ECONOMIC ANALYSIS

# Adopting Health Economic Research in Radiation Oncology: A Perspective From Low- or Middle-Income Countries

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review articles

abstract

Establishing a new radiation therapy (RT) setup is resource-intensive as it involves substantial capital costs and the recruitment of a skilled workforce. It is essential to incorporate health economic analysis that estimates recurring and nonrecurring expenses on the basis of the national and local needs, infrastructure, and future projections. RT costing exercises can be especially relevant for low- or middle-income countries (LMICs) with more than 70% of the global cancer burden, with access to $<$ 20% of the available resources. This review article summarizes the scope of RT costing exercises in LMICs, the hurdles in conducting them, and possible ways to circumvent them. The purpose of performing costing studies in RT lies in their utility to improve the efficiency of the investment while at the same time helping to address the issues of uniformity and equitable distribution of resources. This will help assess the net benefit from RT in terms of utility and outcome-linked parameters like Quality-Adjusted Life Years. There are numerous barriers to conducting economic evaluations in LMICs, including the lack of national costing values for equipment, data on manpower salary, cost for public and private setups, and indirect costs. The situation is further complicated because of the nonuniform pay structure, lack of an organizational framework, robust real-world data on outcomes, and nonavailability of country-specific reference utility values. Collaborative national efforts are required to collect all elements required to perform health technology assessments. Information from the national and hospital databases can be made available in the public domain to ease access and broader adoption of health economic end points in routine care. Although resource-intensive at the onset, costing studies and health economic assessments are essential for improving the coverage and quality of RT in LMICs.

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## BACKGROUND

Modern medicine is rapidly evolving, thus imparting a dynamic character to clinical practice. Health care is a diverse field and includes an overarching delivery mandate in therapeutic and preventive settings. With the widely expanding armamentarium of drugs, devices, and technology, it is essential to assess the actual benefits of such interventions to humankind weighed against the costs involved. Ideally, resource-adapted evidence-based medicine should dominate clinical practice and health programs. The UN Committee on Economic, Social and Cultural Rights in 2000 quoted that “the right to the highest attainable standard of health includes availability, accessibility, acceptability, and quality.” Although all these aspects remain pertinent, the availability and accessibility to resources largely determine the population health in most countries. Because of the complex interplay of access to treatment, availability of skilled personnel, health care setup (academic *v* nonacademic, high-volume *v* low-volume), health care benefits in the form of coverage of medical expenses, and perceived clarity between clinical effectiveness and cost-effectiveness, clinical practice is expected to diverge from evidence-based medicine.

To achieve the WHO mandate of Universal Health Coverage, various means to prioritize different treatment approaches within the health care system have been established. Health Technology Assessment (HTA) is one of the methods used by many countries to objectively define the priority areas for financial protection that will have comprehensive coverage and primarily benefit the population, especially the informal sector. HTA forms an essential aid in bridging the gap between available evidence and implementation. This is particularly important for low- or middle-income countries (LMICs) that face adverse demand-supply constraints. Although developed countries like the United States, Canada, and the United Kingdom have been using HTA to make policy decisions on the health care system for a few decades, LMICs like India, Pakistan, Thailand, and many African countries have

## CONTEXT

**Key Objective**

Structured costing exercises are essential for providing affordable and equitable Radiation Therapy (RT) for patients with cancer in low- or middle-income countries (LMICs).

**Knowledge Generated**

The majority of LMICs do not have RT costing programs although a few countries like India, Pakistan, and Thailand have initiated the same. The major hurdle for costing exercises includes the lack of infrastructure, including funding and manpower. The availability of data on costs and outcomes of patients is also a significant deterrent.

**Relevance**

Multicentric collaborative efforts, government initiatives, and pragmatic research are essential for successful RT costing studies in LMICs.

also recently adopted this approach to make unbiased decisions for health care interventions. HTA refers to the systematic evaluation of a health technology's properties, effects, and impacts on the social, economic, organizational, and ethical well-being of an individual or a population. This article aims to review the global challenges, scope, and impact of HTA in oncology with particular reference to radiation oncology, focusing on the prevailing scenario in LMICs.

