GUIDELINES FOR CERVICAL CANCER SCREENING IN MALAYSIA

SECOND EDITION | 2023

FAMILY HEALTH DEVELOPMENT DIVISION

GUIDELINES FOR CERVICAL CANCER SCREENING IN MALAYSIA 2023

FAMILY HEALTH DEVELOPMENT DIVISION
MINISTRY OF HEALTH

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FOREWORD

Cervical cancer remains a major burden to many countries worldwide, particularly in under-developed and developing countries. It continues to have a huge impact on women not only physically but also socially and sexually. Globally, cervical cancer is the fourth most common cancer as well as the fourth leading cause of cancer deaths in women with an estimated 604 127 cases and 314 831 deaths in 2020. Nine out of ten of deaths from cervical cancer occur in low- and middle-income countries (LMICs). In Malaysia, the age standardised cervical cancer rate is 6.2 per 100,000 females (2012-2016), making it the third most common cancer in women, with 3,981 new cases reported for year 2012-2016.

Due to its slow progression if detected early, cervical cancer is one of the most preventable and treatable form of cancer. The causal association between HPV and cervical cancer has led to the development of tools that can be used towards the elimination of cervical cancer. HPV testing is now a well-recognized primary screening modality of choice. The development of automated laboratory tests that enable detection of oncogenic HPV infection in cervical samples thus facilitates the widespread introduction of primary HPV screening.

Recognizing the burden of cancer to the Malaysian population, the Ministry of Health has launched the National Cancer Blue Print 2016-2020 which highlighted the Ministry's commitment towards control and prevention of cancers. This framework comprises the stategies to reduce the impact of cancer which include training of healthcare providers, enhancing awareness campaigns, early detection, encouragement of collaborative efforts with multi-agencies, upgrading infrastructure and equipment and other related activities.

The Ministry of Health had introduced cytology screening as a part of family service packages since 1969 that was expanded as a screening modality for cervical cancer detection nationwide in 1995 in Malaysia. Nonetheless, the trend of cytology coverage has never met the targeted threshold which was set at 40 per cent of eligible women aged 30 to 65 years. This mediocre achievement is contributed by several factors such as lack of health education, embarrassment, discomfort, social-cultural barriers, constraints in manpower as well as monetary constraints among other factors.

Approximately 95 per cent of cervical cancer is caused by persistent infection of 'high risk' human papillomavirus (HR HPV). Progression of HPV infected epithelial cells to invasive cancer is a long-term process and may take 10 to 15 years. Therefore, initiating an effective cervical cancer control

programme through enhancing HPV vaccination and promoting screening is crucial in ensuring the acceleration of cervical cancer elimination.

The discovery of HPV's role in causing cancer has also led to the development of HPV vaccine to prevent cervical cancer. A school-based HPV vaccination was first introduced in 2010, targeting 250,000 13-year old school girls annually.

The global COVID-19 pandemic has generated compelling public interest worldwide in the effectiveness of screening and vaccination to safeguard the population against an infectious disease. The global experience of combatting COVID-19 has provided additional opportunities to seek the newly created resources to combat HPV. Advances in molecular testing has led the World Health Organization (WHO) to develop guidelines for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, that encompass a strong recommendation to use HPV DNA detection as primary screening test rather than cytology method which increases the predictive power for future cancerous outcomes. Self-sampling in HPV testing may overcome the societal barriers and negative attitudes towards screening. In line with the WHO's strategy, Malaysia aims to screen at least 70% of eligible women twice a lifetime with HPV testing.

This guideline was first developed in 2019 to assist health personnel in standardising the cervical cancer screening programme as well as managing abnormal results from HPV screening test (based on primary HPV test and biopsy confirmed cervical pre-invasive lesions).

I would like to congratulate and thank all the experts who have contributed towards the development of this revised guideline.

I hope that this guideline will improve the programme's performance in order to achieve the targets of cervical cancer elimination and ultimately ensuring the health and well-being of the women in the country.

Dr. Mohd Safiee bin Ismail

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ABBREVIATIONS

AEC-US	Atypical Endocervical Cells of Undetermined Significant
AIS	Adenocarcinoma in-situ
ASC	Atypical Squamous Cells
ASC-H	Atypical Squamous Cells, Cannot Rule Out High Grade Squamous Intra-epithelial Lesion
ASCUS	Atypical Squamous Cells of Undetermined Significance
CIN	Cervical Intra-Epithelial Neoplasia
GP	General Practitioner
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HSIL	High Grade Squamous Intra-Epithelial Lesion
HrHPV	High Risk Human Papilloma Virus
IPES	Integrated Package of Essential Services
IPPF	International Planned Parenthood Federation
JK	Health Nurse
JM	Community Nurse
LBC	Liquid-based Cytology
LSIL/ LGSIL	Low Grade Squamous Intra-Epithelial Lesion
MLT	Medical Laboratory Technologist
MO	Medical Officer
MOH	Ministry of Health

NAT	Nucleic Acid Test
PCR	Polymerase Chain Reaction
PPK	Health Care Assistant
PPP	Medical Assistant
PT	Administrative Officer
HSIL	High Grade Squamous Intra-Epithelial Lesion
SCC	Squamous Cell Carcinoma
SIL	Squamous Intra-Epithelial Lesion
SO	Science Officer
STI	Sexual Transmitted Infection
VIA	Visual Inspection with Acetic Acid
VILI	Visual Inspection with Lugol Iodine

1. INTRODUCTION

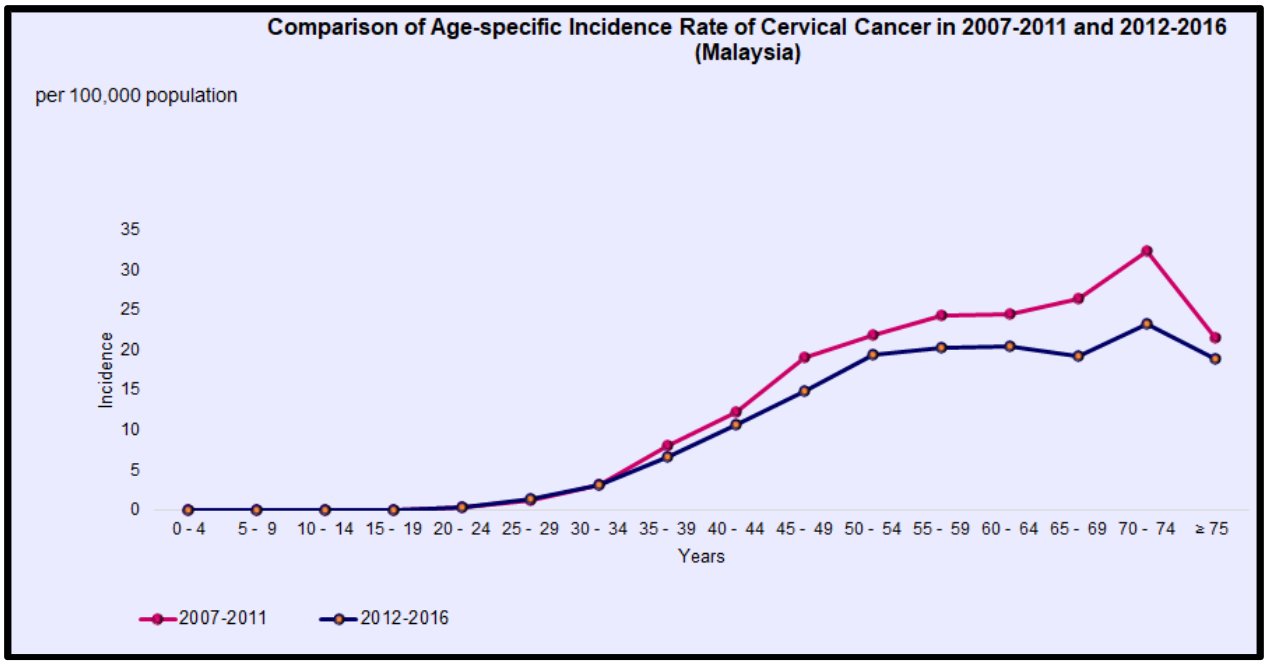
1.1 Cervical Cancer Screening- The Malaysian Landscape

In Malaysia, cervical cancer is the third most common cancer among females and ranked ninth in Malaysia among other cancers (Azizah et al., 2019). The number of new cases and deaths is estimated to increase by 64 per cent and 87 per cent in 2040, respectively, if no immediate action is taken (Zhao et al., 2022). The incidence of cervical cancer starts to rise among women aged 35 years and reach its peak between 50 to 65 years (**Figure 1)** (Azizah et al., 2019).

The conventional cytology was initiated in 1969 as a part of family planning programme and was expanded nationwide through the launch of the National Cytology Screening Programme in 1998, targeting all eligible women aged 20 to 65 years old. It is an opportunistic programme where cytology are offered to women who attend primary care clinics and maternal and child health clinics (Othman & Rebolj, 2009). The main objectives of this programme are prevention and early detection of cervical cancer and ensuring early treatment as well as sufficient follow up of patients (Division of Family Health Development, 2004).

The Ministry of Health provides approximately 75 per cent of the cytology screening in the country without incurring any cost to the public. However, women who undergo cytology screening services at the other agencies such as university hospitals, private facilities and non-government organizations may have to pay out of pocket or those covered by insurance will be paid by the insurance companies. The primary screening tool used in cervical cancer screening in the Ministry of Health facilities is cytology method either liquid-based cytology or conventional cytology. Liquid-based cytology (LBC) is a screening technique which is deemed superior to the conventional cytology (Strander, Andersson-Ellström, Milsom, Rådberg, & Ryd, 2007).

Despite the wide availability of screening services, the screening uptake has remained poor among eligible women, ranging between 23 to 26 per cent; and this coverage has declined up to 50 per cent pursuing COVID-19 pandemic (Ministry of Health Malaysia, 2020). This is further intensified by a lack of a national screening registry which affects the data quality.



Source: Malaysian National Cancer Registry Report (2007-2011 and 2012-2016)

Figure 1 Age-specific incidence rate of cervical cancer in 2007-2011 and 2012-2016 in Malaysia

1.2 HPV Vaccination Programme In Malaysia

Countless countries have integrated HPV vaccination into their national vaccination programme in their effort to make HPV vaccination their primary strategy in the prevention and eradication of cervical cancer. Since 2006, three vaccines have been approved for global use by WHO, which are bivalent HPV-16/18 vaccine (Cervarix®), quadrivalent HPV-6/11/16/18 vaccine (Gardasil®) and nonavalent HPV-6/11/16/18/31/33/45/52/58 (Gardasil®). Malaysia had successfully introduced HPV vaccination in the Malaysian National Immunization Programme in 2010. The decision to proceed to this strategy was supported by local and international cost–effectiveness studies. Aljunid, et al (Ezat & Aljunid, 2010) who led a study on the local mathematical model of HPV vaccine, projected that the introduction of HPV vaccination will potentially prevent 89 per cent of cervical cancer and save substantial annual cost for HPV-related treatment. Other considerations included vaccine efficacies

(World Health Organization, 2017), high immunogenicity among adolescents, prophylaxis property of the vaccine and feasibility reasons.

This strategy which aims to protect the girls prior to their sexual debut provides an excellent opportunity to decrease the incidence of cervical cancer over time. The National HPV Immunization Programme focuses on vaccinating school girls aged 13 years old through school-based health service package. This national programme was implemented in 2,958 public and private secondary schools registered under the Ministry of Education throughout Malaysia. The consent forms and printed HPV health education materials were delivered to the parents through school teachers one week prior to the first dose vaccination. This was conducted through scheduled school visits by the various school health teams at district level to ensure HPV vaccination was spaced at month 0, 1 and 6 as well as reach completion within the same year. The updated WHO recommendations in 2022 suggests that a single dose of HPV vaccine confers comparable efficacy and duration of protection as a 2-dose schedule (mondiale de la Santé & World Health Organization, 2022).

A systematic review and meta-analysis in 2018 concerning population level impact which includes data from 60 million individuals and up to 8 years of post-HPV vaccination have shown remarkable evidence of reduction in HPV prevalence among girls and young women, decreased anogenital wart among boys and significant reduction in CIN2 + (Drolet, Bénard, Pérez, & Brisson, 2019). There was also evidence of vaccine cross-protection and herd immunity effects among boys and older women from girls-only vaccination programmes. Concerning vaccinating males, a study conducted in the United States, found that the cost-effectiveness of male vaccination appeared less favourable when compared to an increased female vaccination coverage (Chesson, Ekwueme, Saraiya, Dunne, & Markowitz, 2011). In Malaysia, the prevalence of vaccine-targeted HPV 16/18 decreased 91% among women aged 18 to 24 years, from 4.0% in 2013-2015 to 0.4% in 2019-2020 (S. P. Khoo et al., 2022). The observed decline in prevalence of vaccine targeted HPV genotype among younger women, a decade after the national HPV vaccination programme is an early indication of its effectiveness in reducing the burden of cervical cancer.

1.3 HPV and Cervical Cancer

Cervical cancer is a rare outcome of an unresolved HPV (oncogenic) infection, currently defined as persistent presence of HPV DNA in repeated testing of cervical specimens. Human papillomavirus

(HPV) is the most common viral infection of the reproductive tract. Most sexually active women and men will be infected at some point in their lives and some may be repeatedly infected.

The peak time for acquiring infection for both women and men is shortly after becoming sexually active. HPV is sexually transmitted, but penetrative sex is not required for transmission. Skin-to-skin genital contact is a well-recognised mode of transmission.

Over 100 different types of human papillomavirus (HPV) have been identified and there are more than 40 anogenital HPV types, 15 of which are classified as 'high risk' or oncogenic as they are associated with anogenital cancer, including squamous and adenocarcinoma of the cervix (Daling, 1996). Persistent infection with oncogenic HPV types is generally subclinical, but may result in the development of a range of anogenital tumours including cancers of the cervix, anus, penis, vulva as well as vaginal HPV infections that usually clear without any intervention within a few months, and about 90 per cent clear within 2 years (Lowy & Schiller, 2006) (**Figure 2**). Women with persistent infections, especially with HPV 16, are at significantly higher risk of cervical cancer and its immediate precursor lesion, cervical intraepithelial neoplasia (CIN) grade 3 (CIN3) (Brotherton & Gertig, 2011; Trimble & Frazer, 2009). More than 70% of cervical squamous cell carcinomas and approximately 78% of cervical adenocarcinomas are caused by oncogenic HPV types 16 and 18 (International Collaboration of Epidemiological Studies of Cervical Cancer, 2007). HPV 16 is the most carcinogenic, accounting for about 55–60% of cervical cancers, while HPV 18 accounts for a further 10–15% of cervical cancers (Muñoz et al., 2003).

In many industrialised countries, the prevalence of HPV infections in young adult females may range between 30 per cent and 80 per cent and the lifetime probability of ever encountering HPV is as high as 80 to 90 per cent. Most of these infections clear spontaneously without clinical signs or symptoms.

An estimated 4 to 10 per cent of the HPV infected women will become persistent carriers until they reach middle age and these women are the high-risk group for cervical cancer and probably for any other HPV-related cancer. In Malaysia, the incidence of HPV infection among healthy women is reported to be approximately 7 per cent (Su Pei Khoo et al., 2018).

The time lag between the peak of HPV infection and the peak of cancer incidence is two (2) to four (4) decades, making the initial infection and precursor lesions of cervical cancer an appropriate window for screening and early detection.

