FACTORS ASSOCIATED WITH CERVICAL CANCER AMONG WOMEN OF REPRODUCTIVE AGE GROUP IN SWAZILAND

by

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Submitted in accordance with the requirements for the degree of

MASTER OF ARTS IN PUBLIC HEALTH

In the subject

Health Studies

at the

UNIVERSITY OF SOUTH AFRICA

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15 November 2018

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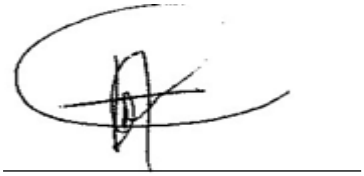
I declare that the above dissertation is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references.



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DEDICATION

This dissertation is dedicated to my family, friends and colleagues. To my late parents Richard and Busisiwe, I just wish you both were here.

Your patience and encouragement are beyond measure. I thank the Almighty for you. I would not have achieved this degree without your encouragement.

Lastly, a special appreciation to my colleagues and friends for unceasingly inspiring and believing in me when I doubted myself, your reassuring words pushed me to keep on going.

ACKNOWLEDGEMENT

First and foremost, I would like to thank the Almighty God for giving me strength during my studies. I also convey my heartfelt gratitude to the following individuals:

- To my supervisor Dr. D.S.K Habedi, thank you for your guidance, support and encouragement. Your expertise and knowledge did not go unnoticed. I have gained overwhelming wealth of knowledge from you. I would not have done it without you.
- A heartfelt appreciation to the Cancer Registry in the Swaziland Ministry of Health; Ms Xolile Dlamini and Ms Lomalanga Hlophe for the all the support during the exercise.
- Swaziland Ministry of Health, thank you for granting me permission to study, therefore contributing to my professional development.
- To my statistician Mr MT Mamahlodi thank you very much for the hard work and the enthusiasm you put in contributing to the study results. You were exceptionally great.
- To my friends and colleagues thank you very much for your patience and support; it is appreciated.

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ABSTRACT

The study is informed by inadequate information on factors associated with the prevalence, incidence and mortality of cervical cancer cytological abnormalities in Swaziland. The aim of the study was to explore and describe factors associated with cervical cancer among women of reproductive age between 15 and 49 years in Swaziland. Quantitative descriptive design with a data extraction tool was used to retrospectively generate observational data from 1748 patients' records in Mbabane Government Hospital from January 2014 through to December 2014. Bivariate logistic regression was used to establish relationship between cervical cancer and each explanatory variable. The overall prevalence of cervical cytology test results was 24.9%. The combination of marital status, HIV status, ART status, age at sexual debut have been identified as factors associated with cervical abnormalities. Most importantly, the results will also serve as evidence for the development of a national cervical cancer screening policy and also strengthening the cancer registry in Swaziland.

Keywords: Age; cervical cancer; cytological abnormalities; incidence, mortality; prevalence; reproductive; women.

LIST OF ABBREVIATIONS

AJCC	American Joint Committee on Cancer
ASR	Age-Standardized Rate
CIN	Cervical Intraepithelial Neoplasia
CpG	Carcinogenic potential Group
CT	Computed Tomography
DNAm	Deoxyribonucleic acid methylation
FIGO	Féderation Internationale de Gynécologie etd'Obstétrique
GCPs	Good Clinical Practices
GDMPs	Good Data Management Practices
HPV	Human Papilloma Virus
IARC	International Agency for Research on Cancer
IUD	Intrauterine Contraceptive Device
LVSI	Lymphovascular Space Invasion
NACT	Neoadjuvant Chemotherapy
PCGTs	Polycomb Group Proteins Target Genes
PLND	Pelvic Lymphadenectomy
PLoS	Public Library of Science
RT	Radiation Therapy
SNHRRB	Swaziland National Health Research Review Board
SNCR	Swaziland National Cancer Registry
SRHU	Sexual Reproductive Health Unit
STIs	Sexually Transmitted Infections
TNM	Tumor size, Lymph Nodes, Metastases
UNFPA	United Nations Population Fund
VIA	Visual Inspection Assessment
WHO	World Health Organization

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CHAPTER 1

ORIENTATION TO THE STUDY

1.1 INTRODUCTION

This chapter provides an orientation to the study. It outlines the background of the research problem, the statement of the research problem, the aim and objectives of the study. In addition, chapter discusses the significance of the study, the theoretical framework of the study, the definition of key concepts, an overview of the research method and an overview of the structure of the dissertation.

1.2 BACKGROUND INFORMATION ABOUT THE RESEARCH PROBLEM

Cervical cancer is the second leading cause of cancer deaths for women globally, with an estimated 88% of deaths occurring in the developing world. Available technologies have dramatically reduced mortality in high-income settings, yet cervical cancer receives considerably little attention on the global health policy landscape (Parkhurst & Vulimiri 2013:1093). Su, Wu, Scotney, Ma, Monie, Hung and Wa (2010:110) demonstrate that cervical cancer is the second most common cause of cancer in women worldwide, with approximately 510 000 new cases and 288 000 deaths reported annually. Every year, over half a million women die from cervical cancer worldwide. More than 85% of these deaths occur in low and middle-income countries. The World Health Organisation (2013:2) corroborates that cervical cancer is the second most common cancer in women affecting more than 1.4 million women worldwide with an increase estimates of new cases from 493,000 in 2002 to 528,000 in 2012 and 274,000 deaths in 2002 and 266,000 deaths in 2012. In sub-Saharan Africa, 34.8 new cases of cervical cancer were diagnosed per 100 000 women annually, and 22.5 per 100 000 women die from the disease (Ferlay, Soerjomataram, Ervik, Dikshit, Eser, Mathers, Rebelo, Parkin, Forman, & Bray 2013:2). Cervical cancer is gradually becoming a rare disease in many developed countries; this is not the case with many countries in sub-Saharan Africa. Cervical cancer is the most common cancer in women in sub-Saharan Africa and second to breast cancer in northern Africa (Anorlu 2008:41).

Swaziland is not sparred from the burden related to cervical cancer among women. It is the most common malignant disease in women accounting for 31% (Swaziland Ministry of Health 2016:12). A total of 13.4 % of female respondents reported to had never had a screening test for cervical cancer in their lifetime and 21.7 % ever screened among those aged between 30 and 44 years. This translates to about one in every five women aged 30-49 years had ever had a screening test for cervical cancer (Swaziland Ministry of Health 2014:15). There are some cost effective interventions in low and middle income settings that can help with the management of cancer, including primary prevention and early detection (WHO, 2012: 27-31). The Papanicolaou test, commonly called the Pap test or smear, has been the gold standard method for cervical cancer screening worldwide and has been effective only in high-income countries. In low-income settings, the visually inspecting of the cervix after applying a staining solution of acetic acid (VIA) or Lugol's iodine (VILI) remained as most effective method at identifying women with pre-cancerous lesions compared to the Pap Smear test (Cervical Cancer Action, 2012:12).

1.3 STATEMENT OF THE RESEARCH PROBLEM

Swaziland developed cervical cancer guidelines in 2013, since then cervical cancer screening and prevention has become an essential part of a comprehensive sexual and reproductive health services for women. In addition, the Swaziland National Cancer Registry (SNCR) has been re-established to inform response to the burden of cancers in the country through a systematic process. Currently, there is inadequate information on the factors associated with the prevalence, incidence and mortality of cervical cancer cytological abnormalities. Moreover, cervical cancer most commonly occurring among women in the country is accounting for 31% of all cancers (Swaziland Ministry of Health, 2016:12). Therefore, it is important to study factors that are associated with cervical cancer among women of reproductive health in Swaziland. Guided by reliable data, the correct interventions for saving lives and improving the conditions of cancer patients and their families can be introduced.

1.4 AIM OF THE STUDY

The aim of this study was to explore and describe factors associated with cervical cancer among women of reproductive age between 15 and 49 years in Swaziland.

1.4.1 Research objectives

The specific objectives for this study were:

- To determine the baseline demographic characteristics of women of reproductive age between 15 and 49 years diagnosed with cervical cancer at Mbabane Government Hospital in Swaziland in 2014.
- To determine the baseline clinical characteristics of women of reproductive age between 15 and 49 years diagnosed with cervical cancer at Mbabane Government Hospital in Swaziland in 2014.
- To determine the prevalence of cervical cancer among women between 15 and 49 years at Mbabane Government Hospital in Swaziland in 2014.
- To determine the risk factors associated with cervical cancer among women between 15 and 49 years at Mbabane Government Hospital in Swaziland in 2014.

1. 5 RESEARCH QUESTIONS/HYPOTHESES

- What are the baseline demographic characteristics of women of reproductive age between 15 and 49 years diagnosed with cervical cancer at Mbabane Government Hospital in Swaziland in 2014?
- What are the baseline clinical characteristics of women of reproductive age between 15 and 49 years diagnosed with cervical cancer at Mbabane Government Hospital in Swaziland in 2014?
- What is the prevalence of cervical cancer among women between 15 and 49 years at Mbabane Government Hospital in Swaziland in 2014?
- What are the risk factors associated with cervical cancer among women of reproductive age between 15 and 49 years at Mbabane Government Hospital in Swaziland in 2014?

1.6 SIGNIFICANCE OF THE STUDY

The proposed study will greatly benefit and assist Swaziland in several ways:

- To help plan cervical cancer screening coverage.

- To support the development of a national cervical cancer screening policy.
- To assist in planning towards strengthening the cancer registry in Swaziland.
- To inform the development of an opportunistic integrated Sexual and Reproductive Health Programme.

1.7 DEFINITIONS OF KEY CONCEPTS

Age refers to the length of time that a person has lived or a thing has existed (Schwall, Hedge & Borman 2012:169). For the context of this study, age refers to the number of years women of reproductive age diagnosed with cervical cancer have lived.

Cancer is a term used for the malignant, autonomous and uncontrolled growth of cells and tissues. Such growth forms tumours, which may invade the tissues around the cancer and cause new growths similar to the original cancer in distant parts of the body, called metastases (WHO, 2014:38). In the context of this study, cancer refers to malignant growth or tumour in the surrounding tissue of cervix of women of reproductive age between 15 and 49 years of age.

Cervical pertains to many areas where tissues narrow to a neck-like passage (Whitlock, 2018:5). In the context of this study, cervical refers to abnormal cells in the lining of the cervix of women of reproductive age between 15 and 49 years of ages diagnosed with cancer of the cervix.

Factors refer to and events, characteristics, or other definable entities that bring about a change in a health condition or other defined outcome (Australian Institute of Health and Welfare 2015:1). In the context of this study, factors refer to the following: socio-demographic: age, place of residence, region, and marital status; reproductive: parity, history of contraceptives; Behavioural: sexual debut, number of lifetime partners, smoking, alcohol, history of STIs and Clinical: family history of cancer, menarche, history of STIs, serology, ART start, PAP smear results, and VIA results.

