FOREWORD

Cervical cancer continues to be an important reproductive health problem for women throughout the world. Each year around 5,27,624 new cases occur, with an incidence of 14 per 100,000 women population. Nearly 80% of these cases occur in the developing world. Around 50% of the world burden is borne by South and South East Asia.

Cervical cancer is a disease that develops slowly and its precancers can be easily detected and treated. Therefore, an early and timely screening is very essential to prevent this cancer. Implementation of Pap smear screening has reduced incidence of this cancer in the industrialized countries. However, such programs have been difficult to establish in the developing world. This is one of the main reasons why cervical cancer rate is higher in these countries. It is estimated that only about 5% of women living in developing world get screened as compared to more than 70% of women in the USA and Northern Europe.

In Bhutan, cervical cancer is the most common cancer diagnosed in our women, with an estimated incidence of 20/100,000 women population. More than half are diagnosed in late stages, leading to high mortality. Since the radiation, which is the main stay of treatment for cervical cancer, is not available in the country, cervical cancer continues to be the most common cancers referred out for radiation.

National Pap Smear Screening Program was established in Bhutan in October 1999, but went nationwide only in 2006. Visual Inspection with Acetic acid (VIA) is also being done to women between 30 to 45 years of age as an adjunct method to Pap smear screening. Despite the free screening services, incidence and mortality due to cervical cancer did not change significantly over the past years. Low coverage, inadequate capacity of health workers and lack of awareness among women among other reasons could be the contributing factors. It is highly essential to scale up Pap smear screening services, especially in the wake of introduction of HPV vaccination in the country since 2010, which could lead to complacency among health workers.

This book has been designed to be used as a reference and guideline for all levels of service providers to standardize the cervical cancer screening and treatment services in the country. We hope to offer better services to our women, thus helping them to preserve their reproductive health as long as they live.

TASHI DELEK

(NimaWangdi)
Secretary
Ministry of Health
1. **INTRODUCTION**

Worldwide, cervical cancer is the second most common cancer among women. In the year 2012 there were 5,27,624 new cases (source: Globocan 12) and 85% of this cancer is diagnosed in the developing countries and 50% of the world burden is borne by South and South East Asia. This difference in incidence and death between industrialized and the developing countries is mainly due to either lack of or poor quality of screening services.

In Bhutan, it is the most common cancer diagnosed in women. The peak incidence is between 40-49 years in our country. Most are diagnosed in later stage, 45% or more in stage III and above, leading to high mortality. A local study showed poor 5 year overall survival rate with poor survival even for stage IB (65% vs 85% in literature). The incidence and mortality has not changed over the last decade indicating that our screening program is yet to show impact.

*Figure1: Age distribution of morbidity and mortality due to cervical cancer in the last 7 years (2007 to 2013)*

The morbidity and mortality associated with this cancer has impact not only on the life of these women, but also on their families. A woman with cervical cancer lives with bleeding, foul smelling discharge, leaking urine/feces or severe pain for many months. She dies when she is still socio-economically productive leaving behind children who are small or dependent *(see figure 1)*. Besides, the government spends a lot of money getting these patients treated in centers outside Bhutan. Cervical cancer is still the most common cancer referred for radiation.

This is a cancer that is not only curable if diagnosed early, but is also preventable if a good screening program exists. It must have a defined target population, high coverage, high quality cyto-laboratories with quality assurance system, and good follow up mechanism and effective treatment. We do have screening program, but coverage and follow up of women with abnormal smears need to be improved. Unless more than 50% of target population is covered by screening with more than 80% adhering to follow up and treatment of precancer, morbidity and mortality due to cervical cancer will not reduce *(see figure 2)*.
Figure 2: Incidence and mortality due to cervical cancer in the last decade showing no change. Number of deaths reported has increased since 2010 due to improved registration and follow up. (These figures are based only on registered cases).

In developing countries, Pap smear did not work due to involvement of so many levels of people and need of so many logistics. Therefore, newer methods have been sought, and Visual Inspection with Acetic acid (VIA) is one of the promising methods that may be used as either adjunct or alternative to Pap smear in low resource countries like ours. In Bhutan at present, we have adopted VIA as an adjunct to Pap smear in women 30-45 years of age. These women should first have Pap smear taken followed by VIA. This is to improve sensitivity of Pap smear. Women with positive VIA can also be referred for colposcopy immediately or cryotherapy on the spot. This will then help reduce loss of follow up. VIA alone could not be provided as an alternative to Pap smear in Bhutan because providers need longer and more intensive training followed by regular supervision by gynecologists, both of which are not possible at present.

Besides secondary prevention with Pap smear screening and VIA, HPV vaccination with quadrivalent vaccine was also launched in 2010, through a school based mass campaign where more than 49,000 girls between 12-18 years of age were vaccinated. From 2011 onwards, vaccine was offered to 12 year olds through routine vaccination program based at health centers. Because of logistic problems, vaccine is now being offered through the school based program. All girls studying in class VI will be vaccinated irrespective of age.

There has been no study to show that vaccinated women should have different screening schedules. Besides, presently available vaccines protect only against HPV types 16 and 18 that cause about 70% of cervical cancers. Therefore, girls that have received vaccination also must undergo routine screening from the age of 25 years instead of doing it from 30 years as advised on vaccination cards. It is of utmost importance that health workers should not be complacent about screening just because vaccination is being given to all our girls.

Due to the fact that most of women will be vaccinated, newer and more sensitive method of screening may be introduced in our country in future. HPV testing is now being offered as a co-test with Pap smear in many developed countries. When these 2 methods are used, screening interval can be increased to 5 years. HPV testing is either offered as primary test followed by cytology in test positive women or cytology is used as primary screening with HPV as triaging method for women with ASCUS before they undergo colposcopy. HPV testing should not yet be used as sole screening method and it is not cost effective to screen women younger than 30 years with HPV. In Bhutan, we are doing HPV testing only in research settings at present.
II. Cervical cancer

Cervical cancer affects the cervix of uterus in the female reproductive system. It develops due to persistent infection with one of the high risk HPV types.

Natural history of cervical cancer

Women get Human Papilloma Virus (HPV) infection when they become sexually active. HPV infection peaks in women 20-29 years old women. In most cases, the infection is transient and is cleared by one to two years. But, in about 20% of women, it may persist and lead onto abnormal changes in the cervical epithelium. This is known as Cervical Intraepithelial Neoplasia (CIN). Some of these lesions may turn into cancer 10-15 years later on, depending upon the type of HPV infection and the host immunity. These precancer lesions are easily detectable by screening methods like Pap smear and they can be treated effectively.

HPV is a non-enveloped double stranded DNA virus. It is highly species specific and epitheliotrophic. Out of 100 HPV types, 40 of them infect anogenital areas. These viruses are either oncogenic (high risk types) or non oncogenic (low risk types). More than 99% of cervical cancer specimens contain high risk type HPV DNA; 70% contain DNA of HPV type 16 and 18. Cervical cancer is a rare long term outcome of persistent infection with one of the high risk HPV types. In Bhutan, 73% of women with cervical cancers harbored HPV type 16 and 18. Rest contained 31, 45, 58 and 59 (source: HPV Prevalence Study, year 2012)
Risk Factors
Epidemiological studies have identified number of factors that play a significant role in the development of cervical cancer.

- **Early age at marriage** is one of the most important risk factors. This is because HPV infection acquired in very young girls is more likely to give rise to cellular abnormalities in the cervix.

- **Multiple sexual partners** increase the risk of exposure to HPV infection. Presence of other STIs also acts as cofactors in the development of CIN and invasive cancer.

- **Low socio-economy and low education**: Women of low socio-economy are more likely to either not enroll in school or drop out early leading to early marriage and have more children. Due to low literacy, they are also less likely to participate in screening due to ignorance and lack of awareness.

- **Multiparity**: Every time a woman delivers, her cervix undergoes repair. During repair there are immature dividing cells that are susceptible to HPV infection.

- **Smoking**: Nicotine and by products of smoking are thought to increase a woman’s relative risk for cervical cancer because their concentration in the cervical mucus decreases the immune capability of the cervical tissue.

- **Immuno-suppression**: Immuno-suppression due to any reason leads onto persistence of HPV infection with more likelihood of developing cellular atypia. HIV positive women are at higher risk of developing cervical cancer. Cervical cancer is one of the AIDS defining cancers.

- **Lack of screening program**: Lack of an effective screening program also acts as a risk factor. Women who regularly undergo screening and adhere to follow up and treatment are unlikely to get cancer compared to those who never do it.

