RESEARCH ARTICLE

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Economic Evaluation of Cervical Cancer Screening by HPV DNA, VIA, and Pap smear Methods in Indonesia

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Abstract

Background: Cervical cancer occurs 80% in developing country including Indonesia and take place in the first rank of incidence rate and third rank in mortality rate in Asian Pacific. Natural history of cervical cancer gives a potential to get accurate screening method. Cervical cancer screening m in Indonesia use VIA and Pap smear method for women in age range 30 to 50 years old. Recently, HPV DNA test has been recommended in international and national policy as primary screening method for cervical cancer. This research aims to asses cost-effectiveness and economic implications of specific cervical cancer screening modalities. **Methods:** Cost-effectiveness analysis was conducted from societal perspective. Cost data was collected from four hospitals in Indonesia. Direct medical costs were derived from discussions with an expert panel and hospital billing data, aligning with current practice guidelines. Direct and indirect non-medical costs were estimated from patient interviews. Effectiveness data for the screening methods were extracted from a systematic review of existing literature. Markov model design was used for cost-effectiveness analysis. Budget impact analysis used healthcare perspective method from its billing for cervical cancer patients. **Results:** Cervical cancer screening costs are calculated using direct medical, non-medical, and indirect expenses. Regarding to cost-effective analysis by incremental cost-effective ratio (ICER), pap smear for every 3 and 5 years is more cost-effective than VIA. HPV DNA also has the potential to be cost-effective. The budget impact analysis investigates scenarios, with a focus on negotiation-based cost reductions for HPV DNA testing. Controlling HPV DNA tariffs at USD 8.76 proves cost-effective. **Conclusion:** In conclusion, pap smear is the most cost-effective modality, while HPV DNA has the potential to be cost-effective by reducing the unit cost. Despite favorable outcomes, challenges in implementation suggest a phased approach for resource equalization before full deployment.

Keywords: Cervical cancer- screfrening- HPV DNA- cost-effective analysis

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Introduction

More than 80% of cervical cancer occurs in developing country, including Indonesia. Nearly 9 from 10 women with cervical cancer died from an advanced stage in 76% of cases. Based on Global Cancer Incidence, Mortality, and Prevalence (Globocan) 2018, Indonesia was placed first of cervical cancer incidence among other Asian Pacific countries and in second rank of cervical cancer mortality after Nepal [1]. Natural history of cervical cancer requires about 20 years, so it has a big chance to be prevented. An accurate screening method is required to screen and detect

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earlier an abnormality in cervix [2].

The costs associated with cervical cancer treatment are notably substantial. In the United States, the expenses of cervical cancer treatment in the final year of life typically reaches USD 118,000 for patients under 65 years old and USD 79,000 for those over 65 years old [3]. Research conducted in Brazil examining the costs of cervical cancer treatment indicates that direct medical costs per year, from the payer's perspective amount to USD 523,218 and USD 581,965 from the healthcare facility's perspective. These figures do not encompass the additional 3.5% of non-medical direct costs that patients are required to bear [4].

Screening scope in Indonesia is still under 10% of the target population that also means it is still far away from the WHO standard [5]. Cervical cancer elimination program from WHO targeted that cervical cancer incidence in all countrycountries could reach 4 cases per 100,000 population. This strategy consists of HPV vaccination program for girls in 15 years old, screening with high performance examination for women in 35 years old and 45 years old, and treatment for women with precancer lesion and invasive cancer [6,7]. Nowadays, cervical cancer screening program in Indonesia use VIA and Ppap smear methods with women in age range 30 – 50 years old as target population. However, VIA still the most frequent used than papsmear. Papsmear is considered difficult to be implemented in developing countries since require large fund, it needs safe transportation to carry specimen with object glass, and require trained health workers for cytology analysis [8]. Recently, HPV DNA methods is recommended for cervical cancer screening. Most of the literature mentioned that HPV DNA method is more effective than papsmearPap smear to detect precancer lesion and invasive cancer. Hence, it is poured into policy recommendations both in international or national as primary screening [1,6]. Unfortunately, HPV DNA method in Indonesia is still minimal and no specific regulations.

