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# Cost effectiveness of fruquintinib for colorectal cancer: a systematic review

Mona Thangamma AG[1], Shree Rath[2], Andria J N Sirur[3], Vijaya Kumar Uthakalla[4], Santenna Chenchula[5], Swati[6], Tuhin James Paulo[7], Debopriya[8], Chanchal Goyal[9], Ujjawal Sharma[10], Gopal Vinod[11], Firdaus Samad[12], Arindam Biswas[13], Sree Sudha T Y[14]*

[1] Manipal Academy of Higher Education Karnataka, India.
[2] All India Institute of Medical Sciences, Bhubaneswar, Odisa, India.
[3] Department of Commerce, Manipal Academy of Higher Education Karnataka, India.
[4] Community Medicine, Dr. NTR University of Health Sciences, Alluri Sitarama Raju Institute of Medical Sciences, Eluru, India.
[5] All India Institute of Medical Sciences Bhopal, India.
[6] Mahatma Gandhi Institute of Medical Sciences, Wardha, Maharashtra, India.
[7] Department of Pharmacy Practice, ISF, College of Pharmacy Moga Punjab, India.
[8] Department of Pharmaceutics, Delhi Pharmaceutical Sciences and Research University New Delhi, India.
[9] Department of Health Research, Centre for Evidence for Guidelines, New Delhi, Delhi, India.
[10] Department of Human Genetics and Molecular Medicine, Central University of Punjab Bhatinda, India.
[11] Welcome Trust Research Lab, CMC, Vellore, India.
[12] Public Health, Indian Institute of Public Health Martin Luther Christian University Shillong, India.
[13] Public Health (Allied health), Indian Institute of Public Health Martin Luther Chritian University Shillong, India.
[14] Department of Pharmacology, All India Institute of Medical Sciences Deogharh, India.

*Correspondence: sudha.pharmacology@aiimsdeoghar.edu.in

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## Evidence in Context

- Colorectal cancer is a major health and economic challenge globally.
- Economic evaluations used advanced cost-effectiveness models comparing Fruquintinib with other treatments.
- Fruquintinib is cost-effective in China, with better ICER values than Regorafenib.
- Its cost-effectiveness is not supported when compared to placebo, exceeding economic thresholds.
- Findings emphasize the integration of economic and clinical outcomes in treatment decisions, with current data limited to China.

To view Article

## Abstract

**Background:** Colorectal cancer, one of the most prevalent cancers globally, originates from polyps in the colon or rectum, which can develop into cancer over time. It remains a leading cause of cancer-related deaths, imposing significant economic and healthcare burdens. As the incidence of colorectal cancer continues to rise, particularly in developing healthcare systems, understanding the economic impact of treatment options is critical for informing clinical decisions and shaping healthcare policies.

**Methods:** Following PRISMA guidelines, an extensive literature search was conducted through databases including PubMed, Embase, and Scopus up to 7 October 2024. The inclusion criteria targeted studies utilizing cost-effectiveness analysis frameworks like Markov and Partitioned-Survival models, comparing fruquintinib to other cancer treatments. Key outcome measures focused on Incremental Cost-Effectiveness Ratios and Quality-Adjusted Life Years.

**Results:** Of the 49 articles screened, seven studies were eligible for inclusion. These studies provided a detailed economic evaluation of Fruquintinib against Regorafenib, placebo, and best supportive care. Notably, Fruquintinib was cost-effective in the Chinese healthcare setting with an ICER of $26,508 per QALY compared to $35,607 for Regorafenib. However, it did not meet cost-effectiveness thresholds when compared with placebo, with an ICER exceeding three times the GDP per capita in China, reflecting the economic challenges of implementing new cancer treatments.

**Conclusion:** Fruquintinib shows promise as a cost-effective treatment for metastatic colorectal cancer, particularly in healthcare settings like China, providing significant QALY gains compared to traditional therapies. However, its adoption is highly dependent on local economic thresholds and healthcare systems. While this study underscores the need to integrate economic and clinical outcomes in cancer treatment decisions, the drug's approval and data are currently limited to China, making it difficult to conclude its cost-effectiveness globally.

