health
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REPUBLIC OF SOUTH AFRICA

2030 NDP

Cervical Cancer Prevention and Control Policy

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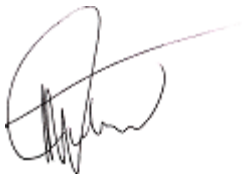
FOREWORD

Cervical cancer, along with maternal deaths, has been identified as a national priority in South Africa as well as other Sub-Saharan African countries. Cervical cancer is the second most common cancer among women in South Africa, after breast cancer. Due to limited access to prevention, early diagnosis and treatment, cervical cancer is often fatal. According to the National Cancer Registry, there were 5 785 new cases in 2012, i.e. an age standardised incidence rate of 24.17 per 100 000 women.

In order to mitigate the impact of cervical cancer on health and socio economic development, the country needs to implement a comprehensive cervical cancer prevention and management programme. This entails implementation of three interdependent strategies, namely: (i) reducing oncogenic HPV infections, (ii) detecting and treating cervical pre-cancer, and (iii) providing timely treatment and palliative care for invasive cancer.

This policy update takes the above strategies into account. It also recognises technological advancements in cervical cancer prevention methods and new evidence on prevention and treatment approaches in the context of an endemic HIV epidemic. Furthermore, this policy makes provision for all women over the age of 30 years to undergo three free cervical cancer screening tests at ten year intervals in South Africa's public health sector. It also clarifies the availability and screening cycles for women living with HIV.

Cervical cancer prevention and control is part of a broad based Sexual and Reproductive Health (SRH) programme implemented by the national Department of Health. A number of concurrent health system interventions operating through other government priority programmes ensure that the necessary infrastructure, medical technology, competent health workforce, and other resources are provided to facilitate effective implementation and monitoring of these policy recommendations.



Dr Aaron Motsoaledi
Minister of Health
Date: June 2017

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The national Department of Health would like to acknowledge the exceptional contributions of the writing group. The authors of this document would like to make it clear that any conclusions in this document and standards are derived from the literature evidence and are not necessarily their opinions.

The contributors consist of surgeons, oncologists, radiologists, nuclear physicians, pathologists, obstetricians and gynaecology specialists. In addition, experts in various fields including the civil society and other interest groups were contacted when necessary for further opinions.

It is also worth noting that although considerable reference was made to the World Health Organization (WHO) guidelines, the cervical prevention and control policy, 2017 document is aligned to the healthcare situation in South Africa. The department would like to acknowledge the following team members:

NDOH leads: Dr Pearl Holele and Dr M Makua
Clinical experts: Prof. Lynette Denny, Dr Mary Kawonga and Dr Nancy Kidula
Cervical policy costing: Naomi Lince-Deroche, Craig van Rensburg and Daphne Ncube (HE2RO)
Monitoring and Evaluation: Ronelle Niit (and team)
Other key contributors/technical experts: Prof. Greta Dreyer, Prof. Jennifer Moodley, Melanie Pleaner, Prof. Helen Rees, Dr Sinead Delany-Moretlwe, Admire Chikandiwa, Saiqa Mullick, Pedro Pisa, Prof. Gerhard Lindeque, Prof. Sam Monokoane, Dr T L Msibi; Dr Manivasan Moodley, Prof. Jay Bagratee, Dr A Kambaran and Dr N Mayat from KwaZulu-Natal, Dr Elizabeth Mbizvo and Dr Shaidah Asmal, Suzette Jordaan and team and Ministerial Advisory Committee for cancers (Chair and team)
National Department of Health contributors: Dr Anban Pillay, Dr Peter Barron, Thembi Zulu, Gavin Steel, Jane Riddin, Bilqees Sayed, Keshika Sivnannan, Vuyiswa Lebese, Dineo Tshikedi, Dimpho Chweneyagae, Prof Melvyn Freeman and Sandyha Singh
Partners and CSOs: S Meyer, M Seguin, L Pretorius, N Kotschan, Linda Greeff, Gail Walters and Fran Lewis

MP Matsoso
Director-General: Health
Date: June 2017

ABBREVIATIONS AND ACRONYMS

AIDS	acquired immunodeficiency syndrome
ART	Antiretroviral therapy
ASCUS	Atypical Squamous Cells of unknown significance
ASIR	Age Standardised Incidence Rate
CIN	Cervical intraepithelial neoplasia
CIS	Carcinoma in situ
DBE	Department of Basic Education
DHET	Department of Higher Education and Training
DHIS	District Health Information System
DNA	Deoxyribonucleic acid
DOH	Department of Health
EPI	Expanded Programme on Immunisation
HIS	Health Information System
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
hrHPV	High risk Human Papilloma Virus
HSIL	High grade squamous intraepithelial lesions
ICC	Invasive cervical cancer
ICPD	International Conference on Population and Development
IARC	International Agency for Research on Cancer
LBC	Liquid based cytology
LEEP	Loop electrosurgical excision procedure (same as LLETZ)
LLETZ	Large loop excision of the transformation zone (same as LEEP)
LSIL	Low grade squamous intraepithelial lesions
M&E	Monitoring and evaluation

MCC	Medicines Control Council
MCWH	Maternal, child and women's health
MDG	Millennium Development Goal
MTSF	Medium Term Strategic Framework
NCFP	National contraception and fertility planning policy and service delivery guidelines
NCR	National Cancer Registry
NHLS	National Health Laboratory Service
NIDS	National Indicator Data Set
NSDA	National Service Delivery Agreement
NSP	National Strategic Plan for HIV, STIs and TB
Pap smears	Papanicolaou smears
PCR	Polymerase chain reaction
PHC	Primary health care
RNA	Ribonucleic acid
SACEMA	South African Centre for Epidemiological Modelling and Analysis
SMS	Short messaging system
SA	South Africa
SRH	Sexual and reproductive health
STI	Sexually transmitted infection
TB	Tuberculosis
TOP	Termination of pregnancy
UN	United Nations
VIA	Visual inspection with acetic acid
WHO	World Health Organization

INTRODUCTION

Cervical cancer is one of the most common cancers diagnosed in women in South Africa. The main cause of cervical cancer is infection of the cervix by the Human Papillomavirus (HPV), of which strains 16 and 18 are the most common types associated with the development of cervical cancer.

Cervical cancer is a relatively unique cancer in that it has a long precursor phase, during which risk and abnormalities can be detected by screening. Screening can now be done using either cytology, SVA (single visit approach) or by detection of persistent infection with high risk types of HPV. If a positive screening test is left untreated, a woman is at high risk of developing cervical cancer over a five to 30 year period. Once these abnormalities are detected and treated, progression to invasive cancer of the cervix can be prevented.

The national Department of Health has a broad based programme to address several women's health issues, including cancer of the cervix. Organised cervical cancer screening for eligible women is the central element within the department's existing cervical cancer prevention strategy. This policy updates the existing strategy to take into account technological advancements in cervical cancer prevention and new evidence on screening, approaches and methods in context of the HIV epidemic.

This updated policy also makes provisions for the introduction of primary prevention of cervical cancer through HPV vaccination of young girls aged nine to12 and the promotion of awareness regarding HPV prevention through safe sex practices and dual protection (barrier plus other methods of contraception). It also provides for secondary prevention by strengthening cytology screening and introducing in the public sector both HPV DNA-based screening where resources permit and SVA, which is referred to as test-and-treat, in resource-limited settings where treatment immediately follows a positive screening test such as VIA (visual inspection with acetic acid). The policy makes provision for three free cervical cancer screening tests in ten year intervals for all HIV negative, asymptomatic women over the age of 30 attending public sector health services. It also introduces new guidelines for cervical cancer screening for women living with HIV. Screening these target groups has been proven most effective at detecting and preventing cervical cancer in women by numerous international and local research studies.

A number of concurrent health system interventions through other government priority programmes will ensure that the necessary infrastructure, medical technology, and material and information resources will be provided to facilitate implementation and monitoring of these policy provisions. For example, the policy makes provision for: integrating HPV vaccination within strengthened school health services; training of staff to effectively screen, diagnose, manage and treat cervical pre-cancer; adequate referral mechanisms to ensure continuity of care for women with positive screening test results; infrastructure and resources to treat women with positive screening test results; and community mobilisation to create demand for services.

WHAT'S NEW IN THE REVISED POLICY

Alignment to the global framework: The development of this policy contributes to the country's commitment to Sustainable Development Goal (SDG) 3: *"Ensure healthy lives and promote well-being for all at all ages".* It responds to the SDG target 3.7, which calls for governments to ensure universal access to sexual and reproductive healthcare services, including information, education and the integration of reproductive health into national strategies and programmes by 2030. All the guiding principles, action areas and selected targets of the Global Strategy for Women's, Children's and Adolescents health *(namely: "ensure universal health coverage and access to quality essential services and vaccines; and "reduce by one third preventable mortality from non-communicable diseases by 2030)* are alluded to in this policy.

Alignment with national priorities and frameworks: This policy revision is guided by the South African National Health Insurance (NHI) white paper which recommends for massive reorganisation of the healthcare system to create a new platform for health service provision. The policy also responds to a number of critical national priorities, including:

- The National Development Plan 2030 goals
- The increasing quadruple burden of disease in South Africa
- The high prevalence of HIV and non-communicable diseases (NCDs) in South Africa
- The scale up of HPV immunisation initiated in 2014
- Current implementation of the primary healthcare (PHC) re-engineering strategy
- The introduction of National Health Insurance (NHI) in South Africa

Integration: The policy compliments other existing policies and guidelines which aim to ensure universal access to sexual and reproductive health services such as the National Contraception and Fertility Planning Policy and associated service delivery guidelines, the HPV vaccination Standard Operating Procedure (SOP) and health sector HIV Prevention Strategy (2016) and Palliative care Policy **(2016)**.

Holistic approach and outcome focus: Unlike the previous cervical cancer screening policy, which was restricted to screening services, this policy offers guidance for a full continuum of care and includes prevention, screening, diagnosis, treatment, and palliative care services. It further outlines the minimum service delivery package for the different levels of care (the community; primary healthcare facilities; district, regional and tertiary hospitals; and private institutions).

Special considerations: As the policy is aligned with WHO recommendations, special considerations for high risk groups are considered; such as women living with HIV, women with other immunosuppressive conditions, sex workers, adolescents, and migrants.

Community engagement and involvement: The policy explains the role of civil society organisations and provides for a communication strategy to increase awareness of cervical cancer at the community level as well as increase demand for and utilisation of cervical cancer prevention and control services.

Technological advances: The policy takes cognisance of the availability of new screening technologies, the technological advances in primary prevention, screening and treatment of pre-cancerous lesions and proffers different alternatives depending on available resources.

SECTION A: BACKGROUND AND CONTEXT

CHAPTER 1: BACKGROUND

Cancer is a largely preventable disease; however, its incidence has been rising and it is already a leading cause of death in many low and middle-income countries (LLICs). In 2008, less than 170 million healthy lives were lost to cervical cancer. South Africa contributed 25% of infection-related cancers (cervix, stomach and liver). In the same year, the age-adjusted-disability- years of lives lost (daily) per 100 000 women was estimated at 641/100 000 in South Africa compared to 58/100 000 in Australia and New Zealand

Globocan 2012 statistics further estimated that globally, 266 000 women died from cervical cancer in 2012, revealing a significant rise in mortality cases compared to those in 2008. In Africa, it is thought that approximately 80 000 women are diagnosed with cervical cancer per year, and over 50 000 women die from the disease. In other words nearly 70 per cent of women diagnosed with cervical cancer die from the disease. This is despite cervical cancer being both preventable and curable if detected in its early stages. Furthermore, data show a high prevalence, poor prognosis and diagnosis at ages younger than 35 especially in LMICs including South Africa. In women co-infected with HIV, the mean age of diagnosis is 10 to15 years younger.

Detection, treatment and follow-up of pre-invasive lesions place a huge burden on an already overloaded primary and district health facilities. Its treatment requires radiation, which is expensive and is mostly done at tertiary and quaternary hospitals. Costs for staffing, facilities and direct treatment are also exorbitant. In addition most patients need to travel long distances for treatment and follow-up, and they incur additional out of pocket expenses towards accommodation and other living expenses for the duration of treatment.

The impact of cervical cancer on communities is complex and is aligned with high levels of poverty, cultural factors, social justice, gender, race, ethnicity and geography. Poor women present with advanced disease have less access to diagnosis and treatment and have a much higher case to fatality rate than women in high income countries (HIC s).