Given that problem, a cost-effective screening method is needed to control cervical cancer cases. All this time, economic evaluation about cervical cancer screening especially in Indonesia is still limited. This study is important to evaluate in economic aspects of cervical cancer screening methods as a reference for decision maker in the future.

Materials and Methods

This research is an economic evaluation study, a systematic evaluation method of properties and effects of health technology. This study was conducted from May 2021 until May 2022 in Indonesia. The type of economic evaluation that is carried out is a cost and consequences analysis using a societal perspective. We divided the method section based on the main step that used to mesure the outcome. Those step are costing analysis, cost-effective analysis, and budget impact analysis.

Costing Analysis

A societal perspective was used in costing analysis [9–12]. Direct medical cost requires information about cost of each screening method and follow-up treatment cost from normative cost calculation, and overall therapy cost from primary and secondary data. Primary data can be obtained from patient interview about their personal billing (out of pocket). From interview, direct non-medical cost and indirect cost can also be obtained when patients accessed the screening and treatment for cervical cancer. Whereas secondary data can be provided by hospital billing and national assurance claim (BPJS Kesehatan), Subunit of Cancer Directorate of Non-Communicable Diseases, e-catalog, and laboratory examination tariff.

Cost-Effectiveness Analysis

Cost-effectiveness analysis used societal perspective to look for cost estimation and outcome from cervical cancer screening methods such as VIA, Pap smear, or HPV DNA. In this model, the target population was woman aged 30 – 50 years old. Each screening method may also have variations in screening interval as well as the screening program itself. As a principle, modeling was carried out to estimate impact of each screening program to natural history of disease, expected life years, and expected quality-adjusted life years [13]. Markov model using lifetime time horizon with 3% discount rate was the choice to consider health-state in accordance with natural history of cervical cancer [11,12,14]. Parameter used in the model consists of cost, clinical outcome, and quality of life. Cost parameter that calculated in this model were direct medical cost, Sensitivity analysis was done in this study to define effect size of the parameter towards ICER estimation. Sensitivity analysis used one-way sensitivity analysis that presented by Tornado diagram and probabilistic analysis that presented by Cost-Effectiveness Plane and Cost-Effectiveness Acceptability Curve.

Budget Impact Analysis

Cervical cancer screening program in this era uses VIA and Pap smear with interval time in 5 years. For the future, non-genotyping HPV DNA method every 5 years can be used to replace Pap smear gradually. Population for screening target in budget impact analysis is woman aged 30 years by cohort for next 5 to10 years. Target population is new population and recurrent population that received re-screening. For calculation of cost impact considering target population, pre cancer cases, cervical cancer incidence potential, screening cost, pre cancer treatment cost, and cancer treatment cost. Pap smear will gradually be replaced with HPV DNA and nationally used in fifth year. This stage start from province with highest cervical cancer incidence and screening rate, so within 5 year it will reach entire country. This study analyzes in budget impact for the next 10 years and used healthcare's perspective according to cost calculation from healthcare billing. It was similar to previous study in a different country [15].

Results

Based on cost-effective analysis, if compared to no screening, all modalities of cervical screening have potential cost-effective for examination every 3 years or 5 years. This results was analysed from Incremental

Cost-Effective Ratio (ICER) that explained about cost-difference for each screening modalities. A modality was considered to be cost-effective if it has an ICER less than three times of Gross Domestic Product (GDP). If compared to each modality, HPV DNA vs VIA every 3 year and HPV DNA vs Pap smear every 3 year and 5 year have more than three times of GDP, so those were not cost-effective. If the HPV DNA screening cost was reduced into USD 8.76, so that the ICER will not more than once of GDP and become the most cost-effective modality than pap smear and VIA.

Cost Analysis:

The calculation of medical expenses encompasses direct medical costs, direct non-medical costs, and indirect costs. Direct medical costs are allocated to screening, the treatment of precancerous lesions, and cervical cancer treatment. As screening methods, VIA has the lowest direct medical costs, while HPV DNAHPV DNA represents the screening modality with the highest costs. The primary cost driver for HPV DNAHPV DNA is the support cost, specifically the laboratory expenses for cervical fluid samples. Furthermore, the budget impact analysis scenario considers the minimum value of the HPV DNA test, set at 125 thousand based on negotiations between POGI (Obstetrist and Gynecologist association) and suppliers.

