

# IMAP Statement on preventing cervical cancer

Cervical cancer, largely preventable, is one of the main causes of cancer death in women. Most women die of the disease when they are still in the workplace and caring for their families, at a high cost to society and to the economy.

## Introduction

This Statement has been prepared by the International Medical Advisory Panel (IMAP) and was approved in November 2016.

Cervical cancer, largely preventable, is one of the main causes of cancer death in women. In 2012, 528,000 new cases of cervical cancer were diagnosed and 266,000 women died of the disease, nearly 90 per cent of them in low to middle income countries. Deaths due to cervical cancer are projected to rise by almost 25 per cent over the next 10 years.<sup>1</sup> Most women die of the disease when they are still in the workplace and caring for their families, at a high cost to society and to the economy.

Cervical cancer prevention encompasses a wide range of interventions, which provide IPPF Member Associations with multiple opportunities within the continuum of care to decrease mortality and morbidity from the disease. These opportunities include community engagement and policy change as well as clinical interventions. These activities can be incorporated into existing services to enhance them and provide a wider service offer to women. As such, they form one of the key components of the Integrated Package of Essential Services which promotes basic service provision for the most pressing sexual and reproductive health needs of the population.

## The purpose of this Statement

This Statement is intended to provide up-to-date information on cervical cancer, outline activities for its prevention, and provide recommendations to support Member Associations on the practical ways that they can assimilate interventions in their settings so that cervical cancer prevention care is integrated as part of sustainable health provision, in line with IPPF's mission.

## Intended audience

This Statement is primarily intended for use by IPPF Member Associations for all their clinical and non-clinical staff. The content is also aimed at other organizations, activists and researchers, and policy and decision makers who are working to improve sexual and reproductive health coverage in resource-poor settings by making use of existing human resources for health.

## Key facts about cervical cancer

The primary cause of cervical pre-cancer and cancer is persistent infection with human papilloma virus (HPV). HPV infection is a common sexually-acquired infection and will resolve without treatment in most women and men. It also causes genital warts in both sexes. In a minority of cases, HPV does not resolve and in women this may lead to the development of cervical pre-cancer lesions. If not treated, this could progress to cancer over a period of 10–20 years.

Women living with HIV are especially at risk because they are more likely to develop persistent human papilloma virus infections at an earlier age and to develop cancer sooner. Other risk factors include early age of first sexual activity, smoking, multiple sexual partners and having partners with multiple partners, co-infection with other sexually transmitted infections, high parity and young age at first birth. The use of oral contraception for more than five years is indirectly associated with cervical cancer.

The extended timeline between exposure to HPV and development of disease gives multiple points at which screening and other preventative measures could result in improved health outcomes in a timely, acceptable way with low-cost interventions.<sup>2</sup>

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## Primary prevention of cervical cancer

HPV vaccination protects women from human papilloma virus infection prior to initiation of sexual activity. Vaccines provide protection from HPV 16 and 18 which are the two high risk HPV types that most commonly cause cervical cancer and are responsible for approximately 70 per cent of cases. Two vaccines that prevent infections from high risk HPV types 16 and 18 are currently licensed in most countries. One of these vaccines is quadrivalent and reduces cervical cancer by 70 per cent. It also prevents infections from HPV types 6 and 11 which cause 90 per cent of genital warts. A newly registered nonavalent vaccine (9vHPV), which protects against an additional five HPV sub-types, prevents 90 per cent of invasive cervical cancer, high grade pre-cancer and genital warts.<sup>3</sup>

It should be noted that cervical screening is still required even if a woman is vaccinated because vaccines do not protect against all HPV types. Older women who have not been vaccinated will also need access to screening. It is important to administer the vaccine to young girls because the vaccines do not treat existing HPV infection.