Reproductive refers to being capable of producing new life or offspring (Siegel & Swanson, 2004:773). In this study, reproductive refers to the capability of women of reproductive age to conceive and have children.

Women refer to an adult female person (Jenkins, 2016:394). For the purposes of this study, women refer to adult female human beings between the ages of 15 and 49 years diagnosed with cervical cancer.

Reproductive age refers to capability of women between the ages of 15 and 49 years diagnosed with cervical cancer to conceive and have children (WHO, 2013:16).

1.8 RESEARCH DESIGN AND METHODS

1.8.1 Setting

The study was conducted in the Hhohho Region at Mbabane Government Hospital, a referral centre for all cancer cases in Swaziland.

1.8.2 Population

Records for all patients diagnosed with cervical cancer from January 2014 through to December 2014 made up the study population. Data for 2014 were critical because it was the year when the cancer registry was established in Swaziland. The study findings provided baseline information for future references. Inclusion of women aged between 15 and 49 years is because of being in their reproductive age groups, sexually active and to improve screening tests for cervical cancer.

1.8.3 Participant Sampling

Census sampling includes all records that met the inclusion criteria made it possible to determine the prevalence of cervical cancer among women between 15 and 49 years at the study site.

1.8.4 Data Collection

The researcher adapted the existing data extracting tool from Swaziland National Cancer Registry in order to ensure validity and reliability. Identified cervical cancer risk factors in line with programme guidelines were retrieved. Data under the following categories were extracted; socio-demographic: age, place of residence, region, and marital status; reproductive: parity, history of contraceptives; Behavioural: sexual debut, number of lifetime partners, smoking, alcohol, history of STIs, and clinical: family history of cancer, menarche, history of STIs, serology, ART start, PAP smear

results and VIA results. Data were read into MS Excel spreadsheet for storage and management.

1.8.5 Data Analysis

Data were then exported into STATA version 12.0 for analysis. In order to describe the data and prepare for analysis socio-demographic, behavioural, frequencies distributions were produced for all categorical variables and were summarised as proportions. Furthermore, the prevalence of clinical abnormalities in cervical cancer screening was established.

A chi-square test was used to establish associations between the outcome variables and explanatory variables; age, marital status, age at first sex, age at first menstruation, number of live births, number of lifetime partners, smoking, alcohol, history of cervical cancer, HIV status, and ART status.

All explanatory variables were recoded as categorical variables in order to use bivariate logistic and multivariate regression methods. Bivariate logistic regression was used to establish the relationship between cervical cancer and each explanatory variable using chi-square. Multivariate logistic regression was built based on bivariate logistic results if explanatory were below significance level of $p<0.20$. The significance level (alpha or p-value) of the study was set at 0.05.

1.9 SCOPE OF THE STUDY

The study was limited to cervical cases in Mbabane Government Hospital and those diagnosed from January 2014 through to December 2014 only. The study was also limited to extraction of patient data without an interaction with patients. Against this background, the researcher could not determine the sample size because the study sample size was dependent on the aggregated data available in the dataware-house.

1.10 OVERVIEW OF THE RESEARCH METHOD

The study looked at extraction of variables for patients diagnosed with cervical cancer using a structured data extraction tool and stored on excel spreadsheet. The extracted variables were coded in numerical values and in line with a relevant data dictionary.

For the purposes of this study, the researcher used observational retrospective design to describe factors associated with cervical cancer among women of reproductive age in Swaziland. Census sampling includes all records that met the inclusion criteria were studied to make it possible to determine the prevalence of cervical cancer among women between 15 and 49 years at the study site. The researcher adapted the data extracting tool from Cancer Registry Department to use as an existing data extraction instrument.

1.11 ETHICAL CONSIDERATIONS

The researcher observed all the ethical principles outlined in the University of South Africa (Unisa) Research Policy as well as the universal ethics principles. Ethical approval was obtained from the Ethics Committees of the University of South Africa. Permission to conduct the study was obtained from Swaziland National Health Research Review Board (SNHRRB). More details on ethical considerations are included in Chapter 3.

1.12 STRUCTURE OF THE DISSERTATION

The dissertation was structured into five chapters with a list of references and relevant supporting documents following the fifth chapter. The first chapter provides an overview of the study and articulates the context of the research problem that underpinned the study. The second chapter covers the literature relevant to the topic of the study. The third chapter described the research methodology. The fourth chapter focuses on the presentation and discussion of the research findings. Lastly, the fifth chapter provides a summary of the results, the recommendations based on the research findings, and the limitations of the study.

1.13 CONCLUSION

This chapter provided an introduction and background to the research problem, as well as the research purpose and objectives, significance and foundation of the study and a brief section on the research design and methodology. The next chapter will provide a detailed literature review.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

The previous chapter provided an introduction, background and foundation of the study. This chapter discusses the literature review conducted by the researcher in keeping with the aim of this study. The study sought to explore and describe factors associated with cervical cancer among women of reproductive age between 15 and 49 years in Swaziland. Relevant literature from previous studies on factors associated with or contributing to cervical cancer was reviewed. The scope of this literature review, therefore, covers evidence from textbooks, published and unpublished research, scientific reports, and other credible sources of scientific work done globally, mainly on cervical cancer. Searches of published articles, journals and the proceedings of major conferences were also done. Mesh phrases used for the search included cervical cancer and cervical cancer Africa. Several sources were consulted, including medical and research textbooks, the latest relevant journals, World Health Organisation (WHO) publications, programme reports, the Internet and several Swaziland Ministry of Health reports. The Internet search engines used include Google scholar PubMed and Public Library of Science (PLoS). Iin addition, endnote was used to compile the list for literature for easy management and reference.

2.2 OUTLINE OF THIS CHAPTER

The term scientific literature refers to theoretical and research publications in scientific journals, reference books, text books, government reports, policy statements and other materials about the theory, practice and results of scientific enquiry (Garrard, 2016:4). The outline of the chapter is as follows:

- Cervical cancer situation at global level;
- Cervical cancer in Africa;
- Cervical cancer in Swaziland;
- Risk factors associated with cervical cancer;
- Causes for cervical cancer;
- Cervical cancer prevention;
- Diagnosis of cervical cancer;

- Cervical cancer staging; and
- Treatment of cervical cancer;
- Conclusion.

2.3 CERVICAL CANCER SITUATION AT GLOBAL LEVEL

According to WHO (2014:20), cervical cancer is one of the gravest threats to women's lives. It is estimated that over a million women worldwide currently have cervical cancer. Most of these women have neither been diagnosed nor do they have access to treatment that could cure them or prolong their lives. In 2012, 528 000 new cases of cervical cancer were diagnosed, and 266 000 women died of the disease, nearly 90% of them in low- to middle-income countries.

Without urgent attention, deaths owing to cervical cancer are projected to rise by almost 25% over the next ten years. Cervical cancer occurs worldwide, but the highest incidence rates are found in Central and South America, East Africa, South and South-East Asia, and the Western Pacific. On the contrary, over the past three decades, cervical cancer rates have fallen in most of the developed world, largely because of screening and treatment programmes (WHO, 2014:8).

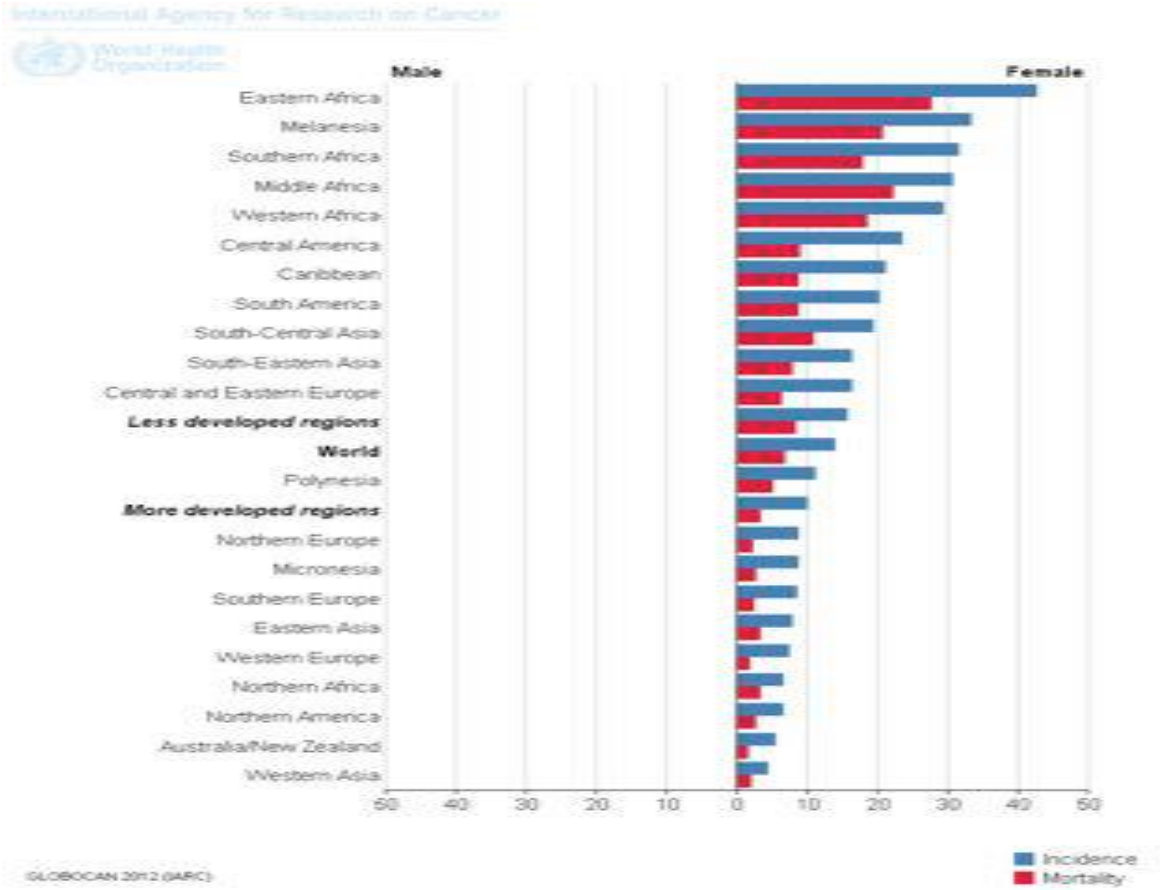

Figure 2.1: Cervical Cancer: Estimated Age-Standardised Rate (World / Regions) per 100,000 (AfriEDev.Info:1)

Cervical cancer is the fourth most common cancer in women, and seventh overall, with an estimated 528,000 new cases in 2012 (AfriEDev.Info, 2014:1). The majority of the global burden (around 85%) occurs in the less developed regions, where it accounts for almost 12% of all female cancers. There were an estimated 266,000 global deaths from cervical cancer in 2012 accounting for 7.5% of all female cancer deaths. Almost nine out of ten (87%) cervical cancer deaths occur in less developed regions. Mortality varies between different regions of the world, with rates ranging from less than 2 per 100,000 in Western Asia, Western Europe and Australia/ New Zealand to more than 20 per 100,000 in Middle/Central Africa 22.2, and Eastern Africa 27.6. Western Africa is not far behind at 18.5 (AfriEDev.Info, 2014:1).

