

**EPIDEMIOLOGICAL PROFILE OF CERVICAL CANCER IN LIMPOPO PROVINCE,
2013 TO 2015**

By

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DECLARATION

I, Lekota Provia Maggy, declare that **EPIDEMIOLOGICAL PROFILE OF CERVICAL CANCER IN LIMPOPO PROVINCE, 2013 TO 2015** is my own original work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete reference and that this work has not been submitted before any other degree at any other institution.

SIGNATURE

DATE

DEDICATION

This research is dedicated to the following people:

- To my lovely daughter Tshegofatso and her dad Themba.
- My brother Thabang, my sisters Lesedi and Martha, my mother Rebecca and my father Wilson.
- To the screeners of pap smear and cytotechnicians at Limpopo province and the whole country and globally, not forgetting Prof van Bogaert of National Health Laboratory services, at Polokwane hospital who passed away in 2015.
- To all the women who screened for pap smear in Limpopo province and the whole world and also those who try their best in implementation of strategies to prevent cervical cancer around the world.

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ABSTRACT

Background: Cancer of the cervix is the fourth most common cancer affecting women worldwide and is currently considered as a sexually transmitted cancer. This type of cancer is caused in most cases by a viral infection, Human Papilloma Virus (HPV) strains 16 and 18. Cervical screening aims to prevent invasive cervical carcinoma by detection and treatment of its precursors cervical intraepithelial neoplasia grade 2 (CIN2) and, particularly, grade 3 (CIN3). The current study aimed at determining the distribution of cervical cancer and the association of cervical cancer with HIV infection in Limpopo Province.

Methods:

The current study used quantitative retrospective method to systematically review the available data on Papanicolaou (Pap) smears from National Health Laboratory Services at Polokwane hospital from the year 2013 to 2015. The data was kept anonymously by not using the names of the patients and ethical clearance was received from the Turfloop Research Committee of University of Limpopo in consideration of section 14, 15, 16, and 17 of National Health Act 61 of 2004. The data was exported to excel spreadsheet and cleaned before exported into SPSS 23.0 software which was used for data analysis.

Results:

The findings from the current study show a decline of 33% in the number of Pap smears that were submitted for cytology between 2013 (82 041) and 2015 (23 527) in Limpopo province. However, the study revealed that there is an increase in prevalence of cervical cancer from 16.7% in 2013 to 19.2% in 2015 in Limpopo Province. In the same period this rural province already demonstrates a high burden of cervical cancer among the middle aged women. The positive cervical smears were classified as cervical intraepithelial neoplasia (CIN) I, II, or III and therefore, 78.5% were CIN I, 21% CIN II and 0,5% CIN III. HIV infections have been found to be associated with cervical cancer as the prevalence of cervical cancer among HIV positive women was found to be 25% and most of the affected women are the middle aged group.

Conclusion:

The screening coverage for cervical cancer has decreased in Limpopo Province but the prevalence of cervical cancer has increased by 2.5% therefore, this translates to the need for community awareness about prevention of cervical cancer. Majority of the cases were classified as CIN 1 at 78.5% which can be cured if treatment started early. The Limpopo Province should therefore strengthen strategies to integrate HIV and cervical cancer services as it was found that there is a strong association between the HIV and cervical cancer.

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ABBREVIATION

ACS	:	American Cancer Society
AIDS	:	Acquired Immunodeficiency Syndrome
CIN	:	Cervical intraepithelial neoplasia
HIV	:	Human Immunodeficiency Virus
NHLS	:	National Health Laboratory Services
PAP	:	Papanicolous (test)
SEER	:	Surveillance Epidemiology and End Results
STI	:	Sexually transmitted infection
UNPD	:	United Nations Population Division
WHO	:	World Health Organisation
VIA	:	Visual Inspection with Acetic acid
HPV	:	Human Papilloma Virus

DEFINITION OF CONCEPTS

Cervical cancer-it is cancer of the neck (cervix) of the uterus. It develops in the tissues of the cervix of female reproductive organ (Arbyn et al., 2011). This definition will be used as is in this study.

Screening-is the method applied to a population aimed to identify the disease before it manifest in order to allow early treatment and effective management (Ferlay et al., 2012). In this study, screening refers to examination of women to detect any presence of cellular changes in the cervix.

Vaccination- is the prevention of the disease by administration of a prepared antigenic material into the body to stimulate the development of antibodies to provide immunity against specific agent (WHO, 2013). In the current study, vaccination of HPV is recommended for girls aged 9 years to 13 years old prior to the debut of sexual activity.

Human Papillomavirus (HPV) - is a sexually transmitted virus. It is passed on through genital contact (such as vaginal and anal sex) and can cause genital cancers such as cancer of the vulva (Botha, et al., 2010). In this study it is certain types of HPV that are classified as “high-risk” because they lead to abnormal cell changes and can cause cervical cancer.

1. CHAPTER: ONE

1.1 Introduction

The aim of the study was to investigate the epidemiological profile of cervical cancer and association of HIV with cervical cancer in Limpopo Province from 2013 to 2015. This chapter presents background information about cervical cancer, problem statement, significance, research question, aim and objectives of the study.

1.2. Background

Cervical cancer is the fourth most common cancer affecting women worldwide (WHO, 2012). Cervical cancer is currently considered as a sexually transmitted cancer and is caused in most cases by a viral infection, Human Papilloma Virus (HPV) strains 16 and 18 (WHO, 2012). Most of women who are sexually active are in contact with the virus (Botha, Bruno, Dreyer, Mouton and Guidoizzi, 2010). The HPV virus is found in 99.7% of cervical cancers, so they are considered as a major cause of cancer of the uterus (Bunduki, Matumo and Vahaviraki, 2015). Cervical cancer develops in the tissues of the cervix of female reproductive organ and is a serious female health problem affecting mostly middle aged women with about 80% occurring in developing countries (Sankaranarayanan, Swaminathan, Brenner, 2011).

According to Singh, S. and Badaya, (2012) Sub-Saharan Africa has recorded the highest incidence for cervical cancer in recent years. The incidence of cervical cancer can be attributed to high prevalence of Human Papilloma Virus (HPV) and also other co-factors like use of long term birth control pills, high parity, and increased number of sexual partners, smoking and also lack of screening programmes (Zhao, Lewkowitz and Chen, 2012). Higher incidence of cervical cancer is observed in some countries in Africa where the disease affects women from 30 years of age (Paul, Tiwary and Chouhuryl, 2011).

The National Cancer Registry (NCR) within the National Health Laboratory Service (NHLS) is the principal cancer surveillance system in South Africa (SA) and maintains the largest repository of cancer data in the country. The NCR is mandated through recent legislation to monitor SA's national cancer burden (NDOH, 2011). NCR was

established in 1986 as a voluntary, pathology-based cancer reporting system, it now receives over 100 000 cancer reports annually and about 80 000 of them are new cases in South Africa, on the basis of which cancer incidence is calculated (NDOH,2011). In Limpopo Province, it is estimated that 40 000 of cervical cancer patients are diagnosed annually, of which 13.7% of them are new cases while most of them are repeating cases (NDOH, 2011). Data collected from the system are used for research, for educational purposes and to inform decision-making for cancer prevention and control policies in SA (NDOH, 2011).

1.3. Research problem

There is a high incidence of death among cervical cancer patients in South Africa (NDOH, 2011). This is due to poor access to screening and treatment services, limited human and financial resources. In Limpopo province most of women are dying due to cervical cancer, where most of them are young ones.

According to the World Health organization (WHO, 2012), the introduction of vaccines that prevent HPV infection, combined with a comprehensive cervical cancer screening and treatment policy, is a key to addressing the burden of cervical cancer (WHO, 2013).

An estimated 20% of asymptomatic women in South Africa have never had one or more Papanicolaou (Pap) smears (Mamahlodi, Kuonza, and Candy, 2013), this makes them to be likely to present late for screening and therefore putting their lives in danger of contracting Cervical cancer, and complications. The precursors of cervical cancer can be detected and treated, if individuals present early for screening (Mamahlodi, et al., 2013). Knowing the epidemiological profile of women diagnosed with cervical cancer will assist in profiling communities which are vulnerable and presenting with high prevalence of cervical cancer. This will be done in order to prioritize screening and health education in a bid to fight the disease.

1.4. Significance of the study

Cervical cancer screening aims to prevent invasive cervical carcinoma by detection and treatment of its precursors cervical intraepithelial neoplasia grade 2 (CIN2) and, particularly, grade 3 (CIN3). Our study will provide cervical cancer trends in Limpopo

Province to determine the effectiveness of the screening programmes and also determine the disease risk factors. This will assist in advising the policy makers on the variations by period of diagnosis and changes in risk factors in women. The current study will also provide recommendations to ensure that women who have previously not undergone screening do go for screening in order to reduce the incidence of cervical cancer by understanding the risk factors associated with cervical cancer and mortality related to it the general population.

