ORIGINAL ARTICLE

Cost-effectiveness analysis of colonoscopy for screening colorectal cancer in Indonesia using Markov Model

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ABSTRACT

Colorectal cancer (CRC) is one of the top three diagnosed cancers worldwide and the second leading cause of cancer-related deaths, imposing a significant economic burden. In this context, early detection is crucial for effective management. The primary detection method particularly for high-risk individuals is colonoscopy but screening has not been widely adopted and the participation rate and the colonoscopy screening compliance rate were low. Pharmacoeconomic investigations are essential for evaluating the costs and effectiveness of colonoscopy screening for colorectal cancer. Therefore, this research aimed to conduct a cost-effectiveness analysis using a Markov model for a cohort of 100,000 adults aged 45 to compare the outcomes of screened and unscreened scenarios. The Markov model developed in this study consists of three main stages: the health stage, the colorectal cancer stage, and the death stage. The parameters used in this study include the probabilities at each stage, costs, the sensitivity and specificity of colonoscopy, utilities at each stage, and the discount rate. One-way and probabilistic sensitivity analyses were conducted to address uncertainty. Meanwhile, the Incremental Cost-Effectiveness Ratio (ICER) of screening colonoscopy compared to no screening for adult patients was found to be cost-effective and valued at USD 6,191.15/QALY (Quality-adjusted Life Year). This value was significantly below the Cost-Effectiveness Threshold (CET) assumed to be USD 14,759.10. Based on the cost-effectiveness acceptability curve at a willingness to pay (WTP) threshold of USD 5,500, the probability of being cost-effective for colorectal cancer screening increased and consistently reached 100% at a WTP level of USD 9,000. Colonoscopy screening was cost-effective when analyzed using the Markov model, as suggested by ICER value exceeding three times the Gross Domestic Product (GDP) of Indonesia. Future research could explore alternative interventions, such as biennial colonoscopy, and compare the result with other screening methods.

Keywords:
pharmacoeconomics; colorectal cancer; screening; colonoscopy; CEA

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INTRODUCTION

Colorectal cancer (CRC) is one of the three most commonly diagnosed cancers worldwide and the second leading cause of cancer-related mortality after lung cancer.[1] World Health Organization (WHO) reported that there were 1.9 million new cases and over 930,000 deaths due to colorectal cancer in 2020. The incidence will increase to 3.2 million cases per year (63%) and 1.6 million deaths annually (73%) in 2040.[2] Furthermore, the high incidence of colorectal cancer correlates with significant economic impacts. The estimated global cost is approximately 2.8 trillion, while in Europe, the economic burden is around €191 billion per year. These data show that colorectal cancer has a substantial global economic impact, with healthcare costs being the largest contributor to the burden.[3]

The key to successful management of colorectal cancer is early detection, allowing for potentially curative surgical interventions. However, a significant number of patients in Indonesia present with advanced stages of the disease, and this leads to low survival rates regardless of the treatment provided. Early detection of colorectal cancer is an essential effort to improve quality of life.[4] Several research have reported that early detection efforts in various countries have been proven effective in reducing mortality rates associated with the condition. Meanwhile, more cases can be identified at earlier stages through proper screening guidelines. Screening methods for colorectal cancer include the Fecal Occult Blood Test, Sigmoidoscopy, Colonoscopy, Virtual Colonoscopy, and DNA Stool analysis. Colonoscopy is the most commonly used detection method recommended for all cancer risk categories.[4,5] The method is the gold standard procedure widely used in the diagnosis and treatment of colonic mucosal disorders, such as colorectal cancer.[6] Purnomo et al (2023)[7] conducted research on the prevalence of colorectal cancer screening in Semarang, where the participation rate was 63% and the colonoscopy screening compliance rate was 70.27%. Therefore, colorectal cancer screening based on primary care should be considered in line with the level of public compliance.