## Secondary prevention

Secondary prevention of cervical cancer consists of the following interventions:

- Assess for the presence of cervical pre-cancer with **screening** methods – human papilloma virus DNA testing, visual inspection with acetic acid or cytology.
- Screening is followed by **treatment** of women who screen positive with cryotherapy or excision of pre-cancerous areas with loop electrosurgical excision procedure.
- In higher resource settings, screening may be combined with a diagnostic test in the form of biopsy – ‘screening, diagnosis and treatment’.

It is imperative that all programmes that aim to reduce mortality and morbidity from cervical cancer should provide **both screening and treatment** as a minimum, using the most effective interventions that the context allows. Treatment should occur at the same time as screening in a ‘single visit approach’ wherever possible so that women are not lost to follow-up for treatment.

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## Screening with human papilloma virus DNA testing

Key technical facts:

- HPV testing is an objective test that detects the viruses which cause cervical cancer. It performs better than cytology when predicting risk of developing high grade or invasive disease.<sup>4</sup> It is recommended as the first triage test in all settings.
- A sample of cells is taken from the cervical area with a swab or brush either by a health care professional using a speculum during a pelvic examination or from high in the vagina by the woman herself (self-sampling).
- Human papilloma virus DNA testing can replace screening tests in some basic contexts as it is a reliable test for diagnosing HPV when it is present.
- Because it does not confirm presence of pre-cancer, best practice combines HPV DNA testing with a second test (either a specific HPV test or cytology) for increased sensitivity for the presence of pre-cancer.

## Screening and treatment in low resource settings

### SCREENING WITH HUMAN PAPILLOMA VIRUS DNA

In low resource settings, test kits such as careHPV™ are designed for self-sampling and can be used as a primary screening test. These do not require electricity and can be carried out in small spaces with results on the same day, with limited training. While the results are not as sensitive as those taken by a health care provider,<sup>5</sup> self-sampling in this context is recommended to reach women who do not have access to a regular screening programme, as screening uptake and detection of moderate grade pre-cancer has been shown to increase with self-collection. This could reduce cost by bypassing a provider and increase convenience to the woman.<sup>6</sup>

When an HPV DNA test is positive, women can be referred for a second screening test and treatment as below. If additional tests are unavailable, then a direct referral for treatment is recommended.

### SCREENING WITH VISUAL INSPECTION WITH ACETIC ACID (VIA)<sup>7</sup>

Key technical facts:

- This method uses inspection of the cervix with the naked eye after application of dilute (3–5 per cent) acetic acid. Pre-cancerous changes are visible and described as ‘acetowhite’.
- Visual inspection with acetic acid requires use of a speculum and light source and a trained health care provider. After applying the acetic acid using a swab, the provider waits for at least one minute.
- Any acetowhite changes that remain after one minute are more likely to be associated with cervical pre-cancer or cancer.
- In basic settings, visual assessment for treatment may be used after positive HPV DNA testing results.
- Women should receive treatment if VIA is used as primary screening and the result is abnormal.

The advantages of VIA are that it does not require many resources. It is relatively cheap and the supplies required are locally available, and it does not need laboratory facilities. Results are immediate so treatment can be given at the same visit. Training for providers from a wide range of cadres can be accomplished in a few days using a competency-based approach.

While visual inspection with acetic acid is a simpler test to perform than cytology, it is still invasive and requires the use of a speculum to inspect the cervix. Unlike cytology or biopsy, it does not definitively diagnose the grade of any pre-cancerous lesions and is also a subjective test depending on the skills and experience of the provider performing the examination. Training should therefore be facilitated through validated programmes, and skills must be used regularly with refresher courses provided.

Quality control and quality assurance for VIA is particularly important because it can be liable to inter-observer variation especially for low grade pre-cancerous changes. This can be achieved through supervision and routine monitoring which will require significant resource planning. Even with training, VIA has a high false-positive rate; in other words, more women will be sent for treatment than is necessary.

Cervical cancer prevention initiatives are multi-dimensional and provide Member Associations of all backgrounds with opportunities to contribute to the reduction of mortality and morbidity.