Lastly, the current research will add value into determining the effectiveness and optimal use of HPV screening in decreasing the incidence of and mortality due to cervical cancer. This will also assist in determining the optimum screening interval and the optimal ages at which to start and stop screening. Further research after this current study will be needed to determine how long screening can be delayed after first sexual activity and whether women with certain risk profiles require different screening protocols.

1.5. Aim of the study

Aim of the study was to investigate the epidemiological profile of cervical cancer and association of HIV with cervical cancer in Limpopo Province, 2013 to 2015.

1.6. Objectives of the study

1. To describe the demographic characteristics of women diagnosed with cervical cancer in Limpopo Province.
2. To determine association of HIV with cervical cancer in Limpopo Province.

1.7. Research question

What is the epidemiologic profile of cervical cancer in Limpopo Province from 2013 to 2015?

CHAPTER TWO:

2. LITERATURE REVIEW

2.1. Introduction

Chapter two discusses the literature review on the burden of cervical cancer around the world, strategies to reduce cervical cancer, complications of late screening and awareness and health education.

Human papillomavirus (HPV) infections cause virtually all of the more than 500000 cases of invasive cervical cancer per year and mortality worldwide (Ault, 2006; Schiffman, Wentzensen, Wacholder, Kinney, Gage and Castle, 2011). Cervical cancers occur primarily at the cervical transformation zone. The transformation zone is a ring of tissue located where the squamous epithelium of the vagina meets, undermines, and replaces the glandular epithelium of the endocervical canal (Schiffman et al., 2011). HPV is a contact infection and it is spread among the sexually active individuals by sexual contact (Ault, 2006). Genital HPV infection is predominantly, but not exclusively, a sexually transmitted infection and about 50% to 80% sexually active women are infected by this virus at least once in their lifetime (Banura, Mirembe, Katahoire Namujju, Mbonye and Wabwire, 2011).

Cervical cancer is known to be a preventable disease through the detection of cervical cancer precursors, historically using cytology of the cervix as the primary screening test (Botha and Richter, 2015). Screening is found to be the best method for early detection of cervical cancer (Hoque, 2013). The aim of cervical screening is to reduce the incidence of cancer by the detection and treatment of precursors (Mark, 2012). A secondary aim of screening is the early detection of invasive disease, which might improve the prognosis and also reducing mortality from the disease (Mark, 2012). Papanicolau smears are used in the classical primary screening technique, HPV DNA testing, introduced in 2008, is well diffused in developed countries and is taking off in developing countries with a potentially significant reduction in the numbers of advanced cervical cancers and deaths (American Cancer Society, 2012).

2.2. Epidemiology of human papillomavirus infection

The human papilloma viruses (HPVs) are DNA double strand viruses and of small size which approximately 8000 pairs of bases and it has cohabited with the human species over many years suffering relatively few changes in their genetic composition (Castellsagué, 2008). There is scientific indication that cervical cancer is in fact a sequel to a long term unresolved infection by certain genotypes of the HPV (Castellsagué, 2008). Thus, it has been estimated that at least half of all sexually active individuals will acquire HPV at some point in their lives, whereas at least 80% of women will acquire an HPV infection by age 50 (Ault, 2006). The current challenge is that the probability of HPV infection per sexual act is not known but is clearly high (Schiffman, Castle Jeronimo, Rodriguez and Wacholder, 2007)

It has been found that over 100 HPV genotypes exist and these are divided into two groups which are high-risk (HR) and low risk (LR) depending on their potential to cause cancer. There are about 15 high-risk (oncogenic) cancer causing HPV genotypes that are responsible for 5% of all human cancers but predominantly cervical cancer and other anogenital cancers (Desruisseau, et al., 2010; Banura et al., 2011). But the subtypes which are most associated with approximately 99.7% of all cervical cancers are the HPV 16 and HPV 18 (Banura et al., 2011; Schiffman et al., 2011).

The natural history of cervical cancer has been extensively studied and there is now a substantial body of molecular, clinical and epidemiological evidence that persistent infection of the cervix with oncogenic types of human papillomavirus (HPV) is an essential event in the pathogenesis of cervical cancer (Denny, 2012). Men play an important role in HPV transmission as HPV DNA has been detected in the genitalia of up to 73% of healthy men (Banura et al., 2011). HPV infection accounts for an estimated 530,000 cervical cancer cases (~270,000 deaths) annually, with the majority (86% of cases, 88% of deaths) occurring in developing countries (Tota, et al., 2011).

2.2.1 The burden of cervical cancer

Cervical cancer is a public health problem around the world, especially in developing countries, where 80% of cases are reported annually (WHO, 2011). The burden of cervical cancer is higher in low- to middle-income countries, due to poor access of screening and treatment services and limited human and financial resources (WHO, 2013).

2.2.1.1 The global burden of cervical cancer

Worldwide, women in developing countries account for about 85% of both annual cases of invasive cervical cancer, ICC estimated at 493,000 and annual deaths from ICC estimated at 273,500 (Tota et al., 2011). Cervical cancer is the second most common cancer among women worldwide, with an estimated 528,000 new cases in 2012 (Ferlay et al., 2012). There were an estimated 266,000 deaths from cervical cancer worldwide in 2012, accounting for 7.5% of all female cancer deaths. The average risk of dying from cervical cancer before age 75 is three times higher in the less than in more developed regions (Ferlay et al., 2012).

Cervical cancer was ranked the third most common cancer globally, ranking after breast and colorectal cancer estimated at 1.3 million cases and 0.57 million cases respectively. It has also been ranked the fourth most common cause of cancer deaths ranking below breast, lung, and colorectal cancer (Denny and Anorlu, 2012). Approximately 528 000 new cervical cancer cases were estimated to be diagnosed globally per year, with 266 000 deaths due to cervical cancer in 2012 (WHO, 2013).

India has the world's largest burden of cervical cancer about 122, 844 women are diagnosed with cervical cancer and 67, 477 die from disease (Sreedevi, Javed and Dinesh, 2015). Cervical cancer is also a public health problem in Europe, specifically across the whole of Eastern Europe (Maree et al., 2011) and Western Europe had 9 318 cases of cervical cancer and 3 794 deaths for the same period, in a total population of 96

million women (Arbyn et al., 2011). The burden of cervical cancer was the lowest in Finland and the highest in Lithuania (Arbyn et al. 2007; Maree, Wright and Makua, 2011). The difference of incidence of cervical cancer between the regions of lower and higher levels of development is due to the absence of national cervical cancer screening programmes in the low-to middle-income countries (Soerjomataram et al., 2012). The majority of women who develop the disease in these countries seek treatment at a later stage, when treatment is no longer effective (WHO, 2011).

2.2.1.2 The burden of cervical cancer in Africa

Africa is the region which has the highest burden of cervical cancer (Arbyn et al., 2011; Maree et al.; 2011). Approximately 80 000 women were diagnosed with cervical cancer, and 60 000 women died from cervical cancer, in African population of 270 million women at risk of developing cervical cancer (aged 15 years and older) during 2008 (Denny and Anorlu, 2012; Shantal et al., 2014). In Sub-Saharan Africa, cervical cancer is the most common cause of cancer death in women (23.2% of the total) , the incidence and mortality rates for cervical cancer are 34.8 and 22.5 per 100 000 respectively which is the highest of any world region (Denny and Prendiville,2015). More than 85% of incidence cases and deaths from cervical cancer occur in low-resource countries where the initiation and maintenance of cervical cancer screening programs have proved impossible (Jemal, Bray, Forman, O'Brien, Ferlay and Center , 2012).

There is however a variance of cervical cancer incidence in African regions in which the highest rate 40 cases per 100,000 has been reported in Eastern and Southern Africa. Cervical cancer is the leading cause of cancer-related death among women in Eastern, Western and central Africa (Arbyn et al., 2011). In Southern Africa the highest incidence of cervical cancer is found in Lesotho and Swaziland as these two countries have neither screening programs nor any anticancer treatment facilities

and have 1 and 2 doctors per 10,000 populations, respectively (compared with 8/10,000 in South Africa and 27/10,000).

2.2.1.3 The burden of cervical cancer in South Africa

It has been estimated that at least 30 000 women die of cervical cancer in South Africa annually (WHO, 2010). Cervical cancer is currently the primary cancer amongst the women in South Africa, with annual new cases of approximately 6742 in African women and 3681 deaths (Botha and Richter, 2015). Black women are most affected as the incidence is nearly 3 times higher in Black women compared to White women – 35 per 100 000 versus 12 per 100 000 (Maree et al., 2011).

