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Evaluating the economic screening of cervical cancer using IVA, HPV DNA, and histology methods: Systematic review

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ABSTRACT

Background: Cervical cancer is a common malignancy causing cancer-related deaths worldwide. Evidence suggests that adequate screening can reduce cervical cancer-related deaths. Screening for cervical cancer can be done using Visual Inspection of Acetic Acid (VIA), HPV DNA and cytology. The economic burden of cancer patients is substantial ranging from US$8,066 to 22,888 per patient. Health cost effectiveness was comparative in the analysis of costs and consequences for the three screening methods. VIA is the most cost-effective primary screening test for cervical cancer. **Purpose**: To review the research results of a full economic evaluation to encourage the specific cervical cancer screening methods used to enhance the detection of precancerous lesions in women's cervix. **Method:** This systematic review used the PRISMA ScR framework with a literature search using 3 databases, namely Pubmed, Wiley, and Google Scholar, with years of publication from 2009 – 2023. The data that has been obtained is carried out by critical appraisal using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS). **Results:** Based on the search for 3,973 selected articles, 7 match the inclusion criteria. This systematic review discovered three major themes: the utility value of health status, cost and analysis. **Conclusion:** The most cost-effective cervical cancer screening is by VIA. HPV DNA and pap smear based cytology techniques have been reported to show high sensitivity and specificity respectively including being expensive and resource intensive. In contrast the VIA technique has moderate sensitivity and specificity but is less expensive Various developed countries have used Pap or HPV DNA cytology tests as the main screening method, which can lead to a 50-70% reduction in cervical cancer incidence, while in developing countries using VIA tests as a cervical cancer screening method.

1. Introduction

Cervical cancer is a malignancy that is a common cause of cancer-related death worldwide (Boardman, 2019). Cervical cancer has a massive economic impact. For instance (Wu et al., 2020) research revealed that cervical cancer costs per patient in China's Henan region varied from US$8,066 to 22,888 from the time of diagnosis to one year following discharge.

Human papillomavirus (HPV) infection with a high-risk serotype leads to cervical cancer. Untreated HPV infection can result in the development of precancerous lesions and malignity. Early

diagnosis and precancerous lesions treatments offer significant potential for intervention because neoplastic development can take years or even decades. WHO identifies cervical cancer as a potential that can be eliminated in this type of cancer. Nonetheless, cervical cancer remains underdiagnosed at this time in clinical exams, particularly in underdeveloped nations (World Health Organization., 2019).

There is proof that effective screening can lower the fatalities caused by cervical cancer. As per the global strategy for eliminating cervical cancer, it is possible to eliminate cervical cancer by the end of this century if in 2030: (a) By the age of 15, 90% of girls have received the entire HPV vaccine, (b) At ages 35 and 45, 70% women are screened with the high-performance test.; and (c) 90% women with invasive cancer are managed, as are 90% women with precancer that have been treated. According to the worldwide HPV vaccination market analysis, just 13% of girls will have received their full dose of vaccine and be protected against cervical cancer by 2021. These findings highlight the need for more rigorous cervical cancer screening in eligible and at-risk groups (World Health Organization., 2020).

Cervical cancer screening can be conducted by various methods, including Acetic Acid Visual Inspection (IVA), HPV DNA testing, and cytology. IVA is an examination by directly applying diluted acetic acid/vinegar (3-5% concentration) to the cervix. After waiting for about one minute, you will see white patches if there are dysplastic cells (precancerous stages). The Pap Smear examines cervical cells using liquid cytology. These screening techniques' diagnostic value, accuracy, and cost interactions vary within the healthcare system (Huy et al., 2019).

