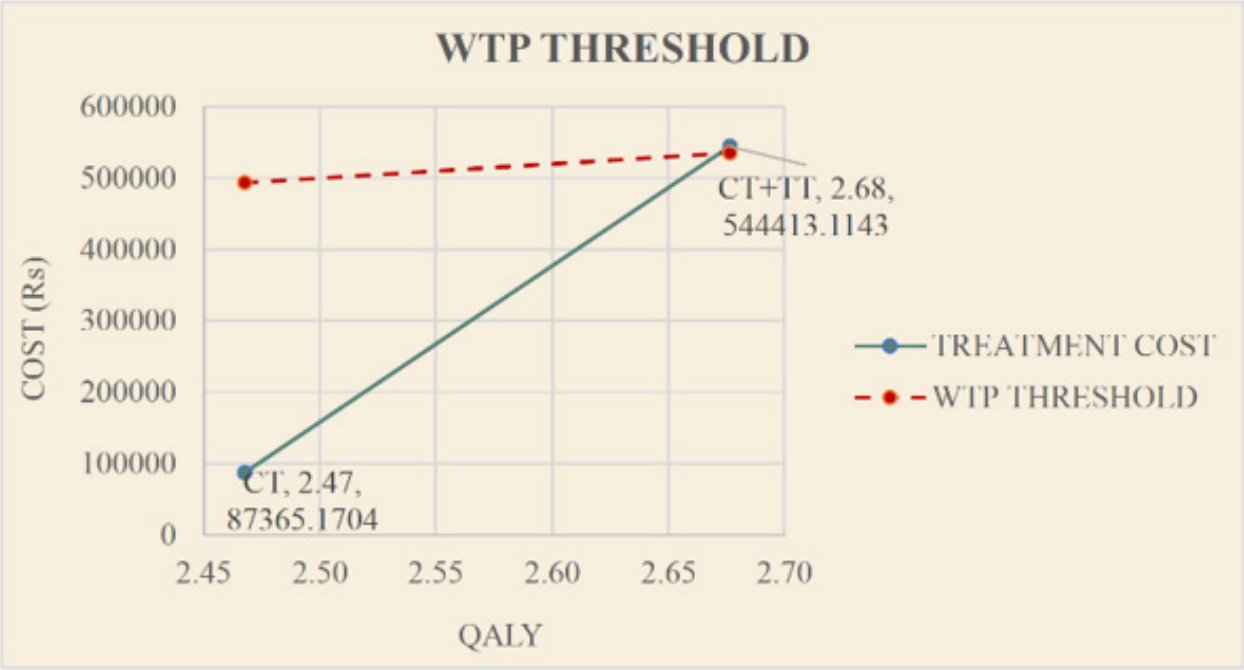

Figure 1: Cost-Effectiveness Vs WTP Threshold.

Cost-effectiveness plane comparing conventional Chemotherapy (CT; ***n***=61) and Bevacizumab-Based Combination Therapy (CT+TT; ***n***=49) against the Willingness-To-Pay (WTP) threshold of INR 2,00,000 per QALY (dashed line). The x-axis represents incremental QALYs gained and the y-axis represents incremental cost (INR). CT is plotted within the cost-effective quadrant (below WTP threshold); CT+TT is plotted above the threshold, indicating it is not cost-effective at the defined WTP limit.

Table 3: Direct medical costs of Bevacizumab-Based Combination Therapy (CT+TT) regimens over a six-month treatment period (*n*=49).