Regardless of where it occurs, cervical cancer has an overwhelmingly negative impact on women, families and communities. Most women become economically inactive after diagnosis of cancer; many are chronically ill and debilitated for the remainder of their lives. Due to bleeding, discharge and fistulation, many patients die socially isolated, in severe discomfort and in pain and in healthcare systems that lack adequate palliative care, anti-cancer therapies and pain control (only 11 countries in SSA are able to provide oral opiates for pain control).

The high morbidity and mortality from this disease has a devastating impact on society. Cancer is responsible for the premature removal of many economically active women, mothers and grandmothers from society. This poses not only a financial burden on the family, but also social and emotional trauma to other members of the family, alteration in family structure because young children must drop out of school and become care-givers, loss of household amenities and generally a significant fall below the poverty line.

CHAPTER 2: The south african context

This section describes the current status of cervical cancer in South Africa based on the available data from different data sources. It is acknowledged that the data presented may not be entirely representative due to information gaps and limited up-to-date data sources. Available data from South African National Cancer Registry (NCR) collected in 2010, despite having limitations, highlights several important key observations about progress in the prevention of cervical cancer in South Africa and affirms the need for cervical cancer prevention and control to remain a national priority. It also provides the baseline for decision making in this policy in line with the strategic objectives of the country.

South Africa has a pathology-based NCR, which was established in 1986 and is the main source of cancer statistics. It collates and analyses cancer cases diagnosed in pathology laboratories (public and private) and reports annual cancer incidence rates stratified by age, sex and population groups. The NCR was incorporated into the National Institute for Occupational Health (NIOH) in 2009 and receives data on about 80 000 cases per year, of which 60 000 are new cases.

Cervical cancer ranks as the leading cause of female cancer deaths in South Africa, particularly affecting women in the reproductive age group from 15 to 44 years. Recent estimates suggest that given a population of 19.35 million women aged 15 and older who are at risk of developing cervical cancer, 7 735 women are diagnosed annually with cervical cancer and 4 248 die from the disease. This translates to a case fatality rate of greater than 50 per cent, and is equivalent to an age standardised mortality rate of 17.9 per 100 000 women per year. In 2008, cervical cancer reportedly accounted for an estimated 81 394 years of life lost (YLL) among women in South Africa. The number of diagnosed cases may still be on the increase and the morbidity and mortality pattern in the majority of women may be compounded by presentation (in over 75% of cases) with late stage disease, which is more difficult and more expensive to treat effectively.

Making reference to available local data, the NCR in 2011 recorded 4 907 cases of cervical cancer (compared to 5 627 cases of breast cancer). Of these 4 056 (82.7%) were diagnosed in black women as compared to only 437 cases of cervix cancer diagnosed in white women. Overall, cervical cancer represented 4 907/ 31 910 or 15 per cent of all cancers diagnosed in women compared to breast cancer, 6 849/ 31 910,

which accounted for 21 per cent of cancers in women. Using data on histological and cytological diagnosed cases of cervical cancer as provided by the NCR in 2003 and 2010 the overall “Age Standardised Incidence Rate” (ASIR) was 22.7 per 100 000 and 22.3 per 100 000 women respectively.

Of note, the ASIRs in black women in 2003 and 2010 were 26.7 per 100 000 and 26.1 /100 00 respectively, compared to 19.02 /100 000 and 16.3/100 000 in coloured women, 12.96 /100 000 and 12.91/100 000 in white women, and 10.57/100 000 and 8.04/100 000 in Asian women. This population reveals considerable racial disparities in the magnitude of cervical cancer with significantly higher ASIRs in black women. These statistics may reflect inequities in access to effective cervical cancer prevention and control services. This needs to be taken into consideration when designing the implementation framework of this policy.

Despite the existence of a national cervical cancer screening programme since 2002, cervical cancer incidence has remained unchanged. And the prognosis associated with a cervical cancer diagnosis is poor with half of cervical cancer cases estimated to result in death. The mean age of diagnosis of cervical cancer is about 45 years in South Africa, despite many cases occurring before the age of 35. Black women and women living with HIV bear a disproportionate burden of cervical cancer disease reflecting lack of access to comprehensive and effective integrated care.

Information on cervical cancer screening in the public sector in South Africa is captured in the country’s District Health Information Software (DHIS). According to the DHIS, there has been an increase in the national cervical cancer screening coverage rate for women who are 30 years and older from 54.5 per cent in the 2014/15 financial year to 57.4 per cent in second quarter of the 2015/16 financial year.

With regard to the prevalence of the different levels of dysplasia as derived from cytology and histology reports of just over 16 per cent of screened women who potentially had cervical cancer precursors, the National Health Laboratory Service (NHLS) 2014 report indicated that eight per cent of patients had low grade squamous intra-epithelial lesions (LSIL), 4 per cent had high grade SIL (HSIL), 4.1 per cent had atypical squamous cells of underdetermined significance (ASCUS), 0.3 per cent had a malignancy, and 0.1 per cent had atypical glandular cells of undetermined significance (AGUS).

Factors contributing to high cervical cancer incidence in South Africa

The following factors contribute to high incidence rates, especially among black and HIV-positive women. These factors have therefore been taken into consideration in this revised policy:

- **Socio economic status and place of residence** (urban versus rural): Women who live in rural areas are disadvantaged regarding access to appropriate information and access to services. Even in some cases where a woman has access to a primary healthcare facility for screening, her referral to the next level of care is delayed due to poverty or financial challenges.
- **Educational level:** The default community messaging strategy is through written material. Furthermore the medium of communication is in English, which excludes most of the women living in rural areas, whose first language of communication is not English.
- **Social arrangement of the family:** Women in some communities are largely not decision makers in relation to health seeking patterns, especially for sexual and reproductive health issues, due to their economic reliance on their male partners. In other communities the decision to seek medical advice is made by the elderly woman in the family who may not be adequately informed.
- **Access to services:** The healthcare system in South Africa is still largely hospi-centric with a focus on curative care. In addition, the availability of specialised health care services in South Africa is not equitably distributed according the needs of the community. Thus there are areas where advanced services are available and accessible while other parts of the country only offer basic healthcare services. The situation is exacerbated by the severe shortage of specialists such as oncologists, radiation oncologists, appropriately trained surgical specialists and nurses trained in oncology.
- **Healthcare worker skills:** Weak health worker competencies attributable to inadequate training contributes to a delay in diagnosis and referral to the next level of care for definitive treatment.
- **Stigma:** Due to the stigma associated with cervical cancer, patients tend to delay seeking treatment early or even disclosing the condition.

PATHOPHYSIOLOGY

Persistent infection of the cervix with high-risk or oncogenic types of Human Papillomavirus (HPV) – most notably HPV types 16 and 18 – is well established as a necessary cause of cervical cancer. HPV infection of the genital tract is mostly acquired by sexual contact with most people getting infected with HPV shortly after onset of sexual activity; and is a prerequisite for the development of pre-invasive cervical intra-epithelial neoplasia (CIN grades 1, 2, 3), also known as low and high grade squamous intraepithelial lesions (LSIL and HSIL) (pre-cancer) and for progression to invasive cervical cancer.

Although very common, not all HPV infections persist and only a small proportion progress to cervical dysplasia and ultimately cancer. It is estimated that between 10 and 20 per cent of infections with oncogenic types will result in cervical dysplasia. Left untreated and in the absence of immunosuppression or other risk factors for expression, a mere one per cent ultimately progress to invasive cancer. Fortunately, progression from cervical dysplasia to overt cancer typically takes between 5 and 30 years-- thus a window of opportunity for screening, early detection and treatment.

Oncogenic potential is type specific, which has important bearing for prevention by both vaccination and screening. In South Africa, infection by some oncogenic HPV types is very common, with a recent study reporting a prevalence of 54 per cent in an urban /peri-urban population, while pre-cursor lesions were detected in about 10 per cent of all women. HPV 16 and 18 together account for more than 60 per cent of cervical cancer in South Africa, with HPV 45 and HPV 35 each detected in about 10 per cent of tumours.

It is well known that HIV infection increases the risk for HPV acquisition, as well as the risk for development of overt cervical cancer. Women infected with HIV have higher incidence, higher prevalence, higher HPV viral loads and an increased risk of persistent infection with HPV. They also have a higher likelihood of infection with multiple HPV sub-types, greater prevalence of oncogenic subtypes, a higher prevalence of cervical cancer precursors and a faster progression rate to more severe lesions. The HPV prevalence, persistence and viral load also tend to increase with decreasing CD4 counts and increasing HPV-RNA levels. In addition, recurrent abnormalities after treatment for precursor lesions are more common, and therefore these women have a higher risk of death from cervical cancer. Antiretroviral therapy does not eradicate this risk. These interactions have important implications for both HIV and cervical cancer programming and are addressed in this policy.

CHAPTER 3: Cancer control methods

Cervical cancer control is founded on Primary Healthcare principles which emphasise that *"prevention is better than cure."* Primary prevention refers to the prevention of the disease before the precursor phase starts, while secondary prevention is used for the detection and treatment of the asymptomatic pre-cancer phase. When invasive disease develops, the negative impact of the disease on the patient and society must be prevented by early diagnosis and provision of the most effective treatments available - called tertiary prevention. Cervical cancer can thus be prevented through operationalization of all these strategies.

3.1 Primary prevention

Primary prevention of cervical cancer entails preventing the acquisition of HPV infection and the development of cellular changes in the cervix. Good general immunity, prevention of smoking, improved nutrition and sexual health all impact on the risk of incident and persistent HPV infection, and the risk to develop precursor lesions on the cervix. As such, health education and services, for example: sexual health education tailored to the age group; providing contraceptive counseling and services including condoms, prevention of tobacco use and support for cessation may be employed within the package of primary prevention interventions. For HIV positive women early initiation of antiretroviral medication and maintaining good cell mediated immunity may have a positive impact on HPV specific immunity.

The most effective strategy available to primarily prevent this infection is by vaccination against the most common oncogenic HPV types, namely types 16 and 18. HPV vaccines are indicated for pre-pubertal girls and offer most hope to effectively stop the epidemic of cervical cancer in the developing world. Furthermore, studies have shown sufficient immune response in HIV positive children, hence they too can receive the HPV vaccine. Consequently, many countries (including some BRICS - and Sub-Saharan African countries) have successfully started to integrate HPV vaccination into their immunisation and vaccine programmes. In South Africa, the HPV vaccination programme was initiated in 2014, through the Integrated School Health Programme, and is implemented jointly with the Departments of Basic Education and Social Development.

These vaccines work best if administered prior to exposure to HPV. Both vaccines prevent over 95 per cent of HPV infections caused by HPV types 16 and 18, and also have some cross-protection against other less common HPV types which cause cervical cancer. One of the vaccines also protects against HPV types 6 and 11 which cause anogenital warts. The positive effect of HPV vaccination on national cervical cancer prevalence is expected to be seen within 20 years (depending of coverage), but the effect may be evident earlier as was seen with the dramatic reduction in the incidence of genital warts in Australia, where a very effective national vaccination programme targeting over 80 000 STI clinics was implemented. Herd immunity will eventually also lower the incidence of the disease among the unvaccinated cohort, but this is foreseen only when the majority of girls have been vaccinated.

With this in mind, the policy expects to scale up collaborative efforts between the Departments of Health and Basic Education to ensure increased access to and uptake of HPV vaccination for adolescent girls in school.

3.2 Secondary prevention

Screening refers to the testing of women without symptoms to detect cancer risk. The main goal is to detect persistent HPV infections and cancer precursor lesions so that they can be treated in time. This can be achieved most effectively by screening the correct target population in a structured rather than opportunistic way. Well-organised screening programmes have been shown to effectively reduce the incidence of and mortality from cervical cancer, even in low and middle-income countries.

Essential requirements for an effective screening programme include targeting the correct age group, high coverage of the population at-risk using a screening test with excellent sensitivity and good predictive value, effective treatment of women with abnormal screening tests, reliable laboratory services, a functional follow-up and referral system and effective communication between the different aspects of the screening programme. For this reason, coordination, careful monitoring and quality control are all essential.

Spontaneous or opportunistic screening has a low impact on the incidence of and mortality from cervical cancer because it fails to reach older women, results in poor coverage and repeated or over-screening of lower risk groups. Coordinated strategies to inform and educate women are needed to inform women at risk about cervical cancer

prevention, screening, early detection and treatment of pre-cancer. A functioning health system infrastructure to deliver prevention and treatment services is essential in this regard. This policy therefore advocates for institution of resilient health systems to support the scale up and assure effectiveness of this programme.

Cytology-based screening programmes have been in existence for over 50 years. It has the largest evidence base that screening leads to a reduction in cancer related mortality. The costs of screening have been shown to increase in proportion to increasing the age range and the number of scheduled examinations and decreasing the screening cycle.