Health cost-effectiveness is compared in the cost-consequence analysis for the three screening methods. The cost-effectiveness of resource-limited settings such as India and South Africa revealed IVA is the most affordable primary cervical cancer screening test (Cromwell et al., 2021). However, the affordability of cervical cancer screening is focused and limited by using different methodologies and generalizations across the past, which are often not possible due to several internal and external factors. There is a lack of a consistent method for highlighting economic evaluations, so there is a need for a methodological approach that can describe the systematic differences in the various effectiveness and economic assessments of the two screening methods for cervical cancer (Turner et al., 2019). Numerous industrialized nations have utilized Pap, HPV DNA, and cytology examinations as the main screening method, which can lead to a 50-70% reduction in cervical cancer incidence. From a macroeconomic perspective, global investment in cervical cancer prevention strategies could save up to $1 trillion due to increased disease-free years of life and decreased treatment costs. While techniques such as It has been reported that HPV DNA testing and cytology-based pap examinations demonstrate high sensitivity and specificity (World Health Organization., 2023). However, they also incur significant costs and require substantial resources.

Furthermore, the authors only select based on cost-effectiveness models for review. The authors did not assess the quality of the study methodology, which could affect the validity of the result but only focused on the cost-effectiveness of IVA, HPV DNA and Cytology screening methods.

This systematic review used the CEA/CUA study for cervical cancer screening using Visual Acetic Acid Inspection (IVA), HPV DNA and Cytology.

2. Methods

The research method used was Systematic Review (SR). A systematic review's primary steps were: constructing research questions, identifying search keywords, searching relevant databases, and selecting articles, both abstract and full text, extracting articles based on criteria for selection and reviewing the articles' quality.

2.1. Research Question

The framework used is PICO (Population, Intervention, Comparison, Outcome) which is available in Table 1 below:

Table 1. PICO *Framework*

P	I	C	O
Precancerous lesions	HPV DNA	Iva and Cytology	ICER

Review question

Considering a perspective society, what evidence is provided from a full economic evaluation to support specialized cervical cancer screening techniques to enhance the identification of women's cervical precancerous lesions?

2.2. Search Strategy Design

The search strategy was to locate studies published through clinical trials and peer review. The sources utilized by the author include Pubmed, Wiley, and Google Scholar databases. A database search was carried out in July 2023. In searching for articles, the keywords used were ((((((((((((((((((((((((((Uterine Cervical Neoplasms[MeSH Terms]) OR (Cervix OR (cervical) OR (cervico OR (cancer)) OR (cancerous)) OR (precancer*)) OR (precancer*)) OR (premalignan*)) OR (carcinoma*)) OR (adenocarcinoma*)) OR (neoplas*)) OR (dysplas*)) OR (dyskaryos*OR (tumor])) AND (Human Papillomavirus DNA Tests OR (VIA test*)) OR (visual inspection*)) OR (visual screening)) OR (visual examination*)) OR (visual detect*)) OR (visual test*)) OR (naked eye*)) AND (Papanicolaou Test)) OR (Papanicolaou test*)) OR (Pap test*)) OR (Pap smear)) OR (Papanicolaou smear).

The researcher establishes the inclusion and exclusion criteria for choosing relevant articles. The inclusion criteria were original research articles published between 2009 – 2023, in Indonesian and English, Full-Text, WHO documents or reports/certain formal organizations and relevant articles regarding effectiveness, economic evaluation and cervical cancer screening methods. Exclusion Criteria: Opinion papers. The Prisma-Scr flowchart below describes the number of articles found and the filtering procedure:

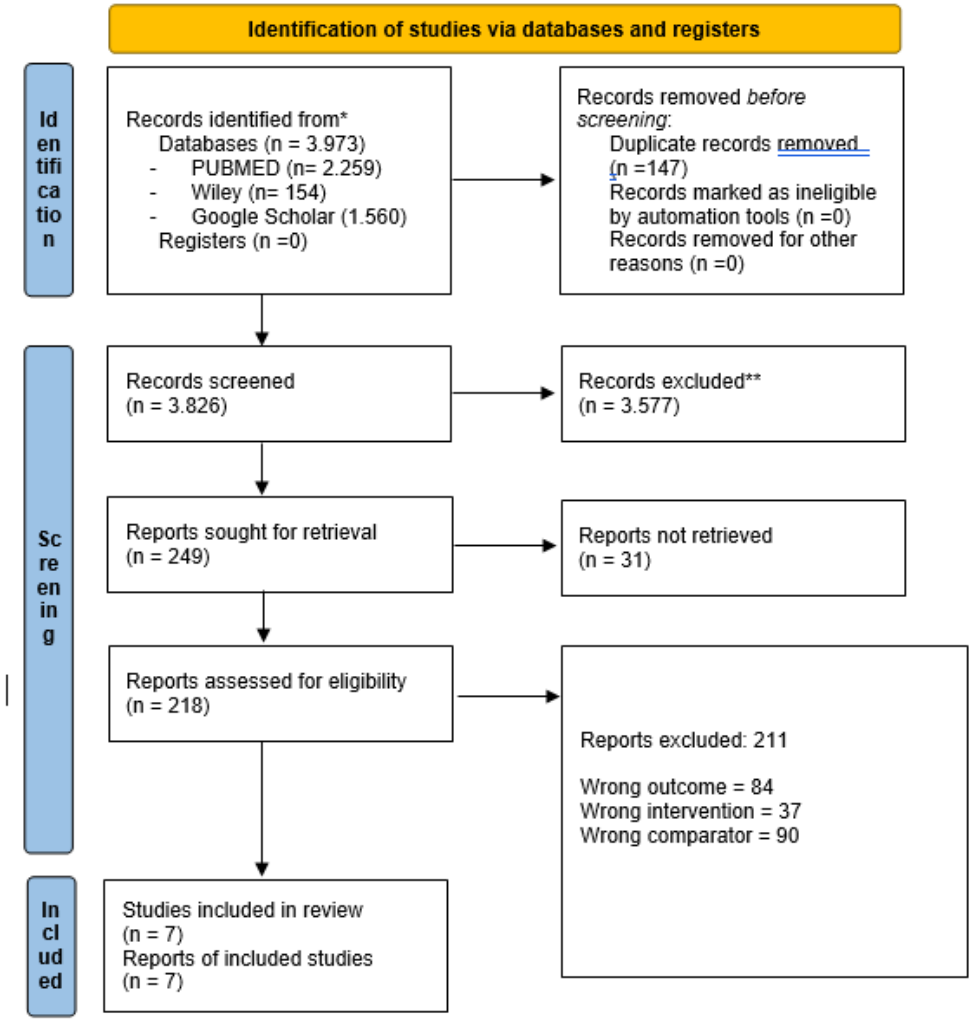

Fig. 1. Prisma ScR flow chart (Tricco et al., 2018)

Some articles are excluded from obtaining articles that match the research questions. This study identified eight relevant articles, then evaluated them using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) tool, a set of guidelines for reporting health economic evaluations. It was developed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) in 2013 and updated in 2022. The CHEERS guidelines help researchers ensure that health economics evaluations are clear, transparent and reproducible.