***Keywords:*** *global burden of disease study, GBD, air pollution, cardiovascular disease, age-period-cohort, joinpoint regression, India*

# Introduction

Colorectal cancer (CRC) is a type of cancer that primarily affects the colon and rectum, which are parts of the large intestine. This form of cancer begins with the development of noncancerous growths called polyps on the inner lining of the colon or rectum. Over time, some of these polyps can transform into colorectal cancer. It's one of the most common types of cancer worldwide and a leading cause of cancer-related deaths [1].Colorectal cancer ranks as the third most prevalent cancer worldwide, contributing to approximately 10% of all cancer cases in 2020, there were approximately 1.93 million new cases and 0.94 million deaths due to colorectal cancer globally.The incidence of CRC is expected to rise significantly by 2040, with estimates suggesting a 63% increase in new cases and a 73% increase in deaths [2].

Colorectal cancer treatment integrates multiple modalities tailored to disease stage and specific patient factors. Surgery is typically the first-line treatment for localized colorectal cancer, meaning cases where the disease has not spread to other organs. Surgery aims to remove the cancerous tissues, and if the cancer is caught early, it can be highly effective. However, surgery is less effective in cases where the cancer has spread (metastasized) to other parts of the body [3]. For more advanced cases, Chemotherapy, including combinations like FOLFOX and FOLFIRI, plays a crucial role, particularly in advanced stages, although side effects and varying effectiveness pose challenges [4]. Targeted therapies such as EGFR inhibitors (e.g., cetuximab, panitumumab) are employed based on specific genetic markers in tumours, but mutations like KRAS can limit their efficacy [5]. Radiation therapy is another option, typically used alongside chemotherapy or for palliative care in advanced stages, restricted by its potential toxicity. Lastly, immunotherapy benefits patients with certain genetic markers like MSI-H or dMMR, offering significant advantages to those responsive to immune checkpoint inhibitors. Each treatment option balances benefits and limitations, necessitating personalized approaches based on detailed genetic and molecular tumour profiling [4]. Fruquintinib is a selective inhibitor of vascular endothelial growth factor receptors (VEGFR) 1, 2, and 3. It works by targeting and inhibiting the action of these receptors, which play a crucial role in the angiogenesis process that supplies blood to tumours. By blocking these pathways, fruquintinib hampers tumour growth and proliferation, making it an effective treatment option for conditions like metastatic colorectal cancer.Fruquintinib has been approved in China and recently by the FDA for use in specific mCRC cases [6].

The treatment of colorectal cancer imposes a significant economic burden both through direct medical costs and indirect costs such as lost productivity. Direct costs include hospital stays, chemotherapy, radiation, and surgical procedures. In the U.S., colorectal cancer has substantial financial implications, with significant out-of-pocket costs for patients, which can lead to financial toxicity. For example, patients often face high annual costs for treatments like chemotherapy, which can be as high as $5,600 per year [7]. Managing these costs within healthcare systems is challenging due to the expensive nature of cancer care and the need for prolonged treatment for many patients. Advanced therapies and the need for ongoing care, including primary treatment and follow-up, and management of side effects drive the high costs [8].This systematic literature review aims to provide a comprehensive assessment evaluating the cost-effectiveness of Fruquintinib for colorectal cancer. It helps determine whether these new treatments provide value relative to their costs, considering both their efficacy in extending quality-adjusted life years and their impact on healthcare expenditures.This analysis is vital for healthcare decision-makers, enabling informed decisions regarding the inclusion of new treatments in clinical practice, which can ultimately influence health policy and funding allocations.

**Review Question**

What is the cost-effectiveness of Fruquintinib for treating colorectal cancer compared to standard therapies, in terms of incremental cost-effectiveness ratio (ICER), quality-adjusted life years (QALYs), and overall healthcare costs?