## NEED FOR HTA IN ONCOLOGY

Oncology practice is driven by evidence-based medicine because of the need to balance the risk of disease progression and treatment toxicity versus the benefit gained from cancer control, which also imparts longevity. Cancer treatments differ from nononcologic conditions in the necessity of multidisciplinary management involving a combination of cancer surgery, cytotoxic or cytostatic therapies like chemotherapy, targeted therapy, hormonal therapy or immunotherapy, and radiation therapy (RT). In addition to this, other diagnostic clinical services (pathology, radiology, and nuclear medicine) and allied disciplines (physiotherapy, dietetics, dentistry, stoma care, social work, palliative care, and emergency care) are essential and closely integrated into cancer treatment. For example, in RT, HTA requires precise and comprehensive estimation of recurring and nonrecurring costs and their utilization, primarily because of the significant initial capital investment and the requisite collaboration with other specialists like radiation physicists, dosimetrists, radiation therapy technologists, information technology specialists, engineers, and oncology nursing.

On the basis of the existing health systems, many countries have developed RT costing models for value and resource utilization. The Ontario model and the ESTROHERO time-driven activity-based costing tool are the most established models that have been extensively reported and used in the literature.[1-3] Although the framework for HTA guidance has taken root in a few LMICs like India, Pakistan, Thailand, Indonesia, Brazil, and Argentina, it is still being taken up in other LMICs and low-income countries (LICs).

## THE PROBLEM

The Lancet Oncology Commission report states that the most common cancers in LMICs include head and neck, breast, and uterine cervical cancers. These have an approximate RT utilization rate of 74%, 87%, and 71%, respectively.[1,4] Although the importance of RT costing data already available from high-income countries to date cannot be overestimated, an accurate estimation of the RT costs can resolve many pertinent issues exclusive to LMIC. For example, although Telecobalt machines have been abandoned in most developed nations favoring Intensity-Modulated Radiation Therapy (IMRT)–compatible linear accelerators, cobalt machines still play a significant role in plugging the gaps in RT coverage in various parts of Africa and Asia.

By 2030, LICs and LMICs are likely to have more than 70% of the global cancer burden and access to $<$ 20% of the available resources.[1] In 2013, the Global Task Force on Radiotherapy for Cancer Control (GTFRCC) was commissioned to understand the global demand for RT and to quantify the investment needed to achieve global equity. The proposed model suggested that by 2035, 12 million patients per year in LMICs would benefit from RT. Moreover, investment for meeting RT needs by 2035 was estimated to result in $278.1 billion US dollars (USD) net in benefits and save 26.9 million life-years for an investment of $184 billion USD. By contrast, the cost of inadequately treated cancer had already reached $895 USD billion in 2010.[5]

These overarching models encompassing multiple countries and continents give a comprehensive overview of the focus areas for workforce optimization and resource allocation. However, within each country, the situation can be vastly disparate. The Lancet Commission reported that 36 countries do not have access to a single RT machine, which is alarming.[1] Lack of infrastructure coupled with a deficiency of trained workforce (Radiation Oncologists, Medical Physicists, and Radiation Therapy Technologists) in LMICs forms the major challenge in these regions. For example, Munshi et al[6] in 2020 estimated the number of teletherapy machines in India to be around 600, which is far less than the estimated units despite indigenous technology development. Moreover, less than 40% of the teletherapy machines are located in India's northern and eastern parts, accounting for more than 60% of the population.[7] The clustering of machines in a few states and cities within these states is a significant barrier to access to radiotherapy. Although the trained human resources pool is increasing, the HTA needs to assess the practicability of custom duty rebates, explore public-private partnerships, and expand the capacity for indigenous technology development.