Table 2. Data Charting

No	Authors/ Country	Title	Population	Intervention	Comparison	Outcome	Purpose	Model	Article Type	Screening Mechanism	Results
1	Chauhan, 2020 India (Chauhan, 2020)	Cost-effectiveness of strategies for cervical cancer prevention in India	Women aged 30 -65 years	DNA HPV Test	Visual Inspection with Acetic Acid (VIA), papanicolau Test	ICER	To examine the affordability of various cervical cancer screening systems and the availability of human papillomavirus (HPV) vaccination in India.	Markov model on MS Excel spreadsheet	Cost-Utility Analysis (CUA)	The least frequent screening method is pap smears conducted every 10 years, while the most frequent is HPV DNA screening perfomed every 3 years. In terms of costs, Opting for VIA screening every 10 years is the most cost-effective approach, whereas conducting HPV DNA testing every 3 years is the most costly strategy.	Screening with VIA 5 and 10 years is cost-effective at a single GDP per capita. India should implement a screening program with a 5-year VIA, which adds US$ 829 (INR 54,881) in costs for each quality-adjusted life year (QALY) gained. Both HPV vaccination alone and combined with screening (utilizing VIA every 5 and 10 years) are considered cost-effective, as they result in (ICERs) ranging from US$ 86 (INR 5,693) to US$ 476 (INR 31,511) per QALY gained compared to neither vaccination nor screening.
2	Termrungruangler, 2019 Thailand (Termrungruanglert, 2017a)	Cost-effectiveness analysis of HPV primary screening and dual stain cytology triage compared with cervical cytology.	A cohort of women aged 30-65 years	Primary HPV	PAP smear	ICER	To evaluate the clinical and financial benefits of p16/Ki-67 dual staining cytology for primary screening of the human papillomavirus (HPV) compared to cytology.	Excel-based Markov model	Cost Effectiveness Analysis (CEA)	Compared to a conventional pap smear, p16/ki-67 double staining as a triage method for HPV primary screening demonstrated greater sensitivity without specificity.	With an ICER of 1.395 per QALY, using p16/ki-67 double staining as a triage method was more efficient and costly than traditional cytology. The model results demonstrate that screening HPV-positive women in the Thai population aged 30-65 with the HPV genotyping test as the primary screening test paired with double staining cytology as triage is more cost-effective than conventional Pap cytology.
3	School Of Public Health, 2019	Health Technology Assessment of strategies for	Women aged 30-65 years	DNA HPV	PAP smear, IVA	ICER	To compare 3 screening strategies, namely IVA,	Markov model on MS Excel spreadsheet	Cost-Utility Analysis (CUA)	Cervical cancer screening with iva and HPV DNA testing. Samples	The lifetime OOP decrease per woman due to cancer case screening ranges from INR 636 (USD 9.6) to INR 810

No	Authors/ Country	Title	Population	Intervention	Comparison	Outcome	Purpose	Model	Article Type	Screening Mechanism	Results
	India (Chandigarh, 2022)	cervical cancer screening in India					Pap Smear and HPV DNA Test, at three different places screening intervals every 3, 5 and 10 years.			were also taken for pap smears for women screened positive for HPV DNA.	(USD 12.2). Finally, The research found that IVA every five years is the most economical screening technique among various screening strategies in the Indian context.
4	Shi, dkk (2011) Cina (Shi, 2011)	Evaluation of primary HPV-DNA testing to visual inspection methods for cervical cancer screening in rural China; an epidemiologic and cost-effectiveness modeling study	662 women aged 15-59 years	HPV	Visual Inspection with Acetic Acid (VIA)	ICER	to undertake a thorough cost-effectiveness evaluation and various screening modalities' impact on cancer incidence and death, comparing the benefits of HPV treatment screening and visual inspection in rural China.	Markov Model	Cost Effectiveness Analysis (CEA)	The VIA screening method was compared to a "Gold Standard" diagnosis based on biopsies taken from all four quadrants. The data was re-analyzed to characterize VILI's accuracy after a negative VIA. Then assess colposcopy.	According to this analytical model, primary care HPV screening in rural China is preferable to visual inspection screening approaches, especially as part of a screening program Savings (LYS) per year with ICER (US$ 557) (for VIA) to $959 (for HPV treatment) in comparison to no intervention referring to Shanxi province's $2,975 per capita GDP in 2008.
5	J Van Rosmalen et al, 2012 Belanda (Rosmalen, Kok, et al., 2012)	Cost-effectiveness of cervical cancer screening: cytology versus human papillomavirus DNA testing	women aged 30-60 years	DNA HPV	HPV test, Cytology test	ICER	to evaluate the efficiency of cytology and HPV testing in terms of cost.	MISCAN Model	Cost Effectiveness Analysis (CEA)	Primary screening uses cytology tests and HPV tests, while triage, namely cytology triage for those who are positive for HPV and HPV triage for those with mild HPV.	The most economical method is primary HPV testing by cytology triage. Using cost-effectiveness limits of €20,000 and €50,000 per QALY resulted in an ideal screening program with 3 and 7 screening rounds.