# Methods

**Search Strategy**

This systematic literature review conforms to the highest standards of quality and transparency,

Adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines for economic evaluations, as detailed in PRISMA 2020 (Table S1) [9]. The review protocol was carefully designed and registered with the International Prospective Register of Systematic Reviews to ensure thoroughness and reduce bias (CRD42024598835). Our search strategy involved three key phases and utilized both MeSH terms and free text to target essential domains such as “Colorectal Cancer” (condition), cost (outcome), Fruquintinib (intervention), and a global context. Boolean operators "OR" and "AND" were used to effectively combine these terms. The initial search included databases like MEDLINE (PubMed) and Google Scholar and was expanded to others such as Embase (Ovid), Scopus, and Web of Science, covering all records up to 7 October 2024. Additionally, we performed backreferencing and forward citation tracking to identify relevant studies that might not have been captured in the initial searches, by reviewing the references of the included studies. The complete search strategy is presented in Table S2.

**Inclusion Criteria**

**Population:** Patients of all age groups diagnosed with colorectal cancer, irrespective of disease severity, gender, ethnicity, education, socioeconomic status, or geographical location.

**Intervention**: Fruquintinib

**Comparators:** Studies with or without a comparator

**Outcomes**

**Costs:** The total costs from multiple perspectives including societal, patient, healthcare payer, healthcare provider, and the ICER.

**Types of Studies:** Included studies with cost-effectiveness analyses (CEA), studies with both experimental (randomized controlled trials, quasi-experimental studies), and observational designs. Also, modelling studies such as decision trees, Markov, and simulation models are considered [10].

**Exclusion Criteria:** Excluded are studies that do not report on Fruquintinib or only provide data on patient-reported outcomes, utilities, or quality of life without associated cost details. Reviews, editorials, commentaries, methodological papers, and articles not published in English are also excluded.

**Study Selection**

A thorough and systematic method was used to select studies for inclusion in this review. We used Nested Knowledge software to screen identified studies for efficiency and consistency. Two independent reviewers (MT, NC) screened titles, abstracts, and full texts of all studies deemed potentially relevant to minimize bias and ensure objectivity. Disagreements were settled by consensus or, if needed, arbitration by a third reviewer (MN).

**Data Extraction**

A standardized form on Nested Knowledge was used to ensure the accuracy and reliability of data extracted from the studies included. Baseline characteristics and outcome data were independently extracted by two reviewers (MT and NC) from each study. These characteristics encompassed details such as author information, year of publication, study country, type of economic evaluation (EE), analytical approach, study perspective, population, and intervention specifics. The extracted outcome data primarily included mean costs and incremental cost-effectiveness ratios (ICERs). Any discrepancies encountered during the extraction process were resolved by consensus or, if required, arbitration by a third reviewer (MN).

**Quality Assessment**

Two independent reviewers (MT,NC) assessed the quality of the included studies using the CHEQUE checklist for model-based studies. The CHEQUE checklist evaluates model structure, data quality, parameter estimation, sensitivity analysis, and transparency. The scoring system is typically categorical, often using a Likert scale to rate each criterion from 'poorly addressed' to 'excellently addressed’. The final score, often an aggregate of these individual scores, provides a quantitative measure of the study's overall quality. This scoring system allowed for a quantitative assessment of the methodological quality of the included studies.

### Data Synthesis

Due to various factors like location, healthcare system specifics, timeframes, and analytical perspectives, outcomes of economic evaluations can vary widely. Guidelines often advise against combining primary outcomes from studies with significant differences in clinical environments or methodologies, as this heterogeneity can complicate meta-analyses by violating necessary pooling assumptions. To navigate these challenges, we adopted a structured narrative synthesis method to collate the economic evidence [11]. This approach involved a detailed presentation of each study's characteristics, methodological rigor, and findings. By evaluating these individual contributions, it was possible to discern overarching trends and areas of agreement, despite the inherent variability. For clarity and comparability in our analysis, we compiled a table titled "Overview of Studies Evaluating Fruquintinib for Metastatic Colorectal Cancer" (Table 1) [12].