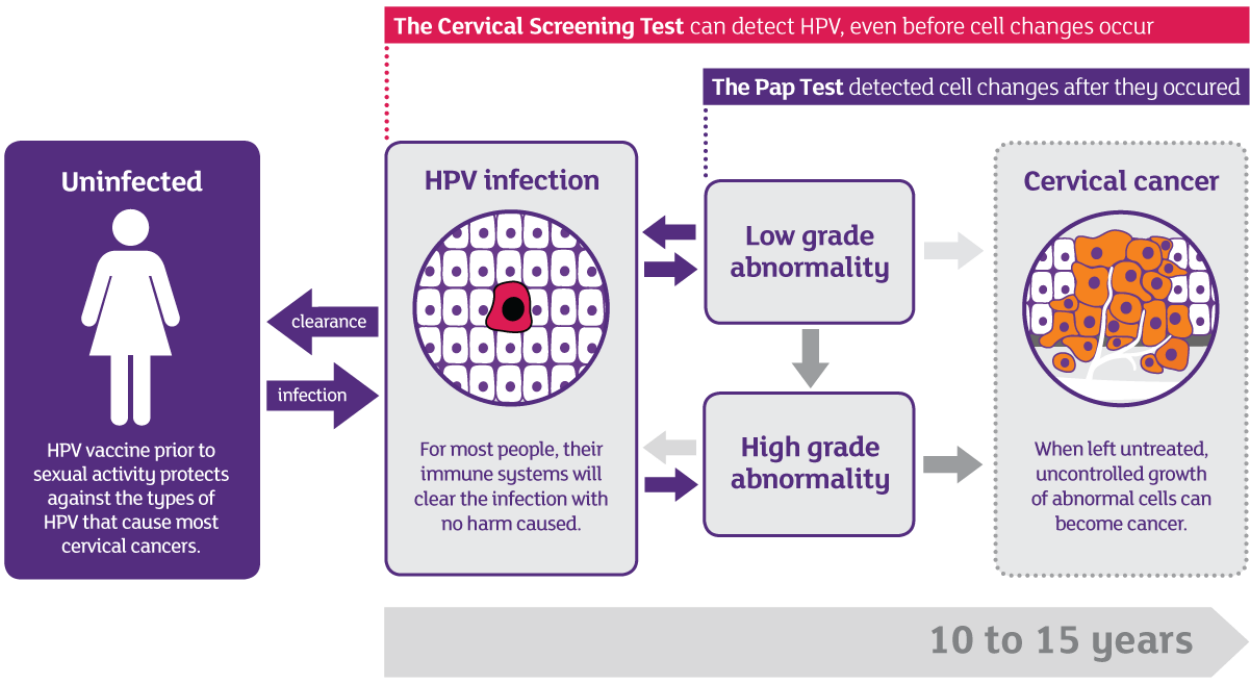


Figure 2 Pathogenesis of cervical cancer

2. RATIONALE FOR PRIMARY HPV TESTING

Persistent infection with high risk (HR) HPV is necessary for the development of cervical cancer and its precursor lesions. However, only a very small percentage of them progress to these disease states. This discovery has led to important technological advances, including the development of molecular tests for HPV to identify women with precancerous cervical lesions.

Cytological screening for cervical cancer precursors has been very successful in countries where adequate resources exist to ensure high quality and good coverage of the population at risk performed every three years. The extensive use of this tool has produced a tremendous reduction in cervical cancer incidence and invasive disease in developed countries (Devesa et al., 1987); however the success of this tool is influenced by many factors including behavioural and infrastructure factors.

Papanicolaou (Pap) smear was initiated as the primary screening tool to detect early precursors to cervical cancer by the Ministry of Health (MOH) in 1969. Currently, multi-agencies are involved in

providing cytology screening services for Malaysian women in embracing the cancer screening programme. These agencies include MOH, the National Population and Family Development Board of the Ministry of Women, Family and Community Development, private clinics and hospitals, university hospitals and army hospitals.

In 1996, the second National Health & Morbidity Survey (NHMS II) revealed that only 26 per cent of eligible women underwent cervical cancer screening using cytology while in 2006 (NHMS III) this proportion had doubled to 43.7 per cent. However, five (5) years later, the NHMS 2011 reported that only 12.8 per cent of eligible women had cytology examination (Institute for Public Health (IPH), 2008).

Over the years, it was found that the cytological abnormalities are primarily due to infection with HPV; however, various inflammatory conditions or sampling variations can result in false positive cytology results. Triage of an abnormal cytology result may involve repeat testing, colposcopy and/or biopsy. A histologically confirmed high-grade lesion must be surgically removed or ablated in preventing the development of invasive cervical cancer. Thus, there is a need for a test with a higher sensitivity to decrease this unnecessary repeated testing.

Due to the relationship between persistent infection with oncogenic HPV types and the development of cervical cancer, testing for the presence of oncogenic HPV DNA in cervical cell specimens has the potential to identify women at increased risk of developing cervical cancer (Cancer Council Australia, 2022). Women in whom oncogenic HPV types are not detected are at very low risk of CIN3 or cancer for at least 5 years (Dillner et al., 2008; Katki et al., 2011). HPV DNA testing has proven to be more sensitive than cytology in cervical cancer screening as it detects high-grade lesions earlier, thus preventing more cervical cancers (Rijkaart et al., 2012; Ronco et al., 2010). Substantial evidence, including data from randomised trials in developed countries, has shown HPV testing in primary screening is superior to cytology (Franceschi et al., 2011; Ronco et al., 2014; Sankaranarayanan et al., 2009).

However, the possible advantages offered by HPV-based screening require a well-organized programme with good compliance with screening and triage policies.

3. OBJECTIVES

i. To provide a systematic guideline for the cervical cancer screening programme in Malaysia
ii. As a guide and reference for health personnel involved with cervical cancer screening
iii. To standardize the management of abnormal results based on primary HPV screening test
iv. To provide a standard management of the biopsy confirmed cervical pre-invasive lesions

4. SCREENING POLICY

4.1 Target Age Group

HPV test is **recommended to sexually active women** aged **30 to 65 years**. However, women younger than 30 years can be offered cytology screening (conventional / liquid-based cytology). For women who exceed 65 years AND never had any routine screening, HPV testing can be offered.

4.2 Screening Intervals

Those eligible for cytology screening, the initial screening is yearly for two (2) years. If the results were normal, then a 3-yearly cytology is indicated.

Those eligible for HPV test, the screening interval will be every 5 years for those who are tested HPV negative.

4.3 Management for HPV Positive Results

Women who are HPV positive should follow the flowchart (Refer **Figure 12).**

4.4 Screening Personnel

Self-sampling by women or by health-care professional (provider sampling).

4.5 Reporting Personnel

4.5.1 Cytology Based Screening

Pathologists and Cytotechnologists

4.5.2 HPV Test

Laboratory based: Scientific officers or pathologists.

5. SCREENING METHODS

5.1 HPV Test

HPV test is a molecular technique using a sample of cervical cells, to detect the presence of Human Papillomavirus (HPV). This guideline specifically refers to partial genotyping (i.e. the detection of HPV16 and 18 versus other carcinogenic types) to identify women who at the highest risk of cervical cancer among those tested positive for HPV. HPV test is also validated as a reflex testing test for ASC-US and Low-Grade Squamous Intraepithelial Lesion (LSIL).

Many developed countries have adopted HPV testing as a primary screening tool. Incorporation of HPV testing into cervical cancer screening programmes has resulted in increased disease detection and lengthening the screening interval.

5.1.1 The Platform

HPV testing has been shown to be more effective in the detection of precancerous changes of the cervix compared to cervical cytology on a clinically validated platform for population-based screening. HPV can be detected through tests that identify high-risk HPV types, either by signal amplification (hybridisation techniques) or target amplification (PCR) of a viral DNA fragment (with partial genotyping) (**Table 1**).

In a clinical setting where self-sampling is utilised, PCR-based target amplification has been consistently shown to have higher sensitivity and greater clinical utility. Therefore, only PCR-based tests can be used to evaluate self-collected samples. Furthermore, in self-collection, the platform should offer a cellularity control, to avoid “false negative” results that are caused by incorrect sampling.

Laboratory-based HPV testing must be clinically validated in population studies [FDA approved or CE-IVD (European Conformity, in vitro diagnostic for specimens derived from humans) marked, both MDA approved]. Alternatively, tests that are FDA approved or CE-IVD marked, (both MDA approved) and have been validated in cross sectional comparisons with other validated tests, using the benchmarks articulated by Meijer et al. (Meijer, Berkhof, Heideman, Hesselink, & Snijders, 2009) may be used.

To ensure compliance to a Good Laboratory Practice, each designated laboratory shall have a test protocol in place.

Clinically validated HPV test (minimum FDA/CE certified or equivalent) and MDA certified (under Act 737) shall be used in this screening.

Table 1 Examples of Available HPV Nucleic Acid Test (NAT) Methodology

TEST	TECHNIQUE	PRODUCT
DNA	Target Amplification	GP5+/GP6+ bio PCR-EIA
	Amplification and genotyping of HPV-16 and HPV-18	Cobas HPV test (Roche) Xpert HPV (Cepheid) Abbott RealTime High Risk (HR) HPV assay PapilloCheck Onclarity (BD) Anyplex II (Seegene)
RNA	Amplification of E6/E7 proteins	Aptima HPV Assay PreTect HPV-Proofer HV

The clinical sensitivity of an HPV test is an important consideration in screening programmes. POCT's sensitivity and specificity exceeds 90 per cent and 40 per cent respectively. For a laboratory-based HPV testing, the pooled sensitivity ranges from 88.6 to 91.1 per cent and the pooled specificity ranges from 89.7 to 90.0 per cent (Koliopoulos et al., 2017).

5.1.2 Sample Analysis

Sample analysis can either be performed in a central laboratory (batch testing) or as a Point of Care Test (POCT) (as approved by the state POCT committee), depending on the geographical area and resource accessibility. Furthermore, for a laboratory-based HPV testing, the selected test must be clinically validated in population studies (FDA approved or CE-IVD marked, both MDA approved) and performed in accredited laboratories (under Molecular Lab/Unit). In contrast, several validated POCT ports will be placed in selected healthcare facilities and managed by authorized personnel.

5.1.3 Specimen Collection

The representatives from the manufacturer will provide a detailed information regarding the procedures involved in specimen collection. The medium or device used by the healthcare practitioners (provider sampling) or the clients (self-sampling) in collecting the lower vaginal specimen must be suitable and validated for the use of HPV test as intended by the manufacturer.

The specimen container must be screwed on properly to prevent spillage or contamination. The specimen shall be properly labelled and accompanied with relevant clinical history using HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (PS 1/98 (Pindaan 2020)) or HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (*PS 1/98* (Pindaan 2023)).

5.1.4 Transportation of Specimen

The specimen should be **transported as soon as possible** (should not exceed 14 days after collection). It does not require cold-chain management but should be stored at room temperature (<30°C).

5.1.5 Analytical Process

The processes involved must comply with:

i. Authorised and competent personnel shall perform the test.
ii. The test procedure shall follow the manufacturer's insert kit.
iii. The laboratory must demonstrate the validation of the collection device by referring to peer reviewed publications or by undertaking its own validation studies.
iv. The Laboratory Turn-Around Time (LTAT) should be within **14 working days**.

5.1.6 HPV Results

- The result is reported qualitatively:
  - Positive for HPV 16/18
  - Negative for HPV 16/18
  - Positive for HPV non 16/18 subtype
  - Unsatisfactory
- Result is unsatisfactory if the Internal Control is invalid.
- An example of the report is portrayed in **Table 2**.
- The requesting officers will receive the reports via web-based, email, fax, or hardcopy.
- The leftover specimen shall be kept at room temperature for at least 2 weeks after the report has been released and can be stored up to 4-10 weeks if kept at 2-8° C.

Table 2 Example of an HPV Test Report

SPECIMEN	Cervico-vagina
TEST RESULTS	PCR for Oncogenic HPV and genotype: HPV 16 – Detected/Not Detected HPV 18 – Detected/Not Detected HPV (non 16/18) – Detected/Not Detected Unsatisfactory
RECOMMENDATION	**Follow the 'Management of HPV Result'**

(Refer **Appendix 4** for A Sample of HPV Report)

5.1.7 Laboratory Waste Disposal

Disposal of leftover specimens shall follow the standard guideline of clinical waste management.

5.2 Cytology Based Screening

Cytology tests (including the Papanicolaou smear test and liquid-based cytology (LBC) identify atypical cervical cells through the preparation and interpretation of slides using microscopy by a trained expert.

5.2.1 Conventional Cytology

A sample from cervical scrape is obtained using a cervical brush/broom and is smeared directly onto a glass slide. The sample is immediately fixed (within 5 seconds) with 95% alcohol and stained with Papanicolaou stain for microscopic examination.

5.2.2 Liquid-based Cytology

A sample from cervical scrape is obtained using cervical brush/broom and suspended in a vial of preservative for transport to the laboratory. The sample is processed and placed onto a glass slide and stained with Papanicolaou stain for microscopic examination. The choice of technology must be FDA approved or equivalent.

In those screened high risk HPV positive (HPV 16/18 and non-16/18), liquid-based cytology is indicated to triage this cohort. This is termed as **Reflex Liquid-Based Cytology**. The sample collection will be carried out by the health care providers at the health clinics. These samples will be sent to the designated cytology laboratories which are equipped with adequate resources which include equipment as well as dedicated, trained cytotechnologists and anatomical pathologists. The reporting format shall follow the **PS 2/2019** format (**Appendix 5**).

5.3 Other Methods

In low resource areas, other options of cervical screening can be adopted such as Visual Inspection with Acetic Acid (VIA) / Visual Inspection with Lugol Iodine (VILI). VIA testing is a visual examination (without magnification) of the cervix after application of dilute acetic acid to identify aceto-white lesions (VIA is considered positive) that require treatment (e.g. ablation or excision) or further evaluation. VIA is inappropriate in postmenopausal women or when the transformation zone is no longer visible. VILI, in contrast is considered positive when the affected cervical tissue turns into yellow after Lugol application.

6. TAKING SAMPLES

6.1 General advice prior to sample collection HPV Test / Cytology

i. Avoid taking cervical cancer screening during normal menstruation. If abnormal or prolonged menses, refer to a medical officer.
ii. Avoid sexual intercourse 48 hours prior to the procedure.
iii. Do not douche or insert any form of medication or tampons (vaginal creams, foams, films, or jellies or spermicides) into the vagina 48 hours prior to the procedure.
iv. Any cervical lesion seen should be referred to a gynaecologist.
v. Can be performed after 6 weeks postpartum.

6.2 HPV Test

6.2.1 Requirements for HPV Sampling in Health Clinics

i. Request form (HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (*PS 1/98 (*Pindaan *2020)*) or (HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (*PS 1/98* (Pindaan 2023).

ii. Flocked swab (Not to be replaced by other swabs for example cotton or microbiology swab) or any types of sampling device
iii. Specimen container with preservative.
iv. Laminated guide card for women

6.2.2 Self-Sampling HPV Test (Vaginal Sample)

HPV self-sampling kit can be in many forms. Refer **Figure 3.**

Instructions to women on self-sampling (English and Malay) (As per **Figure 4** and **Figure 5**).

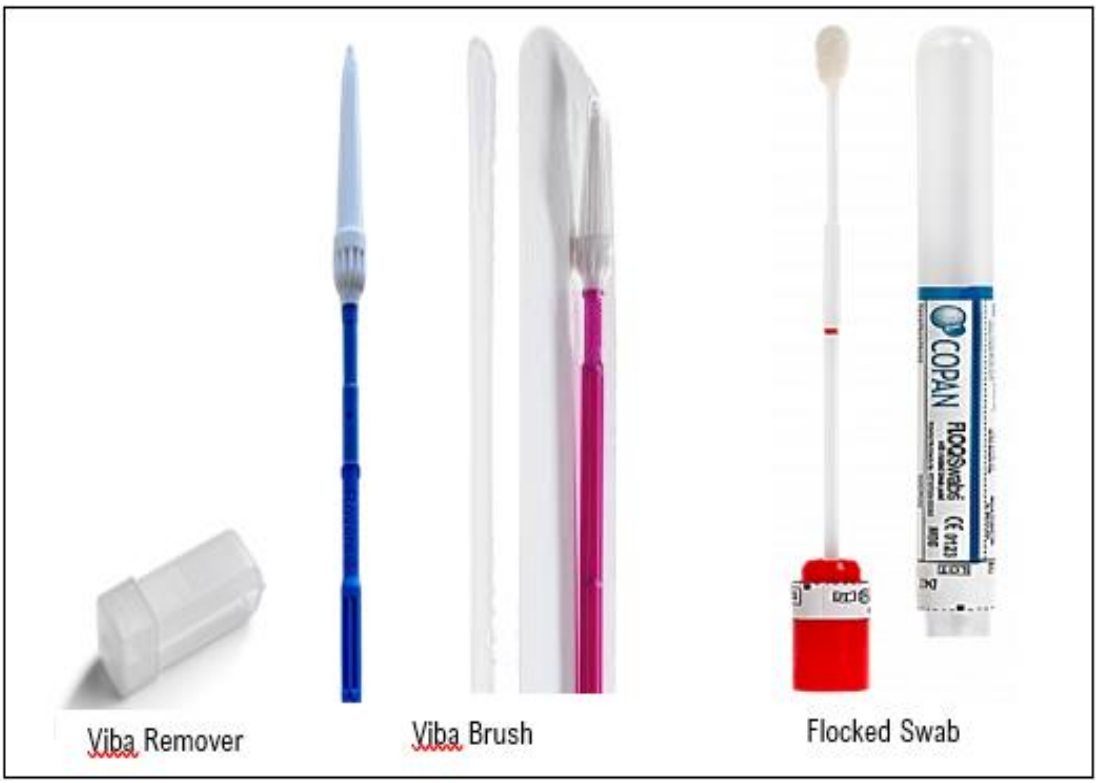


Figure 3 HPV test sampling devices

How to perform a self-sampling HPV test (depends on the self-sampling devices available in the health facilities)

The clinic/facility will provide a conducive and clean place to perform the HPV test.