Su et al. (2010:110) demonstrate that cervical cancer is the second most common cause of cancer in women worldwide, with approximately 510 000 new cases and 288 000 deaths reported annually. The World Health Organization (2012:10) corroborates

that worldwide, cervical cancer is the second most common malignant disease among women, with nearly 80% of cases arising in less developed countries.

Annually, over half a million women die from cervical cancer worldwide, with more than 85% of these deaths occurring in low- and middle-income countries. WHO (2013:2) corroborates that cervical cancer is the second most common cancer in women affecting more than 1.4 million women worldwide with an increase estimates of new cases from 493,000 in 2002 to 528,000 in 2012 and 274,000 deaths in 2002 and 266,000 deaths in 2012. Moreover, the cost of the prevention vaccination is such that it will likely remain unavailable for most women in many parts of the world (WHO, 2013:2).

2.4 CERVICAL CANCER IN AFRICA

Africa with a population of 267.9 million women aged 15 years and older at risk of developing cervical cancer, approximately 80,000 women are diagnosed with cervical cancer per year, and just more than 60,000 women die from the disease (Denny & Anorlu, 2012:1434). Cervical cancer is gradually becoming a rare disease in many developed countries. However, this is not the case with many countries in sub-Saharan Africa. For example, in sub-Saharan Africa, 34.8 new cases of cervical cancer were diagnosed per 100 000 women annually and 22.5 per 100 000 women died from the disease (International Agency for Research on Cancer, 2013:2).

High-risk parts of Africa, with estimated age standardised rate (ASR) of over 30 per 100,000, include: Eastern Africa 42.7; Southern Africa 31.5; Middle/ Central Africa 30.6; – with Western Africa on the border line of high risk at 29.3 (AfriEDev.Info, 2014:1). Mortality from cervical cancer in Africa is very high. Because of poor access to high quality screening and treatment services, the majority of cervical cancer deaths (85%) occur in women living in low- and middle-income countries (United Nations Population Fund 2011:5). Cervical cancer is a largely preventable disease, but worldwide it is one of the leading causes of cancer death in women. Most deaths occur in low- to middle-income countries (WHO 2012:37). According to IARC (2013:2), cervical cancer is an avoidable cause of death among women in sub-Saharan Africa.

Table 2.1: World countries with the top 20 highest incidence of cervical cancer in 2012

Rank	Country	Age-Standardised Rate per 100,000 (World)
1	Malawi	75.9
2	Mozambique	65.0
3	Comoros	61.3
4	Zambia	58.0
5	Zimbabwe	56.4
6	Tanzania	54.0
7	Swaziland	53.1
8	Burundi	49.3
9	Bolivia	47.7
10	Guyana	46.9
11	Madagascar	44.6
12	Uganda	44.4
13	Mali	44.2
14	Rwanda	41.8
15	Senegal	41.4
16	Kenya	40.1
17	Guinea	38.4
17	Lesotho	38.4
19	Suriname	38.0
20	Fiji	37.8

Source: GLOBOCAN 2012 v1.1 http://globocan.iarc.fr

2.5 CERVICAL CANCER IN SWAZILAND

According to Bruni, Barrionuevo-Rosas, Albero, Aldea, Serrano, Valencia, Brotons, Mena, Cosano, Muñoz, Bosch, de Sanjosé, and Castellsagué (2016:6), about 223 cases of cervical cancer are annually notified among the 411 787 women at risk for cervical cancer (Female population aged >=15 years) in Swaziland. The crude incidence rate for cervical cancer is 36 per 100,000 populations. Swaziland lies in the regions with highest incidence rates where there is neither screening programme nor any anti-cancer treatment facilities that have one and two doctors per 10,000 populations (Denny & Anorlu, 2012:1434). Swaziland Ministry of Health (2016:12)

corroborates that the country is not sparred from the burden related to cervical cancer among women; it is the first most common malignancy in women accounting for 31% of all female cancers. A total of 13.4 % of female respondents reported to had never had a screening test for cervical cancer in their lifetime and 21.7 % ever screened among those aged between 30 and 44 years. Therefore, this translates to about one in every five women aged 30-49 years had ever had a screening test for cervical cancer (Swaziland Ministry of Health, 2014:15).

Table 2.2: Cervical cancer incidence in Swaziland, Southern Africa and World (estimations for 2012)

Indicator	**Swaziland**	**Southern Africa**	**World**
Annual number of new cancer cases	223	8,652	527,624
Crude incidence rate per 100,000 women per year	36.0	29.3	15
Age-standardised incidence rate per 100,000 women per year.	53.1	31.5	14.0
Cumulative risk (%) at 75 years old	5.0	3.1	1.4

Sources: GLOBOCAN 2012 v1.2 Available from: http://globocan.iarc.fr.

As indicated in Table 2.2, available reports that cervical cancer morbidity was estimated at 36.0/100 000 women per year. On another note, cervical cancer mortality was estimated at 19.1//100 000 women per year as indicated in Table 2.3.

Table 2.3: Cervical cancer mortality in Swaziland (estimations for 2012)

Indicator	**Swaziland**	**Southern Africa**	**World**
Annual number of deaths	118	4,721	265,672
Crude mortality rate per 100,000 women per year	19.1	16.0	7.6
Age-standardised mortality rate per 100,000 women per year	31.0	17.9	6.8
Cumulative risk (%) at 75 years old	3.0	1.9	0.8

Sources: GLOBOCAN 2012 v1.2 Available from: http://globocan.iarc.fr.

In response to cervical cancer being leading among female cancers and also increasing cases, Swaziland developed cervical cancer guidelines in 2013. Since then, cervical cancer screening and prevention have become an essential part of a comprehensive sexual and reproductive health services for women. In addition, the Swaziland National Cancer Registry (SNCR) has been re-established to inform response to the burden of cancers in the country through a systematic process.

2.6 RISK FACTORS ASSOCIATED WITH CERVICAL CANCER

According to the Alliance for Cancer Prevention (2014:1), a risk factor is anything that increases a person's chance of developing cancer. Although risk factors often influence the development of cancer, most do not directly cause cancer. Some people with several risk factors never develop cancer, while others with no known risk factors do.

Age at sexual debut, lifetime number of sexual partners, history of sexually transmitted infections, sexual activity, HIV and human papillomavirus (HPV) are linked to the likelihood of becoming infected with cervical cancer (The Lancet, 2017: 849). Long-term use of oral contraceptives is associated with increased risk; women with HIV and AIDS are also at increased risk of cervical cancer. In the same vein, Raghavendra, Nitturu, and Kamble (2014:8) attest that women with sexual behavioural variables have higher odds of cervical cancer and these associations were found to be statistically significant. These variables include early age at first coitus, the time interval since first exposure, history of extra marital sex in husband and wife; reproductive variables like parity, lack of genital and menstrual hygiene, previous history of sexually transmitted diseases and lastly, dietary factors like lower frequency of fruit consumption.

According to Bahmanyar, Paavonen, Naud, Salmerón, Chow, Apter, Kitchener, Castellsagué, Teixeira, Skinner, and Jaisamrarn (2012:443), their analysis in the Papilloma Trial against cancer in young adults (PATRICIA) showed a significant association between several behavioural risk factors. The latter include not married or living with a partner, smoking, young age at first sexual intercourse, higher number of

sexual partners, longer duration of hormonal contraceptive use, condom use, and history of STIs, and infection with cervical cancer.

The study will review factors that include Human papilloma virus (HPV), immune system deficiency, history of alcohol, first menstrual age, history of STIs, history of smoking, age, onset of sexual intercourse activity, number of lifetime partners, history of contraceptives, and multiple pregnancies. The study will also focus on these factors because in 2014, the Swaziland Cancer Registration tools were limited to these factors.

2.7 CAUSES OF CERVICAL CANCER

2.7.1 Human papillomavirus (HPV) infection

Cervical cancer, caused by sexually acquired infection with HPV, continues to be a public health problem worldwide as it claims the lives of more than 270,000 women every year (UNFPA, 2011:5). This virus is most commonly passed from person to person during sexual activity. According to Colombo, Carinelli, Colombo, Marini, Rollo, and Sessa (2012:vii27), HPV is detected in 99% of cervical tumours, in particular the oncogenic subtypes such as HPV 16 and 18.

There are different types, or strains, of HPV, and some strains are more strongly linked with certain types of cancers. Bahmanyar et al. (2012:441), in the PATRICIA trial conducted in a number of countries, corroborate that HPV is the causal agent in virtually all cervical pre-cancer and cancer. Currently, 13 HPV types are believed to be carcinogenic, of which types HPV-sixteen and HPV-eighteen cause approximately 70% of cervical cancer. Infection with HPV types is a necessary, although not sufficient, cause of almost all cases of cervical cancer. The progression from HPV infection to cervical cancer occurs over a series of 4 steps: HPV transmission, acute HPV infection, persistent HPV infection leading to precancerous changes, and invasive cervical cancer (Vesco, Whitlock, Eder, Burda, Senger & Lutz, 2011: 698).

2.7.2 Immune system deficiency

A lowered immune system can be caused by immune suppression from corticosteroid medications, organ transplantation, treatments for other types of cancer, or from HIV and AIDS. Women who are HIV positive are at particular risk of progression to invasive

cervical cancer (The Lancet, 2017:856). In a study in South Africa, Shimange (2017: 52) corroborates that owing to the HIV pandemic, sero-positive patients presented with invasive cervical carcinoma ten years earlier than their sero-negative counterparts.

According to WHO (2014:42), cervical cancer is a defining illness of AIDS, that women living with HIV and other immunocompromised women have a higher prevalence of HPV (the risk of infection increases with the degree of immunosuppression) and a higher prevalence of persistent HPV infection and infection with multiple high-risk HPV types. Consequently, this increased susceptibility to HPV infection leads to a greater risk of pre-cancer and cancer at younger ages, which increases with the degree of immunosuppression; an increased risk of developing invasive disease up to ten years earlier than in women not infected with HIV; and more frequent presentation with advanced disease with smaller chance of survival for five years.

2.7.3 History of sexually transmitted infections (STIs)

Women who have genital herpes have a higher risk of developing cervical cancer. Co-infection with other sexually transmitted agents, such as Chlamydia trachomatis and herpes simplex virus, may be associated with risk for HPV infection (Vesco et al., 2011:699).