In low resource settings, services can be initiated with the best elements available, which can evolve with support over time, with the priority to move towards HPV vaccinations for maximum long-term public health benefit.

### TREATMENT WITH CRYOTHERAPY

Key technical facts:

- Cryotherapy freezes abnormal areas on the cervix by applying a highly cooled metal disc (cryoprobe).<sup>8</sup>
- The low temperature of the cryoprobe is achieved using a tank with compressed carbon dioxide (CO<sub>2</sub>) or nitrous oxide (N<sub>2</sub>O) gas.
- Cryotherapy can be performed by any provider who is skilled in pelvic examination and trained in cryotherapy.
- Treatment takes about 15 minutes and is associated with only mild discomfort so no anaesthesia is required. Following cryotherapy, the frozen area regenerates to its normal state.

The most significant advantage of cryotherapy is that it is performed at the same time as a positive visual inspection with acetic acid. Compressed gas tanks should be in place to ensure a seamless service. Robust infection prevention and appropriate care of the equipment are essential. The patient should also be advised that she may have a profuse, watery discharge after treatment and to avoid sexual intercourse until this stops (or use a condom if intercourse cannot be avoided). As with VIA, training and supervision are essential to maintain skills.

## Screening and treatment in high resource settings

### SCREENING WITH HPV DNA

In settings where more resources are available, accuracy can be improved using a second test (either another HPV test for specific types or cytology).<sup>9</sup> If this second test is positive, referral should be made for colposcopy and biopsy where they are available, as below.<sup>10</sup> If cytology is negative, the woman can be rescreened for HPV DNA after 12 months.

### SCREENING WITH CYTOLOGY

Key technical facts:

- Cytology involves taking a sample of cells from the cervix using a wooden spatula or brush.
- The 'smear' sample is either fixed on a slide at the facility (Pap smear) or placed in a transport medium (liquid-based cytology) and then sent to the laboratory where experts examine the cells in the sample under a microscope.
- If abnormal cells are seen on microscopic examination, the extent of their abnormality is classified using the Bethesda System.<sup>11</sup>

The main advantage of cytology is that it is better at predicting the presence or absence of disease compared to visual inspection with acetic acid, resulting in fewer women being treated than those screened with VIA. Cytology requires more resources – skilled personnel, training, equipment and laboratory costs. There is also a risk of loss to follow-up because of delays in treatment related to the time it takes to assess a specimen, which could be days or even weeks.

### DIAGNOSTIC TESTS

Diagnostic tests are performed if either screening test is positive and before treatment. Such tests can reduce the number of women who need treatment as not all women who screen positive with any method have pre-cancer or cancer, because no test can be 100 per cent accurate. As with cytology, an additional step at this stage can cause delay and potential loss to follow-up.

Diagnostic methods include colposcopy, which uses specialized equipment to visualize the cervix with magnification. Small biopsies can be taken at the same time, which determine the degree of abnormality present. To be beneficial, both require specific high level skills and equipment.

### TREATMENT OF PRE-CANCER

Key technical facts:

- Removal of pre-cancerous changes should be carried out with loop electrosurgical excision procedure (LEEP), **not** cold knife cone.<sup>12</sup>
- LEEP is the removal of abnormal areas from the cervix using a loop made of thin wire powered by an electrosurgical unit.
- LEEP serves a dual purpose – it treats the pre-cancer by removing the affected tissue, and it also produces a specimen for pathological examination.
- The procedure can be performed under local anaesthesia on an outpatient basis and usually takes less than 30 minutes. The patient should stay at the outpatient facility for a few hours to ensure that bleeding does not occur.
- Patients should avoid sexual intercourse for one month or use a condom if intercourse cannot be avoided.

Loop electrosurgical excision procedure should only be performed by a trained health care provider who has demonstrated competence in the procedure and who can recognize and manage intra-operative and post-operative complications such as haemorrhage. It is therefore best carried out in facilities that can manage complications.