Data on cervical cancer treatment is derived from hospital billing records, with Table 1 presents the first-year treatment costs. Stage 1 cancer treatment has the lowest cost, averaging USD 5,691 while Stage 3 requires the highest cost at USD 6,763. The average cost for cervical cancer treatment is USD 6,343.9, and subsequent years incur lower expenses compared tocost the first year.

Cost-Effectiveness Analysis

A cohort study involving 100,000 women aged 30-50 demonstrated that screening for cervical cancer every 3 years is effective in reducing cancer incidence. The HPV DNA modality exhibits superior sensitivity compared to VIA and Pap smear, resulting in the best outcomes (Figure 1). Screening every 3 years surpasses the outcomes of screening every 5 and 10 years. Without screening, the cancer incidence rate is 1,879 with 1,409 deaths. Every 3 years, VIA reduces the incidence rate to 1,147 with 810 deaths, Pap smear to 1,048 with 728 deaths, and HPV to 955 with 653 deaths (Supplementary files, Table 2).

Cost and output estimates based on this modeling consider screening costs, pre-cancerous lesion treatment, and cancer treatment, viewed from a discounted perspective. Life years and QALYs are used to measure outcomes. Compared to screening every 3 years, the no-screening scenario has the lowest total costs at USD 77.13, closely followed by VIA screening every 3 years at USD 96.09. Pap Smear totals USD 120.65, and HPV is USD 262.93 (Table 2). However, the 10 years expected

Table 1. Cervical Cancer Treatment Cost in First Year

Stadium	n	Mean	SE	Min	Median	Max
1	85	USD 5,691	344	USD 346.7	USD 6,190	USD 13,470.3
2	283	USD 6,121.8	171.2	USD 325.6	USD 6,335	USD 21,584.1
3	275	USD 6,763	197.8	USD 211.9	USD 6,805.8	USD 27,021.2
4	41	USD 6,419.7	561.5	USD 910.6	USD 6,178	USD 18,124.4
Total	684	USD 6,343.9	120.2	USD 211.9	USD 6,523.7	USD 27,021.2