The situation with brachytherapy is even grimmer than with teletherapy[7,8]. Although the age standardized rate of carcinoma of the uterine cervix has declined worldwide, it continues to be a significant public health concern in most LICs/LMICs. Intracavitary brachytherapy is an indispensable modality and an integral component in the RT treatment for these cancers. However, the economic viability of the initial capital investment, periodic source changes, the requirement of an operating room (OR), low utilization rate, and alternatives like IMRT/stereotactic body radiotherapy deter many hospital administrators from procuring an independent brachytherapy setup.[7] Interestingly, many centers are now adopting a collaborative approach, with one center equipped with brachytherapy catering to the needs of several centers.[7] Another strategy is installing a Co-60 brachytherapy setup instead of Ir-192, as Co-60 requires very few source changes compared with Ir-192. Although a Co-60 brachytherapy setup might have a marginally higher initial cost because of the higher source cost and shielding requirements, it has been found to be cost-favorable in middle-income countries like Peru.[9]

The above considerations on resource scarcity, resulting in low access, apply to treatment delivery and treatment planning equipment, such as simulators and planning systems as well.

The foremost challenge in radiation oncology is optimal utilization of scarce and costly technology. Also, there is a dearth of trained personnel and technical infrastructure to support a system capable of effectively treating common cancers. Finally, uniform accessibility to RT machines in a large population with variable population density and cancer incidences requires meticulous planning from the government and the private setups. Also, a stringent process of quality assurance, training, and research is required for achieving these goals.

## HURDLES FOR HTA IN LMICs

Estimating the benefits of health interventions and comparing these interventions in terms of monetary value is an arduous task for all disciplines of medicine in LMICs.

Costing models like time-driven activity-based (TD-ABC) analysis adopted in the ESTRO-HERO rely on assigning a monetary value to resources and workforce for estimating treatment costs in various scenarios.[1,10] In LMICs, the estimation of these monetary values is especially complicated because of variations in the type of setup (public *v* private *v* public-private partnership), workforce, patient load, remuneration, insurance status, and, most importantly, the nonavailability of public data toward any of these components. Hence, a spending approach with a defined perspective (provider, payer, and societal) similar to the TD-ABC model of ESTRO-HERO will be more feasible than a microcosting process in LMICs. Structured country-level economic research for deriving monetary values for resources and infrastructure is required in LMICs.

A second methodology is Cost-Effectiveness Analysis, defined as the incremental cost divided by changes in health outcomes. Although other end points have been proposed (like the number of new cancers prevented), the two most common health outcomes used are either survival or quality of life. Although appealing, a significant roadblock in the real-world setting pertains to a lack of reliable outcome data about disease status, morbidity, and quality of life and assigning value to these health states, especially true in the LMIC setting. Real-world evidence is more applicable to Asian countries because of the minority representation of Asian patients in clinical trials and the fact that reimbursement decisions are not made at market entry.[11] One of the most commonly used methods of Cost-Effectiveness Analysis relies on assigning health states to individuals by using questionnaires like EQ-5D-5L and subsequently estimating end points like Disability-Adjusted Life Years or Quality-Adjusted Life Years.[12] However, a validated reference population value set of most LMICs, except Thailand and India, is still not available.

A commonly used estimate for calling an intervention cost-effective in the United States is the incremental cost-effectiveness ratio of $50,000 USD/life-year saved. This threshold has been derived from a cohort of patients with End-Stage Renal Disease requiring dialysis in the United States in the 1980s.[13,14] A generalized cost-effectiveness threshold valid across countries/regions is impossible to generate because of differences in economic profile, existing socio-demographic profile, the available health care facilities, and the proportion of earnings spent by the government on health care. Hence, multiple countries have proposed different thresholds for what constitutes a cost-effective intervention for them. In 2013, the NICE guidelines published its national threshold, which gave the reference values for the technology appraisals with explicit value in the form of a range of GB£20,000-30,000 per Quality-Adjusted Life Years for a structured threefold decision-making process (< GB£20,000, GB£20,000-30,000, and > GB£30,000). Similarly, for Canada, an oncology-specific ceiling threshold value of CAN$75,000 was suggested in 2009. For countries that do not have a specified ICER, the WHO suggested a threshold value for a cost-effective intervention as one to three times the country's gross domestic product for averting a Disability-Adjusted Life Years.[15] Efforts are underway now in many countries to establish a formal cost-effective threshold.