No	Authors/ Country	Title	Population	Intervention	Comparison	Outcome	Purpose	Model	Article Type	Screening Mechanism	Results
6	Shalini L Kulasingam et al, 2009/ Kanada (Kulasingam et al., 2009)	Human papillomavirus testing with Pap Triage for cervical cancer prevention in Canada: a cost-effectiveness analysis	women aged 25 to 30 years and over	HPV	HPV test, Pap smear test	ICER	to ascertain the HPV test's sensitivity and specificity, either by itself or combined with a pap smear.	Markov Model	Cost Effectiveness Analysis (CEA)	Primary screening uses only the HPV or Pap smear test, while for triage, namely Pap smear with HPV triage or HPV with Pap smear triage.	The results Based on the article, it was found that the strategy for testing HPV with Pap was associated with an ICER <$50,000 per life. Pap followed by HPV triage was also associated with an ICER earned <$100,000 per year. At 25 years of age, triage Pap for women with positive HPV is more economically efficient in decreasing the occurrence of cervical cancer. The screening method currently recommended in Canada.
7	I H-I Chow et al, 2010/Taiwan (Chow, 2010)	Cost-effectiveness analysis of human papillomavirus DNA testing and pap smear for cervical cancer screening in a publicly financed healthcare system	30-year-old healthy woman	Pap smear, DNA HPV	The Pap test, the combination of HPV DNA test with pap smear for triage, and the combination of HPV DNA test with pap smear.	ICER	To evaluate the long-term cost-effectiveness of HPV DNA testing and Pap smear strategies in Taiwan for cervical cancer screening.	Markov Model	Cost Effectiveness Analysis (CEA)	Pap smear screening uses the pap smear test, while for triage, namely HPV, The combination of DNA test with pap smear as a triage method, and the use of HPV DNA test in conjunction with pap smear.	The increased cervical cancer screening frequency from a single Pap test per year to an HPV DNA test followed by Pap smear triage every five years, with an ICER of $1,247,000 per QALY acquired, may result in financial gains, mainly in countries with publicly funded healthcare systems

3. Results and Discussion

From the 7 articles obtained, the study quality was evaluated using the CHEERS critical appraisal tools, and all studies that met the inclusion criteria were included. The cheers statement has 28 statements, explanatory reports, elaborations accompanied by tools and usage guides. In each statement there are 2 categories, namely Yes (Y) and No (T). For each assessment can be seen in the table below :