SE, Standard Error; Currency in US Dollar 2021

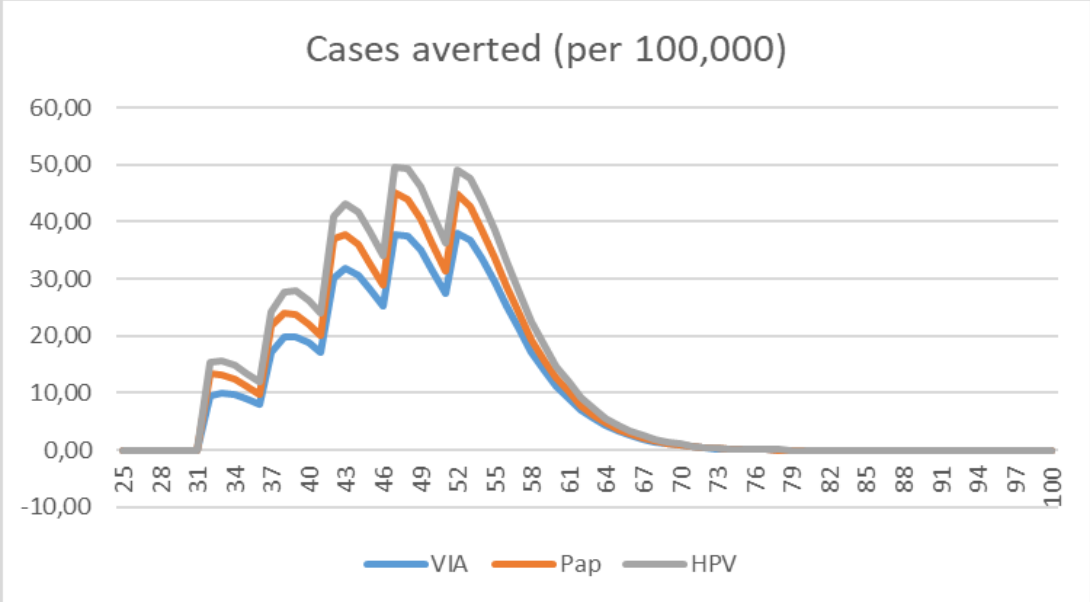


Figure 1. Cervical Cancer Case Averted Per 100.000

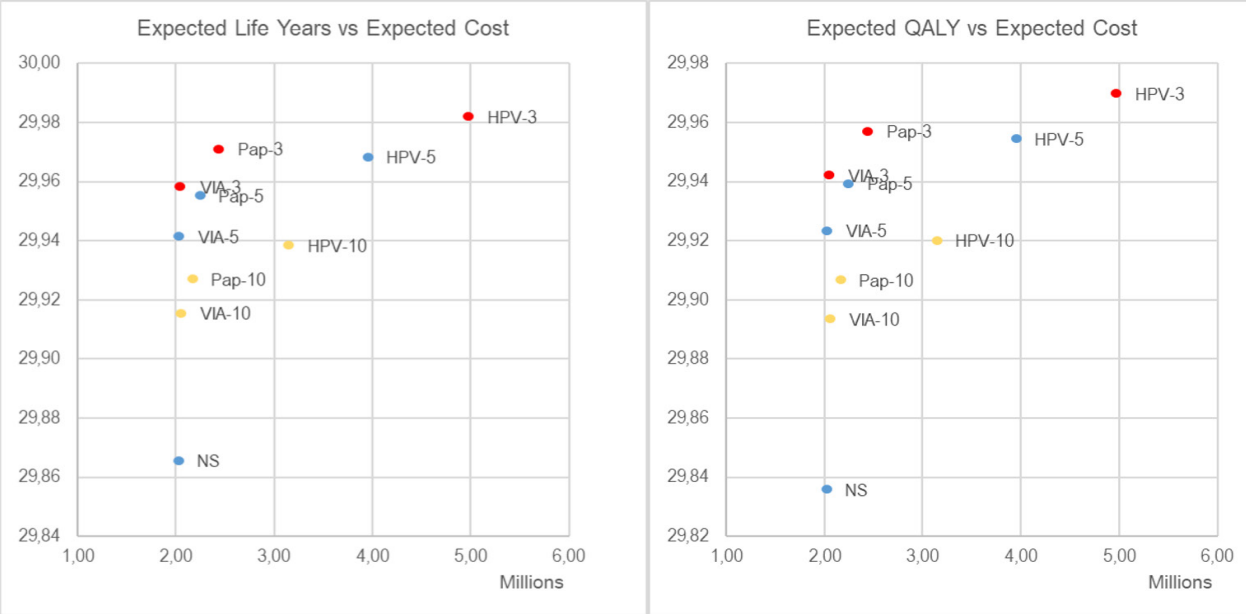


Figure 2. Expected Life Years vs Expected Cost and Expected QALY vs Expected Cost

Table 2. Lifetime Health and Cost Consequences (Base-case)

		Expected Cost				Expected Outcome	
		Discounted				Discounted	
Screening type	Freq	Screening	Treatment	Cancer	Total	Life years	QALY
Screening option							
No screening	0	-	-	USD 77.13	USD 77.13	19.247	19.228
VIA	3	USD 28.34	USD 9.75	USD 58.00	USD 96.09	19.284	19.273
	5	USD 19.58	USD 6.85	USD 64.20	USD 90.62	19.277	19.264
	10	USD 11.81	USD 4.13	USD 70.89	USD 86.83	19.267	19.252
Pap Smear	3	USD 63.21	USD 6.90	USD 50.54	USD 120.65	19.289	19.279
	5	USD 43.67	USD 4.99	USD 56.78	USD 105.44	19.282	19.271
	10	USD 26.34	USD 3.02	USD 66.05	USD 95.41	19.271	19.258
HPV	3	USD 210.78	USD 7.87	USD 44.29	USD 262.93	19.294	19.285
	5	USD 145.61	USD 5.78	USD 49.85	USD 201.23	19.288	19.278
	10	USD 87.84	USD 3.52	USD 61.19	USD 152.55	19.276	19.263

VIA, Visual Inspection with Acetic Acid; HPV, Human Papilloma Virus; QALY, Quality-Adjusted Life Year; Currency in US Dollar 2021