The implementation of colorectal cancer screening has not been widely adopted up to a certain point. Factors contributing to the lack of colorectal cancer detection strategies include costs, the comfort of the test, and test accuracy. Cost is the primary concern, particularly regarding reimbursement by insurance.[7] In Indonesia, the government and the National Health Insurance Agency have not established tariff policies for the use of colonoscopy. However, some hospitals have set standards for colorectal screening through colonoscopy. The main challenges in the detection are the high cost of colonoscopy, which is not covered by the government, and the low level of public awareness regarding colorectal cancer.[7] Pharmacoeconomic analyses are crucial for evaluating the costs and effectiveness associated with screening compared to the absence of screening. The results can serve as a reference for developing policies regarding colorectal cancer screening in Indonesia.

MATERIALS AND METHODS

Model Overview

The formulation of the Markov model starts with examining the disease progression using a decision tree model adapted from Ahn and Ha.[8] The decision tree model shows that detection through colonoscopy leads to four main outcomes, namely true negative, false negative, true positive, and false positive. These four outcomes certainly affect the interpretation of the results from the screening process, as reported in Table 1.

Markov model was developed to simulate a cohort hypothesis including 10,000 adult patients aged 45 years, with screening cycles occurring every 10 years (Figure 1b). The time horizon used was 30 years[9] and the model analyzed the population without and with colonoscopy screening. In addition, the analysis focuses on total costs and utilities. Cost-effectiveness is assessed from the provider's perspective by comparing the populations with and without colonoscopy screening.

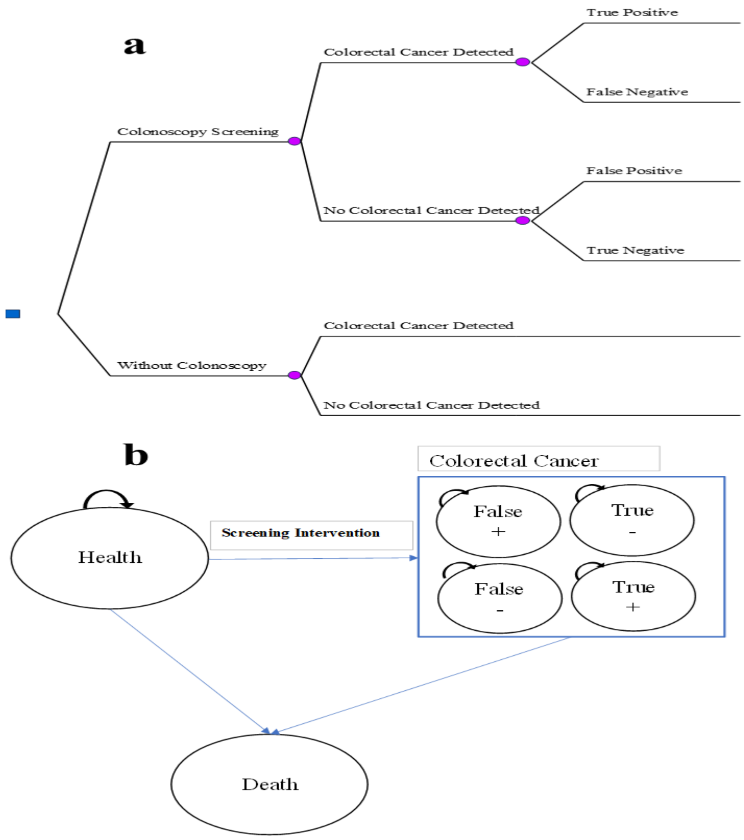

Figure 1. Model in Cost-Effectiveness Analysis
(1a. Decision Tree Model; 1b. Markov Model)

Table 1. Measurement of Each Colorectal Cancer Condition

Conditions	Measurement
True Positive	Health population x probability health to health x sensitivity + CRC population x probability CRC to CRC
False Negative	Health population x probability health to health x (1-sensitivity) + CRC population x probability CRC to CRC
True Negative	Health population x probability health to health x specificity + CRC population x probability CRC to CRC
False Negative	Health population x probability health to health x (1-specificity) + CRC population x probability CRC to CRC

Note: Probability, sensitivity, and specificity value according to the table 2; Health population and CRC population based on Monte-Carlo cohort simulation.