Overall few countries in the developing world have been able to successfully implement a cytology-based screening programme. This is due to the complex, human, financial and 'bricks and mortar' infrastructure and resources required to initiate and to sustain such programmes. Much of the existing cytology screening is opportunistic or sporadic, with low population coverage. And it tends to include young women in urban areas, resulting in minimal or no reduction in cervical cancer incidence or mortality burden. This policy institutes supportive health systems and target the higher risk age groups in order to maximise yields and ensure efficiency and effectiveness.

Addressing the resource intensive constraints that have negatively impacted the implementation of cytology in LMICs has led to the evaluation of alternative cervical screening tests including VIA and HPV testing.

The table below depicts the performance of alternative strategies for primary cervical cancer screening based on systematic reviews and meta-analysis of diagnostic test accuracy studies.

Generally HPV test has the highest sensitivity, while cytology has the highest specificity.

Screening method	Pooled sensitivity %	Pooled specificity %
VIA	69 - 77	82 - 87
HPV	94 - 95	84 - 90
Cytology	70 - 84	88 - 95

The findings also show that VIA is able to detect over 70 per cent of true positives and over 80 per cent of true negatives. These findings complement the existing WHO recommendation that VIA is a suitable test for primary cervical cancer screening in Sub-

Saharan Africa. Slightly higher false positivity rates were noted when VIA was used. However, the variation in false negative values was minimal and not statistically significant. In implementing a screening programme, the absolute numbers of false positives following screening with VIA are small and this should be weighted *vis-a-vis* the higher coverage and the lower costs of screening.

Based on promising results from several randomised trials, a number of countries in SSA are using the VIA as a screening approach in order to rapidly increase access and coverage of cervical cancer screening services. The advantages of VIA include the fact that it can be offered at primary healthcare level by non-physician health workers, it uses minimal commodities and supplies, it does not require laboratory support, the results are available immediately and treatment can be offered in the same visit (screen and treat / SVA). However, the test is highly reliable on user perception and thus may result in high false positivity rates leading to overcalling and overtreatment. Nevertheless, the accuracy of the reader has been noted to improve over time especially with frequent screening and adequate supervision.

HPV DNA testing

HPV DNA testing is recognised as the ideal cervical cancer screening method because of its high sensitivity, specificity, positive and negative predictive value, objectivity and reproducibility. Randomised controlled trials (RCTs) have shown that HPV testing not only detects more CIN two to three lesions at screening, but also leads to their substantial reduction in subsequent rounds of screening and a 70 per cent reduction in subsequent invasive cancer. A RCT in India reported 50 per cent reduction in invasive cervical cancer mortality following a single round of HPV testing compared to VIA and cytology.

Despite its promising performance, the costs, logistics and technology requirements for successful implementation of current commercially available HPV testing are challenges for under-resourced health systems in LMICs. Newer technologies, such as

GeneXpert, a PCR-based test that has been extensively used for diagnosis of tuberculosis in SSA, including South Africa, detects 15 high risk types of HPV within one hour and can be performed in very resource restricted environments. While the test is currently expensive, it is the best 'point of care' HPV testing technology and it may make the test and treat approach feasible, changing the future of HPV testing.

> *In areas where there are no current screening services, HPV testing should be considered, particularly point of care testing. There are over 250 GeneXpert machines throughout South Africa, and they can all be used for HPV testing – it is simply the reagents in the cartridges that need to be changed. The initial capital expenditure will therefore be minimal. The current commercially available test is FDA approved.*

Self-sampling has been shown to be an acceptable and effective modality which can dramatically increase coverage in a number of settings particularly among harder to reach populations. The precise use of self-sampling in the context of national screening programs remains to be defined.

Inherent in any screening strategy are the trade-offs between the characteristics of the test (i.e. sensitivity to maximise precursors detected and specificity to minimise overtreatment) and programmatic issues such as population coverage and the necessary diagnostic and treatment procedures, costs and quality control.

This policy recommends for the use of Liquid based cytology (LBC) as the preferred screening method in the country. Where there is a functioning cytology service with skilled healthcare workers, good supply management, methods of communication between the laboratory and the clinics and patients and providers, and strong linkage to treatment facilities then these services should be consolidated and upgraded. The policy further proposes to offer VIA as the screening approach in resource constrained regions pending the national scale up of liquid based cytology and the roll out of HPV testing. It also recommends that self-sampling and the creation of regional laboratories be investigated, particularly in rural areas. Finally this policy intends to institutionalise quality assurance for all the screening approaches in order to foster accuracy and reliability of the tests.

Treatment of pre-cancer

It is crucial that screening, regardless of the test is used, is linked to a reliable treatment programme. The treatment of pre-cancerous lesions is an essential part of secondary prevention and can either involve surgery (cryotherapy, cryopen, thermal coagulation) or use excisional techniques e.g. LEEP/ LLETZ.

In addition, alternative management protocols such as the single visit approach (SVA), also known as test and treat, in which women are screened and treated at the same visit have been investigated in clinical trials and the feasibility, safety and acceptability of SVA with VIA and cryotherapy has been demonstrated in Thailand and several sub-Saharan African countries. The test and treat approach does not obviate the need for counselling or careful explanation on the need for follow-up. Further, an aspect of the test and treat approach that has not been well evaluated is the added complexity of point of care testing and treatment at a primary care level. How to integrate this approach into other women's and general health interventions needs careful evaluation and planning.

Colposcopy

When using cytology or HPV test for screening, treatment is preceded by colposcopic evaluation and conducted under colposcopic guidance. This facilitates more thorough evaluation of the cervix including biopsy of the lesion. Histological evaluation of the biopsy specimen is critical especially for diagnosis of early invasive cancer of the cervix. With appropriate training and supervision, the skill can be task shared with nurses so as to improve access. This policy recommends that colposcopy services should therefore be made available at primary and district levels and screening should be nurse-driven with support from medical officers and specialists where appropriate.

3.3 Tertiary intervention

Tertiary intervention focuses on people who are already affected by invasive cervical cancer, with the goal to improve quality of life, reduce disability, minimise complications and restore function. This is done by diagnosing and treating the disease or providing palliative care. Treatment must therefore be made available to all women whenever cervical cancer is detected

A multidisciplinary approach to the management of cervical cancer has been shown globally to achieve the best results. Tertiary prevention should therefore include several professionals (surgeons, medical and radiation oncologists, pathologists, clinical psychologists, social workers, etc.). It is essential to ensure that a full social history of the patient is elicited, including the impact of the diagnosis and treatment on her roles and responsibilities in society. Notably, South Africa provides temporary disability grants which can relieve some of the threats created by low income.

Critical to a favourable outcome for women diagnosed with cervical cancer is the process of staging. Staging cancer is the centre of deciding the appropriate treatment. Diagnosis of early stage disease can be done using excisional procedures such as cone biopsy, LLETZ or clinically. Cervical cancer is staged from one to four; and treatment in each stage is individualised.

Surgery is the mainstay of treatment in early stages of the disease. For stage 1a1, a simple hysterectomy is usually sufficient. However, for stage 1a2, 1b1 and 2a1 removal of pelvic lymph nodes which requires a higher level of surgical skill and hospital facilities is necessary. For other stages, radiation (with or without chemotherapy) are the main forms of primary treatment. Radiation and chemotherapy can also be given in an adjuvant setting-after primary surgery, or as palliative treatment in women with metastatic or recurrent disease.

Careful monitoring of women being treated for cervical cancer is essential and requires attention to detail, precise evaluation of symptoms, and separating out symptoms related to the disease versus those caused by complications of treatment or co-morbidities such as lung, cardiovascular, HIV, etc. Involvement of other stakeholders such as family, communities, hospices and home carers is crucial. All actors involved in the care of the woman should ensure the highest possible quality of care including respect, dignity and upholding of the rights of the patient.

The management of invasive cervical cancer forms an important part of this policy document. Improved screening is expected to allow diagnosis at an earlier stage of disease for women who did not benefit from disease prevention strategies. Early detection of invasive disease leads to improved cure rates and improved survival.

Therapeutic cancer treatments including surgery for early stages, radiation and chemo-radiation are mostly available at tertiary facilities. Post treatment all women need follow up for a minimum of three to five years

For women who either cannot tolerate or benefit from therapeutic options, more radical treatment options, effective supportive and palliative treatment should be offered. This policy recommends for the development of palliative care services nationally with medical palliation, including pain control, care facilities and home care support as an integral service of primary and secondary healthcare facilities.

SECTION B: POLICY FRAMEWORK

CHAPTER 4: Enabling legislation, guidance documents

Various national legislative and policy frameworks support implementation of this Cervical Cancer Prevention and Control Policy (CCPCP). These existing national policies and strategies provide an enabling framework for prioritising cervical cancer control and present opportunities for linking the cervical cancer prevention programme with other national priorities. The national frameworks are described below.

Enabling national legislation

The Constitution of South Africa (No. 108 of 1996) and the National Health Act (Act No. 63 of 2003) provide overarching guidelines to protect the rights of the citizens and prevent discrimination of women regarding access to quality healthcare service. Services are rendered in an equitable and non-discriminatory manner in terms of sexual orientation, sexual preferences, sexual identity, race gender, age and culture, with due regard for what is suitable and appropriate for individual clients' needs.

Policies, strategic plans, programmes and declarations

Taken together, the following domestic policies and guidelines will facilitate integration of service provision in order to comprehensively address cervical cancer prevention and control needs of women in the country. They include: The Strategic Plan for Maternal, New-born, Child and Women's Health (MNCWH) and Nutrition in South Africa (2012-2016), the National Contraception and Fertility Planning Policy and its accompanying service delivery guidelines (2012), the National Strategic Plan for HIV, Sexually Transmitted Infections (STIs), and Tuberculosis (TB) (2012-2016) *(details other interventions for addressing transmission of infections)* and the Non-Communicable Disease (NCD) Strategy *(addresses cancer among other NCDs).* The Integrated School Health Policy and the Policy Guidelines for Youth and Adolescent Health also provide platforms for the implementation of this policy.

Policy framework and strategy on cancer in South Africa will provide additional guidance on the following:

- strengthening support and monitoring of the National Cancer Registry in order to monitor the burden and outcomes of the disease
- provision of overall structural organisation of the cancer service within the facilities, primary healthcare , district hospitals, regional hospitals and tertiary and quaternary hospitals
- regulation of the pharmaceutical and non-pharmaceutical requirements of the medical management of cancer treatment
- establishment of a planned patient transport system that ensures access to high level services.

CHAPTER 5: Policy goals and strategic objectives

5.1 Policy goals

The overall purpose of this policy is to improve women's health and well-being by decreasing cervical cancer-related morbidity and mortality. Specifically, the policy has two goals.

Goal 1: Reduce the incidence of invasive cervical cancer by implementing effective primary and secondary prevention interventions.

Goal 2: Improve the quality of life and reduce morbidity and mortality of women diagnosed with invasive cervical cancer.

5.2 Strategic objectives

This policy articulates four strategic objectives that will be achieved in order to attain these goals.

Goal 1: Strategic objective

1.1. To reduce the incidence of oncogenic HPV infections by 5% from 25% (2017) to 20% (2022) in HIV negative women and from 60% (2017) to 55% (2022) in HIV positive women through scaling up of the HPV vaccination programme.

1.2. To reduce the incidence of invasive cervical cancer from 31.7/100 000 women in 2017 to 20 per 100 000 by 2022 through implementation of HPV vaccination of adolescent girls concurrently with an effective cervical cancer screening programme.

Goal 2: Strategic objectives

2.1: To decrease age-standardised mortality rate from cervical cancer of 18/100 000 women (currently) to 15 per 100 000 by 2022 through promoting early detection and treatment of HG SIL and overt cancer.

2.2. To improve quality of life of women with terminal cancer through provision of palliative care and support in alignment with the palliative care policy framework and strategy.

Each strategic objective has a set of sub-objectives, which represent the intermediate outcomes that this policy seeks to achieve on the path to achieving the aforementioned improvements in health status at population level. These sub-objectives are articulated in more detail in ***"Section D: Monitoring and Evaluation",*** of this document.

