original reports abstract

Cost Effectiveness of Bevacizumab Plus Chemotherapy for the Treatment of Advanced and Metastatic Cervical Cancer in India—A Model-Based Economic Analysis

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PURPOSE Patients with advanced and metastatic cervical cancer have a poor prognosis with a 1-year survival rate of 10%-15%. Recently, an antiangiogenic humanized monoclonal antibody bevacizumab has shown to improve the survival of these patients. This study was designed to assess the cost effectiveness of incorporating bevacizumab with standard chemotherapy for the treatment of patients with advanced and metastatic cervical cancer in India.

METHODS Using a disaggregated societal perspective and lifetime horizon, a Markov model was developed for estimating the costs and health outcomes in a hypothetical cohort of 1,000 patients with advanced and metastatic cervical cancer treated with either standard chemotherapy alone or in combination with bevacizumab. Effectiveness data for each of the treatment regimen were assessed using estimates from Gynecologic Oncology Group 240 trial. Data on disease-specific mortality in metastatic cervical cancer, health system cost, and out-of-pocket expenditure were derived from Indian literature. Multivariable probabilistic sensitivity analysis was undertaken to account for parameter uncertainty.

RESULTS Over the lifetime of one patient with advanced and metastatic cervical cancer, bevacizumab along with standard chemotherapy results in a gain of 0.275 (0.052-0.469) life-years (LY) and 0.129 (0.032-0.218) quality-adjusted life-years (QALY), at an additional cost of $3,816 US dollars (USD; 2,513-5,571) compared with standard chemotherapy alone. This resulted in an incremental cost of $19,080 USD (7,230-52,434) per LY gained and $34,744 USD (15,782-94,914) per QALY gained with the use of bevacizumab plus standard chemotherapy.

CONCLUSION Addition of bevacizumab to the standard chemotherapy is not cost effective for the treatment of advanced and metastatic cervical cancer in India at a threshold of 1-time per-capita gross domestic product.

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INTRODUCTION

Cervical cancer is the second most common cancer affecting women in low- and middle-income countries.[1,2] South East Asia region contributes to around 33% of the global cases and mortality caused by cervical cancer; India alone accounts for around 65% of this burden.[1,2] Most of the cervical cancer cases in India are diagnosed in locally advanced stage (83% International Federation of Gynecology and Obstetrics [FIGO] stage II-IVA).[3] Nearly 15%-61% of affected women develop recurrence or metastasis usually within the first 2 years of completing the treatment.[4]

Patients with advanced (recurrent and persistent) and metastatic cervical cancer usually have a poor prognosis with a 1-year survival rate between 10%-15%.[5] Presently, doublet chemotherapy of cisplatin and paclitaxel is the standard of care for the management of these patients.[6] However, as a result of acquired resistance to platinum-based chemoradiotherapy for locally advanced disease, response rate with cisplatin-based therapy is poor.[7] Recently, an antiangiogenic humanized monoclonal antibody drug bevacizumab, an inhibitor of vascular endothelial growth factor, has shown to improve the survival of patients with advanced cervical cancer.[6] The only randomized controlled trial, Gynecologic Oncology Group (GOG)-240, shows that the addition of bevacizumab to the chemotherapy significantly improves both progression-free survival (8.2 months *v* 6.0 months) and overall survival

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CONTEXT

Key Objective

Is adding bevacizumab to standard chemotherapy a cost-effective option for treatment of advanced and metastatic cervical cancer in India, a country that has a huge burden of cervical cancer?

Knowledge Generated

Using a Markov model for analysis, the study results show that the use of bevacizumab enhances the survival by 0.276 life-years, and it increases the cost by 3.58 times compared with conventional chemotherapy alone. An incremental cost of $34,744 US dollars per quality-adjusted life-year gained makes bevacizumab plus chemotherapy a cost-ineffective treatment for patients with advanced and metastatic cervical cancer in India.

Relevance

Treatment of advanced cervical cancer with bevacizumab is associated with high cost, and the decision on its reimbursement under insurance programs is dependent on evidence for cost effectiveness. Adding bevacizumab to chemotherapy is not a cost-effective alternative to chemotherapy alone; hence, doublet chemotherapy should be continued as standard therapy for advanced and metastatic cervical cancer treatment in India.