Parameter Inputs

Figure 1b shows that the state of health, population suffering from colorectal cancer, and death are observed in the design of the Markov model. In the population stage indicated for colorectal cancer, the conditions are categorized into true positive, true negative, false negative, and false positive according to the progression concept in the decision tree. True negative and true positive represents a negative and positive test indicating the absence and presence of colorectal cancer, respectively. False negative refers to a negative test result despite the patient having the disease, and false positive describes a positive test result when the patient does not have the disease[10]. These four test outcomes can show biases in the screening process, reporting the necessity for sensitivity and specificity to be incorporated into the Markov model.

All patients in the cohort simulation are assumed to be in a healthy state, with the possibility of transitioning from normal condition to colorectal cancer. In this condition, healthy patients can also transition to the death state. The parameters used in this analysis include probability values, direct medical costs, screening effectiveness, and utility (Table 1). The probabilities were obtained from Wang et al.[11], which relates to the incidence of colorectal cancer events following colonoscopy screening, measured as the incidence rate per 10,000 person-years. The incidence rate related to mortality was derived from the probability of health to death due to colorectal cancer. The transition probabilities for health to health and CRC to CRC events are presented in the matrix.

Table 2. Parameter Input in Markov Model

Parameter	Distribution	Values	Source
Probability			
Health to Health	Beta	0.99398	Matrix (1-P Health to CRC-P Health to Death)
Health to CRC	Beta	0.00392	Wang et al.[11]
Health to Death	Beta	0.002101	Lee et al.[12]
CRC to Death	Beta	0.000068	Lee et al.[12]
CRC to CRC	Beta	0.999932	Matrix (1-P CRC to Death)
Cost			
Colonoscopy	Gamma	USD 39.39	Peraturan Wali Kota Tangerang Selatan[13]
Colorectal Cancer Treatment	Gamma	USD 1938.21	Amalia et al.[14]; Peraturan Wali Kota Tangerang Selatan[13]; Senore et al.[15]
Effectiveness			
Sensitivity of Colonoscopy (True Positive)	Beta	0.89	Hassan et al.[16]
Sensitivity of Colonoscopy (False Negative)	Beta	0,11	Hassan et al.[16]
Specificity of Colonoscopy (True Negative)	Beta	0,26	Hassan et al.[16]
Specificity of Colonoscopy (False Positive)	Beta	0,74	Hassan et al.[16]

Parameter	Distribution	Values	Source
Utility			
Health	Beta	1	
CRC	Beta	0.713	Kristin et al.[17]
Death	Beta	0	

Abbreviation: P=Probability; CRC=Colorectal Cancer; USD=United States Dollar

Cost data were obtained from sources and the values were converted to US dollars using the exchange rate as of June 2024 (1 USD = IDR. 16,276). Cost of colonoscopy screening was derived from South Tangerang City Mayor's Regulation No. 5 of 2023, which amounts to IDR. 636,500 (USD 39,39). Cost method for colorectal cancer therapy used weighting based on each cancer stage in association with each treatment.

Model Outcome

The total lifetime costs and quality-adjusted life years (QALYs) were estimated. The incremental cost-effectiveness ratio (ICER) was calculated by dividing the incremental costs of colonoscopy screening versus no screening by the corresponding incremental QALYs. Colonoscopy screening was deemed cost-effective if the ICER was below the willingness-to-pay (WTP) threshold of three times the GDP per capita, as recommended for Indonesia. Both costs and utilities were discounted at a rate of 3%, in line with Indonesian guidelines for health economic evaluations. All analyses were performed using Microsoft® Excel.