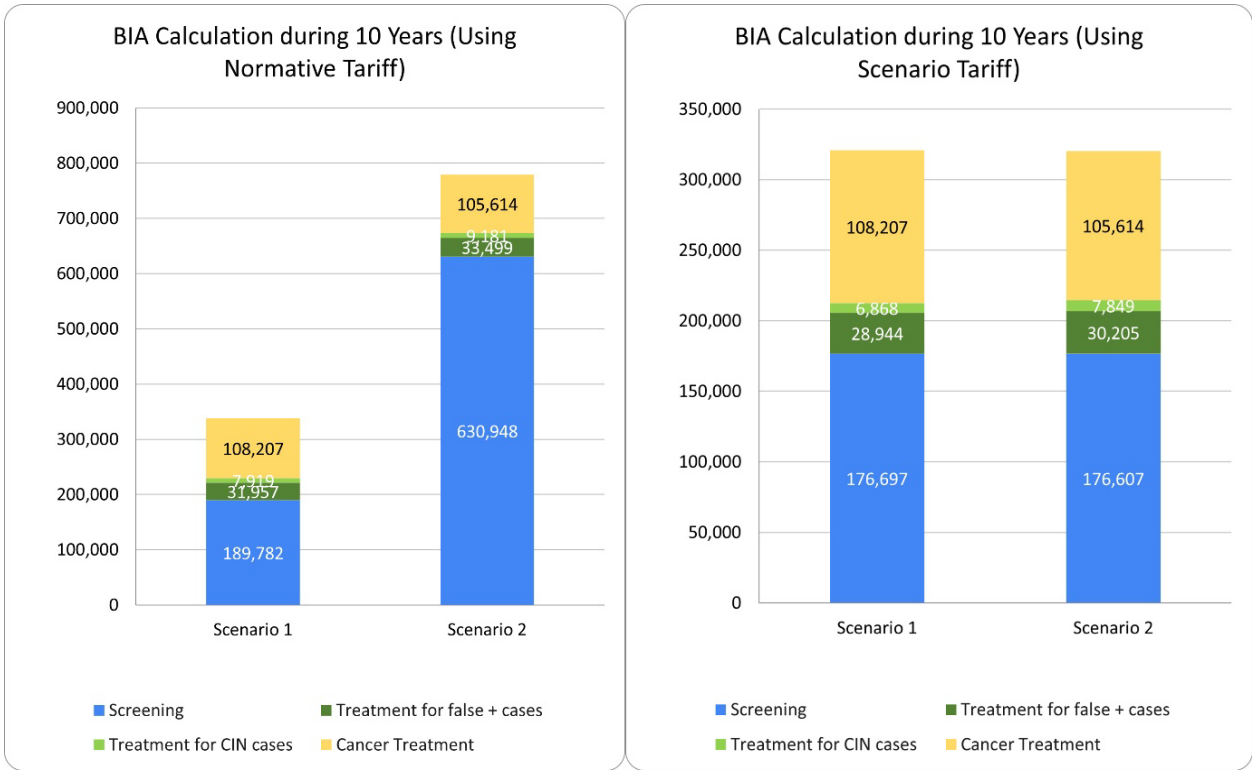
total cost has the cheapest cost than other screening frequency.

Plotting life expectancy and QALYs (X-axis) against estimated costs (Y-axis) reveals the no-screening scenario with the lowest costs and outcomes. VIA, Pap Smear, or HPV screening every 3 years shows higher outcomes with greater costs (Figure 2).

Table 3. Incremental Cost-Effectiveness Ratio Every 3 Years and 5 Years

Modality	ICER Per QALY (3 years)	ICER Per QALY (5 years)
VIA vs NS	USD 438.27	USD 382.65
Pap smear vs NS	USD 874.71	USD 672.02
HPV vs NS	USD 3,365.95	USD 2,568.53
Pap vs VIA	USD 3,781.65	USD 2,156.21
HPV vs VIA	USD 13,968.24	USD 8,467.05
HPV vs Pap smear	USD 26,106.18	USD 15,473.22

