REVIEW ARTICLE

A NARRATIVE REVIEW OF THE COST-EFFECTIVENESS OF BEVACIZUMAB IN COLORECTAL CANCER TREATMENT

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ABSTRACT

Introduction: Colorectal cancer (CRC) is one of the most prevalent malignancies globally and a major cause of cancer-related mortality. Bevacizumab, a monoclonal antibody targeting vascular endothelial growth factor (VEGF), has demonstrated clinical efficacy in combination with chemotherapy for metastatic CRC (mCRC). However, its high cost raises concerns regarding cost-effectiveness, particularly in resource-limited settings. **Objective:** This study aimed to evaluate the cost-effectiveness of adding bevacizumab to chemotherapy through a narrative review of recent economic evaluations. **Methods:** A literature search was conducted in PubMed, Scopus, and ScienceDirect to identify studies published between 2020 and 2025. Six eligible studies were included, most of which were conducted in high- or upper-middle-income countries. Data on incremental cost-effectiveness ratios (ICERs), quality-adjusted life years (QALYs), and willingness-to-pay (WTP) thresholds were extracted and analysed. **Results:** All studies used ICERs as the primary outcome and applied country-specific WTP thresholds. The majority concluded that adding bevacizumab was not cost-effective, primarily due to high ICERs exceeding WTP thresholds. Although clinical benefits such as improved progression-free and overall survival were reported, the economic value of bevacizumab remains limited due to its high cost, complex manufacturing, and originator pricing. One study suggested potential cost-effectiveness with biosimilar bevacizumab, and another supported optimized dosing strategies. **Conclusion:** In conclusion, while bevacizumab offers clinical advantages, its addition to standard chemotherapy in mCRC is generally not cost-effective under current pricing. Further context-specific research is needed to support informed decision-making, especially in constrained healthcare systems.

Keywords: : Bevacizumab, colorectal cancer, cost-effectiveness, chemotherapy

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Article History Details

Received: 26 Januari 2026
Revisiedi: 10 Maret 2026
Acceptedi: 26 April 2026

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INTRODUCTION

Colorectal cancer (CRC) ranks among the three most commonly diagnosed cancers worldwide and is the second leading cause of cancer-related deaths. Data from GLOBOCAN 2020 indicate approximately 1.9 million new CRC cases globally (1,2). Around 15% of cases are diagnosed at stages 0–I, 20–30% at stage II, 30–40% at stage III, and 20–25% at stage IV. A considerable number of patients are diagnosed at advanced stages (III/IV), with nearly one-third developing metastatic disease over time (3,4).

The standard approach for managing metastatic CRC involves systemic chemotherapy, often using doublet regimens such as FOLFOX or FOLFIRI, or more intensive triplet regimens like FOLFOXIRI (5,6). In recent years, targeted therapies have been developed to address specific molecular characteristics and tumor locations. One such agent is Bevacizumab, an FDA-approved monoclonal antibody that inhibits vascular endothelial growth factor (VEGF). It has been shown to enhance the effectiveness of multi-drug chemotherapy and fluoropyrimidine-based treatments in metastatic cases (7,8).

Multiple clinical trials have assessed the impact of adding Bevacizumab to standard chemotherapy. Findings from phase III studies suggest improved overall survival (OS), progression-free survival (PFS), and treatment response rates when Bevacizumab is included. However, the high cost of these therapies remains a concern. For example, a four-cycle course of Bevacizumab can cost approximately USD 4,000. In healthcare systems with limited financial resources, it becomes essential to assess whether the clinical benefits of such high-cost treatments justify their economic burden (9,10,11).

Accordingly, this study aims to assess the cost-effectiveness of Bevacizumab in the treatment of metastatic colorectal cancer, with particular focus on its value in settings with constrained healthcare budgets.

METHODS

Study design

A comprehensive literature search was conducted using major academic databases, including Scopus, PubMed, and ScienceDirect, targeting publications from 2020 to 2025. Two distinct search strategies were developed to capture the broadest range of relevant studies, focusing on the keywords: cost-effectiveness, Bevacizumab, and colorectal cancer. In addition to database searches, the reference lists of identified articles and relevant review papers were manually screened to uncover any additional eligible studies. An overview of the study identification and selection process is illustrated in Figure 1.