2.7.4 Age

Girls younger than 15 years rarely develop cervical cancer. The risk goes up between the late teens and middle thirties. Women over 40 years remain at risk and need to continue having regular cervical cancer screenings, which include both a Pap test and HPV test. Teschendorff, Menon, Gentry-Maharaj, Ramus, Weisenberger, Shen, Campan, Noushmehr, Bell, Maxwell, and Savage (2010:442) conducted a study on deoxyribonucleic acid methylation (DNAm) profiling of 48 age-matched cervical smear samples from premenopausal women with normal smears (HPV-positive and negative) and smears exhibiting dysplasia (all HPV-positive; Supplemental material). They verified that the age of samples with dysplasia did not differ from the normal smears (Wilcoxon test, P = 0.86). Despite the relatively small sample size and narrow age range of this premenopausal sample set, it was found that Polycomb group proteins target genes (PCGTs) and 69 age-PCGT Carcinogenic potential group (CpG) subset were preferentially hyper-methylated with age.

2.7.5 Age at sexual debut

Delaying commencement of sexual activity and avoiding early and repeated birth are strong considerations in the fight against cervical cancer options which are hardly open to girl 'brides', vulnerable to intimidation and sexual violence (AfriEDev.Info, 2014:1). According to Plummer, Peto and Franceschi (2012:2640), in International Collaboration of Epidemiological Studies of Cervical Cancer that the odds ratios for invasive cervical carcinoma were approximately proportional to the square of time since first intercourse (exponent 1.95, 95% CI: 1.76–2.15) up to age 45. First cervical infection with HPV often occurs soon after first sexual intercourse. Therefore, early age at first intercourse is a reasonable proxy for early age at first exposure to HPV.

2.7.6 Oral contraceptives

Some research studies suggest that oral contraceptives may be associated with an increase in the risk of cervical cancer. Castellsagu, Díaz, Vaccarella, de Sanjosé, Muñoz, Herrero, Franceschi, Meijer, and Bosch (2011: 1023) conducted in a study on copper intrauterine contraceptive device (IUD) and cervical cancer, after adjusting for relevant covariates, a strong inverse association was found between ever use of copper IUDs and cervical cancer (odds ratio 0·55, 95% CI 0·42–0·70; p<0·0001). This suggested that copper IUD use might act as a protective cofactor in cervical carcinogenesis.

2.7.7 Smoking

According to Roura, Castellsagué, Pawlita, Travier, Waterboer, Margall, Bosch, De Sanjosé, Dillner, Gram, and Tjønneland (2014: 463), tobacco smoking is a cited cause of cervical cancer, but whether it causes cervical malignancy independent of HPV infection is unclear. Here, strong associations were found between most measures of tobacco smoking and the risk of cervical intraepithelial neoplasia of Grade 3/carcinoma in situ and invasive cervical cancer, after taking into account past exposure to HPV infection. Quitting smoking was associated with a two-fold risk reduction. The findings confirm the role of tobacco smoking in cervical carcinogenesis and show that quitting the habit has important benefits for cancer protection.

2.8 Causes for cervical cancer

According to the Anticancer Fund (2012:5), it has become clear that essentially all cervical cancers are caused by certain types of HPV infection, caused by sexual contact or even by skin-to-skin contact. HPV is very frequent in the general population that almost all adult women have at some time contracted HPV. However, in the overwhelming majority of cases, HPV infection resolves within six months to two years without causing any signs of disease. A persistent infection with the so-called high-risk (carcinogenic, cancer causing) HPV types, notably HPV types 16 and 18, which are the most common types found in cervical cancer cases worldwide, is necessary for cancer to develop. However, this is not sufficient as the development of cervical pre-cancerous lesions and cervical cancer takes several years (decades) to occur. Bahmanyar et al. (2012:441) underscore that HPV is the causal agent in virtually all cervical pre-cancer and cancer. Currently, 13 HPV types are believed to be carcinogenic, of which types HPV-16 and HPV-18 cause approximately 70% of cervical cancer.

2.9 Cervical cancer prevention

Well-organised cervical screening programmes or widespread good quality cytology can reduce cervical cancer incidence and mortality. The introduction of HPV vaccination could also effectively reduce the burden of cervical cancer in the coming decades. According to the Anticancer Fund (2012:5), when detected early, the treatment of cervical cancer is simple and effective. Therefore, the main risk factor for life threatening cervical cancer is failing to have regular gynaecological examinations and Pap smears. Vesco et al. (2011:699) argue that one reason why cytological screening for cervical cancer has been so successful is that cervical cancer does not develop suddenly, it is preceded by precancerous changes of the cervix that are known as cervical intraepithelial neoplasia (CIN).

According to WHO (2014:52), a comprehensive programme includes three interdependent components: primary, secondary and tertiary prevention. The interventions included in each component are described in figure 2.2.

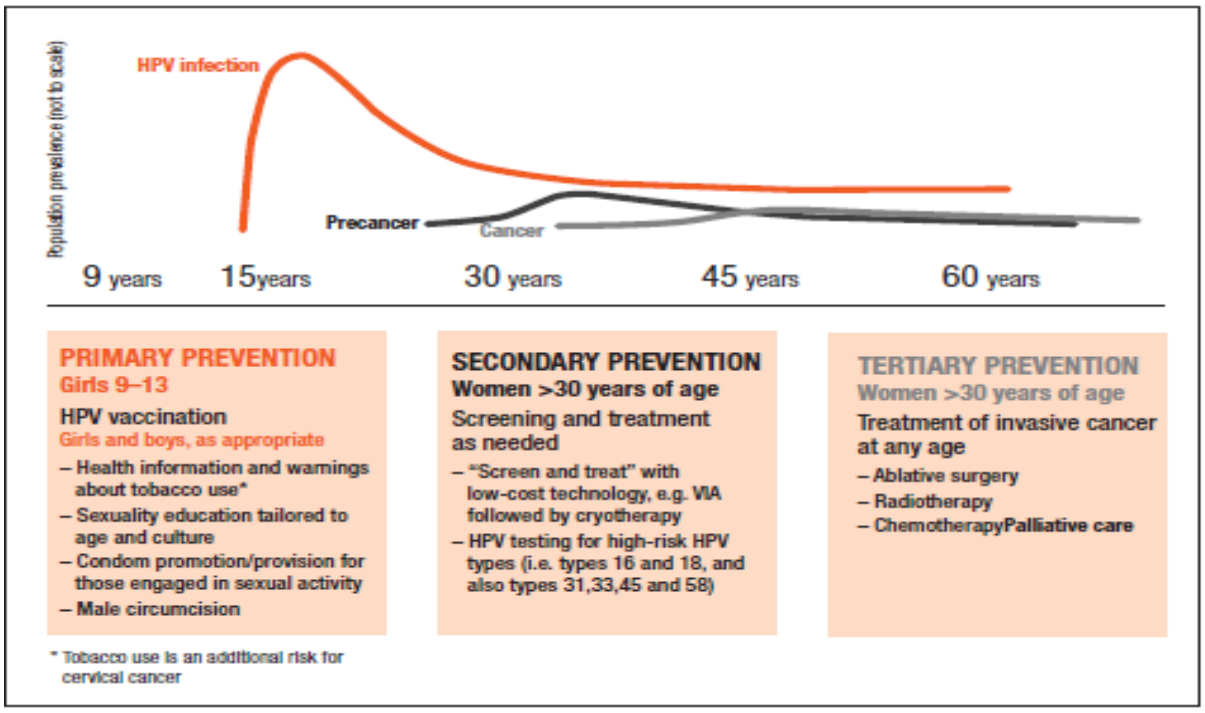

Figure 2.2: The WHO comprehensive approach to cervical cancer prevention and control: Overview of programmatic interventions over the life course to prevent HPV infection and cervical cancer (WHO, 2013: 52).

In the HPV vaccination era, it is expected that the cervical cancer incidence will be reduced, especially in those developed countries where large-scale immunization has been introduced. Most developed countries have introduced HPV vaccines into routine vaccination programmes and more than 60 million doses have already been distributed in 2010, which could guarantee a protection rate of ~70% (Colombo, Carinelli, Colombo, Marini, Rollo & Sessa, 2012: vii27).

2.10 Diagnosis of cervical cancer

The Anticancer Fund (2012: 5) indicates that early detection of cervical cancer can easily be made by an examination of swaps or smears from the cervix surface, obtained during a gynaecological examination. Cervical cancer must be suspected when there are abnormalities upon gynaecological examination. The latter include severe abnormalities in cervical smears; there is bleeding outside of menstruation periods; and there is bleeding after sexual intercourse. According to Colombo et al (2012: vii27), the WHO recognises three categories of epithelial tumours of the cervix: squamous, glandular (adenocarcinoma), and other epithelial tumours, including

neuroendocrine tumours and undifferentiated carcinoma. Squamous cell carcinomas account for ~70%–80% of cervical cancers and adenocarcinomas for 10%–15%. Early cervical cancer is often asymptomatic while locally advanced disease could cause symptoms, including abnormal vaginal bleeding, also after coitus, discharge, pelvic pain, and dyspareunia. Some early cancers are not appreciable and even deeply invasive tumours may be somewhat deceptive on gross examination. If examination is difficult or there is uncertainty about vaginal/ parametrial involvement, this should be done under anaesthesia together with a radiotherapist.

According to Vesco et al. (2011:699), cervical cytology results are not diagnostic of cervical intraepithelial neoplasia (CIN) or cancer, biopsy and histologic confirmation are required for diagnosis. The above statement means that for countries to successfully manage cervical cancer, guidelines should articulate screening procedure, including when to start and stop.

The Anticancer Fund (2012:6) postulates that diagnosis of cervical cancer is based on clinical examination; Pap smear test; colposcopy; histopathological examination; Bethesda cytological examination; routine laboratory examination of blood and urine, and also medical imaging examination.

2.11 STAGING OF CERVICAL CANCER

According to Colombo et al. (2012:vii28), the cervical cancer Féderation Internationale de Gynécologie etd'Obstétrique (FIGO) classification is based on clinical examination. The FIGO classification is based on tumour size, vaginal or parametrial involvement, bladder/rectum extension, and distant metastases. It requires radiological imaging such as chest X-ray and intravenous pyelogram. A comparison between The American Joint Committee on Cancer (TNM) classification and FIGO staging is shown in Table 2.2.

