Philippine Society for Cervical Pathology and Colposcopy

The PSCPC Clinical Practice Guidelines for the Management of Abnormal Cervical Cancer Screening Results

in cooperation with

DISCLAIMER

This guideline is intended to be used by obstetrician-gynecologists, general practitioners, and primary care providers. Although adherence to this guideline is encouraged, it should not restrict the clinicians in using their clinical judgment and considering patient's values, needs and preferences while handling individual cases. Clinicians and relevant stakeholders must always exercise sound clinical decision-making as the individual patient's history and current physical status dictate and while their responses to treatment may vary.

Payors and policymakers, including hospital administrators and employers, can also utilize this CPG, but nonconformance to this document should not be the sole basis for granting or denying financial assistance or insurance claims. Recommendations from this guideline should not also be treated as strict rules on which to base legal action.

Developers of this CPG are aware of its limitations. Evidence summaries are based on the best available scientific evidence as of the time of its formulation. However, certain aspects of the screening may not have been addressed by the clinical trials and observational studies, and as such, evidence bases are therefore not all inclusive. Considerations on these aspects were still deemed necessary in the current contexts of primary care.

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ACKNOWLEDGEMENT

This CPG was initiated, prepared and funded by the Philippine Society for Cervical Pathology and Colposcopy (PSCPC). The PSCPC neither imposed any condition nor exerted any influence on the operations and the final output formulation.

The CPG Steering Committee was responsible for overall organization and management and is accountable for the quality of the CPG. The members include Maria Julieta V. Germar, MD (PSCPC), Renee Vina G. Sicam, MD (PSCPC), Ian Theodore G. Cabaluna RPh, MD, Gdip (Epi), MSc (cand.), Maria Virginia S. Abalos, MD (PSCPC), Jay-Ar T. Sorreda, MD (POGS) and Concepcion D. Rayel, MD (PSCPC).

The Technical Working Group undertook extensive work in (1) searching and synthesizing the evidence while ensuring objectivity in each stage of the process, (2) presenting the evidence in the panel discussion, and documenting and writing the final report. They were also indispensable in carrying out the legwork, coordinating among various individuals, groups, and committees, and facilitating the *en banc* meeting. The members of the group are the following: Ian Theodore G. Cabaluna RPh, MD, Gdip (Epi), MSc (cand.), Rogelio N. Velasco, Jr. MD, MSc (cand.), Rich Ericson C. King, MD, MSc (cand.), Howell Henrian G. Bayona, MSc, Kerwyn Jim C. Chan, MSc (cand.), Joseff Karl U. Fernandez, MD, Richmond Paul E. Goce, MD, Timothy Hudson David Culasino Carandang, MD, FRSPH

Lastly, this guideline is invaluable because of the contribution and participation of panelists from different sectors of healthcare who committed their time and effort to share their knowledge, experience, and expertise in analyzing the scientific evidence and their values and preferences in formulating the recommendations with consideration of patients and the current healthcare system in the country.
The panel members are the following: Ma. Theresa G. Fiji-Aliga, MD (Philippine Academy of Family Physicians), Genalin F. Amparo, MD (Jose R. Reyes Memorial Medical Center), Clarito U. Cairo, Jr. MD (Department of Health), Betha Fe M. Castillo, MD (Philippine Obstetrical and Gynecological Society), Mary Judith Q. Clemente, MD (Philippine Infectious Diseases Society for Obstetrics and Gynecology), Michele A. Hernandez-Diwa, MD (Philippine Society of Pathologists), Tristan Jediah V. Labitad, MD (Philippine Society of Public Health Physicians), Jericho Thaddeus P. Luna, MD (University of the Philippines - Philippine General Hospital), Daphne Oseña-Paez (Patient Advocate), and Jean Anne B. Toral, MD, MSc (Collaboration/Manila Declaration: Call to Action Against Cervical Cancer).

EXECUTIVE SUMMARY

The Clinical Practice Guidelines for the Management of Abnormal Cervical Cancer Screening Results is an output of the Philippine Society for Cervical Pathology and Colposcopy. This clinical practice guideline is a systematic synthesis of evidence to address the management of abnormal cervical cancer screening results among adult females, which include ASCUS on cytology and positive high risk HPV DNA test. This CPG provides three (3) recommendations on prioritized questions in the management of abnormal cervical cancer screening results.

Recommendations are based on the appraisal of the best available evidence on each of the three identified clinical questions. The CPG is intended to be used by general practitioners and specialists in the primary care setting, policy makers, employers and administrators, allied health practitioners and even patients. The guideline development process followed the widely accepted Grading of Recommendations, Assessment, Development, and Evaluation or the GRADE approach. It included 1) identification of critical questions and critical outcomes, 2) retrieval of current evidence, 3) assessment and synthesis of the evidence base for these critical questions, 4) formulation of draft recommendations, 5) convening of a multi-sectoral stakeholder panel to discuss values and preferences and assess the strength of the recommendations, and 6) planning for dissemination, implementation, impact evaluation and updating. The recommendations in this CPG shall hold and will be updated after 3 years or when new evidence arise.

SUMMARY OF RECOMMENDATIONS

Recommendation	Certainty of Evidence	Strength of Panel Recommendation
Question 1: Among adult females with Pap smear of ASCUS, should HPV DNA, repeat Pap smear after 1 year or colposcopy be done?		
1. We suggest either repeat cytology after six months or immediate HPV triaging compared with colposcopy in screening for cervical cancer among adult females with ASCUS.	Very Low	Weak
Question 2: Among adult females with HPV 16/18 on genotyping, should VIA, cytology or colposcopy be done?		
1. We suggest colposcopy over cytology or VIA for adult females who are positive for either HPV 16 or 18.	Low	Weak
Question 3: Among adult females with other HPV high risk types on genotyping, should VIA, cytology or colposcopy be done?		

1. We suggest colposcopy over cytology triage for adult females who are positive for other high-risk HPV types (non-16/18).	Very Low	Weak
2. We suggest colposcopy over VIA/VILI triage for adult females who are positive for other high-risk HPV types (non-16/18).	Very Low	Weak

INTRODUCTION

Cervical cancer remains to be the leading gynecologic malignancy in the Philippines. Human Papilloma Virus (HPV) is deemed as the "necessary cause" of cervical cancer, with multiple sexual partners, multiparty, immunocompromised-state, smoking and use of oral contraceptive pills as risk factors[1]. At least 70% of the cases are caused by HPV types 16 and 18. Aside from these, other oncogenic or high-risk HPV (hrHPV) genotypes are associated with cervical intraepithelial neoplasia and cervical carcinoma[2]. In May 2018, a Call to Action for the elimination of cervical cancer was initiated by the WHO with targets for vaccination, screening and access to treatment by year 2030.

In the Philippines, national implementation of primary prevention of girls aged 9-14 years old through HPV vaccination started in 2016. However, only 5% of the intended population have received their final HPV dose[3]. The Department of Health adopted VIA as the primary screening method for 25-55 year old women, but only a minority of women (less than 1 in 10) have been screened[4]. Thus, cervical cancer remains to be a significant disease in the country.

The Philippine Society of Cervical Pathology and Colposcopy is a non-stock, non-profit organization, that aims to disseminate knowledge in uterine cervical pathology and colposcopy. Since its incorporation in 2002, it has held workshops and continuing medical education activities for promotion of knowledge on cervical cancer screening and the practice of colposcopy, a diagnostic procedure that detects premalignant disease and early cervical cancer. In 2019, in its collaboration with four other Obstetrical and Gynecological specialty/subspecialty societies to address Cervical Cancer in the country, namely SGOP, AOGIN-Philippines, PIDSOG and POGS, its role was designated as screening to streamline the efforts for a cervical cancer-free Philippines.

The PSCPC previously created guidelines for screening and management of abnormal results in 2012. Since then, many international screening guidelines have been published in recent years which are advocated by several organizations, such as the WHO and American Society for Colposcopy and Cervical Pathology (ASCCP). In general, most guidelines are in agreement that HPV DNA testing is the recommended primary screening test.

The Department of Health and the National Institutes of Health through the Philippine Guidelines on Periodic Health Examination (PHEX) recently created recommendations on the method, age and frequency of cervical cancer screening in the country[5]. As HPV DNA testing is emerging to be the method of choice screening in the country, guidelines as to the subsequent management of a positive test is needed. Updates through genotyping has enabled the division of HPV to HPV-16/18 and other high risk HPV genotypes. PSCPC, in the form of this CPG, will give recommendations on both of these positive results.

Most obstetrician-gynecologists still perform Pap smear (conventional or liquid-based cytology) in primary screening for cervical cancer. Not all obstetrics-gynecologists are trained in performing VIA and HPV DNA test is not available in all institutions. In this time of transition from Pap smear to HPV DNA testing as primary screening, clinicians should be guided on the management of abnormal Pap smear result. The most common abnormal Pap smear result is ASCUS and the management of such will be addressed in this CPG. It is envisioned that more questions will be added to the PSCPC CPG in the subsequent years.

The objective of this CPG is to give guidance to obstetrician-gynecologists and general physicians who perform cervical cancer screening as to the next steps in the management of abnormal screening results showing the following: 1.) ASCUS on cytology 2), positive for high risk HPV 16/18 3) and positive for other high risk DNA types.

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GUIDELINE DEVELOPMENT METHODOLOGY

Organization of the Process

Following the international standards, the DOH (1) outlined the guideline development process into four phases: 1) preparation and prioritization, 2) CPG generation, 3) CPG appraisal, and 4) implementation in the Manual for CPG Development[1].