HIV- positive women are 3 to 5 times more likely to develop cervical lesions that could become cancerous (MacPhail, 2013). In South Africa, approximately 13% of the female are living with HIV/AIDS and this makes a high-risk environment for the acquisition of cervical cancer in South Africa (Botha and Richter, 2015). In South Africa, the cervical cancer, screening coverage (proportion of women over the age of 30 years) is low (Denny,2015).

2.2.1.4 The burden of cervical cancer in Limpopo

In Limpopo province estimates for cervical cancer in 2000 were 56% (Bradshaw, Nannan, Laubscher, Groenewald and Joubert, 2000). In most rural health facilities of Limpopo Province, it shows that few women were screened for cervical cancer (Mamahlodi, et al., 2010). Approximately 500 patients are seen daily at Tshilidzini Hospital which is in rural area of Limpopo Province and fifty-three percent of these patients are women, but only 16.2 percent of these women access cervical cancer screening annually (Mudau, Tagli and Mabunda, 2016). Most of them who develop the disease seek treatment much later when it is at an advanced stage which treatment is no longer effective due to lack of knowledge on cervical screening and attitude of women (Mudau, Tagli and Mabunda, 2016).

The Hoedspruit Training Trust and the Global Women's Health Division of Mount Sinai Medical Centre in NY initiated a programme called "The Hoedspruit Endangered Species Center(HESC)" to integrate cervical cancer screening into the HIV services provided at Hlokomela, using a see and treat approach, approaching, providing screening and treatment at the same visit (HESC,2015). The procedure is performed by applying 5% acetic acid or ordinary table vinegar and it is called VIA (visual inspection with acetic acid (HESC, 2015).

2.5. Strategies to reduce cervical cancer

Strategies that aim to ensure that all women are screened at the appropriate interval and receive adequate follow-up are most likely to be successful in further reducing cervical cancer incidence and mortality in the communities (Moyer, 2012). Health education programmes that promote abstinence, conscientious condom use, or both, could reduce the risk of cervical cancer at the population level (Schiffman et al., 2007). Vaccination programmes against HPV infection have been developed and introduced in many countries with an aim to reduce the incidence of cervical cancer (Schiffman et al., 2007).

2.5.1. The Screening Programmes for Cervical Cancer.

Secondary prevention of cervical cancer is detectable in the early stages through screening for precancerous cervical lesions the method of cytology- based Papanicolaou test, commonly known as Pap smear (Botha et al., 2010). Screening programmes purpose is for early detection of cancer, in order to reduce mortality and morbidity from cervical cancer (Botha et al., 2010). If cancer is detected in the early stages, it is preventable or curable by surgical removal of the precancerous lesions (Mamahlodi et al., 2013).

The screening programmes have considerably decreased the incidence and mortality rates in developed countries but there are no screening programmes of women in most developing countries (Hoste et al., 2013). About 85% of all

cervical cancer related deaths reported were from developing countries which have poor set ups of screening programs or minimally effective (Seinfeld,2015). It is recommended that the first Pap smear should be taken at age 21 years or within three years of onset of sexual activity. It is different in developing countries where the first Pap smear is taken at the age of 30-35 years (Botha et al., 2010). Never having had a Pap smear is considered as one of the highest risk for development of cervical cancer (Botha et al., 2010). An analysis of population-based surveys indicates that coverage of cervical cancer screening in developing countries is 19% compared to 63% in developed countries and ranges from 1% in Bangladesh to 73% in Brazil (Stewart, 2014). Older and poor women who are at highest risk of developing cancer are least likely to undergo screening (Subramanian, 2013).

In developing countries the demand of cervical cytology (Papanicolaou test) are too complex (Seinfeld,2015).The study designed to find alternative tests to cytology, specifically to allow point- of- care testing to enable women to be screened and treated in a single visit, without the necessity for complex and expensive laboratory investigations as well as colposcopy and histological examination (Seinfeld,2015). They have demonstrated that visual inspection with acetic acid (VIA) is an alternative sensitive screening method (Subramanian, 2013). It is cheap and non-invasive, and can be done in a low level health facility like a health centre (Subramanian, 2013). VIA provides instant results and those eligible for treatment can receive treatment of the precancerous lesions using cryotherapy on the same day and in the same health facility. This “see and treat” method ensures adherence to treatment soon after diagnosis, hence stemming the problem of failing to honour patient referrals (Denny, 2012).

2.5.1.1 Public Health Importance of Screening

Disease prevention strategies can be categorised as primary prevention and secondary prevention (Paul and Fabio, 2014). Primary prevention aims to reduce the risk of an individual to contract a particular disease by

eliminating the etiological agents from the environment. In cervical cancer, the most important risk factor for development of premalignant and malignant disease is human papillomavirus (HPV) infection (Botha and Dochez, 2012).

HPV is the most common sexually transmitted infection (STI) around the world. The virus is primarily spread by direct skin-skin contact (Botha et al., 2010). Women who are sexually active have a lifetime risk of up to 80% to be infected with one or more HPV types (Karin, 2012). The goal of cervical cancer screening is to identify pre-lesions and early-stage invasive lesions, as treatment of these lesions may stop progression of the disease. Routine screening has a good chance of detecting most premalignant infection and or cellular changes (Mamahodi et al., 2013).

2.5.1.2. Complications of late screening

Cervical cancer screening serves as a model for the success of a screening program. The age-adjusted incidence of and mortality rates from cervical cancer in the United States have decreased by more than 50% between 1975 and 2008 (SEER, 2011). Screening for cervical cancer from patient aged 10 years to 19 years is complicated by lower rates of detection and higher rates of false-positive results than in older women (SEER, 2011).

Lack of awareness and knowledge about cervical cancer among women was found equally responsible for late presentation of patients and advanced stage at diagnosis of cervical cancer (Yu et al., 2005). Inadequate knowledge of cervical cancer about etiology, screening, diagnostic procedure and treatment among health care practitioners (WHO, 2006; Tran et al., 2011) lead to the misdiagnosis of cervical cancer and unnecessary consultations. Health care practitioners should be given training and skills about cervical cancer diagnostic, which will improve the diagnosis of cervical cancer at advanced stage (Mayor, 2011).

The increased risk of late reporting is usually found among women who have lower education (Denny and Prendiville, 2015). Cervical cancer is difficult to cure once symptoms develop and is fatal if left untreated. Prognosis is strongly dependent upon the stage of disease at detection and treatment. Late-stage disease is associated with low survival rates after surgery or radiotherapy (Paul and Fabio, 2014).

2.5.2 Awareness and health education

It has estimated that 20% of asymptomatic women in South Africa have never had one or more Pap smears (Castle, De Sanjose, and Qiao, 2012). The main obstacle is not necessarily the cost of the screening test, but it is the complexity and shortage of the infrastructure for the screening programs. And this include trained healthcare practitioners, healthcare equipment required to conduct screening, sample transport, and public sector laboratories with adequate trained personnel who can screen, diagnose and guarantee rigorous quality control. A data information system must be able to deliver back the results of the patient so that healthcare providers can ensure the necessary follow-up and interventions by trained healthcare providers (Wright and Kuhn, 2012).

Lack of knowledge with regard to cervical cancer and cervical cancer prevention opportunities for women and healthcare workers is also of concern (Sibiya, 2012). An estimated 8.8-million South African women who are eligible for cervical cancer screening have not yet been screened even once in their lifetime (National Cancer for Health Statistics, 2012). Every step in the screening process needs to be thoroughly considered by a multidisciplinary team of experts, including primary health nurses and doctors, public health specialists, pathologists and gynecologists (Sibiya, 2012).

The reason for high incidence and mortality from cervical cancer in sub-Saharan Africa is lack of awareness of cervical cancer among the population, health-care providers and policymakers; limited access to high-quality health-care services

and cervical screening programmes; and lack of functional referral systems (Mark, 2012). In Uganda the limitations on levels of population awareness about cervical cancer include perceptions, beliefs and knowledge about cervical cancer risk factors and symptoms (Paul and Fabio, 2014).

Weak healthcare systems, lack of financial and human resources, competing health needs, war and civil strife, and widespread poverty have prevented many governments from supporting cervical cancer prevention programs in developing countries (Denny and Prendiville, 2015). In United Kingdom (UK), knowledge and understanding of cancer risk factors and outcomes of cancer treatments influenced individuals' intentions and actual participation in cancer prevention programmes (Zhao, Lewkowits and Chen, 2012).