Table 2.4: Comparison of TNM categories and FIGO staging

TNM categories	**FIGO stages**	
TX Primary		Tumour cannot be assessed.
T0		No evidence of primary tumour.
Tisb		Carcinoma in situ (pre-invasive carcinoma).
T1	I	Cervical carcinoma confined to uterus (extension to corpus should be disregarded).
T1ac	IA	Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximum depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of ≤7.0 mm. Vascular space involvement, venous or lymphatic, does not affect classification.
T1a1	IA1	Measured stromal invasion ≤3.0 mm in depth and ≤7.0 mm in horizontal spread.
T1a2	IA2	Measured stromal invasion >3.0 mm and ≤5.0 mm with a horizontal spread of ≤7.0 mm.
T1b	IB	Clinically visible lesion confined to the cervix or microscopic lesion >T1a/IA2.
T1b1	IB1	Clinically visible lesion ≤4.0 cm in greatest dimension.
T1b2	IB2	Clinically visible lesion >4.0 cm in greatest dimension.
T2	II	Cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina.
T2a	IIA	Tumour without parametrial invasion.
T2a1	IIA	Clinically visible lesion ≤4.0 cm in greatest dimension.
T2a2	IIA2	Clinically visible lesion >4.0 cm in greatest dimension.
T2b	IIB	Tumour with parametrial invasion.
T3	III	Tumour extends to pelvic wall and/or involves lower third of vagina, and/or causes hydronephrosis or non-functioning kidney.
T3a	IIIA	Tumour involves lower third of vagina, no extension to pelvic wall.

T3b	IIIB	Tumour extends to pelvic wall and/or causes hydronephrosis or non-functioning kidney.
T4	IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to stage IV.
T4a	IVA	Spread of the growth to adjacent organs.
T4b	IVB	Spread to distant organs.

Source: Colombo, N., Carinelli, Colombo, A., Marini, Rollo and Sessa (2012:vii28). Available from http://annonc.oxfordjournals.org

2.12 TREATMENT OF CERVICAL CANCER

2.12.1 Primary treatment

According to Colombo et al. (2012: vii29), depending on stage, primary treatment consists of surgery, radiotherapy, or a combination of radiotherapy, and chemotherapy. Definitive radiation therapy should consist of pelvic external beam radiation with high-energy photons and intracavitary brachytherapy, and must be administered at high doses (>80–90 Gy) and in a short time (<55 days), with the best technological resources available.

Table 2.5: Cervical cancer treatment according to stage

Stage	**Treatment**	**Issue**
IA1	Conization or simple hysterectomy ± salpingo-ophorectomy and pelvic lymphadenectomy (PLND) if lymphovascular space invasion (LVSI)	Conservative surgery
IA2	Conization/ radical trachelectomy or modified radical hysterectomy and PLND	Adjuvant computed tomography/, radiation therapy (CT/RT) if risk factors (LVSI, G3, positive resection margins, multiple nodes)

IB1, IIA	Radical hysterectomy and PLND	Adjuvant CT/RT if risk factors (LVSI, G3, positive resection margins, multiple nodes)
IB2, IIB–IV	Combination CT/RT with cisplatin	Neoadjuvant chemotherapy (NACT) to large bulky tumours prior CT/RT

Source: Colombo et al (2012:vii28). Available from http://annonc.oxfordjournals.org

Pelvic lymphadenectomy (PLND); lymphovascular space invasion (LVSI); computed tomography (CT); neoadjuvant chemotherapy (NACT); radiation therapy (RT).

2.12.2 Management of advanced/metastatic disease

Patients with metastatic or recurrent cervical cancer are commonly symptomatic. The role of chemotherapy in such patients is palliative, with the primary objective to relieve symptoms and improve quality of life (Colombo et al., 2012:vii30). The response rates after previous chemotherapy are worse compared with chemotherapy naïve patients. Cisplatin is considered the single most active cytotoxic agent. Overall, the duration of the objective response to cisplatin in patients with metastatic or recurrent disease remains disappointing and survival in such patients is only ~7 months. There is no clear dose response effect. Cisplatin-based combination therapy, such as cisplatin–paclitaxel and cisplatin–topotecan, has been extensively investigated in clinical trials. Only the cisplatin–topotecan combination reported an overall survival advantage compared with monotherapy.

2.12.3 Response evaluation and follow-up

According to Colombo et al. (2012:vii31), no definitive agreement exists on the best post-treatment surveillance. Computed tomography (CT) or positron emission tomography (PET) scan should be performed as clinically indicated. A clinical visit with gynaecological examination including Pap smear is usually performed every three months for the first two years, every six months for the next three years and yearly thereafter. Marth, Landoni, Mahner, McCormack, Gonzalez-Martin and Colombo (2017:iv81) highlight that patients should return to annual population-based general physical and pelvic examinations after five years of recurrence-free follow-up.

2.13 CONCLUSION

Cervical cancer remains a huge health problem and is driven by an array of risk factors. These include socio-demographic, behavioural, and clinical. In line with the aim of the study, namely, to explore and describe factors associated with cervical cancer among women of reproductive age between 15 and 49 years in Swaziland the review searched for literature on categories of risk factors as highlighted from chapter 2.6 to 2.7.2. The purpose of this review was to look at the situation of cervical cancer from a global level, down to African perspective before focusing on Swaziland situation. Different guidelines were further reviewed to establish ways of prevention, causes, diagnosis, staging, and treatment for cervical cancer. In summary, the situation of cervical cancer from a broad to the local perspective, including risk factors is well documented in the literature.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 INTRODUCTION

The study was conducted with the aim of describing and exploring factors associated with cervical cancer among women of reproductive age between 15 and 49 years in Swaziland. This was done with the view of recommendations on which factors should be the focus for the country in the fight against cervical cancer. In this chapter, research design and methodology of the study are discussed in detail including, study population, sample, the data collection tool, data collection process, data management, ethical considerations, reliability, validity, and analysis.

3.2 METHODOLOGICAL FOUNDATION

The study was conducted within the objectivist epistemological perspective. According to Yilmaz (2013:312), the objectivist epistemology seeks to develop explanatory universal laws in social behaviours by statistically measuring what it assumes to be a static reality. It emphasises the measurement and analysis of causal relationships between isolated variables within a framework, which is value-free, logical, reductionist, and deterministic, based on a priori theories. A quantitative approach endorses the view that psychological and social phenomena have an objective reality that is independent of the subjects being studied.

3.3 RESEARCH DESIGN

Grove, Burns and Gray (2013:43) assert that a research design is a pattern that should be followed to maximise control over factors that could interfere with a study's outcomes. The purpose of a descriptive design is to identify patterns of variables, to describe and define variables, to identify initial links among variables, and to compare and contrast on variables of interest. For the purposes of this study, the researcher used an observational retrospective design to describe factors associated with cervical cancer among women of reproductive age in Swaziland. It attempted to "connect the dots" by identifying factors associated with cervical cancer among women of reproductive age.

3.3.1 Quantitative research

Quantitative research can be conceptually divided into two types: descriptive and associational. Grove et al (2013:43) maintain that a research design is a pattern that should be followed to maximise control over factors that could interfere with a study's outcomes. The purpose of a descriptive design is to identify patterns of variables, to describe and define variables, to identify initial links among variables, and to compare and contrast on variables of interest. Yilmaz (2013:311) defines quantitative research as a type of empirical research into a social phenomenon or human problem, testing a theory consisting of variables which are measured with numbers and analysed with statistics in order to determine if the theory explains or predicts phenomena of interest. In view of the above literature, for the purpose of this study, the researcher used quantitative, analytical, associational, observational, and retrospective design to describe factors associated with cervical cancer among women of reproductive age in Swaziland. A statistician was consulted in development of the questionnaire, data capturing and analysis.

This study was quantitative in nature because it explored and described factors associated with cervical cancer among women of reproductive age between 15 and 49 years in Swaziland. The study only looked at extracted variables of patients diagnosed with cervical cancer by using a structured data extraction tool and stored on MS Excel spreadsheet. The extracted variables were coded in numerical values and in line with a relevant data dictionary.

3.4 RESEARCH METHODS

3.4.1 Population

The researcher needed to know what characteristics the study participants should possess, and clarify the group to whom study results can be generalised by identifying the population to be studied. A population is all the individuals or objects with common, defining characteristics (Polit & Beck, 2010:75). The study population included records of all women diagnosed with cervical cancer at Mbabane Government Hospital from January 2014 through to December 2014. Data from 2014 was used because Swaziland had just developed cervical cancer guidelines and also cervical cancer screening and prevention become an essential part of a comprehensive sexual and

reproductive health services for women. In addition, the Swaziland National Cancer Registry (SNCR) was re-established to inform response to the burden of cancers in the country. The study focused on women aged between 15 and 49 years because of being in their reproductive age groups, sexually active and to improve screening tests for cervical cancer.

3.4.2 Inclusion criteria

The inclusion criteria were as follows:

- Clinical records of all women who tested for cervical cancer between January 2014 and December 2014.
- Women aged between 15 and 49 years old and diagnosed with cervical cancer at Mbabane Government Hospital.

3.4.3 Exclusion criteria

Conversely, the exclusion criteria were as follows:

- Clinical records of all women who did not test for cervical cancer between January 2014 and December 2014.
- Records of all women whose records were incomplete.
- Women aged below 15 years and above 49 years old diagnosed with cervical cancer at Mbabane Government Hospital.

3.4.4 Sample

According to Polit and Beck (2010:75), researchers typically collect data from a sample, which is a subset of the population. A sample is clearly more practical and less costly than collecting data from an entire population. A carefully selected sample can provide data representative of the population from which it is drawn. However, the risk is that the sample might not adequately reflect the population's traits. All the records of women between ages of 15 and 49 years diagnosed with cervical cancer constituted the sample. Data from the patients' files and registers were extracted and stored in a database for statistical analysis.

3.4.5 Sampling

According to Bhattacherjee (2012:65) Sampling is the statistical process of selecting a subset (called a "sample") of a population of interest for purposes of making observations and statistical inferences about that population. There are two main types of sampling, namely, probability and non-probability sampling. Non-probability sampling is a sampling technique in which some units of the population have zero chance of selection or where the probability of selection cannot be accurately determined (Bhattacherjee, 2012:69). The researcher employed non-probability sampling because cervical cancer was diagnosed at the referral hospital where records of all patients who tested positive for cervical cancer from January 2014 through to December 2014 constituted the sample.

3.4.6 Sampling method

According to Dattalo (2010:1), although random sampling is considered by many researchers as the gold standard methodological procedure for maximising external validity and optimising sample size, in practice, random sampling often is difficult to implement. Therefore, non-probability sampling methods used to balance a sample's composition in terms of characteristics and diversity. The study population included records of all women diagnosed with cervical cancer at Mbabane Government Hospital from January 2014 through to December 2014. Census sampling whereby all records that meet the inclusion criteria were studied to make it possible to determine the prevalence of cervical cancer among women between 15 and 49 years at the study site.

3.4.7 Research setting

Polit and Beck (2010:223) assert that data for quantitative studies sometimes are collected in real-world settings, such as in clinics or people's homes. Other studies are conducted in highly controlled environments established for research purposes. Another important design decision concerns how many different sites will be involved in the study.

The study was conducted at Mbabane Government Hospital, a referral centre for all cancer cases in Swaziland as mandated by the Ministry of Health in Swaziland. Data collected in 2014 were critical because it was the year when the cancer registry was

established in Swaziland so that findings provided baseline information for future reference.