One-Way and Probabilistic Sensitivity Analysis

The impact of parameter uncertainty is evaluated using one-way sensitivity analysis for each model parameter as presented in a tornado diagram. Parameters for probability, cost, and discount rates are adjusted by ±25% from the initial values, while effectiveness and utility data are represented using the minimum and maximum values reported in the literature.

Probabilistic sensitivity analysis (PSA) is conducted to assess the impact of parameter uncertainty using Monte Carlo simulation. The results of PSA report multiple new ICER values simultaneously for 1,000 new cases. These values represent the interaction of uncertainty across all included parameters and the output is depicted in Cost-Effectiveness Acceptability Curve (CEAC).

RESULTS

Base-Case Analysis

Table 3 presents the results of costs and utilities after discounting for the population receiving colorectal cancer screening compared to those without screening. The population undergoing colonoscopy screening incurred higher costs and experienced greater utility. ICER value obtained was USD 6,191.18/QALY, which is below the threshold of three times GDP (Figure 2).

Table 3. ICER Value Based on Baseline Analysis

	Cost (USD)	QALY
Without Colonoscopy	20,349,315	1,590,212
Colonoscopy	534,149,218	1,673,201
Incremental	513,799,903	82,989
ICER	USD 6,191.18/QALY	
Assuming GDP in Indonesia	USD 4,919.7	
3x GDP	USD 14,759.1	

Abbreviation: GDP=Gross Domestic Product; QALY=Quality-Adjusted Life Year

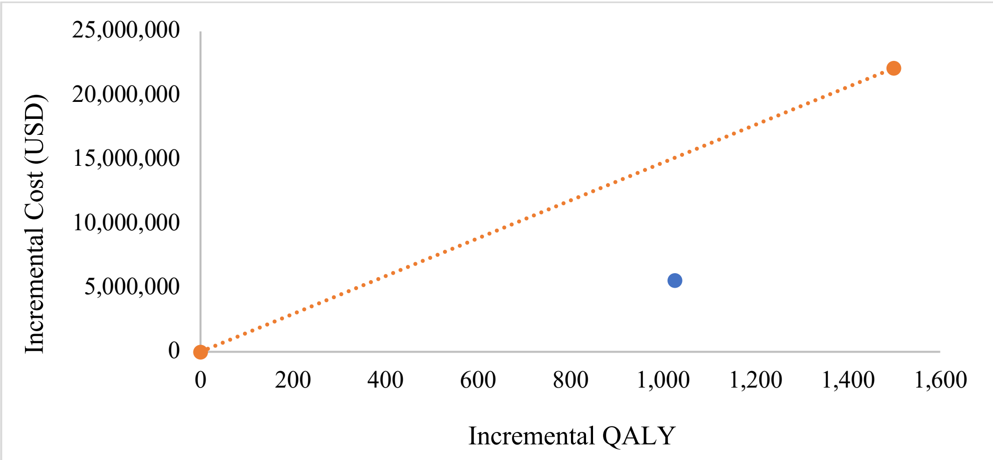

Figure 2. Cost-Effectiveness Threshold (CET) in Baseline Analysis

Note: Orange dots = 3 times the GDP of Indonesia in 2023; blue dots = ICER value in the base-case analysis

One-Way Sensitivity Analysis

One-way sensitivity analysis was conducted by varying the parameter values from base-case values to assess the impact on ICER. The differences in ICER values between the minimum and maximum input parameters are shown in the tornado diagram (Figure 3).

Based on the tornado diagram, the discounting rate of utility and cost of treating colorectal cancer are the parameters with the greatest impact on the differences in ICER values. In contrast, the specificity of colonoscopy for true negative results is not very sensitive to changes in the ICER value.