The Philippine Society of Cervical Pathology and Colposcopy conceptualized the creation of Clinical Practice Guidelines on the Management of Abnormal Cervical Screening Results in the Philippines in 2021. The members of the society underwent a workshop in creation of CPG by a private company. A Steering Committee was formed composed of the officers of the PSCPC and obstetrician and gynecologists practicing in Luzon, Visayas and Mindanao. In the preparation and prioritization phase, the Steering Committee (SC) set the CPG objectives, scope, target audience, and clinical questions. They identified and formed the working groups involved in creating the evidence base and finalizing the recommendations for each clinical question included.

The guideline questions were developed using the PICO (population, intervention, comparator, and outcome) format. The SC developed the questions consulting the technical working group and the consensus panel. The questions prioritized were the following:

1. Among adult females with Pap smear of ASCUS, should HPV DNA, repeat Pap smear after 1 year or colposcopy be done?
2. Among adult females with HPV16/18 on genotyping, should VIA, cytology or colposcopy be done?
3. Among adult females with other HPV high risk types on genotyping, should VIA, cytology or colposcopy be done?

The technical working group composed of the evidence review experts (ERE) and technical adviser were tasked to review existing CPGs, appraise, and summarize the evidence, and draft the initial recommendations. The evidence summaries were then presented to the consensus panel members to finalize the recommendations.

The consensus panel consisted of multisectoral representatives tasked to review the evidence summaries and develop recommendations during the *en banc* meeting. In the meeting, they prioritized critical and important outcomes; discussed necessary considerations revolving around the recommendations and voted on each recommendation and its strength.

Creation of the Evidence Summaries

The ERE searched and appraised research articles related to the clinical question. The results of the appraisal of existing CPGs and their evidence summaries determined the need for a systematic search (Date of Last Search: June 30,2022) in electronic databases (MEDLINE via PubMed, CENTRAL, Google Scholar) for the need to do de-novo systematic reviews and meta-analysis for each question. Relevant local databases and websites of medical societies were also utilized in the search. Keywords were based on PICO (MeSH and free text) set for each question. The ERE also contacted authors of related articles to verify details and identify other research studies for appraisal, if needed.

At least two reviewers worked on each PICO question. Evidence reviewers appraised the directness, methodological validity, results, and applicability of each relevant article included. RevMan, STATA, and GRADEPro were used for the quantitative synthesis of important clinical outcomes for each question. The ERE generated evidence summaries for each of the three questions. Each evidence summary included evidence on the burden of the problem, and diagnostic performance, benefits, harm, and social and economic impact of the screening test/intervention. Evidence/information that will facilitate in the decision

(i.e. cost of screening test, cost-effectiveness studies, qualitative studies) were also included in the evidence summaries. The Quality of Evidence was assessed using the GRADE approach[2] (Table 1).

Table 1. Basis for Assessing the Quality of the Evidence using GRADE Approach

Certainty of Evidence	Interpretation
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Factors that lower quality of the evidence are:

- Risk of bias
- Important inconsistency of results
- Some uncertainty about directness
- High probability of reporting bias
- Sparse data/Imprecision
- Publication bias

Additional factors that may increase quality are:

- All plausible residual confounding, if present, would reduce the observed effect
- Evidence of a dose-response gradient
- Large effect

The evidence was synthesized based on the screening cascade framework (Figure 1). Direct evidence was given high priority. They are studies that evaluated the effect of screening strategies or intervention on patient important outcomes such as mortality or morbidity. In cases where direct evidence is scarce, indirect evidence were also utilized. These are research that studied certain aspects of the cascade such as the diagnostic performance of the screening test and/or confirmatory test, or the effectiveness of early therapy.

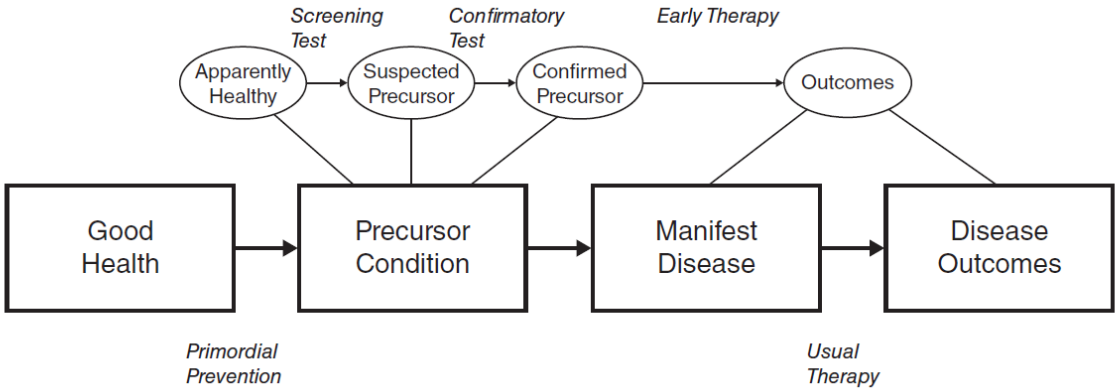

Figure 1. Screening Cascade. Adopted from: Dans A, Dans L, A. SM. Painless Evidence-Based Medicine. Second ed: John Wiley

Composition of the CPG Panel

The Steering Committee and technical adviser finalized the members of the consensus panelists, considering possible conflicts of interests of each panel member. To ensure fairness and transparency, the

composition was guided by the DOH manual[1]. Content experts and other key stakeholders were invited to join the CP. The key stakeholders included family physicians, public health physicians, pathologists, policymakers, and patient advocates. See Annex A for list of members.

Formulation of the Recommendations

Screening tests were recommended based on the following criteria[3,4]:

1. The burden of illness must be high.
2. The tests must be accurate.
3. Early treatment must be more effective than late treatment.
4. Diagnostic tests and early treatment must be safe.
5. The cost of the screening strategy must be commensurate to the potential benefit.

Draft recommendations were formulated based on the quality of evidence, trade-offs between benefit and harm, cost-effectiveness, applicability, feasibility, equity, resources and uncertainty due to research gaps.

The strength of each recommendation (i.e. strong or weak) was determined by the panel considering all the factors mentioned above. Strong recommendation means that the panel is "confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects" while weak recommendation means that the "desirable effects of adherence to a recommendation probably outweigh the undesirable effect but is not confident."[5]

The recommendation for each question and its strength was determined through voting. A consensus decision was reached if 75% of all CP members agreed[2]. If consensus was not reached in the first voting, questions, and discussions were encouraged. Two further rounds of voting on an issue were conducted. Evidence-based draft recommendations were also revised based on input arrived at by consensus in the *en banc* discussions.

Managing Conflicts of Interest (COI)

The Steering Committee facilitated the whole CPG formulation process, but their members had no direct participation in assessing and synthesizing the evidence, generating the evidence summaries and evidence-based draft recommendations of the Evidence Review Experts, and voting on final recommendations during the *en banc* consensus panel review. They invited the relevant organization to nominate individuals who can become part of the consensus panel.

Each nominee completed and submitted a declaration of interest form and their curriculum vitae. The SC screened the nominees for any possible conflict of interest that may bias their decisions. Those with significant potential COI were not allowed to vote during the deliberation. See Annex B for the list for COI management.

External Review

Three independent stakeholders reviewed the draft guidelines on the clarity, acceptability, applicability and feasibility of the recommendations and gave their feedback to the steering committee. Their feedback was taken into consideration. The reviewers found the recommendations to be clear, acceptable and feasible. The reviewers did not make changes to the recommendations. Suggestions regarding providing a practical version for readers such as an algorithm, timely updating, dissemination and monitoring of the guidelines were noted by the steering committee and are included in future activities.

Planning for Monitoring, Dissemination, Implementation and Update

The SC will develop a program of monitoring to determine the best practices of relevant stakeholders in the adherence and impact of this guideline. Monitoring the use of this CPG may also be a subject of research by interested parties.

The SC will discuss with relevant stakeholders such as DOH and PhilHealth to prepare a dissemination plan after being cleared by the DOH National Practice Guideline Program. Preliminary plans include making guidelines available on websites, press conferences, social media sites, professional society conventions, and journal publications. A simple concise version with an algorithm will also be provided. This CPG will be updated after 3 years or when new evidence requiring immediate review of the recommendation emerges.

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BURDEN OF CERVICAL CANCER

Cervical cancer has a high disease burden globally. It is the fourth most common cancer worldwide and has an age-standardized mortality rate of 162 per 100, 000 population.[1] It is estimated to account for 604,000 new cases and 342,000 deaths among women in 2020 worldwide.[1,20] There is a wide disparity in the incidence and mortality of cervical cancer among developed and undeveloped countries with 85% of cases and deaths occurring in Low to Middle Income Countries (LMIC)[2] . Although a preventable disease, highly effective screening modalities and vaccination are not widely available in developing countries. As of 2020, only 44% of women in LMICs have been screened for this disease compared to more than 60% in high-income countries[3] .

Cervical cancer is the second most common cancer among Filipino women, with 5,479 and 4,052 new cases and deaths respectively in 2020.[1] It is also the fourth leading cause of cancer-related death among women in the Philippines. Its overall 5-year survival rate has not changed at 44% between 1980 to 2010.[4] The relatively high mortality rate (1 in 10,000 women) was attributed to lack of screening for early detection and inaccessible treatment services in the country. [4,5]

Almost all cervical cancers are caused by the human papillomavirus (HPV).[6] At least 70% of the cases are caused by HPV types 16 and 18. Aside from these, other oncogenic or high-risk HPV (hrHPV) genotypes are associated with cervical intraepithelial neoplasia (CIN; HPV-6, 11, 31, 34, 33, 35, 39, 42, 44, 45, 51, 52, 56, 58, 66) and cervical carcinoma (HPV-31, 45, 33, 35, 39, 51, 52, 56, 58, 66, 68, 70).[7] Various risk factors associated with HPV infection and cervical cancer among Filipino women include smoking, low socioeconomic status, high parity ($\geq$5 pregnancies), young age at first intercourse, use of oral contraceptives, and risky sexual behaviors.[5]

The annual costs associated with cervical cancer treatment in the United States (US) is USD 441 million, with mean costs of USD 50,846 and USD 27,656 for the first and second years after diagnosis respectively.[8] In China, the average total costs per case from diagnosis to one year after final discharge were varied from USD 8,066-22,000, and the quality-adjusted life years (QALYs) lost ranged from 0.05-0.26.[9] In addition to economic burden, cervical cancer is also associated with various physical and psychological burden. Among 384 Filipino cervical cancer patients in a tertiary hospital, the prevalence rates of anxiety, depression, and combined anxiety and depression were 8.6%, 35.7%, and 6.5% respectively.[10] Various factors including age, employment status, cancer stage, time since diagnosis, chemoradiation treatment, and psychological support were associated with these conditions.