3.4.8 Ethical issues related to sampling

In the non-probability sampling, data were extracted from patients' files and registers. Approval to conduct the study was sought in the following manner:

- An approval letter to conduct the study was requested from the Swaziland National Health Research Review Board (SNHRRB).
- An ethical clearance certificate was obtained from the University of South Africa Department of Health Studies' Higher Degrees Committee
- Permission letter to conduct the study was requested from Mbabane Government Hospital.
- Permission letter to conduct the study was requested from Sexual Reproductive Health Unit (SRHU).

3.5 DATA COLLECTION

According to Polit and Beck (2010:339), data collection concerns the gathering of data to address research questions. A variety of quantitative data collection approaches exist; the primary methods are self-reports, observations, review of existing data, and bio-physiologic measurements. In this study data from a clinic register, other patients' files and cards were extracted.

3.5.1 Description of data collection tool

Existing records are an important data source for nurse researchers. A wealth of data gathered for other than research purposes can be fruitfully exploited to answer research questions. Hospital records, patient charts, care plan statements, and the like all constitute rich data sources to which nurse researchers may have access (Polit & Beck, 2010:338).

Quantitative methods require the researcher to use a pre-constructed standardised instrument or pre-determined response categories into which the participants' varying perspectives and experiences are expected to fit (Yilamz, 2013:313). For the purposes of this study, an existing data extraction instrument from Ministry of Health Cancer

Registry Department was used to extract data. Permission to use the tool was granted by the department. The data extraction tool has cervical cancer patients' variables of interest under different categories, namely, socio-demographic, behavioural, reproductive, and clinical risk factors. The hospital uses a number of tools to store patients' records. These include patients' files, cards and patient-care registers.

The following categories and variables were identified in the different source documents:

- Socio-demographic: age, place of residence, region, and marital status;
- Reproductive: parity, history of contraceptives;
- Behavioural: sexual debut, number of lifetime partners, smoking, alcohol, history of STIs; and
- Clinical: family history of cancer, menarche, history of STIs, serology, ART start, PAP smear results, and VIA results.

3.5.2 Data collection procedure

Identified cervical cancer risk factors in line with programme guidelines were retrieved as per the different variables in the extraction tool. Cervical cancer patients' variables of interest including socio-demographic, behavioural, reproductive and clinical risk factors were extracted from patients' records including; patients files, cards and patient-care registers.

Data under the following categories were extracted; Socio-demographic: age, place of residence, region, and marital status; Reproductive: parity, history of contraceptives; Behavioural: sexual debut, number of lifetime partners, smoking, alcohol, history of STIs and Clinical: family history of cancer, menarche, serology, ART start, PAP smear results and VIA results. Data were extracted and stored in excel spreadsheet then exported into STATA 13.0 (Stata corp.college station, Texas, USA) for analysis

3.6 DATA MANAGEMENT AND ANALYSIS

Data were stored in MS Excel spreadsheet after extraction then exported into STATA 13.0 for cleaning before analysis. Study unique identifiers were captured to maintain anonymity of participants and security was ensured by password protection and encryption according to Good Data Management Practices (GDMP) and Good Clinical Practices (GCP). Data were further checked for possible errors and missing values

through running of frequencies, such that any issues were addressed by going back to the data sources to verify the data. The researcher was guided by the supervisors and a qualified statistician as an expert in the field to ensure GDMP and GCP.

Percentages and proportions were used to estimate the prevalence of reproductive women diagnosed with cytological abnormalities from January 2014 through to December 2014. The prevalence of cytological abnormalities diagnosed in women aged 15 to 49 years of age was compared using a chi-square test. The strength and magnitude of association of the factors related to cervical cancer screening programme were tested using Spearman's rho correlation test. The significance level (alpha or p- value) of this study was be set at 0.05. This means that if a mean or a proportion from a sample is likely to occur more than alpha then the researcher fails to reject the null hypothesis.

3.7 VALIDITY AND RELIABILITY OF THE STUDY TOOLS

According to Yilmaz (2013:317), reliability means consistency or the degree to which a research instrument measures given variable consistently every time it is used under the same condition with the same subjects. It is important to note that reliability applies to data not to measurement instruments. Validity refers to the accuracy and trustworthiness of instruments, data, and findings in research. Nothing in research is more important than validity (Bernard, 2010:53).

In order to ensure validity and reliability, the researcher adapted the data extracting tool from Cancer Registry Department to use as an existing data extraction instrument. A data quality system was put into place to ensure the extraction of quality data for analysis. Data collection was standardised, where a standard operating procedure was developed with instructions detailing how data would be extracted and stored and maintained. Periodical review of data collection was undertaken by the researcher to help to identify gaps in data extraction.

3.8 ETHICAL CONSIDERATIONS

The study was not in contact with patients. Instead, data were extracted from patients' files and registers. Approval to conduct the study was sought in the following manner;

- An approval letter to conduct the study was requested from the Swaziland National Health Research Review Board (SNHRRB).
- An ethical clearance certificate was obtained from the University of South Africa (Unisa) Department of Health Studies' Higher Degrees Committee.
- Permission letter to conduct the study was requested from Mbabane Government Hospital.
- Permission letter to conduct the study was requested from Sexual Reproductive Health Unit (SRHU).

The researcher did not foresee any risks because patients' identifiers were not extracted, but instead, a study identification number was used to link patients' records with data. Most importantly, the researcher worked with knowledgeable research officers who were also trained in ethical procedures before conducting the study.

The researcher has received training on procedures to protect participant confidentiality and GCP. The researcher worked with knowledgeable research officers who were also trained on the data extraction tool and on GDMP to ensure adherence to ethical issues before conducting the study. They were also made to sign confidentiality agreement by the researcher as part of GCP. Patient health information (PHI) was protected, for example; name, telephone number, residential address or other personal details did not appear on any of the extracted records. No patient records left the hospital. Even during the data extraction exercise, a separate room was used, and records returned to filing room upon finish. Extracted data in the electronic tool were password-protected to prevent unnecessary interference.

There was no gift or any monetary arrangements in the study; only data were extracted from patients' files and registers or records at no cost.

3.9 CONCLUSION

This chapter described the methodology followed by the researcher to address the research question. It provided the rationale and motivation for the selected methodology. It also examined how the ethical principles were observed to collect, manage, analyse data to produce results for the study. In the next chapter, the results of the study are presented and discussed.

CHAPTER 4

ANALYSIS, PRESENTATION AND DESCRIPTION OF THE RESEARCH FINDINGS

4.1 INTRODUCTION

In chapter 3 methodology was described, including rationale and motivation for the selected methodology. In this chapter, the main research findings of the study are presented and discussed. The discussion will focus on the research objectives of the study and compare the research findings with existing literature. These results are introduced by the presentation and discussion of the characteristics of the respondents. A conclusion is provided at the end of the chapter. The specific objectives for this study were as follows:

- To determine the baseline demographic characteristics of women of reproductive age between 15 and 49 years diagnosed with cervical cancer at Mbabane Government Hospital in Swaziland in 2014.
- To determine the baseline clinical characteristics of women of reproductive age between 15 and 49 years diagnosed with cervical cancer at Mbabane Government Hospital in Swaziland in 2014.
- To determine the prevalence of cervical cancer among women between 15-49 years at Mbabane Government Hospital in Swaziland in 2014.
- To describe risk factors associated with cervical cancer among women between 15-49 years at Mbabane Government Hospital in Swaziland in 2014.

4.2 DATA MANAGEMENT AND ANALYSIS

Data were stored in MS Excel spreadsheet after extraction then exported into STATA version13.0 for cleaning before analysis. Study unique identifiers were captured to maintain anonymity of participants and security was ensured by password protection and encryption according to GDMP and GCP. Data were further checked for possible errors and missing values through running of frequencies, such that any issues were addressed by going back to the data sources to verify the data. The researcher was guided by the supervisors and a qualified statistician as an expert in the field to ensure GDMP and GCP.

The following categories and variables were used in the study:

- Socio-demographic: age, place of residence, region, and marital status;
- Reproductive: parity, history of contraceptives;
- Behavioural: sexual debut, number of lifetime partners, smoking, alcohol, history of STIs; and
- Clinical: family history of cancer, menarche, history of STIs, serology, ART start, PAP smear results and VIA results.

The significance level (alpha or p-value) of the study was set at 0.05. This means that if a mean or a proportion from a sample is likely to occur more than alpha then the researcher accepts the null hypothesis. In order to establish prevalence of socio-demographic, behavioural, frequencies distributions were produced for all categorical variables and were summarised as proportions. Furthermore, the prevalence of clinical abnormalities in cervical cancer screening was established.

A chi-square test was used to establish associations between the outcome variables and explanatory variables; age, marital status, age at first sex, age at first menstruation, number of live births, number of lifetime partners, smoking, alcohol, history of cervical cancer, HIV status, and ART status.

All explanatory variables were coded and categorical variables in order to use bivariate logistic and multivariate regression methods. Bivariate logistic regression was used to establish relationship between cervical cancer and each explanatory variable using chi-square. Multivariate logistic regression was built based on bivariate logistic results if explanatory were below significance level of $p<0.20$.

4.3 RESEARCH RESULTS

4.3.1 Background characteristics

A total of 1748 records were initially extracted in line with the inclusion criteria of age group 15-49 years. Frequency distribution of baseline demographic characteristics of women of reproductive age between 15 and 49 years screened for cervical abnormalities at Mbabane Government Hospital in Swaziland in 2014 (n=1748) are shown by the Table 4.1.

4.3.2 Distribution of socio-demographic factors (n=1748)

Table 4.1: Distribution of socio-demographic, reproductive, behavioural, clinical factors (n=1748)

Socio-demographic variables	Categorisation	Frequency	Percent
Age group	16 to19 years	30	1.7
	20 to24 years	264	15.1
	25 to 29 years	385	22
	30 to34 years	397	22.7
	35 to 39 years	278	15.9
	40 to 44 years	213	12.2
	45 to 49 years	181	10.3
Urban Rural	Rural	870	49.8
	Urban	878	50.2
Region Name	Hhohho Region	1,174	67.2
	Lubombo Region	74	4.2
	Manzini Region	468	26.8
	Shiselweni Region	32	1.8
Marital Status	Divorced	39	2.2
	Married	841	48.1
	Single	839	48
	Widow	24	1.4
	Missing	5	0.3

Age was initially analysed as a continuous variable where it was established that the age of patients ranged from 16 to 49 years. The median age of the patients was 32 years. Age was then categorised into age groups of five-year age bracket as per national survey guides on age categorisation. It can also be noted that distribution of number of patients screened for cervical abnormalities at age group of 16-19 years was lower than other age groups, rose steadily, and with a pick at age group of 30-34 years then started declining in the following age group of 35-39 years. A graphical presentation is shown in Figure 4.1.