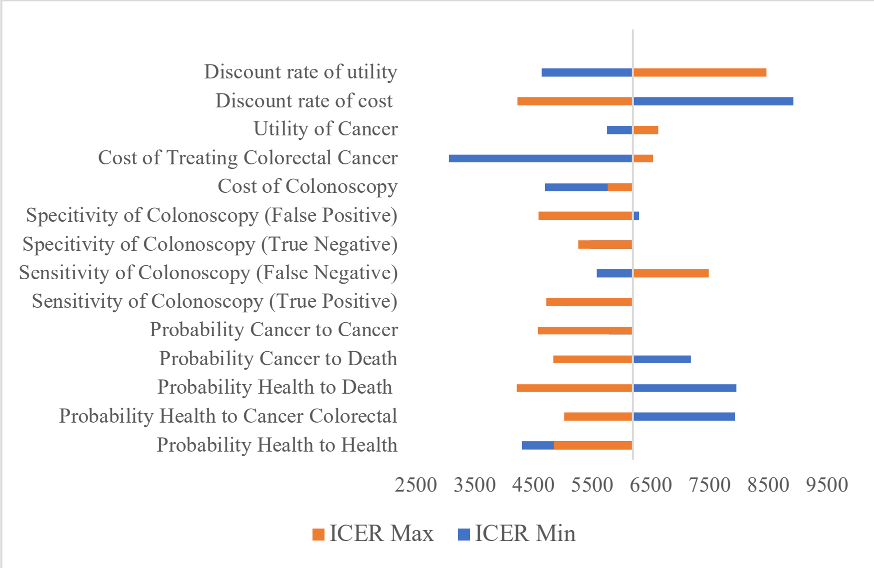

Figure 3. Tornado Diagram Based on One-Way Sensitivity Analysis

Probabilistic Sensitivity Analysis

According to the results of PSA, the ICER values are distributed in quadrant I with an effective mean. Based on the CEAC (Figure 5), colonoscopy screening has increased constantly to one after the intersection of the curves. The method has a greater likelihood of being cost-effective, while the without-screening curve shows a consistent decline after intersecting with the screening curve since the option is not recommended.