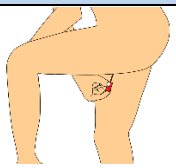
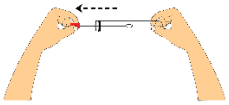
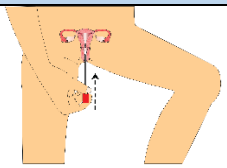
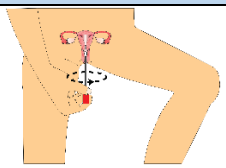
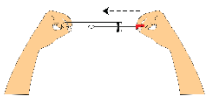
Step 1	Step 2	Step 3	Step 4	Step 5
				
POSITION • Undress from the waist down. • Remove your underwear. • Ensure you are in a comfortable position.	**REMOVING THE SWAB** • Twist the swab cap to loosen the swab from the plastic tube. • Hold the plastic tube. • Place the plastic tube at a safe and clean place.	**INSERTING THE SWAB** • Gently spread open the folds of skin at the opening of your birth canal (vagina). • Remove the swab and hold the swab on the red line. • Insert the swab into the birth canal until red line.	**TAKING THE SAMPLE** • Rotate the swab for 10 times. • Remove the swab from the birth canal. • Make sure the swab is not contaminated after removal.	**RETURNING THE SWAB** • Insert the swab back into the plastic tube. • Return the tube to the nurse. • An appointment will be given to inform the result. • If you have any problems, speak to the nurse.

Figure 4 Self-sampling HPV test English

Bagaimanakah cara untuk mengambil ujian HPV kendiri

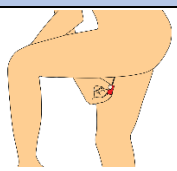
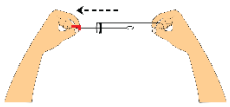
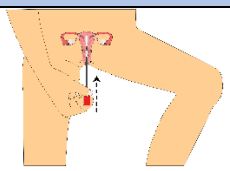
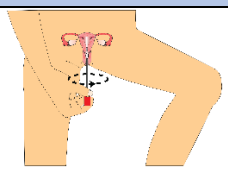
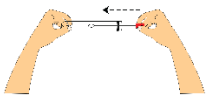
Langkah 1	Langkah 2	Langkah 3	Langkah 4	Langkah 5
				
KEDUDUKAN • Tanggalkan pakaian dari aras pinggang ke bawah • Tanggalkan seluar dalam anda • Pastikan anda berada dalam kedudukan yang selesa	**KELUARKAN SWAB** • Pusingkan penutup swab untuk melonggarkan swab dari tiub plastik. • Pegang tiub plastik. • Letakkan tiub plastik di tempat yang selamat dan bersih.	**MASUKKAN SWAB** • Buka lipatan kulit pada saluran faraj dengan perlahan. • Keluarkan swab dan pegang swab di atas garis berwarna merah. • Masukkan swab ke dalam saluran faraj sehingga garis yang bertanda merah.	**PENGAMBILAN SAMPEL** • Putarkan swab sebanyak 10 kali. • Keluarkan swab dari saluran faraj. • Pastikan swab tidak dicemari selepas dikeluarkan.	**KEMBALIKAN SWAB** • Masukkan swab ke dalam tiub plastik. • Serahkan tiub plastik kepada jururawat. • Janji temu akan diberi untuk memaklumkan keputusan. • Sila berhubung dengan jururawat sekiranya terdapat sebarang kesukaran.

Figure 5 Self-sampling HPV Test in Malay Language

6.2.3 Assisted Sampling HPV Test by The Healthcare Provider (Provider Sampling)

Health-care professionals must be prepared to take vaginal swabs for HPV sampling for women who are not confident in performing self-sampling. This sampling is done with the women in supine position **WITHOUT** using a speculum.

6.2.4 Repeating HPV Tests for Unsatisfactory Results

Health-care professionals are required to repeat HPV test **using liquid-based cytology sampling method**. **The sample is sent for HPV test.**

The request form [(HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (*PS 1/98 (*Pindaan *2020)*) must be stamped **"UNSATISFACTORY HPV TEST"** on the right-hand side (**Appendix 2 or Appendix 3**).

The specimen container should be labelled "**HPV testing**".

6.3 Taking Samples for Cytology Based Screening

6.3.1 Instruments for Taking Cervical Smears

i. Bivalve vaginal speculum (CUSCO) - all sizes preferably disposable
ii. Swabs
iii. Normal saline
iv. Hand gloves
v. Cervical sampler broom, Cervex-Brush® Combi, endocervical brush or spatula
vi. Request form - HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (*PS 1/98 (*Pindaan *2020 or* HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (PS 1/98 *2023)*.
vii. Adequate light source
viii. Couch and screen

6.3.2 Additional Instruments for Conventional Smear

i. Frosted end glass slide and 2B pencil or ordinary glass slide and diamond pencil.
ii. Fixative – 95% ethyl alcohol in coplin jar or alcohol spray
iii. Slide mailer

6.3.3 Instrument for Liquid-based Cytology

i. Preservative vial

6.3.4 How to Take a Cervical Smear

1. Complete the cytology request form - HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (PS 1/98 (Pindaan 2020) or HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (PS 1/98 (Pindaan 2023)) and label the glass slide or vial.
2. Wash your hands and wear gloves.
3. Examine the woman in a dorsal position.
4. Swab the introitus with normal saline.
5. Wet the bivalve speculum using sterile water or normal saline **(DO NOT USE LUBRICANT).**
6. Introduce the speculum into the vagina carefully avoiding contact with the cervix (for conventional smear, bleeding from the cervix will interfere with the evaluation of smear).
7. Visualize the cervix. If there is discharge, take a swab for microscopic examination and send for culture and sensitivity if indicated. Remove excess discharge before taking the cervical sample.
8. Obtain an adequate sample from the cervix using the appropriate sampler device (cervical sampler broom, Cervex-Brush® Combi, endocervical brush or spatula (refer **Figure 6**) according to the sample type.

6.3.5 Taking a cervical smear in peri- and post-menopausal women

No.	For Pre-Menopausal Women	For Peri And Post-Menopausal Women
1.	**Cervical sampler broom** Rotate 3 to 5 times 360 degrees in the cervical os. **OR**	**Cervical sampler broom** Rotate 3 to 5 times 360 degrees in the cervical os. **PLUS** **Endocervical brush** Obtain a sample from the endocervix by gently inserting the endocervical brush into the endocervical canal while ensuring that you can see the lower row of the brush/bristles. Rotate 90 degrees (a quarter rotation).
2.	**Cervex-Brush® Combi** Insert the central part of the brush into the cervical os and rotate clockwise twice. **OR**	**Cervex-Brush® Combi** Insert the central part of the brush into the cervical os and rotate clockwise twice. **OR**
3.	**Spatula** Rotate once or twice, keeping in close contact with the ecto-cervix. **PLUS** **Endocervical brush**: Obtain a sample from the endocervix by gently inserting the endocervical brush into the endocervical canal while ensuring that you can see the lower row of the brush/bristles. Rotate 90 degrees (a quarter rotation).	**Spatula** Rotate once or twice, keeping in close contact with the ecto-cervix. **PLUS** **Endocervical brush** Obtain a sample from the endocervix by gently inserting the endocervical brush into the endocervical canal while ensuring that you can see the lower row of the brush/bristles. Rotate 90 degrees (a quarter rotation).

Note:
For clinics without endocervical brushes, healthcare staff should ensure that when using cervical sampler broom, the center (tip) of the broom should be directed into the cervical os and rotate the broom 3 to 5 times. The sample should be smeared onto the labelled glass slide in one direction (**Figure 8**).

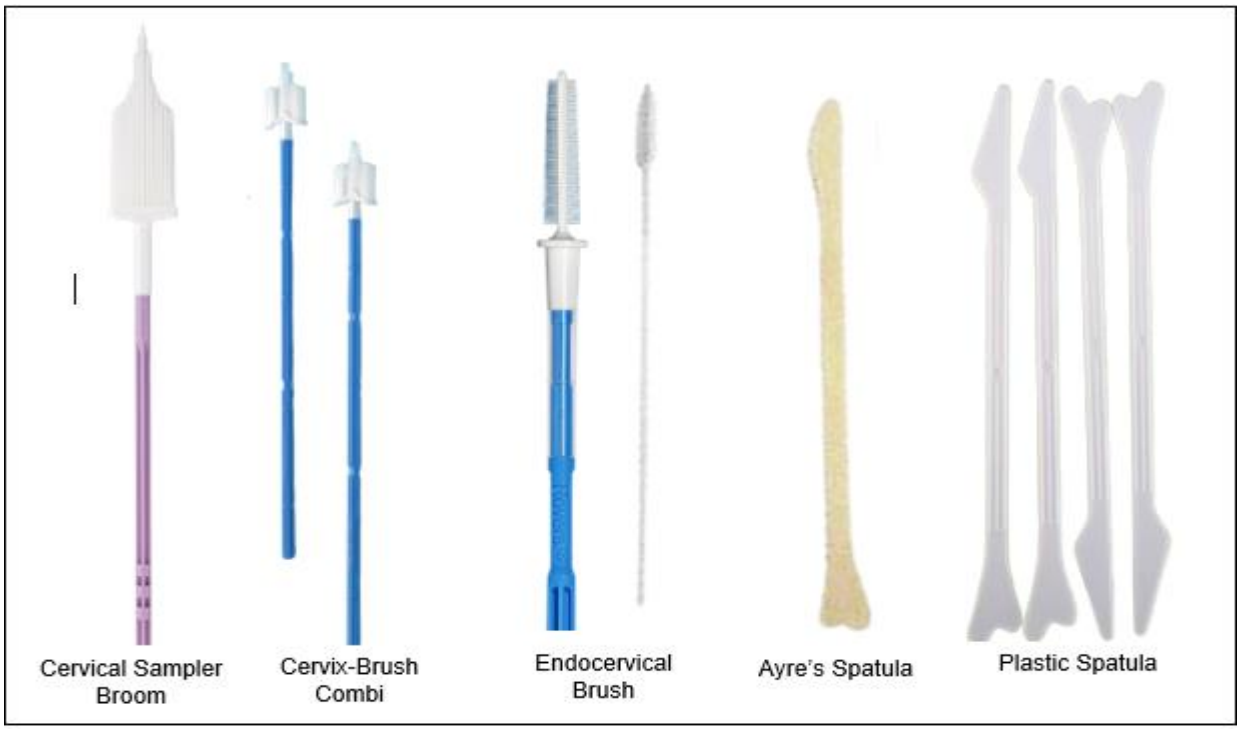


Figure 6 Cervical Sampling Device

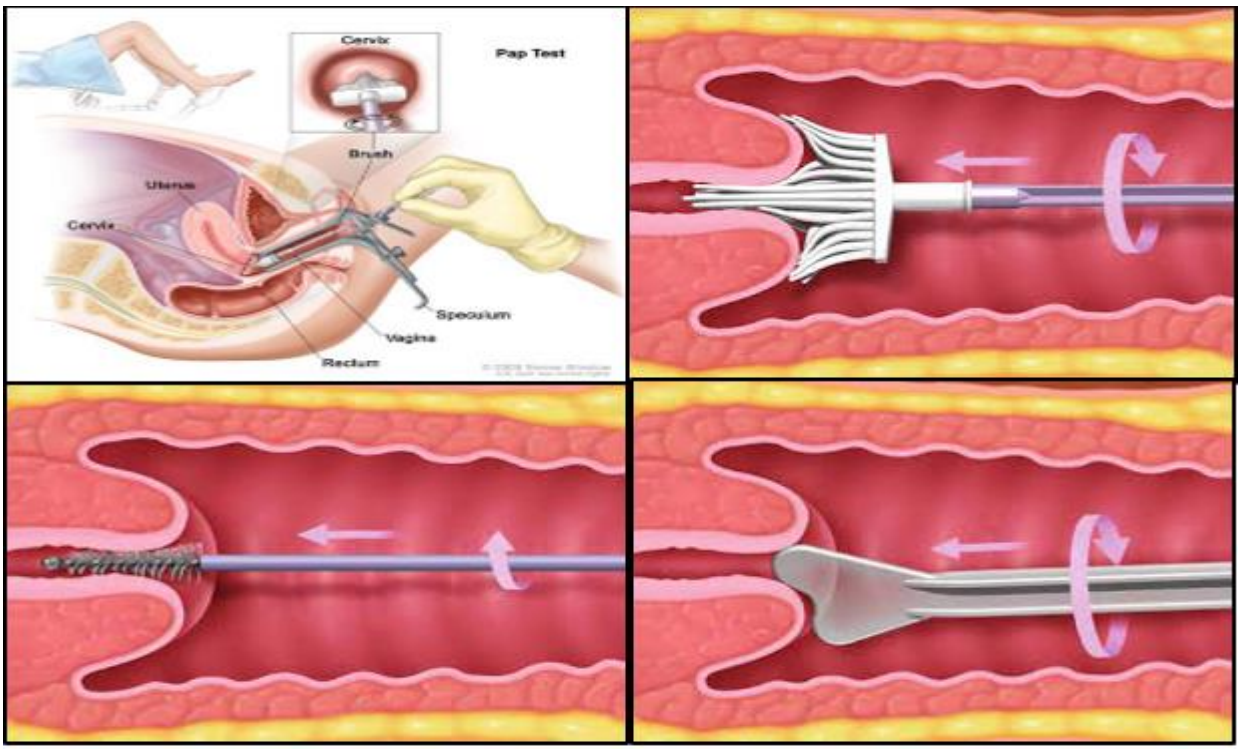


Figure 7 Rotation of cervical sampling

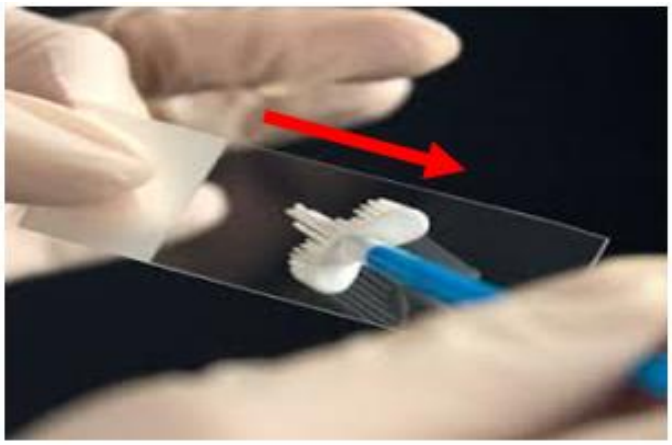


Figure 8 Smearing the sample using a cervical sample broom in one direction for conventional smear

Liquid-based:

Obtain an adequate sample from the cervix including the transformation zone. Follow the instruction according to user manual, example:

ThinPrep:

360 degrees rotation 3x. Rinse the brush vigorously inside the preservative vial by swirling and pushing against the vial wall 10 times. Discard the brush.