Current management

Screening programs have been proven to reduce the incidence and mortality from cervical cancer in countries where these have been widely implemented. The World Health Organization (WHO) considers HPV screening followed by immediate treatment among adult women as the secondary prevention for cervical cancer (with HPV vaccination for girls aged 9-14 years as the primary approach).[6] Ablative treatment with cryotherapy, thermal ablation, or excision treatment may be given to women who are found to have precancerous lesions based on screening. Treatment options for invasive cervical cancer include surgery, chemotherapy, and radiation therapy, depending on the stage of the disease.[6]

WHO recently published an updated guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention.[11] It strongly recommended HPV DNA as the primary screening test for the general population of women and women with human immunodeficiency virus (HIV). It also suggested the use of HPV DNA test in either a “screen-and-treat approach” or a “screen, triage and treat approach” together with other tests such as cytology, visual inspection of the cervix by acetic acid (VIA) or with Lugol’s iodine (VILI), and colposcopy. Seven algorithms for screening and treatment of cervical cancer were identified.[12]

WHO suggested using HPV genotyping as a triage to primary HPV DNA screening test (Algorithm 4).[12] Patients who test positive for HPV 16/18 will be recommended for treatment, while those who test positive for other hrHPV types will undergo VIA triage and treatment. Another approach (Algorithm 6) involved using hrHPV DNA as the primary screening test followed by colposcopy triage.[12] Despite these recommendations, the optimal screening strategy for women who test positive for other hrHPV genotypes remains unclear.

Women with high-grade cytological lesions may undergo direct visualization through colposcopy. In contrast, among patients with low-grade cytological abnormalities, several management options exist[13,14]. Women classified cytologically ASCUS are more common among younger women, and present a management dilemma among clinicians. HPV testing plays a key role in the triaging of these patients due to higher sensitivity and similar specificity compared to repeat cytology. Incorporation of HPV testing in among patients with ASCUS can increase the detection of cervical intraepithelial neoplasia (CIN) through colposcopy[15-17]. Although cytology is readily available, HPV testing is not widely accessible with financial concerns a major limitation to the majority of Filipinos. Colposcopy, on the other hand, entails significant resources and may potentially cause adverse events such as bleeding[18].

Women who test positive for HPV 16/18 on genotyping are recommended colposcopy by the American Society for Colposcopy and Cervical Pathology[19]. However, WHO is more lenient, as it recommends either undergoing partial genotyping, colposcopy, VIA or Cytology as these have similar benefits, harms, and programmatic costs[12].

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Question 1. Among adult females with Pap smear of ASCUS, should HPV DNA, repeat Pap smear after one year, or colposcopy be done?

Population	Adult females with Pap smear of ASCUS
Screening Intervention	HPV DNA test, repeat Pap smear
Linked Treatment	Psychiatric medications and behavioral interventions
Comparison	Colposcopy
Outcomes	Development of CIN 2+, CIN 3+ or invasive cancer, mortality, HPV infection, preterm birth, adverse events, acceptability, costs, feasibility, equity
Subgroups	By age, risk factors

RECOMMENDATION

We suggest either repeat cytology after six months or immediate HPV testing over colposcopy in screening for cervical cancer among adult females with ASCUS.

(Very low certainty of evidence, weak recommendation)

Benefits and Harms of the Tests

The search identified three RCTs (n = 7, 484) that evaluated either HPV testing or repeat cytology against immediate colposcopy among women aged 18 to 81 years old with ASCUS on cervical cytology conducted in USA, Colombia and Sweden[12-14] (**Appendices 1 and 2 of the Supplementary evidence for question 1**). The ASCUS-LSIL Triage Study and the ASCUS-COL Trial compared three interventions while Dillner et al examined HPV triaging with immediate colposcopy. In all the studies, HPV DNA triage was performed using Hybrid Capture II, while repeat cytology was performed at six-month intervals. Outcomes evaluated were CIN2 and CIN3 or worse until the end of 24 months of follow-up. The studies were assessed for risk of bias **(Appendix 4: Supplementary evidence for question 1)** and the GRADE approach was used to evaluate the certainty of evidence **(Appendix 5: Supplementary evidence for question 1).**

Detection of cervical intraepithelial neoplasia, invasive cancer and mortality

1. HPV triage versus immediate colposcopy (3 studies, n=5,430)

Triage testing using HPV DNA, when compared to immediate colposcopy, resulted in a similar number of diagnoses of CIN2+ (10.2 vs 10.9%, RR: 0.96, 95% CI: 0.83, 1.12), and CIN3+ (5.2 vs 5.1%, RR: 1.04, 95% CI: 0.83, 1.31).

Five and ten women were diagnosed with invasive cancer in the HPV triage and immediate colposcopy arms, respectively (0.19 vs 0.36%, RR: 0.57, 95% CI: 0.21, 1.60), while three women in each arm were found to have adenocarcinoma in situ (RR: 1.03, 95% CI: 0.21, 5.11).

The certainty of evidence for CIN2+ was deemed moderate due to risk of bias as a result of the lack of blinding among colposcopists in one study, while that of CIN 3+ and invasive cancer was low and very low, respectively, due to the additional issue of serious / very serious imprecision of the interval estimates.

2. Repeat cytology versus immediate colposcopy (2 studies, n=4,099)

Repeat cytology, when compared to immediate colposcopy, resulted in similar or fewer diagnoses of CIN2+ (6.4 vs 7.4%, RR: 0.86, 95% CI: 0.69, 1.08), and similar or more diagnoses of CIN3+ (3.7 vs 3.1%, RR: 1.17, 95% CI: 0.84, 1.62).

Four women were diagnosed with invasive cancer – one in the repeat cytology group and three in the immediate colposcopy group (RR: 0.43, 95% CI: 0.06, 2.88).

The certainty of evidence for CIN2+ and CIN3+ were deemed low, while that of invasive cancer was very low due to the lack of blinding among colposcopists in one study and serious to very serious imprecision of the interval estimates.

Outcomes	**No. of Studies** *(no. of participants)*	**RR (95% CI)**	**Interpretation**	**Certainty of Evidence**
HPV triage versus immediate colposcopy				
CIN2+	3 (n=5,430)	0.96, 95% CI: 0.83, 1.12	Equivalent	Moderate
CIN3+	3 (n=5,430)	1.04, 95% CI: 0.83, 1.31	Inconclusive	Low
Invasive cancer	3 (n=5,430)	0.57, 95% CI: 0.21, 1.60	Inconclusive	Very low
Repeat cytology versus immediate colposcopy				
CIN2+	2 (n=4,099)	0.86, 95% CI: 0.69, 1.08	Inconclusive	Low
CIN3+	2 (n=4,099)	1.17, 95% CI: 0.84, 1.62	Inconclusive	Low

Invasive cancer	2 (n=4,099)	0.43, 95% CI: 0.06, 2.88	Inconclusive	Very low

Relevant subgroups

No data was available from the three RCTs regarding outcomes for specific subgroups.

Adverse events

Indirect evidence from the TOMBOLA trial conducted in the UK among women with mild dyskaryosis or borderline nuclear abnormalities and were randomized to either immediate colposcopy or repeat cytology showed higher pain, bleeding and discharge among patients who underwent immediate colposcopy[11]. Although anxiety and distress were less common in the colposcopy arm after 6 weeks of assessment, there was no significant difference between the two arms in anxiety and depression after 30 weeks (Table 4). No data was retrieved on the adverse events among those who underwent HPV testing compared with immediate colposcopy.

Table 4. Harms associated with screening (repeat cytology versus immediate colposcopy)

Adverse events	Repeat cytology	Immediate colposcopy	RR (95% CI)	Quality of evidence	Interpretation
Pain	145/968	304/782	0.39 (0.32, 0.46)	Very low	Favors repeat cytology
Bleeding	166/967	366/781	0.37 (0.31, 0.43)	Very low	Favors repeat cytology
Discharge	83/964	267/780	0.25 (0.20, 0.32)	Very low	Favors repeat cytology
Anxiety	6 weeks after procedure 121/900 30 months after randomization 143/887	6 weeks after procedure 59/751 30 months after randomization 146/949	6 weeks 1.71 (1.27, 2.30) 30 months 1.05 (0.85, 1.29)	Very low	Favors IC at 6 weeks but no difference at 30 months
Depression	6 weeks after procedure 68/902 30 months after randomization 108/887	6 weeks after procedure 50/757 30 months after randomization 101/948	6 weeks 1.14 (0.80, 1.62) 30 months 1.14 (0.89, 1.48)	Very low	Favors IC at 6 weeks but no difference at 30 months

Diagnostic Performance of the Tests

Accuracy of HPV triaging

In a meta-analysis investigating the diagnostic accuracy of HPV triaging and cytology, the absolute sensitivity of HPV triaging using Hybrid Capture 2 assay was 90.9% (95% CI 85.7 to 94.4%) for CIN2+ while the sensitivity for CIN3+ was 94.8% (95% CI 89.6 to 97.5%). The pooled specificity was 60.7% (95% CI 52.9 to 68.0%) and 56.6% (95% CI 39.4 to 72.3%) for CIN2+ or CIN3+, respectively[15].