Member Associations should develop relationships with national or international bodies to procure the vaccines to enable a sustainable supply chain.

### HOW OFTEN SHOULD WOMEN BE SCREENED AND ATTEND FOR FOLLOW-UP CARE?

Member Associations should be aware of national cervical cancer prevention guidance on ages and intervals for screening as this will dictate local programming. The following is recommended as a minimum:

- Screening should be performed at least once for women aged 30–49 years – the target age group where most benefits can be achieved.<sup>13</sup> The recommended age range and frequency for high resource settings is a maximum of five-yearly between the ages of 25 and 65 years.<sup>14</sup>
- Women who test negative with visual inspection with acetic acid or cytology should be re-screened after three to five years.<sup>15</sup>
- Among women who test negative with HPV testing, re-screening should be done after a minimum interval of five years.<sup>16</sup>
- All women who have been treated for pre-cancer should be re-screened after one year.
- Women with HIV should be screened for HPV at time of diagnosis if sexually active, and screened twice as many times in their lifetime as the general population.<sup>17</sup>
- The management of abnormal screening results for HIV-positive women with positive screening is the same as in the general population.
- Post-partum women can be offered primary screening six weeks post-delivery and visual inspection with acetic acid at six months.
- Women can stop screening in high resource settings at 65 years if they have had consistently negative results during the previous 15 years or longer. In low resource settings, screening can cease at 49 years.

### Tertiary prevention and palliative care

A small number of women will be diagnosed with cancer at screening. They need to be referred for treatment of invasive cancer with surgery, radiotherapy, chemotherapy or a combination in a tertiary level facility. Palliative care should be able to ensure that quality of life for women and their families is optimized using medical and non-medical means in primary and secondary care.<sup>18</sup>

Lower level providers can offer opportunistic counselling during visits for other services such as testing for reproductive tract infections, contraception and antenatal care, and can provide signposting on where and when to go for screening.

## Summary recommendations and opportunities for intervention\*

### SERVICE DELIVERY

- It is crucial to assess the demographics of the target population to determine whether cervical cancer prevention activities will have a positive impact. Community activities should be planned before the service is set up, with a special focus on the importance of vaccination and screening for young women.
- Cost-effectiveness of vaccination requires assessment to determine delivery strategy (health facility, school, community outreach).<sup>19</sup>
- The World Health Organization recommends vaccination of adolescent girls before sexual activity commences<sup>20</sup> and increasing access by combining this with other interventions simultaneously – the ‘one system multiple intervention’ approach.<sup>21</sup> It is recommended that opportunities to partner and support government vaccination interventions, either as a planned activity or on an opportunistic basis, should be investigated to safely co-administer with other childhood vaccinations such as diphtheria, tetanus and pertussis (DTP) and hepatitis B.
- Member Associations should develop relationships with national or international bodies to procure the vaccines to enable a sustainable supply chain.
- Clinical intervention will only succeed in reducing mortality and morbidity from cervical cancer where **screening** is combined with **treatment** of pre-cancer and cancer.
  - The service delivery approach that is recommended is the single visit approach which leads to fewer women lost to follow-up. This requires training providers in screening, treatment with cryotherapy or loop electrosurgical excision procedure, and providing continuous supportive supervision and adequate equipment.
  - Where screening takes place with no opportunity for immediate treatment, the preferred alternative is treatment at the same site at a separate time by suitably equipped and trained outreach teams. Referring to a

second facility at a separate time increases loss to follow-up as does performing an additional diagnostic test.

- Excellent services depend on inter-connection among levels of service across a geographical area.
- Referral mechanisms for those who require further investigations, treatment or palliative care must be agreed at the service planning stage. Member Associations must build relationships with tertiary facilities to enable onward referral for cancer cases diagnosed during screening. They may also have opportunities to influence policy about the availability of opiates, guidance on community prescribing and maintaining the supply chain.