SurePath:

360 degrees rotation 5x in clockwise manner. Drop the detachable cytobrush head into the preservative vial. Rinse the cervical sampler broom in the preservative vial (A) OR drop the detachable head device into the preservative vial (B) according to the user manual (**Figure 9**).

Others: Follow collection method from the package insert / user manual.

Note:

i. Position of transformation zone (TZ) varies according to age. Selection of sampling device should be in accordance to the location of transformation zone. (**Figure 10A and Figure 10B)**
ii. Smear should be taken before performing bimanual examination
iii. During colposcopic examination, smear should be taken before applying acetic acid

Figure 9 Transferring of sample into the vial containing preservative

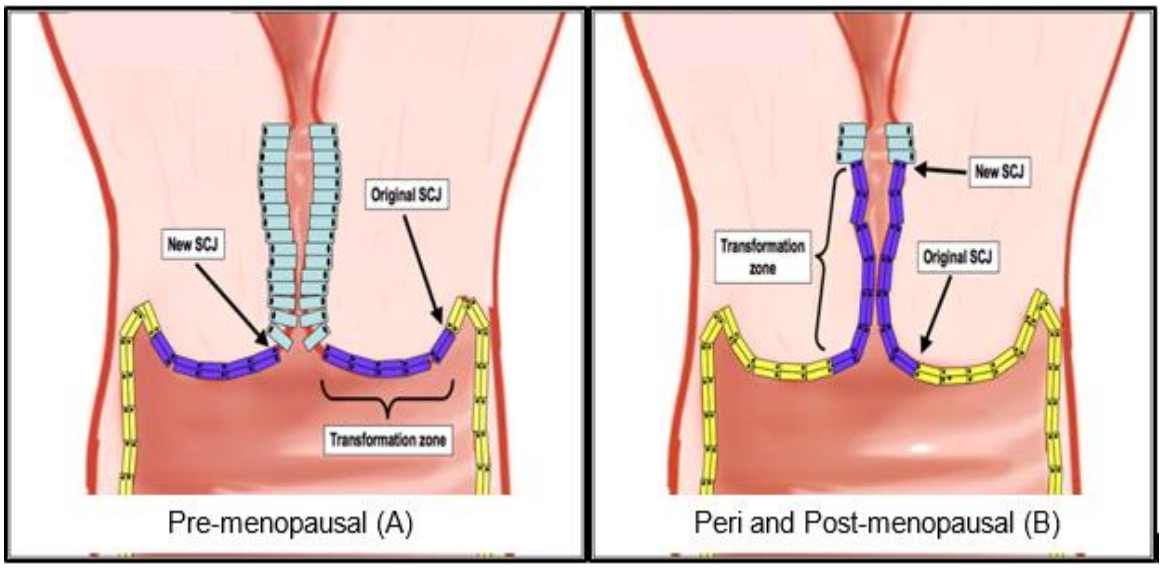


Figure 10 Position of transformation zone (TZ).

Figure 10 (B) is TZ for post-menopausal women in which both cervical sampler broom and endocervical brush should be used.

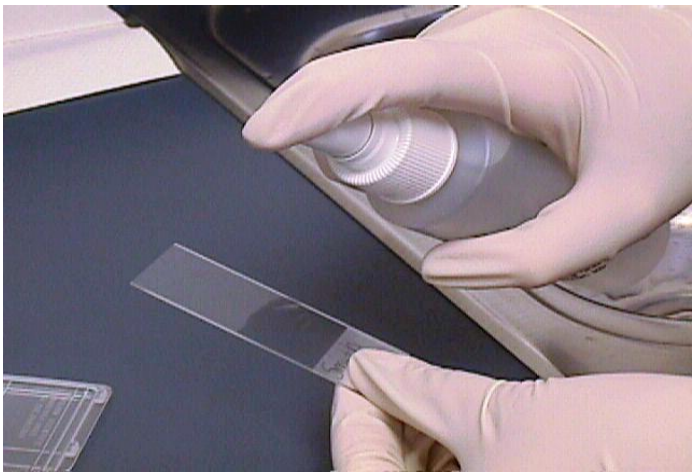
Fixation:

Conventional

a) After taking the smear, immediately (within 5 seconds) dip the slide into a coplin jar containing 95% ethyl alcohol for 30 minutes. Once completed, stand the slide on the slide rack to drain excess fluid.

OR

b) Immediately spray fixed (within 5 seconds). The slide should be placed 15 to 25 cm from the nozzle and spray at the right angle (Refer **Figure 11**).



Note: Distance of the nozzle to slide is about 15-25cm (6-10 inches). The sprayed preservative should cover the whole smear area.

Figure 11 Fixation of smear by alcohol spray

NOTE:

- The fixative (95% ethyl alcohol) must be placed in a covered container to avoid evaporation.
- The fixative must be changed regularly
- Do not allow the smeared slide to dry before fixation
- Endocervical brush may be used in severely atrophic cervix
- Ensure correct labelling of slide and completion of form
- Details of previous smears (if relevant) must be stated in the request form

6.3.6 Reasons for Unsatisfactory Cytology

Insufficient sample
Inadequate fixation time (less than 30 minutes)
Delay in dipping the slide in the fixative
Blood-stained smear
Thick uneven smear
Excessive discharge/ thick inflammatory exudate (on the slide)
Broken slide beyond repair
Usage of lubricant before taking smear
Dirty and contaminated slides

7. PREPARING THE SAMPLES BEFORE SENDING TO THE LABORATORY

7.1 Preparation for HPV Samples

i. Label the samples and request forms using 2 unique identifiers (preferably using barcode if available).
ii. Ensure the identification details on the samples and request forms are matched.
iii. Suspend the flocked swab into the container with preservative fluid or any other sampling device which follows the preparation manual from the manufacturer.
iv. Tighten the cap to prevent spillage or contamination.
v. Place the samples into biohazard plastic bags.
vi. Transport the samples at room temperature **(stable up to 35^{0}C)** with the request forms to the designated laboratory **as soon as possible** not exceeding 14 days after collection.

(The details of the preparation will be explained by the manufacturer.)

7.2 Preparation for Cervical Samples Using Conventional Smear and LBC

i. Label the samples and request forms with 2 unique identifiers (preferably using barcode if available).
ii. Ensure the identification details on the samples and request forms are matched.
iii. For conventional smear, place the slide/s in the slide mailer.
iv. Transport the slide or the sample vial with the request form to the laboratory. Avoid delay in sending the slide/sample and keep the slide in a dry environment to prevent fungal contamination.

7.3 Preparation for Cervical Samples Using LBC for Unsatisfactory HPV Test

i. Label the samples and request forms with 2 unique identifiers (preferably using barcode if available).
ii. Ensure the identification details on the samples and request forms are matched.
iii. For conventional smear, place the slide/s in the slide mailer.
iv. Send the slide or the sample vial with the request form to the laboratory. Avoid delay in sending the slide/sample and keep the slide in a dry environment to prevent fungal contamination.
v. The Request Form (HPV TEST/ CYTOLOGY (CYTOLOGY/LBC) REQUEST FORM (PS 1/98 (Pindaan 2020)) must be stamped "**UNSATISFACTORY HPV TEST**".
vi. The specimen container should be labelled for "HPV testing".

8. MANAGEMENT OF HPV TEST RESULTS

8.1 Management Algorithm of HPV Test Results

Please refer to **Figure 12** below for the summary of clinical management**.**

Unsatisfactory

For women with an unsatisfactory HPV test, repeat HPV test using liquid-based medium as soon as possible but not more than 12 weeks. The method follows the steps for taking a cervical smear using liquid-based **but the sample is sent for HPV test**.

Negative high-risk HPV

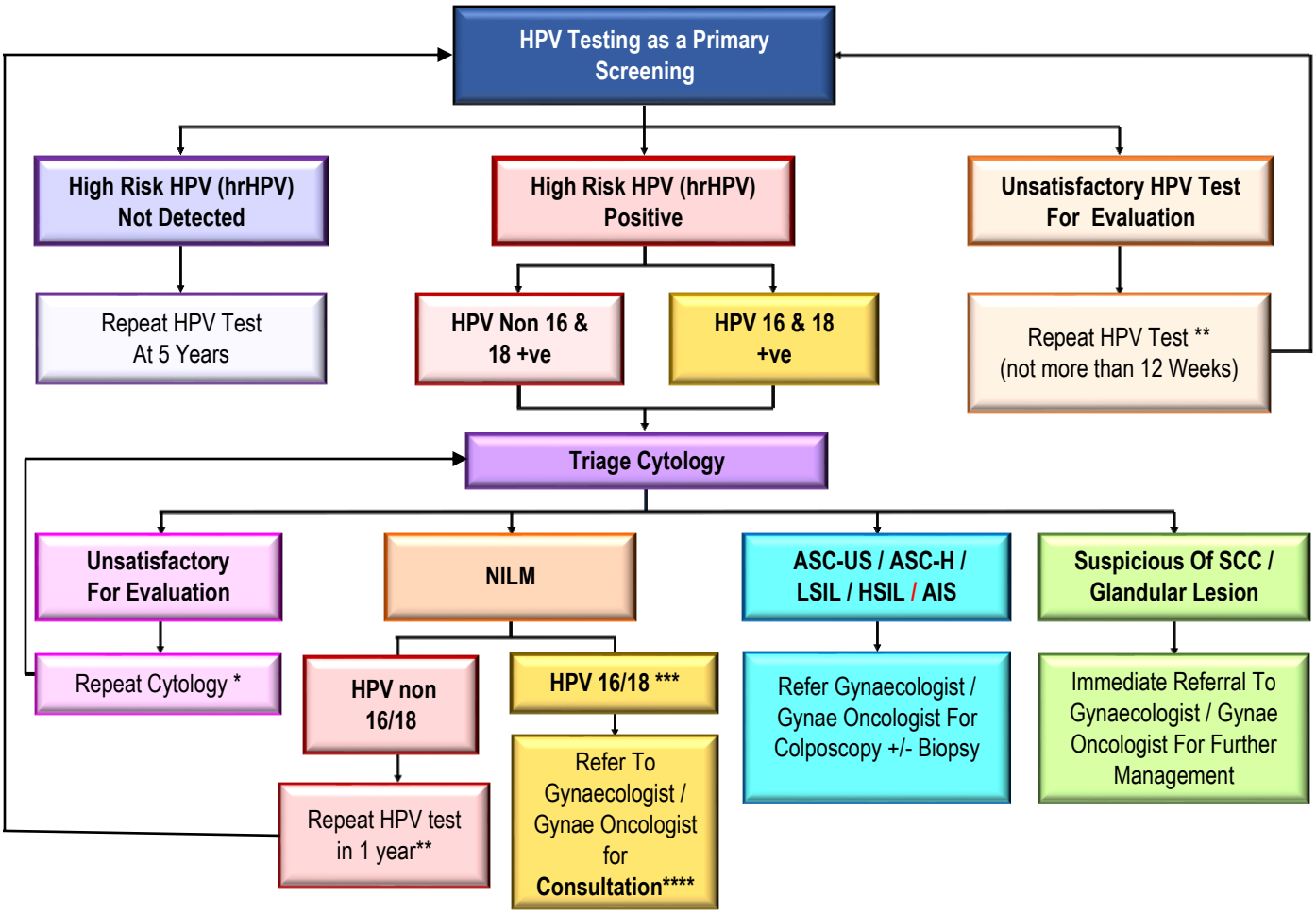
For women with a negative HPV test, they should be offered the next screening test not earlier than 5 years.

High risk positive 16/18

Women with positive oncogenic HPV (**16/18**) results are required to undergo triage liquid-based cytology. Negative LBC cases should be consulted with gynae-oncologists regarding subsequent management. Those women whose LBCs are reported as ASC-US or ASC-H or LSIL or HSIL or AIS, should be referred to gynaecologists or gynaelogical oncologists for colposcopy. In the case where LBC reports suspicious of squamous cell carcinoma or any glandular lesions, immediate referral to a gynaecological oncologist is indicated.

High risk positive non-16/18

Women with positive oncogenic HPV (**non 16/18**) results are required to undergo triage liquid-based cytology. Negative LBC cases should repeat HPV tests in one year **using LBC medium**. Those women whose LBCs are reported as ASC-US or ASC-H or LSIL or HSIL or AIS, should be referred to gynaecologists or gynaelogical oncologists for colposcopy. In the case where LBC reports suspicious of squamous cell carcinoma or any glandular lesions, immediate referral to a gynaecological oncologist is indicated.



* At best immediately, but not more than 3 months.

** Repeat HPV test using LBC medium

***Options of management remain a matter of contention solely because of cost effectiveness associated with cytology re-triage. Based on Athena Trial, patients were subjected for colposcopy and biopsy. Data showed that 10% of CIN II and CIN III in this cohort of patients (with negative cytology/NILM). Malaysian unpublished data reported that 6.25% of CIN II and CIN III in this cohort. It remains a matter of contention, in deciding the cut of point in subjecting patients for colposcopy and biopsy (5% or 10%).

****Consultation for risk assessment and further management

Figure 12 Management of HPV Test Results

8.1.1 Exit Criteria for Cervical Cancer Screening

Cervical screening test can be discontinued for women after 65 years with **two negative consecutive** HPV tests in the preceding 10 years, with the latest test performed within the last 5 years. However, for those without prior HPV test, two negative consecutive cytology reports with the latest performed within the last 3 years, screening can be discontinued.

9. MANAGEMENT OF CYTOLOGY RESULTS

For centres that utilizes cytology as primary screening, the management of cytology results are as the following:

9.1 Management of Unsatisfactory Smear

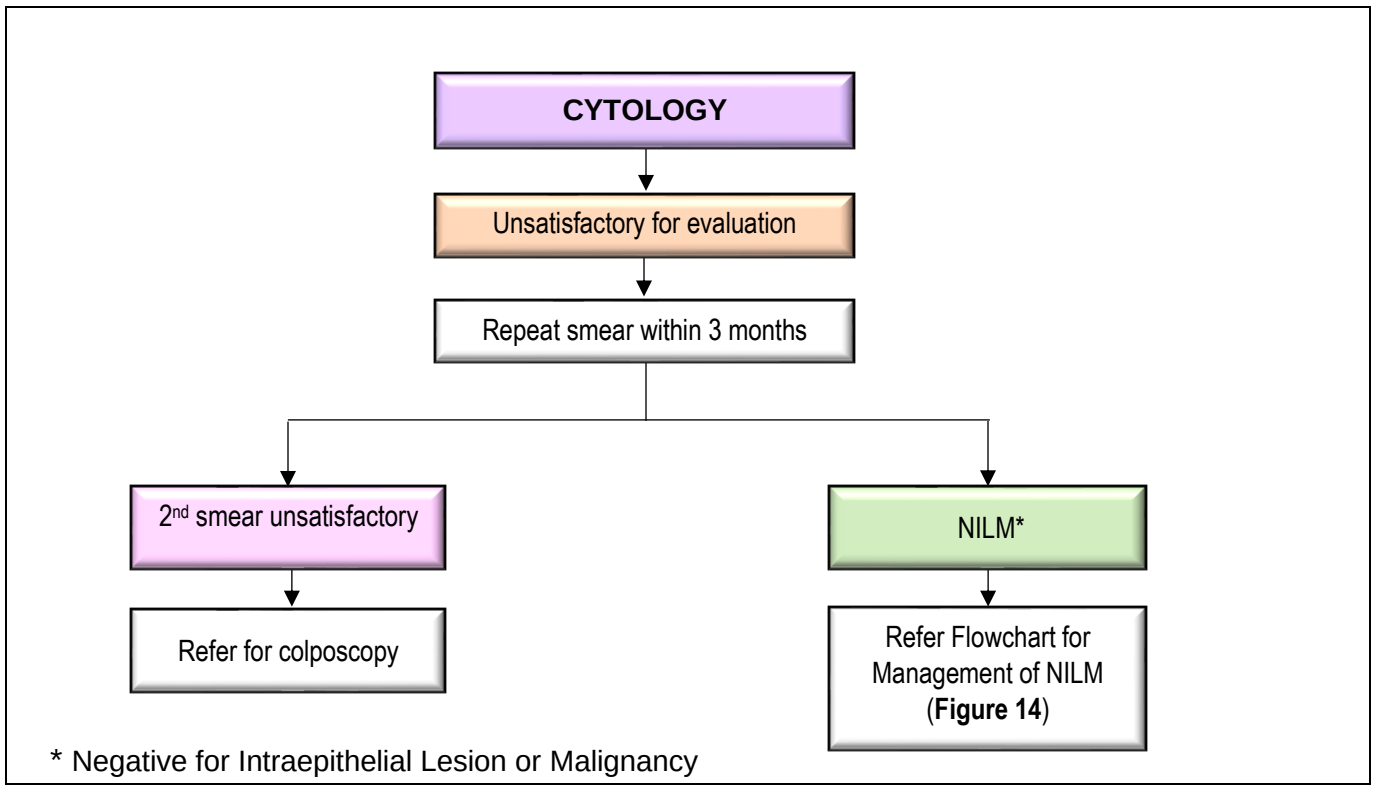


Figure 13 Management of Unsatisfactory Smear

9.2 Management of Normal Smear

9.2.1 Management of Negative for Intraepithelial Lesion or Malignancy (NILM)

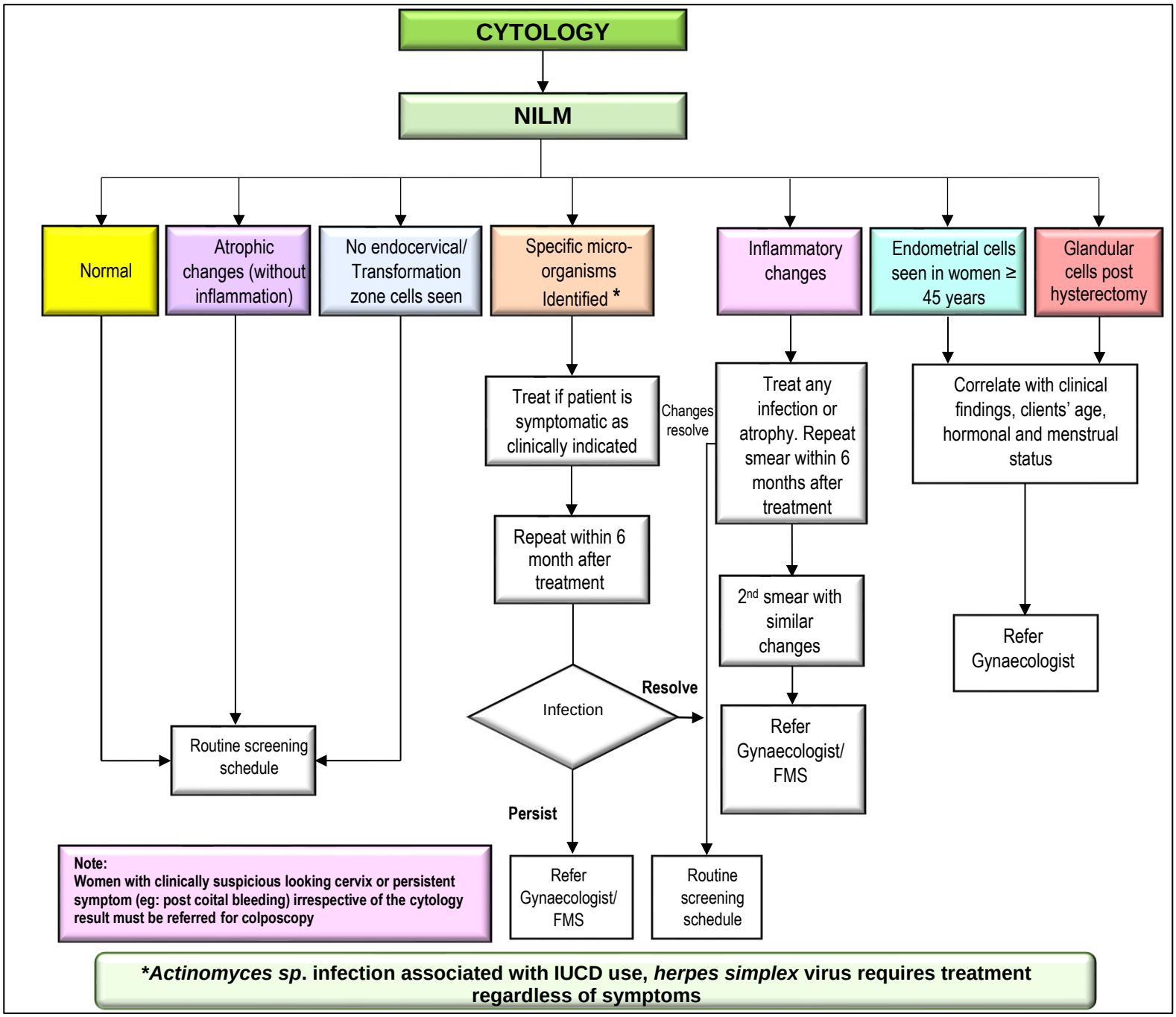


Figure 14 Management of Negative for Intraepithelial Lesion of Malignancy (NILM)

9.3 Management of Abnormal Cytology

9.3.1 Squamous Cell Abnormalities

1. Atypical Squamous Cells

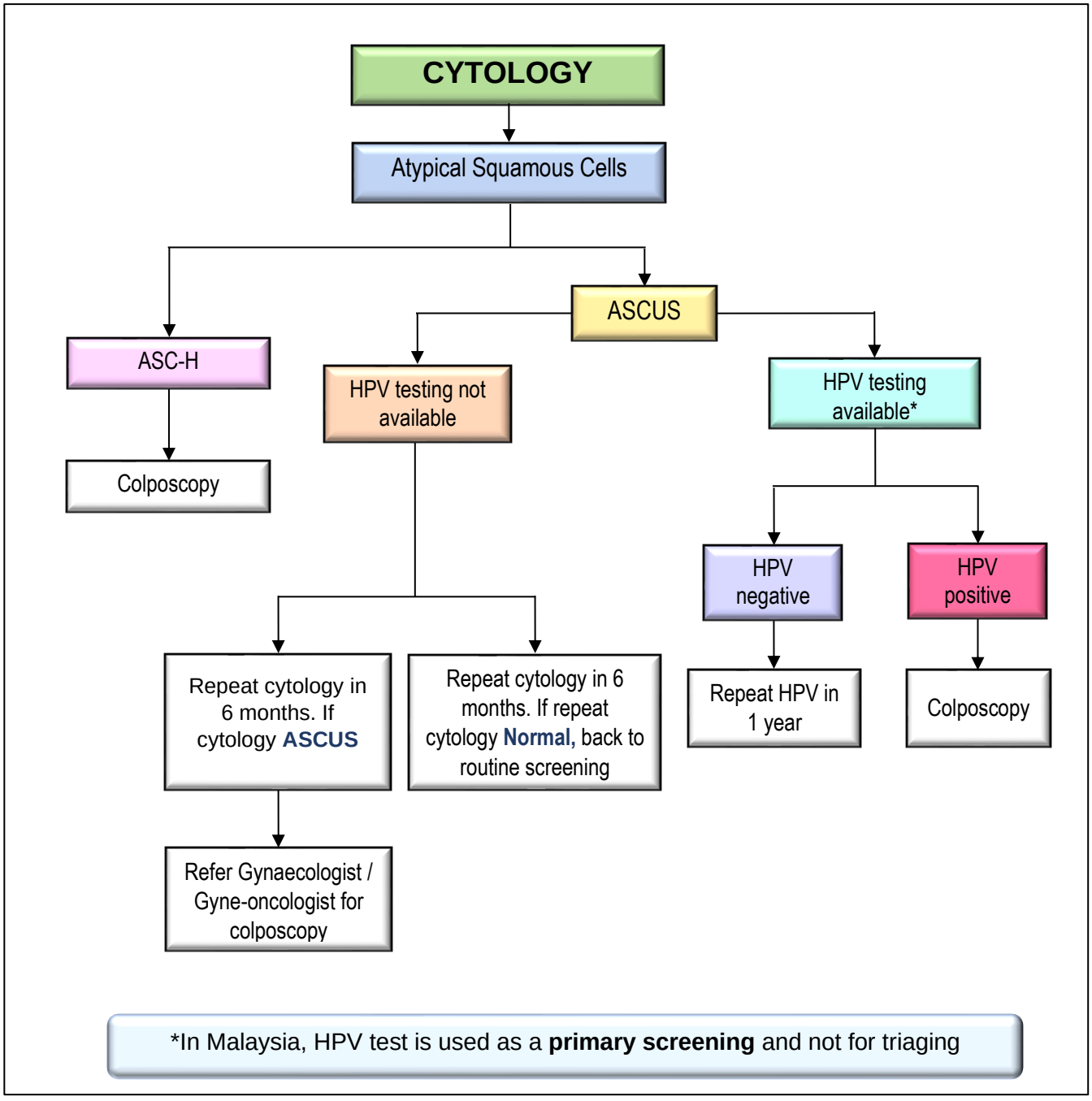


Figure 15 Management of Atypical Squamous Cells

2. Low-grade Squamous Intraepithelial Lesion (LSIL)

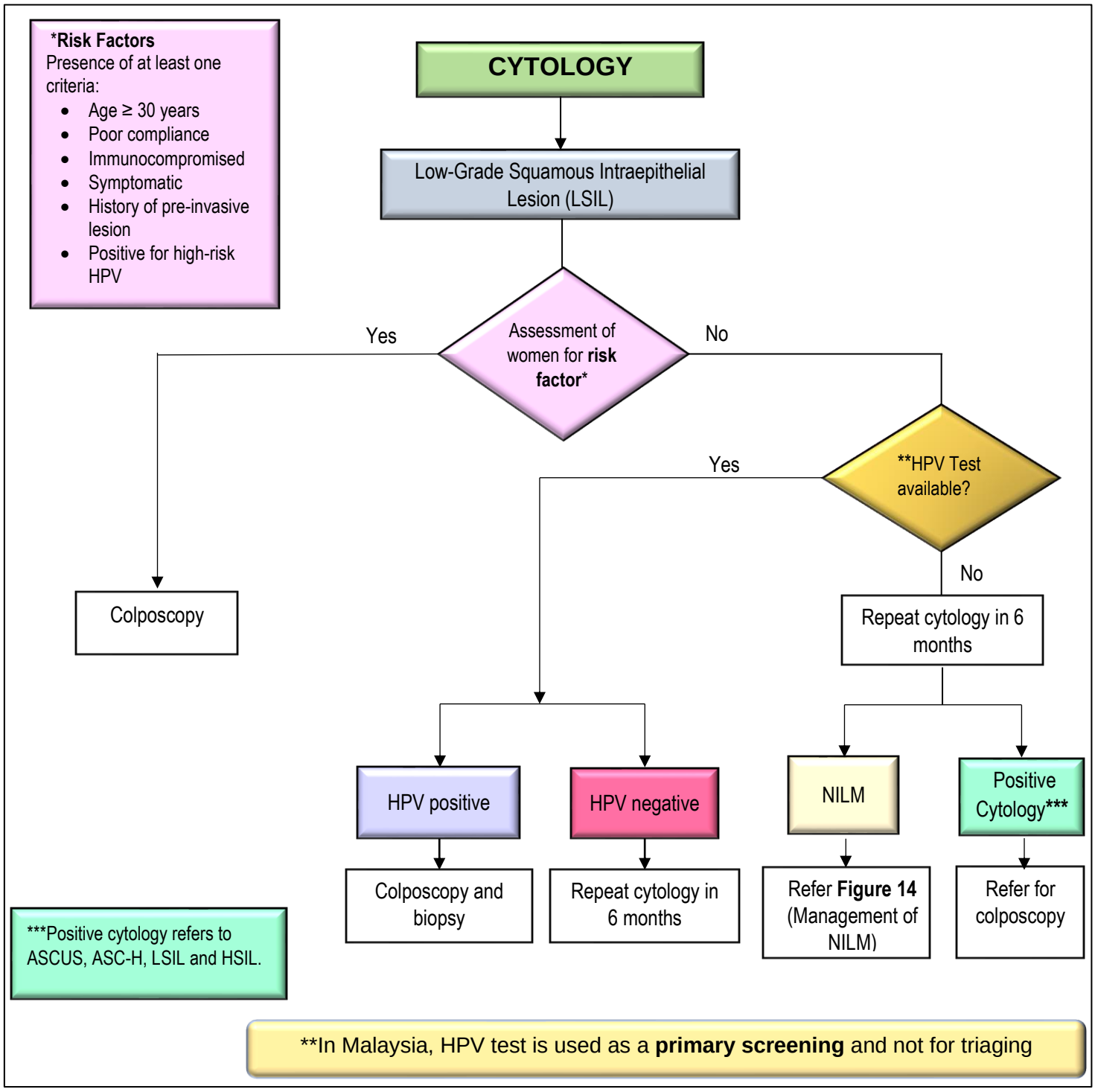


Figure 16 Management of Low Grade Squamous Intraepithelial Lesion (LSIL)

3. High-grade Squamous Intraepithelial Lesion (HSIL) and Squamous Cell Carcinoma (SCC)

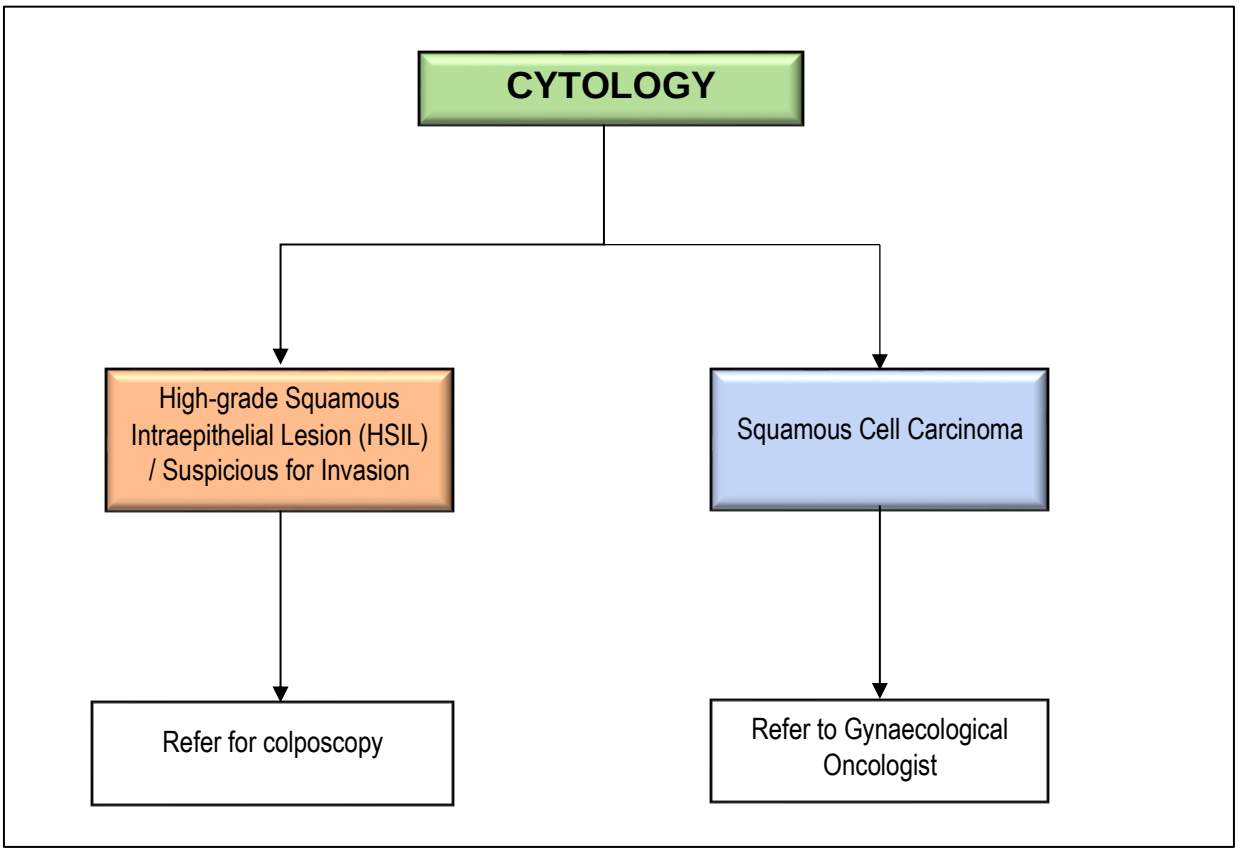


Figure 17 Management of High-grade Squamous Intraepithelial Lesion and Squamous Cell Carcinoma