5.3 Strategic enablers

Successful implementation of this policy depends on a number of strategic enablers. Strengthening existing health system is essential to ensure that these strategic enablers are in place to support policy implementation

The strategic enablers for this policy have been identified and include:

- skilled and motivated health workforce (management, service providers and laboratory personnel),
- strengthened laboratory capacity including quality assurance mechanism
- appropriately equipped health facilities,
- efficient supply, delivery and maintenance of vaccines and medical equipment and screening and treatment supplies / commodities
- community engagement for increased demand for and utilisation of services
- strong referral and feedback linkages between levels of care to ensure continuity of care for clients,
- effective strategic information and monitoring and evaluation system
- multisectoral engagement

These strategic enablers have been articulated in various existing national reforms, strategies and policies such as: the National Development Plan, the Negotiated Service Delivery Agreement for health sector, Primary Healthcare re-engineering, the national Department of Health 10-point plan, the National Health Insurance policy, and the National HIS Strategy. Health system strengthening to support this cervical cancer control policy will thus be done in accordance with these existing instruments.

5.4 Principles

The cervical cancer prevention programme will be guided by important universal principles that have been adopted by the national Department of Health and will employ a rights based approach. These include: the principles of equity, universal health coverage and access to care, quality of care, employment of safe and acceptable techniques and technologies (beneficence), efficiency and cost effectiveness, sustainability and accountability. Further, guided by the principle of integrated health planning and service delivery, HPV vaccination and cervical cancer screening interventions will be integrated within the national primary healthcare strategy, while treatment for invasive cancer will be integrated at all levels of healthcare as appropriate.

SECTION C: CANCER CONTROL PACKAGES OF CARE

CHAPTER 6: Levels of care

6.1 Overview

Activities aimed at meeting the goals of this policy will take place at all levels of care: community, primary healthcare, and higher levels of care. Figure 2 below provides a general overview of the expectations for each level of care. Further detail is provided in subsequent chapters. The overlap or duplication of activities across levels is meant to reflect the integrated nature of service delivery and to facilitate timely access to screening and treatment services.

Figure 1: Recommended services to be provided at various levels of care

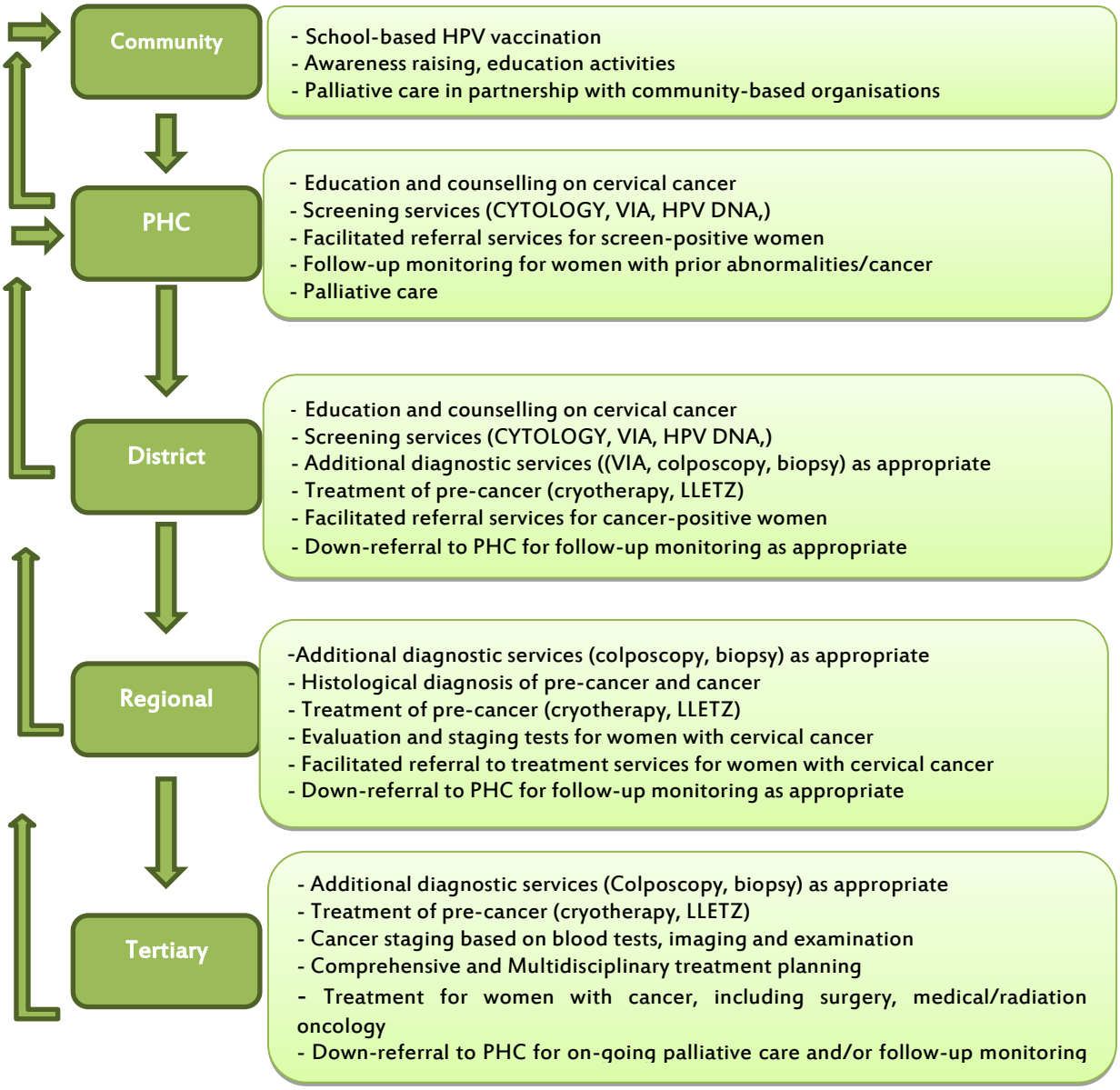
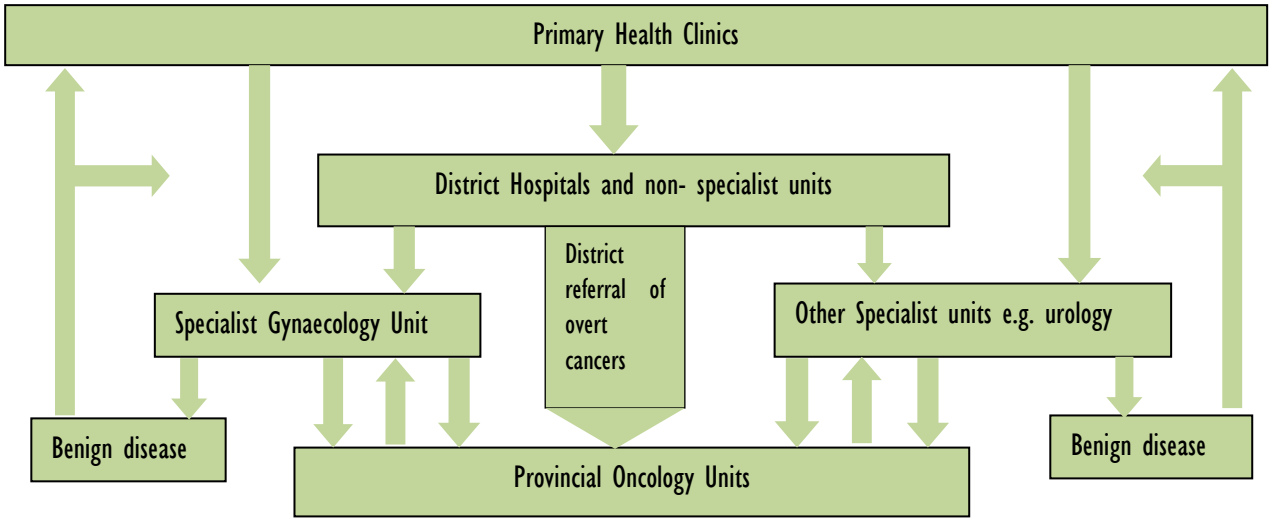


Figure 2: Summary of levels of care and referral pathways



CHAPTER 7: Primary prevention of the disease

Strategies for primary prevention of cervical cancer include HPV vaccination, voluntary medical male circumcision and promoting a healthy lifestyle amongst sexually active women. HPV vaccination has been shown to be the most cost-effective strategy in the prevention of cervical cancer.

Policy statement 1:

The HPV vaccine should continue to be offered to ALL pre-pubertal girls aged nine to 12 years, in order to primarily protect them against HPV types 16 and 18.

7.1 The HPV vaccine

Primary prevention of cervical cancer will be achieved by providing HPV vaccines to pre-pubertal girls between ages nine to 12 years at all primary schools across the country. The HPV vaccination programme in South Africa utilises the bivalent vaccine and is currently implemented through the Integrated School Health Programme through the joint efforts with the Departments of Health, of Basic Education and Social Development. Two different vaccine preparations are currently available in South Africa and globally:

- the **bivalent vaccine** (Cervarix®) targets HPV 16 and 18, which are the main causes of cervical cancer worldwide. In addition this vaccine prevents a large proportion of non-16 and non-18 associated pre-cursor lesions as well, thus affording high efficacy against cervical cancer
- the **quadrivalent vaccine** (Gardasil®) targets HPV 16 and 18 as well as HPV 6 and 11, affording extra protection against genital warts.

Both vaccines induce and seem to sustain a strong immune response. Both have excellent safety records with almost no serious adverse events directly related to the vaccines. Both vaccines very effectively prevent HPV 16 infection and associated lesions.

Recommendation: Two doses of HPV vaccine should be given to each girl, six months apart. To reach this target group, HPV vaccines should be administered to girls in

primary school between Grades four and seven, who are usually between ages nine and 12 but may include girls up to age 15.

Prophylactic vaccines such as the HPV vaccine should ideally be administered prior sexual debut, when acquisition of HPV infection is likely to occur. Antibody levels and immunity are highest when administered to younger individuals. Many recent studies demonstrate that immunological response to two doses is not inferior to three, especially when younger recipients are considered. As resources expand, the target group for the vaccine may be redefined to extend benefit to boys and to target other diseases caused by HPV among males and females.

7.2 Voluntary medical male circumcision (VMMC)

Male medical circumcision is included in the health sector HIV prevention strategy in order to reduce HIV transmission, an outcome which may also impact on HPV transmission and progression to cervical dysplasia. The strategy outlines several interventions for men who require circumcision.

7.3 Lifestyle modification

Good general immunity, prevention of smoking, improved nutrition and sexual health all impact on the risk of incident and persistent HPV infection and the risk of developing precursor lesions on the cervix.

CHAPTER 8: Secondary prevention screening for and diagnosis of pre-cancerous lesions

In order to protect those women who do not benefit from primary prevention, secondary prevention will be necessary for at least two decades after implementing the HPV vaccination programme. Secondary prevention will be achieved by providing screening for the early detection of high risk pre-cancerous lesions, and treatment of these lesions.

Policy statement 2: Cervical cancer screening will continue to be offered by the public healthcare system free of charge to all eligible women as a national priority.

Recommendations: Cytology-based screening, particularly via pap smear, is currently and will continue to be the method of choice in the short-term. LBC and HPV based screening will be phased in based on resource availability. The aim is for LBC and HPV based screening tests to constitute 50 and 20 per cent of all screening tests performed in the public health sector by 2020, respectively; and 30 and 60 per cent of all tests by 2030.

It is also recognised that in certain areas where there are significant resource constraints, alternative screening tests, such as VIA, that do not require laboratory facilities and are based on inspection of the cervix with a light source and a speculum will also continue to be the method of choice, in the short-term.

In view of the cost-effectiveness and accuracy of the HPV DNA testing, the country will progressively transition to this method of screening as the gold standard in all provinces.

8.1 Method availability - screening

Globally, there are multiple options for screening for cervical cancer as a result of new approaches and technological advancements in recent years. However, given the current inequitable distribution of resources within and across provinces, districts and sub-districts in South Africa, this policy makes special provision for use of different screening services depending on the availability of resources. The following screening tests will thus be available as part of this policy:

- **Cytology (conventional):** Cervical screening in South Africa has traditionally been done using conventional cervical cytology (also called a papanicolaou, or pap smear). *It is a human and laboratory resource intensive method* which involves using a device to collect cells from the cervical face and endocervix and spreading the cells on a glass slide for reading by a trained cytologist at a laboratory. Cervical cytology testing by pap smear is one of the oldest methods of screening. It has resulted in successful and significant reduction in incidence of invasive cancer in countries where it is consistently practiced and provided in an organised manner. The slide also serves as a permanent record and can be reviewed for quality assurance.

- **Cytology (liquid):** LBC is considered to be an alternative to conventional cytological investigations. A spatula or brush/broom-like device is used to collect cells (in the same way as for conventional cytology), and then the cells are put into a liquid medium and transported to the laboratory for processing and reading. This ensures a good quality and clean slide which is easier to interpret, and reduces the need for repeat pap smear thus saving costs. HPV DNA tests (described below) can also be performed with samples collected and analysed using LBC. Result categories are the same as for conventional cytology.