Table 3. Methodological Quality Assessment

No	Questions	A1	A2	A3	A4	A5	A6	A7
1	Title. Mention the interventions being compared and identify the study as an economic evaluation.	Y	Y	Y	Y	Y	Y	Y
2	Abstract. Present a well-organized summary emphasizing the context, main methods employed, results obtained, and alternative analyses.	Y	Y	T	Y	Y	Y	Y
3	Provide the context for the study, including the research question and its practical significance in guiding decision-making within policy or practice.	Y	Y	Y	Y	Y	Y	Y
4	Determine whether a plan for health economic analysis was formulated and its availability.	T	Y	Y	Y	Y	Y	Y
5	Outline the traits of the study population, including age range, demographics, socioeconomic factors, and clinical characteristics.	Y	Y	Y	Y	Y	Y	Y
6	Offer pertinent contextual details that could impact the findings.	Y	Y	Y	Y	T	Y	Y
7	Explain the interventions or strategies being compared and provide a rationale for their selection.	Y	Y	Y	Y	Y	Y	Y
8	Specify the viewpoint(s) embraced by the research and the rationale behind their selection.	T	Y	Y	Y	Y	Y	Y
9	Specify the duration of the study and the rationale for its suitability.	Y	Y	T	Y	T	T	T
10	Provide information about the selected discount rate(s) and the rationale behind their selection.	T	T	Y	Y	Y	T	T
11	Explain the specific outcomes to assess the benefit(s) and harm(s).	Y	Y	Y	Y	Y	Y	Y
12	Explain how outcomes capture benefit(s) and harm(s).	Y	Y	Y	Y	Y	Y	Y
13	Provide an overview of the population under study and the methodologies employed to assess and assign value to outcomes.	Y	Y	Y	Y	Y	Y	Y
14	Explain how costs were calculated.	Y	Y	Y	Y	Y	Y	Y
15	Provide the dates when the estimated resource quantities and unit costs were recorded, the currency used and the year of conversion.	Y	T	Y	Y	Y	Y	Y
16	If modeling is employed, provide a comprehensive explanation for its usage. State whether the model is publicly accessible and indicate where it can be accessed.	Y	Y	Y	Y	T	Y	Y
17	Explain any techniques used for analyzing or statistically modifying data, any approaches for extrapolation, and methods employed to validate the utilized model.	Y	Y	Y	Y	Y	Y	Y
18	Explain any approaches employed to estimate the variability of study results among sub-groups.	Y	Y	Y	Y	Y	Y	Y
19	Explain the distribution of impacts among diverse individuals or modifications made to address the needs of priority populations.	T	Y	T	Y	T	Y	T
20	Explain approaches to identify and describe any sources of uncertainty in the analysis.	Y	T	T	T	T	Y	T
21	Explain any methods utilized to involve patients, service recipients, the public at large, communities, or stakeholders (such as clinicians or payers) in the study's design.	Y	Y	Y	Y	Y	Y	Y
22	Provide a comprehensive account of all analytical inputs, such as values, ranges, references, and any uncertainties or assumptions regarding their distribution.	Y	Y	Y	Y	Y	Y	Y
23	Present the average values for the primary cost and outcome categories of interest, and provide a concise summary using the most suitable overall measure.	Y	Y	Y	Y	Y	Y	Y
24	Explain uncertainty regarding analytical judgments, inputs, or projections can impact the findings. Present the impact of selecting the discount rate and time frame, if relevant.	Y	Y	T	T	T	Y	Y

25	Examine any distinctions in the involvement of patients/service recipients, the general public, community, or stakeholders and their impact on the approach or findings of the study.	Y	Y	Y	Y	Y	Y	Y
26	Summarize the main discoveries, restrictions, ethical or fairness concerns that were not addressed and how these factors may affect patients, policies, or practices.	Y	Y	Y	Y	Y	Y	Y
27	Explain the study's funding sources and the funders' involvement in determining, designing, conducting, and reporting the analysis.	Y	Y	T	Y	T	T	Y
28	Report the author's conflicts of interest according to the requirements of the journal or International Committee of Medical Journal Editors.	Y	Y	Y	Y	Y	Y	Y
Total		24	25	22	26	21	25	24

Characteristics Of Evidence Sources

Various characteristics of the seven articles have been chosen, encompassing characteristics related to continent, country, and article type.

a) Articles Characteristics Based on Continent

Table 4. Articles Characteristics Based on Continent

Continent	Amount	Percentage (%)
Asia	5	72
Europe	1	14
America	1	14
Total	7	100

Drawing from the information presented in Table 4, it can be inferred that most of the 5 articles (72%) came from the Asian continent.

b) Article Characteristics Based on Country

Table 5. Article Characteristics Based on Country

Country	Amount	Percentage (%)
Developed countries	3	43
Developing country	4	57
Total	7	100

Table 5 above suggests that most of the 5 articles (57%) came from developing countries (India, Thailand and China).