Symptoms of cervical cancer:
Cervical cancer is frequently asymptomatic in the very early stage of the disease. Later on, following are the frequently encountered symptoms:

- Abnormal vaginal bleeding – It can be inter-menstrual, postcoital, postmenopausal or a woman may have just heavier and more prolonged menstrual flow than usual.
- Excessive or foul smelling vaginal discharge may be there due to superadded infection of necrotic tissue.
- There may be urinary frequency, urgency and backache.
- In advanced cases, there may be:
  - Pain in the pelvic region and/or lower limbs
  - Swelling of lower limbs
  - Renal failure in late stages
  - Passage of urine and feces per vagina (fistulae formation)
- It may be silent for many years till it is well advanced. If Pap smear is done, we may diagnose early.

*If women have symptoms like abnormal bleeding including postcoital bleeding, she should undergo colposcopy even if they have normal Pap smear report.*
Signs

a. General examination:
- Pallor
- Cachexia in advanced cases
- Signs of renal failure due to obstructive uropathy in late cases
- In advanced stage, there may be enlargement of lymph nodes in the abdomen, inguinal region. Scalene node may be palpable.

b. Speculum examination:
- Early lesions present as a rough, reddish, granular area that bleeds on touch. Or cervix may look normal on naked eye examination and we diagnose through abnormal Pap smear.
- Later on, it may be ulcerative, infiltrative or polypoid. The lesion is highly friable and bleeds profusely on vaginal examination or speculum examination. This makes visualization difficult.
- Sometimes, the cervix is just enlarged and hard (barrel shaped) with no obvious lesion
- Where cancer is suspected and no lesion observed, LEEP biopsy should be done.

Fig. 2.1: Invasive cervical cancer
c. **Manual Examination:**
   - Cervix is usually firm and expanded or fleshy. It is highly friable and bleeds profusely. There may be profuse foul smelling discharge too. Vagina and pelvic sidewalls may be involved.

**Types of cervical cancer:**
- **Squamous cell carcinoma** and variants arising from the squamous epithelium that covers the ectocervix
- **Adenocarcinoma** arising from the endocervix which is lined with columnar epithelium. In the past, it used to constitute 5% of cervical cancer (now 18.5-27%).
- **Adeno squamous** (mixture of squamous cell carcinoma and adenocarcinoma)
- Others

**Spread**

*It is a locally invasive and slow growing tumor.* The cancer involves vagina, pelvic wall, bladder and rectum by direct spread. Through lymphatic spread, it reaches pelvic and para-aortic nodes. Through blood, it spreads to lumbar vertebrae, lungs, liver, bone and other structure, including brain.

**Staging:**
Cancer of the cervix can be staged clinically into the following stages:

**Stage I.** The carcinoma is strictly confined to the cervix.

**Stage II.** The carcinoma invades upper third of vagina or part of the parametrium though not up to pelvic wall.

**Stage III.** The carcinoma has extended to the pelvic wall or lower third of vagina. Involvement of ureters may lead to unilateral or bilateral hydrenephrosis.

**Stage IV.** The carcinoma extends to bladder or rectum, or there may be distant spread involving other organs.
Fig. 2.2: A schematic diagram of clinical stages of cancer of cervix
**Diagnosis**
It is suspected from history and clinical findings on vaginal and speculum examinations, and confirmed by biopsy. Colposcopy has an important role in the diagnosis of early (preclinical) cancer. An examination under anesthesia is done to see the extent of the disease and also to stage the cancer.

**Investigations**
- CBC, ABORH grouping, LFT, RFT
- X-ray chest PA view
- CT scan/or MRI
- Cystoscopy where bladder involvement suspected

**Treatment**
Very early stages of cervical cancer may be treated with surgery alone. Cure rate at this stage is same for surgery and radiation. Even after surgery radiation may be needed for some women depending upon histopathology reports. Once spread beyond cervix, radiotherapy is the main stay of treatment. Nowadays, concurrent chemotherapy is given along with external radiation. This is followed by brachytherapy. Women with very advanced stages (IV) are given palliative treatment with radiotherapy or chemotherapy.

---

| All women with diagnosis of any cancer should be referred to JDWNRH |

**Palliative care**
Nowadays, there is a paradigm shift from cure to comfort in cancer care. Pain control is one of the most important aspects, but other symptom control is also important. For example a woman with foul smelling discharge can be given Sitz bath with Betadine or Metronidazole tablets.

---

| Palliative care services should be provided at all levels of health care centers. |

**Follow up of patients with cervical cancer**
A woman with cervical cancer must be followed up regularly, especially in the first 2-3 years. This is because most of the recurrence and deaths occur in the first 2 or 3 years of treatment. Pap smear must be done every 4 months for the first 3 years, every 6 months for the next 3 years and yearly after that. If patients have signs of recurrence like discharge or bleeding, swelling or pain of legs or any pain in the lower abdomen or intractable cough, they should be referred immediately to gynecologist.

---

| As far as possible, a gynecologist should do the follow up of cancer patients, at least once a year. |

**Prognosis**
Clinical stage at presentation is the single most important prognostic factor. Other factors are:
- Size of tumor
- Type and grade of tumor
- Involvement of pelvic lymph nodes etc
The five year survival rate varies from above 85% for stage I to less than 10% for stage
III. PRECANCEROUS LESIONS OF CERVIX

Anatomy and Physiology of Cervix

To understand the pathophysiology of cervical cancer, you must have a good knowledge of anatomy and physiology of cervix.

Cervix is the lower fibro muscular portion of the uterus. It is cylindrical or conical in shape and is 3-4 cm long and about 2.5 cm in diameter. It is supported by ligaments which stretch between the lateral and posterior portion of the cervix and wall of the bony pelvis.

There are two parts of the cervix

- Portiovaginals: This is the lower half of the cervix which protrudes into the vagina with an opening (orifice) called external os.
- Supravaginal portion: It is the upper half of the cervix which meets the body of the uterus at the internal cervical os.

External os
It is an opening through which the cervix opens into the vagina. In parous women it appears as a transverse slit (wide gaping opening). In nulliparous women, it resembles a small circular opening in the center of the cervix.

Uterine cervix is also divided into two parts in relation to the external os.
- Ectocervix
- Endocervix

Ectocervix: This is the portion of the cervix lying exterior to the external os. This part of cervix is readily visible on speculum examination.

Endocervix: This is the portion of the cervix proximal to external os till the level of internal os.

Endocervical canal: It transverses the endocervix and connects the uterine cavity with that of vagina. It is widest in women in reproductive age group, 6-8 mm in width. The external os needs to be stretched or dilated to visualize this portion of the cervix.

Vaginal fornix: The space surrounding the cervix in the vaginal cavity is called fornix which is again divided into:
- Lateral fornix
- Anterior fornix
- Posterior fornix

Structure of cervix
The cervix is composed of thick fibromuscular stroma lined by epithelium. The stroma supports the blood vessels, lymphatics and nerves. Arterial supply is derived from internal iliac artery through the cervical branch of uterine arteries, which descends in the lateral aspects of the cervix at 3 and 9 ‘o clock position. The veins of the cervix run parallel to arteries. The lymphatic vessels from the cervix drain into:
• Common, external and internal iliac nodes
• Obturator and parametrial nodes.

**Epithelial lining of cervix:**
Two types of epithelium cover the cervix:

1. Squamous epithelium
2. Columnar epithelium

The two types of epithelium meet at the original squamo-columnar junction in prepuberal girls.

1. **Squamous Epithelium**

It is stratified non-keratinizing squamous epithelium covering normally a larger area of ectocervix. It is opaque, pale pink in colour and multilayered (15–20 layers of cells). Squamous epithelium may either be:

- Native or original, formed during embryonic life.
- It may have been newly formed as metaplastic epithelium in adult life.

In premenopausal women, the original squamous epithelium is pinkish in colour and the metaplastic squamous epithelium looks somewhat pinkish white on speculum examination.

Histological structure of squamous epithelium of the cervix consist of 4 layers

1. Basal cell layers
2. Parabasel cell layers
3. Intermediate cell layers
4. Superficial cell layers

**Basal cell layers**
It is a single layer of round cells with large dark staining nuclei and little cytoplasm attached to the basement membrane. The basement membrane separates the epithelium from the underlying stroma. HPV infects this layer.

*Figure of HPV infection3*
Parabasal cell layers:
Basal cells divide and mature to form the next few layers of cells called parabasal cells. Parabasal cells contain large dark staining nuclei and greenish blue basophilic cytoplasm.

Intermediate cell layers:
Parabasal cells differentiate and mature to form intermediate cell layers. The intermediate cells are polygonal with abundant cytoplasm and round nuclei. These cells form a basket woven pattern.

Superficial cell layers:
Intermediate cells mature to form superficial cell layers which are composed of large and markedly flattened cells with small, dense pyknotic nuclei and transparent cytoplasm. Intermediate and superficial cell layers contain abundant glycogen in their cytoplasm, which is a sign of normal maturation and development of the squamous epithelium. Lack of glycogen in the cytoplasm of intermediate and superficial cells indicates abnormal or altered maturation.