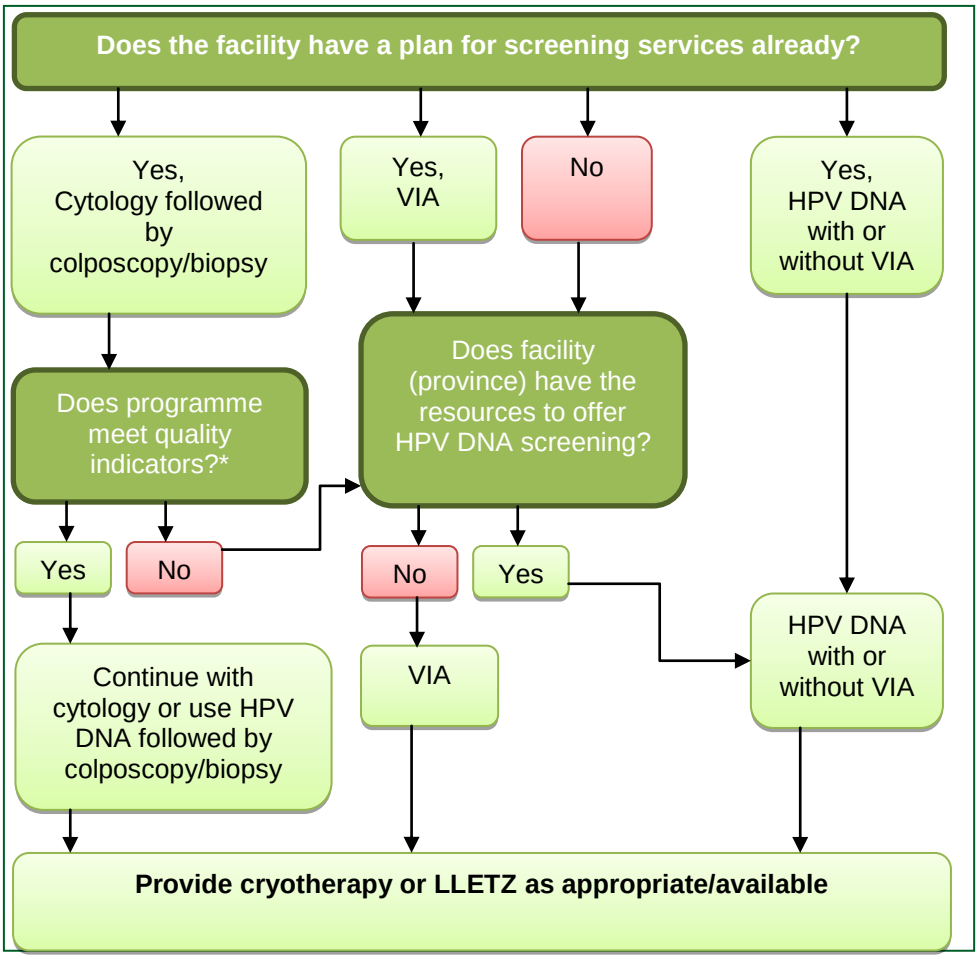
- **HPV DNA testing:** HPV DNA testing is a new technology where women are screened for the presence of high risk HPV (usually types 16 and 18). It is extremely sensitive for current and future ectocervical and endocervical dysplastic lesions. The high sensitivity and the fact that speculum examination is not essential for collection (if the self-testing option is applied) make HPV screening potentially less human resource-intensive option for screening. Further, HPV-

based screening is more effective for the prevention of cancer than a single round of cytology – this is a key benefit for a developing country with a long screening interval. One of the advantages of HPV-DNA testing is the high negative predictive value. It has been demonstrated that the risk of developing CIN 3 after a negative HPV-DNA test is almost zero within six and 10 years respectively. This characteristic of HPV-DNA testing could permit longer inter screening periods and fewer overall screenings during a woman's lifetime. Genetic material can be collected by a healthcare professional or self-collected by the woman. A simple swab is used to "wipe" the cervical face or vaginal wall, and the swab is then deposited into a liquid medium and sent to a laboratory for processing and testing. Results are either positive (high risk HPV DNA present) or negative (no high risk HPV DNA present). Because screening via HPV DNA testing is extremely sensitive, it may identify HPV prior to the development of lesions, allowing for extremely early treatment.

- **Visual inspection with acetic acid (VIA):** Visual inspection with acetic acid is a screening alternative for low-resource settings. The healthcare provider "paints" the cervix with an acetic acid (i.e. vinegar) solution, and uses the naked eye to visualise the results. Lesions appear white. No samples are collected, and no laboratory is required. Results are either positive (lesions) or negative (no lesions). Since VIA is known to have a lower specificity than other methods, there is a potential for over treatment if inspection is not carefully and consistently supervised. The ability of those performing VIA to identify a normal cervix correctly (specificity) seems to improve with practice. Effective training and quality assurance programs are therefore critical to ensuring the effectiveness of VIA. This screening methodology is currently in use in very limited settings in South Africa, usually supported by NGOs.

The figure below summarises options regarding which screening method is advised, based on available resources, including laboratory and specialist services. Details on how to provide each screening method will be included in the clinical guidelines developed as the companion for this policy document.

Figure 3: Decision making guideline for screening (adapted from WHO)



(Quality indicators include Pap adequacy rates, screening coverage rate, ability to refer to treatment, etc.)

8.2 Target groups and frequency of screening

Guidelines for screening frequency are provided for three separate target groups:

> **Policy statement 3:** All women 30 -50 years will be screened for cervical cancer as prescribed in the national policy recommendations below

Target group for screening

- **General or low risk population:** This population is defined as all asymptomatic, 30 years of age or older women who are HIV-negative or who do not know their HIV status. An **unscreened, low-risk woman** is someone 30 years or older who reports that she has never been screened or who had her last screening test more than 10 years ago.

Recommendation: The target age for screening low risk asymptomatic women is from 30 – 50 years. Asymptomatic women under the age of 30 years should not be screened unless infected with HIV. Screening can however be done upon request by women outside these age bracket (<30 or >50).

Screening interval

Women in the low risk target group will be offered screening three times in their lifetime, assuming no abnormalities are found during screening. Screening will be offered first at age 30 and then at 10 year intervals (i.e. at ages 40 and 50).

Recommendation: Structured screening will be offered to the low risk target group as follows: women will be screened three times at 10 year intervals starting at the age of 30 years.

If a woman is first screened at an age older than 30, her last screen may be after age 50. The healthcare provider should consider risk factors for older women, and screen if appropriate. For example, if the woman presents at ages 38 and 48 for her first two screens, at age 58 a risk assessment may be required, (e.g. is she sexually active, is she symptomatic, etc.) prior to offering a third lifetime screen.

Recommendation: All low risk women who are found to have an abnormality during routine screening should subsequently be screened at three year intervals until the screen result is negative. When the result is negative, the woman can return to the 10 year schedule.

HIV-positive or high risk population

Policy statement 4: All HIV positive women will be screened for cervical cancer at diagnosis and subsequently every three years if the screening test is negative and at annual intervals if the screening test is positive for disease as prescribed in the national policy recommendations below.

- All HIV-positive women are considered to be high risk for cervical cancer whether they are receiving antiretroviral (ARV) treatment or not. Women who are recipients of organ transplants are also at high risk. Other women considered high risk are

those with immunosuppressive disease and those on chronic immune suppressing treatment. An **unscreened high risk woman** is any sexually active, high risk woman (regardless of age) who has not been screened in the last three years or who has never had a screening test.

Recommendation: Screening for HIV positive women will be done irrespective of CD4 count and ARV treatment and continued at three yearly or annual intervals (based on the results of the screening) for the duration of the woman's life.

- **Symptomatic women:** This refers to all women who present with any of the symptoms of early cervical cancer as well as women 30 years and older who are treated for a presumed STI. Symptoms of early cervical cancer may include: abnormal vaginal bleeding, persistent /foul smelling vaginal discharge, etc. Women with any of these symptoms should be examined immediately using a vaginal speculum to clearly visualise the cervix, have a screen (cytology, VIA or HPV DNA) if there is no obvious cauliflower-like growths, ulcers or fungating mass , and be referred immediately to the next level of care. Women who do not have symptoms suggestive of cervical cancer but who do have a presumed STI, should have a screen performed regardless of the timing of their last screen.

8.3 Special considerations

The following are special considerations for screening and treatment.

- **Age:** Cervical cancer is rare before the age of 30 years. Screening younger women will detect many lesions that will never develop into cancer; this will lead to considerable overtreatment, and is therefore not cost-effective. The risk of invasive cancer is low in adolescents and there is a high rate of spontaneous regression of squamous intraepithelial lesions among this group. However, in South Africa, HIV incidence is high amongst younger women and girls and therefore screening services will be provided routinely to younger women (i.e. younger than 30 years) from the time that HIV diagnosis is confirmed provided that the young women have previously had sex (i.e. putting them at risk of acquiring HPV).

- **Rural versus urban, rich versus poor:** In acknowledgement of the current inequitable distribution of resources within and across provinces, districts and sub-districts, this policy make special provision for use of different screening services

depending on the level of resources, including specialised staff, available. However, the fundamental principles to consider when establishing a specific management protocol should be the accessibility of services and the delay of progression to disease.

- **Pregnant women:** Screening for cervical cancer should be provided to eligible clients as part of routine preconception care. Furthermore, speculum examination should be part of routine ante natal care evaluation to rule out gross cervical abnormalities. Pregnancy does not preclude screening for cervical cancer and it can be performed up to 20 weeks of gestation to avoid missed opportunity. When taking a pap smear during pregnancy, it is advisable to use the plastic brush /broom to minimise trauma to the cervix. The service provider should be aware that if VIA is performed in pregnancy lesions may look larger than they actually are, while interpretation of pap smear may be more difficult. Pregnant women with abnormal screening results should therefore be advised to come for re- screening –six to 12 weeks after delivery. This is because most lesions shrink or regress spontaneously after delivery.

Should a screening be abnormal or a lesion detected at speculum examination, the patient should be immediately referred to a specialist for colposcopy. Due to the risk of significant bleeding the colposcopist should defer taking a biopsy until at 12 weeks after delivery *unless there is suspicion of invasive cancer*. Treatment for precancerous lesions by cryotherapy, LEEP or cold knife conisation is contraindicated in pregnancy or within 12 weeks postpartum as it is associated with a high rate of complications, including severe haemorrhage. Additionally, when excision is performed during pregnancy there is a high rate of incomplete excision and recurrence. Unless invasive cancer is suspected, any intervention should be delayed until after 12 weeks postpartum when she should be re-evaluated and appropriate treatment provided then.

8.4 Colposcopy

The standard method for diagnosis of cervical precancerous lesions is histopathological examination of tissue obtained through colposcopy directed biopsy.

A colposcope is a low-power, stereoscopic, binocular microscope with a powerful light source used for magnified visual examination of the uterine cervix, to help in the diagnosis of cervical neoplasia. Colposcopy allows the cellular patterns in the epithelium and surrounding blood vessels to be examined, the extent of abnormal lesions to be defined and abnormal areas biopsied. However, due to the limited number of colposcopy facilities in South Africa, and the high prevalence of cervical pre-neoplasia, colposcopic evaluation of all women who screen positive is not always feasible.

The treatment of cervical lesions should ideally be done under the guidance of a colposcopy. Given the range of screening methods/approaches available, including test-and-treat, in certain instances, this step may no longer be mandatory prior to the treatment of pre-cancerous disease. It is therefore recommended that in the interim, treatment without a colposcope should be done pending the progressive increase in availability of colposcopy services.

Recommendation: Colposcopy is a diagnostic tool. However, the treatment of abnormal cervical lesions should ideally be done under the guidance of a colposcopy.

CHAPTER 9: Treatment and care of cervical pre-cancer or risk

The ultimate aim of secondary prevention is to appropriately treat all cervical abnormalities detected by screening. All women in whom cervical abnormalities have been detected (positive screening test) should be managed appropriately depending on the screening result. In most cases precancerous lesions can be treated on an outpatient basis using relatively non-invasive procedures. The methods that are available for the treatment of cervical lesions are summarised here and explained in more detail in the clinical guidelines.

Recommendation: Where resources allow, the standard screening and diagnostic sequence of: cytology, followed by colposcopy, biopsy and histological confirmation, in the event of an abnormal smear, should be followed prior to treatment. Alternatively, a "*screen-and-treat*" approach is recommended, where treatment is provided immediately following an abnormal screening test.