(17 months *v* 13.3 months) in patients with advanced and metastatic cervical cancer.[8] It also showed that the use of bevacizumab was also associated with the occurrence of hypertension, thromboembolism, and gastrointestinal or genitourinary fistulas.

The cost of incorporating bevacizumab to standard chemotherapy is around 13 times higher than that of chemotherapy alone.[7] With limited budgets allocated to the health care sector, it becomes essential to ascertain whether the incremental cost is worth the potential health gains with a newer drug. Previous economic evaluations undertaken in the United States reported that incorporating bevacizumab with chemotherapy for treatment of advanced and metastatic cervical cancer is not cost effective.[7,9]

One of these studies used a static model that did not take into account the transition among various health states.[9] The Markov model used in other study did not include all the necessary health states that could influence the outcome of the study.[7] In view of the methodologic limitations of previous economic evaluations,[7,9] and limited generalizability of the US evidence, we undertook this study to assess the cost effectiveness of bevacizumab plus standard chemotherapy compared with chemotherapy alone for the treatment of advanced and metastatic cervical cancer in India.

METHODS

Model Overview

A Markov model was developed for estimating the lifetime costs and health consequences in a hypothetical cohort of 1,000 patients of advanced and metastatic cervical cancer treated with either chemotherapy alone or chemotherapy with bevacizumab. The health outcomes were evaluated in terms of life-years (LY) and quality adjusted life-years (QALY) lived. All the future costs and consequences were discounted at a rate of 3%.[10,11] The present analysis was based on a disaggregated societal perspective in which both the health system cost and patient-level out-of-pocket expenditure (OOPE) was incorporated.[12] We did not include the indirect cost because of productivity losses. The cost effectiveness was assessed in terms of incremental cost-effectiveness ratio (ICER).

The Markov model (Fig 1) simulates patient's clinical progression during treatment starting with patients in the stable disease/partial response (SD/PR) assumed to be receiving treatment with either of the therapeutic regimen. On the basis of the standard guidelines,[13] both treatment regimens were repeated at 21 days interval until developing progressive disease (PD), severe complications (SC), or complete response (CR). The cycle length of the model was assumed to be one month by rounding up the 21-day interval. The treatment was halted for 1 month for those who develop limited complications (LC), during which the patients are assumed to recover following appropriate treatment. The patients with CR or SC were further assumed to progress and develop PD. Disease-specific mortality was observed only after patients develop PD, and an additional all-cause mortality was also assumed from all the five health states.[14]

In cases of chronic diseases where patients move through different health states, the Markov model allows a possibility to move between different health states and is much better suited than a decision tree, which is more suitable for acute conditions with unidirectional movement. Since the overall survival is short, and there are several other health states such as severe complications, a partitioned survival model does not offer any significant advantage. The Markov model also allows us to estimate costs and utilities using a hypothetical cohort when individual patient-level data are not available. Similar methods have been used in cost-effectiveness analyses for cervical cancer interventions.[7,15]

The model starts with patients at age 55 years, the median age at diagnosis.[3] On the basis of the clinical evidence, we