Accuracy of repeat cytology

The sensitivity was lower at 71.5% (95% CI 62.9 to 78.8%) at ASCUS+ for CIN2+ and 77.9% (95% CI 64.0 to 87.6%) at ASCUS+ for CIN3+. The specificity in predicting the absence of CIN2+ was 68.4% (95% CI 59.9 to 75.8%) for CIN2+ and 57.4% (95% CI 40.36 to 73.0%) for CIN3+[15].

Relative accuracy of the tests

Triage of ASCUS cases with HPV was 27% more sensitive than repeat pap smear using ASCUS+ as the threshold (relative sensitivity: 1.27; 95% CI 1.16 to 1.39) in detecting CIN2+ and 14% more sensitive than repeat pap smear in detecting CN3+ (relative sensitivity 1.14, 95% CI 1.06 to 1.22). The specificity of a repeat smear at the cut-of ASCUS+ was identical to the specificity of HC2 for exclusion of CIN2+ and CIN3+ (relative specificity for CIN2+: 0.99; 95% CI 0.97 to 1.03; relative specificity for CIN3+: 0.99 (0.89 to 1.09)[15].

All forest plots are shown in **Appendix 6: Supplementary evidence for question 1.**

Table 5. Absolute and relative accuracy of HPV triage and repeat cytology in triaging women with ASCUS

Triage test	Outcome	Sensitivity (95% CI)	Specificity (95% CI)	LR+	LR-
HPV	CIN2+	90.9% (85.7 to 94.4%)	60.7% (52.9 to 68.0%)	2.31	0.15
	CIN3+	94.8% (89.6 to 97.5%)	56.6 % (39.4 to 72.3%)	2.18	0.09
Repeat cytology	CIN2+	71.5% (62.9 to 78.8%)	68.4% (59.9 to 75.8%)	2.26	0.42
	CIN3+	77.9% (64.0 to 87.6%)	57.4% (40.3 to 73.0%)	1.83	0.39

Cost Implication

There were no local studies comparing the costs associated with the three screening studies. We estimated costs for each screening strategy using costs obtained from tertiary hospitals in both government and private settings (Table 6).

An estimation of costs related to testing and subsequent management for each strategy (per 1000 patients) is summarized in Table 7. In this estimation, CIN2+ detection rates and colposcopy referral rates were based from the included studies, while the proportion of patients receiving cryosurgery and LEEP were obtained from a local cost utility analysis on cervical cancer screening[16]. Estimated costs have a wide range because both government and private settings were considered.

Table 6. Costs of screening tests, procedures, and professional fees in the Philippines

	Rates (PHP)			
Screening Test	**GOVH**	**PVTC**	**PVTH**	**Professional Fees**
Pap / conventional cytology	685	665	-	600-1000
HPV test	-	5,800	8,666	600-1000
Colposcopy	600	7,000	7562	6,000-20,000
Cryotherapy	1,000	10,000	15,000	6,000-15,000
Loop Electrosurgical Excision Procedure (LEEP)	5,500	15,000	70,000	6,000-20,000

GOVH – government hospital; PVTC – private clinic; PVTH – private hospital

Table 7. Estimation of direct costs associated with various management strategies for ASCUS (per 1000 patients)

Parameter		**Screening Intervention**		
		Screening 1: immediate colposcopy	Screening 2: HPV triage	Screening 3: Repeat cytology
A	CIN2/3+ detection rates	10.9%	10.2%	6.4%
B	Colposcopy referral rates	100%	48.8%	19.3%
C	Proportion of patients with CIN2/3+ receiving cryosurgery per 1,000 ASCUS	100% (n = 109)	100% (n = 102)	100% (n = 64)
D	Proportion of patients with CIN2/3+ receiving conization per 1,000 ASCUS	12.5% (n=14)	12.5% (n=13)	12.5% (n=8)
E	Unit cost of screening intervention per 1,000 ASCUS	Colposcopy PHP 600 – 27,000 X 1,000 **= PHP 600,000 – 27,000,000**	HPV test PHP 5,800 – 9,666 X 1,000 Colposcopy PHP 600 – 27,000 X 488 **= PHP 6,092,800 – 22,842,000**	Cytology PHP 685 – 1,685 X 1,000 X 4 Colposcopy PHP 600 – 27,000 X 271 **= PHP 2,902,600 – 14,057,000**
F	Other direct costs associated with the implementation of the proposed screening intervention per 1,000 hrHPV+ (non-16/18) patients	Cryotherapy PHP 1,000 – 30,000 X 109 Conization	Cryotherapy PHP 1,000 – 30,000 X 102	Cryotherapy PHP 1,000 – 30,000 X 64 Conization

	(C * cost of cryotherapy) + (D * cost of conization)	PHP 5,500 – 90,000 X 14 **= PHP 186,000 – 4,530,000**	Conization PHP 5,500 – 90,000 X 13 **= PHP 173,500 – 4,230,000**	PHP 5,500 – 90,000 X 8 **= PHP 108,000 – 2,640,000**
G	Total cost of screening per 1,000 patients (E + F)	**PHP 786,000 – 31,530,000**	**PHP 6,266,300 – 27,072,000**	**PHP 3,010,600 – 16,697,000**

Equity, Acceptability, and Feasibility

No local study was found specifically assessing stakeholder attitudes and preferences regarding different triage strategies. Available local data related to cervical cancer screening using pap smear showed poor knowledge but positive attitudes towards cervical cancer screening tests among women of different ages.

Awareness and attitudes toward cervical cancer screening

In a survey of awareness and attitudes on cervical cancer screening programs, healthcare workers in one hospital in Cebu reported awareness of the existence and schedule of cervical cancer screening. However, only about 25% expressed an understanding of the purpose of such screening tests as well as eligibility criteria. Nonetheless, positive attitude toward screening was noted as more than 90% expressed willingness to submit themselves for screening.[17]

Poor knowledge on HPV infection, screening, and prevention were also reported in another study conducted in Baguio involving 81 women in their reproductive age. Most of the respondents have not undergone screening tests or HPV vaccination due to feelings of anxiety, inability to communicate their desire to get screened, cost of the vaccine, and lack of information.[18]

Among female adolescents (n=107) seeking consultation in a NCR-based hospital, most (> 75%) were not aware of cervical cancer screening HPV prevention but were willing to receive the vaccine if given for free.[19] These findings of poor awareness of cervical cancer screening through pap smear were also echoed in another survey involving 256 female college students in Cebu.[19]

Methods to improve acceptability

A quasi-experimental study was done 1999 to determine interventions to improve pap smear compliance among Filipino women. In total, 2,500 Filipino women 15-50 years old from 8 rural and 5 urban areas throughout the Philippines participated. Compliance to pap smear screening was predicted by civil status, level of education, number of children, family history of cancer, and perceived risk of having cancer. Cost of screening was found to be a factor affecting decisions to seek cervical examinations. The study proposed having a well-planned nationwide cervical cancer screening program characterized by focused public health education campaigns, accessible and equipped screening centers with complementary treatment facilities, and subsidized by the government or private health insurance systems.[20] A before and after study design involving female patients aged 21-65 years consulting an outpatient Family Medicine Clinic in UP-PGH showed that an opportunistic screening program increases the screening uptake of women (from 2% to 27%) when given during waiting hours or regular consultations. In addition, more women (38%) preferred VIA over pap smear (16%) as the screening procedure.[21]

Recommendations from Other Groups

Table 5. Summary of Key Recommendations from Different Groups

WHO[17]	WHO suggests that women from the general population and women living with HIV who have screened positive on a cytology primary screening test and then have normal results on colposcopy are retested with HPV DNA testing at 12 months and, if negative, move to the recommended regular screening interval. Conditional recommendation, low-certainty evidence
American Society of Colposcopy and Cervical Pathology (ASCCP)[22]	ASCCP recommends assessing risk for CIN3+ before doing colposcopy, treatment or surveillance through combination of current results including HPV testing and cytology, and past history. They recommend repeat HPV testing or cotesting at 1 year for patients with minor screening abnormalities indicating HPV infection with low risk of underlying CIN 3+ (e.g., HPV-positive, low-grade cytologic abnormalities after a documented negative screening HPV test or cotest).

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Question 2. Among adult females with HPV16/18 on genotyping, should VIA, cytology or colposcopy be done?

Population	Adult females with HPV DNA 16/18
Screening Intervention	VIA, cytology
Comparison	Colposcopy
Outcomes	Development of CIN 2+, CIN 3+ or invasive cancer, mortality, HPV infection, preterm birth, adverse events, acceptability, costs, feasibility, equity
Subgroups	By age, risk factors

RECOMMENDATION

We suggest colposcopy over cytology or VIA for adult females who are positive for either HPV 16 or 18. *(Very low certainty of evidence, weak recommendation)*

Benefits and Harms of the Tests

Search Strategy

A comprehensive systematic search was performed (Date of last search: June 30, 2022) in Medline, CENTRAL, and Google Scholar (**Appendix 1: Supplementary evidence for question 2**). Characteristics of included studies are shown in **Appendix 2: Supplementary evidence for question 2** while the risk of bias (RoB) assessments are shown in **Appendix 3: Supplementary evidence for question 2**.