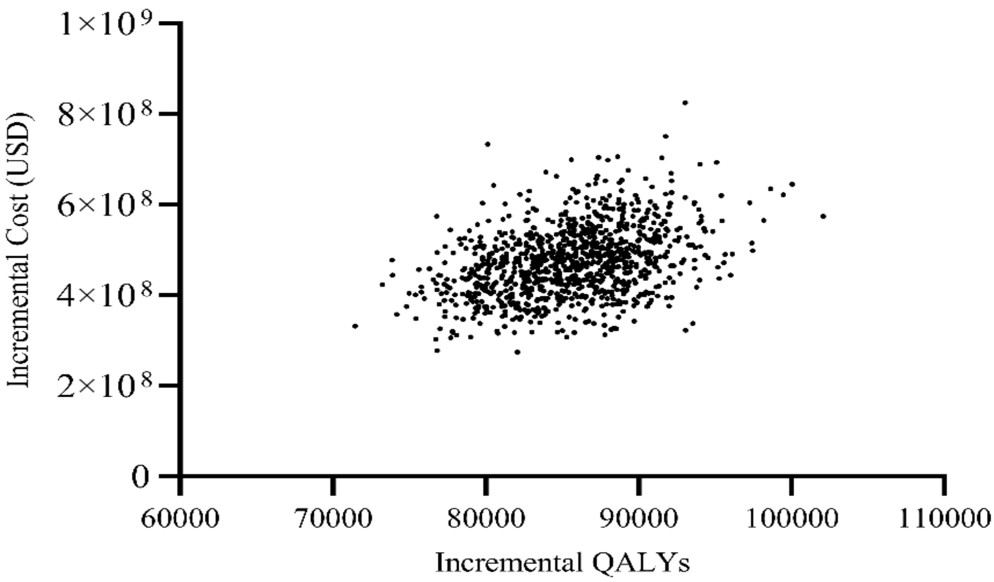

Figure 4. Probabilistic Sensitivity Analysis

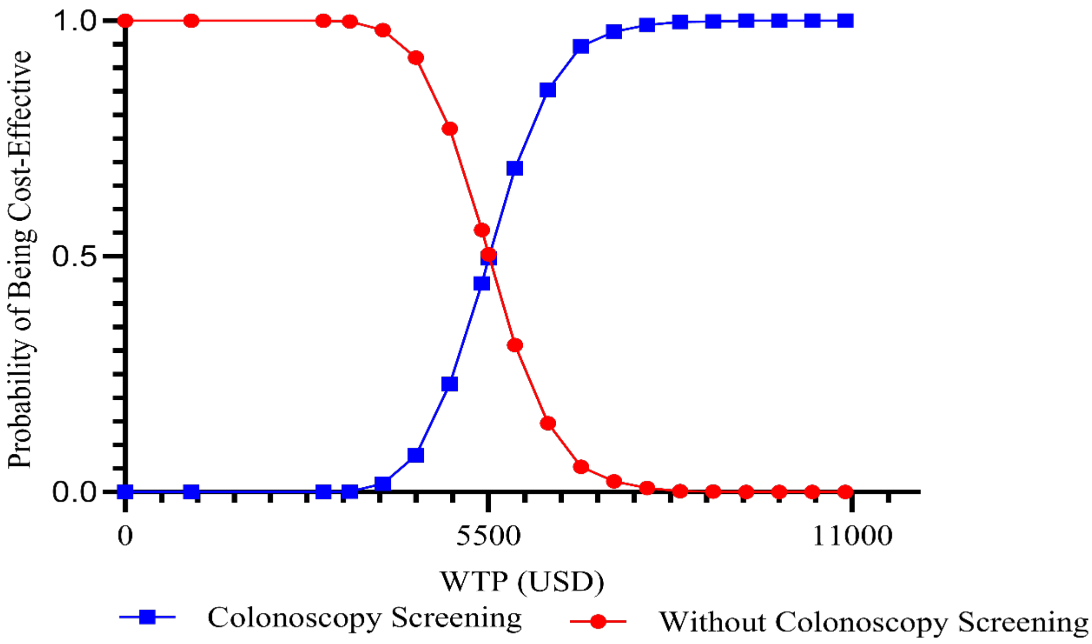

Figure 5. Cost-Effectiveness Acceptability Curve (CEAC)

DISCUSSION

Colorectal cancer represents a significant threat to human health, and screening has been reported as an effective strategy to reduce the burden. Different countries have established screening guidelines for colorectal cancer sequentially. However, screening has not been fully implemented in Indonesia due to several factors, including a lack of knowledge and community engagement, insufficient screening tools, and costs not covered by the National Health Insurance.[18] Antara[19] also stated that colonoscopy surveillance was crucial for the early detection of recurrences, precancerous lesions, and metachronous cancers in patients with colorectal malignancies at Sanglah General Hospital in Bali, Indonesia.

This research was conducted to assess the long-term cost-effectiveness analysis of colorectal cancer screening using colonoscopy from a healthcare provider's perspective. The results show that the costs of colonoscopy screening and utilities are higher than the population without screening. Colorectal cancer incidence and mortality in hypothetical cohorts of 10,000 high-risk individuals enter each strategy at 45 years of age. The incremental cost per QALY for colorectal cancer screening varied from USD 6,191.18/QALY, placing the ICER value in quadrant 1. This required careful consideration from decision-makers regarding the classification of the intervention as cost-effective. The results related to Cost-Effectiveness Threshold (CET) can be seen in Figure 4. Globally, this assessment is based on CET derived from the willingness to pay (WTP) threshold. According to WHO recommendations, an intervention is considered cost-effective and highly cost-effective when the ICER value is less than three and one times the national annual GDP per capita, respectively.[20] Indonesia has a GDP value of approximately IDR 75,000,000 (USD 4,919.7), making the CET to be IDR 225,000,000 (USD 14,759.1).[21]