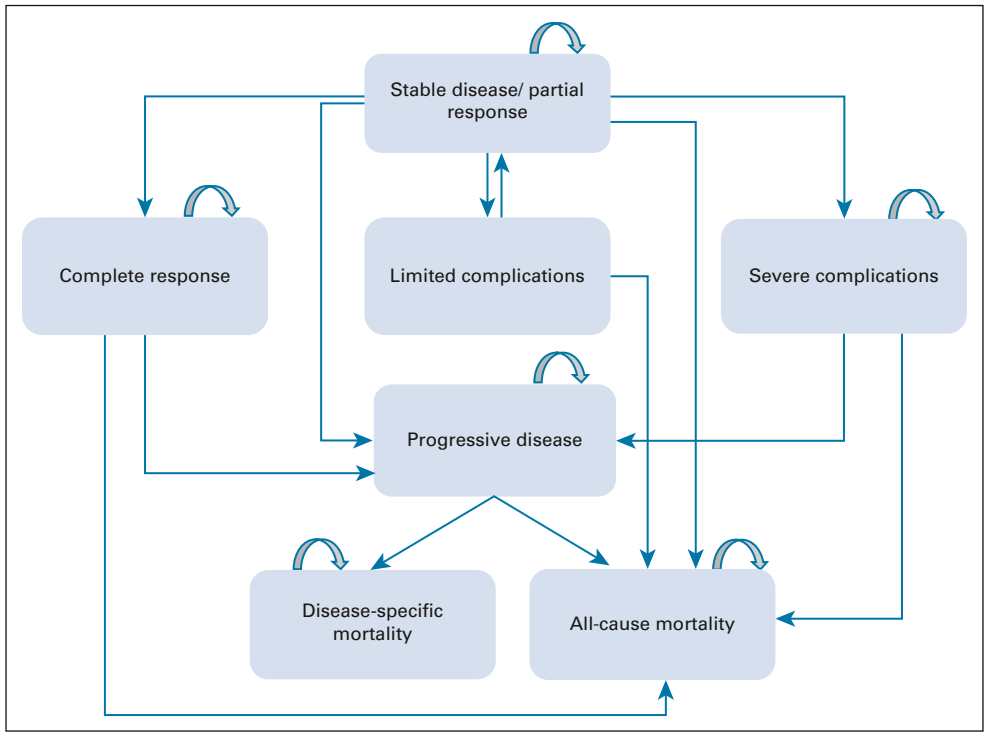

FIG 1. Model structure.

assessed CR after completion of six treatment cycles.[13] LC included grade 2 or higher hypertension, whereas grade 3 or higher thromboembolism and fistula represented SC. In addition, nausea/vomiting and grade 4 or higher neutropenia represented acute side effects in both treatment regimens.[7,8] The management of complications and side effects was as per standard treatment guidelines.[16] Patients in PD received palliative care for pain management, vaginal discharge, and vaginal bleeding.[16]

Control and Intervention Arms

On the basis of the current standard of care for advanced cervical cancer cases in India,[8,13] the control arm comprised intravenous cisplatin (50 mg/m^2 on day 1) along with paclitaxel (175 mg/m^2 on day 1), once every 3 weeks. In the intervention arm, intravenous bevacizumab (15 mg/kg on day 1, once every 3 weeks) was added to cisplatin and paclitaxel.

Clinical Parameters and Utility Values

Monthly transition probabilities (Table 1) were derived from the GOG-240 trial.[8,17] On the basis of the method mentioned in the study by Keller et al,[18] the probability of achieving a CR or developing LC or SC was calculated using total number of patients in the SD/PR state (1,416 for patients in the intervention arm and 1,148 in the control arm) throughout the 30-month trial period.[8,18]

Because of lack of data, the probability of progression from CR and SD/PR was assumed to be same. Probability of progression was derived from progression-free survival curves of the GOG-240 trial.[17] We assumed a 90% probability of progression from SC state.[18] The probability of disease-specific mortality was derived from a study reporting stage-specific mortality rates following treatment for cervical cancer from India.[5] Finally, we used the age-specific all-cause mortality rate for the female population of India.[14] Utility values for different health states were obtained by analyzing the data collected from 202 patients with cervical cancer across six large cancer hospitals in India, as part of the Cancer Database for Cost and Quality of Life (CaDCQoL).[19] The patients were administered the EQ-5D-5L tool to measure the health-related quality of life. The Indian tariff values were used to calculate the index utility score for different health states.[20] Since there were not enough sample of patients in PR health state, we estimated the utility value for the same by applying the gradient of utility between the health states of response and LC obtained from published literature (Table 1).[7]

Costs of Treatment

The present analysis included both the health system cost and the patient-level OOPE incurred during the duration of treatment. The health system cost accounted for the outpatient consultations, diagnostics, day care, inpatient stay, etc. The OOPE included expenses incurred on travel, boarding/lodging, food, and user fee. Since the cost of drugs and diagnostics were assessed as part of health system cost, we excluded them from OOPE to avoid double counting. The unit health system cost of specific services was derived from the previously undertaken costing studies from India (Table 2).[21,22] Where published cost data were not available, estimates from reimbursement rates of