Treatment Regimen	Cost Per Cycle (INR)	Dosing Frequency	No. of Cycles (6 months)	Total Cost Per Patient (INR)
Nab-Paclitaxel + Carboplatin + Bevacizumab	80,026.40	Once every 3 weeks	8	6,40,211.20
Paclitaxel + Carboplatin + Bevacizumab	79,019.75	Once every 3 weeks	8	6,32,158.00
Gemcitabine + Bevacizumab	59,063.00	Once every 4 weeks	6	3,54,378.00
Gemcitabine + Oxaliplatin + Bevacizumab	58,131.43	Once every 2 weeks	12	6,97,577.14
Lipodox + Bevacizumab	60,359.80	Once every 4 weeks	6	3,62,158.80
Lipodox + Carboplatin + Bevacizumab	75,766.00	Once every 4 weeks	6	4,54,596.00
Topotecan + Bevacizumab	65,982.00	Once every 3 weeks	8	5,27,856.00
Topotecan + Cisplatin + Bevacizumab	93,752.00	Once every 3 weeks	8	7,50,016.00
Cyclophosphamide (Endoxan) + Bevacizumab	50,471.50	Once every 3 weeks	8	4,03,772.00
FOLFOX + Bevacizumab	51,784.00	Once every 2 weeks	12	6,21,408.00
Mean ± SD	67,435.58 ± 14,127.47	-	-	5,44,413.11 ± 1,43,754.25

CT+TT = Chemotherapy Plus Targeted Therapy (bevacizumab); BEV = Bevacizumab; INR = Indian Rupees (2024-2025 prices). Costs represent drug acquisition costs only. All values reported as Mean ± SD for the average row. ICUR for CT+TT vs. CT: ICUR =(5,44,413.11 - 87,365.17) ÷ (2.676 - 2.468) = INR 21,88,200.99 per QALY gained.

progression-free survival with bevacizumab-based regimens, albeit with notable toxicity and cost implications (Prieto and Sacristán, 2003; Whitehead and Ali, 2010). The cost per QALY for CT alone (INR 35,406) was well within the WTP threshold of INR 2,00,000, confirming its cost-effectiveness. In contrast, the ICUR for CT+TT (INR 21,88,200/QALY) substantially exceeded this threshold, indicating that combination therapy is not cost-effective under current Indian economic conditions. These findings are particularly relevant given India's resource-constrained healthcare environment, where GDP-based WTP thresholds are significantly lower than those applied in high-income settings. A threshold-based sensitivity analysis indicated that bevacizumab-based combination therapy would require an approximately 91% reduction in incremental cost to become cost-effective at the predefined WTP threshold of INR 200,000/QALY, suggesting that the study conclusions are robust to reasonable variations in WTP assumptions.

Pearson correlation analyses demonstrated a weak-to-moderate positive association between treatment cost and QOL improvement in both groups (CT: r=0.28; CT+TT: r=0.49), with linear regression explaining approximately 24.2% of QOL variation in the CT+TT group. While higher-cost regimens showed some association with better QOL outcomes, the relatively low R^2 values indicate that cost alone is not a determinant of QOL improvement; clinical, psychological, and disease-related factors likely contribute substantially.

This study has several strengths. The prospective design and use of validated QOL instruments (EORTC QLQ-OV28 and City of Hope instrument) enhance the reliability of QOL and QALY estimates. Real-world cost data from hospital billing records improve generalisability to the Indian tertiary care context. Baseline quality-of-life scores were comparable between groups, although potential selection bias inherent to the observational design remains.

Limitations include the relatively small sample size, particularly in the CT+TT group (*n*=49), and the six-month follow-up period, which may not fully capture long-term survival benefits and late toxicities associated with bevacizumab-based therapy. As an observational study, treatment allocation was physician-directed, introducing the possibility of selection bias and confounding by indication. The economic analysis included direct drug acquisition costs only and did not account for adverse event

Table 4: Cost-QOL correlation analysis and cost-utility summary for CT and CT+TT treatment groups.

