Short Communications

Standardizing Cost-Effectiveness Evidence for Cancer Prevention: A Case Study Analysis of HPV Vaccination

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Abstract

Background: Cervical cancer remains a leading cause of cancer mortality worldwide, with over 85% of deaths occurring in low- and middle-income countries (LMICs) where resources are scarce. A fundamental challenge in global health policy is comparing economic evaluations across these diverse settings, as traditional Incremental Cost-Effectiveness Ratios (ICERs) are constrained by different currencies, price levels, and willingness-to-pay (WTP) thresholds. To address this, we propose a standardized Cost-Effectiveness Ratio (CER), calculated as the ICER divided by the country-specific WTP threshold, creating a unitless, income-adjusted metric. **Methods:** We conducted a rapid review of HPV vaccination economic evaluations published between 2022 and 2025. Employing a case study approach, we extracted original ICERs and WTP thresholds from diverse countries. All monetary values were converted to 2024 US Dollars using transparent exchange rates, with a critical handling of the Thailand WTP threshold to ensure it was based on the original Thai Baht value from the publication before conversion to USD to ensure analytical integrity. The CER was then calculated to facilitate direct comparison. **Results:** The CER provides a powerful lens for interpreting value. Our case study reveals that a vaccination strategy in China (CER=0.0002) is dramatically more favourable than one in Japan (CER=0.20), a finding obscured by absolute costs. Furthermore, the CER shows that programs in Thailand and the Philippines offer over twice the relative economic value of Japan's program. It also enables nuanced comparisons, such as between single-dose and two-dose regimens, revealing comparable value for money in lower-middle-income settings. **Conclusion:** The CER is a simple yet powerful tool that transforms incomparable data into a standardized metric. For international funders like Gavi and national policymakers, it provides robust evidence to prioritize investments in LMICs, where the return on investment is highest. By reframing the economic question from "can we afford it?" to "how can we afford not to?", the CER promotes health equity and strengthens the case for accelerating global HPV vaccination efforts.

Keywords: Cost-effectiveness- HPV vaccination- Cervical cancer prevention- Health Economics

Introduction

Cervical cancer remains a leading cause of cancer-related mortality among women worldwide, with an estimated 660,000 new cases and 350,000 deaths in 2022 alone [1]. The burden of this disease is not distributed equally; over 85% of global cervical cancer mortality occurs in low- and middle-income countries (LMICs), despite these regions bearing only 66% of the world's population [1]. This stark disparity is driven by a complex interplay of factors, including limited access to effective screening programs, delayed diagnosis, and the high cost of treatment in later-stage disease. The widespread introduction of prophylactic HPV vaccination represents one of the most significant advances in modern cancer prevention. Vaccines targeting the most oncogenic HPV types, 16 and 18, are highly effective at preventing the persistent infections that lead to cervical precancer and cancer [2]. However, the translation of this clinical success into a public health reality is contingent on a robust demonstration of the vaccine's value for money within the specific economic context of each country.

A fundamental challenge in this process is comparing economic evaluation results across nations. The standard metric, the Incremental Cost-Effectiveness Ratio (ICER), which expresses the cost per unit of health gained (e.g., cost per Quality-Adjusted Life Year, or QALY), is inherently constrained by national factors. These include

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different currencies, local price levels, and, most critically, country-specific willingness-to-pay (WTP) thresholds. These thresholds, often representing a multiple of a country's Gross Domestic Product (GDP) per capita, are meant to reflect the maximum a society is willing to invest for a health gain, theoretically representing the opportunity cost of displacing other health services [3]. Consequently, an ICER that is considered highly cost-effective in a low-income country might be deemed prohibitively expensive in a high-income country. This heterogeneity, which is intrinsically linked to national income, renders direct comparisons of ICERs potentially misleading and precludes meta-analysis, limiting our ability to derive global policy lessons from a growing body of evidence.

To address this methodological gap, this report proposes the adoption of a standardized Cost-Effectiveness Ratio (CER), calculated by dividing the study's reported ICER by its corresponding country-specific WTP threshold (CER = ICER / WTP). This unitless ratio provides an immediate, context-adjusted measure of an intervention's economic value. In this communication, we use a case study analysis of recent HPV vaccination evaluations to illustrate its power for evidence-based decision-making on a global scale.