There is also a considerable variation reported in the nature of health care economic evaluation (HEE) guidelines for carrying out HTA across various countries. A review of the methodology used in various countries for HEE was published recently by Sharma et al.[16] Here, the authors bring out the similarities in the fundamental principles (type of economic evaluation, time horizon, and measure of health outcomes) and differences (study perspective, discount rate, comparator, and cost components) in the various national HEE guidelines. A similar publication presents the specific challenges that different Asian countries face while incorporating HTA-related research in health care decision making.[17]

## WAY FORWARD

The political will, policymakers, and researchers have to come together to reconcile and complement efforts to achieve the common goal of universal health coverage. The technical expertise for health economic assessment projects may be lacking in countries embarking upon HTA exercises. International collaborations and aid by agencies like IAEA and WHO can provide the technical expertise for the initial phase of these projects and train local manpower adequately for future projects. The government's role is central in introducing HTA projects in the country. Formation of a central institutional framework to critically review the available evidence and inform not only about the cost-effectiveness and clinical effectiveness of a wide range of health interventions like drugs, devices, technologies, and programs but also the gain concerning equity or financial risk protection is essential. A central body for HTA will also ensure the standardization of HTA initiatives across the country. Another major setback in HTA activities is the lack of quality data. Prospective large-scale cancer registries incorporating data on outcomes and toxicities can be a cost-effective long-term solution for the same rather than hospital-based data. National reference cost data are one of the fundamental requirements for carrying out HTA activities. The reference value set of a country with a similar sociodemographic profile for that cancer may be used if country-specific data are unavailable. However, the results may be inconsistent.[14] The problems of HTA exercises and their potential solutions are summarized in Table 1.

**TABLE 1.** Hurdles in RT Costing in Low- or Middle-Income Countries and Proposed Solution(s)

| Hurdle | Proposed Solutions |
|---|---|
| Lack of methodology addressing region-specific issues | Cooperation with international experts, setup national committees/bodies |
| Lack of quality patient data on survival and toxicity | Setting up prospective registries, shifting to electronic medical records |
| Lack of data on cost of equipment | Initial uniform assignment of cost of equipment followed by actual cost estimation |
| Lack of data on cost of manpower | Estimation on the basis of national average with a possible consensus by national radiation oncology bodies |
| Lack of reference data sets | Use data sets from countries with similar clinic-demographic profile, National Projects for estimation of reference value |
| Resistance to RT costing exercises | Generate awareness, develop health economics workshops for training, demonstrate efficacy in the decision-making process of costing exercises undertaken in other parts of the world |

Abbreviation: RT, radiation therapy.

## RT COSTING EXERCISES SPECIFIC TO RADIATION ONCOLOGY

RT cost calculation practices have evolved from an unspecified or nonsystematic method to a time-driven, activity-based costing (spending) method.[18] The latter approach is especially relevant as RT mainly uses medical resources (equipment and personnel) that cannot be directly traced to a single treatment. In addition to the fact that costing literature on RT remains scarce, Defourny et al also reported that most studies provide incomplete information about the exact costing methodology used and concerning the time horizon, discount rate, or sensitivity analysis performed.[2,19] Ideally, the costing method should be chosen on the basis of the purpose of the economic evaluation and the perspective. The TD-ABC process used in the ESTRO-HERO project divided the cost into three layers: central is the external beam radiation therapy (EBRT) core, which involves the cost of human and capital resources and of activities dedicated to the external beam RT pathway, including the time spent on these activities. In addition to this central TD-ABC part, two other layers estimate the costs incurred in a well-functioning radiation oncology department, embedded in multidisciplinary oncology setup: The direct Radiation Oncology support, including personnel (eg, quality managers) and equipment (eg, for dosimetry, information technology) and indirect activities in multidisciplinary oncology not related to the strict pathway of EBRT, but in which some of the radiation oncology personnel is involved, such as chemotherapy delivery.[2] In LMICs, the microcosting method will be challenging and time-consuming for estimating these direct and indirect costs. Another factor to be considered is that microcosting de facto focuses on very specific questions and indications, and hence, that the effort done cannot be expanded to other indications, whereas a TD-ABC as described in HERO allows us to calculate the cost of all indications in a radiation oncology department or in a country.