Individual Sources of Evidence Results

Several themes were identified in the Systematic Review conducted by the researcher:

Table 6. Mapping Theme

Theme	Sub Theme	Article
Health Status Utility Value	Health Status Utility Value	A1, A3
Cost	1. Cost	A1, A2, A3, A4
	2. Effectiveness	A1, A3, A4, A5, A7
Analysis	1. Sensitivity	A1, A2, A3, A4, A5, A6, A7
	2. Threshold	A5

Evidence Summary

Based on the 7 chosen articles, it was found that they met the systematic review objectives, namely to discuss the utility value of health status, cost and analysis.

a. Health Status Utility Value

The HrQoL assessment can use a standard tool, namely the EQ-5D-5L (Chauhan, 2020). The FIGO classification says that the Individuals aged 18 to 70 years who underwent treatment for confirmed cervical cancer based on histological examination were at one of the stages I-IVb. According to oncologist consultation, the quality of life (HRQoL) tends to stabilize 4 - 5 months after treatment. Thus, patients with problems regarding cervical cancer can be resolved within 4 months after treatment and are eligible and interviewed during follow-up during outpatient care in the radiotherapy department to assess the quality of life (Termrungruanglert, 2017b). The results of a study (Don Husereau, 2022; Lewandowska et al., 2020) that there are differences in HRQol between Han people and ethnic minorities with cervical cancer and precancerous lesions. HPV vaccine awareness is low among women with cervical cancer and precancerous lesions in southwest China, many women have not even undergone screening. Nationality, economic hardship, menopausal status and screening participation may affect HRQoL in women with cervical cancer and precancerous lesions.

b. Cost

1) Cost

The introduction of the HPV vaccine for teenage girls was also relatively affordable to avoid cervical cancer. At 5and 10-year frequencies, immunizing teenage girls for HPV at the same time as screening women with IVA seems to be a more cost-effective strategy than neither vaccination nor screening. Long-term, when the cohort of young women immunized with HPV reaches 30 years of age, and the IVA screening frequency should be determined based on the vaccination coverage of HPV in the cohort (Chauhan et al., 2020; Irham, 2023). Testing for high-risk human papillomavirus (hrHPV) is the most cost-efficient. The hrHPV testing technique can reduce expenses and discover additional cervical intraepithelial neoplasia 2 or higher (CIN2+) than the screening cytology strategy (Chow et al., 2010; Rosmalen, Van, et al., 2012). Among the non-dominance strategies, The most expensive option is IVA every 5 years, incurring an extra expense of INR 21,196 (USD 320) per QALY gained. Introducing the HPV vaccine alongside IVA every 5 years result in an estimated 90% cancer cases and deaths reduction compared to 5-year IVA alone, at an additional cost of INR 20,537 per QALY acquired. Screening becomes more cost-effective as treatment coverage (Tricco et al., 2018). In general, the cost-effectiveness of IVA techniques has been demonstrated, assuming consistent test results over some time. Due to the visual inspection testing low cost, IVA techniques with greater screening frequencies are anticipated to outperform HPV-treating strategies at lower frequencie (Chandigarh, 2022; Chauhan, 2020).

2) Effectiveness

VIA or HPV is the most efficient alternative for screening and cytology-based screening proved to be the least effective and costly screening method, as the lowest screening in papsmear every 10 years and the highest in HPV DNA screening is done every 3 years. According to cost, performing VIA every 10 years was the cheapest strategy while HPV DNA every 3 years was the most expensive. Insights from developed nations indicate that employing both Pap smear and HPV DNA screening methods is effective and economically efficient, decreasing cervical cancer incidence and mortality by more than half (Shi et al., 2011; Wuriningsih & Distinarista, 2019). The relative order of testing

technologies in reducing cervical cancer incidence and mortality is VIA (least effective); VIA/VILI; careHPV@1.0 pg/ml, and careHPV@0.5 pg/ml (most effective) (Shi et al., 2011).

c. Analysis

1) Sensitivity

It has been reported that HPV DNA and cytology-based pap smear techniques have high sensitivity and specificity, including being expensive and resource intensive. In contrast, IVA is less expensive but has modest sensitivity and specificity. According to (Termrungruanglert, 2017b) and (Chandigarh, 2022), In comparison to traditional Pap smears, using p16/ki-67 double staining as a triage method for HPV primary screening demonstrated better sensitivity without specificity loss. Improved screening results in a lower precancerous lesions prevalence and a lower annual incidence and cervical cancer mortality rate.