Detection of Cervical Intraepithelial Neoplasia (CIN) in HPV 16/18 positive women

There was no direct evidence found that compared the performance of VIA, cytology, or immediate colposcopy in the detection of CIN in women who test positive for HPV 16/18. All literature in the search strategy subjected HPV 16/18-positive women to immediate colposcopy. Seven RCTs in total were found which used this strategy to get the detection rates of CIN2+ and CIN 3+ in this population[7-13]. Tables 2 and 3 report the detection rate of CIN2+ and CIN 3+ for immediate colposcopy and cytology respectively in the included studies. Around 11 to 17 % of patients who were positive for HPV 16/18 had CIN after undergoing immediate colposcopy.

Table 2. Detection rates for CIN 2+ and CIN 3+ of immediate Colposcopy (N=1,889)

Outcome	Studies (N)	Detection rate %	95% CI %

CIN 2+	6 RCTs (1,889)	17.3	13.6 to 21.4
CIN 3+		11.1	7.6 to 15.2

Table 3. Detection rates for CIN 2+ and CIN 3+ of patients who underwent co-testing for HPV and Cytology

Outcome	Studies (N)	Detection rate %	95% CI %
CIN 2+	2 RCTs (760)	34	30.6 to 37
CIN 3+	3 RCTs (1864)	17.9	7.1 to 32.3

Diagnostic Accuracy of Cytology, VIA, and Colposcopy in the Detection of CIN in HPV-positive women

The diagnostic performance of Cytology, VIA, and Colposcopy for the detection of CIN 2+ and CIN 3+ in women positive for high-risk HPV infection was presented by the WHO in the latest edition of screening and treatment of cervical, pre-cancer lesions for cervical cancer prevention guidelines[14]. This extensive report included a meta-analysis of related studies up to February 2020. Table 4 shows the number of included studies, sensitivity, specificity, and likelihood ratios of the said diagnostic modalities in the detection of CIN 2+ and CIN 3+ in HPV-positive women. Colposcopy was noted to have the highest sensitivity, specificity and positive likelihood ratio, and having the least negative likelihood ratio. VIA, on the other hand, had the lowest sensitivity and positive likelihood ratio among these tests.

Table 4. Diagnostic accuracy of Cytology, VIA, Colposcopy in the detection of CIN2+ and CIN 3+ in patients who are positive for high-risk HPV infection.

Test (outcome)	# Included Studies	Sensitvity (95% CI)	Specificity (95% CI)	LR+	LR-
Cytology (CIN 2+)	39	0.71 (0.65 – 0.77)	0.75 (0.69 – 0.80)	2.8	0.38
VIA (CIN 2+)	19	0.65 (0.55 – 0.75)	0.73 (0.65 – 0.81)	2.4	0.48
Colposcopy (CIN 2+)	7	0.83 (0.79 – 0.86)	0.75 (0.66 – 0.83)	3.3	0.23
Cytology (CIN 3+)	28	0.78 (0.69 – 0.77)	0.73 (0.67 – 0.78)	2.8	0.31
VIA (CIN 3+)	18	0.68 (0.57 – 0.78)	0.74 (0.65 – 0.82)	2.6	0.43

Colposcopy (CIN 3+)	6	0.86 (0.78 – 0.92)	0.72 (0.61 – 0.83)	3.1	0.19

Harms of Colposcopy Testing

Colposcopy is associated with complications such as bleeding, pain or discomfort, and, discharge and infections, especially if punch biopsy and treatment procedures such as loop electrosurgical excision is performed. Table 5 is a summary of studies by Drolet in 2012 on Anxiety following an abnormal cytology result and a study by the TOMBOLA group which reported adverse events in women following cervical punch biopsy and electrosurgical excision[15,16]. These studies involved the use of self-administered questionnaires on women undergoing these diagnostic exams. Following punch biopsy, about half of patients will experience pain, and 21% will experience moderate to severe bleeding. The treatment of CIN through electrosurgical excision causes a higher percentage of patients experiencing pain (67% vs 53%) and moderate to severe bleeding (53% vs. 21%).

Table 5. Health-related problems and adverse effects of conventional cytology, punch biopsy and electrosurgical excision.

	Proportion of women reporting a health problem			
Event	Health Problem	Total	Light/Mild	Moderate and Severe
Pap test	Symptoms at least 2–7 days	13%		
Abnormal test	Anxiety at least 12 weeks	35%		
Punch biopsy	Pain	53%	25%	28%
	Bleeding	79%	58%	21%
	Discharge	46%	32%	14%
Treatment *Electrosurgical excision*	Pain	67%	34%	33%
	Bleeding	77%	24%	53%
	Discharge	63%	21%	42%

Cost Implication

Among the RCTs included in the analysis, there were no direct cost-utility studies comparing the interventions stated in the problem. In published data across other countries, HPV testing was more expensive compared to VIA or cytology [7,11]. Co-testing with cytology and HR-HPV testing performed better in detecting CIN 2+ lesions compared to cytology and HR-HPV testing alone, but with the greatest costs[7]. The WHO guidelines suggest any test (cytology, colposcopy, genotyping, or VIA) after a positive HPV DNA test, and the costs for these are highly dependent on the resources and systems in place for a particular country [17].

A 2015 local study showed VIA screening every 5 years was the most cost-saving strategy for the Philippine setting [18]. Whereas in a large-scale study in Canada (FoCAL trial), a screening strategy with the use of HPV test followed by reflex cytology on a positive result had lower overall costs and was able to detect a larger number of CIN2+ lesions compared to liquid-based cytology alone. They also found out HPV testing every 4 years produces similar outcomes compared to Cytology-based screening every 2 years at a lower cost[19]. The current prices of tests for cervical cancer screening are shown in the table below, comparing the costs from a public healthcare institution to a private healthcare institution, as well as additional professional fees. It is important to note that not all services are available and provided for in public general hospitals in the Philippines.

Table 6. Costs of different interventions (in Philippine Peso) in the Philippine General Hospital, against Private institutions with estimated professional fees (as of July 2022)

INTERVENTION	PGH	PRIVATE HOSPITAL[b]	PF RANGE
Cytology/Conventional Pap Smear	685	665	600-1000
HPV test + Liquid Based Cytology		8,000	600-1000
HPV test		5,800-8,666	600-1000
Liquid Based Cytology	1,915	1,628	600-1000
Colposcopy	600	7,000-7,562	6,000-20,000
Cryotherapy	1,000	10,000-15,000	6,000-15,000
Conization	5,500	15,000-120,000	40,000-80,000
Loop Electrode Excision Procedure (LEEP)	5,500	15,000-70,000	6,000-20,000

[a]PGH: Philippine General Hospital
[b]Private Institution pricing from Qualimed Manila (FMAB) and St Lukes Medical Center Global City.

Psychosocial Impact

The reception and implications of HPV testing have been studied in a 2009 study in Greater Manchester. The study used the General Health Questionnaire (GHQ) tool to assess psychological distress and compare across the experimental groups. In the table below, there were no significant differences between the GHQ scores between those blinded to the HPV results against those whose HPV status was revealed regardless of HPV or cytology status. There was only weak evidence for psychosocial morbidity associated with a positive HPV result. Sexual satisfaction was reduced in women who were cytology negative and were revealed to have positive HPV [20].

Equity, Acceptability, and Feasibility

The majority of new cases of cervical cancer and morbidities associated with it occur in low-resource countries. Southeast Asia was ranked seventh for incidence of cervical cancer and sixth in mortality related to cervical cancer among other regions of the world in 2020. It is projected that 95% of deaths due to cervical cancer in 2030 will have occurred in low to middle income countries [21]. Lowering the incidence of cervical cancer with screening preventive strategies is underutilized as coverage for these procedures is poor in these countries. A systematic review by Chua et al noted that for Southeast Asia, factors that affect reluctance to cervical cancer screening most often are psychological or emotional (fear and embarrassment), and knowledge-related (lack of information and awareness). Patient education-based approaches may be key moving forward, as the study likewise noted demographics (increased age inversely related to screening tests), perception, attitudes, and beliefs (preferring family needs over health, patriarchal issues), to be possible facilitators towards better cervical cancer screening implementation [21,22].

With some countries shifting towards use of HPV testing for cervical cancer, reports of anxiety and concern have been an issue due to it being a test for a sexually transmitted illness. An acceptability study of the use HPV screening was done as a part of the FOCAL trial, and 63% of the patients were accepting of its use as cervical cancer screening. The receipt of a positive HPV result was concerning to the patients not for a possibility of cancer but rather who they got it from, and 75% of respondents reported that a positive result would affect their current relationship. The patients likewise identified government programs and healthcare providers to provide proper information that may influence decision making towards HPV testing and cervical cancer screening [24].

Self-sampling HPV test may be used to overcome cost and multiple barriers towards cervical cancer screening, especially in low to middle income countries [25]. The results of this test were 86.7 to 97.5% in concordance with provider collected samples. A review by Mulki showed that most participants reported that HPV self-sampling had the benefit of convenience of doing the procedure at home, less embarrassment, and less travel. However, there were concerns on proper procedure, cleanliness, and quality of samples obtained. Follow up of these patients were likewise a concern, as those needing further testing and treatment would have to travel and go to clinic centers. Cultural beliefs likewise may play a role in the acceptability of this testing, as there are women who report asking permission from their husband prior to engaging in the test. Improved government support for training healthcare workers should likewise be a priority as they are the ones who assist and follow-up the patients who did self-sampling[25].

Recommendations from Other Groups

For women who test positive for HPV 16/18 on genotyping, the American Society for Colposcopy and Cervical Pathology recommends a direct referral for colposcopy, especially in women who underwent co-testing with HPV testing and cytology but with unsatisfactory cytology result[23]. Whereas according to the World Health Organization guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention published in July 2021, patients who test positive for HPV DNA can either undergo partial genotyping, colposcopy, VIA or Cytology as these have similar benefits, harms, and programmatic costs,

hence decision should be dependent on feasibility and availability [17]. For women who test positive for HPV 16 or 18 on genotyping after a positive HPV DNA screening, a screen, triage, and treat approach with the use of ablative procedures can be entertained depending on the patient's eligibility after application of acetic acid. In both of these guidelines, cited triage strategies using HPV testing employed the use of Hybrid Capture II, an assay which tests positive or negative depending on the presence or absence of either one or a combination of the high-risk HPV genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68, and low-risk HPV genotypes 6, 11, 42, 43 and 44.