Data Extraction

Data extraction was performed independently by three reviewers using a standardized template. Key information extracted from the included studies is summarized in Tables 1 and 2. The extracted data cover various aspects such as author, study region, analytical perspective, population characteristics, type of economic modeling, time horizon, discount rate, interventions, measures of effectiveness (e.g., QALYs or DALYs), incremental cost-effectiveness ratios (ICERs), sensitivity analyses, and decision-making criteria

RESULTS

The database search yielded possible studies for the review. The number was reduced to after removal of duplicates and an initial selection on the basis of titles. After screening of the titles, abstract, and full text, six studies were included in this review. The detailed of study review can be seen in figure 1.

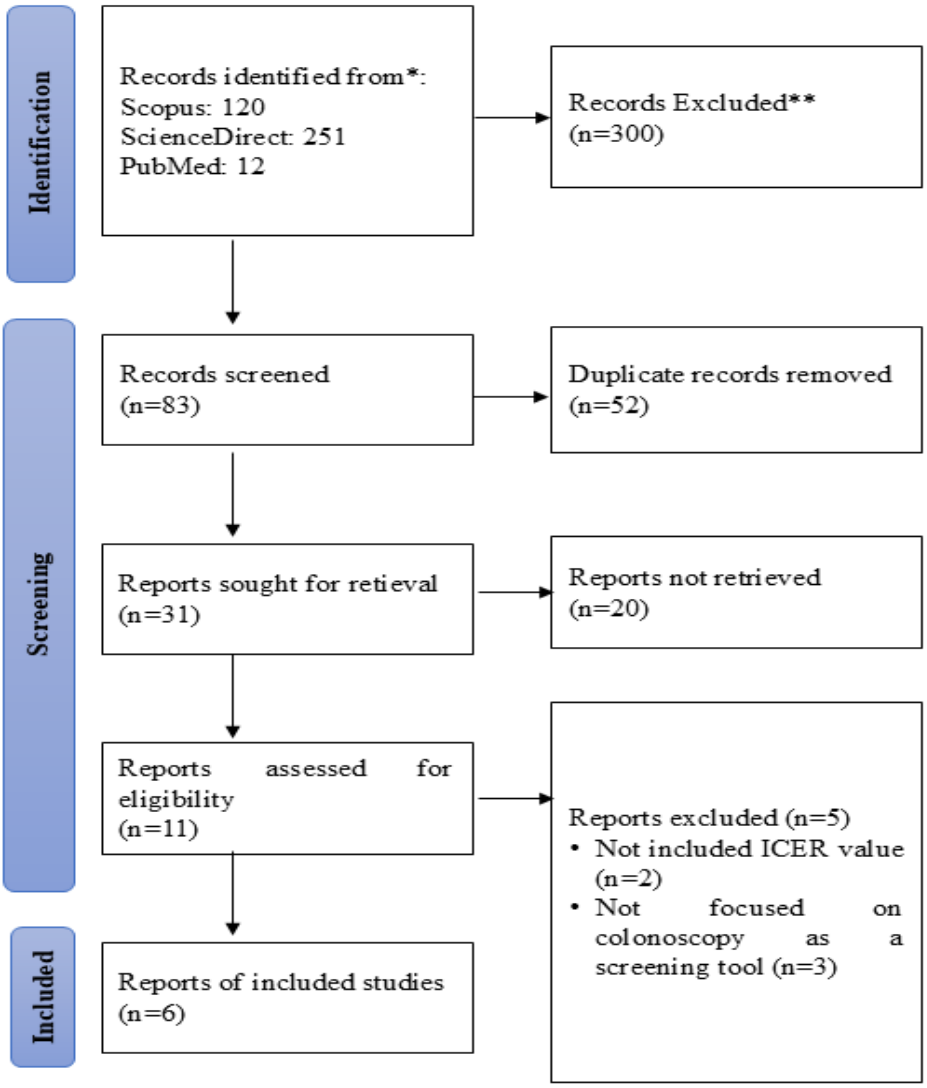

Figure 1. PRISMA flow diagram in the study selection stage

Note: *Consider, when feasible, reporting the number of records identified from each database or register searched (rather than the total number across all databases/register.
**When automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools (excluded by years range, limited only English articles, limited only original research article).

Study characteristics

The six studies included different regions (Table 1); most focused on high income country (HIC), such as Canada, China, Japan, Taiwan and two categorized on upper-middle income country (UMI), such as Iran and Indonesia (12-17). The perspectives were conducted from societal, payer, and provider. The majority of studies (3 of 6) focused on combination of bevacizumab with usual chemotherapy, one study focused on different type of Bevacizumab, one study focused on different dose, and one study focused on different chemotherapy's combination. All studies population is in stage IV / metastatic colorectal cancer.