The maturation of squamous epithelium of the cervix is dependent on estrogen. If estrogen is lacking, full maturation and glycogenation do not take place. So, after menopause, the cells do not mature beyond the parabasal cell layers. As a result the epithelium becomes thin and atrophic. On speculum examination it appears pale with sub epithelial petichial hemorrhages, which is easily prone to trauma and infection.

Abnormal Nuclei:
- In superficial and intermediate cells, indicates LSIL
- In parabasal and basal cells, indicates HSIL

Fig. 3.1 Stratified squamous epithelium (x20)

Columnar Epithelium:
The endocervical canal is lined by columnar epithelium. It is also known as glandular epithelium. It is composed of a single layer of tall cells with dark straining nuclei close to the basement membrane. On visual examination it appears red, as underlying capillaries can be seen more easily due to its single layer.

At its upper limit it merges with the columnar epithelium of the endometrium and at its lower limit it merges with the squamous epithelium at the squamo columnar junction. It
covers a variable extent of ectocervix depending upon the woman’s age, reproductive and hormonal status. The columnar epithelium does not form a flattened surface in the cervical canal, but is thrown into multiple longitudinal folds protruding into the lumen of the canal, giving rise to papillary projections. It forms several invagination into the cervical stroma forming endocervical crypts (endocervical glands). On visual examination, the surface of the cervical canal gives grainy appearance. Localized growth over the endocervical columnar epithelium may produce cervical polyp, which is a red mass protruding from the external os. Mitosis and glycogen production are absent in columnar epithelium.

*Fig. 3.2: Columnar epithelium (x40)*

Original squamo-columnar junction:
It appears as sharp line with a step, due to the difference in the height of squamous and columnar epithelium.

The location of squamo-columnar junction in relation to the external os is variable over a women’s lifetime and depend upon factors like age, hormonal status, birth trauma, OCP use, pregnancy etc. It is not visible during childhood. It becomes visible after puberty and early reproductive period. In late thirties and menopause, its original site is marked by presence of crypt openings or Nabothian cysts. Or, you can faintly see it as the lower end of transformation zone.

*Fig. 3.3: Squamocolumnar junction (SCJ) (x10)*
**New squamo columnar junction:**
When columnar epithelium on the ectocervix is exposed to the acidic vaginal environment after puberty, destruction and eventual replacement of the columnar epithelium by newly formed metaplastic squamous epithelium occurs. Metaplastic processes mostly start at the original SCJ and proceed centripetally towards the external os. Thus a new SCJ is formed between the metaplastic squamous epithelium and the columnar epithelium. The location of the new SCJ progressively moves on the ectocervix towards the external os and is inside cervical canal on completion of reproductive life and onset of menopause. The area between the new and old SCJ is known as the transformation zone (TZ). This area contains immature cells, which may get infected by HPV. New SCJ is an important landmark in VIA and colposcopy since most of the atypia lies near this in the transformation zone. It is essential to see the upper limit of the TZ or new SCJ in its entirety or we might miss CIN or cancer.

*Fig. 3.4: The entire new squamocolumnar junction (SCJ) is visible and hence the colposcopic examination is satisfactory; the transformation zone (TZ) is fully visualized. The metaplastic squamous epithelium is pinkish-white compared to the pink original squamous epithelium.*

**Immature squamous metaplasia**
The term immature squamous metaplasia applies when there is little or no stratification in the newly formed metaplastic epithelium. It does not produce glycogen. In the majority of women, it develops into mature squamous metaplastic epithelium. In about 20% of women with HPV infection, viral DNA gets incorporated into host DNA causing intraepithelial neoplasia/lesion or CIN.

**Transformation zone:**
This is a region of the cervix where columnar epithelial is being replaced by the new metaplastic squamous epithelium. It corresponds to the area of cervix between the original and new squamo columnar junction. In premenopausal women the transformation zone is fully located on the ectocervix. After menopause the transformation zone may move into the cervical canal. It is important to see the upper end of TZ in VIA and Colposcopy.

*Fig. 3.5: Transformation zone and its boundaries*
CIN (cervical intraepithelial neoplasia)
This is development of abnormal cells due to persistent HPV infection with integration of viral DNA into host DNA (CIN)

1. CIN I: Lower one third of epithelium is abnormal
2. CIN II: Lower two-third of epithelium is abnormal
3. CIN III/carcinoma-in-situ (CIS): When full thickness is involved
4. Invasive carcinoma: When basement membrane breaks through and underlying stroma is invaded

CIN II and III/CIS are known as high grade CIN and are considered to be the true precursors of invasive cancer. The terminology CIN is mostly used to describe histopathology (biopsy) reports whereas SIL (squamous intraepithelial lesion) is usually used for giving cytology reports (see TBS in the Annex).

CIN I/II/III figure (picture)
Natural history of cervical cancer precursors

Despite women’s frequent exposure to HPV, development of cervical neoplasia is uncommon. Most cervical abnormalities caused by HPV infection are unlikely to progress to high-grade CIN or cervical cancer. The long time frame between initial infection and overt disease indicates that several cofactors (e.g., genetic differences, hormonal effects, micronutrient deficiencies, smoking, or chronic inflammation due to other STIs) may be necessary for disease progression. Spontaneous regression of CIN may also indicate that many women may not be exposed to these cofactors. Several studies have addressed the natural history of CIN, with particular emphasis on disease regression, persistence and progression. They have revealed that most low-grade lesions are transient; most of them regress to normal within relatively short periods or do not progress to more severe forms. High-grade CIN, on the other hand, carries a much higher probability of progressing to invasive cancer, although a proportion of such lesions also regress or persist. It appears that mean interval of progression of precursors to invasive cancer is some 10 to 15 years.

- Oncogenic type of HPV infecting the metaplastic cells near SCJ is the first step in the development of preneoplastic lesion of the cervical cancer.
- Persistent infection with one or more of the oncogenic subtypes of HPV is a necessary cause for cervical neoplasia.
- The high grade cervical intraepithelial lesions are seen in young women in their thirties and if left untreated, they develop into invasive cancer in their forties and fifties.
- If intervention are done when these women have only preneoplastic lesion, none or very few of them will have cancer later on.

**Fig. 3.6: Cytological changes due to HPV infection, LSIL**

![Cytological changes due to HPV infection, LSIL](image)

IV. PREVENTION OF CERVICAL CANCER
Cervical cancer has a long preclinical phase known as CIN. This can be easily picked up by screening and treated effectively, thus making this cancer a preventable disease.

There are 3 types of prevention:

1. **Primary prevention**
   - Education of people to prevent HPV infection
• Vaccination against HPV (now available in Bhutan too)

2. Secondary Prevention
• Screening
• Early detection of cancer (this will improve survival)

3. Tertiary Prevention:
• Treatment
• Avoid complications

This is to prolong life and improve quality of life of a woman even if death cannot be averted.

Primary prevention is by HPV vaccination. There are two types of vaccine developed. One is bivalent (Cervarix) and protects against HPV 16 and 18. It is given at 0, 1 and 6 months. The other one is quadrivalent (Gardasil) and contains vaccine against HPV 16, 18, 6 and 11. 6 and 11 are low risk types that cause genital warts. This vaccine is given at 0, 2 and 6 months. The vaccines are most effective if given to prepuberal girls. In some countries, boys are also being vaccinated.

We must not be complacent because of vaccination, because it will take more than 20 years to show results. Vaccination protects against 70% of cervical cancers only.

Secondary prevention
Secondary prevention is done by different screening methods. Among them, Pap smear, HPV testing and visual methods like VIA and VILI are the commonest ones used in different countries.

Pap smear
It is a proven method for cervical cancer screening. Where this program exists, and is of good quality, it has brought down morbidity and mortality due to cervical cancer to a large extent.

What is Pap smear?
There is constant shedding of cells from the cervix and vagina. Pap smear studies these cells leading to identification of women with abnormalities in the cervix. It is by treating these lesions that we can prevent development of cervical cancer. Pap smear is one of the success stories in medical history. But, to be effective following must be in place:

• Defined target population
• High coverage
• Good quality Cytolaboratory and
• Strict adherence to follow up and treatment by women.

In Bhutan, our target population is all women between 25 to 65 years of age regardless of HPV vaccination status. All women who are or were sexually exposed should participate in screening.

WHEN SHOULD IT BE DONE?
• In women who are menstruating it must be done in mid cycle as far as possible (7 to 10 days after menstruation stops).
• In women with amenorrhoea or in menopause or who had hysterectomy, it can be done any time
• In women who have delivered or had an abortion/miscarriage, it should be done after three months.