9.3.2 Glandular Cell Abnormalities

1. Atypical Glandular Cells and Adenocarcinoma

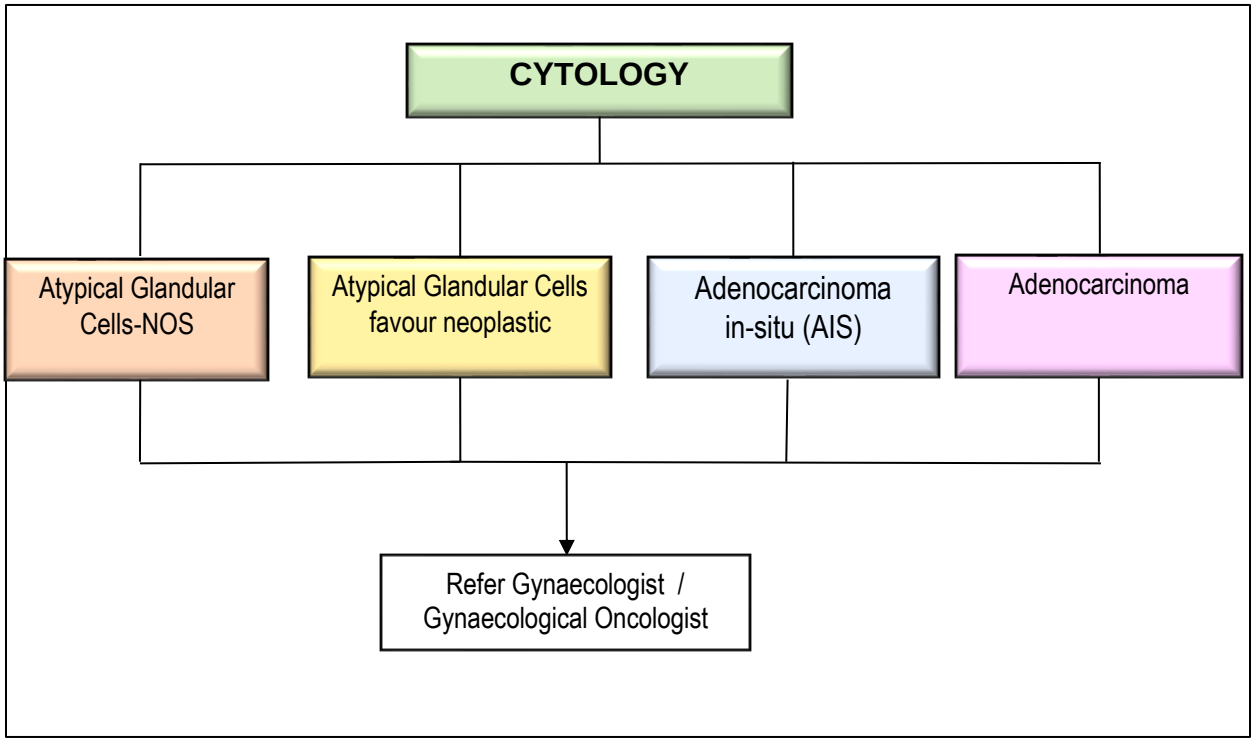


Figure 18 Management of Atypical Glandular Cells, Adenocarcinoma in-situ (AIS) and Adenocarcinoma

9.3.3 Management of Women Aged 45 Years and Above with Presence of Endometrial Cells on Cytology

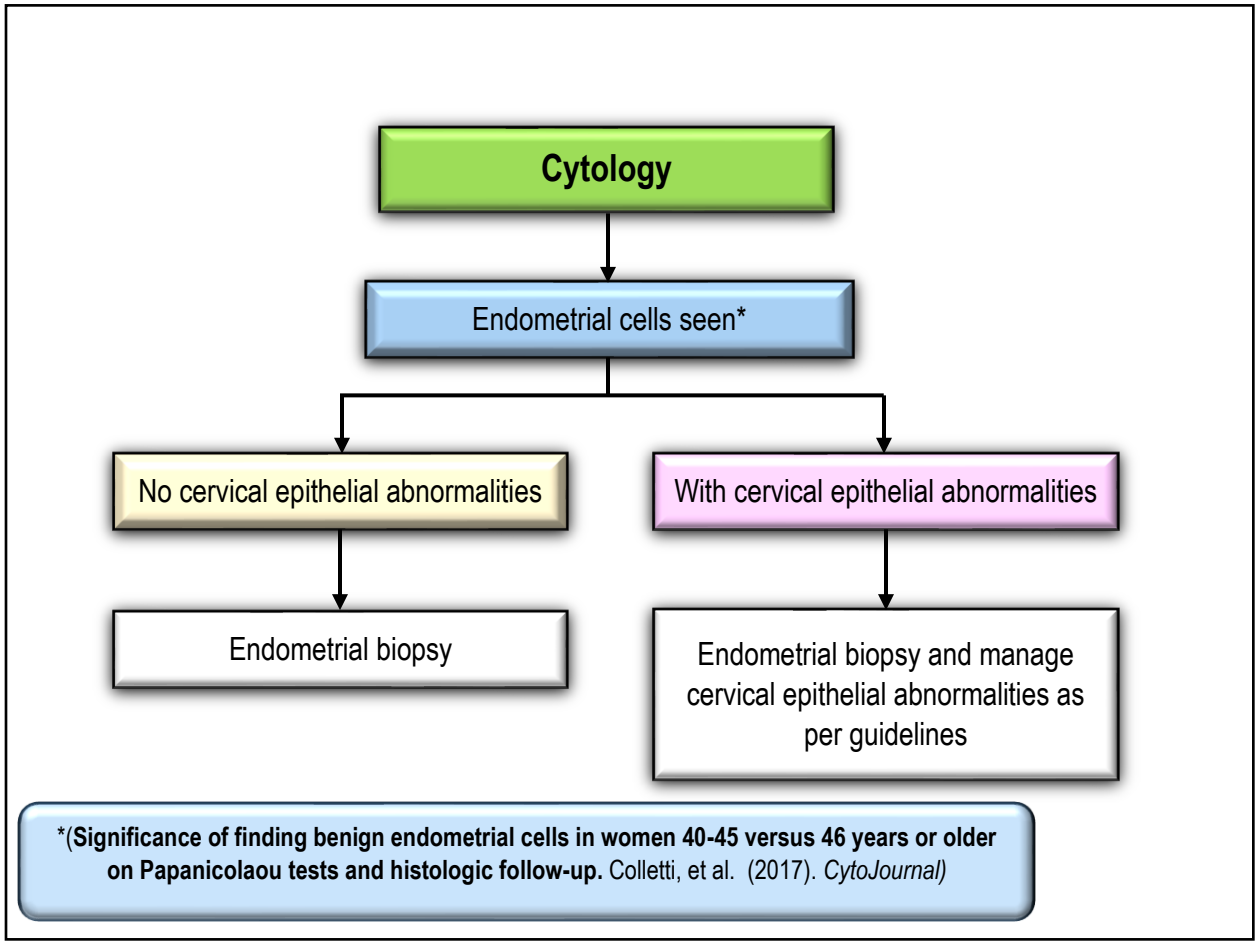


Figure 19 Management of Women >45 Years Old with Endometrial Cells on Cytology

9.4 Cytology Guidelines Post Hysterectomy

Table 3 Guidelines for Cytology Following Hysterectomy

No.	Status	Action
1.	Hysterectomy for benign disease: a. Normal cytology history. b. Benign histopathology of cervix with no dysplastic or neoplastic changes.	In the absence of symptoms, may not require further screening.
2.	Subtotal hysterectomy	Should continue to have cytology according to normal screening schedule.
3.	Hysterectomy where histology is unknown	Should have one baseline vault smear. If this is normal, further screening should be based on clinical indication.
4.	Immunosuppressed women	Should continue to have vault smears at yearly intervals.
5.	Women with history of CIN 2 and 3: a. If excision margin was involved or histological assessment is inadequate	Follow-up should be at the discretion of the gynaecologist. In general, vault cytology should be taken at least yearly until 65 years.
	b. CIN 2 / 3 completely excised at hysterectomy	Yearly vault cytology for 5 years followed by two yearly until 65 years.
6.	Women previously treated for invasive gynaecological malignancy	Should be followed up by a gynaecologist, preferably a gynaecological oncologist.
7.	Glandular cells post hysterectomy	Correlate with clinical findings, clients' age and hormonal status. If abnormal, refer to a gynaecologist.

9.5 Management of Abnormal Cytology and CIN in Pregnancy

- Colposcopic examination should be undertaken to exclude invasive disease by a colposcopist.
- If a high-grade lesion is suspected on colposcopy, refer to a gynaecologist or gynaecological oncologist for a biopsy if indicated to exclude possible invasive disease. Cervical biopsy is safe in pregnancy.
- For histology confirmed CIN 2 or 3, colposcopic review should be done in the second or the third trimester to exclude any possible progression to invasive disease.
- Treatment of CIN should be deferred until at least 6 weeks postpartum, when the lesion should be reassessed.

9.6 Indications for Colposcopy

The following conditions are indicated for colposcopy:
Suspicious looking cervix
Unexplained post-coital bleeding, blood-stained vaginal discharge, and postmenopausal bleeding
Persistent unsatisfactory cytology on 2 occasions, 3 months apart
Persistent inflammatory cytology on 3 occasions
Persistent Atypical Squamous Cells of Undetermined Significance (ASC-US) on 2 occasions
Atypical Squamous Cells of Undetermined Significance (ASC-US), positive for high-risk HPV
Atypical Squamous Cells –cannot exclude high grade lesion (ASC-H)
Persistent Low Grade Squamous Intraepithelial Lesion (LSIL) on 2 occasions, 6 months apart
Low Grade Squamous Intraepithelial Lesion (LSIL) with high risk factors
High Grade Squamous Intraepithelial Lesion (HSIL)
Squamous Cell Carcinoma (SCC)
Atypical Glandular Cells (AGC)
Adenocarcinoma
Positive for high-risk HPV DNA with positive cytology

9.7 Screening in Special Population

9.7.1 Screening in Pregnancy

The World Health Organization (WHO) emphasises that pregnancy is not the ideal time for taking cervical samples for cytology screening because it can give misleading results. However, for symptomatic patients, the standard screening and management should be followed. If the cervical cancer screening is due during pregnancy, it may be postponed to the 6-week postpartum visit.

9.7.2 Screening in Immunocompromised Population

An immunocompromised host is defined as a patient who does not have the ability to respond normally to an infection because of an impaired or weakened immune system. This inability to fight infection can be caused by a number of conditions, including diseases (for example, diabetes, human immunodeficiency virus [HIV] infection), malnutrition, and drugs (Cherry J, Harrison G, Kaplan S, Steinbach W, & Hotez P, 2019).

9.7.2.1 High Risk Immunocompromised Clinical Conditions Requiring Frequent Screening Includes:

- All HIV positive women.
- All women who had undergone solid organ transplant (SOT).
- All women with clinical conditions requiring them to take 2 or more immunocompromised medication.

9.7.2.2 Screening Recommendation in Immunocompromised Population

Cervical cancer screening is recommended for all sexually active immunocompromised women.

- Screening modality:
    - Cervical cytology for women for all sexually active women less than 30 years.
    - 3-yearly HPV primary screening for women aged 30 years old and above.
    - Those who are tested positive with any high-risk HPV strains should be sent for colposcopy instead of doing a cytology triage.

- Age for exit from screening: lifetime screening

Note: HIV prevalence in Malaysia among the population was 67,000 (0.4%) in 2021. Among women aged 15 years and above, approximately 7,000-8,000 women were infected with HIV (Center of Disease Division, 2022)

10. TRAINING HEALTHCARE WORKERS IN HPV TESTING

Health workers are required to be well informed about the natural history of cervical cancer, as well as HPV testing, interpreting HPV test results, follow-up, and counselling for women. This training should be provided for the health care providers involved in cervical cancer screening, particularly at the primary care level such as the family medicine specialists, public health physicians, medical officers, nurses, and assistant medical officers as well as at the secondary and tertiary care levels comprising gynaecologists, pathologists, scientific officers, and medical laboratory technologists.

10.1 Training Objectives

The objectives of this training are to enable the health care professionals to:

i. Communicate information about HPV testing and cervical cancer screening.
ii. Teach and assist lower vaginal sampling for HPV testing.
iii. Provide information and counselling to women, before and after the HPV test is taken.
iv. Communicate and convey the HPV results in the most appropriate manner.
v. Ensure proper follow-up according to the available guidelines.

10.2 Training Topics

Training topics that should be included:

(Should be tailored to the target group according to services provided)

Table 4 Training Modules for HPV Training to Healthcare Workers

Modules	Topics
Module 1	Cervical Cancer Control Programme in Malaysia: Integrating HPV Test as A Screening Tool in Primary Care
Module 2	Natural History of HPV Infections and Cervical Cancers
Module 3	HPV Sampling Technique
Module 4	Management of HPV Test Results
Module 5	HPV Test Reporting Format
Module 6	Data Monitoring and Surveillance

11. EDUCATIONAL MATERIAL

Educational materials are provided to each State Health Departments and regular trainings are conducted by the core team.

12. QUALITY ASSURANCE FOR BATCH TESTS

12.1 Laboratory

The laboratory should comply with ISO 15189 standard and retain a documented quality assurance process that includes (but is not limited to) the following:

12.1.1 Sampling

Internal Quality Control (QC) shall be included to assess the adequacy of the human DNA material present in the sample. The laboratory involved should monitor the rate of unsatisfactory specimens and provide feedback to the referring clinicians.

12.1.2 Analytical

Both positive and negative controls shall be included in every batch of the testing. The laboratories involved shall participate in External Quality Assurance (EQA) Programme for HPV test and Gynae-cytology module.

13. INFORMATION SYSTEM AND MONITORING

13.1 Data Monitoring and Surveillance

Each clinic is required to identify an officer to monitor the implementation of the services. To mitigate the communication between the primary care and the hospitals, liaison officers should be appointed at the hospital laboratories and the gynaecology clinics. Documentation of data is managed by using Excel spreadsheet. Please refer to the manual for entering of data into the e-reten. Data from the e-reten is transferred to the e-compilation reten (google sheet) which incorporates data from all the clinics in each state.

13.2 Future Development in Data Monitoring and Surveillance

It is crucial to develop a networking system which enables sharing of electronic medical records (eMR) and electronic medication management (eMeds) from all health centres, hospitals, and data centres. A screening registry will improve the surveillance and monitoring system. Health facilities should be connected to available cloud available and public Internet with enterprise grade reliability and performance in order to rise to the challenges of data surveillance.