Section A: Pearson Correlation -Treatment Cost vs. Quality-of-Life Outcomes		
Correlation Parameter	**CT (Chemotherapy alone) (*n*=61)**	**CT+TT (Combination Therapy) (*n*=49)**
Cost vs. Change in QOL	r=0.278; R^2=0.077	r=0.492; R^2=0.242
Cost vs. Post-treatment QOL	r=0.326; R^2=0.106	r=0.371; R^2=0.138
Cost vs. Baseline QOL	r=0.129; R^2=0.017	r=-0.196; R^2=0.038
Section B: Cost-Utility Analysis Summary		
Parameter	CT (Chemotherapy alone) (***n***=61)	CT+TT (Combination Therapy) (***n***=49)
Mean cost per cycle (INR)	10,734.06±4,402.14	67,435.58±14,127.47
Total cost per patient (INR)	87,365.17±35,460.39	5,44,413.11±1,43,754.25
QALY (Mean ± SD)	2.468±0.509	2.676±0.482
Cost-utility ratio (INR/QALY)	35,406.11	2,03,413.51
Incremental cost (INR)	-	4,57,047.94
Incremental QALY	-	0.209
ICUR (INR/QALY)	-	21,88,200.99
WTP threshold (INR/QALY)	2,00,000	2,00,000
Cost-effective vs. WTP threshold?	Yes	No

CT=Chemotherapy alone (*n*=61); CT+TT = Bevacizumab-Based Combination Therapy (*n*=49). Section A: Pearson correlation coefficient (r) and coefficient of determination (R^2) between treatment cost and QOL parameters. Section B: CUR = total cost ÷ total QALY; ICUR = incremental cost ÷ incremental QALY. WTP threshold: INR 2,00,000/QALY (≈ USD 2,410), based on India's per capita GDP (2025). Statistical analysis: Pearson correlation and simple linear regression performed using Microsoft Excel 2021. INR = Indian Rupees; QALY = quality-adjusted life year; CUR = Cost-Utility Ratio; ICUR = Incremental Cost-Utility Ratio; WTP = Willingness-To-Pay.

management, supportive care, caregiver burden, productivity losses, or other indirect costs. In addition, cost data were derived from a single institution and may not be generalisable across all healthcare settings in India.

CONCLUSION

In conclusion, while bevacizumab-based combination therapy provided superior clinical outcomes, its ICUR far exceeds current WTP thresholds in India. These findings highlight the need for equitable pricing strategies, health technology assessment frameworks, and policy discussions on subsidising targeted therapies in resource-limited settings. Future prospective studies with larger samples and extended follow-up are needed to better define the long-term cost-utility profile of bevacizumab in Indian ovarian cancer care.

In this prospective study, bevacizumab-based combination Chemotherapy (CT+TT) produced significantly greater QOL improvement and higher QALY gains than chemotherapy alone in ovarian cancer patients. However, with an ICUR of INR 21,88,200.99/QALY against a WTP threshold of INR 2,00,000/QALY, CT+TT was not cost-effective under current Indian economic conditions. Chemotherapy alone remained cost-effective and should be considered the standard-of-care option in resource-limited settings. These findings support the need for equitable drug pricing policies and health technology assessment to improve access to targeted therapies for patients where clinical benefit justifies their use.

ABBREVIATIONS

BEV: Bevacizumab; **BLPLND:** Bilateral Pelvic Lymph Node Dissection; **BSO:** Bilateral Salpingo-Oophorectomy; **CT:** Conventional Chemotherapy or Chemotherapy alone; **CT+TT:** Bevacizumab-Based Combination Therapy or Chemotherapy Plus Targeted Therapy; **CUR:** Cost-Utility Ratio; **EORTC QLQ-OV28:** Ovarian cancer-specific quality-of-life questionnaire module; **FPC:** Finite Population Correction; **GDP:** Gross Domestic Product; **ICUR:** Incremental Cost-Utility Ratio; **INR:** Indian Rupees; **QALY:** Quality-Adjusted Life Year; **QOL:** Quality of Life; **TAH+BSO:** Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy; **WTP:** Willingness-To-Pay; **USD:** United States Dollars; **SD:** Standard Deviation; **α:** Statistical significance level; **r:** Pearson correlation coefficient; **R^2:** Coefficient of determination; **p:** *p*-value; **n:** Sample size or number of patients.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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