Time-horizon and discount rate

For cost-effectiveness analyses of Bevacizumab added, these studies were generally based on a lifetime perspective (4 of 5), and just one only using 4-years' time-horizon. For discount rate, most of studies using discount rate ranging 3%-5%, and two studies not using discount rate.

Table 1. General Characteristics of Selected Articles

Study	Region	Perspective	Population	Method	Time Horizon	Discount Rate
Lu et al (12)	Canada	Payer	mCRC patients	Retrospective cohort study	Lifetime	-
Li et al (13)	China	Provider	Patient with first progression of metastatic colorectal cancer	Markov Model	4-years	5%
Kristin et al (14)	Indonesia	Provider	Patient with metastasis colorectal cancer	Markov Model	Lifetime	3%
Sugiura et al (15)	Japan	Payer	Patients with chemo refractory metastatic colorectal cancer	Markov Model	Lifetime	3.5%
Shi et al (16)	Taiwan	Societal	Patients with metastatic colorectal cancer	A long-term and prospective cohort study	Lifetime	3%
Jafari et al (17)	Iran	Societal	Stage IV Colorectal Patients	Decision Tree Model	Lifetime	-

Study outcomes

Outcomes of the six selected studies publications are provided in Table 2. The effectiveness of therapeutic regimens mostly took QALYs. All the cost data is used US$. All the studies include ICER as the main outcomes, which are the most important measurement indicators in an economic evaluation, especially ICER. All studies using WTP threshold to make a decision of cost-effective on the interventions. We identified three studies is compared combination chemotherapy and Bevacizumab with only chemotherapy (13-15). All studies found the addition of Bevacizumab to be not cost-effective. This is caused by all ICER values being above the WTP thresholds used in each country. One study compares the newest type Bevacizumab, namely Bevacizumab biosimilars, the result is probability being cost-effectiveness in WTP threshold $50,000 (12). One study compare different dose of chemotherapy is Irinotecan, will be cost-effective at a WTP $26,263.5/QALY.(16) One study compares Bevacizumab+FOLFOX 6 with Cetuximab+FOLFOX 6, Cetuximab was more cost-effective for adding to FOLFOX 6 (17).

For the sensitivity analysis, most of the studies conducted a one-way sensitivity analysis, as well as a probabilistic sensitivity analysis, which demonstrated the impact of the results of all the combined uncertainty for all the parameter values.

DISCUSSION

To the best of our knowledge, this is the first review to comprehensively summarize economic evaluations concerning the addition of Bevacizumab to chemotherapy in patients with metastatic colorectal cancer. We identified six studies that assessed the cost-effectiveness of this intervention in such patients. These studies were categorized based on the similarities in intervention types and outcome measures.

This study analyses the cost-effectiveness of adding bevacizumab to standard therapy for metastatic colorectal cancer. Due to article length constraints, we did not perform a formal quality assessment of the included reports.

Table 2. Cost-effectiveness Analysis in Selected Studies

Study	Interventions	Comparator	QALYs	LY	Cost	ICER	Sensitivity Analysis	Conclusion
Lu et al (2024)	Bevacizumab biosimilars	Originator Bevacizumab	Int: 0.63 Com: 0.64	Int: 0.87 Com: 0.87	Int: $84,162 Com: $90,541	$637,900/QALYs	Alternative scenarios including (1) using a 2-year time horizon and (2) calculating total 1-year and 2-year patient-level costs and effects by biosimilar subgroups	Probability being cost-effectiveness in 99,9% in WTP Threshold $50,000
Li et al (2023)	Bevacizumab plus chemotherapy	Chemotherapy alone	Int: 0.85 Com: 0.73	Int: 1.18 Com: 4	Int: $30,789 Com: $8,027	$188,904/QALYs	One-way sensitivity analysis and PSA	Not cost-effective at the WTP threshold of $38,201.