**Pap smear must not be done in presence of any type of bleeding. If a woman who has never done Pap smear presents with abnormal bleeding, refer her for colposcopy.**

### Registration and Filling of Forms
You must maintain a Pap smear register in your RH clinic. Register all the demographic information of a patient, including mobile and CID numbers. Write her obstetric and menstrual history and whether she is on any type of contraception. Keep a big space or one whole page of the register for each patient. This is because you must not change her Pap smear number once you have given it. When she comes for subsequent smears, you must add /1, /2, /3. For example a patient in Thimphu has X12 as her number. On repeat visit you must not change her original number on the card but write X12/1 on request form and slide. You must advise the patient never to lose her card and to bring it to the RH clinic every time she is called for a Pap smear. She must understand that this card will be with her till she is of 65 years of age. **Fill the forms properly with correct information (see the form in Annexure III)**

### How Should Pap Smear Be Taken?
Before making a patient lie down on the examining table make sure you have a numbered slide and fixative spray nearby (if you have no assistant). There must also be good source of light. Put a speculum to expose the cervix. Do not do vaginal examination or use any lubricant on the speculum. Scrape the transformation zone all around with Allesbury’s spatula with its tip inside the os. Smear it on the slide and quickly spray the fixative onto the slide, from a distance of 10cm. If there is bleeding on taking smears, refer her for colposcopy. If her menstruation is due or has just stopped, call her back after the next cycle or in mid-cycle. If inflammation is present (presence of discharge with foul smell, pruritus or pain lower abdomen), treat it first and do the smear after two weeks or after her next menstrual period. Spray fixative will be prepared and issued by cytology laboratories. *(For screening interval refer to protocol: Annexure II).*

### Packing and Transportation of Slides
After the slide is dried, put into slide boxes and transfer to the nearest cyto-laboratory within 7 days of collection

**Advantages of Pap smear as a screening method**

- Widely accepted screening method
- Practical (safe, easy and non invasive)
- Affordable
- Acceptable to women
- Acceptable sensitivity (70%) and specificity (80%)
- Permanent record of screening in a form of a slide

**Disadvantages of Pap smear**
Requires
- Materials like slides, spatulas, and speculum
- Reagents
- Microscopes
- Reliable transports of slides
- Trained cyto-technicians and cyto-pathologists

If any of these are missing, the entire program may break down. Besides, long waiting time for report leads to loss of follow up.

VISUAL INSPECTION WITH ACETIC ACID (VIA)

What is it?
Cervix is painted with 5% acetic acid and naked eye observation is done after one minute. If there are precancerous lesions, these areas become white (VIA positive). Women who test positive are either treated on the spot or referred. When treatment like cryotherapy is offered at the same visit, it is called single visit approach.
If no white lesions are seen, VIA is negative. The test is then repeated after three years.

Advantages of VIA
- Test is simple and non invasive
- Nurses can do it
- It can be done anywhere
- There is immediate report
- Sensitivity is more than that of Pap smear (80%)
- Treatment can be done at the same visit

Disadvantages
- It cannot be done in women more than 45 years and less than 30 years
- Intensive training and quality control are needed
- Low specificity (60%) leads to over treatment, but there is no harm
- No tissue for histopathology for retrospective study

In Bhutan, VIA is done as an adjunct to Pap smear in women 30-45 years of age.

What is the target population?
Women in the age group of 30 to 45 years who are or were sexually exposed must undergo VIA testing. This is because precancer lesions (CIN) are frequently found in this age group and the new SCJ is easily visible in most of these women.

Who should do it?
Health workers trained in VIA

Instruments and Supplies:
- Examining table
- Light source
- Bivalve speculums (Cusco or Graves)
- Instrument tray or container
- Cotton swabs
- New examination gloves, or surgical glove
- Dilute (3-5%) acetic acid solution (white vinegar is acceptable)
- 0.5% chlorine solution for disinfection
• A record form (refer to annexure X)

**When should it be done?**

• At any time after the menstruation has stopped
• In women who have delivered or had abortion it should be done after three months
• In a woman with amenorrhoea, other than pregnancy, it can be done anytime.

**Registration and filling of forms**

• Maintain a VIA register (Annexure IX)
• Fill the forms properly (Annexure X)

**How to perform VIA**

**Pre-test counseling and client Assessment:**

Take a brief reproductive history, including risk factors

**Step 1**

• Inspect the external genitalia and check the urethral opening for discharge
  • Palpate Skene’s and Bartholin’s glands for tenderness
  • Tell the woman that the speculum is about to be inserted and she may feel some pressure

**Step 2**

• Gently insert the speculum fully or until resistance is felt and slowly open the blades to reveal the cervix
• Adjust the speculum and light source so that the entire cervix can be seen

**Step 3:** When the cervix can be seen in its entirety, fix the blades of the speculum in the open position so that it will remain in place with the cervix in view

**Step 4:** Move the light source to see the cervix clearly

**Step 5:** Look at the cervix and check for evidence of infection, such as whitish purulent discharge; ectopy; grossly apparent tumors or cysts, ulcers or lesions

**Step 6:** Use a clean cotton swab to remove any discharge, blood or mucus from the cervix

**Step 7:** Identify the cervical os and SCJ, and the surrounding area

**Step 8:** Soak a clean swab in dilute acetic acid solution and apply it thoroughly to the cervix

**Step 9:** Once the cervix has been washed with the acetic acid solution, wait 1 minute for it to be absorbed and look for any acetowhite reaction to appear

**Step 10:** Inspect the SCJ carefully. Check to see if the cervix bleeds easily. Look for any raised and thickened white plaques
Step 11: As needed, reapply acetic acid or swab the cervix with a clean swab to remove any remaining mucus, blood or debris that develops during the inspection and may obscure the view.

Step 12: When visual inspection has been completed, use a fresh cotton swab to remove any remaining acetic acid from the cervix and vagina.

Step 13: Gently remove the speculum
- If the VIA test is **negative**, place the speculum in 0.5% chlorine solution for 10 minutes for decontamination
- If the VIA test is **positive** and the woman chooses treatment, place the speculum on the HLD tray or container for use during cryotherapy

Step 14: Perform bimanual examination and rectovaginal examination (if indicated), Check for:
- cervical motion tenderness
- pregnancy
- uterine abnormality
- enlargement or tenderness of adnexa
Flow chart of VIA/VIA followed by Cryotherapy

Perform VIA

VIA negative
   - Repeat VIA in three years

VIA Positive
   - Recommend Cryotherapy
     - Counsel clients
       - Accept for Cryo
         - Has cervicitis
           - Treat with antibiotics
           - Cryo after two weeks
         - No cervicitis
           - Immediate cryotherapy

VIA at one year
   - VIA negative
     - Repeat VIA after three years
   - VIA positive or cancerous lesions
     - Refer for further evaluation or cancer treatment

Suspected cancer
   - Do not accept cryotherapy
     - Refer to Gynecologist

Cryotherapy is provided at the 3 Regional Referral Hospitals and Phuntsholing Hospital
V. FOLLOW UP OF PAP SMEAR REPORTS

1. NORMAL PAP SMEAR
   Repeat Pap smear after 3 years. If women have abnormal bleeding, refer for colposcopy.

2. AIR DRIED/INADEQUATE SMEAR
   Give patient the same number and repeat smear after 2 months. Unsatisfactory rate should be less than 5% if your technique of smear taking is good.

3. INFLAMMATORY CHANGES / INFLAMATION:
   Give: Tab Metronidizole 400mg BD for 7 days/or 2 g HS stat.
   Tab Doxycycline 100mg BD for 7 days.
   Repeat Pap smear after 2 months. If there is repeated inflammation, inspect cervix. If it looks normal and woman has no discharge/contact bleeding etc, she can follow normal interval of screening. If cervix has suspicious lesion, do a VIA or refer her for colposcopy. The inflammatory cells may obscure proper study of cells and we may miss CIN or cancer.

4. BACTERIAL VAGINOSIS
   Give: Tab Metronodizole 400mg BD for 7 days or 2 g HS stat.
   Repeat Pap smear after 2 months.
   If repeated BV, ignore and repeat Pap smear after 3 years (do not repeat treatment unless symptomatic).

5. TRICHOMONAS VAGINALIS
   Give: Tab Metronidizole 400mg BD for 7 days.
   Or single dose of Metronidazole 2 gm stat at night.
   Treat both partners at the same time. Do STI counseling. Repeat Pap smear after 2 months.

6. CANDIDA/FUNGAL EFFECT
   Give: Clotrimazole vaginal Pessary 2 HS for 3 nights
   or Fluconazole 150 mg. orally stat.
   Repeat Pap smear after 2 months.

7. HERPES SIMPLEX
   Give: Acyclovir 400 mg orally TDS for 7 days (for both partners)

8. Epithelial cell abnormalities: HPV INFECTION, LSIL, HSIL, CARCINOMA-IN-SITU, SQUAMOUSCELL CARCINOMA, ADENOCARCINOMA, ASCUS, AGUS.