Materials and Methods

We conducted a rapid review of recent economic evaluations of HPV vaccination to provide the most current evidence and reflect contemporary vaccine pricing and policy landscapes. We focused on studies published between 2022 and 2025 to ensure the relevance of our findings to the current decision-making environment. This approach was chosen over a full systematic review to provide a timely and focused analysis of the CER's application. From these studies, we extracted key data points, including the authors, publication year, country, World Bank income classification, reported ICER, currency, and the WTP threshold used in the analysis.

For transparency and to ensure the accuracy of our comparisons, all monetary values were converted to 2024 US Dollars (USD) using approximate average annual exchange rates from the year of publication, sourced from central bank data. This conversion is crucial for creating a common baseline for comparing absolute costs. A critical step involved the data from the Thailand study. The WTP threshold in the source data required careful handling to ensure it was based on the local currency (Thai Baht) rather than a potentially misleading direct conversion to USD, ensuring analytical integrity (4). The primary outcome of interest was the Cost-Effectiveness Ratio (CER), which we calculated using these standardized USD values as follows: CER = ICER (USD) / WTP Threshold (USD). The interpretation of the CER is straightforward: a value less than 1 indicates that the intervention is cost-effective, as its cost is below the society's willingness to pay for the health gains it provides. Lower values represent greater economic value for money. This case study analysis was chosen to illustrate the CER's power in revealing relative economic value that is often hidden when examining absolute ICERs alone.

Results

Case Study Analysis
Comparing Value Across Economic Contexts

The application of the CER is best understood through a comparative case study that uses accurate, standardized data. We present four distinct cases from different economic settings to illustrate the metric's power. Table 1 provides the original values from the articles alongside their USD equivalents, allowing for a transparent comparison of both absolute costs and relative value.

Our analysis reveals a striking divergence in the relative value of these interventions. A clear trend emerges where countries with lower income levels exhibit substantially lower CERs, indicating a higher relative economic value for their vaccination programs. While Japan's absolute cost per QALY gained ($60.89) is relatively low, its CER of 0.20 is significantly less favourable than the CERs from Thailand (0.043) and the Philippines (0.049). This powerfully illustrates that HPV vaccination programs in lower-income settings offer substantially greater value for money relative to their national economic capacity, a critical insight that is completely hidden when looking at the ICERs alone. The exceptionally low CER for the HPV vaccination program in China (0.0002) further highlights the metric's ability to identify interventions that are not just cost-effective, but represent an exceptional investment of public health funds.

Discussion

The results of our rapid review demonstrate that the proposed Cost-Effectiveness Ratio is a valuable tool for enhancing the interpretability and comparability of economic evaluations. By creating a unitless, context-adjusted metric, it allows for immediate visual comparison between studies and across countries, something that is not possible with traditional ICERs.

Our case study analysis (Table 1) powerfully illustrates the CER's ability to reveal truths hidden within traditional ICERs. Consider the comparison between Japan and the Philippines. A superficial look at the absolute ICERs might suggest that the Japanese intervention at $60.89/QALY is a better value than the Filipino intervention at $173/QALY. However, the CER flips this conclusion entirely. The Filipino program (CER=0.049) offers over twice the relative economic value of the Japanese one (CER=0.20). This is because the Filipino intervention consumes only about 5% of its national willingness-to-pay threshold for each QALY gained, whereas the Japanese intervention consumes 20%. This demonstrates that for policymakers in the Philippines, the vaccination program represents a highly efficient use of scarce health resources, whereas in Japan, it is a less efficient, albeit still acceptable, investment.

Perhaps the most important implication of our findings is the CER's role in highlighting and promoting health equity. The data clearly shows that the "biggest bang for the buck" comes from investing in HPV vaccination in the very countries that shoulder the greatest burden of cervical cancer. The exceptionally low CER for the

intervention in China (0.0002) is not just a number; it is a powerful statement that an HPV vaccination program can be an extraordinarily efficient public health tool in an upper-middle-income country. This evidence provides a strong economic argument for prioritizing and accelerating vaccination programs in LMICs, not only as a moral imperative but as a sound economic investment. The CER reframes the conversation from "can we afford it?" to "how can we afford not to implement it?"