Incremental cost-effectiveness ratio (ICER) is statistic method used for analysing cost-effectiveness of health-care intervention. In this study, ICER was used to evaluate the most cost-effective of cervical cancer screening methods. The ICER estimates per QALY between screening modalities were calculated for 3 years and 5 years. Some results exceed three times GDP, especially in comparisons involving HPV. The ICER estimates between HPV and VIA every 3 years require around USD 13,968.24 per QALY and every 5 years require greater costs of USD 8,467.05 per QALY. Similarly, the comparison between HPV and Pap Smear every 3 years needs 372 million and every 5 years demands USD 15,473.2, exceeding 3 times of GDP with standard of 1 GDP per capita for Indonesia at USD 4,032.85 in 2020. Although above twice GDP, the



Currency in US Dollar 2021

Figure 3. Budget Impact Analysis Calculation during 10 Years

estimated ICER between HPV and VIA every 5 years is still considered cost-effective as it remains below 3 GDP (Table 3).

Based on normative costing calculation, HPV DNA screening cost in USD 38.05 with ICER estimation more than 3 times so it is not cost-effective. In order to produce a cost-effectiveness, for HPV DNA tests every 3 years, achieving an ICER of 1 GDP compared to VIA or Pap Smear would require cost reductions to USD 14.83 or USD 14.51 respectively. If the test is conducted every 5 years, costs could be reduced to USD 21.64 or USD 17.99 (Supplementary files, Table 3).

One-way sensitivity analysis is depicted by a Tornado diagram (Supplementary files, Figure 1 and Figure 2). In this analysis, the most influential factors are the screening cost itself and the sensitivity to CIN2+. When compared to no screening, all three modalities can minimize the ICER to a negative value for VIA and Pap smear, and approach zero for HPV DNA modality. In the comparison between HPV DNA,VIA, and Pap smear, if the price of HPV DNA can be reduced to USD 8.76, it can minimize the ICER, making it more cost-effective compared to IVA and Pap smear. This is because HPV DNA screening can detect more cases of precancerous lesions, which can be treated, preventing them from developing into cancer cases. However, these results can be obtained under the condition that screening modalities are repeated at the same intervals, either every 3 years or 5 years in this study.

Probablistic sensitivity analysis that was done every 3 years and 5 years showed that every screening modalities are cost-effective (Supplementary files, Figure 3 and Figure 4). Probabilistic sensitivity analysis every 3 years showed that HPV DNA is superior in output but require greater cost compared to VIA and Pap smear. The same pattern has been discovered for every 5 years screening time. In line with the high testing costs, the ICER values for HPV DNA are greater than 3 times the GDP compared to VIA and Pap smear screening every 3 years, as well as compared to Papsmear every 5 years. Cost-effectiveness acceptability curve showed that all modalities are cost-effective for any amount of WTP per QALY (Supplementary files, Figure 5). If compared to Pap smear, HPV DNA has 60% effectivity of 3 times GDP, and has 80% effectivity of 3 times GDP compared to VIA. However, if the setting up of cutoff is 1 GDP, HPV DNA has the smallest effectivity than VIA or Pap smear.

Budget Impact Analysis

This study examines 30-year-old women, totaling an estimated 2.11 million individuals according to 2023 projections by the Indonesian Central Statistics Agency (BPS). Current cervical cancer screening coverage falls short of the desired target. In the BIA scenario, the aim is to achieve 100% coverage by the fifth year and continue this trend until the tenth year. According to, BPJS Health 2015-2019 data, 66% of cervical cancer screenings in Indonesia use Pap smear, while 34% use VIA. The BIA proposes a gradual shift from Pap smear to non-genotyping HPV DNA screening, prioritizing areas with high cancer incidence rates.

Calculation results using the Markov model for 10 years reveal that the second scenario (VIA, Pap smear, and HPV DNA) sees a 145,390 increase in cases receiving pre-cancer therapy compared to the first scenario (VIA

and Pap smear). However, the second scenario shows 665 fewer cancer cases over 10 years.