All abnormal Pap smear reports are signed out by a pathologist

- ASCUS and LSIL are known as equivocal Pap reports.
- LSIL: Do immediate colposcopy, regardless of age of the women.
- ASCUS: Repeat Pap smear after 6 month if woman is less than 40 years. If repeat smear is abnormal, then do colposcopy. If the women are more than 40
years, do immediate colposcopy. If normal, repeat after 3 years. Only 7-17% of women with ASCUS have CIN II/III and 15-30% of those with LSIL have CIN II/III. If biopsy negative, no need of LEEP.

- ASC-H: Here, immediate colposcopy is advised since 40% of women have high grade CIN. If biopsy or colposcopy negative, repeat Pap smear after 6 months. If report abnormal, including ASCUS/LSIL, LEEP must be done.

- 70-75% of women with HSIL have high grade CIN and 1-2% have invasive cancer. Therefore, LEEP is advised if colposcopy is unsatisfactory, biopsy negative or CIN I or cervix looks normal.

- See and treat: If unreliable for follow-up, you can do LEEP instead of taking a biopsy. This decreases number of visits to hospital and loss of follow up too.

9. INFLAMMATION IN PATIENT WITH IUCD (Intra Uterine Contraceptive device)

If normal, repeat every 3 years.

10. ABNORMAL SMEAR IN PATIENT ON OCP (oral contraceptive pill)
- Stop OCP for 3 months.
- Then repeat Pap smear.
- If report is still abnormal, refer for colposcopy.
- If normal, she can follow normal interval of screening

11. ABNORMAL SMEAR DURING PREGNANCY OR AT THE POSTNATAL VISIT

Repeat Pap smear 3 months after delivery/abortion.

12. PATIENTS/PARTNER WITH HIGH RISK BEHAVIOUR
Women with multiple partners or whose spouse has multiple partners and women with STD or HIV must do Pap smear yearly instead of doing every 3 years

Women who had hysterectomy for reason other than cervical /endometrial cancer and CIN lesions need not undergo Pap smear screening.

If endometrial cells seen in menopausal women, she should have fractional curettage (first do ECC and then endometrial biopsy)

13. FOLLOW UP OF A PATIENT TREATED FOR CARCINOMA OF THE CERVIX

Do Pap smear every 4 months for the first 3 years, every 6 months for the next 3 years, and yearly after that. She must see a Gynecologist at least once a year. If she has signs of persistent or recurrent disease or her Pap smear report is abnormal, she must immediately be seen by a Gynecologist. Send the slides to a Laboratory where there is a pathologist.
14. FOLLOW UP OF PATIENTS TREATED FOR CIN

All those patients that have been treated for CIN must do Pap smear and colposcopy after one year. This is to ensure cure. If both Pap smear and colposcopy are normal, they can undergo screening every 3 years. It holds true for all patients who had treatment for CIN irrespective of the type of treatment she received (conization, cryotherapy, LEEP, diathermy coagulation or hysterectomy).

COLPOSCOPY

Colposcopy is an important back up for cervical cancer screening whatever method may be used. Pap smear leads to suspicion of a lesion by finding abnormal cells. Colposcopy helps in locating the source of abnormal cells and confirming it by biopsy. Sensitivity of Pap smear is about 75%. It goes up to 95% when combined with Colposcopy.

What is it?

It is a low power, stereoscopic, binocular field microscope with a powerful light source used for magnified visual examination of the uterine cervix. It helps in diagnosis of cervical neoplasia/cancer. Most common indication is abnormal Pap smear or VIA positive. It is also done when a cervix looks suspicious or history suggests presence of cancer (postcoital, intermenstrual, postmenopausal bleeding or contact bleeding/ or spotting).

Cervix is observed after applying normal saline, 5% acetic acid and Lugol’s iodine solution in successive steps. The most important step is with acetic acid. Abnormal lesions become white and biopsy can be taken. The findings are documented on a special card, for future reference.

TREATMENT OF CIN

1. CIN I

This is known as low grade CIN and is mostly transient, especially in women below 30 years of age. These women should be followed up with colposcopy 6 monthly for 18 to 24 months and treated if found persistent. But, if you are unsure about compliance, it is better to treat the woman than follow up. Mode of treatment depends on size and location of the lesion. She must undergo Pap smear and colposcopy after one year of treatment. If both normal, she can enter normal screening intervals.

2. CIN II/III/CIS

Here the treatment should be done with excision or ablation depending upon size of lesion. If lesion is small and SCJ seen entirely, cryotherapy can be done. Otherwise, LEEP is the treatment of choice. When a woman is older or has completed family, or her cervix is completely flushed with uterus, she may opt for hysterectomy. It is also done if there are other indications like fibroma or DUB.

MODALITIES OF TREATMENT

Evidence supports the high effectiveness of simple methods like LEEP and cryotherapy. Cold conization (using knife) and hysterectomy are costly and more risky for patients.
LEEP and cryotherapy services are available in all Regional Hospital and P/ling Hospital. Cryotherapy is being done by trained female Health Assistants who work in colposcopy clinics.

In counseling patients, who undergo screening procedures, the health care providers must be able to describe types of treatments in simple words to patients who need them, so that these patients make informed choices.

1. **Cryotherapy**
   It involves freezing of cervix using either compressed carbon dioxide or nitrous oxide as coolant. Treatment consists of applying this gas to the cervix through a probe for a 3 minute freeze, followed by thawing for 5 minutes and freezing again for another 3 minutes. This is called ‘double freeze’ technique.

   It is a simple procedure using simple equipment. It is easy to learn and does not need electricity or anesthesia. It has very few side effects. The only disadvantage is there is no tissue for histology.

*Fig. 5.1: (a) The iceball on the cervix immediately after cryotherapy (b) Appearance 2 weeks after cryotherapy (c) 3 months after cryotherapy (d) 1 year after cryotherapy*
2. **LEEP (Loop Electro surgical Excision Procedure)**

Excision of cervical lesions with LEEP is done by applying a low-voltage, high frequency alternating current to a thin wire loop and slowly passing it across the cervix (see Figure 5.2). The raw area is then cauterized with a ball-type electrode to stop the bleeding. Lastly, Monsels’s paste (Ferric subsulfate which is a hemostatic agent) is applied on the area and the vagina is tightly packed. The pack is removed after 3-4 hours and patient sent home. If no active bleeding, packing may not be done.

This procedure is also called LLETZ (large loop excision of transformation zone) since the logic behind this excision is to remove whole of TZ in which CIN is located. Part of endocervical canal is also removed.

Advantage of this procedure is the presence of tissue for histology. Its disadvantages are need of anesthesia (local or general), electricity and a complicated set of instruments. Users must also undergo proper training.

*Fig. 5.2: Excision of an ectocervical lesion with one passes*

3. **Conization (with cold knife)**

Under regional or general anesthesia, cervix is excised in the shape of a cone, using a knife. After disinfecting and painting the cervix with Lugol’s Iodine, ties are applied at 3 and 9 o’clock positions. Then, whole of iodonegative area (transformation zone) on the ectocervix is cut with knife, removing also part of endocervical canal to a height of about 2 cm. The raw area is cauterized (or sutured sometimes) to control bleeding and tight packing of vagina is done. Patient is kept overnight and discharged next day after removing the pack and ensuring there is no active bleeding.

The advantage of this procedure is that it can be used where LEEP and cryotherapy may not be advisable (when invasion or glandular atypia is suspected or the SCJ is deep inside canal).