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Question 3. Among adult females with other HPV high risk types on genotyping, should VIA, cytology or colposcopy be done?

Patients:	Adult females with other high-risk HPV types (non-HPV-16/18)
Diagnostic Intervention:	Cytology triage Visual inspection of the cervix with acetic acid (VIA) triage
Comparison:	Direct colposcopy
Anticipated Outcomes:	Cervical cancer, High-grade cervical intraepithelial neoplasia or worse (CIN 2+, CIN 3+), mortality, HPV infection, preterm birth, adverse events (major infections or bleeding, procedure-associated pain, cervical stenosis, infertility, spontaneous abortion, perinatal deaths, premature rupture of membrane, unnecessary interventions, increased viral shedding in women living with HIV), acceptability, costs, feasibility, equity
Subgroups:	By age (< 30, 30-49, > 49) By risk factors (HIV positivity; smoking history; multiple sexual partners; condom use)
Purpose of the tests:	Screening for cervical cancer
Linked treatments:	chemotherapy, radiation, cervical cryosurgery, cervical cryotherapy, excision

RECOMMENDATIONS

1. We suggest colposcopy over cytology triage for adult females who are positive for other high-risk HPV types (non-16/18). *(Very low certainty of evidence, weak recommendation)*

Consensus Panel Concerns: Although the available evidence favoring colposcopy over cytology triaging is derived from urban settings and is of very low certainty (serious indirectness, lack of local studies on cost-effectiveness, absence of evidence of harm of cytology), the panel still suggest colposcopy over cytology to avoid inequity by ensuring practice of colposcopy in both urban and rural areas and avoid confusion among clinicians regarding insufficiency of evidence. Colposcopy is perceived to be the best test for adult females who are positive for other high-risk HPV types (non-16/18) by the consensus panel after evaluating the current evidence.

2. We suggest colposcopy over VIA/VILI triage for adult females who are positive for other high-risk HPV types (non-16/18). *(Very low certainty of evidence, weak recommendation)*

Consensus Panel Concerns: Although the available evidence supporting colposcopy over VIA/VILI triaging is derived from rural settings and is of very low certainty (very serious indirectness, absence of evidence of harm of VIA/VILI), the panel still suggest colposcopy over VIA/VILI to avoid inequity by ensuring practice of colposcopy in both urban and rural areas and avoid confusion among clinicians regarding insufficiency of evidence. Colposcopy is perceived to be the best test for adult females who are positive for other high-risk HPV types (non-16/18) by the consensus panel after evaluating the current evidence.

Benefits and Harms of the Tests

Evidence for this review was informed by 1 multi-center, open-label RCT in China. In urban settings, colposcopy detected more CIN2 cases but had similar CIN3 yields as cytology triage. In rural settings that involved patients positive for any hrHPV genotype, colposcopy was superior to VIA/VILI for CIN3+ detection. Similar disease yields were noted for VIA/VILI triage and cytology. No data on adverse effects were available. Estimates are based on very low to low certainty of evidence.

One randomized controlled trial (RCT)[11] was included after a systematic search of MEDLINE and CENTRAL (**Appendices 1 and 2 of the Supplementary evidence for question 3**). Another RCT from Australia was excluded as it compared dual-stained cytology with conventional cytology.[12] Three other RCTs and 16 observational studies reporting prognostic data for hrHPV types were also found but excluded due to serious indirectness (**Appendix 4: Supplementary evidence for question 3**). **Appendix 3: Supplementary evidence for question 3** provides a detailed summary of the characteristics of the included studies.

A population-based, multi-center, open-label RCT[11] in China evaluated different triage strategies for women aged 35-64 years (median 47) in both urban (n=18,176) and rural sites (n=15,385). Women from urban sites testing positive for non-16/18 hrHPV were randomly assigned to cytology or direct colposcopy, while those in rural sites received either VIA/VILI, cytology, or direct colposcopy as triage options. Partial HPV genotyping of cervical exfoliate cell specimens for non-16/18 HPV types was done only in the urban sites using polymerase chain reaction (PCR) tests (Cobas 4800 or Liferiver hrHPV kit). In rural areas, a hybrid capture-based careHPV (QIAGEN) assay was used to analyze brush specimens. Outcomes assessed were CIN2, CIN3+, and colposcopy referral rates after a follow-up period of 24 months. The study was assessed for risk of bias **(Appendix 5: Supplementary evidence for question 3)** and the GRADE approach was used to evaluate the certainty of evidence **(Appendix 6: Supplementary evidence for question 3).**

Cervical intraepithelial neoplasia (CIN2, CIN3+) (1 RCTs, N = 2,689, Very Low Certainty of Evidence)

Urban Settings: Cytology vs Colposcopy

Among patients screened in urban settings, direct colposcopy yielded higher CIN2 detection rates compared to cytology triage (5.1% vs. 1.4%; RR=0.28 [95% CI 0.13 to 0.60]) as well as CIN2+ (7.4% vs. 2.3%).[11] When only CIN3+ lesions were considered, the advantage of colposcopy over cytology triage was less evident (Table 1). Certainty of evidence was downgraded to low due to serious risk of bias as well as high attrition rate (15%) among patients in the cytology arm who were positive for ASCUS but did not proceed with colposcopy.

Rural Settings: Cytology vs Colposcopy

Among patients screened in rural settings, no clear advantage was noted for cytology triage in detecting CIN2 and CIN3+ cases when compared to direct colposcopy.[11] It should be noted that data on other hrHPV genotypes were not available for rural settings; thus, the outcomes may have been influenced by results from women positive for HPV-16/18.

Rural Settings: VIA/VILI vs Colposcopy

Greater CIN3+ detection rates were noted for direct colposcopy compared to VIA/VILI triage (4.5% vs. 2.8%; RR=0.23 [95% CI 0.09 to 0.58]) in the rural setting. However, results were inconclusive when only CIN2 lesions were considered.

Rural Settings: Cytology vs. VIA/VILI

Cytology and VIA/VILI exhibited similar CIN2 detection rates (3.2% vs 2.31%; RR 1.40 [95% CI 0.55 to 3.57]). Cytology identified more CIN3+ cases than VIA/VILI (2.8% vs. 1.0%), but this finding was not statistically significant (RR 2.64 [0.82, 8.56]) and was affected by serious imprecision.

Table 1. Clinical outcomes of different triage methods for women positive for other high-risk HPV types.

Outcomes (follow-up period)	**No. of Studies** (no. of participants)	**Effect Estimate** Risk Ratio [95% CI]	**Interpretation**	**Level of Certainty**
Comparison 1: Cytology triage vs. direct colposcopy *(Urban settings)*				
CIN2 (24 months)	1 (1,139)	0.28 [0.13, 0.60]	Favors colposcopy	Low ⊕⊕◯◯
CIN2+ (24 months)	1 (1,139)	0.31 [0.17, 0.57]	Favors colposcopy	Low ⊕⊕◯◯
CIN3+ (24 months)	1 (1,139)	0.39 [0.14, 1.08]	Inconclusive	Low ⊕⊕◯◯
Comparison 2: Cytology triage vs. direct colposcopy *(Rural settings)*				
CIN2 (24 months)	1 (1070)	1.14 [0.50, 2.61]	Inconclusive	Very Low ⊕◯◯◯
CIN2+ (24 months)	1 (1070)	0.82 [0.46, 1.46]	Inconclusive	Very Low ⊕◯◯◯
CIN3+ (24 months)	1 (1070)	0.62 [0.26, 1.44]	Inconclusive	Very Low ⊕◯◯◯
Comparison 3: VIA/VILI triage vs direct colposcopy *(Rural settings)*				
CIN2 (24 months)	1 (1332)	0.81 [0.40, 1.65]	Inconclusive	Very Low ⊕◯◯◯
CIN2+ (24 months)	1 (1332)	0.46 [0.27, 0.78]	Favors colposcopy	Very Low ⊕◯◯◯
CIN3+ (24 months)	1 (1332)	0.23 [0.09, 0.58]	Favors colposcopy	Very Low ⊕◯◯◯
Comparison 4: Cytology triage vs. VIA/VILI triage *(Rural settings)*				
CIN2 (24 months)	1 (698)	1.40 [0.55, 3.57]	Inconclusive	Very Low ⊕◯◯◯
CIN2+ (24 months)	1 (698)	1.79 [0.88, 3.65]	Inconclusive	Very Low ⊕◯◯◯
CIN3+ (24 months)	1 (698)	2.64 [0.82, 8.56]	Inconclusive	Very Low ⊕◯◯◯

CIN, cervical intraepithelial neoplasia; VIA/VILI, visual inspection of cervix with acetic acid or Lugol's iodine

Other outcomes

hrHPV prevalence

The included trial[11] reported a prevalence rate of 9.51% (n=18,176) for all hrHPV genotypes in urban areas, while a prevalence of 12.7% (n=15,385) was recorded in rural areas. Among women in urban settings, the prevalence rates of HPV-16/18 and other hrHPV genotypes were 2.24% and 7.26% respectively. Data on hrHPV genotypes were not available for women in the rural settings.