**Table 1: Overview of Studies Evaluating Fruquintinib for Metastatic Colorectal Cancer**

| Study, Year | Country | Population | Intervention | Comparator | Quality |
|---|---|---|---|---|---|
| Yao et al, 2019(19) | China | Metastatic Colorectal Cancer | Fruquintinib | Regorafenib | High |
| Peng et al,2020(18) | China | Metastatic Colorectal Cancer | Fruquintinib | Placebo | High |
| Zhang et al,2020(20) | China | Metastatic Colorectal Cancer | Fruquintinib | Best Supportive Care (BSC) | High |
| Guan et al, 2021(15) | China | Metastatic Colorectal Cancer | Fruquintinib | Regorafenib | High |
| Kusi et al,2023(17) | USA | Metastatic Colorectal Cancer | atezolizumab+/-cobimetinib (ATE+/-COB), fruquintinib (FRU), regorafenib (REG), TAS-102+/-bevacizumab (TAS+/-BEV) | Biosimilar Placebo | High |
| Huang et al,2024(16) | China | Refractory Metastatic Colorectal Cancer | Fruquintinib | Placebo | High |
| Cho et al,2024(14) | USA | Refractory Metastatic Colorectal Cancer | Regorafenib dose optimization (ReDO), rifluridine/tipiracil and bevacizumab (TAS-BEV), | Fruquintinib | High |

The ICER and standardized cost-effectiveness measures were utilized to analyze the results across the included studies. Most studies adhered to the World Health Organization's recommended threshold, where an intervention is considered very cost-effective if its ICER is less than the GDP per capita of the country. It is deemed cost-effective if the ICER is less than three times the GDP per capita. Conversely, interventions with an ICER equal to or exceeding three times the GDP per capita are not cost-effective. Some studies employed local cost-effectiveness thresholds to enhance relevance to their specific settings [13].

## Results

### Study Selection

After conducting a comprehensive search of multiple databases, a total of 49 records from Embase (24), PubMed (8), and Scopus (10), with an additional 7 from Web of Science. Before screening, 23 duplicate records were removed, leaving 26to be screened. Of these, 16 records were excluded due to factors such as inappropriate intervention (1), irrelevant outcome (4), unsuitable publication type (5), and incompatible study design (6). 10 records were sought for retrieval, all of which were successfully obtained and assessed for eligibility. However, 3 reports were subsequently excluded due to publication-type issues. Ultimately, 7 [14-20] studies were included in the review (Figure 1).

### Quality Assessment

The methodological assessment of the included studies was rigorously conducted using the CHEQUE checklist, specifically tailored for evaluating model-based research [21]. This comprehensive checklist facilitated a detailed examination of the methodological rigor and data quality inherent within the seven model-based studies included in the review. Each study was scored on a scale of 100, reflecting the robustness of its overall quality. Further details are provided in Table S3.

**Overview of the Studies**

The main characteristics of the studies are summarized in Table1, andthemethods and results are summarized in Table4S. In Table 1 the included studies provide a summary of studies focusing on the treatment of metastatic colorectal cancer from 2019 to 2024. The studies were chiefly conducted took place in China and the USA, exploring interventions predominantly focusing on Fruquintinib,either as monotherapy or in combination with Atezolizumab, and against comparators like Regorafenib,placebo, and best supportive care (BSC). 5 studies evaluated Fruquintinib, as a standalone treatment or 2 studies in combination with other cancer therapies.