Its disadvantages are that it needs anesthesia, electricity and hospitalization besides carrying more risks of complications like hemorrhage (about 12%). Some patients need readmission and blood transfusion. It is also not good for women who have not completed family since it leads to more scarring of cervix than the above procedures.
Advice/information that must be given to patients after performing any of the 3 procedures (it should be printed and given to patients post procedure):

1. There will be vaginal discharge lasting for 3-4 weeks, which is normal.
2. There might be bleeding between the 10th and 14th day post-procedure. They must report to the health center if bleeding is heavy.
3. Report to health center immediately if there is fever, pain lower abdomen or foul smelling discharge. Presence of infection/inflammation is a contraindication for all the 3 procedures. This is to avoid infection later on. Any infection present should be treated beforehand.
4. Remove CuT before cryotherapy/LEEP/conization. Reinsert after 3 months.
5. Sexual exposure must be avoided for 4 weeks,
6. Patients must come for follow up after 1 year (do Pap and Colposcopy).
**Table 5.1: The indications of the three procedures are given in the tables below.**

<table>
<thead>
<tr>
<th>Indications for cold-knife conization</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The lesion extends into the endocervical canal and it is not possible to confirm the exact extent</td>
</tr>
<tr>
<td>• The lesion extends into the canal and the farthest extent exceeds the excisional capability of the LEEP cone technique (maximum excisional depth of 1.5 cm).</td>
</tr>
<tr>
<td>• The cytology is repeatedly abnormal, suggesting neoplasia, but there is no corresponding colposcopic abnormality of cervix or vagina on which to perform biopsy.</td>
</tr>
<tr>
<td>• Cytology suggests a much more serious lesion than that which is seen and biopsy-confirmed.</td>
</tr>
<tr>
<td>• Cytology or colposcopy shows atypical glandular cells that suggest the possibility of glandular dysplasia or adenocarcinoma</td>
</tr>
<tr>
<td>• Endocervical curettage reveals abnormal histology.</td>
</tr>
<tr>
<td>• There should be no cervico-vaginitis or PID</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Eligibility criteria for cryotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The entire lesion is located in the ectocervix without extension to the vagina and/or endocervix</td>
</tr>
<tr>
<td>• The lesion is visible in its entire extend and does not extend more than 2 to 3 mm into the canal</td>
</tr>
<tr>
<td>• The lesion can be adequately covered by the largest available cryotherapy probe (2.5 cm): the lesion extends less that 2mm beyond the cryotherapy probe</td>
</tr>
<tr>
<td>• CIN is confirmed by cervical biopsy/colposcopy or suspected on VIA</td>
</tr>
<tr>
<td>• There is no evidence of invasive cancer</td>
</tr>
<tr>
<td>• The endocervical canal is normal and there is no suggestion of glandular dysplasia</td>
</tr>
<tr>
<td>• The woman is not pregnant</td>
</tr>
<tr>
<td>• If the woman has recently delivered, she is at least three monthas post-partum</td>
</tr>
<tr>
<td>• There is no evidence of pelvic inflammatory disease or cervico-vaginitis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Eligibility criteria that must be met before LEEP is performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CIN is confirmed by cervical biopsy, when possible</td>
</tr>
<tr>
<td>• If the lesion involves or extends into the endocervical canal, the distal or cranial limit of the lesion should be seen: the furthest (distal) extend us no more than 1 cm in depth</td>
</tr>
<tr>
<td>• There is no evidence of pelvic inflammatory disease (PID), cervicitis, vaginal trichomoniasis, bacterial vaginosis, anogenital ulcer or bleeding disorder</td>
</tr>
<tr>
<td>• If the woman has recently delivered, she should be at least three months post-partum</td>
</tr>
<tr>
<td>• Women with hypertension should have their blood pressure well controlled</td>
</tr>
<tr>
<td>• The woman must give written consent to have the treatment after being thoroughly informed as to how it is performed and the probabilities of its effectiveness, adverse effects, complications, long-term sequel, and alternative ways that are available to manage her problem.</td>
</tr>
</tbody>
</table>
Factors that affect a Pap Smear Program

1. Informing the public on cervical cancer and importance of its prevention through Pap smear will attract as many women as possible. Try to reach the unreached

2. Coverage

Each health center should know your target population so that you are able to calculate coverage. Aim to cover more than 70% of your clients all the time. Always try to recruit new clients instead of repeatedly doing Pap on old clients.

3. Reporting time of Pap smear

Long reporting time affects program. There must be co-ordination in the districts to ensure transport of slides to cyto-centers as fast as possible. Reports also must be collected in time and disbursed so that women are not left to anxiety. Also ensure that every woman that has done Pap smear gets her report.

4. Unsatisfactory smear rate should be less that 5%

5. Follow up of abnormal smears

All women with abnormal Pap smear report must be sent for colposcopy within 2 months. Prior appointment with colposcopy center must be arranged by the referring center. This ensures that a woman does not need repeated visit to a colposcopy center for service and decreases loss of follow up. Remember that it is by treating all women with precancers that helps to prevent future cancers. Pap smear itself has no intrinsic value if this part of program fails. Each health center must have a list of women with abnormal Pap smear and record dates of Colposcopy and treatment.

6. Quality Assurance in cytology

All abnormal reports should be signed out by a Pathologist

- 10% of negative smears must be read by pathologists quarterly or 6 monthly
- If women with normal Pap smear reports develop cancer, her slides must be reviewed by pathologist
- Regular refresher training for cyto-technicians
VI. IEC and Counseling

Information Education Communication
Information on cervical cancer screening and prevention is limited to communities having access to mass media like Kuensel and BBS. Even the most effective media in the country that is health care providers are not trained enough to give correct information on cervical cancer and its prevention. For a screening program to be successful, information plays a key role. Group and individual counseling is a must. This will help women adhere to screening and decrease loss of follow up. There should be pre and post-test counseling.

Health care providers should know and be able to use basic counseling techniques. These techniques will help them establish a relationship with the client. If a woman believes in the competence and honesty of the provider, she will be more likely to have the test and if necessary accept treatment and return for a follow up visit. In addition, she will be more likely to motivate others who need screening tests.

Pretest counseling

Women must be told the following:

- What is cervical cancer?
- What are its signs and symptoms?
- What are risk factors?
- How it is treated?
- How it can be prevented?
- How pap smear/VIA is done?
- When and who should do them?

Posttest counseling

- What you found and reassure
- When to collect report?
- Importance of collecting report?
- What to do in the event of abnormal and normal reports?

Follow up visit

- Result of Pap smear
- Schedule for next visit
- Procedures like Colposcopy and types of treatment available
- Timeframe of referral and treatment

(There should be linkage between Pap smear and Colposcopy Centers. Number of women referred, with their particulars like name, age, address and CID number should be communicated to the Colposcopy Centers. The latter in turn must give feedback on who have reported must be communicated.)

Target Group

1. Women of 25 to 65 years:
CIN and cervical cancer are most common in this age group. Though they are at higher risk of developing cervical cancer, many of them have completed child bearing and therefore are not likely to access reproductive health services. Special approaches are required to inform them of the needs for and availability of screening services.

2. **Adolescent girls**
HPV infection acquired in this age may induce dysplasia, which may then progress to cancer sometimes. They are more vulnerable to HPV infection because of physiological changes in the cervix and there is also likelihood of multiple sexual partners at this stage of life. These girls must be informed on risk of multiple partners and importance of HPV vaccination.

3. **Adolescent boys and sexually active males**
Male sexual partners including adolescent males are responsible for spread of HPV infection from one partner to the other, if safe sex is not practiced. They must be sensitized to be responsible and must take part in disease and pregnancy prevention. Adult males can also help the woman to access cervical cancer screening services.

4. **Health care providers**
Program success depends upon ability of the existing providers in adopting a public health oriented approach to screening and treatment. They must have skills necessary to counsel clients and to provide quality services and respect women’s concerns and needs.

Methods and Media
All available opportunities should be used to inform the target population identified about cervical cancer:

1. Interpersonal communication (IPC) during household visits, at health center during MCH clinics and any other gathering at individual and group level
2. Printed materials like
   * Leaflets
   * Posters
   * Brochures
   * Flip charts
   * Flash cards
3. Audio visual – like Music for health part IV, slides
4. Mass media - Kuensel and BBS (radio/TV), hotline counseling, website for health and cervical cancer.
VII. MONITORING AND SUPERVISION
Monitoring and supervision of the Pap smear activities will be carried out to study the effectiveness of the cervical cancer prevention. It will be carried out both at the central and district level in a coordinated fashion.

Monthly reporting on Pap smear activities will be done by health centers to the DHSO and he will submit quarterly reports to the RH Program (see Annex VII for reporting format) Supervision will be made annually around July at the centers of Pap smear collection and screening, to oversee the quality and quantity of Pap smear collection, quality of reporting and to sort out constraints faced by cyto-technicians and health workers taking smears.