Cost components in BIA calculation include screening cost, pre cancer treatment cost, and cervical cancer treatment cost. Screening cost and pre cancer treatment cost in BIA calculation used 2 tariff schme, normative tariff and scenario tariff. For cervical cancer screening approaches, BIA presents two scenarios. The first scenario maintains the current approach (VIA and Pap smear), while the second scenario gradually transitions to non-genotyping HPV DNA. In scenario 2, pre-cancer screening and treatment costs are higher due to the more expensive unit cost for HPV DNA screening, despite fewer cancer cases. In normative tariff, total costs for scenario 2 over 10 years amount to USD 779,242 or similar with 2.3 times higher than scenario 1 amounting to USD 337,865. Controlling the HPV DNA tariff at USD 8.76, with Pap smear and VIA tariffs at USD 8.76 and USD 1.75, respectively, results in lower total costs for scenario 2, both in pre-cancer screening and treatment, as well as cancer treatment. The HPV DNA program cost USD 320,275 , it was nearly USD 460,000 lower than normative tariff (Figure 3). From these findings, we can conclude that for shorterm scenario 2 will gives a higher cost, while for longterm it will needs less cost for cervical cancer treatment cost because the number of cervical cancer cases would be in smaller amount caused by accurate early detection of cervical cancer. It would be recommended if scenario 1 shift to the scenario 2 gradually in a longterm.

Discussion

The unit costs of cervical cancer screening, calculated using the normative costing method, are as follows: HPV DNA at USD 38.05, VIA at USD 2.35, and Pap Smear at USD 9.17. When compared with other studies, VIA has the lowest unit cost compared to other screening modalities. Lince-Deroche et al. calculated the costs of several cervical cancer screening modalities, including HPV DNAHPV DNA at USD 6.31, VIA at USD 4.26, and Pap smear at USD 9.50 [16]. Study in India showed that cost of screening for cervical cancer were USD 5.2 for VIA, USD 9.8 for Pap smear, and USD 14.8 for HPV DNA [17]. They also practiced HPV vaccination to decrease cervical cancer cases, proven by 60% decline of cases and related mortality caused by HPV 16/18 in the lifetime of 100,000 adolescent girls using cohort analysis. Compared to no vaccination, routine VIA screening every 5 or 10 years combination with HPV vaccination resulted more cost-effective of ICER per QALY [17]. Singapore provides subsidies to Singaporean citizens and permanent residents (PR) in the cervical cancer screening program using Pap smear and HPV DNA modalities at polyclinics. The cost for a Pap smear is USD 10.77 and USD 16.1 for HPV DNA for Singapore citizens. Meanwhile, PR is USD 16.1 for Pap smears and 24.25 for HPV DNA [18].

The analysis of direct medical costs for cervical cancer patients, derived from hospital billing for each stage (I to IV), revealed costs of USD 6,190, USD 6,335, USD 6,805.8, and USD 6,178 for the first year respectively. The following year it was USD 261.45, USD 336.56, USD 431, and USD 1,754.56. When compared with the calculation of cervical cancer treatment in Mexico, the cost of cancer treatment in Indonesia from the same perspective (hospital) is slightly more [19]. As well as study in Mexico, a cost-effectiveness study in India also divided health system cost for invasice cancer treatment into four steps of treatment such as outpatient consultation and diagnostic, surgery, 3-dimensional radiotherapy, and brachytherapy. Treatment using 3-dimensional radiotherapy required more treatment cost than others . Treatment using 3-dimensional radiotherapy required more treatment cost than others [17].

Corresponding to cost-effectiveness analysis reluts, the most effective screening modality is pap smear every 5 years and 3 years, following with HPV DNA every 5 years, because the all three modalities have an ICER per QALY below once GDP per capita. However, HPV DNA vs VIA per three years with ICER per QALY USD 13,968.24 has cost-effective potential because its below three times GDP per Capita. Meanwhile, HPV DNA vs Pap Smear (every three years and every five years) with ICER values of USD 26,106.18 and USD 15,473.22 respectively are not cost-effective (above three times GDP per Capita). Based on these results, the modality that is considered to have the most cost-effective potential is a Pap smear every five years, for each increase in the QALY value it costs USD 2,156.21 (Table 3).