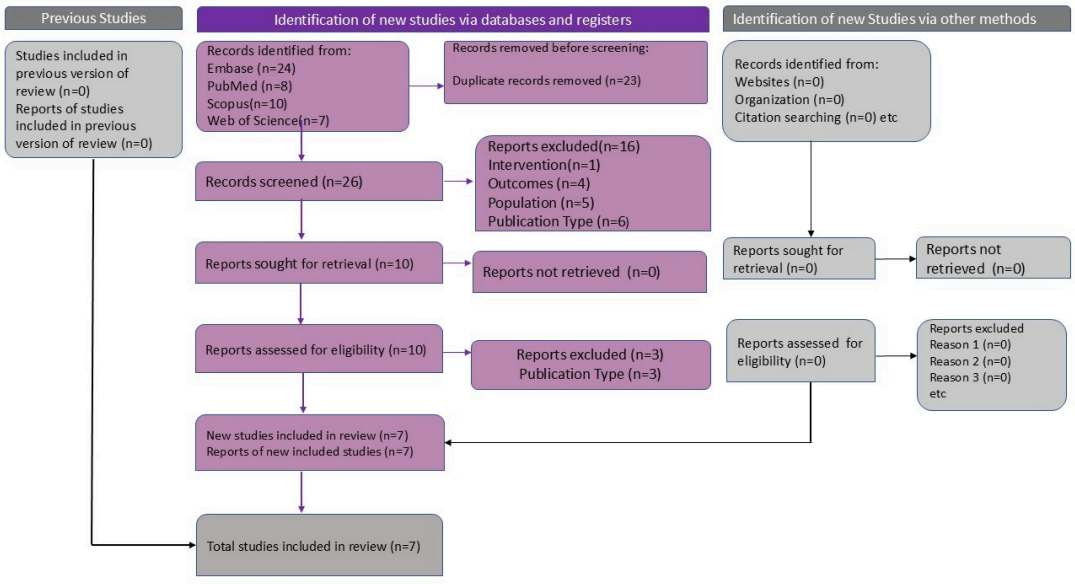


**Figure 1: PRISMA flowchart depicting article screening and selection process**

Table 4S in the provided document outlines the methods and results of the included studies, focusing on different economic evaluation frameworks and the cost-effectiveness of treatments for metastatic colorectal cancer. These studies utilize predominantly CEA using Markov and Partitioned-Survival models to measure the long-term cost-effectiveness and utility of different therapeutic interventions, in terms of QALYs.

The study by Yao et al [19] employed a Markov model to evaluate Fruquintinib against Regorafenib, concluding that Fruquintinib was cost-effective in the Chinese healthcare context due to its lower cost of $33,536 compared to $35,607 for Regorafenib and superior QALY gain of 0.274 versus 0.246. Peng et al [18] also assessed Fruquintinib, against a placebo. Despite showing higher effectiveness with a QALY of 0.640 against 0.478 for the placebo, the study determined that it did not meet the local cost-effectiveness threshold, emphasizing the economic challenges of new cancer drugs. Zhang et al [20] explored Fruquintinib combined with BSC), revealing that the combination did not meet cost-effectiveness criteria, with incremental costs per QALY gained reaching $36,253.94, which was beyond the accepted limits.Guan et al [15]. further evaluated Fruquintinib against Regorafenib using a Markov model and noted that although Fruquintinib has a higher upfront cost, it proves to be cost-effective over time with a better health outcome, achieving a QALY of 0.74 compared to 0.75 for Regorafenib and an ICER of CNY 1,529,196.84 per QALY ($231,676/QALY). In contrast, Kusi et al [17] in the USA examined multiple drug combinations including Atezolizumab and Fruquintinib, finding that combinations like TAS-102 with Bevacizumab were more economical, particularly in later-line treatment scenarios, the most favorable ICERs being substantially lower than single-agent therapies.

Huang et al [16] targeted refractory metastatic colorectal cancer in China, comparing Fruquintinib to placebo using a Partitioned-Survival model. The study endorsed Fruquintinib as a feasible option, contingent on a specific willingness-to-pay threshold, with its cost-effectiveness calculated at $35,974.31 per QALY. Finally, Cho et al [14] assessed the cost-effectiveness of Regorafenib dose optimization (ReDO) versus other combinations in the US, demonstrating that ReDO was economically favourable when compared to alternatives like TAS-BEV and Fruquintinib, with an ICER of $790,988 per QALY, highlighting its economic viability in complex treatment regimens.