HPV is a new technique developed through public or private cooperation between Qia Gen Inc (Gaithersburg, MD) and PATH (Seattle, WA, USA) that has demonstrated excellent sensitivity for identifying cervical intraepithelial neoplasia grade 2 and higher (CIN2+) (Shi et al., 2011). The threefold utility disadvantage associated with time spent in triage This would render strategy I (primary cytology with HPV triage) the most economical option. In cases where 10% of women with a positive initial test fail to attend triage, opting for primary cytology screening (Strategy I) emerges as the most economically efficient decision. The liquid-based Pap smear will have comparable sensitivity but lower specificity than the conventional one. Pap smears every 5 and 3 years, HPV-Pap every 5, 3, and every year, and each year combined increases and discounted QALY magnitudes and the alternatives cost as anticipated (i.e., annual screening programs are the most effective and the most costly).

2) Threshold

Maintaining the screening cost-effectiveness to establish the minimum coverage required for treatment, a threshold analysis specific to the situation is necessary for positive screening and the cervical cancer risk/ HPV infection lifetime incidence (Auliya, 2022). Based on the probability of HPV infection, a subgroup analysis was performed to examine the screening effect among those with low incomes (bottom 1/3 income group) and non-poor (upper 2/3 income group), among the income groups concerned. In the threshold analysis, it was found that the HPV test is the least expensive. In the base case analysis, The HPV test laboratory price was €33.87 or equivalent to IDR 562,990, and the annual utility loss due to triage was 2.2 days of life. If the laboratory expense for the HPV test exceeds €42 IDR 698,187, conducting primary cytology screening would be a more cost-effective option compared to primary HPV testing (for € 20,000 or IDR 332,470,000 cost-effectiveness threshold QALY) or more than €41 or IDR 681,563 (for €50,000 or IDR 831,175,000 per QALY threshold). Primary cytology screening proves to be the most economically efficient approach as it minimizes the loss of utility resulting from time spent in triage, reducing it from 2.2 days per year to a minimum of 6 days per year.

4. Conclusion

Cervical cancer is a prevalent malignancy that results in cancer-related deaths worldwide. Adequate screening can reduce cervical cancer-related deaths. Acetic Acid Visual Inspection (IVA), HPV DNA, and cytology can be used to screen for cervical cancer. Pap or HPV DNA cytology tests have been used as the major screening method in a number of developed countries, which can lead to a 50-70% decrease in the cervical cancer incidence. From a macroeconomic perspective, global investment in cervical cancer prevention strategies could result in Potential savings of up to $1 trillion resulting from an increase in disease-free years of life and decreased treatment costs. While techniques such as It has been reported that HPV DNA testing and cytology-based pap examinations exhibit high sensitivity and specificity, they also entail significant costs and require substantial resources.

The most cost-effective cervical cancer screening is the IVA. It has been reported that HPV DNA and cytology-based pap smear techniques exhibit high sensitivity and specificity, including being expensive and resource intensive. In contrast, the IVA technology is less expensive but has modest sensitivity and specificity.

5. Recommendation

The government and health institutions need to increase public awareness about the importance of cervical cancer screening and ensure easy and affordable access to Pap cytology tests or HPV DNA, which have proven effective in decreasing cervical cancer incidence. Cervical cancer is a global problem that affects many countries. Therefore, Improving international collaboration in cervical cancer screening program research and implementation is crucial. By sharing knowledge and experience, we can achieve faster global progress in tackling this problem.

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