### INTEGRATION

- Service planning should consider the potential impact of introducing new interventions on the overall quality of all services provided and not to increase strain on existing activity. Plans should consider how any potential shortcomings will be addressed.
- Cervical cancer prevention activities should align with and complement existing reproductive health services. During the planning phase, consider the ages of women and girls who attend and consider non-medical interventions that can run side by side with clinical services. This includes raising awareness of the symptoms of cervical cancer, plus the benefits of screening and vaccination in conjunction with other sexual health messaging including HIV testing.

Examples:

- If there is a bias in favour of child health, a targeted approach in favour of HPV vaccinations may be the most appropriate service.
- Counselling (but not screening) can take place as part of routine antenatal/post-natal care by midwives.
- Integrating cervical cancer prevention messaging in contraceptive counselling.
- Community-based activities should also involve men, for increased awareness raising.
- Lower level providers can offer opportunistic counselling during visits for other services such as testing for reproductive tract infections, contraception and antenatal care, and can provide signposting on where and when to go for screening.
- Consider training lower level providers to provide screening and treatment services to increase uptake in low resource settings.

\* Further details on initiating a prevention programme can be found in chapter 2: *Comprehensive Cervical Cancer Control. A Guide to Essential Practice*.<sup>1</sup>



### QUALITY ASSURANCE

- When selecting providers for the screening programme, clinical competencies should be assessed prior to training.
- Training in a validated programme and follow-up supportive supervision are mandatory for providers to ensure quality is high and that skills are maintained. Logistics for training, follow-up and audit should be resourced appropriately and planned in advance of training and roll-out of services.
- Coordinated planning of quality improvement activities is essential to programme success; this includes assessing safety effectiveness and how service users experience screening and treatment.
- Monitoring and evaluation should include data collection on serious adverse events, complications and loss to follow-up as well as numbers screened and percentage treated. This includes monitoring of HPV vaccinations by dose and age to ensure that adverse events are recorded.<sup>22</sup>
- HPV testing in each setting must be validated because differences in storage, temperature and transport could affect test accuracy.
- Where possible, screening activities should contribute to a national organized programme network to strengthen national cervical cancer prevention efforts. This includes registering women with disease nationally if such an infrastructure exists.

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### ADVOCACY AND EXTERNAL ENGAGEMENT

- At national level, Member Associations should advocate for the importance of screening and treatment especially where a national consensus is absent, including at tertiary level and in national policy and guidelines.
- Partnerships are critical to coordinate procurement and support of services, for cooperation, for behaviour change communication about the benefits of cervical cancer prevention therapies and to dispel myths about vaccination.
- Ensure procurement and logistics of supplies and equipment at sustainable levels with ministries of health and other relevant agencies.

### Conclusions

Cervical cancer prevention initiatives are multi-dimensional and provide Member Associations of all backgrounds with opportunities to contribute to the reduction of mortality and morbidity.

For planning at national and regional levels, the following should be assessed: affordability, cost-effectiveness and sustainability of introducing HPV vaccines, the screen-and-treat approach and a referral system for treatment at national level.

In low resource settings, services can be initiated with the best elements available, which can evolve with support over time, with the priority to move towards HPV vaccinations for maximum long-term public health benefit. In areas where no mass screening exists, infrastructure for HPV testing, diagnosis and treatment should be developed.

New treatments such as cold coagulation and cryopen, which bypass some of the challenges with gas cylinders, are promising innovations for low resource settings. These are being investigated with positive results in pilot and research projects.

The service delivery approach that is recommended is the single visit approach which leads to fewer women lost to follow-up.

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## WHO WE ARE

The International Planned Parenthood Federation (IPPF) is a global service provider and a leading advocate of sexual and reproductive health and rights for all. We are a worldwide movement of national organizations working with and for communities and individuals.



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