Supervisory team:
- Program Officer, Reproductive Health, DoPH
- Focal person for cervical cancer screening program
- Representative from cytolaboratory

Monitoring tools
- Checklist
- Verbal interaction
- Check patients’ records and register
- Observe techniques and procedures
- Observe if any/how counseling is done
- Check reagents, equipment, instruments
- Quality assurance activities

Monitoring Indicators

Facility level
- No. of women screened within a given time
- No. of unsatisfactory smears
- No. of abnormal smears recorded
- No. of follow up for abnormal smear
- No. of patient who received treatment for CIN
- No. of patient referred to a higher center for treatment
- No. of reports not received
- Reporting time

Central level
No of patients referred to Kolkota for radiation
No of patients recorded in the tumor register
No of patients who have died of the cancer of cervix in the reported year

Laboratory level
No of smear received vs screened
Regular availability of reagent and equipments/supplies
Staining procedures – crosscheck
Random crosscheck of screened slides
(10% of normal smear to be sent for cross check every month)
Total backlog in the cyto-laboratory
6 monthly random checking of 10% of negative slides from regional centers (where pathology services available)
**Evaluation**

The technical committee (list attached) will meet every 3 years to evaluate the program, oversee progress and to identify constraints and recommend solution to the cervical cancer screening program.
THINGS NEEDED FOR DOING A PAP SMEAR
Before you start calling women for Pap smears, be sure you have the following items:

- Pap smear register
- Pap smear cards
- Pap smear request forms
- Gloves
- Cusco’s speculum of different sizes
- A good light source (spotlight/or torch)
- Allysbury spatulas
- Frosted glass slides
- Fixing solution or spray
- At least 2 slide boxes to store and transfer the slides

If possible, Cusco’s speculum and Allysbury spatula should be sterilized. Do not use Savlon to clean the genital area and do not use any fluid to moisten Cusco’s speculum. Do not do any vaginal examination before doing a Pap smear. Do not do VIA before Pap smear if the 2 modalities are being done at the same time on the same client.
Annexure – II

PROTOCOL FOR SCREENING

1. Age group 25-65 years

2. Modality of taking smear – with Allysbury, sand cytobrush. If abnormal cervix besides erosion is observed, the patient must be referred for colposcopy.

3. If report is inflammation, treat and repeat Pap smear after 2 months. If repeated inflammation, ignore if cervix looks normal. Treat if there is discharge with pruritus, foul smell, or pain abdomen. Do Pap smear after 3 years.

4. Interval of screening – 3 years

5. Modality of reporting – TBS (The Bethesda System 2001)

6. Follow-up of abnormal smears – All women with LSIL, HSIL AGUS, and ASCUS must be referred to gynecologists for colposcopy and further management.

7. Central tumor Register for gyn cancers to be maintained in JDWNRH till Cancer Registry is established

8. Storage of information in soft ware and as slides for at least 10 years
Anexxure III    Screening Test Qualities (and their interpretation)

Following are the commonly used test qualities

**Sensitivity:**  Proportion of women testing positive among those who are diseased  
(For Pap smear it is about 70%)

**Specificity:**  Proportion of women testing negative among those who are non diseased  
(For Pap smear it was found to be about 80%)

**PPV (positive Predictive value):**  Proportion of women having disease among those with positive result

**NPV (negative predictive value):**  Proportion of women having no disease among those with negative result

**Sensitivity and specificity:**  Measure the intrinsic value of diagnostic tests. They are good measures for comparing relative value of different tests with regard to identifying true disease or non-disease.

**PPV+ NPV:**  Measure the clinical utility of the test when applied to a specific population in a particular environment.

Pap smear has lower sensitivity than VIA, but has higher specificity. We may miss CIN with Pap smear, but it leads to less over treatment than VIA which has higher sensitivity, but lower specificity.
### Annexure IV

(Front view)

MINISTRY OF HEALTH  
DEPARTMENT OF PUBLIC HEALTH  
PAP SMEAR REQUEST FORM

<table>
<thead>
<tr>
<th>Pap smear No:</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>Occupation</td>
</tr>
<tr>
<td></td>
<td>CID No.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date of collection</th>
<th>Husband’s name</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Husband’s occupation</td>
</tr>
<tr>
<td></td>
<td>Address in detail:</td>
</tr>
<tr>
<td></td>
<td>Telephone/mobile no:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Marital status</th>
<th>single/married/divorced/widow</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of marriages</td>
<td>:</td>
</tr>
<tr>
<td>No. of marriages of husband</td>
<td>:</td>
</tr>
<tr>
<td>No. of pregnancies</td>
<td>:</td>
</tr>
<tr>
<td>Age at 1st pregnancy</td>
<td>:</td>
</tr>
<tr>
<td>Sexual activity</td>
<td>presently active/formally active/never been</td>
</tr>
<tr>
<td>Sexual partners ever had</td>
<td>one/two/&gt;three</td>
</tr>
<tr>
<td>Age at 1st marriage (years)</td>
<td>&lt;15/15-19/20-24/25-20/&gt;30</td>
</tr>
<tr>
<td>Past history of STD</td>
<td>never/once/twice/&gt;3</td>
</tr>
<tr>
<td>Contraception</td>
<td>nil/barrier/OCP/DMPA/IUD/TL/VO</td>
</tr>
<tr>
<td>Any hormonal therapy</td>
<td>:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous Pap smear</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of LMP</td>
<td>( if Hysterectomy, done for what)</td>
</tr>
<tr>
<td>Last delivery/abortion</td>
<td>:</td>
</tr>
<tr>
<td>Intermenstrual bleeding</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Postcoital bleeding</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Contact bleeding</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Cervical erosion</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Summary of present symptoms, if any:</td>
<td>Discharge/bleeding/pruritus/low abd. Pain</td>
</tr>
</tbody>
</table>

| Treated for CaCx | - Surgery: Yes/No |
|                 | - Radiotherapy: Yes/No |
|                 | - Chemoradiation: Yes/No |
|                 | - Chemotherapy: Yes/No |
|                 | - When treated: Yes/No |
INSTRUCTIONS:

Λ Use same client number on every subsequent Pap smear for the same patient.
Λ Do not take smears when there is bleeding PV
Λ Fill in the form on the reverse side completely and clearly
Λ Screen all women who are sexually active (20 – 60 years)
Λ If there is:  
  : Intermenstrual bleeding
  : Postcoital bleeding
  : Any abnormality of the cervix (except erosion)

Send the patient to a gynecologist, do not take Pap smear
### Annex V

**MINISTRY OF HEALTH**  
**DEPARTMENT OF PUBLIC HEALTH**  
**PAP SMEAR REPORT FORM**

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s No:</td>
<td>Name:</td>
</tr>
<tr>
<td></td>
<td>Age:</td>
</tr>
<tr>
<td></td>
<td>Occupation</td>
</tr>
<tr>
<td></td>
<td>CID No.</td>
</tr>
<tr>
<td></td>
<td>Husband’s name:</td>
</tr>
<tr>
<td></td>
<td>Husband’s occupation:</td>
</tr>
<tr>
<td></td>
<td>Address:</td>
</tr>
<tr>
<td></td>
<td>Tel/mobile No:</td>
</tr>
</tbody>
</table>

#### SPECIMEN ADEQUACY
- ( ) Satisfactory for evaluation
- ( ) Unsatisfactory for evaluation (reason) ……………

#### INTERPRETATION/RESULT
- ( ) Negative for Intraepithelial lesion or malignancy

##### SPECIFIC ORGANISMS
- ( ) *Trichomonas vaginalis*
- ( ) Fungal organisms morphologically consistent with *Candida species*
- ( ) Shift in flora suggestive of *Bacterial vaginosis*
- ( ) Bacterial organisms morphologically consistent with *Actinomyces species*
- ( ) Cellular changes consistent with *Herpes simplex virus*

##### OTHER NON NEOPLASTIC FINDINGS
- ( ) Reactive cellular changes associated with
  - ( ) Inflammation
  - ( ) Radiation
  - ( ) Intrauterine contraceptive device (IUD)
- ( ) Glandular cells status post hysterectomy
- ( ) Atrophy
- ( ) Endometrial cells in a women ≥ 40 years of age

#### EPITHELIAL CELL ABNORMALITIES

##### SQUAMOUS CELL
- ( ) Atypical Squamous Cells of Undetermined Significance (ASCUS)
- ( ) Low Grade Squamous Intraepithelial Lesion (LSIL) encompassing *HPV infection*
- ( ) High Grade Squamous Intraepithelial Lesion (HSIL) encompassing:
  - Moderate dysplasia/CIN II, Severe dysplasia/CIN III, CIS

##### GLANDULAR CELLS
- ( ) Atypical Glandular cells of Undetermined significance (AGUS)
- ( ) Atypical endocervical cells of Undetermined significance
- ( ) Atypical endometrial cells of Undetermined significance
- ( ) Endocervical adenocarcinoma in situ
- ( ) Adenocarcinoma:
  - ( ) Endocervical type
  - ( ) Endometrial type
  - ( ) Extruterine
  - ( ) Not otherwise specified

#### Recommendations:
- ( ) Smear unsatisfactory, please repeat……………………………………………………
- ( ) Repeat smear in………..month
- ( ) Repeat smear after anti-inflammatory treatment
- ( ) Gynaecological examination
- ( ) Biopsy necessary

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyto Technician:</td>
<td></td>
</tr>
<tr>
<td>Cyto Technologist:</td>
<td></td>
</tr>
<tr>
<td>Pathologist:</td>
<td></td>
</tr>
<tr>
<td>Date of report:</td>
<td></td>
</tr>
</tbody>
</table>