Efforts to perform RT costing exercises and evaluations have been initiated in various LMICs. A time-driven activity-based analysis comparing RT costing in different income settings was reported in 2017 by Van Dyk et al.[20] The base case cost/course was $5,368 USD in HICs and $2,028 USD in LICs. It was, moreover, clearly demonstrated that the better the scarce and costly resources are used, the lower the costs: in LICs, the cost/course (in USD) for 4-hour, 8-hour, 12-hour, and 16-hour shifts model was estimated to be 5,853, 2,967, 2,028, and 1,544, respectively. Besides the longer operational hours, the authors also suggested a model wherein the treatment preparation, simulation, and planning could be centralized with treatment delivered in satellite centers.

Similar to the national-unit cost of health care services for drugs and commonly used medical equipment, there is a need to generate similar unit cost data for the various RT processes like conventional planning, 3 Dimensional Conformal Radiation Therapy, IMRT, Image Guided Radiation Therapy, and stereotactic body radiotherapy, taking into consideration the course length of RT, complexity of planning, frequency of imaging for verification, and need for adaptive RT.[21] As mentioned above, in many LMICs, the human resource requirement is gradually being met. Tremendous advancements in telemedicine and automation can help circumvent workforce requirements for certain aspects of RT, which do not require a direct patient interaction, such as RT planning, audit, and review. The thrust on promotion and commercialization of the indigenous technology for high-end teletherapy machines with the capability of advanced procedures like IMRT can help solve the crisis of the teletherapy machine gap in LMICs. However, these new machines need to be critically reviewed both for quality and from the health economic point of view before widespread distribution.

Finally, although, on the one hand, basic RT facilities like telecobalt and brachytherapy are scarce in many LMICs, what cannot be ignored is the influx of advanced RT equipment, including TomoTherapy, Gamma Knife, CyberKnife, proton therapy, and MRI Linear Accelerators. Although expensive technology should continue to be adopted whenever feasible, the policymaker can carve out a deal with the private sector to share this investment with patients who deserve this technology. By contrast, technology and processes are being developed to procure these resources in the public sector. A typical example is a proton therapy setup. The initial capital investment of a standard single gantry and three-gantry proton therapy setup in an LMIC is roughly equal to the cost of 10-15 and 30-35 single energy Linear Accelerator, respectively. There is a definite room for implementing advanced technologies even in LMICs, and the capital cost of different RT technologies cannot be compared directly. Although the cost-effectiveness of protons has not been explicitly studied for LMICs, multiple cost-effectiveness analyses compare photons and protons across countries. Most of these emphasize appropriate patient selection for making protons cost-effective. A systematic review of various indications found protons to be cost-effective for pediatric cancers, selected head neck cancers at risk of mucosal toxicity, and left-sided breast cancers.[22,23] Hence, the focus before and during adopting advanced technologies in LMICs should be on cost efficiency, appropriate patient selection, reimbursement strategies, and clinical trials to optimally use these technologies.

In conclusion, the cognizance of the need for systematic evaluations and health economic assessments in LMICs cannot be overstated. Being a technology-intensive branch, new technologies, techniques, and modalities are being introduced in radiation oncology at a rapid pace. With the proportion of cancer cases likely to rise significantly in these countries, RT costing exercises and health technology and economic assessment should be one of the top priorities in our countries to evolve effective and sustainable solutions for the community. Although a challenging task, multicentric/multi-institutional collaborative efforts are required to accomplish this.


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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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