Study	Interventions	Comparator	QALYs	LY	Cost	ICER	Sensitivity Analysis	Conclusion
Kristin et al (2021)	Bevacizumab + FOLFOX/FOLFIRI/XELOX	FOLFOX/FOLFIRI/XELOX	**Secondary data:** Int: 2.07 Com: 1.90 **Real word data:** Int: 3.50 Com: 2.62	-	**Secondary data:** Int: $38,720 Com: $30,552 **Real-world data** Int: $67,774 Com: $42,789	**Secondary data:** $49,312/QALY **Real-world data** $28,446/QALY	One-way sensitivity analysis and PSA	Not cost-effective at the WTP threshold of $10,800/QALY in Indonesia. Will be 80% cost-effective at 300 million IDR.
Sugiura et al (2021)	Bevacizumab+TAS-102	TAS-102 monotherapy	Int: 0.732 Com: 0.501	-	Int: $8424.188 Com:$3434.834	$21,553.630/QALY	One-way sensitivity analysis and PSA	Not cost-effective at a WTP of less than $50,000 per QALY
Shi et al (2022)	dose escalation of irinotecan + Bevacizumab	Irinotecan + Bevacizumab	Int: 1.88 Com: 1.65	-	Int: $54,742 Com: $54,608	$583/QALYs	PSA and USA	Cost effective at a WTP $26,263.5/QALY
Jafari et al (2023)	FOLFOX6+Bevacizumab	FOLFOX6 +Cetuximab	Int: 0.19 Com: 0.22	-	Int: $16,746.13 Com: $15,191.05	Dominated	One-way sensitivity analysis and PSA	FOLFOX6+Cetuximab was more cost-effective (dominant) than FOLFOX6+Bevacizumab

Based on the findings, the addition of bevacizumab may not be considered cost-effective. The incremental cost-effectiveness ratio (ICER) per quality-adjusted life year (QALY) is widely regarded as the gold standard in economic evaluations. According to the World Health Organization (WHO) Commission on Macroeconomics and Health, an intervention is considered highly cost-effective if the ICER is less than the country's per capita gross domestic product (GDP), and cost-effective if the ICER is less than three times the per capita GDP or falls within the country's willingness-to-pay (WTP) threshold (18).

All studies reviewed suggest that the addition of bevacizumab is not cost-effective. However, its effectiveness in combination therapy is greater than chemotherapy alone. Previous research has demonstrated that the bevacizumab plus FOLFOX treatment strategy is superior to FOLFOX alone (19,20). The combination of bevacizumab with chemotherapy enhances clinical outcomes, leading to a significant increase in progression-free survival and overall survival (21). Bevacizumab functions as an angiogenesis inhibitor, effectively blocking the binding of vascular endothelial growth factor A (VEGFA) to its receptors, VEGFR-1 and VEGFR-2. This mechanism induces beneficial alterations in tumor vasculature, ultimately inhibiting tumor growth (22).

One study reported that the addition of bevacizumab, when compared with other targeted therapies such as cetuximab, is not cost-effective (17). This finding is consistent with the study by Song et al. (2024), which indicated that although bevacizumab improves anti-tumor activity and disease control, cetuximab and panitumumab demonstrate stronger therapeutic effects (20). Moreover, cetuximab has been shown to enhance the efficacy of irinotecan and radiotherapy in experimental systems (23).

The high cost of add Bevacizumab made these regimens being not cost-effective. All studies conduct the high cost of adding Bevacizumab, compare with chemotherapy alone or Cetuximab. This high cost caused by multiple factors such as, the expensive biological production process, the price of originator price, and non-effective cost in several contexts (12,14).

This review has several limitations. First, only recent studies published between 2020 and 2025 were included, which may limit the comprehensiveness of the evidence base. Second, we did not conduct a formal quality assessment of the included studies due to constraints on article length. Third, the studies included in this review were heterogeneous in terms of design, population, and outcome measures, which precluded the possibility of performing a meta-analysis. Therefore, this review provides a comparative analysis rather than a quantitative synthesis. Further research is needed to comprehensively assess the cost-effectiveness of bevacizumab as an add-on therapy.

CONCLUSION

This review is the first to comprehensively synthesize economic evaluations of adding bevacizumab to chemotherapy in patients with metastatic colorectal cancer. Although clinical evidence supports the enhanced effectiveness of bevacizumab in combination with chemotherapy—demonstrating improved progression-free and overall survival—the current body of literature consistently indicates that this intervention is not cost-effective. High incremental costs, largely attributed to the complex production process of biologics and pricing strategies of originator drugs, result in unfavourable ICERs that exceed commonly accepted willingness-to-pay thresholds.

The comparative analysis of six studies highlights that, while bevacizumab

offers clinical benefits, its economic value remains limited, especially when compared to chemotherapy alone or alternative targeted therapies such as cetuximab. Due to methodological limitations—including lack of quality assessment and heterogeneity across studies—a meta-analytical approach was not feasible. Further high-quality, context-specific research is necessary to better assess the cost-effectiveness of bevacizumab in diverse healthcare settings and to inform policy decisions regarding its use.

Acknowledgements

The authors were financially supported by the PRODIA EDUCATION AND RESEARCH INSTITUTE (PERI).

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