The cost-effectiveness of Fruquintinib for treating metastatic colorectal cancer has been evaluated in several studies using incremental cost-effectiveness ratios (ICER), quality-adjusted life years (QALYs), and overall healthcare costs. Compared to standard therapies like Regorafenib, Fruquintinib generally demonstrates a favorable economic profile in the Chinese healthcare context. For instance, Yao et al [19] reported that Fruquintinib, costing $33,536 versus $35,607 for Regorafenib, achieved a slightly higher QALY of 0.274 compared to 0.246, resulting in a cost-effective ICER of $26,508 per QALY. Similarly, Guan et al (15)found Fruquintinib to be cost-effective despite its initial cost, showing an ICER of CNY 1,529,196.84 per QALY ($231,676/QALY) due to its long-term health benefits. However, studies such as Peng et al [18], which compared Fruquintinib to placebo, noted that while Fruquintinib provided significantly better QALYs (0.640 vs. 0.478 for placebo), it did not meet the cost-effectiveness threshold, with an ICER higher than the three-times GDP per capita in China, making it less economically viable. Furthermore, when combined with BSC, Fruquintinib's ICER was reported at $36,253.94 per QALY, exceeding acceptable limits according to Zhang et al [20]. These findings indicate that the cost-effectiveness of Fruquintinib depends significantly on the chosen comparator and healthcare setting, with its economic viability being more favorable when compared directly with Regorafenib than when assessed against placebo or in combination therapies.

# Discussion

This comprehensive systematic review focusing on the cost-effectiveness of Fruquintinib for treating metastatic colorectal cancer reveals nuanced insights into its economic viability across diverse healthcare systems. This study reviewed, andsynthesized findings from the studies, explores the variability in cost-effectiveness, discusses the impact of healthcare economic thresholds, and suggests future research directions and policy implications.The significant regional differences in the economic evaluation of fruquintinib. In China, studies such as Yao et al.(19) (2019) and Guan et al [15] demonstrate that Fruquintinib is cost-effective compared to Regorafenib, given its lower cost and slightly better QALY outcomes. However, Peng et al [18] present a contrasting scenario where Fruquintinib does not meet the local cost-effectiveness threshold when compared to placebo. This divergence primarily reflects the high cost of Fruquintinib relative to the economic standards set by local health authorities, which is a common challenge for newer oncology drugs in developing countries where pricing strategies and healthcare funding are critical barriers to access.

The economic evaluations highlight the critical impact of drug pricing on the adoption of new treatments. The ICER values, pivotal in determining cost-effectiveness, vary substantially based on the drug's price relative to the economic context. For instance, Zhang et al [20] found that combining Fruquintinib with BSC does not meet cost-effectiveness criteria, with costs per QALY gained exceeding acceptable limits. This finding suggests that while Fruquintinib may offer clinical benefits, its cost relative to incremental health gains does not justify its use in combination therapies under stringent economic evaluations.The U.S.-based study by Kusi et al [17] indicates that certain combinations, such as TAS-102 with Bevacizumab, provide more economical options in later-line treatment scenarios. These results imply that Fruquintinib's value is contingent not only on its standalone merits but also on its role within broader therapeutic regimens. This variability in findings across different combinations and treatment lines underscores the need for personalized medicine approaches in economic evaluations, where the benefits of treatment can be maximized for specific patient groups.

The findings from this SLR necessitate careful consideration from policymakers and healthcare providers. The decision to include Fruquintinib in treatment protocols should consider its clinical benefits and its cost-effectiveness within the specific economic landscape of a healthcare system. As newer treatments like Fruquintinib come to market, there is an urgent need for policies that address drug pricing and reimbursement criteria to ensure these innovations are accessible and economically viable for the populations they serve.Future research should aim to collect more comprehensive real-world data on the long-term outcomes and cost implications of using Fruquintinib. Longitudinal studies and post-marketing surveillance could provide deeper insights into its effectiveness and economic impact over extended periods and across diverse populations. Additionally, comparative studies involving newer biologics and targeted therapies could help contextualize Fruquintinib's position within the evolving landscape of colorectal cancer treatments.