2.5.3 Vaccination against HPV

Most developed countries have introduced HPV vaccines into routine vaccination programs, to reduce cervical cancer incidence and more than 60 million doses have already been distributed in 2010, which could guarantee a protection rate of approximately 70 % (WHO, 2013). The current quadrivalent HPV vaccine provides protection against high-risk HPV types 16 and 18, and also against low-risk types 6 and 11, which cause 90% of genital warts. The target age groups for vaccination against HPV infection vary in different countries, the vaccine is aimed mainly at girls between the ages of 9 and 12 years because it is most effective when given before the onset of sexual activity. This is mainly because it has no effect against HPV infection which is transmitted sexually once it has been acquired (Brotherton, Fridman, May, Chappell, Saville and Gertig, 2011).

Two vaccines have been developed that prevent the acquisition of high-risk HPV types linked to cervical cancer and one of the vaccines is proven that it also protect against genital warts (WHO, 2013). The introduction of vaccines that prevent HPV infection together with cervical cancer screening and treatment policy is the key to addressing the burden of cervical cancer (WHO, 2013). The WHO (2012) recommends the vaccination of 9-13-year-old girls, prior to sexual activity. The best primary method for prevention of cervical cancer is HPV

vaccination of girls before screening (Karin, 2012). HPV vaccination in the public health sector is still to be seen in the developing world, due to high vaccine cost (Karin, 2012).

More than hundred countries in the world have been licensed to use HPV vaccine and many countries have incorporated vaccine in their routine vaccine programme (Markowitz , Tsu and Deeks , 2012).In United States of America it has been found that 98% of paediatrician and 88% of family practice physician are offering the HPV vaccine to their female patients(Daley , Crane and Markowitz, 2010). Many countries that have low cervical cancer rates have implemented HPV vaccine but full coverage was not achieved in any country (Limia and Pach´on, 2011).

In South Africa vaccine programme was introduced in some schools for girls in grade 4 (Snyman, Dreyer, Visser, Botha and van der Merwe, 2015). It is predicted that in future cervical cancer vaccination will be more cost effective and much more effective than screening for cervical cancer (Mnisi, Dreyer, Richter, Horton and Snyman , 2013). At 100% coverage with vaccination alone, the reduction in the lifetime risk of cancer will be 61%; with the combination of vaccination and screening, the reduction will increase to 75% (NDOH, 2011). The World Health Organization has recommended that routine HPV vaccination be included in national immunisation programmes (Goldie, Kohli, and Grima, 2004). In KwaZulu-Natal Province of South Africa, it has been found that the vaccine completion rate was very high as 99.7%, 97.9% and 97.8% for the first, second and third doses respectively (Moodley , Tathiah , Mubaiwa and Denny,2013).

3. CHAPTER THREE: RESEARCH METHODOLOGY

3.1. Introduction

This chapter discusses research method, research design, study site, study population, sampling and sample size used to acquire subjects, including data collection procedure, data analysis, the process to minimize bias, measures taken to ensure validity and reliability and ethical considerations regarding the study.

3.2. Research Method

The method used in the study was quantitative method. Quantitative method is a systematic emphasize objective measurements and the statistical, mathematical or numerical analysis of data collected through questionnaires and surveys or by manipulating pre-existing statistical data using computational techniques (Brink et al., 2012).

3.3. Research design

Retrospective study is a study that looks back in time to study events that have already occurred (Wright and Kuhn, 2012). The study was a quantitative in nature and follows a retrospective study design where secondary data on reported cervical cancers and HIV status was collected from existing data of cervical smears patient in the National Health Laboratory Services of Pietersburg Hospital in Limpopo Province.

3.3.1. Sampling

3.3.1.1. Study population

The target population is the group of individuals having one characteristic that distinguishes them from other groups (WHO, 2012). The study population for our study was database of all women who were screened for cervical cancer in Public Health facilities from Limpopo Province.

3.3.1.2. Sampling

From this database, all patients screened for cervical cancer from 2013 to 2015 were extracted to be our main focus.

3.3.1.3. Ethical issue related to sampling

The data was kept anonymously; the names of the patients were not appearing on the data.

3.3.1.4. Sample size

Sample is the group of participants in a study selected from the target population from which the researcher generalizes to the target population ((WHO, 2013). The sample size was patients screened for cervical cancer from 2013 and 2015 in Limpopo Province. About 5000 of the specimen were screened for cervical cancer in Limpopo province per month, for which around 1200 were found to be positive (have cervical cancer). A secondary data of all Pap smears tested at NHLS Polokwane for the period 2013 to 2015 was used in the current study.

3.3.1.5. Study site

The Limpopo Province consists of five districts: Waterberg, Sekhukhune, Vhembe, Mopani and Capricorn. Data was collected from National Health Laboratory Services in Pietersburg Hospital which is a referral laboratory where cervical smears specimen collected from all of the districts in Limpopo Province. These samples were analyzed at Pietersburg Hospital.

3.3.2. Data collection

3.3.2.1. Data collection approach and method

The data was extracted from the existing database of patients who were screened for cervical cancer at National Health Laboratory Services in Pietersburg Hospital of Limpopo Province from the system called tracker and exported into excel. Therefore, the main focus was on confirmed cervical cancers screening.

3.3.2.1.1. Inclusion criteria

According to the national cervical screening policy, (SADOH, South African Department of Health), Limpopo Province offers cervical screening for free to women who access primary health services in the province. Therefore, all data of women screened for and diagnosed with cervical cancer from 2013 to 2015 was included in the study.

3.3.2.2.2. Exclusion criteria

The data of women screened for cervical cancer which does not consist of all the demographics needed in the study was not included.

3.3.2.2. Development and testing of data collection instrument

There was no instrument used as this was a secondary data from Central Data Warehouse (CDW) of National Health Laboratory services. The data variables included the date smear was collected, the women's ages at smear collection, the district of residence, HIV status of women and smear cytology results.

3.3.2.4. Data collection process

Data was extracted from the records of NHLS, cleaned and converted to SPSS v23, 0 software to be analyzed.

3.3.2.5. Ethical consideration related to data collection

Data or information was not to be used in contravention of Section 14, 15, 16, and 17 of National Health Act 61 of 2004 and the promotion of access of information Act 2 of 2000. Data was used ethically for the purpose which was applied for. It was stored in a confidential manner by separating patient identifying details from laboratory data and stored the master list that links patient identifying details to study patient identifiers in separate secure place. The analysis and interpretation of the results was discussed in a separate environment from the laboratory.

3.3.3. Data analysis

After extracting the data from the NHLS database, the data was exported to excel spreadsheet and cleaned before exported into SPSS v23.0 software which was used for data analysis. The following analysis was done after consultation with the biostatistician at University of Limpopo:

3.3.3.1. Descriptive analysis

Descriptive statistics such as frequencies and inferential statistics was calculated using chi square test association. Data was presented using graphs; bar or pie graphs and

tables to present distribution and association. A 2x2 table was also used to test sensitivity which is the ability of a test to identify those with a disease (true positive rate) and specificity, the ability of a test to identify those without a disease (true negative rate).

3.3.3.2. Odds ratios

The odds of having the disease is the ratio of the probability that the disease will occur to the probability that the disease will not occur (Chatterjee and Hadi, 2015). The odds and relative odds (odds ratios) was calculated as these were used as useful ways of using the information in cross tabulations where one dimension of the table was an outcome of interest (whether 2x2 tables or more complicated). This helped to determine the odds of the probability of women having cervical cancer against demographic characteristics and the type of contraceptives used. An odds ratio or relative risk of 1 implied that the event is equal likely in both groups, while an odds ratio or relative risk greater than 1 implied that the event is more likely in the first group.

3.3.3.3. T-test

The independent student t-test was used for variables having two categories as it assesses whether the mean difference of two groups was statistically significant. This test was performed at the 95% confidence level. The p-value of less than 0.05 in the study was considered significant.

3.4. Reliability and Validity

3.4.1. Reliability

Reliability is the consistency and dependability of a researcher of a research instrument in measuring a variable, equivalence and internal consistency (Brink, Van der Walt and van Rensburg, 2012); Reliability means “repeatability” or “consistency” of the results. In our study, internal consistency was used to assess the consistency and reliability of the screening test results across all samples which described sensitivity (Se), and specificity (Sp), this was able to measure how accurately the test identifies those with cervical cancer and those without cervical cancer. The accuracy of the result was

calculated from a 2x2 table for sensitivity (the true positive) and specificity (the true negative) to check if they give consistent results.

3.4.2. Internal and External Validity

Validity is the ability of an instrument to measure the variable that it is intended to measure (Brink et al., 2012). To ensure internal validity, the secondary data received from NHLS was evaluated against NHLS data management standards for correctness and validated by cytology Department. External validity was obtained by comparing the study with other related studies from different population.