If comparing the three methods to no screening, VIA every five years emerges as a highly cost-effective screening option, with a cost of only USD 382.65 per additional QALY gained. This result in line with Chauhan et al. showed that VIA always had the lowest cost than other screening methods compared to no screening This cost is still far from one time Indonesia's GDP per Capita, so it has the potential to still be very cost-effective. A systematic review that was conducted to evaluate cervical cancer screening methods in low and middle income countries (LMIC) conclude that HPV testing and VIA were most cost-effective that cytology. That was also more suitable for LMICs because that will reduce health system infrastructure requirements [20]. If cytology method is used, it would require more laboratory tools then increase the screening cost with no optimum results. Recent study showed that nowadays HPV DNA is the most effective cervical cancer screening option for LMICs especially for woman starting from age 30 years for every 5 years or 10 years. By assuming 70%, cervical cancer age-standardized mortality rates will reduced around 63-67% with HPV testing every 5 years. Screening method using VIA or cytology every 3 years was found less effective in a cancer cases nor costs than HPV testing every 5 years [21].

According to the data presented in Figure 2, when comparing the expected life years and QALYs against VIA costs every three years, there is a potential for greater cost savings compared to Pap Smear screenings every five years.. In the figure it is explained that VIA every three years has higher QALY outcomes and lower costs than Pap Smear every five years. In this study, VIA was the most cost-effective cervical cancer screening modality

with an ICER value of USD 829 (far below India's GDP: 1890 GDP). VIA every three years and HPV DNA every five years are dominated by Pap smears every three years. These results contradict the results of [17,22].

The research team believes that the results of this study have good internal and external validity and can be generalized to the Indonesian situation. Cervical cancer screening method using HPV DNA testing relatively new in Indonesia and has not been implemented in most region in Indonesia, so research team used normative cost approach to calculate the unit cost. In addition, in normative cost calculations, screening modalities are used as cost components obtained from the Indonesian e-catalog LKPP prices, as well as BIA calculations that use BPJS Health claims data and screening coverage from the PTM sub-directorate. Cost parameter for cancer treatment cost components in every stage of cancer was obatained from real word data such as hospital billing. Quality of life, direct non medical cost, and indirect medical cost also was obtained from four referral hospital. This research is also comprehensive, involving multidiscipline background form variation perspective, and would be used as recommendation for national policy in Indonesia that have not been done before.

This study limitation include that research team experienced difficulty in bottom-up costing of laboratory cost component because there was still a lack of HPV DNA testing. No variance of error and no inclusion of allowance and profit margin calculation become limitation of normative costing in this study. Uncertainty of cost sources also becomes other limitation in looking for cost information. In cost-effective analysis model of this study, patient was assumed to move to next stage of cancer sequential and can't jump into two or more next stage of cancer. For target population of budget impact analysis models was not suitable enough with recent practical condition because BIA cohort was following to CEA cohort models.

In conclusion, compared to no screening, all modalities are cost-effective. Although VIA is the most frequent methods used in Indonesia, this study find that pap smear for every 5 years is the more cost-effective than HPV DNA if compared to VIA on this study. However, HPV DNA testing every 5 years is also considered potential cost effective because it has an ICER per QALY below once of GDP per capita. In the future, if the screening method shift using scrnario to combine with HPV DNA testing, it would be more effective because HPV DNA testing can detect more precancerous lesions that could be treated to prevent cancer cases. Despite the potential for favorable outcomes, the implementation of HPV DNA screening faces challenges, and a phased approach is crucial to ensure fair distribution of resources prior to full implementation.

Author Contribution Statement

Authors who played role in building concept and design were FH, AVI, MFR, PL, HS, FME, JAT, AT, LSM, WH, YS, MN. The acquisition of data were done by FH, AVI, MFR, PL, HS, FME, TWU, AT, BA, ABH. Then the data were continued to be analyzed and interpreted by FH, AVI, MFR, PL, HS, FME, JAT, AT, MN. Manuscript was drafted by FH, AVI, MFR, PL, HS, MLS, FME, JAT, AT, LSM, WH, MN, YS then critically revised in terms of important intellectual content by FH, MFR, AVI, PL, HS, MLS, JAT, TWU, AT, BA, ABH, MN. All authors approved this manuscript for publication.

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General

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Approval

This work was approved by Ministry of Health Republic of Indonesia.

Ethical Declaration

This work was ethical approved by Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada – Dr. Sardjito General Hospital with approval number KE/FK/1006/EC/2021.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Study Registration

Not applicable.

Conflict of Interest

The author declare that the research was reported receiving grants from BPJS Kesehatan during the study and there was no financial issue that could be construed as potential conflict of interest.

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