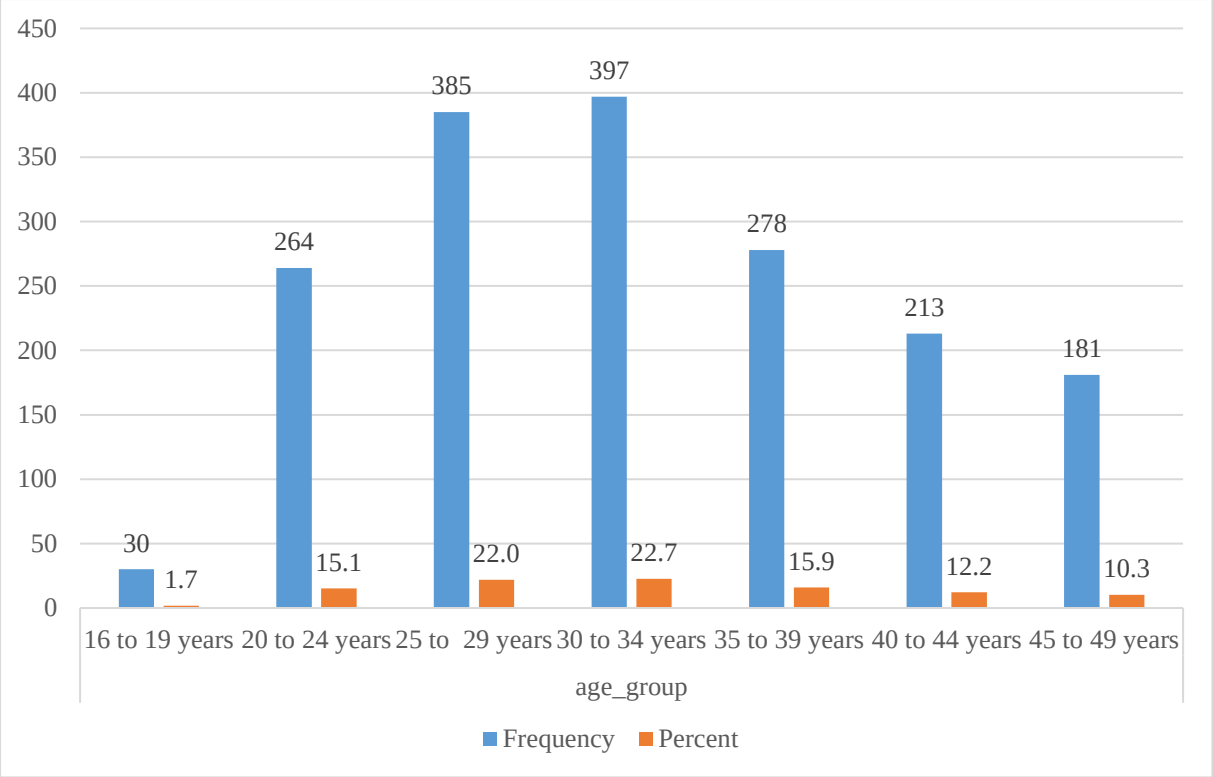

Figure 4.1: Age group distribution of patients screened for cervical abnormalities

Patients came from all parts of the country. Their locations fall in the four regions of the country, namely, Hhohho, Manzini, Lubombo, and Shiselweni regions respectively. These patients were mostly referred from their peripheral health facilities to Mbabane Government Hospital as the main referral facility for cervical cancer.

The majority of the patients came from Hhohho Region while the minority came from Shiselweni Region. The hospital where the study was carried out is located in the Hhohho Region, and is closer to the Manzini which might be associated with the higher number of patients. Lubombo and Shiselweni regions are quite far from Mbabane government referral hospital. There was no difference in distribution of patients by location; 50% neither came from rural nor urban locations.

Not all patients indicated their marital status. Only four had missing status. As a result, they were excluded in the description by marital status. About 48% indicated that they were single and also the same percentage indicated that they were married. Widows indicated the least with one percent. A different picture was established in a study on knowledge, attitudes, and demographic factors influencing cervical cancer screening

behaviour of Zimbabwean women where the majority (70%) were married while 11% were in other relationship status (Mupepi, Sampselle & Johnson, 2011: 946).

4.3.3 Distribution of reproductive factors (N=1747)

Figure 4.2 below indicates that the majority of the patients have children that are less or equals to three while a few patients have less than three children. One patient did not indicate the number of children.

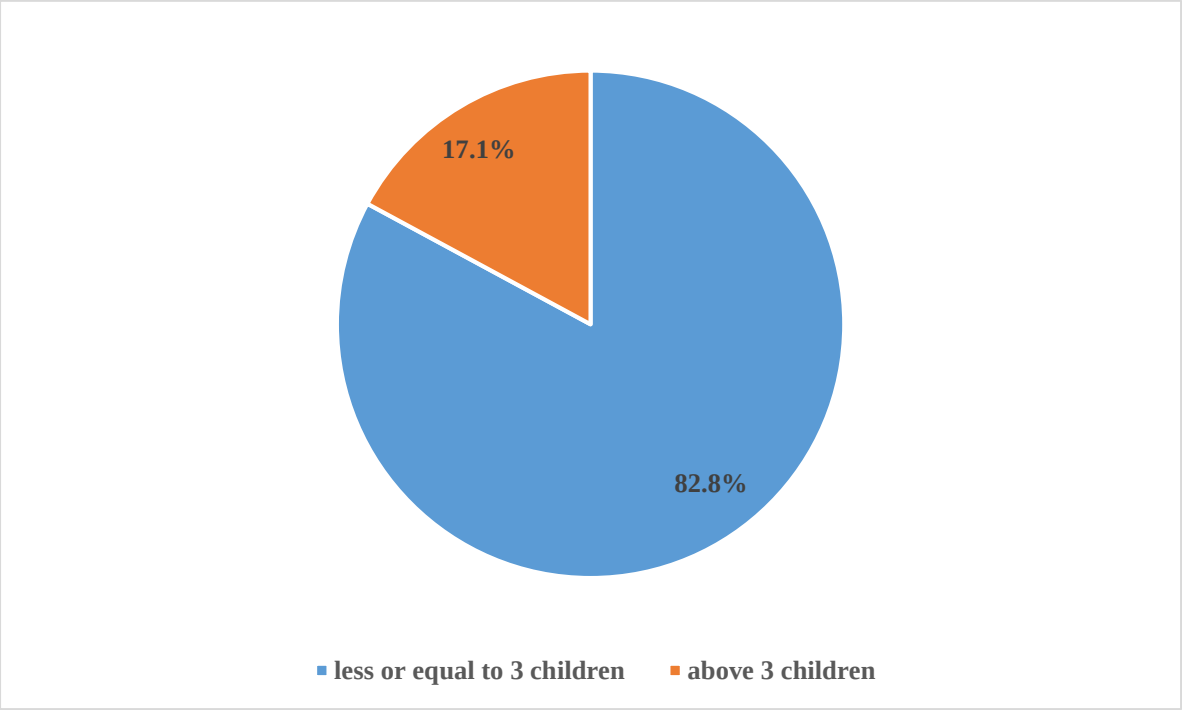

Figure 4.2: Number of children

The picture above is corroborated by the Central Statistics of Swaziland (2016: 96) where the total fertility rate (TFR) is defined as a synthetic measure that denotes the number of live births a woman would have if she were subject to the current age-specific fertility rates throughout her reproductive years (15-49 years) at three children.

4.3.4 Distribution of behavioural factors (N=1748)

A number of behavioural variables were extracted for analysis, these included sexual debut, number of lifetime partners', smoking, alcohol and history of STIs. Their descriptive statistics are shown in Table 4.2.

Table 4.2: Distribution of behavioural factors (N=1748)

Behavioural variables	Categorisation	Frequency	Per cent
Sexual debut category	0 to 9 years	3	0.2
	10 to 19 years	1,103	63.1
	20 to 29 years	615	35.2
	Missing	6	0.3
Number of lifetime partners	0 to 2	892	51
	3 to 5	687	39.3
	6 to 8	73	4.2
	9 to11	52	3
	12 to14	3	0.2
	15 to17	6	0.3
	18to20	4	0.2
	21to23	2	0.1
	Missing	29	1.7
Smoke	No	1,646	94.2
	Yes	102	5.8
Alcohol	No	1,561	89.3
	Yes	187	10.7
History of STIs	No	1,289	73.7
	Yes	459	26.3

Table 4.2 indicates that the majority (63.1%) of patients had their sexual debut between the age group 10 to 19 years. A total of 3 patients indicated that they never had sex in their lives. When patients were asked on the number of lifetime partners, the numbers ranged from zero to 23 and some chose not to respond. The majority (51%) of patients indicated that they had two or less partners in their lifetime. About two patients indicated that their number of lifetime partners ranged from 21 to 23. About 26.3% had history of STIs. Early sexual debut is a measure of youth risk behaviour. Delayed sexual debut helps reduce the risk of HIV and AIDS, STIs, risk of cervical cancer, and unwanted pregnancies (Central Statistical Office Swaziland, 2016:251).

Patients were asked about smoking habits and 94.2% indicated that they do not smoke. About 10.7% of the patients indicated that they take alcohol. According to Park, Kim, Seo, Kang and Lim (2016:371), they explored the prevalence of smoking, alcohol consumption, physical activity, and obesity in cervical cancer survivors and examined associations between socio-demographic factors and each health behaviour. Alcohol drinking was negatively correlated with educational level, which is consistent with previous data on cancer survivors who had undergone hematopoietic cell transplantation. The combination of the above risks could increase the risk of cervical cancer.

4.3.5 Distribution of clinical factors (N=1748)

A number of clinical variables were extracted for analysis. These included HIV status, antiretroviral therapy, age at first menstruation, and history of cervical cancer. Their descriptive statistics are shown in Table 4.3.

Table 4.3: Distribution of clinical factors (N=1748)

Clinical variables	Categorisation	Frequency	Per cent
HIV status	Negative	1,055	60.4
	Positive	588	33.6
	Missing	105	6.0
On antiretroviral therapy	No	1,054	60.3
	Yes	364	20.8
	Missing	330	18.9
Age at first menstruation	10 to14 years	1,090	62.4
	15 to19 years	642	36.7
	20 to 24 years	12	0.7
	Missing	4	0.2
History of cervical cancer	No	1,565	89.5
	Yes	183	10.5

Table 4.3 indicates that 60.4% patients were HIV negative while 33.6% were HIV positive. According to Swaziland Ministry of Health (2017:70), the prevalence of HIV among adults aged 15 years and older in Swaziland is 27.0%: 32.5% among females and 20.4% among males. This translates to approximately 200,000 people living with HIV (PLHIV) aged 15 years and older. About 20.8% indicated to be on antiretroviral

therapy, while 18.9% had missing antiretroviral therapy status. About 62.4% of the patients had their first menstruation at 10 to 14 years. About 10.5% indicated that they had a history of cervical cancer.