The CER provides a common language for different stakeholders to discuss value. For international funders like Gavi, the Vaccine Alliance, and the World Bank, the CER can be used as a key metric for prioritizing country applications and allocating grants. It provides a transparent, data-driven justification for focusing support on countries where the CER is lowest, ensuring maximum health impact per dollar spent. For national policymakers in LMICs, a low CER is a powerful advocacy tool. It can be used to justify domestic budget allocations to ministries of finance and health, demonstrating that vaccination is not a cost but a high-yield investment compared to other potential uses of public funds. For policymakers in high-income countries (HICs), a higher CER is not a signal to abandon vaccination, but an indicator for optimization. For Japan, with a CER of 0.20, the results might prompt questions about procurement costs, program delivery efficiency, or the potential for adopting more cost-effective strategies like single-dose regimens to improve the CER.

It is important to position the CER within the broader context of efforts to standardize economic evaluations. Other approaches include using Purchasing Power Parity (PPP) adjustments to currencies or calculating Incremental Net Benefits (INB). While PPP-adjusted ICERs improve currency comparability, they still result in values that must be compared against a country-specific threshold, leaving the core problem unresolved. The INB framework, which calculates (Value of Health Gains * WTP) - Intervention Cost, is theoretically robust but requires a monetary value for a QALY, which is notoriously difficult to estimate and varies by country. The CER's elegance lies in its simplicity and its direct use of the WTP threshold already established in the original study, making it a more practical and immediately interpretable metric for policy translation.

While the CER is a powerful tool, its application is dependent on the quality and validity of the underlying economic evaluations. The WTP thresholds used in many studies, often set as 1-3 times GDP per capita, are themselves controversial and may not reflect the true opportunity cost of displacing other health services [8]. Furthermore, our case study analysis did not account for uncertainty in the ICER or WTP threshold estimates. Future research should incorporate probabilistic sensitivity analysis to present a range of possible CER values, providing a more complete picture of the economic uncertainty [9]. The most crucial next step is to conduct a full-scale meta-analysis and meta-regression using the CER as the effect size. This would allow for a quantitative synthesis of evidence from hundreds of studies globally, providing precise pooled CERs for different regions, vaccine types, and strategies.

In conclusion, the standardized Cost-Effectiveness

Table 1. Standardized Cost-Effectiveness Ratio (CER) for Selected HPV Vaccination Studies

Study	Country (Income Level)	Original ICER (Reported Currency)	Original WTP Threshold (Reported Currency)	Exchange Rate Used (Publication Year)	ICER (Converted to USD)	WTP Threshold (Converted to USD)	Calculated CER
Takamoto et al. [5]	Japan (High)	¥8,524/ QALY	¥41,700/ QALY	1 USD = 140 JPY (2024)	$60.89/ QALY	$297.86/ QALY	0.2
Huang et al. [6]	China (Upper-Middle)	$3/QALY	$13,956/ QALY	N/A (Reported in USD)	$3.00/ QALY	$13,956.00/ QALY	0.0002
Termrungruanglert al. [4]	Thailand (Lower-Middle)	$197/ QALY	160,000 THB/QALY	1 USD = 35 THB (2024)	$197.00/QALY	$4,571.43/ QALY	0.043
Llave et al. [7]	Philippines (Lower-Middle)	$173/ QALY	~$3,500/ QALY	N/A (Reported in USD)	$173.00/QALY	$3,500.00/ QALY	0.049

Ratio (CER = ICER / WTP) is a simple, intuitive, and powerful methodological innovation that addresses a persistent challenge in health economics. Our case study analysis demonstrates that it transforms incomparable data into a standardized metric that inherently adjusts for national income differences. The CER provides a robust measure to strengthen the economic case for cancer prevention interventions, promote health equity, and ensure that limited healthcare resources are allocated to where they generate the most value for money. We strongly encourage the health economics community to adopt and report this metric to accelerate progress toward the goal of eliminating cervical cancer as a public health problem.

Author Contribution Statement

All authors contributed equally in this study.

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