One of the significant strengths of this review is its inclusivity of diverse geographical and healthcare contexts, primarily from China and the USA, providing a broad perspective on the economic evaluations of Fruquintinib. The studies utilize robust economic evaluation frameworks such as Markov models and Partitioned-Survival models, which are well-regarded for their ability to simulate long-term outcomes and healthcare costs effectively. These models help in understanding the long-term value of treatments in chronic conditions like metastatic colorectal cancer, making the findings highly relevant for long-term healthcare planning and policy development. Moreover, the review captures a range of comparators from standard chemotherapies like Regorafenib to supportive care highlighting Fruquintinib's role in various therapeutic regimens and its comparative effectiveness.

However, the review also faces several limitations. The primary constraint is the variation in economic thresholds and cost-effectiveness standards across different countries, which can lead to inconsistent conclusions about Fruquintinib's cost-effectiveness. For example, while it may be considered cost-effective in one country due to lower healthcare costs or different willingness-to-pay thresholds, it may not be in another with higher cost standards or stricter economic evaluations. This variability can complicate the application of the review's conclusions across different national health systems. Additionally, most studies reviewed were conducted in high-resource settings, potentially limiting the generalizability of the findings to lower-resource settings where economic constraints are more stringent, and healthcare infrastructure may not support expensive cancer treatments Decision-making regarding the inclusion of fruquintinib in treatment protocols should be informed by both its clinical benefits and its economic viability within the specific economic landscape of a healthcare system. There is a need for dynamic policies that can adapt to the economic evaluation of new treatments and modify drug pricing and reimbursement criteria accordingly.

# Conclusion

This systematic review demonstrates that fruquintinib shows promise as a cost-effective treatment for metastatic colorectal cancer, particularly in healthcare settings like China, providing significant QALY gains compared to traditional therapies. However, its adoption is highly dependent on local economic thresholds and healthcare systems. While this study underscores the need to integrate economic and clinical outcomes in cancer treatment decisions, the drug's approval and data are currently limited to China, making it difficult to conclude its cost-effectiveness globally.

**Abbreviations**

BSC: Best supportive care

CEA: Cost-effectiveness analyses

CRC: Colorectal cancer

ICER: Incremental cost-effectiveness ratio

QALYs: Quality-adjusted life years

ReDO: Regorafenib dose optimization

VEGFR: Vascular endothelial growth factor receptors

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## References

[1] WHO. Colorectal Cancer. WHO. 2023. *[Available from: [Article][Crossref][PubMed][Google Scholar]*

[2] Hossain MS, Karuniawati H, Jairoun AA, Urbi Z, Ooi J, John A, et al. Colorectal Cancer: A Review of Carcinogenesis, Global Epidemiology, Current Challenges, Risk Factors, Preventive and Treatment Strategies. Cancers (Basel). 2022;14(7). *[Crossref][PubMed][Google Scholar]*

[3] Salva de Torres C, Baraibar I, Saoudi González N, Ros J, Salva F, Rodríguez-Castells M, et al. Current and Emerging Treatment Paradigms in Colorectal Cancer: Integrating Hallmarks of Cancer. International Journal of Molecular Sciences. 2024;25(13):6967. *[Crossref][PubMed][Google Scholar]*

[4] Gmeiner WH. Recent Advances in Therapeutic Strategies to Improve Colorectal Cancer Treatment. Cancers. 2024;16(5):1029. *[Crossref][PubMed][Google Scholar]*

[5] Adebayo AS, Agbaje K, Adesina SK, Olajubutu O. Colorectal Cancer: Disease Process, Current Treatment Options, and Future Perspectives. Pharmaceutics. 2023;15(11):2620. *[Crossref][PubMed][Google Scholar]*

[6] Lavacchi D, Roviello G, Guidolin A, Romano S, Venturini J, Caliman E, et al. Evaluation of Fruquintinib in the Continuum of Care of Patients with Colorectal Cancer. International Journal of Molecular Sciences. 2023;24(6):5840. *[Crossref][PubMed][Google Scholar]*