Colposcopy referral rates

Among hrHPV+ patients who received triage in rural settings, 22% (n=218) received colposcopy based on cytology results while 27.1% (n=480) underwent colposcopy based on VIA/VILI testing.[11] The study concluded that colposcopy referral rates could be reduced by 70-80% if hrHPV-positive women were triaged by cytology (2.8%) or VIA/VILI (3.4%), compared with direct colposcopy in rural sites. In urban

settings, 27.3% (n=548) of participants were consequently referred to colposcopy after testing positive on cytology triage.

Adverse events

Adverse events were not measured or reported in the included RCT.

Diagnostic Performance of the Tests

Combined testing

A systematic review and network meta-analysis of 27 prospective studies involving healthy asymptomatic women (n=185,269) compared the accuracy of various cervical screening strategies in detecting ≥CIN2.[13] Most studies showed high risk of bias arising from the randomization process, variations in outcome measurement, and missing data. **Co-testing of cytology and hrHPV testing with either-positive criterion (OR rule) was the most sensitive (1.000 [95% CI 0.994 to 1.000]) and least specific (0.846 [95% CI 0.753 to 0.907])**, while using the both-positive criterion (AND rule) for the same combination of tests was the most specific (0.994 [95% CI 0.989 to 0.997]) and least sensitive (0.345 [95% CI 0.183 to 0.519]). Standalone hrHPV tests showed higher sensitivity estimates (0.941 [95% CI 0.872 to 0.976]) than cytological testing alone (0.611 [95% CI 0.499 to 0.710]).[13]

Standalone tests

Another systematic review (n=488,739) provided pooled accuracy estimates of standalone tests in detecting ≥CIN2.[14] The review included 64 primary studies conducted among healthy and asymptomatic women with intact cervix, aged 15-80 years with history of sexual activity, with no history of screening or treatment for cervical neoplasms. True-positives were defined as ≥CIN2 cases on histopathology. Based on 21 studies, clinician-sampled HPV tests showed a slightly lower pooled sensitivity (0.79 [95% CI 0.64 to 0.88]) but higher specificity (0.92 [95% CI 0.87 to 0.96]) compared to VILI testing (sensitivity: 0.81 [95% CI 0.68 to 0.90]; specificity: 0.87 [95% CI 0.82 to 0.91]). VIA test, self-sampled HPV test, conventional pap smear, liquid-based cytology also had lower sensitivity estimates at 0.66 (95% CI 0.58 to 0.74), 0.54 (95% CI 0.44 to 0.63), 0.54 (95% CI 0.41 to 0.66), and 0.52 (95% CI 0.25 to 0.77) respectively when compared to VILI testing, but showed higher specificity estimates at 0.88 (95% CI 0.84 to 0.90), 0.96 (95% CI 0.92 to 0.97), 0.93 (95% CI 0.87 to 0.96), and 0.94 (95% CI 0.88 to 0.97) respectively.[14]

Cost Implication

No local economic evaluations were found on HPV DNA testing as a cervical cancer screening method. Our cost analysis found direct colposcopy as the most expensive strategy, followed by cytology triage, and VIA triage. A quasi-randomized study in China found hrHPV+cytology co-testing to be the most costly. In terms of cost-effectiveness, very low to low certainty evidence from other econometric modeling studies done in other countries showed that direct colposcopy is a more cost-effective triage strategy over conventional cytology among women positive for hrHPV.

Resources required

Table 2 shows the costs of cervical screening tests and linked treatments in various public and private hospitals in the Philippines, which were obtained from the Philippine Society for Cervical Pathology and Colposcopy (PSCPC) on July 26, 2022. The table also provides the estimated costs of professional fees charged by physicians for each procedure.

Table 2. Costs of cervical screening tests, linked treatments, and professional fees in the Philippines

	Rates (PHP)			
Screening Test	**PGH**	**PGH FMAB**	**SLMC-GC**	**Professional Fees**
Pap / conventional cytology	685	665	-	600-1000
HPV test with liquid-based cytology	-	8000	-	600-1000
HPV test	-	5,800	8,666	600-1000
Liquid-based cytology	1915 (outpatient) 2010 (semi-private) 2205 (suite)	-	1628	600-1000
Colposcopy	600	7,000	7,562	6,000-20,000
Cryotherapy	1,000	10,000	15,000	6,000-15,000
Conisation	5,500	15,000	120,000	40,000-80,000
Loop Electrosurgical Excision Procedure (LEEP)	5,500	15,000	70,000	6,000-20,000

PGH: Philippine General Hospital; FMAB: Faculty Medical Arts Building; SLMC-GC: St. Luke's Medical Center Global City

In both best- and worst-case scenarios, direct colposcopy appeared to be the most costly screening strategy (PHP 7.5 to 31.7 million), followed by cytology triage (PHP 4.6 to 11.4 million). VIA triage was the least expensive screening strategy (PHP 2.7 to PHP 9.95 million). Total cost of screening using the different triage strategies were estimated (Table 4) for every 1,000 patients patients testing positive for other hrHPV types and using data on CIN detection rates and colposcopy referral rates from the Zhang et al 2021 RCT[11] as well as cost data from hospitals in the Philippines (Table 2) and a cost-utility analysis study by Guerrero et al in 2015[2] on cervical cancer screening (**Appendix 7: Supplementary evidence for question 3)**.

Table 3. Estimation of direct costs associated with various cervical screening strategies

Screening Strategy	Total cost of screening per 1,000 hrHPV+ (non-16/18) patients	
	Best-case (cheapest)	**Worst-case (most expensive)**
Screening 1: Direct colposcopy	₱7,573,000	₱31,782,000
Screening 2: Cytology triage + colposcopy	₱4,614,300	₱11,442,426
Screening 3: VIA/VILI triage + colposcopy	₱2,747,100	₱9,959,302

Number needed to screen (NNS)

The number needed to screen (NNS) was used to estimate the number of women who need to undergo cervical cancer screening to detect a single CIN2 or CIN3+ case, based on the prevalence estimates in the included study.[11] NNS is obtained by computing the inverse of the absolute risk reduction in the intervention group (Table 3).

When compared with direct colposcopy, 2,724 and 7,161 hrHPV+ women in urban settings need to undergo cytology triage to detect an additional CIN2 and CIN3+ case respectively. In the rural setting, 5,855 hrHPV+ women need to undergo cytology triage to detect one CIN3+ case when compared to colposcopy. A negative NNS was obtained with cytology triage for detecting a CIN2 case when compared to colposcopy in the rural setting, suggesting that the triage strategy may detect more CIN2 cases than direct colposcopy. However, it should be noted that the estimates were imprecise for this comparison. For VIA/VILI triage, 19,039 and 2,925 hrHPV+ women in rural settings need to be screened to detect an additional CIN 2 and CIN3+ case respectively when compared to direct colposcopy. When compared to VIA/VILI triage, cytology triage needs to be conducted on 10,877 and 5,845 hrHPV+ women in rural settings need to be screened to detect a single CIN2 and CIN3+ respectively.

Table 4. Number needed to screen to detect a single CIN2 or CIN3+ case

Outcomes (follow-up period)	**No. of Studies** (no. of participants)	**Risk with intervention** (Rt)	**Risk with control** (Rc)	**Absolute Risk Reduction (ARR)** Rc – Rt	**Number Needed to Screen (NNS)** 100/ARR
Comparison 1: Cytology triage vs. direct colposcopy *(Urban setting)*					
CIN2 (24 mo)	1 (1,139)	1.4%	5.1%	3.7%	2,724
CIN3+ (24 mo)	1 (1,139)	0.9%	2.3%	1.4%	7,161
Comparison 2: Cytology triage vs. direct colposcopy *(Rural setting)*					
CIN2 (24 mo)	1 (1070)	3.2%	2.8%	-0.4%	-25,373
CIN3+ (24 mo)	1 (1070)	2.8%	4.5%	1.7%	5,855
Comparison 3: VIA/VILI triage vs direct colposcopy *(Rural setting)*					
CIN2 (24 mo)	1 (1332)	2.3%	2.8%	0.5%	19,039
CIN3+ (24 mo)	1 (1332)	1.0%	4.5%	3.4%	2,925
Comparison 4: Cytology triage vs. VIA/VILI triage *(Rural setting)*					
CIN2 (24 mo)	1 (698)	3.2%	2.3%	0.9%	10,877
CIN3+ (24 mo)	1 (698)	2.8%	1.0%	1.7%	5,845

Cost-effectiveness

The costs to detect a case of CIN2+ or CIN3+ with hrHPV screening alone, cytology screening alone, or hrHPV + cytology co-testing was estimated in a quasi-randomized study from China involving 182,119 women aged 35-64 years screened presenting in primary healthcare facilities.[15] ***High-risk HPV and cytology co-testing was the most expensive strategy*** with an estimated cost of RMB 36,154 (~PHP 300,000) to detect each CIN2+ case, followed by standalone hrHPV and cytology at RMB 34,943 yuan and 34,561, respectively. For detecting a CIN3+ case, standalone hrHPV testing was the least expensive strategy (RMB 54,078 / PHP ~450,000), while hrHPV+cytology co-testing was the most expensive strategy (RMB 112,480 / PHP ~936,000). These costs were estimated under the following assumptions: 100,000 women screened, 6359 (~6%) undergoing colposcopy, 0.5% CIN2+ incidence, and 0.1% CIN3+ incidence.[15]

An economic evaluation in China used a Markov model to simulate a cohort of women (n=100,000) aged 30-59 years over a 20-year period.[16] The costs, utilities, and benefits of using five cervical screening strategies (i.e. HPV DNA testing every 3 and 5 years, LBC testing every 3 years, and HPV with LBC triage every 3 and 5 years) were compared. ***HPV DNA testing with colposcopy triage every three years was found to be the most cost-effective strategy in reducing cumulative risk of cervical cancer*** (833 per 100,000; 44% reduction), prolonging life years (868.78 years), and increasing quality-adjusted life years (3,333 QALYs per year). It also had the lowest incremental cost-effectiveness ratio (ICER) at 160,206.14 RMB (PHP ~1,300,000) per life year saved. However, no screening strategy was found to be cost-effective because they were all higher than the willingness-to-pay threshold of China (1 GDP per capita).[16]

Similarly, another Markov model in South African compared different triage strategies against no screening after a positive HPV DNA test. ***HPV DNA test followed by colposcopy was found to be more cost effective than HPV DNA+cytology triage*** with an ICER of 14,947 Rand/QALY (PHP ~49,000) and 18,258 Rand/QALY (PHP ~60,000), respectively.[17]

Equity, Acceptability, and Feasibility

No local study was found specifically assessing stakeholder attitudes and preferences regarding different triage strategies following a positive high-risk HPV test result. Available local data related to cervical cancer screening using pap smear showed poor knowledge but positive attitudes towards cervical cancer screening tests among women of different ages. Compliance to such screening programs can be improved through opportunistic screening or well-planned national screening programs that address educational and economic barriers.