TABLE 1. Model Input Parameters

Parameters	Value (SE)	Source
Monthly transition probabilities for the control arm		
SD/PR to CR	0.0148 (0.0015)	17
SD/PR to LC[a]	0.0035 (0.0003)	17
SD/PR to SC[a]	0.0043 (0.0004)	17
SD/PR or CR to PD	0.1420 (0.0145)	17
SC to PD	0.90 (0.0918)	7
PD to disease-specific mortality	0.1680 (0.0171)	5
Monthly transition probabilities for the intervention arm		
SD/PR to CR	0.0219 (0.0022)	17
SD/PR to LC[a]	0.0389 (0.0039)	17
SD/PR to SC[a]	0.0218 (0.0022)	17
SD/PR or CR to PD	0.0789 (0.0080)	17
SC to PD	0.90 (0.0918)	7
PD to disease-specific mortality	0.1680 (0.0171)	5
Age-specific all-cause annual mortality rates, years		
55-59	0.0103 (0.0010)	14
60-64	0.0163 (0.0016)	14
65-69	0.0251 (0.0025)	14
Health state utility values (quality of life)		
SD	0.406 (0.0414)	[b]
PR	0.521 (0.0531)	[c]
CR	0.694 (0.0708)	[b]
LC	0.304 (0.0310)	[b]
SC	0.213 (0.0217)	[b]
PD	0.213 (0.0217)	[b]

Abbreviations: CaDCQoL, Cancer Database for Cost and Quality of Life; CR, complete response; LC, limited complications; PD, progressive disease; PR, partial response; SC, severe complications; SD, stable disease.

[a]Limited complications include hypertension; severe complications include thromboembolism and fistula (both genitourinary and gastro-intestinal fistula).

[b]Denotes CaDCQoL study data used.

[c]Denotes percentage gradient of response to limited complication from the literature of Minion et al.[7]

central government health scheme was used.[23,24] Price of drugs was assessed from procurement prices of Rajasthan Medical Services Corporation.[25] The information on type and quantity of health services (including diagnostics) used by the patient in a particular health state was derived on the basis of the standard guidelines and clinician's expert opinion.[13] The cost of the drugs was calculated assuming an average weight and height of 55 kg and 162 cm, respectively, for an Indian female.[30]

Sensitivity Analysis

A multivariable probabilistic sensitivity analysis was undertaken to estimate the effect of joint parameter uncertainty.[31] Under probabilistic sensitivity analysis, all cost parameters were assigned gamma distribution, whereas utility values and probabilities/proportions were assigned beta distribution. SE was used to create a distribution around the point estimate of a parameter. In cases where SE was not reported, a variation of 40% and 20% on either side of the base value was used for cost and clinical parameters, respectively. The median value of ICER along 2.5th and 97.5th percentiles was calculated using 999 Monte Carlo simulations.[32] Univariate sensitivity analysis was also undertaken to assess the effect each parameter on ICER. Univariate sensitivity analysis was done to assess the impact of uncertainty in individual parameters on the ICER value. The results have been reported using a tornado diagram in Figure 2, to reflect the variation in resulting ICERs with the variation in the parameters. The parameter value was decreased and increased by 20%, to see its effect on deterministic ICER. Further, the effect on ICER with a discount rate of 5% was assessed. Lastly, the effect on the ICER value by considering the price of branded version of bevacizumab in India was also assessed.

Ethical Approval

Ethical approval was obtained from Institutional Ethics Committee of Post Graduate Institute of Medical Education and Research, India, with reference number IEC-03/20202-1565.

RESULTS

Absolute Outcomes

Table 3 reports the absolute and incremental discounted median cost, health outcomes, and cost-effectiveness ratio of treating patients with advanced and metastatic cervical cancer with either of the therapeutic regime. Per-patient LY and QALY lived following treatment with chemotherapy alone was 1.06 (0.93-1.20) years and 0.46 (0.36-0.56) years, respectively. Similarly, a patient after treatment with bevacizumab plus chemotherapy lived a total of 1.33 (1.19-1.49) LY and 0.585 (0.48-0.70) QALY. Furthermore, the total lifetime cost incurred was $1,478 US dollars (USD; 1,308-1,692) and $5,295 USD (4,012-7,030) for a patient treated on chemotherapy alone and bevacizumab plus chemotherapy, respectively.