9.1 Methods for the treatment of cervical abnormalities

9.1.1 Negative, CIN1

Cervical Intraepithelial Neoplasia (CIN) is a premalignant lesion graded as either stage 1, 2 or 3, depending on degree of severity. CIN2 or CIN3 (High grade SIL), can progress to cervical cancer if left untreated. A colposcopic biopsy resulting in a negative or CIN1 outcome should be managed under a "wait-and-see" approach. Women should be called back for re-screening with cytology in three years.

Recommendation: Before implementing conservative management for clients with CIN 1 (the "wait and see approach"), ensure that the woman can be traced, and that she will comply with the follow up regimen including returning for the scheduled re-screening visits.

9.1.2. CIN2, CIN3, and adenocarcinoma in situ

Policy statement 5: All women found with HG-SIL or CIN 2/3 will be offered appropriate pre-cancer treatment using ablative or excisional methods.

Ablative or excisional methods are available for treatment of CIN 2/3, or adenocarcinoma in situ. Ablative methods are meant for treatment only. Excisional methods allow for collection of tissue for further diagnosis or confirmation of treatment success. These methods are described below.

Ablation therapy: Superficial ablation of cervical lesions can be done with cryotherapy or laser or electrical cauterisation. Cervical ablation is suitable for small or lower-grade lesions which are not circumferential and where all margins are clearly visible. Criteria and instructions for ablation are included in the clinical guidelines. In summary:

Electro coagulation diathermy (ED): This procedure involves using electric current to destroy diseased tissue. The current is delivered to the tissue through needle or ball electrodes. The most common ED-type procedure is Large-Loop Excision of the Transformation Zone (LLETZ) (also called LEEP in some areas). With LLETZ, an electrical wire is used to ablate the transformation zone between the ecto and endo-cervix. LLETZ is available in the public sector in South Africa and has historically been recommended for treatment of cervical lesions.

Cryotherapy: Cryotherapy essentially involves freezing lesions using a probe made cold with nitrous oxide. This treatment method is widely accepted and used in many settings globally and can be performed as an outpatient procedure. It is offered in limited settings in South Africa; however, under this policy, use is encouraged for areas where access to LLETZ services is limited. It can be performed by trained nurses and is often used as part of a same day screen-and-treat programme following VIA for screening. It can also be used for treatment after cytological or HPV DNA screening however this will involve a two-step process.

Laser cauterisation (or vaporisation): This method utilises a carbon dioxide laser beam to vaporise lesions. It is not widely available in South Africa. In other settings, it is often performed as an outpatient, hospital-based service under general anaesthesia.

Excision methods: These methods involve removing, or excising, lesions which can be sent to a laboratory for examination.

LLETZ: LLETZ can also be used to excise lesions in the transformation zone. LLETZ is suitable for any cervical lesion, including large, endocervical and severe lesions which

are more difficult to treat with cryotherapy. It offers a dual advantage in that tissue from large and high risk lesions that is excised during the LLETZ excision procedure can be sent to the laboratory for histological examination.

- **Cold Knife Excision/ Cold Knife Conization:** These methods are not recommended for treatment of pre-cancer due to high morbidity, high cost and the need for general anaesthetic. Rather it is recommended to strengthen referral pathways in the short term and in the medium to longer term develop outpatient treatment clinics (with cryotherapy or LLETZ) to increase access to appropriate treatment services.

9.2 Management based on results from VIA

As noted above, in some settings colposcopic biopsy is not used for final diagnosis prior to treatment of lesions. Where VIA screening is used, cryotherapy or LLETZ can be provided to women with positive results (based on eligibility criteria for the treatment method as specified in the clinical guidelines).

9.3 Follow-up care

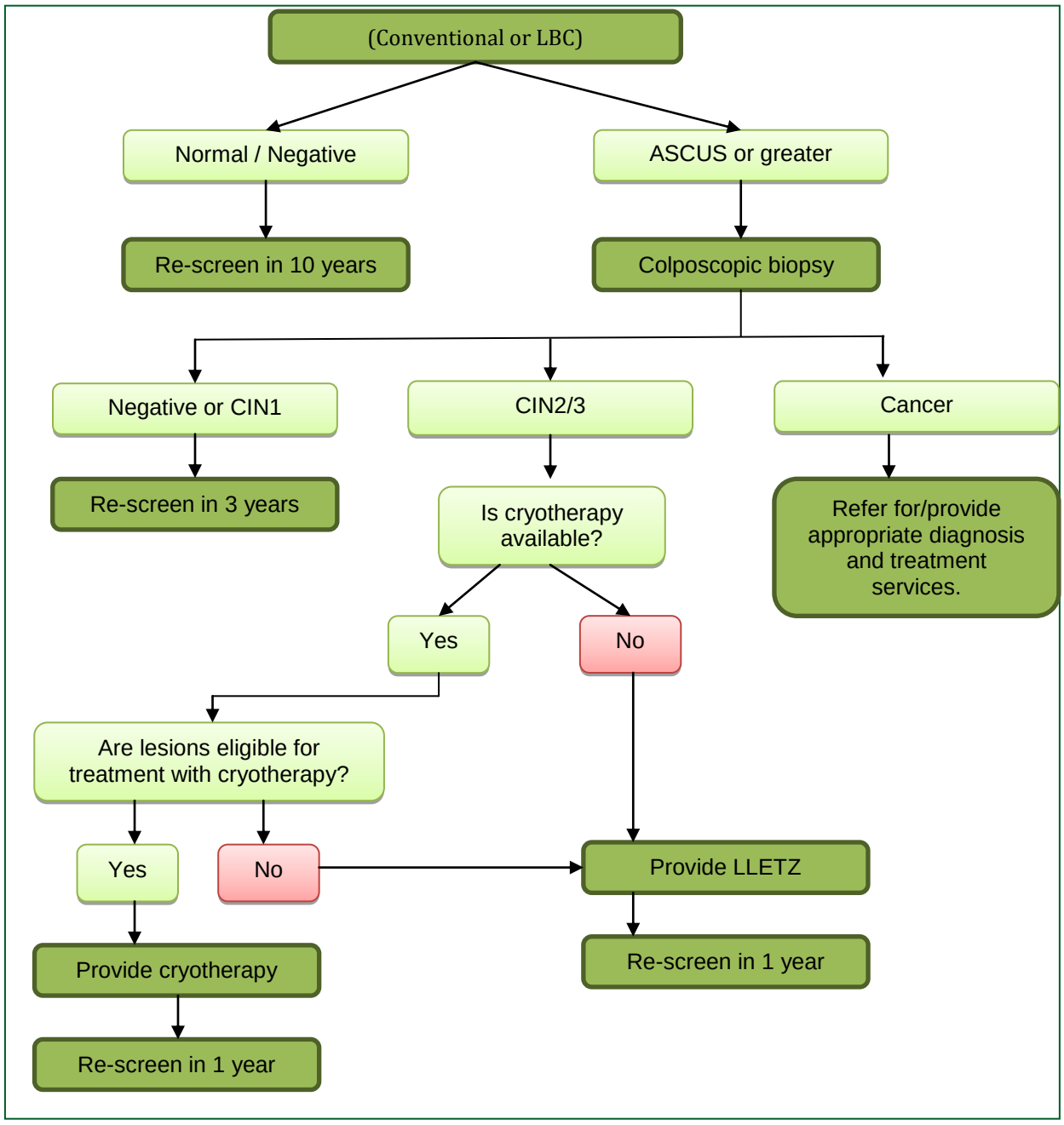
After treatment of cervical lesions or a positive VIA, women should have one follow-up visit (see clinical guidelines for the appropriate interval) and have a screening test three years after treatment, unless they are HIV-positive in which case they should have a follow up screening test one year after treatment.

Follow-up services must be offered at all screening facilities. Therefore, after treatment, all patients should be down referred to the screening facility. When cytology has returned to normal, the recommended screening interval should be followed, i.e. ten yearly for low risk women and three yearly for high risk women.

CHAPTER 10: Screening/diagnosis and treatment algorithms

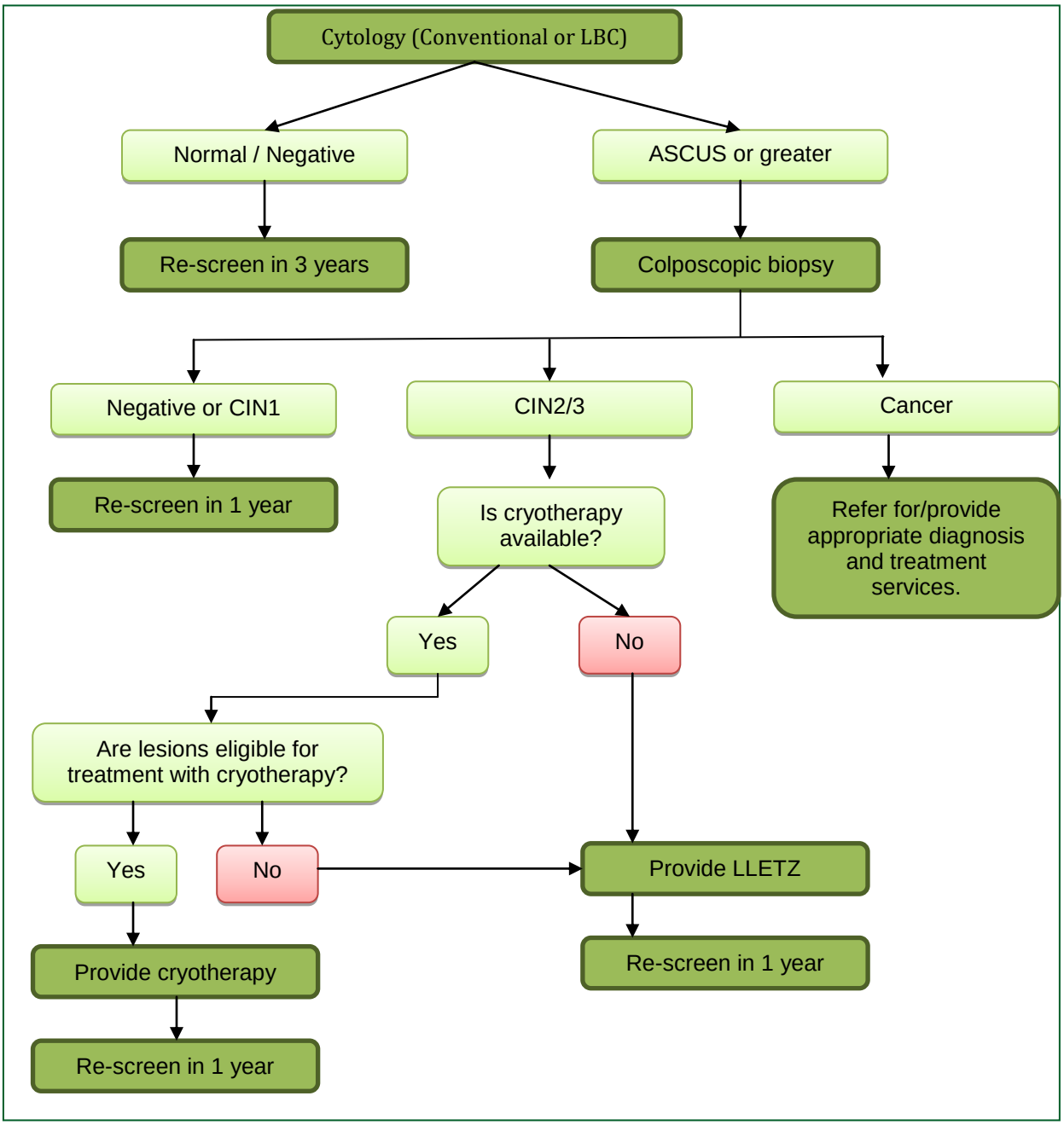
10.1 Screening with cytology for general or low risk population

Figure 4: Low risk group: Screening, diagnosis and treatment (cytology) (adapted from WHO)