[7] ACSCAN. The Costs of Colorectal Cancer: American Cancer Society Cancer Action. American Cancer Society Cancer Action Network. . *Available from: [Article][Crossref][PubMed][Google Scholar]*

[8] Bhimani N, Wong GYM, Molloy C, Dieng M, Kelly PJ, Hugh TJ. Lifetime direct healthcare costs of treating colorectal cancer: a systematic review. The European Journal of Health Economics. 2023;24(4):513-37. *[Crossref][PubMed][Google Scholar]*

[9] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. bmj. 2021;372. *[Crossref][PubMed][Google Scholar]*

[10] Thangamma Ag M, Vidyadharan B, Daniel RP, Sirur A, Kumar P, Thunga PG, et al. Cost and cost-effectiveness of treatments for rheumatic heart disease in low- and middle-income countries: a systematic review protocol. JBI Evid Synth. 2024;22(9):1886-97. *[Crossref][PubMed][Google Scholar]*

[11] Mandrik OL, Severens JLH, Bardach A, Ghabri S, Hamel C, Mathes T, et al. Critical Appraisal of Systematic Reviews With Costs and Cost-Effectiveness Outcomes: An ISPOR Good Practices Task Force Report. Value Health. 2021;24(4):463-72. *[Crossref][PubMed][Google Scholar]*

[12] Campbell M, McKenzie JE, Sowden A, Katikireddi SV, Brennan SE, Ellis S, et al. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. Bmj. 2020;368:l6890. *[Crossref][PubMed][Google Scholar]*

[13] WHO. New cost-effectiveness updates from WHO-CHOICE. WHO. 2021. *[Available from: [Article][Crossref][PubMed][Google Scholar]*

[14] Cho S, Bekaii-Saab TS, Hocum BT, Grossman J, Appukkuttan S, Babajanyan S, et al. Cost-effectiveness analysis of later-line treatments for refractory metastatic colorectal cancer. Journal of Clinical Oncology. 2024;42(16_suppl):3525-. *[Crossref][PubMed][Google Scholar]*

[15] Guan X, Li H, Xiong X, Peng C, Wang N, Ma X, et al. Cost-effectiveness analysis of fruquintinib versus regorafenib as the third-line therapy for metastatic colorectal cancer in China. J Med Econ. 2021;24(1):339-44. *[Crossref][PubMed][Google Scholar]*

[16] Huang Z, Zhou L, Zheng H, Zhan M. Cost-effectiveness analysis of fruquintinib in Chinese patients with refractory metastatic colorectal cancer. Int J Clin Pharm. 2024;46(4):872-80. *[Crossref][PubMed][Google Scholar]*

[17] Obeng-Kusi M, Roe D, Erstad BL, Abraham I. Cost-effectiveness analysis of later-line therapies for metastatic colorectal cancer (mCRC) based on a novel methodology of network meta-analysis (NMA) of survival curves. Journal of Clinical Oncology. 2023;41(16_suppl):3605-. *[Crossref][PubMed][Google Scholar]*

[18] Peng Z, Hou X, Huang Y, Xie T, Hua X. Cost-effectiveness analysis of fruquintinib for metastatic colorectal cancer third-line treatment in China. BMC Cancer. 2020;20(1):990. *[Crossref][PubMed][Google Scholar]*

[19] Yao L, Han J, She L, Ding D, Liao M, Hu H, et al. Cost-effectiveness for metastatic colorectal cancer. Journal of Clinical Oncology. 2019;37(15_suppl):e15003-e. *[Crossref][PubMed][Google Scholar]*

[20] Zhang PF, Xie D, Li Q. Cost-effectiveness analysis of fruquintinib as third-line treatment for patients with metastatic colorectal cancer. Tumori. 2020;106(5):400-5. *[Crossref][PubMed][Google Scholar]*

[21] Kim DD. Developing Criteria for Health Economic Quality Evaluation Tool. Value in Health. 2023. *[Crossref][PubMed][Google Scholar]*