Awareness and attitudes toward cervical cancer screening

In a survey of awareness and attitudes on cervical cancer screening programs, healthcare workers in one hospital in Cebu reported awareness of the existence and schedule of cervical cancer screening. However, only about 25% expressed an understanding of the purpose of such screening tests as well as eligibility criteria. Nonetheless, positive attitude toward screening was noted as more than 90% expressed willingness to submit themselves for screening.[18]

Poor knowledge on HPV infection, screening, and prevention were also reported in another study conducted in Baguio involving 81 women in their reproductive age. Most of the respondents have not undergone screening tests or HPV vaccination due to feelings of anxiety, inability to communicate their desire to get screened, cost of the vaccine, and lack of information.[19]

Among female adolescents (n=107) seeking consultation in a NCR-based hospital, most (> 75%) were not aware of cervical cancer screening HPV prevention but were willing to receive the vaccine if given

for free.[20] These findings of poor awareness of cervical cancer screening through pap smear were also echoed in another survey involving 256 female college students in Cebu.[20]

Methods to improve acceptability

A quasi-experimental study was done 1999 to determine interventions to improve pap smear compliance among Filipino women. In total, 2,500 Filipino women 15-50 years old from 8 rural and 5 urban areas throughout the Philippines participated. Compliance to pap smear screening was predicted by civil status, level of education, number of children, family history of cancer, and perceived risk of having cancer. Cost of screening was found to be a factor affecting decisions to seek cervical examinations. The study proposed having a well-planned nationwide cervical cancer screening program characterized by focused public health education campaigns, accessible and equipped screening centers with complementary treatment facilities, and subsidized by the government or private health insurance systems.[21]

A before and after study design involving female patients aged 21-65 years consulting an outpatient Family Medicine Clinic in UP-PGH showed that an opportunistic screening program increases the screening uptake of women (from 2% to 27%) when given during waiting hours or regular consultations. More women (38%) preferred VIA over pap smear (16%) as screening procedure.[22]

Recommendations from Other Groups

The 2nd edition of the WHO guideline for screening and treating cervical pre-cancer lesions for cervical cancer prevention suggested doing colposcopy, VIA, or cytology as possible triage options.[9] No specific triage method was identified as superior on the basis of their benefits and harms; rather, WHO stated that the choice of triage method will depend on feasibility, training, and program considerations. The American Society of Colposcopy and Cervical Pathology (ASCCP) suggested the use of cytology triage for all positive HPV results, regardless of genotype.[23] The European Cooperation on Development and Implementation of Cancer Screening and Prevention Guidelines (ECCG) provided similar recommendation in using cytology triage for women testing positive for hrHPV genotypes. However, they recommended against direct referrals to colposcopy for all HPV-positive women since it did not have considerable benefits over cytology triage.[24]

Table 5. Recommendations from Other Groups

Group	Recommendation	Basis for recommendation
WHO 2021[9]	WHO suggests using an HPV DNA primary screening test either with triage or without triage to prevent cervical cancer among the general population of women. In a screen, triage and treat approach using HPV DNA detection as the primary screening test among the general population of women, WHO suggests using partial genotyping, colposcopy, VIA OR cytology to triage women after a positive HPV DNA test.	**Conditional recommendation** **Moderate-certainty evidence**
ASCCP 2020[23]	ASCCP suggests using additional reflex triage testing (e.g. cytology) for all positive primary HPV screening tests results, *regardless of genotype*. If the primary HPV screening test results are positive for HPV-16/18 and reflex triage testing from the same laboratory specimen is not feasible, referral for colposcopy before obtaining additional testing was suggested. If the test results are HPV-16/18 positive and triage testing is not performed before the colposcopy, ASCCP suggests the collection of an additional triage test at the colposcopy visit.	**Conditional recommendation** **Low-certainty evidence**
ECCG 2015[24]	The guideline recommends cytology triage for women testing positive for hrHPV at primary screening. Depending on the result of the cytology triage, women testing positive for HPV should be referred to repeat testing or colposcopy. Direct colposcopy of all HPV-positive women was not recommended.	**Strong recommendation** **High-certainty evidence** **Conditional recommendation** **High-certainty evidence**

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Annex 1

PSCPC CPG WORKING GROUPS

Steering Committee

Project Director: Maria Julieta V. Germar, MD (PSCPC)
Project Head: Renee Vina G. Sicam, MD (PSCPC)
Technical Adviser: Ian Theodore G. Cabaluna RPh, MD, Gdip (Epi), MSc (cand.)

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Jay-Ar T. Sorreda, MD (POGS)
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Consensus Panel Facilitator: Maria Asuncion A. Silvestre, MD

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Genalin F. Amparo, MD (Jose R. Reyes Memorial Medical Center)
Clarito U. Cairo, Jr. MD (Department of Health)
Betha Fe M. Castillo, MD (Philippine Obstetrical and Gynecological Society)
Mary Judith Q. Clemente, MD (Philippine Infectious Diseases Society for Obstetrics and Gynecology)
Michele A. Hernandez-Diwa, MD (Philippine Society of Pathologists)
Tristan Jediah V. Labitad, MD (Philippine Society of Public Health Physicians)
Jericho Thaddeus P. Luna, MD (University of the Philippines - Philippine General Hospital)
Daphne Oseña-Paez (Patient Advocate)
Jean Anne B. Toral, MD, MSc (Collaboration/Manila Declaration: Call to Action Against Cervical Cancer)

External Reviewer

Mary Christine F. Palma, MD
Carlo L. Evangelista, MD, FPAFP
Christia S. Padolina MD

Annex B

Declaration of Conflict of Interest

NAME	REPRESENTATIVE	DECLARATION OF INTEREST	DISPOSITION
Consensus Panel			
Amparo, Genalin	JRMMC	Part-time specialist in JRRMMC (2019-present) and Dr. Jose Fabella Memorial Hospital (2012-present) Board Member of PSCPC (Jan 2021-Dec 2022) and SGOP (Jan-Dec 2022) Stocks in 2 hospitals under construction: North Valley Medical Center and Allied Care Experts (ACE) - Mandaluyong	Can vote but must declare potential conflicts
Clemente, Judith	PIDSOG	None to declare	No action required
Figi-Aliga, Ma. Theresa	PAFP	None to declare	No action required
Cairo, Clarito	DOH	Program Manager for Philippine Cancer Prevention and Control of the Department of Health	Can vote but must declare potential conflicts
Hernandez-Diwa, Michelle	FAP	Bought shares in a hospital ongoing construction (Great Valley Medical Center) Subspecialty is molecular pathology; in charge of molecular laboratories that will offer HPV testing	Cannot vote but can share their expertise during the panel meeting
Toral, Jean	Collaboration	Member of the Implementation Research Advisory Group (IRAG) for Study to Understand Cervical Cancer Early Endpoints and Determinants (SUCCEED)	Can vote but must declare potential conflicts

		Goes to 4 clinics; offers cervical cancer screening services in Manila, Quezon City, and Caloocan	
Luna, Jericho Thaddeus P.	PGH	Philippine Society for Fertility Preservation (PSFP) (2019-2022)	Can vote but must declare potential conflicts
Oseña-Paez, Daphne	Patient Advocate	None to declare	No action required
Castillo, Betha Fe	POGS	None to declare	No action required
Steering Committee			
Germar, Maria Julieta		Co-author of an evaluation of Visual Inspection of the cervix with acetic acid (VIA) workshop (2019) Co-author, Cost of Cervical cancer diagnosis and management (2015-2022)	Must declare their potential conflicts
Sicam, Renee Vina		Stocks in Makati Medical Center	Must declare their potential conflicts
Cabaluna, Ian Theodore		Project lead in the updating of the National Guideline for Periodic Health Examination Program Manager in the DOH-funded program on the development of primary care and cancer national guidelines	Must declare their potential conflicts
Abalos, Maria Virginia S.			
Sorreda, Jay-Ar T.		Medical Officer III, Eastern Bicol Medical Center (May 2021 to present)	Must declare their potential conflicts

		Vice-President, Catanduanes Medical Society (May 2021- May 2023)	
Rayel, Concepcion D.		Stocks in Davao Doctor's Hospital	Must declare their potential conflicts
Technical Working Group			
Velasco, Rogelio N.		Author in PHEX (Guideline on cervical cancer screening)	Must declare their potential conflicts
King, Rich Ericson C.		None to declare	No action required
Bayona, Howell Henrian G.		None to declare	No action required
Chan, Kerwyn Jim C.		None to declare	No action required
Fernandez, Joseff Karl U.		None to declare	No action required
Goce, Richmond Paul E.		None to declare	No action required
Carandang, Timothy Hudson David Culasino		None to declare	No action required
Silvestre, Ma. Asuncion		None to declare	No action required