Incremental Cost, Outcomes, and Cost Effectiveness

As reported in Table 3, over the lifetime of a patient with advanced and metastatic cervical cancer, treatment with bevacizumab results in a gain of 0.275 LY (3.30 life-months) and 0.129 QALY (or 1.55 quality-adjusted life-months) at an additional cost of $3,816 USD (2,513-5,571) compared with standard chemotherapy alone. This results in an incremental cost of $19,080 USD (7,230-52,434) per LY gained and $34,744 USD (15,782-94,914) per QALY gained with the use of bevacizumab. As per Indian guidelines, we compared the value of ICER with one-time per-capita gross domestic product (GDP) of India to

TABLE 2. Cost Parameters

Parameters	Value (SE)		Source
	₹	USD	
Health system cost			
Outpatient consultation (per visit)	639 (131)	9 (2)	21
Day care for chemotherapy (per visit)	1,038 (111)	14 (1.5)	22
Inpatient care (per bed day)	3,207 (655)	43 (9)	21
PET scan	14,663 (1,693)	198 (23)	23
Chest x-ray	60 (7)	0.81 (0.09)	23
CT chest	4,500 (519)	61 (7)	23
CT abdomen	4,500 (519)	61 (7)	23
MRI abdomen	5,000 (1,020)	67 (14)	24
CBC + RFT + LFT	585 (119)	8 (1.6)	[a]
CBC + RFT	360 (73)	5 (1)	[a]
Biopsy	1,362 (145)	18 (2)	22
Coagulogram	553 (113)	7.5 (1.5)	24
OOPE			
User fee (per visit)	279 (56.9)	3.7 (0.76)	[b]
Other direct nonmedical expenditure (per visit)	1,509 (172)	20.3 (2.32)	[b]
Price of drugs			
Cisplatin per mg	3.36 (0.685)	0.04 (0.009)	25
Paclitaxel per mg	1.80 (0.367)	0.024 (0.004)	25
Bevacizumab per mg (Biosimilar)	35.86 (7.31)	0.48 (0.098)	25
Bevacizumab per mg (branded drug)	297 (60.6)	4.0 (0.817)	26
Cost of management of complications/side effects			
Fistula per procedure	16,000 (3,265)	216 (44)	24
Thromboembolism per month	3,075 (628)	42 (8.5)	[a]
Neutropenia per month	30,850 (6,296)	416 (85)	[a]
Hypertension per month	284 (58)	4 (0.8)	27
Nausea and vomiting per month	154 (31)	2 (0.4)	[a]
Grade 3 nausea and vomiting	209 (43)	3 (0.6)	[a]
Cost of best supportive care			
Gastrointestinal bleeding lifetime	738 (151)	10 (2)	[a]
Vaginal discharge lifetime	162 (33)	2 (0.4)	[a]
Pain per month	607 (124)	8 (1.7)	[a]
2DRT	4,888 (997)	66 (13)	24

NOTE. All the cost estimates in this study pertains to the base year of 2020. The unit costs that were derived from the previous studies were inflated accordingly, on the basis of the GDP deflator indices for India.[28] Cost estimates are presented both in ₹ as well as USD. Conversion rate for the year 2020 of 1 USD = 74.13₹ was used.[29]

Abbreviations: 2DRT, two-dimensional radiotherapy; ₹, Indian rupees; CaDCQoL, Cancer Database for Cost and Quality of Life; CBC, complete blood count; CT, computed tomography; LFT, liver function test; MRI, magnetic resonance imaging; OOPE, out-of-pocket expenditure; PET, positron emission tomography; RFT, renal function test; STG, standard treatment guidelines; USD, United States dollars.

[a]Denotes that cost was derived on the basis of normative costing using standard treatment guidelines and expert opinion, as well as published unit costs and government procurement prices.

[b]Denotes CaDCQoL study data used.[7]

conclude the cost effectiveness of bevacizumab.[12] We found that the use of bevacizumab at an incremental cost of $34,744 USD per QALY gained is much higher than the per-capita GDP of $1,965 USD (₹145,679) for India in 2020 and hence deemed not cost effective. Even using a three-times per-capita GDP value of $5,895 USD (₹437,037) as threshold,[33] bevacizumab is not cost effective for treating advanced and metastatic cervical cancer in India.