14. FLOWCHART FOR HPV DNA TESTING AT PRIMARY CARE FACILITIES

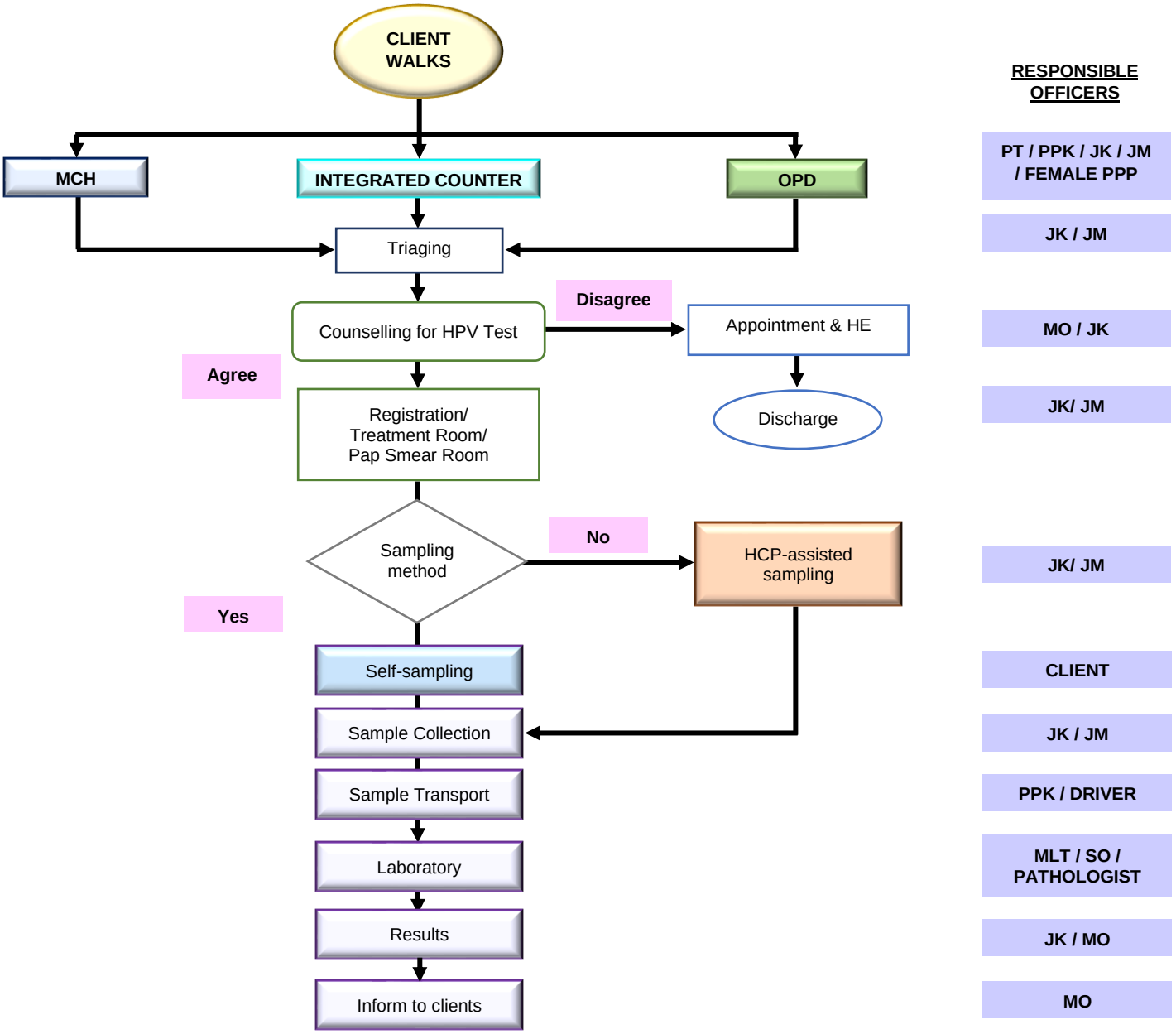


Figure 20 Flowchart for Implementation of HPV Testing At Primary Care Facilities

APPENDIX 1 SCREENING FORM FOR HPV / CYTOLOGY TEST

PS 1/98 PINDAAN 2020

KEMENTERIAN KESIHATAN MALAYSIA
PERKHIDMATAN PATOLOGI

No. Makmal:

BORANG PERMOHONAN UJIAN HPV/ SITOLOGI (PAP SMEAR /LBC)
HPV TEST /CYTOLOGY (PAP SMEAR/LBC) REQUEST FORM

Hospital / Klinik / *Hospital / Clinic* :

BUTIRAN KLIEN / *CLIENT'S DETAILS*

i. Nama / *Name* :

ii. Nombor Kad Pengenalan / *IC. No* :

iii. Etnik / *Ethnicity* :

iv. Tarikh Lahir / *Date of Birth* : (dd) (mm) (yyyy)

v. Alamat : *Address:*

vi. No. Telefon:
(Tel. Bimbit/ Rumah/ *Mobile No./ Home No.*)
Phone No:
(No. Tel. Waris/ Pejabat/ *Next of Kin/ Office*)

vii. Tahap Pendidikan Tertinggi: *Highest Education:*
- ☐ Tidak Bersekolah / *No formal education*
- ☐ Sekolah Rendah / *Primary School*
- ☐ Sekolah Menengah / *Secondary School*
- ☐ Sijil / *Certificate*
- ☐ Diploma / *Diploma*
- ☐ Ijazah dan ke atas / *Degree and above*

viii. Pekerjaan: *Occupation:*
- ☐ K/tangan Kerajaan / *Government Servant*
- ☐ K/tangan Swasta / *Private sector*
- ☐ Bekerja Sendiri / *Self-employed*
- ☐ Suri Rumahtangga / *Housewife*
- ☐ Pesara / *Pensioner*

ix. Pendapatan isi rumah bulanan: *Monthly household income:*
- ☐ ≤ RM 3,999
- ☐ RM 4,000 - RM 7,999
- ☐ ≥ RM 8,000

BUTIRAN SARINGAN / *SCREENING INFORMATION (Tandakan X pada kotak berkenaan)*

i. Tarikh sampel diambil: *Date sample taken:* (dd) (mm) (yyyy)

ii. Jenis sampel: *Type of sample:*
- ☐ Conventional Pap Smear
- ☐ Liquid-based preparation
- ☐ Cervical vagina swab for HPV

iii. Bahagian sampel diambil: *Sampling site:*
- ☐ Serviks / *Cervix*
- ☐ Vagina / *Vagina*

iv. Jenis saringan: *Type of screening:*
- ☐ Baru / *New*
- ☐ Ulangan / *Repeat*

v. Nombor makmal terdahulu: *Previous laboratory No.*
- *HPV*
- *Pap Smear*
- *Histopathology*

vi. Keputusan terdahulu: *Previous diagnosis:*

vii. Pengambilan sampel oleh: *Sampling by:*
- ☐ Sendiri / *Self* (Self-sampling)
- ☐ Anggota Kesihatan / *Healthcare Provider* (Assisted)

RINGKASAN KLINIKAL / *CLINICAL SUMMARY (Tandakan X pada kotak berkenaan)*

i. Body Mass Index (BMI): ..... kg/m² (Berat: ..... kg; Tinggi: ..... m)

ii. Status Hormon: *Hormonal status:*
- ☐ Hamil / *Pregnant*
- ☐ Postpartum / *Postpartum*
- ☐ Pra-menopos / *Pre-menopausal*
- ☐ Menopos / *Menopausal*

iii. Tarikh Haid terakhir: *Last menstrual period:* (dd) (mm) (yyyy)

iv. Bilangan Anak Semasa *Current Parity:*

v. Tarikh Kelahiran terakhir: *Last childbirth:* (dd) (mm) (yyyy)

vi. Tarikh Saringan Pap smear / Ujian HPV Terakhir *Date of Latest Pap smear screening / Latest HPV test:* (dd) (mm) (yyyy)

vii. Sejarah Rawatan : *Treatment history*
- ☐ Kemoterapi / *Chemotherapy*
- ☐ Radiasi di bahagian pelvik / *Pelvic radiation*
  Nyatakan tarikh akhir rawatan:..... *Specify completion date*
- ☐ Pembedahan ginekologi / *Gynaecology surgery*
  Nyatakan / *specify*:.....
- ☐ Tiada / *none*

viii. Kontraseptif /Terapi hormon: *Contraceptive/ hormonal therapy*
- ☐ ADR / *IUCD*
- ☐ Hormon / *Hormone*
- ☐ Nyatakan / *Specify*: .....
- ☐ Tiada / *None* .....

ix. Gejala / Tanda: *Symptom / Sign*
- ☐ Tiada / *Nil*
- ☐ Lelehan dari faraj / *Vaginal discharge*
- ☐ Pendarahan luar biasa / *Abnormal bleeding*
- ☐ Nyatakan / *specify* : .....

x. Serviks : *Cervix*
- ☐ Biasa / *Normal*
- ☐ Luar Biasa / *Abnormal*
- ☐ Tiada serviks / *No cervix*

xi. Maklumat tambahan: *Additional information* .....

MAKLUMAT PEMOHON / *REQUESTING PRACTITIONER*

Nama: *Name*

Jawatan / Cop : *Designation / Stamp*

Tandatangan *Signature*

APPENDIX 2 SCREENING FORM FOR REPEAT HPV TEST USING LBC MEDIUM IN UNSATISFACTORY RESULT

PS 1/98 PINDAAN 2020

KEMENTERIAN KESIHATAN MALAYSIA
PERKHIDMATAN PATOLOGI

No. Makmal:

BORANG PERMOHONAN UJIAN HPV/ SITOLOGI (PAP SMEAR
HPV TEST /CYTOLOGY (PAP SMEAR/LBC) REQUEST FOR

UNSATISFACTORY HPV TEST

Hospital / Klinik *Hospital / Clinic* :

BUTIRAN KLIEN / *CLIENT'S DETAILS*

i. **Nama** / *Name* :
ii. **Nombor Kad Pengenalan** / *IC. No* :
iii. **Etnik** / *Ethnicity* :
iv. **Tarikh Lahir** / *Date of Birth* : (dd) (mm) (yyyy)

v. **Alamat** : *Address:*

vi. **No. Telefon:** *Phone No:*
(Tel. Bimbit/ Rumah/ *Mobile No./ Home No.*)
(No. Tel. Waris/ Pejabat/ *Next of Kin/ Office*)

vii. **Tahap Pendidikan Tertinggi:** *Highest Education:*
- ☐ Tidak Bersekolah / *No formal education*
- ☐ Sekolah Rendah / *Primary School*
- ☐ Sekolah Menengah / *Secondary School*
- ☐ Sijil / *Certificate*
- ☐ Diploma / *Diploma*
- ☐ Ijazah dan ke atas / *Degree and above*

viii. **Pekerjaan:** *Occupation:*
- ☐ K/tangan Kerajaan / *Government Servant*
- ☐ K/tangan Swasta / *Private sector*
- ☐ Bekerja Sendiri / *Self-employed*
- ☐ Suri Rumahtangga / *Housewife*
- ☐ Pesara / *Pensioner*

ix. **Pendapatan isi rumah bulanan:** *Monthly household income:*
- ☐ ≤ RM 3,999
- ☐ RM 4,000 - RM 7,999
- ☐ ≥ RM 8,000

BUTIRAN SARINGAN / *SCREENING INFORMATION (Tandakan X pada kotak berkenaan)*

i. **Tarikh sampel diambil:** *Date sample taken:* (dd) (mm) (yyyy)

ii. **Jenis sampel:** *Type of sample:*
- ☐ Conventional Pap Smear
- ☒ Liquid-based preparation
- ☐ Cervical vagina swab for HPV

iii. **Bahagian sampel diambil:** *Sampling site:*
- ☒ Serviks / *Cervix*
- ☐ Vagina / *Vagina*

iv. **Jenis saringan:** *Type of screening:*
- ☒ Baru / *New*
- ☒ Ulangan / *Repeat*

v. **Nombor makmal terdahulu:** *Previous laboratory No.*
- *HPV*
- *Pap Smear*
- *Histopathology*

vi. **Keputusan terdahulu:** *Previous diagnosis:*

vii. **Pengambilan sampel oleh:** *Sampling by:*
- ☐ Sendiri / *Self* (Self-sampling)
- ☐ Anggota Kesihatan / *Healthcare Provider* (Assisted)

***REPEAT HPV TEST**

RINGKASAN KLINIKAL / *CLINICAL SUMMARY (Tandakan X pada kotak berkenaan)*

i. **Body Mass Index (BMI):** ..... kg/m² (Berat: ..... kg; Tinggi: ..... m)

ii. **Status Hormon:** *Hormonal status:*
- ☐ Hamil / *Pregnant*
- ☐ Postpartum / *Postpartum*
- ☐ Pra-menopos / *Pre-menopausal*
- ☐ Menopos / *Menopausal*

iii. **Tarikh Haid terakhir:** *Last menstrual period:* (dd) (mm) (yyyy)

iv. **Bilangan Anak Semasa** *Current Parity:*

v. **Tarikh Kelahiran terakhir:** *Last childbirth:* (dd) (mm) (yyyy)

vi. **Tarikh Saringan Pap smear / Ujian HPV Terakhir** *Date of Latest Pap smear screening / Latest HPV test:* (dd) (mm) (yyyy)

vii. **Sejarah Rawatan :** *Treatment history*
- ☐ Kemoterapi / *Chemotherapy*
- ☐ Radiasi di bahagian pelvik / *Pelvic radiation*
  Nyatakan tarikh akhir rawatan:..... *Specify completion date*
- ☐ Pembedahan ginekologi / *Gynaecology surgery*
  Nyatakan / *specify*:.....
- ☐ Tiada / *none*

viii. **Kontraseptif /Terapi hormon:** *Contraceptive/ hormonal therapy*
- ☐ ADR / *IUCD*
- ☐ Hormon / *Hormone*
- ☐ Nyatakan / *Specify*: .....
- ☐ Tiada / *None* .....

ix. **Gejala / Tanda:** *Symptom / Sign*
- ☐ Tiada / *Nil*
- ☐ Lelehan dari faraj / *Vaginal discharge*
- ☐ Pendarahan luar biasa / *Abnormal bleeding*
- ☐ Nyatakan / *specify* :.....

x. **Serviks :** *Cervix*
- ☐ Biasa / *Normal*
- ☐ Luar Biasa / *Abnormal*
- ☐ Tiada serviks / *No cervix*

xi. **Maklumat tambahan:** *Additional information* .....