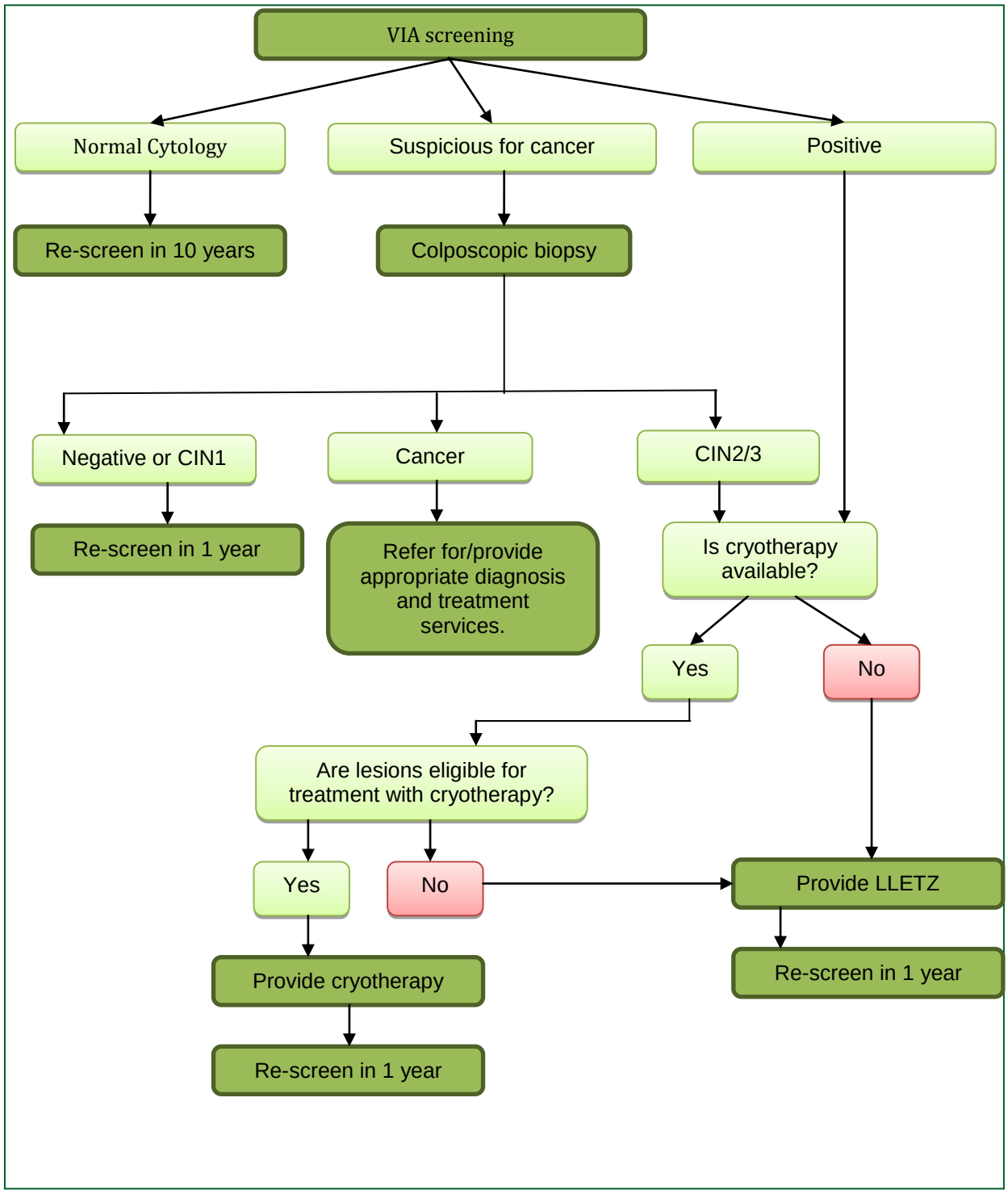
10.2 Screening with cytology in high risk groups and symptomatic women

Figure 5: High risk group: Screening, diagnosis and treatment (cytology) (WHO)



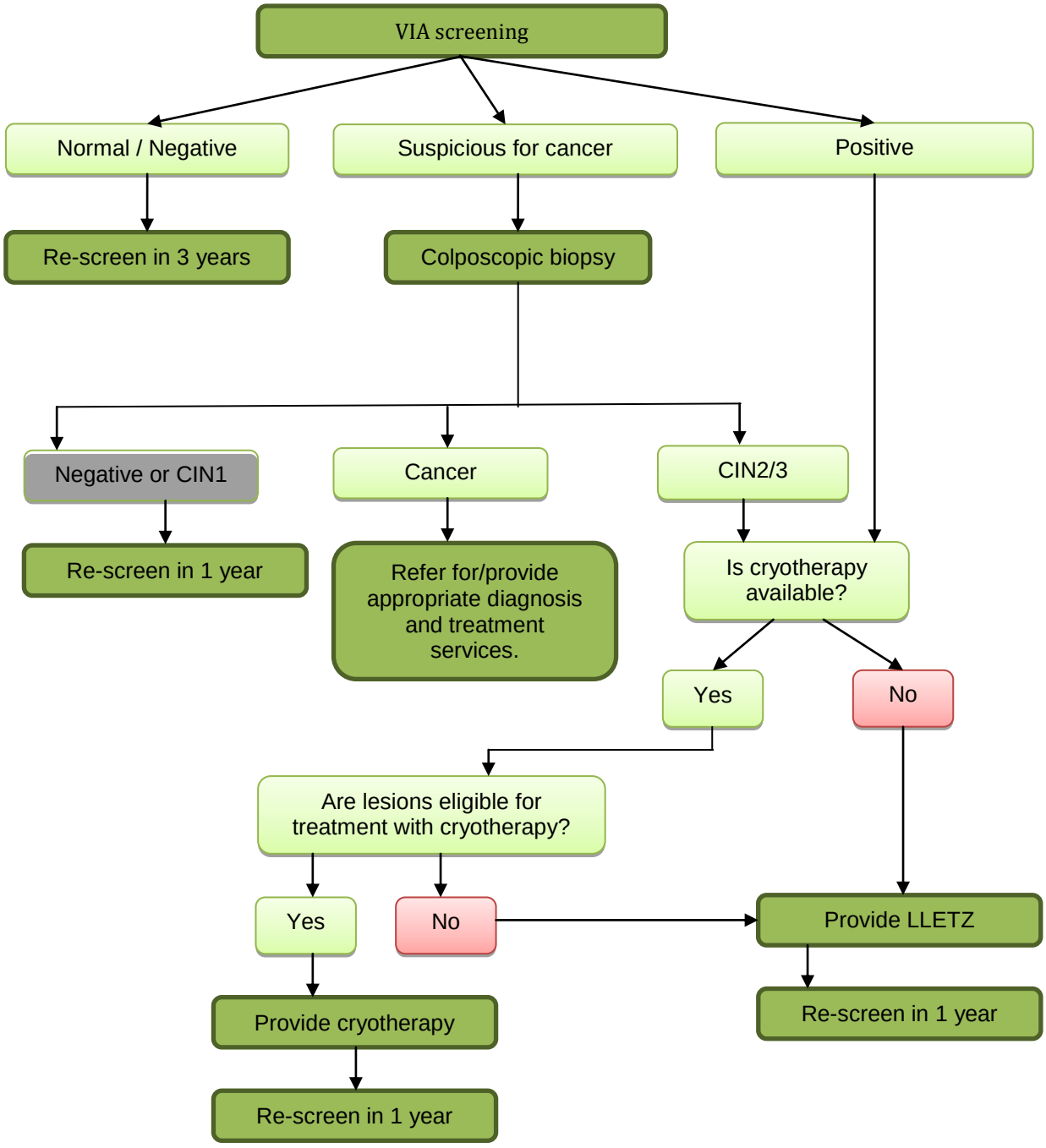
10.3 Screening with VIA for low risk or general populations

Figure 6: Low risk group: Screening, diagnosis and treatment (VIA) (WHO)



10.4 Screening with VIA for high risk populations

Figure 7: High risk group: Screening, diagnosis and treatment (VIA) (WHO)



CHAPTER 11: Treatment and care of cervical cancer

Cancer treatment entails the provision of curative and palliative care, aiming to decrease cervical cancer morbidity and mortality rates, alleviate suffering, and enhance the quality of life in women with potentially terminal disease. Healthcare providers at all levels should know the common symptoms and signs of cervical cancer. If a woman presents with such symptoms, her cervix should be examined visually to determine whether further testing is needed. Furthermore, any woman presenting with a foul smelling discharge should have a speculum examination in order to rule out the possibility of invasive cervical cancer. (This is also known as down staging).

11.1 Cancer diagnosis and staging

Policy statement 6: All women with histologically diagnosed cervical cancer must undergo staging before any treatment is initiated.

Cervical cancer should be biopsy diagnosed and referred for treatment within six weeks of biopsy. Once a histological diagnosis of cervical cancer has been made, the next step is to formulate the most effective therapy for the individual concerned. In order to manage a cervical cancer patient properly, it is essential to understand the extent or "stage" of her disease at the time of diagnosis. This is what is referred to as ***staging***. It is used to determine the best treatment options.

The classification of the International Federation of Gynaecology and Obstetrics (FIGO), which is based on tumour size and the extent of spread of disease in the pelvis and distant organs, is recommended for staging invasive cervical cancer. The extent of growth of the cancer is assessed clinically, supplemented by a limited number of relatively unsophisticated investigations. An exception to the above is staging of micro invasive cervical cancers, which are staged according to pathological criteria of the depth and width of the invasive lesion in relation to the epithelium of origin (which may be either squamous or glandular epithelium). Attention should be paid to the size of the tumour and possible involvement of the vaginal fornices, the parametria (transverse cervical and uterosacral ligaments), the pelvic walls, the bladder and the rectum. Generally severity of cervical cancer progressively increases from stage one to four.

In some cases, a cancer can be “down-staged” or changed form a more severe to a less severe stage through surgical or chemical means.

11.2 Cancer specific and curative services

A range of therapeutic cancer treatments exist, and there is guidance globally on preferred treatment approaches for specific cancer stages. Treatments guidelines for South Africa are provided in the clinical guidelines and include the following:

- **Surgery:** Surgery can be used to remove cancer in early stages, and may be followed by extra or adjuvant therapy if needed
- **Chemotherapy/ Radiation:** Chemotherapy and radiation therapy are additional options for treating cancer. They can be used to cure, or in some cases, halt disease progression

Recommendation: Women should be given all the information about the procedure (including the benefits, risks, potential side effects, recovery time, cost, chances of success, five year survival rates etc.) before it is performed.

With timely diagnosis and optimal treatment, the following are the five year survival rates by stage of cancer:

- Stage IA – 95 -98%
- Stage IB- 75 -85%
- Stage II -65 -75%
- Stage III – 30%
- Stage IV – 5 -10%

In women who are HIV-positive and diagnosed with cervical cancer, ARV treatment must be initiated immediately (if the woman is not currently taking ARVs). ART forms an essential part of therapy for cervical cancer in women who are HIV-positive.

All patients who have undergone treatment for invasive cancer require follow up. The follow up schedules regimens for the different treatments are enunciated in the clinical guidelines.

All facilities that treat patients with cervical cancer, regardless of HIV status, should monitor and report on improvements using the indicators defined in chapter 13.

11.3 Palliative care services

Palliative care services are an essential part of the treatment and care process for any form of cancer. Palliative care is addressed in detail in a separate policy within the national Department of Health. Palliative care can take many forms. Below is a summary of the basic expectations for palliative care under this policy.

- Human resources are required in facilities to manage or oversee the linking of terminally ill patients to appropriate palliative care services.
- Palliative radiation therapy should be provided as appropriate in tertiary facilities to provide effective, comprehensive symptomatic control.
- Medical palliation, including constant availability of analgesics for pain control and incontinence care, should be provided in a home-based support system, and is an integral part of primary healthcare.

SECTION D: Monitoring progress

CHAPTER 12: Monitoring and evaluation

Monitoring and evaluation (M&E) of the cervical cancer control programme is essential. The ultimate purpose of M&E is to: generate an essential set of good quality and reliable measurable indicators and to enable the use of these indicators for monitoring progress with programme implementation and for evaluating impact of the programme on health outcomes.

This section outlines the outcome and impact indicators that will be used for evaluation. A detailed monitoring framework will be developed by the national Department of Health in conjunction with provinces and districts. This framework will define the programme inputs, activities and expected outputs, as well as the input, process and output indicators that will be used to measure progress.

The M&E framework will be aligned to the national HIS Strategy. Health information system (HIS) strengthening (personnel, resources, HIS technology and information management) is essential to enable effective monitoring and evaluation (M&E).