As shown in Figure 3, a cost-effectiveness acceptability curve has been prepared showing the probability of the drug bevacizumab of being cost effective at various willingness-to-pay thresholds. It shows that there is zero probability of bevacizumab being cost effective till the willingness-to-pay threshold is $13,350 USD, which is around 6.8-times the per-capita GDP value of India.

Sensitivity Analysis

Univariate analysis showed that ICER is most sensitive to price and dosage of bevacizumab ($34,771-$23,904 USD; Fig 2). It is also sensitive to utility values of SD ($27,134-$31,930 USD) and PR health states ($26,222-$33,293 USD). Furthermore, when discount rates were varied to 5%, the ICER was $29,756 USD. Decreasing the transition probability to move from SD or CR to PD in case of bevacizumab by 50% and 90% resulted in an ICER of $18,288 USD and $14,691 USD, respectively. If the price of branded drug is considered, the ICER goes up significantly higher—$195,251 USD (112,993-643,595).

Model Validation

The median survival time and survival rate of the control arm was compared with the local epidemiologic data from India. Our study reported a median survival time of 11 months and 2-year survival rate of around 10% following treatment with routine chemotherapy. These model outcomes corroborate with the findings from an Indian prospective cohort study that reported a median survival time and 2-year survival rates of around 9 months and 12%, respectively, among those in stage IV cervical cancer.[5]

We found that the lifetime months gained by a patient treated with bevacizumab plus chemotherapy compared with chemotherapy alone is around 3.3 months. Furthermore, 9.5%, 19.4%, and 34% of patients achieved a complete response, and develop severe and limited complications, respectively, over the duration of treatment regimen given to a cohort of 1,000 patients. All these findings are consistent with the results of the GOG-240 trial.[8,17]

DISCUSSION

For patients with advanced and metastatic cervical cancer in India, chemotherapy is the standard of care. Cisplatin at a dose of 50 mg/m^2 given once in every 3 weeks was a historic standard of treatment for these patients.[34] However, with the use of cisplatin concurrent with radiation in majority of these patients, they become resistant to cisplatin for recurrent or persistent disease.[35] In view of the nature of the disease with poor gains in survival, assessment of toxicity, quality of life, and cost of treatment become paramount.

The GOG-204 trial established paclitaxel and cisplatin as the standard of care for this subgroup of patients with cervical cancer.[8,36] Dismal outcomes after combination chemotherapy focused the attention toward molecular-targeted agents. Cervical cancers are associated with increased levels of vascular endothelial growth factor, which is associated with poor prognosis and is the target of antiangiogenesis therapy such as bevacizumab.[37] GOG-240 established that addition of bevacizumab to the standard chemotherapy increased the response rate and overall survival for these patients.[8]

Globally, 85% of the patients with cervical cancer live in low- and middle-income countries where access and affordability of bevacizumab remain limited.[38] Payers face the difficult choices while determining which interventions to include in the health benefit packages.[39-42] Similar is the case of bevacizumab, which is considered as a costly anticancer drug.[43] The Health Technology Assessment Board of India recommends the use of one-time per-capita GDP of India as the threshold for cost effectiveness.[12] On the basis of the per-capita GDP of $1965 USD (₹145,679) during the year 2020, our findings show that the treatment comprising bevacizumab plus chemotherapy is not cost effective for advanced and metastatic cervical cancer in India. We found that the cost of treating adverse events of this intervention is high, because of which the drug remains cost ineffective even after reducing its prices similar to the prices of control arm drugs. Our study finding is in line with the results of previous economic evaluations.[7,9] Economic evaluations conducted on the use of bevacizumab for other indications such as metastatic renal cancer,[44] metastatic breast cancer,[45] and metastatic colorectal cancer[46] have also shown it to be a cost-ineffective drug.

We need to investigate various measures, besides price reduction, which may help to make this treatment cost effective for India. Currently recommended dose of bevacizumab is 15 mg/kg (once every 3 weeks), which may be reduced to lower doses of 5-10 mg/kg at once every 3 weeks (recommended for colorectal cancer, glioblastoma, ovarian cancer, and renal cell carcinoma) after evaluation in future trials.[47] This will reduce the cost of treatment by nearly 50%. However, with an ICER of $28,069 USD, bevacizumab even with a reduced dosage to 7.5 mg/kg, is not cost effective for the treatment of advanced and metastatic cervical cancer in India.