3.5. The process to minimize bias

Bias is an influence that produces an error which can affect the quality of evidence in both quantitative and qualitative studies (Brink et al., 2012). Researcher bias was minimized by making sure that the researcher did not intervene outcome of the screening results from the laboratory and a biostatistician was involved during data analysis. Reporting and presentation bias was minimized by making sure that the findings of the study were reported and presented as they were with no influence from the external force.

3.6. Ethical considerations

3.6.1. Seeking permission

Permission to conduct the study was obtained from Turf loop Research Ethics Committee (TREC). And permission again was obtained from Department of Health Provincial Research Committee and National Health Laboratory Services to use their data of women in Limpopo Province who were screened for cervical cancer from 2013 to 2015.

3.6.2. Confidentiality and privacy

Confidentiality was maintained by ensuring that information obtained from the data was kept anonymous. The names of the patients on the data were removed and no discussion of the results with laboratory technicians or any other person working in the

laboratory including the data managers occurred. The data and results were only discussed with research supervisors and statistician.

3.6.3. Harm

The study was conducted in such a way that it fulfilled its goals and avoids embarrassment or discomfort, physical and psychological harm to the screeners in the study. Because only database with cervical cancer results was used, no physical or emotional harm was anticipated.

3.6.4. Beneficence

Beneficence generally means doing well, or doing acts of kindness. Over and above refraining from doing harm to others, the principle of beneficence requires that physicians provide, and to the best of their ability, positive benefits such as good health, prevent and remove harmful conditions from patients (Beauchamp, 1994).

The information obtained from the data was not linked to the participants because of no names were mentioned in the study.

3.7. Conclusion

In this chapter research methodology, research design, sampling, data collection, data analysis, internal and external validity and ethical consideration were discussed.

CHAPTER FOUR: RESULTS

4.1 Introduction

The current study aimed to investigate the epidemiological profile of cervical cancer in Limpopo Province from 2013 to 2015. This chapter presents the distribution of cervical cancer and the association of HIV with cervical cancer.

4.2. Distribution of cervical cancer in Limpopo Province

A total of 182 574 cervical cancer screening were done in Limpopo Province from 2013 to 2015 and there has been a decline in the screenings done annually from 82 041 in 2013 to 23 527 in 2015 screenings. Figure 4.1 below presents the prevalence of cervical cancer by year showing a statistically significance increase from 16.7% in 2013 to 19.2% in 2015 at p-value of 0.001.

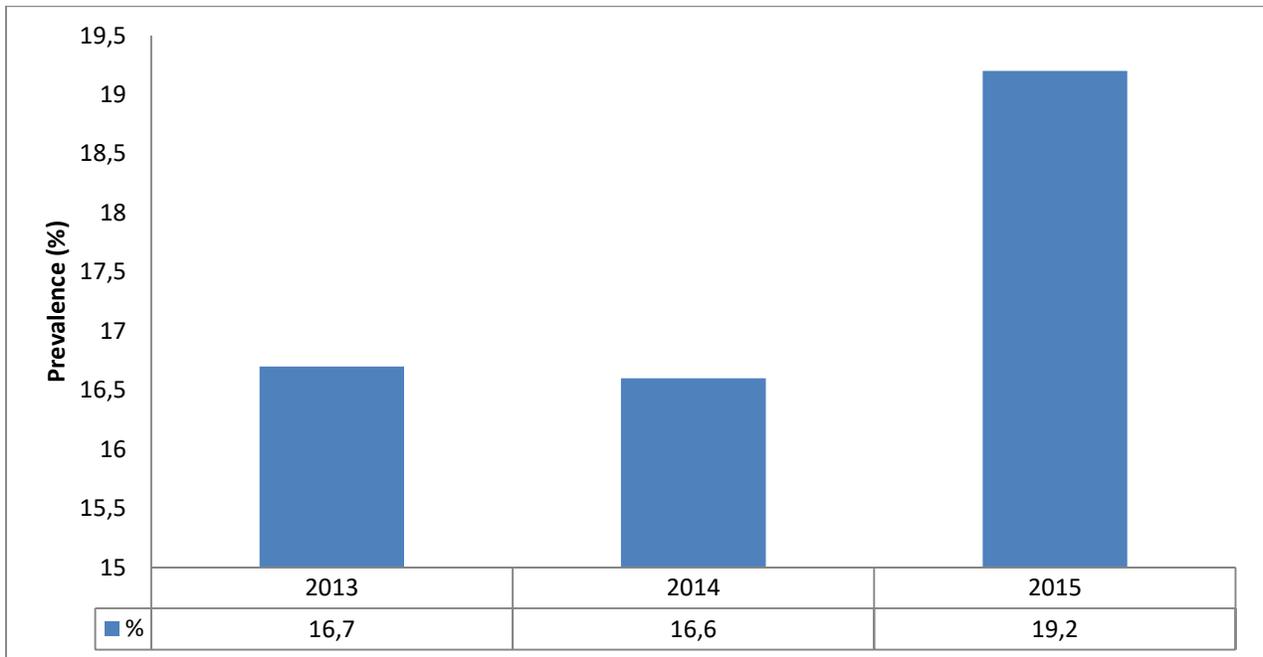


Figure 4.1: Prevalence of cervical cancer by year

The prevalence of cervical cancer by age group as presented in Table 4.1 above shows that the worst affected age group is 35 -44 years at 21.3% in 2013, 21.8% in 2014 and 23.5% in 2015. The lowest affected age group being 15 – 24 years at 10.2% in 2013, 10.6% in 2014 and 15.0% in 2015. All the age groups have shown an increase from the

year 2013 to 2015. All the age groups had an increasing trend in the study period from 2013 to 2015

Table 4.1: Prevalence of cervical cancer by year stratified by age group

	2013 % (95% CI)	2014 % (95% CI)	2015 % (95% CI)
15 – 24	10.2 (9.6 – 10.8)	10.6 (9.9 – 11.2)	15.0 (13.5 – 16.4)
25 – 34	18.9 (18.4 – 19.5)	18.6 (18.1 – 19.2)	21.5 (20.5 – 22.5)
35 – 44	21.3 (20.7 – 21.9)	21.8 (21.2 – 22.4)	23.5 (22.4 – 24.5)
45 – 54	16.5 (15.9 – 17.2)	16.1 (15.4 – 16.7)	19.2 (18.0 – 20.4)
55 – 64	12.4 (11.6 – 13.1)	12.3 (11.5 – 13.0)	14.6 (13.1 – 16.0)
≥ 65	12.8 (12.2 – 13.5)	12.2 (11.6 – 12.9)	13.0 (13.0 – 14.3)

The distribution of cervical cancer by geographical area in Limpopo Province shows that Mopani District had a highest prevalence in 2013 and 2014 followed by Waterberg district in 2015 at 20%, 19% and 21.9% respectively as illustrated in figure 4.1 below. Vhembe District has the lowest cervical cancer prevalence but this district is showing an increasing trend from 14.3% in 2013 to 15.9% in 2015.