MAKLUMAT PEMOHON / REQUESTING PRACTITIONER

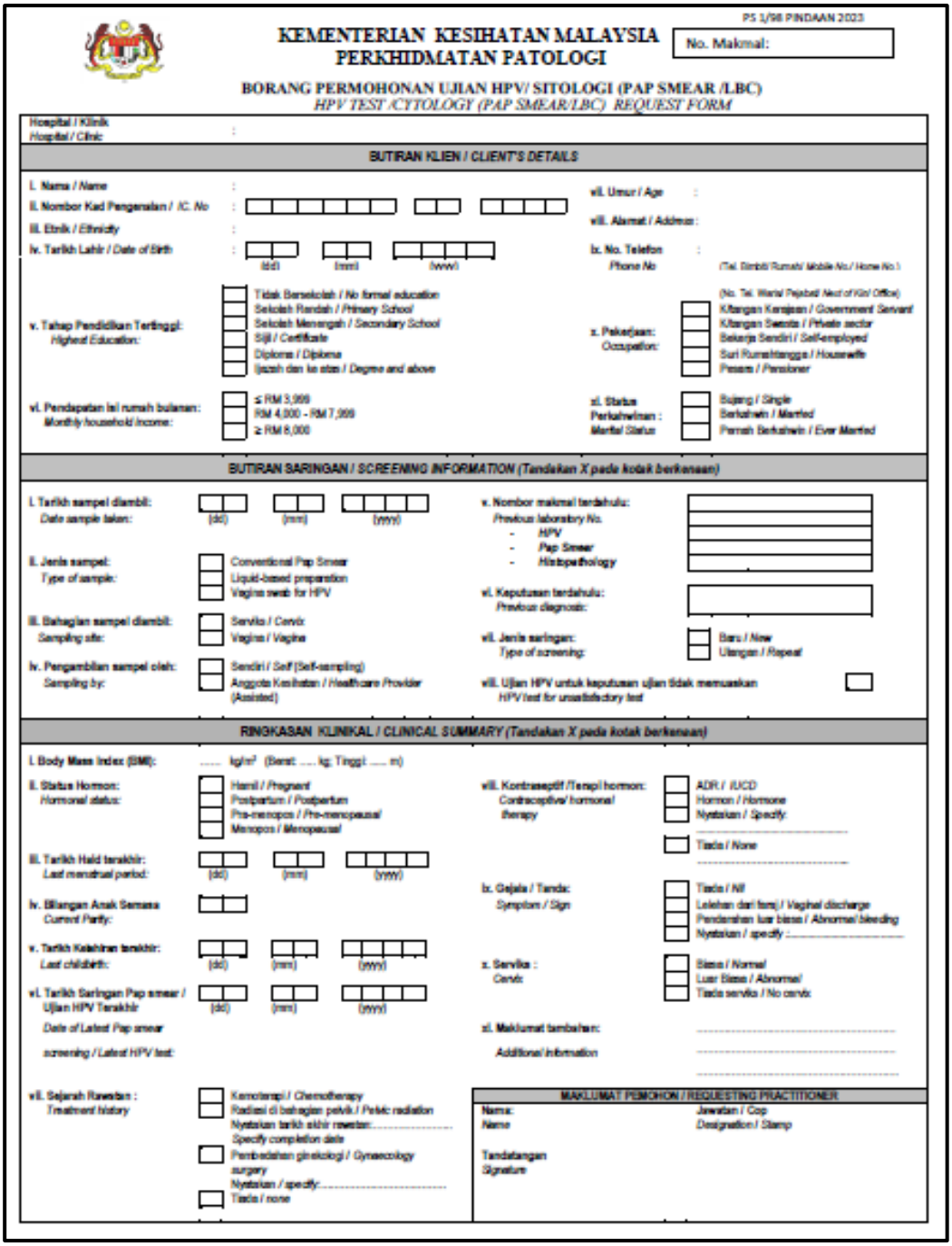
Nama: *Name*

Jawatan / Cop : *Designation / Stamp*

Tandatangan *Signature*

Appendix 3

APPENDIX 3 SCREENING FORM FOR HPV / CYTOLOGY TEST (EDITED 2023)



PS 1/98 PINDAAN 2023

KEMENTERIAN KESIHATAN MALAYSIA
PERKHIDMATAN PATOLOGI

No. Makmal:

BORANG PERMOHONAN UJIAN HPV/ SITOLOGI (PAP SMEAR /LBC)
HPV TEST /CYTOLOGY (PAP SMEAR/LBC) REQUEST FORM

Hospital / Klinik
Hospital / Clinic :

BUTIRAN KLIEN / *CLIENT'S DETAILS*

i. Nama / *Name* :
ii. Nombor Kad Pengenalan / *IC. No* : | | | | | | | | | | | | | |
iii. Etnik / *Ethnicity* :
iv. Tarikh Lahir / *Date of Birth* : (dd) (mm) (yyyy)

vii. Umur / *Age* :
viii. Alamat / *Address* :
ix. No. Telefon / *Phone No* : (Tel. Bimbit/ Rumah/ *Mobile No./ Home No.*)

v. Tahap Pendidikan Tertinggi: *Highest Education:*
- Tidak Bersekolah / *No formal education*
- Sekolah Rendah / *Primary School*
- Sekolah Menengah / *Secondary School*
- Sijil / *Certificate*
- Diploma / *Diploma*
- Ijazah dan ke atas / *Degree and above*

vi. Pendapatan isi rumah bulanan: *Monthly household income:*
- ≤ RM 3,999
- RM 4,000 - RM 7,999
- ≥ RM 8,000

x. Pekerjaan: *Occupation:*
- (No. Tel. Wakil/ Pejabat/ *Next of Kin/ Office*)
- Kakitangan Kerajaan / *Government Servant*
- Kakitangan Swasta / *Private sector*
- Bekerja Sendiri / *Self-employed*
- Suri Rumahtangga / *Housewife*
- Pesara / *Pensioner*

xi. Status Perkahwinan : *Marital Status*
- Bujang / *Single*
- Berkahwin / *Married*
- Pernah Berkahwin / *Ever Married*

BUTIRAN SARINGAN / *SCREENING INFORMATION (Tandakan X pada kotak berkenaan)*

i. Tarikh sampel diambil: *Date sample taken:* (dd) (mm) (yyyy)

ii. Jenis sampel: *Type of sample:*
- Conventional Pap Smear
- Liquid-based preparation
- Vagina swab for HPV

iii. Bahagian sampel diambil: *Sampling site:*
- Servika / *Cervix*
- Vagina / *Vagina*

iv. Pengambilan sampel oleh: *Sampling by:*
- Sendiri / *Self (Self-sampling)*
- Anggota Kesihatan / *Healthcare Provider (Assisted)*

v. Nombor makmal terdahulu: *Previous laboratory No.*
- *HPV*
- *Pap Smear*
- *Histopathology*

vi. Keputusan terdahulu: *Previous diagnosis:*

vii. Jenis saringan: *Type of screening:*
- Baru / *New*
- Ulangan / *Repeat*

viii. Ujian HPV untuk keputusan ujian Sitek memuaskan *HPV test for unsatisfactory test*

RINGKASAN KLINIKAL / *CLINICAL SUMMARY (Tandakan X pada kotak berkenaan)*

i. Body Mass Index (BMI): ..... kg/m² (Berat: ..... kg; Tinggi: ..... m)

ii. Status Hormon: *Hormonal status:*
- Hamil / *Pregnant*
- Postpartum / *Postpartum*
- Pra-menopos / *Pre-menopausal*
- Menopos / *Menopausal*

iii. Tarikh Haid terakhir: *Last menstrual period:* (dd) (mm) (yyyy)

iv. Bilangan Anak Semasa *Current Parity:*

v. Tarikh Kelahiran terakhir: *Last childbirth:* (dd) (mm) (yyyy)

vi. Tarikh Saringan Pap smear / Ujian HPV Terakhir *Date of Latest Pap smear screening / Latest HPV test:* (dd) (mm) (yyyy)

vii. Sejarah Rawatan : *Treatment history*
- Kemoterapi / *Chemotherapy*
- Radiasi di bahagian pelvik / *Pelvic radiation* Nyatakan tarikh akhir rawatan: ..... *Specify completion date*
- Pembedahan ginekologi / *Gynecology surgery* Nyatakan / *specify:* .....
- Tiada / *none*

viii. Kontraseptif /Terapi hormon: *Contraceptive/ hormonal therapy*
- ADR / *IUCD*
- Hormon / *Hormone* Nyatakan / *Specify:* .....
- Tiada / *None* .....

ix. Gejala / Tanda: *Symptom / Sign*
- Tiada / *Nil*
- Leleh an dari faraj / *Vaginal discharge*
- Pendarahan luar biasa / *Abnormal bleeding*
- Nyatakan / *specify* : .....

x. Servika : *Cervix*
- Biasa / *Normal*
- Luar Biasa / *Abnormal*
- Tiada servika / *No cervix*

xi. Maklumat tambahan: *Additional information* .....

MAKLUMAT PEMOHON / *REQUESTING PRACTITIONER*

Nama: *Name* | Jawatan / *Cop Designation / Stamp*

Tandatangan *Signature*

APPENDIX 4 SAMPLE REPORT FOR HPV TEST RESULT

KEMENTERIAN KESIHATAN MALAYSIA
PERKHIDMATAN PATOLOGI
BORANG PERMOHONAN UJIAN HPV/SITOLOGI (PAP SMEAR/LBC)

HPV 2/2019

MOLECULAR VIROLOGY TEST RESULT REPORT

Human Papillomavirus (HPV) Genotyping

NAME :
NRIC NO. :
REGISTRATION NO. :
WARD / KLINIK :
HOSPITAL :
NEGERI :
REQUESTED BY :

SAMPLE DETAILS FOR MOLECULAR VIROLOGY TEST

Sample Type	Self sample / LBC	Date of Test	-
Sample Collection Media		Lab Barcode No.	-
		Date of Sample Collection	-
Sample Transport Condition	with ICE / no ICE	Date of Sample Received	-

RESULT DETAILS FOR MOLECULAR VIROLOGY TEST

QUALITITATIVE Real-time PCR - HPV VIRUS DNA			
Result Interpretation (Tanda X pada kotak berkenaan)	HPV 16	Detected	
		Not Detected	
	HPV 18	Detected	
		Not Detected	
	HPV (non 16/18)	Detected	
		Not Detected	
		INVALID / UNSATISFACTORY	

NOTES :

a) Test method : Real-Time Polymerase chain reaction (RT-PCR).
b) Genotype detection : 16, 18 and other High Risk HPV DNA (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)
c) 'Not Detected' result does not conclusively rule out the agent tested, for the following reasons:
- *Specimens collection not timely.*
- *Specimen deterioration / breakdown of cold chain during storage or transportation.*
- *Detection value lower than limit of detection.*

d) This result shall be interpreted in conjunction with other clinical laboratory findings.
e) This report shall not be reproduced except with written approval from the laboratory.

COMMENTS :

SUGGESTION

	Repeat HPV test at 5 years (HPV not detected
	Repeat HPV test within 12 weeks (Unsatisfactory HPV test)
	For Liquid-based cytology (HPV positive 16/18 and non 16/18)

Authorized by:

..... Date : .....

APPENDIX 5 CYTOLOGY/ LIQUID-BASED CYTOLOGY REPORT

KEMENTERIAN KESIHATAN MALAYSIA
PERKHIDMATAN PATOLOGI
FORMAT LAPORAN SITOLOGI (PAP SMEAR/LBC)
PAP SMEAR /LIQUID BASED CYTOLOGY (LBC) REPORT

PS 2/2019

Name: **I.C. No.:** **Cytology No.:**

A) Type of sample: ☐ Conventional Pap Smear ☐ Liquid-based preparation

Ai) Type of LBC: ☐ SurePath ☐ ThinPrep ☐ Others

B) Sample Adequacy:

☐ **i) Satisfactory for evaluation:**

Endocervical cells/transformation zone cells:
☐ Present ☐ Absent
With:
☐ Obscuring blood
☐ Poor fixation/air drying artifact
☐ Thick uneven smear
☐ Thick inflammatory exudate
☐ Lack of clinical data

☐ **ii) Unsatisfactory for evaluation:**
☐ Scanty squamous epithelial component
☐ Poor fixation/air drying artifact
☐ Obscuring blood
☐ Thick uneven smear
☐ Thick inflammatory exudate
☐ Broken slide beyond repair

C) Interpretation/ Result

☐ **i) Negative for intraepithelial lesion or malignancy (NILM)**

a) Organism present:
☐ Fungal organisms morphologically consistent with Candida spp.
☐ Shift in flora suggestive of bacterial vaginosis
☐ Bacteria morphologically consistent with Actinomyces spp.
☐ Cellular changes associated with Herpes Simplex Virus
☐ Trichomonas vaginalis
☐ Cytomegalovirus (CMV)

b) Other non-neoplastic findings:
☐ Benign cellular changes associated with:
☐ Inflammation/typical repair
☐ Irradiation
☐ Intrauterine contraceptive device (IUCD)
☐ Atrophy
☐ Presence of glandular cells post hysterectomy
☐ Presence of endometrial cells (in woman ≥ 45 yrs of age)

☐ **ii) Epithelial cells abnormalities**

☐ **a) Squamous cell:**
☐ Atypical squamous cells:
☐ of undetermined significance (ASC-US)
☐ cannot exclude HSIL (ASC-H)
☐ Low grade squamous intraepithelial lesion (LSIL)
☐ High grade squamous intraepithelial lesion (HSIL):
☐ Features suspicious for invasion
☐ Squamous cell carcinoma

c) Other malignant neoplasm, specify:
.....
.....
.....

☐ **b) Glandular cells:**
☐ Atypical cells (NOS):
☐ Endocervical cells
☐ Endometrial cells
☐ Glandular cells
☐ Atypical cells, favour neoplastic:
☐ Endocervical cell
☐ Glandular cells (NOS)
☐ Endocervical adenocarcinoma (in-situ)
☐ Adenocarcinoma:
☐ Endocervical
☐ Endometrial
☐ Extrauterine
☐ Not otherwise specified (NOS)

D) Comments: .....
.....
.....

E) Suggestion
☐ Repeat LBC/Pap Smear as Schedule
☐ Repeat Pap Smear 3 - 6 months
☐ Repeat Pap Smear after antimicrobial treatment
☐ Repeat smear after oestrogen therapy
☐ Refer FMS
☐ To get Colposcopy appointment
☐ Refer to Gynaecologist/Gynaecological Oncologist

LAB USE ONLY

Validated by		**Screener**		
Designation		First Screener		Review of previous Pap smear slide: YES / NO (If YES Slide No.: ☐)
Date reporting		Second Screener		
Date Printing		Pathologist		

VALIDATION

Result reviewed by:	Date:
Designation/Stamp:	Action:

JJ021 0427 PNMS-JB

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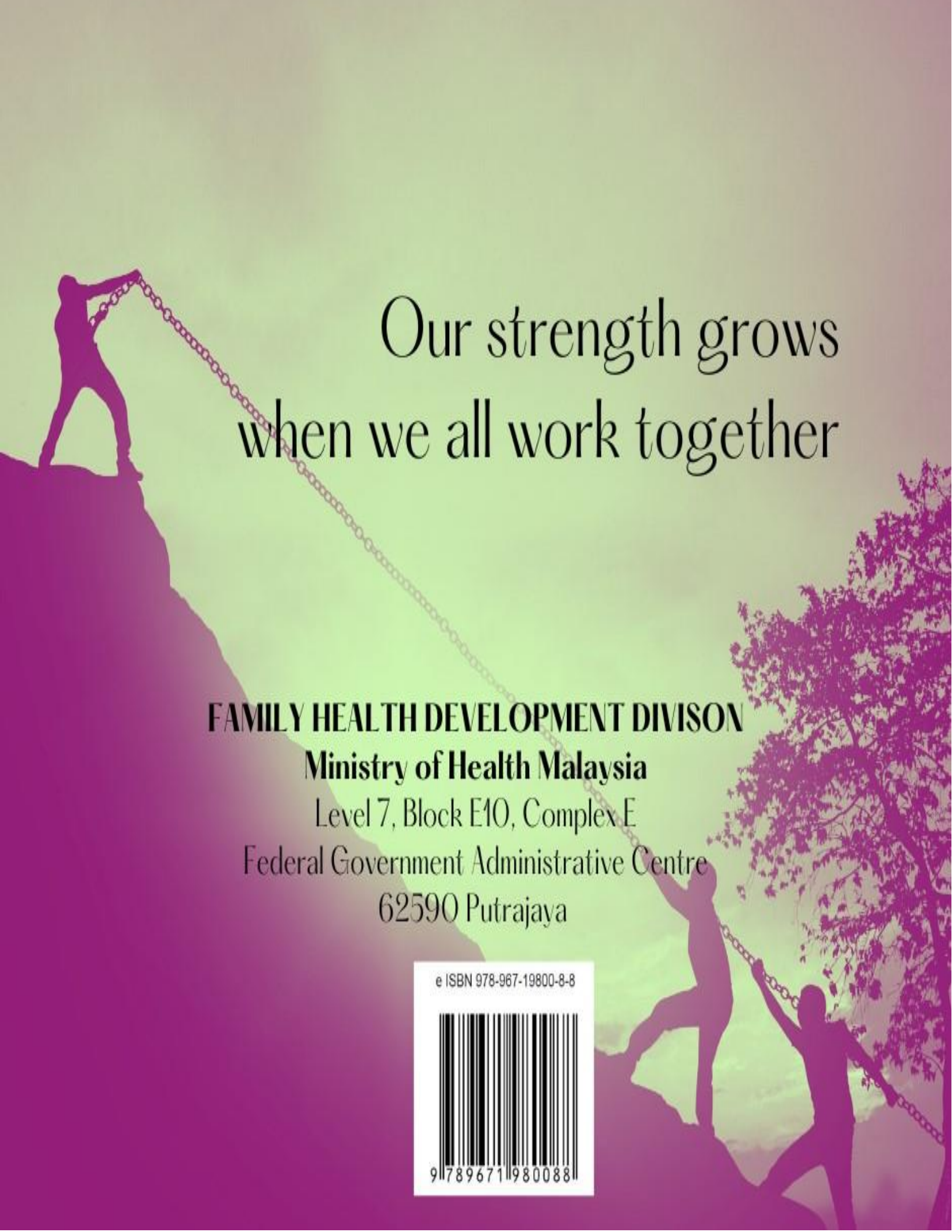

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