Based on CET, the intervention of colorectal cancer screening using colonoscopy is considered cost-effective since the ICER value remains below the CET. According to Phisalprapa et al[22], screening with colonoscopy led to a more cost-effective outcome compared to no screening or using FIT in Thailand. Javadinasab et al.[20] stated that performing a colonoscopy at age 40, with screenings every 10 years was the most cost-effective strategy. Meanwhile, Khalili et al.[23] explained that colorectal cancer detection could reduce mortality rates among adults over 50 compared to populations without screening. Detection of colorectal cancer by any method is cost-effective but the performance of a single colonoscopy every 10 years shows the best result due to a lower ICER value.

This research conducted 14 parameters using one-way sensitivity analyses to assess the robustness of the results. The factors most influential on the ICER value are the discounting rate of utility and cost of treating colorectal cancer. In the parameter of discount utility values, increasing the value at the minimum discount rate leads to a decrease in the ICER from baseline. Meanwhile, ICER value increases from baseline at the maximum discount rate. There is a reduction in health utility values, resulting in an increased ICER. Regarding the parameter of colorectal cancer treatment, incorporating costs at the minimum value caused the ICER to decrease. The sensitivity with a considerable range in colorectal cancer treatment costs is attributed to the limited availability of cost data related to colorectal cancer morbidity.

In PSA using Monte Carlo simulation with 1,000 iterations, the percentage of ICER values below baseline (62.4%) was greater than above baseline (37.6%). At a WTP threshold of USD 5,500, there is an intersection between the curves for the intervention "without screening" and "colonoscopy screening." In this context, the probability that "colonoscopy screening" is more cost-effective than "without screening" is 50%. This reflects a significant uncertainty in cost-effectiveness assessment between the two options. After a WTP threshold of USD 5,500, the probability of being cost-effective for colorectal cancer screening increases and consistently reaches 100% at a WTP level of USD 9,000. The results were consistent with Khalili et al.[23] who reported that colorectal cancer detection using colonoscopy every 10 years was cost-effective. Other research also compared 10-yearly colonoscopy screening cost-effectiveness with blood-based screening[24]. A 10-year interval detection strategy with colonoscopy is the most effective method for improving clinical outcomes because greater benefits are provided in terms of health and reduction of disease risk.

This research is the first to investigate the cost-effectiveness of colorectal cancer screening using colonoscopy and has several limitations. First, all the secondary data used are derived from previous research, which may introduce bias when applied to the Indonesian context. A recommendation for future research is to conduct further analysis using primary or real-world data, particularly concerning costs and utilities. Second, the Markov model used does not specifically represent the actual clinical progression of patients with potential colorectal cancer. In this context, the model only depicts the states of the patients, namely healthy, diagnosed with colorectal cancer, and deceased. Additionally, an initial age of 45 years is used, which limits the generalizability of the result to the onset of screening and colorectal cancer. Third, the model is developed from the perspective of healthcare providers and cost data includes direct medical costs.

RECOMMENDATION

The implementation of colonoscopy screening shows cost-effective results when projected with the Markov model. This is evidenced by the ICER value remaining above three times GDP of Indonesia. A recommendation for future research is to explore other interventions, such as conducting colonoscopy every 5 years, and to make comparisons.

AUTHOR CONTRIBUTIONS

I.K.S.: Conceptualization, methodology, data curation, formal analysis, writing-original draft. D.E.: Supervision, conceptualization, data curation, formal analysis, writing-review&editing. T.M.A.: Supervision, formal analysis, writing-review&editing.

ETHICAL CONSIDERATION

The study was approved by the Ethics Committee of the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada (Approval No. KE/FK/1333/EC/2024, approved on August 30, 2024).

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