Moore et al[48] have identified five factors associated with poor survival in patients with cervical cancer, which include poor performance status, pelvic recurrence, prior radiosensitizing chemotherapy, recurrence within 1 year, and

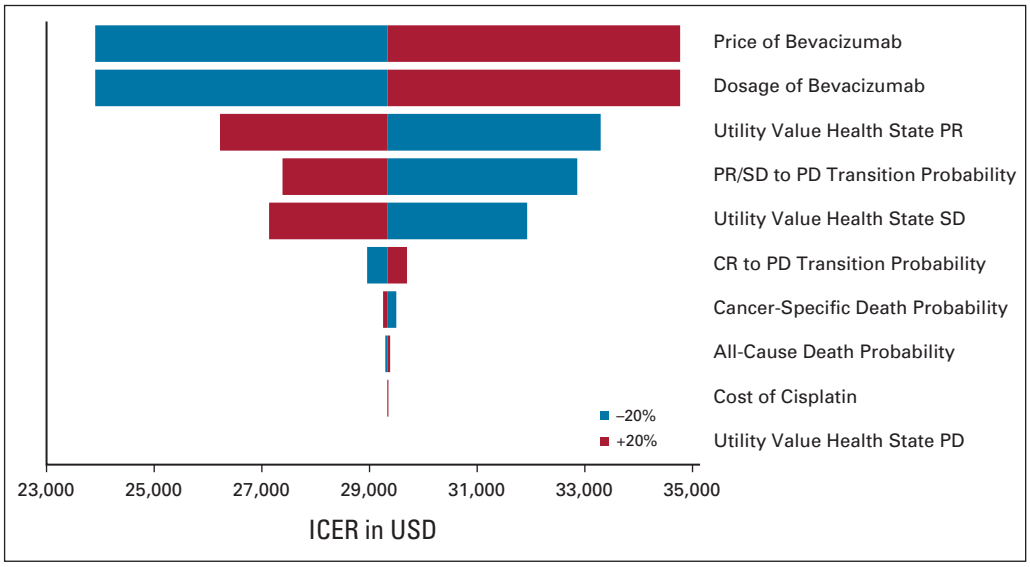

FIG 2. Tornado diagram. CR, complete response; ICER, incremental cost-effectiveness ratio; PR, partial response; SD, stable disease; USD, US dollars.

African American race. In the GOG-240 trial, using Moore's criteria, the hazard ratios for death in low-risk, medium-risk, and high-risk patients were 0.96, 0.673, and 0.536, respectively.[49] However, as shown in our sensitivity analysis, even in the best case scenario, where we reduced the probability to progress in case of bevacizumab by 90% of base value, the drug is not cost effective. This implies that even if the drug was to be used among subgroups where its effectiveness could be more than average, it is unlikely to offer a value for money. Doublet chemotherapy with paclitaxel and cisplatin has a tolerable toxicity profile and reasonable disease control. It is seen to be cost effective in our study and should be continued to be prescribed for resource-limited countries such as India.

TABLE 3. Discounted Probabilistic Median Costs, Health Outcomes, and Cost Effectiveness of Using Bevacizumab Along With Chemotherapy as Compared to Chemotherapy Alone for the Treatment of Advanced and Metastatic Cervical Cancer

Variable	Control Arm	Intervention Arm (biosimilar)
Lifetime cost per patient		
₹	109,617 (96,996-125,501)	392,540 (297,423-521,180)
USD	1,478 (1,308-1,692)	5,295 (4,012-7,030)
Absolute health outcome per patient		
LY lived	1.059 (0.925-1.21)	1.335 (1.195-1.492)
QALY lived	0.456 (0.365-0.555)	0.585 (0.475-0.695)
Incremental cost per patient		
₹	282,922 (186,332-413,041)	
USD	3,816 (2,153-5,571)	
Incremental health outcomes per patient		
LY gained	0.275 (0.052-0.469)	
QALY gained	0.129 (0.032-0.218)	
Incremental cost per LY gained		
₹	1,414,406 (536,004-3,886,952)	
USD	19,080 (7,230-52,434)	
Incremental cost per QALY gained		
₹	2,575,624 (11,69,972-7,035,979)	
USD	34,744 (15,782-94,914)	

NOTE. Values in parenthesis indicate 2.5th and 97.5th percentiles.
Abbreviations: ₹, Indian rupees; LY, life-year; QALY, quality-adjusted life-year; USD, United States dollars.