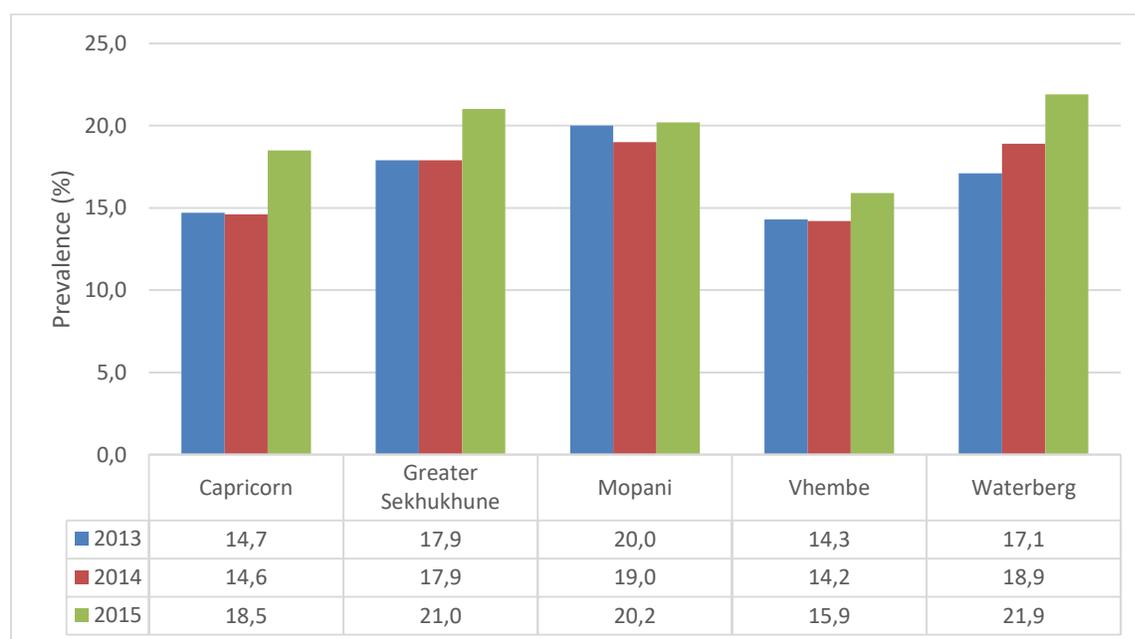


Figure 4.2: Prevalence of cervical cancer by district stratified by year

Within districts, the prevalence of cervical cancer was disproportional by sub-district. All the sub-districts in Capricorn district show an increasing trend from 2013 to 2015 except Molemole sub-district which had a significant decline of 4.7% in 2014 but had an increase of 5.1% in 2015 as presented in table 4.2 above. The increase in Aganang and Lepelle-Nkumpi sub-districts were not statistically significant. Polokwane sub-district had a 3.2% prevalence increase above the 18.5% district prevalence.

All the sub-districts in Greater Sekhukhune had a statistically significant increase of prevalence of cervical cancer from 2013 to 2015 except Elias Motsoaledi and Greater Tubatse. In 2015, the cervical cancer prevalence in Ba-Phalaborwa and Maruleng sub-districts of Mopani Districts were above the district prevalence by 3.1% and 5.6% respectively but the increase within this sub-district per year were not statistically significance.

A statistically significance increase in cervical cancer prevalence was observed in both Mutale and Thulamela sub-districts of Vhembe district for the study period of 2013 to 2015. Musina sub-district in Vhembe district had statistically significant high cervical cancer prevalence above all the sub-districts in Vhembe at 21.9%, 26.3% and 20.3% for 2013, 2014 and 2015 respectively.

Waterberg District had a statistically significance increase of the cervical cancer prevalence from 17.1% in 2013 to 21.9% in 2015 at p-value of <0.0001. All the sub-districts within this district showed an increasing trend during the study period. It is only Mogalakwena sub-district which had a lower prevalence than the district prevalence in all the years while Bela-Bela sub-district had a lower prevalence than the district prevalence by 1.8% and 2.3% in 2013 and 2014 respectively.

Table 4.2: Prevalence of cervical cancer by district stratified by sub-districts over 3-year period.

District	Sub-district	2013	2014	2015	P-value for trend
		% (95% CI)	% (95% CI)	% (95% CI)	
Capricorn	Aganang	12.9 (11.4 – 14.3)	12.9 (11.4 – 14.4)	14.1 (11.2 – 17.0)	0.79
	Blouberg	13.4 (12.4 – 14.3)	13.7 (12.7 – 14.7)	16.1 (14.2 – 17.9)	0.032
	Lepelle Nkumpi	14.7 (13.7 – 15.7)	14.4 (13.4 – 15.4)	16.9 (14.5 – 19.2)	0.140
	Molemole	15.6 (14.1 – 17.0)	10.9 (9.4 – 12.4)	16.0 (12.8 – 19.3)	0.000
	Polokwane	15.7 (14.9 – 16.4)	15.9 (15.2 – 16.7)	21.7 (20.2 – 23.3)	0.000
		% (95% CI)	% (95% CI)	% (95% CI)	
Greater Sekhukhune	Elias Motsoaledi	19.6 (18.3 – 20.9)	18.6 (17.2 – 19.9)	20.6 (18.4 – 22.9)	0.241
	Ephraim Mogale	16.3 (14.7 – 17.8)	14.3 (12.5 – 15.9)	20.9 (17.5 – 24.3)	0.001
	Fetakgomo	14.6 (13.1 – 16.1)	12.6 (11.0 – 14.2)	16.4 (12.9 – 19.9)	0.064
	Greater Tubatse	21.6 (20.5 – 22.8)	21.0 (19.8 – 22.2)	23.3 (20.8 – 25.8)	0.246
	Makhuduthamaga	14.2 (13.0 – 15.4)	18.1 (16.7 – 19.5)	20.9 (18.3 – 23.6)	0.000
		% (95% CI)	% (95% CI)	% (95% CI)	
Mopani	Ba-Phalaborwa	21.6 (20.0 – 23.2)	20.4 (18.7 – 22.1)	23.3 (20.2 – 26.4)	0.228
	Greater Giyani	17.3 (15.4 – 18.6)	14.4 (13.2 – 15.6)	15.4 (12.6 – 18.2)	0.009
	Greater Letaba	21.6 (20.2 – 22.9)	21.5 (20.0 – 22.9)	17.8 (15.4 – 20.1)	0.024
	Greater Tzaneen	18.4 (17.4 – 19.5)	17.8 (16.8 – 18.8)	19.2 (17.5 – 20.9)	0.361
	Maruleng	22.6 (20.9 – 24.3)	23.5 (21.9 – 25.2)	25.8 (22.9 – 28.6)	0.159
		% (95% CI)	% (95% CI)	% (95% CI)	
Vhembe	Makhado	14.2 (13.4 – 15.0)	14.9 (13.9 – 15.8)	15.5 (13.9 – 16.9)	0.272
	Musina	21.9 (19.2 – 24.7)	26.3 (22.9 – 29.8)	20.3 (16.2 – 24.3)	0.049
	Mutale	12.4 (10.8 – 14.1)	12.6 (10.4 – 14.7)	16.4 (13.4 – 19.4)	0.038
	Thulamela	13.8 (12.9 – 14.6)	12.6 (11.8 – 13.4)	15.4 (13.7 – 17.2)	0.007
		% (95% CI)	% (95% CI)	% (95% CI)	
Waterberg	Bela Bela	15.3 (12.6 – 18.1)	16.6 (14.1 – 19.1)	26.4 (18.7 – 33.9)	0.009
	Lephalale	18.8 (16.7 – 20.9)	21.2 (19.3 – 23.0)	26.1 (21.9 – 30.1)	0.004
	Modimolle	21.8 (19.7 – 23.9)	22.9 (20.5 – 25.3)	23.8 (19.1 – 28.4)	0.672
	Mogalakwena	13.8 (12.7 – 14.8)	15.3 (14.2 – 16.4)	17.9 (15.7 – 20.0)	0.002
	Mookgophong	18.4 (15.9 – 20.9)	20.5 (17.8 – 23.2)	25.9 (20.1 – 31.6)	0.042
	Thabazimbi	20.4 (18.4 – 22.5)	23.1 (21.1 – 25.2)	24.8 (20.7 – 28.9)	0.076

Table 4.3: Distribution of cytological diagnoses according to age category among smears submitted to the NHLS from the Limpopo province from 2013-2015

Age in years	Diagnosis	2013	2014	2015	P-value for trend
15 – 24		n (%)	n (%)	n (%)	<0.0001
	Normal	8820 (89.8)	7639 (89.5)	2003 (85.0)	
	CIN I	944 (9.6)	858 (10.1)	346 (14.7)	
	CIN II	54 (0.6)	43 (0.5)	7 (0.3)	
	CINIII	-	-	-	
25 – 34		n (%)	n (%)	n (%)	<0.0001
	Normal	16719 (81.1)	15578 (81.4)	4603 (78.5)	
	CIN I	3304 (16.0)	3170 (16.7)	11448 (19.6)	
	CIN II	595 (2.9)	387 (2.0)	113 (1.9)	
	CINIII	4 (0.02)	3 (0.02)	0 (0.0)	
35 – 44		n (%)	n (%)	n (%)	<0.0001
	Normal	15425 (78.77)	14700 (78.2)	4454 (76.5)	
	CIN I	3152 (16.1)	3292 (17.5)	1161 (19.6)	
	CIN II	1011 (5.2)	794 (4.2)	202 (3.5)	
	CINIII	11 (0.06)	3 (0.02)	2 (0.02)	
45 – 54		n (%)	n (%)	n (%)	<0.0001
	Normal	11529 (83.5)	11608 (83.9)	3571 (80.8)	
	CIN I	1560 (11.3)	1584 (11.5)	3571 (14.4)	
	CIN II	712 (5.2)	626 (4.5)	211 (4.8)	
	CINIII	14 (0.10)	11 (0.08)	2 (0.05)	
55 – 64		n (%)	n (%)	n (%)	<0.0001
	Normal	6180 (87.6)	6188 (87.7)	1922 (85.4)	
	CIN I	485 (6.9)	540 (7.7)	198 (8.8)	
	CIN II	368 (5.2)	316 (4.5)	127 (5.6)	
	CINIII	20 (0.28)	10 (0.14)	3 (0.13)	
≥ 65		n (%)	n (%)	n (%)	0.169
	Normal	9704 (87.2)	8474 (87.7)	2452 (86.9)	
	CIN I	937 (8.4)	7779 (8.1)	258 (9.2)	
	CIN II	468 (4.2)	379 (3.9)	98 (3.5)	
	CINIII	25 (0.22)	24 (0.25)	11 (0.39)	