Proposed indicators to monitor the implementation of this policy:

Strategic objective 1: To reduce the incidence of oncogenic HPV infections by 20% in 2030

Indicator	Definition	Numerator	Denominator	Data source
Coverage of HPV vaccination	Percentage of grade 4 girls (9-12 years) received HPV 2nd dose (fully immunised)	Grade 4 girls 9 - 13 years received 2nd dose	Grade 4 girls 9 – 13 years with signed consent form	
Incidence of oncogenic HPV infection	New cases of oncogenic HPV infection in WRA (15 -49 yrs)	New Cases of oncogenic HPV in WRA	Total number of WRA (15 -49 yrs)	DHIS Surveys

Strategic objective 2: To reduce the incidence of invasive cancer to 20% by 2030

Indicator	Definition	Numerator	Denominator	Data source
Availability of LBC services	Proportion of primary health care facilities providing LBC	Primary health facilities with functional equipment and trained staff for LBC	All primary health care facilities	
Access to cervical cancer screening services	PHC that can provide cervical cancer screening services (any screening method)	Number of PHC facilities with equipment, commodities and competent staff to provide screening- any method	All PHC facilities	DHIS Surveys Mapping
Coverage of cervical cancer screening amongst eligible women	Uptake of screening services by eligible women	Number of eligible women (30 -55 years) who have been screened at least once in the last 10 years	Total number of women 30 – 55 years	DHIS Surveys
Treatment of precancerous lesions	Women with HG-SIL / CIN 2-3 who receive appropriate treatment	Number of Women with HGSIL who receive appropriate excision or ablative treatments	Total number of women with HG SIL	Registers Surveys

Strategic objective 2: To reduce mortality attributed to cervical cancer to 20% by 2030

Indicator	Definition	Numerator	Denominator	Data source
Five year survival of women diagnosed with cervical cancer	Proportion of women with cervical cancer still living 5 years from date of diagnosis	Women diagnosed with cervical cancer still alive 5 years from date of diagnosis	Total number of women diagnosed with cervical cancer	
Incidence of cervical cancer	New cases of cervical cancer	Number of New Cases of cervical cancer diagnosed in women 40 yrs and above	Total number of women 40 yrs and above	DHIS Surveys
Improve quality of life of women with terminal cervical cancer	Women with cervical cancer who receive palliative care	Number of women with terminal cervical cancer who receive hospice care	Total number of women with terminal cervical cancer	

CHAPTER 13: Roles and responsibilities

13.1. Role of community healthcare workers

Counselling services offered by community healthcare workers in primary healthcare facilities is envisaged as the main driver of the education and awareness raising activities. Counselling will be provided free of charge at the primary care level – at all clinics and community health centres, as well as at designated district hospitals in their out-patient departments. Community healthcare workers should provide information on how and where to access screening services with every household visit.

13.2 Role of civil society organisations

Client recruitment through information, education and communication by civil society organisations in a coordinated manner will improve awareness in the community about cervical cancer. Coordinated strategies are needed to inform and educate at-risk women about screening, cervical cancer prevention and the benefits of early detection and treatment. Providing user-friendly and understandable information for eligible women is an essential part of screening to ensure that women understand the rationale for screening and utilise the service. Possible information and educational strategies will include:

Providing information on cervical cancer through one-on-one health education by trained healthcare workers and community dialogues and support groups using various participatory methods.

Developing appropriate information, educational and communication (IEC) materials and strategies that: facilitate dialogue between communities and health workers; engender peer counselling; engage the broader public (e.g. through mass media methods such as radio and TV broadcasts and edutainment programmes); and include important community leaders as advocates for screening.

13.3 Role of academic and research institutions

The continuous technological and evidence based practice are critical to the improvement of the quality of service rendered to patient. The academic and research

institutions if working in a coordinated manner and minimise duplication can enhance the rapid introduction of the technological innovations. The key future research areas include but not limited to:

- early diagnosis to the disease, implementation of the HPV-DNA testing technology
- point of care testing to reduce the lag time between the screening and diagnosis and access to treatment and care
- development of cost effective technology to keep the national cancer registry.

13.4 Role of other sectors/departments

Although the cervical cancer is managed within the Department of Health, the collaboration with other sectors in government to reduce the risk factors that pre-dispose women to the development of cervical cancer is critical.

- Strengthening the comprehensive sexuality education in basic education.
- Reduction in poverty and improvement of the conditions of living for women.
- Reduction of gender based violence and women economic empowerment will contribute to the reduction of mortalities related to cervical cancer.

CONCLUSION

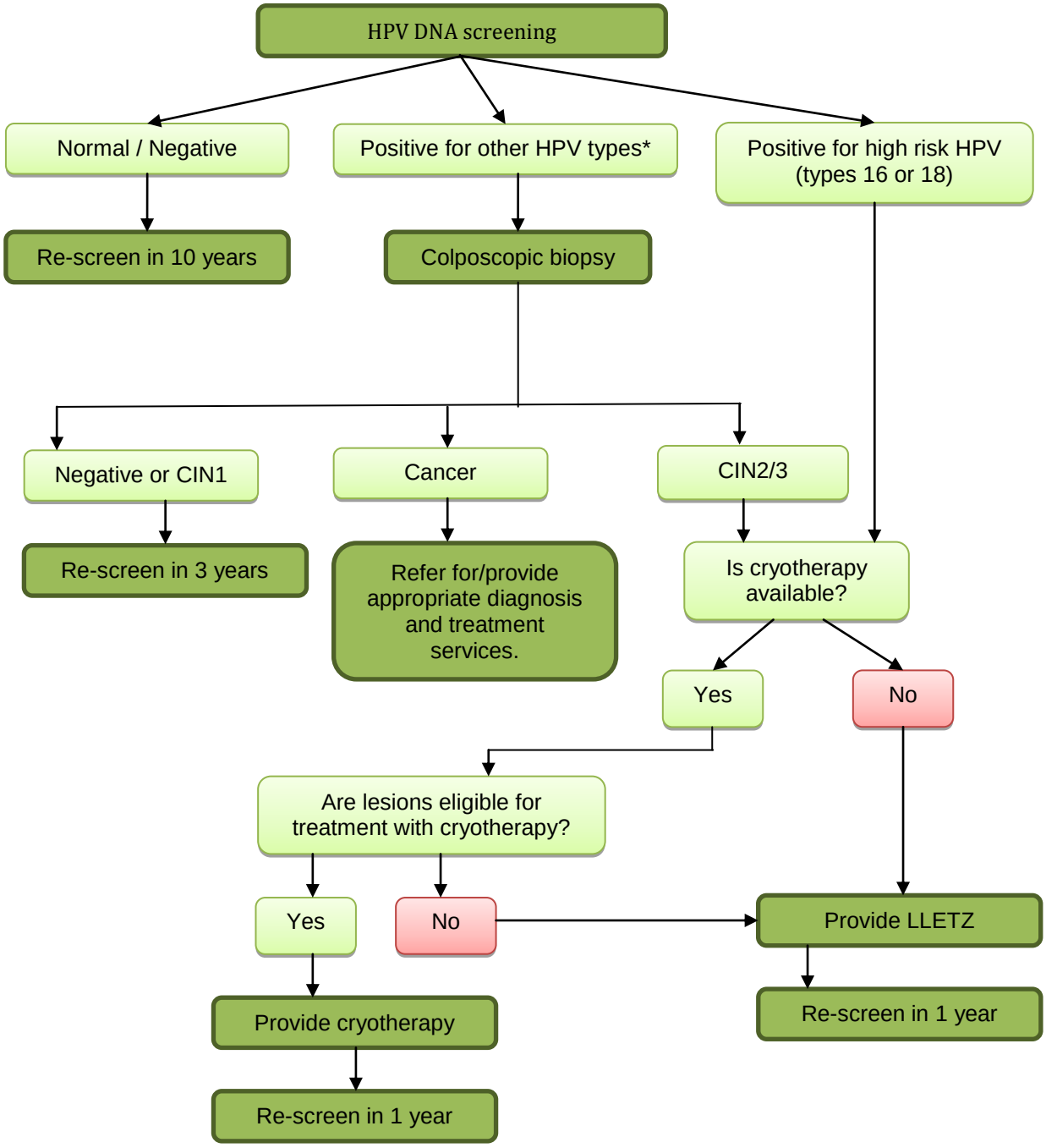
Cervical cancer is a major cause of morbidity and the most common cause of cancer-related death among women in South Africa. Cervical cancer and cervical pre-cancer develop largely as a consequence of persistent infection with high risk HPV.

As stated above, the overall goal of this policy is to improve women's health and well-being by decreasing cervical cancer-related morbidity and mortality in South Africa. This will require strengthening and improving access to screening and treatment services. This will also require strategic enablers such as having a skilled workforce, laboratory capacity, sufficient materials and equipment, strong communication systems, and effective monitoring and evaluation activities.

Fortunately, cervical cancer is largely preventable. HPV vaccination will continue to be implemented as part of the Integrated School Health Programme, collaborating with the Departments of Basic Education and Social Development. Vaccination efforts combined with improved access to screening and treatment services will ultimately contribute to the goals of this policy, improving the quality of life of South African women and families.

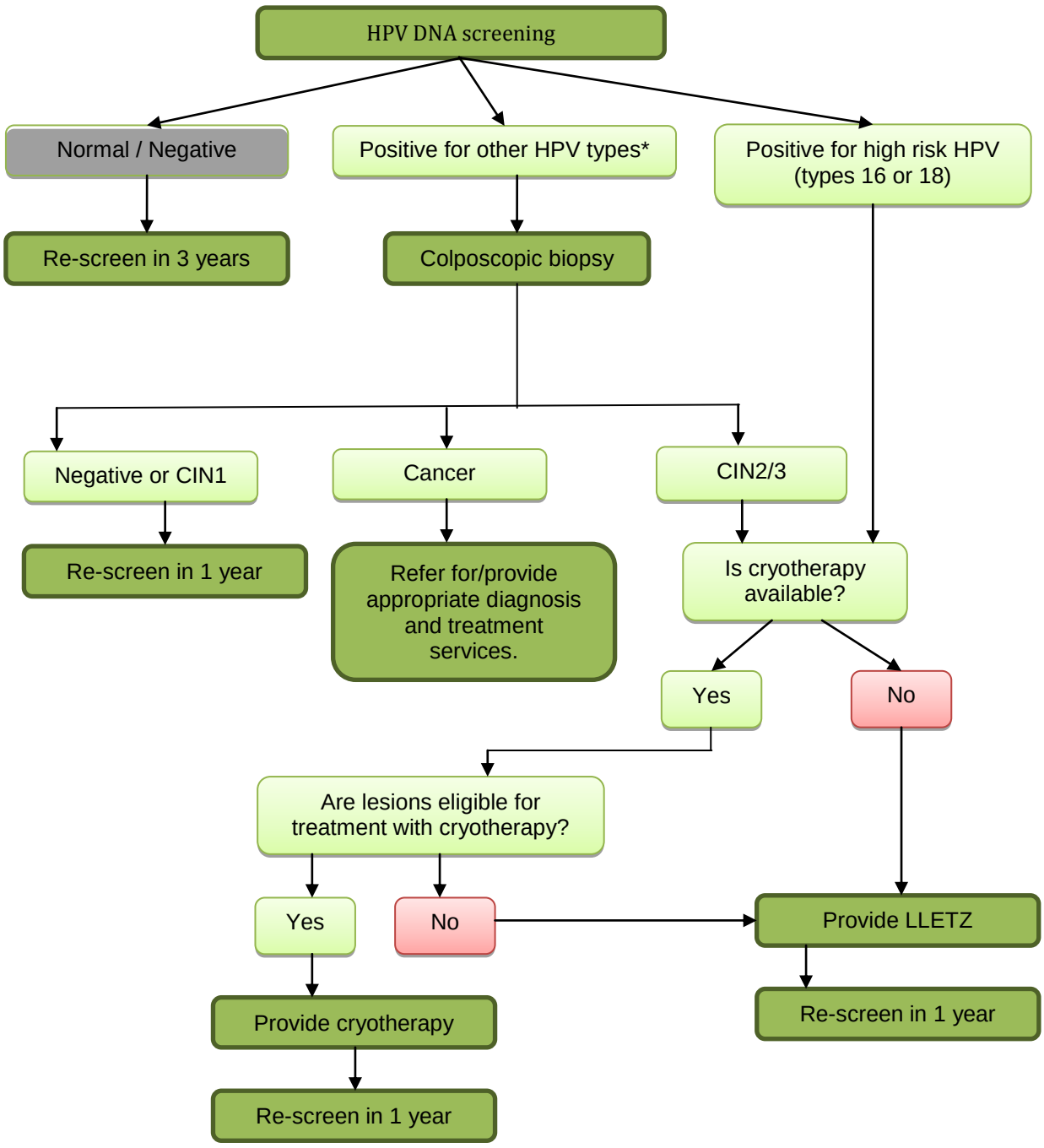
Appendix 1

Figure 8: Low risk group: Screening, diagnosis and treatment (HPV DNA) (WHO)



Appendix 2

Figure 9: High risk group: Screening, diagnosis and treatment (HPV DNA) (WHO)



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