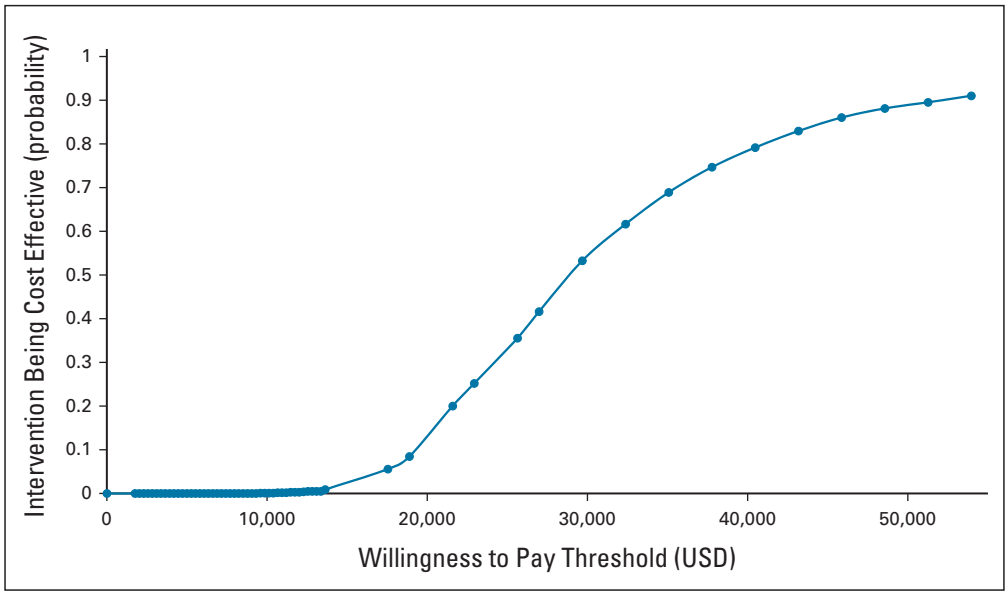

FIG 3. Cost-effectiveness acceptability curve. USD, US dollars.

Given the fact that novel treatments in advanced disease are not cost effective, the focus of disease control strategies should be on prevention. A decline of 70% in cervical cancer in the West is attributed to the effective screening and vaccination against human papillomavirus vaccine.[50] Previous cost-effectiveness analyses have also shown various preventive strategies in the form of screening and vaccination to be cost-effective options for India.[15,51]

On the basis of the standard of care, we had considered chemotherapy regimen of cisplatin plus paclitaxel as the control arm of the study. The effectiveness data from the GOG-240 trial for the control arm were based on the combination of two specific chemotherapy regimens comprising cisplatin plus paclitaxel and topotecan plus paclitaxel. We have assumed that the effectiveness parameters in terms of progression, rate of response, and occurrence of complications would be the same for the chemotherapy regimen of cisplatin plus paclitaxel as it is for the combination as assessed in the GOG-240 trial. Because of relative lack of literature, we assumed that there was a 90% probability of moving from severe complications to progressive disease.[18] A univariate sensitivity analysis to test how this assumption affects the overall findings on cost effectiveness was done. Our univariate sensitivity analysis shows that decreasing this probability from 90% to 30% reduces the ICER value by around 7% only. This lack of major impact on ICER is explained on the basis of the fact that the proportion of individuals who develop severe complications is very small. As a result, we conclude that the findings of our analysis are not sensitive to the assumption of 90% probability of progression.

In conclusion, chemotherapy along with bevacizumab is not a cost-effective alternative when compared with chemotherapy alone at a threshold of either 1-time or 3-times per-capita GDP for treating patients with advanced cervical cancer in India. Doublet chemotherapy with paclitaxel and cisplatin has a tolerable toxicity profile, has reasonable disease control, and is cost effective; hence, it should be continued to be prescribed in standard treatment guidelines for resource-limited countries such as India.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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