CIN I (LSIL, ASC-US, ATYPIA, AGUS)

- AGUS: atypical glandular cells of undetermined significance,
- ASC-US: atypical squamous cells of undetermined significance,
- LSIL: low-grade intraepithelial lesion

CIN II (ASC-H, HSIL)

- ASC-H: atypical squamous cells (cannot exclude high-grade squamous intraepithelial lesion),
- HSIL: high-grade squamous intraepithelial lesion,

CINIII (AIS, Malignant)

- AIS- adenocarcinoma in situ

The overall distribution of the final diagnosis of the smears submitted at the Polokwane NHLS for the period 2013 to 2015 shows that approximately 83% of the cervical smears were negative and 17% positive for cervical cancer and classified as cervical intraepithelial neoplasia (CIN) I, II, or III. Overall of the 17% positive smears, 78.5% were CIN I, 21% CIN II and 0,5% CIN III. Table 4.3 above shows the distribution of cytological diagnoses according to age category and the prevalence of malignant cells enhanced with increasing age from 4% in women aged 15 – 24 years to 25% in women aged 65 years above for the year 2013 (p-value < 0.0001). Similar increasing trend was noted for the year 2014 from 3% in women aged 15 – 24 years to 24% in women aged 65 years and above (p-value < 0.0001). In contrast, the rate of low-grade squamous intraepithelial lesions (LSIL) decreased with increasing age (p-value < 0.0001).

4.3 Association of HIV and cervical cancer

Table 4.4: Prevalence of cervical cancer by HIV status stratified by age group

Age in years	HIV negative % (95% CI)	HIV positive % (95% CI)	Unknown status % (95% CI)	P-value for trend
15 – 24	7.5 (6.8 – 8.0)	26 (24.7 – 28.3)	9.9 (9.3 – 10.4)	P<0.0001.
25 – 34	9.2 (8.6 – 9.7)	32.4 (31.6 – 33.2)	17.1 (16.6 – 17.6)	
35 – 44	10.3 (9.6 – 10.9)	33.9 (33.2 – 34.8)	19.3 (18.8 – 19.9)	
45 – 54	9.3 (8.7 – 9.9)	28.7 (27.7 – 29.8)	14.7 (14.1 – 15.2)	
55 – 64	7.8 (7.0 – 8.6)	25.1 (23.5 – 26.7)	11.2 (10.6 – 11.9)	
≥ 65	8.8 (8.1 – 9.5)	26.8 (25.1 – 28.5)	11.7 (11.1 – 12.2)	

Considering the HIV status of the participants in the current study, high cervical cancer prevalence was observed among HIV positive participants in all age groups as it is presented in Table 4.4 above. The participants who are HIV positive aged 35 to 44 years had the highest prevalence of 33.9% followed by 25 to 34 years and 45 to 54 years at 32.4% and 28.7% respectively.

Table 4.5: Prevalence of cervical cancer among HIV positive women participants per year.

District	2013 % (95% CI)	2014 % (95% CI)	2015 % (95% CI)
Capricorn	29.1 (27.8 – 30.5)	29.1 (29.8 – 30.5)	32.3 (29.8 – 34.7)
Greater Sekhukhune	32.2 (30.7 – 33.6)	33.3 (31.7 – 34.8)	33.2 (30.6 – 35.8)
Mopani	33.4 (31.9 – 34.8)	31.8 (30.4 – 33.3)	30.9 (28.6 – 33.2)
Vhembe	29.4 (27.5 – 31.4)	29.5 (27.5 – 31.4)	29.3 (25.8 – 32.7)
Waterberg	29.3 (27.5 – 30.9)	30.6 (29.1 – 32.3)	30.2 (27.1 – 33.3)

Table 4.5 above presents the prevalence of cervical cancer for participants who are HIV positive stratified by district per year. There has been increasing cervical cancer prevalence in Capricorn, Sekhukhune and Waterberg districts. Mopani district had a decrease from 33.4% in 2013 to 30.9% in 2015. The cervical cancer prevalence among HIV positive women was constant in Vhembe district at approximately 29% for the study period.

Chapter 5: Discussion, Conclusion and Recommendations

5.1. Introduction

This research was aimed at describing the distribution of cervical cancer amongst women in the Limpopo province. Therefore, there were two objectives to be answered in this study which are:

1. To describe the demographic characteristics of women diagnosed with cervical cancer in Limpopo province.
2. To determine the association between HIV and cervical cancer.

5.2 Methodology

The research methodology for the whole study followed a quantitative retrospective design with an aim to systematically review the available data from NHLS Polokwane hospital of pap smears done for the period 2013 to 2015. Similar methodology has been used in several studies to determine the distribution of cervical cancer and its association with HIV. This involved the identification of high-risk human papillomavirus (HPV) types as a necessary cause of cervical cancer offers the prospect of effective primary prevention and the possibility of improving the efficiency of cervical screening programmes (Woodman, Collins, and Young, 2007). The wide range of estimates in the findings of the current study indicates the influence of methodological issues including the sampling method used (scrapes vs. lavage), the sub-site from which the samples were collected (cervical, vaginal or vulvar) and the HPV DNA detection method used (Bosch and de Sanjosé., 2007).

5.3 The distribution of cervical cancer in Limpopo Province.

Screening women for cervical cancer can save lives (CDC, 2013) as this type of cancer is a leading cause of deaths among women worldwide (Hoque et al., 2008). Therefore, screening coverage as a crucial component of providing effective prevention (Gakidou et al., 2008) and in the current study cervical cancer screening dropped by 33% from 2013 to 2015 and this concurs with the notion from the Centre for Disease Control saying the coverage cervical cancer screening in the developing world is low (CDC, 2013). In Limpopo Province the drop in cervical cancer screening might be attributed to

the fact that the province has more rural communities and there are several factors that influence or discourage early diagnosis of diseases such as low socio-economic status, inaccessibility of health facilities, lack of transport and rampant poverty in rural areas (Matsheta, 2008). In contrary to this, in a study conducted by Mamahlodi et al., 2013 on the cervical cancer screening in Limpopo Province, it was found that the number of submitted cervical smears increased by 60% whereas in the current study they have decreased by 32% for the study period.

The current study shows that there has been a statistically significant increase in the prevalence of cervical cancer which concurs with other studies (Castle, 2010; Li et al., 2010). The type-specific prevalence was not estimated in the current study because the provided data did not have the variables on testing for the HPV type. The prevalence of cervical cancer was low among young women which concur with a report from the Centre for Disease Control (CDC, 2013). This is also supported by Smith et al., 2008 saying genital HPV infection in women is predominantly acquired in adolescence, and peak prevalence in middle-aged women appears to differ across geographical regions (Smith et al., 2008). Cervical cancer has declined in women over 65 years old in the current study which is similar to the findings in a study conducted in the United States (Rositch, et al., 2014). This is the age at which cessation of routine cervical cancer screening is recommended. The current study revealed that there has been an overall increasing trend across all five health districts and within sub-districts in the Limpopo province. This concurs with a study conducted by Mamahlodi et al., 2013 on the cervical cancer screening programme in Limpopo province.

Majority of the Pap smears processed in the current study had normal cytology at 83% as compared to 94% in a study conducted in Denmark by Kjær et al., (2008) and the overall prevalence of any type of HPV peaked in women aged 20–24 years in the current study and this was similar in a study conducted by Kjaer et al., (2008). The proportion of cervical intraepithelial neoplasia (CIN) grades in the current study was somehow different to a similar as the study conducted by Gargiulo et al., (2007) in

Italian women as there were high proportion of CIN I at 26.2%, CIN II at 8.9% and CIN III at 7.9% as compared to CIN I at 78.5%, CIN II at 21% and CIN III at 0,5%, in the current study.

5. 4 Association of HIV with cervical cancer in Limpopo Province.