**Annexure VI**  
*(Front view)*
PAP SMEAR CARD

1. Do not lose this card. Ministry of Health
2. Bring this card each time you Department of Public Health come for Pap smear.
3. Remember your Pap smear number.
4. Collect your Pap smear report within two months Name:
5. Collect your Pap smear report within two months Name:
6. Follow the instruction of health personnel Age:

(Behind/Rear view)

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Date</th>
<th>Result</th>
<th>Next visit</th>
<th>If abnormal, colposcopy/treatment done or not</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Annexure VII

MONITORING CHECK LIST FOR THE HEALTH FACILITIES WITH ACTIVE PAP SMEAR SCREENING PROGRAM

Name of the facility: Dzonkghag

Name of the supervisor:

Date of visit:

1. Supplies & Equipment:

- Protocol available: Yes/No
- Training manual available: Yes/No
- Pap smear request forms available: Yes/No
- Pap smear reporting system: Monthly/Quarterly/Annually
- Reagent availability: Adequate/in adequate
- Slides availability: Adequate/inadequate
- Magnel kit: Yes/No
- Light Source: Yes/No
- Speculum: Enough/Not enough
- Spatula: Enough/Not enough
- Drum: yes/No
- Cotton swab: Yes/No
- Autoclave: Yes/No
- IEC materials: Available/Not available

2. Knowledge of the Health personnel (Q&A):

- Are you trained on pap smear collection techniques: Yes/No
- Knowledge on cervical cancer: Yes/No
- Knowledge on pap smear: Adequate/inadequate
- Knowledge on treatment protocol: Adequate/inadequate
- Knowledge on follow up: Adequate/inadequate

3. Observation of skills:

- Attitude towards the clients: Positive/Negative
- Set up of pap smear screening room: Satisfactory/Unsatisfactory
- Enough light: Yes/No
- Infection control measures: Adequate/Inadequate
- Pre and post procedure counseling: Yes/No
- Collection of smear and fixation: Satisfactory/Unsatisfactory
- Packing of slide for transportation: Satisfactory/Unsatisfactory

4. Interview:

- How often do you use the IEC materials: Daily/sometimes/not at all
- How useful is the IEC material: Very useful/Not useful
If not useful, what are the changes that need to be considered

How often do you use IEC materials: daily/some time/not at all
How useful is the IEC material: Relevant/Not relevant
If not relevant, what are the changes that you would like to make:

How often do you use the Magnel kit to counsel the clients?
: Daily/as and when required/Not available
Do you have any problem while providing cervical cancer screening: Yes/No

5. Client’s interview:

Do you know what is Pap smear: Yes/No/Little
From where did you hear about it: .................
Did the health worker explain about the procedures: Yes/No
When will you come for the report: .....................

Comments by the supervisor:

Recommendations by the supervisor:

Signature of the supervisor:
### Annexure VIII

<table>
<thead>
<tr>
<th>Serial Number</th>
<th>Date of Registration</th>
<th>Name of Patient</th>
<th>Age</th>
<th>Age at 1st preg.</th>
<th>Date/s of Pap smear/s</th>
<th>Permanent address</th>
<th>Referred from where</th>
<th>Presenting symptoms</th>
<th>Stage of disease</th>
<th>Referred to Kolkata</th>
<th>Surgery/radiotherapy</th>
<th>Staging in Kolkata</th>
<th>Surgery + radiotherapy</th>
<th>Follow-up</th>
<th>If deceased, date of death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Tumor register

**Instruction:**
Every regional referral hospital should maintain a regional tumor register.
Annually, it should be compiled into the central tumor register which will be maintained in JDWNRH, Thimphu
Annexure IX

MONTHLY PAP SMEAR ACTIVITIES REPORT

<table>
<thead>
<tr>
<th>Activities</th>
<th>25–34yrs</th>
<th>35–44yrs</th>
<th>45-54yrs</th>
<th>55-65yrs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of new clients screened</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of old clients screened</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of woman referred</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LSIL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSIL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reporting Official:

Sign and seal
### Coding for different districts

<table>
<thead>
<tr>
<th>District</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paro</td>
<td>A</td>
</tr>
<tr>
<td>Thimphu</td>
<td>X</td>
</tr>
<tr>
<td>Trongsa</td>
<td>O</td>
</tr>
<tr>
<td>Bumthang</td>
<td>B</td>
</tr>
<tr>
<td>Sarpang</td>
<td>E</td>
</tr>
<tr>
<td>Gelephu</td>
<td>G</td>
</tr>
<tr>
<td>Samtse</td>
<td>SH</td>
</tr>
<tr>
<td>Trashigang</td>
<td>TG</td>
</tr>
<tr>
<td>Monggar</td>
<td>M</td>
</tr>
<tr>
<td>Punakha</td>
<td>P</td>
</tr>
<tr>
<td>Tsirang</td>
<td>T</td>
</tr>
<tr>
<td>Haa</td>
<td>H</td>
</tr>
<tr>
<td>PemaGatshel</td>
<td>PT</td>
</tr>
<tr>
<td>S/Junkhar</td>
<td>SJ</td>
</tr>
<tr>
<td>Gasa</td>
<td>GA</td>
</tr>
<tr>
<td>Lhuntse</td>
<td>L</td>
</tr>
<tr>
<td>Trashiyangtse</td>
<td>TY</td>
</tr>
<tr>
<td>Dagana</td>
<td>DZ</td>
</tr>
<tr>
<td>Chukha</td>
<td>C</td>
</tr>
<tr>
<td>Zhemgang</td>
<td>Z</td>
</tr>
<tr>
<td>Wangdue</td>
<td>W</td>
</tr>
</tbody>
</table>
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>RH</td>
<td>Reproductive Health</td>
</tr>
<tr>
<td>LSIL</td>
<td>Low grade squamous intraepithelial lesion</td>
</tr>
<tr>
<td>HSIL</td>
<td>High grade squamous intraepithelial lesion</td>
</tr>
<tr>
<td>AGUS</td>
<td>Atypical glandular cells of undetermined significance</td>
</tr>
<tr>
<td>STI</td>
<td>Sexually transmitted infections</td>
</tr>
<tr>
<td>HPV</td>
<td>Human Papilloma Virus</td>
</tr>
<tr>
<td>HPE</td>
<td>Histopathology examination</td>
</tr>
<tr>
<td>SCJ</td>
<td>Squamo-columnar junction</td>
</tr>
<tr>
<td>CIN</td>
<td>Cervical intraepithelial neoplasia</td>
</tr>
<tr>
<td>CIS</td>
<td>Carcinoma-in-situ</td>
</tr>
<tr>
<td>TZ</td>
<td>Transformation zone</td>
</tr>
<tr>
<td>LEEP</td>
<td>Loop electrosurgical excision procedure</td>
</tr>
<tr>
<td>LLETZ</td>
<td>Large loop excision of transformation zone</td>
</tr>
<tr>
<td>VIA</td>
<td>Visual inspection with acetic acid</td>
</tr>
<tr>
<td>HLD</td>
<td>High level disinfection</td>
</tr>
</tbody>
</table>
Reference

1. Practical Gynecologic Oncology, III edition: Jonathan S. Bereck and Neville F. Hacher
2. Gynecologic Oncology, Hoskins
5. Large Loop Excision of the Transformation Zone: A practical guide to LLETZ - Water Prendiville
7. Pathology of Early Cervical Neoplasia: Christopher P. Crum, Edmand S. Cibas and Annette R. Lee
8. Manual for Pap smear (developed by RH Program in 1999)
Technical committee for 1\textsuperscript{st} edition

1. Dr. Ugen Tshomo, Gynecologist and Focal Person for Pap Smear Program, JDWNRH
2. Dr. I. K Mohanta, Chief pathologist, JDWNRH
3. Dr. Krishna Sharma, Pathologist, JDWNRH
4. Mr. Dorji, Medical Technologist, JDWNR Hospital
5. Ms. Wangmo, Cyto Technician, JDWNRH
6. Mr. Tshering Dorji, Cyto Technician, Mongar RR Hospital
7. Ms. Dorji Zangmo, ANM, RHU, JDWNRH
8. Ms. Tawmo, ANM, Mongar RR Hospital
9. Ms. Dago Dema, ANM, Paro Hospital
10. Ms. Pem Zam, APO, RH, NCDD, DoPH

Technical committee for 2\textsuperscript{nd} edition

1. Dr. Ugen Tshomo, Gynecologist and Focal Person for Pap Smear Program, JDWNRH
2. Dr. I. K Mohanta, Chief pathologist, JDWNRH
3. Dr. Sonam Gyamtsho, OBGYN, Mongar RR Hospital
4. Ms. Karma Tshering, UNFPA, Thimphu
5. Ms. Ugyen Zangmo, Dy. CPO, RH program
6. Ms. Wangmo, Cyto Technician, JDWNRH
7. Ms. Tshomo, Cyto Technician, Samtse