Our study findings have shown a significant association of HIV and cervical cancer in Limpopo Province as it has been found in another study which has demonstrated the association of HIV with HPV elsewhere (Anorlu, 2008). The prevalence of CIN among HIV positive women was around 25% and 30% which concurs with the findings from sub-Saharan Africa (Anorlu, 2008) as it says HIV-positive women are more likely to have persistent HPV infections than HIV-negative women. Cancer of the cervix is classified as an AIDS-defining cancer, although the risk of invasive cervical cancer in Africa seems less influenced by HIV, and trends do not reflect changing prevalence of infection (Somdyala et al., 2010). This is inconsistent with the findings from the current study as it was found that HIV infection is significantly associated with cancer of the cervix.

5.5. Conclusion

In conclusion, the current study has revealed that the screening coverage for cervical cancer has decreased in Limpopo Province in contrary to the increase in cervical cancer prevalence. CIN I which is the first stage of cervical cancer is dominating as compared to the advanced stages of cervical cancer in Limpopo Province. Cervical cancer was found to be strongly associated with HIV in the current study and this illustrate that there is a need for Limpopo Province to strengthen strategies to integrate HIV and cervical cancer services.

5.6. Recommendations

Cancer of the cervix is a preventable disease and a key aspect of its prevention is the detection of the premalignant form by cervical screening. Therefore, from the current study, it is recommended that the screening programme in Limpopo Province be enhanced to reach more women as the number of screened women was declining.

It is therefore, recommended that cervical cancer prevention program as it has started in primary schools in South Africa should be enhanced focus on HPV vaccination, which is safe, highly efficacious, and, when used in adolescent before sexually active, highly effective and cost-effective. Education about cervical cancer is also needed at schools before teenagers engage themselves to sexual activity.

South Africa has adopted a national policy of offering a free screening to asymptomatic women aged 30 years, followed by 2 further screens 10 years apart. Reviews of the programme suggest major challenges in implementation, even in the more resourced areas of the country. Cervical cancer affect all women of all ages and therefore, cervical cancer screening should be enhanced in Limpopo Province to combat this public health problem and awareness be made to women in rural areas on strategies to prevent cervical cancer.

5.7. Limitations of the study

The available data did not have critical variables risk factors such as (oral contraceptives, socioeconomic factors, number of sexual partners, and screening history of patients) to HPV infection and therefore it was impossible to determine contributory factors to the increase in cervical cancer in Limpopo Province. We are unable to determine whether the overall prevalence of cervical cancer was higher than what would be expected from the general population with or without stratifying it by HIV status because we did not have comparison group from the other province.

5.8. Summary

In summary, cervical cancer is on the rise in Limpopo Province and women of all ages are affected with this condition. This condition affects not only the health and lives of the women, but also their children, families and their communities at large.

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ANNEXURES

Annexure 1: Time frame

Timeline stipulate an overview of the overall plan on each specific step of the study from 2013 to 2015 for samples of approximately 1200 per month.

NO	Items	Apr '16	May '16	Mar '17	Apr '17	May '17	Jun '17	Jul '17	Aug '17	Sep '17	Oct '17
1	Submission of research proposal	X									
2	Acquisition of ethical clearance letter from university		X								
3	Acquisition of approval letter from DOH and NHLS			X							
4	Data collection				X	X					
5	Data analysis						X				
6	Report writing						X				
7	Submission of document for correction							X			
8	Submission of final document								X		
9	End of project										X

Annexure 2: Ethical approval from Turfloop Research Ethics Committee



University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 2212, Fax: (015) 268 2306, Email:noko.monene@ul.ac.za

**TURFLOOP RESEARCH ETHICS
COMMITTEE CLEARANCE CERTIFICATE**

MEETING: 03 November 2016

PROJECT NUMBER: TREC/219/2016: PG

PROJECT:

Title: Epidemiological profile of cervical cancer in Limpopo Province 2013 to 2015
Researchers: Ms PM Lekota
Supervisor: Dr E Maimela
Co-Supervisor: Prof L Skaal
School: Health Care Sciences
Degree: Masters in Public Health


PROF TAB MASHEGO
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE

The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: REC-0310111-031

Note:

- i) Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee.
- ii) The budget for the research will be considered separately from the protocol.
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.

Annexure 3: Letter requesting permission to conduct the study from Department Health, Limpopo Province

Lekota Provia Maggy
University of Limpopo
School of Health Care Science
Cell: 083 689 6166
Work: 015 297 1099
email: tshegonuna@yahoo.com
03 February 2017

The Department of Health
Research Unit
Polokwane
0700

Dear Sir or Madam

Permission to conduct research at the Limpopo Department of Health.

I am studying Masters of public health at the University of Limpopo as a final year student and writing this letter requesting an approval to conduct a research at the Limpopo Department of health where the data will be collected at National Health Laboratory Services.

Hoping that my requests will be considered.

Sincerely Yours

Provia Maggy Lekota
Student no. 9731908

Annexure 4: Permission letter from Department of Health.



LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH

Enquiries: Latif Shamila (015 293 6650)

Ref:4/2/2

Lekota PM
University of Limpopo

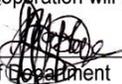
Greetings,

RE: Epidemiological profile of cervical cancer in Limpopo Province 2013 to 2015

The above matter refers.

1. Permission to conduct the above mentioned study is hereby granted.
2. Kindly be informed that:-
 - Research must be loaded on the NHRD site (<http://nhrd.hst.org.za>) by the researcher.
 - Further arrangement should be made with the targeted institutions, after consultation with the District Executive Manager.
 - In the course of your study there should be no action that disrupts the services.
 - After completion of the study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
 - The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
 - The above approval is valid for a 3 year period.
 - If the proposal has been amended, a new approval should be sought from the Department of Health.
 - Kindly note, that the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated.


Head of Department

16/03/2017
Date

18 College Street, Polokwane, 0700, Private Bag x9302, POLOLKWANE, 0700
Tel: (015) 293 6000, Fax: (015) 293 6211/20 Website: <http://www.limpopo.gov.za>

The heartland of Southern Africa – *development is about people*

Annexure 5: Letter requesting a permission to conduct a research project at National Health Laboratory services

Lekota Provia Maggy
University of Limpopo
School of Health Care Science
Cell: 083 689 6166
Work: 015 297 1099
email: tshegonuna@yahoo.com
05 April 2017

The Academic Research Department
National Health Laboratory Services
Sandriham
0100

Dear Sir or Madam

Permission to conduct research at National Health Laboratory Services, Polokwane Laboratory

I am currently working at Polokwane Laboratory as a Laboratory medical Technician in anatomical pathology department and I am busy studying Masters of public health part time at the University of Limpopo as a final year student and I am writing this letter requesting an approval to conduct research at NHLS, Polokwane Laboratory.

My title is Epidemiological profile of cervical cancer in Limpopo Province from 2013 to 2015. As a qualified laboratory medical technician I will follow all the ethics, confidentiality and privacy will be maintained. My data will be collected from April to June as indicated on the proposal.

Hoping that my request will be considered.

Sincerely Yours

Provia Maggy Lekota

Annexure 6: Permission letter for Data collection from NHLS



Academic Affairs and Research
Modderfontein Road, Sandringham, 2031
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Email: babatyi.kgokong@nhls.ac.za
Web: www.nhls.ac.za

25 April 2017

Applicant: Ms Provia Maggy Lekota
Institution: University of Limpopo
Department: School of Health Care Science
Email Address: tshegonuna@yahoo.com
Tel: 015 297 1099
Cell: 083 689 6166

Re: Approval to conduct a study at the National Health Laboratory Service (NHLS) – Polokwane Laboratory

Your application to undertake a research project titled "Epidemiological Profile of Cervical Cancer in Limpopo Province 2013 to 2015" has been reviewed. This letter serves to advise that the application has been approved.

Please note that the approval is granted on your compliance with the NHLS conditions of service and that the study can only be undertaken provided that the following conditions have been met.

- Full Ethics clearance have been obtained from an approved local Ethics Committee
- Processes are discussed with the laboratory manager and/or the pathologist and are agreed upon
- Confidentiality is maintained at participant and institutional level and there is no disclosure of personal information or confidential information as described by the NHLS policy.
- A final report of the research study and any published paper resulting from this study are submitted and addresses to the NHLS Academic Affairs and Research office and the NHLS has been acknowledged appropriately.

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. Once all requirements have been met, please contact the Laboratory Manager Mr Japhta Selapa who will provide approval to communicate with the relevant people. For Data requests, please complete and sign the attached data request form. This should be submitted to academic.research@nhls.ac.za for processing by the Corporate Data Warehouse. Any data related queries may be directed to Zarina Sebat, NHLS Corporate Data Warehouse. Tel: (011) 386 6074 Email: zarina.sebat@nhls.ac.za

Yours sincerely,



Dr Babatyi Malopo-Kgokong
National Manager, Academic Affairs and Research