4.3.6 Cervical cancer screening using Visual Inspection (n=1748)

Visual inspection of the cervix after application of 3-5% acetic acid is a potential alternative to cytology for screening in low-resource countries. According to Grover, Raesima, Bvochora-Nsingo, et al. (2015:2) “See and Treat” (SAT) screening, as an alternative to cytology, is performed through visual inspection after acetic acid (VIA) application to the cervix followed by immediate treatment with cytotherapy for screen positive patients. The study screened for cervical abnormalities using VIA method. Initial results from screening are shown first by many individual results and further categorised into positive or negative as shown in Table 4.4.

Table 4.4: Distribution of cervical screening results by method (N=1748)

Screening Method	Category	Frequency	Per cent
Visual Inspection result	Genital warts	1	0.1
	Not Done	249	14.2
	Not reactive	1,255	71.8
	Cervicitis	232	13.3
	Inflammation	2	0.1
	Missing	9	0.5
Visual Inspection result category	Negative	1,255	71.8
	Positive	235	13.4
	Missing	258	14.8

Table 4.4 shows that the majority (71.8%) of the cases screened negative of cervical abnormalities using VIA. About 14.2% cases could not be screened, while nine cases had missing results. Notably, 13.3% cases screened positive for cervicitis. The different results were then categorised to positive and negative for cervical abnormalities. Those that were categorised as positive for cervical abnormalities include genital warts, inflammation and cervicitis. Conversely, non-reactive ones were categorised as negative for cervical abnormalities. Those not done were added into missing and contributed to 14.8%. Eventually, 13.4% screened positive for cervical abnormalities, using visual inspection method. The evidence-based SAT approach

has been implemented in low-resource settings around the world, such that several South African studies have found the approach cost-effective, safe, and efficacious in screening for and treating cervical dysplasia (Grover et al. 2015:2).

4.3.7 Cervical cytology screening (N=1748)

The study also used the Pap test or cyclonical screening methods to establish any abnormal changes in cells of the cervix. Results from the screening are categorised according to the Bethesda system. The Bethesda system is a list of terms used by laboratories to describe Pap test results in several groups, namely, normal, atypical squamous cells of undetermined significance (ASCUS), atypical glandular cells (AGC), low-grade squamous intraepithelial lesion (LSIL), high grade squamous intraepithelial lesion (HSIL), and cancer. Table 4.5 shows a distribution of pap results by Bethesda category.

Table 4.5: Cervical cytology screening results (N=1748)

Category of Bethesda screening results	Category	Frequency	Per cent
Bethesda results	Negative	1,440	82.4
	ASCUS	19	1.1
	AGC	25	1.4
	HSIL	138	7.9
	LSIL	54	3.1
	Cancer	2	0.1
	Inflammation	25	1.4
	Missing	45	2.6
Bethesda recoded results	Negative	1,440	82.4
	Positive	263	15.1
	Missing	45	2.6

Table 4.5 shows that the majority (82.4%) screened negative while 15.1 % screened positive for cervical abnormalities from the Pap test. Among those that screened positive, a higher percentage (7.9%) showed high grade squamous intraepithelial lesions. A few cases (0.1%) had cancer. A total of 45 cases were missing. According to the American College of Obstetricians and Gynaecologists Frequently Asked Questions161 (2011:2), all patients that screen positive may need further testing

depending on age and the grade of the dysplasia. Sometimes there is more than one option for further testing, with advice from health care provider.

4.3.8 Association between age group and Bethesda results

Age group categories were compared with cytology results according to the Bethesda categories in order to establish distribution of the results by age group as reflected in Table 4.6.

Table 4.6: Association between Age group and Bethesda results

Age group	Negative	Inflammation	AGC	ASCUS	LSIL	HSIL	cancer	Total
16-19 years	28	0	0	1	0	1	0	30
20-24 years	220	6	1	4	5	21	0	257
25-29 years	322	6	2	6	13	27	1	377
30-34 years	323	6	5	3	15	31	0	383
35-39 years	227	4	6	0	10	25	0	272
40-44 years	172	2	7	1	9	17	1	209
45-49 years	148	1	4	4	2	16	0	175
Total	**1440**	**25**	**25**	**19**	**54**	**138**	**2**	**1703**

Pearson chi2(36) = 36.6522 Pr = 0.438

In Table 4.6, the age group 30 to 34 years had more cases of both low-grade squamous intraepithelial lesions (LSIL) and high-grade squamous intraepithelial lesions (HSIL) as compared to the other age groups. Cancer cases were picked in the age group 25 to 29 years and age group 40 to 44 years with one cases in each. More cases of AGC were shown in the age group 40 to 44 years, while more cases of ACUS were established in the age group 25 to 29 years. Seemingly, cases of high-grade squamous intraepithelial lesions increased with age of the women, while cases of low-grade squamous intraepithelial lesions decreased with age. This observation is corroborated by Mamahlodi, Kounza and Candy (2011:8) in a study on cervical cancer screening programme in Limpopo Province of South Africa that the prevalence of HSIL increased with the advancing age of the women (p-value < 0.001). By contrast, the rate of LSIL decreased with increasing age (p-value < 0.001).

4.3.9 Association between Age and visual inspection results

Age group categories were compared with visual inspection application results in order to establish distribution of the results by age group as reflected in Table 4.7.

Table 4.7: Age group distribution of visual inspection application results

Age group	Genital warts	Not done	Not reactive	Cervicitis	Inflammation	Total
16-19 years	0	1	24	4	0	29
20-24 years	1	27	196	38	1	263
25-29 years	0	40	287	57	0	384
30-34 years	0	49	278	68	0	395
35-39 years	0	30	213	32	1	276
40-44 years	0	39	152	21	0	212
45-49 years	0	63	105	12	0	180
Total	1	249	1255	232	2	1739

Pearson chi2(24)=99.8713 Pr = 0.000

Table 4.7 indicates that among the patients screened positive for cervicitis, the majority (68) were contributed by age group 30 to 34 years, while age 16 to 19 years contributed the least number of cases (4). The one case diagnosed with genital warts came from age group 20 to 24 years. VIA picks up more cases probably because of the physiological changes in pregnancy. Therefore, high estrogenic milieu of pregnancy causes an increase in cervical volume through hypertrophy of the fibromuscular stroma, an increase in the vascularity of the entire lower genital tract, more prominent gland opening with tenaciousmucus production, and an increase in stromal edema. The endocervical canal also frequently everts onto the ectocervix. The endocervical canal also frequently everts onto the ectocervix. The vagina becomes more acidic because of higher estrogen levels, and the decidual cells of the cervix show an increase in the nuclear-to-cytoplasmic ratio, together with more prominent nucleoli (Thilagavathi & Greetha, 2016:65).

4.3.10 Prevalence of cervical abnormalities

Results from VIA and cytological results that were categorised as positive or negative were combined to establish overall screening cervical test results as shown in Figure 4.3.

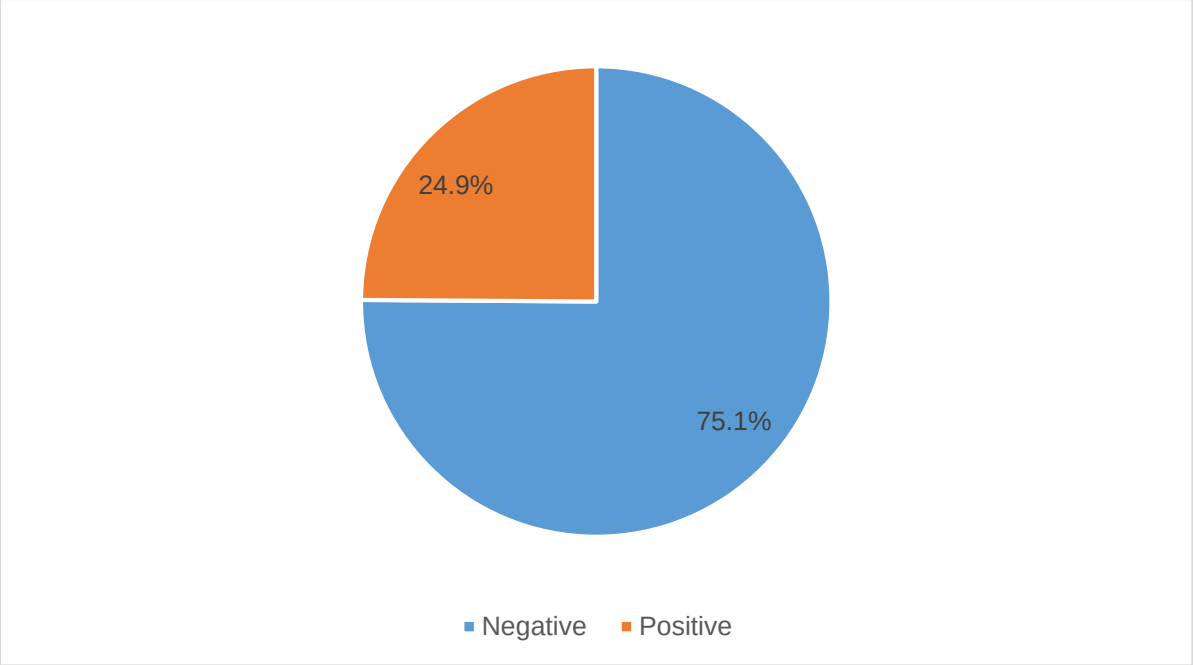

Figure 4.3: Overall screening cervical test results

Figure 4.3 depicts that the overall prevalence of cervical cytology was 24.9% (CI: 22.9-26.9), while those that were screened negative were 75.1%. Ferlay et al. (2012:27) estimated that cervical cancer morbidity and mortality was at 36.0/100 000 and 19.1//100 000 women per year respectively. However, it can be noted that Figure 4.3 shows much lower prevalence. This could be owing to the fact about one in every five women aged 30-49 years had ever had a screening test for cervical cancer (Swaziland Ministry of Health, 2014:15).

4.3.11 Association between age and overall cervical test results

Results from VIA and cytological test results that were categorised as positive or negative were combined to establish overall screening results as shown in Table 4.8.

Table 4.8: Distribution of overall cervical screening results by age group

Age group	Negative	Positive	Total
16-19 years	25	5	30
20-24 years	197	67	264
25-29 years	286	99	385
30-34 years	286	111	397
35-39 years	210	68	278
40-44 years	163	50	213
45-49 years	146	35	181
Total	1313	435	1748

Pearson chi2(6) = 6.5019 Pr= 0.369

Table 4.8 shows that the distribution of number of patients screened for cervical abnormalities at age group of 16-19 years was lower than all other age groups. The numbers of cervical abnormalities increase with age until age group of 30-34 years where it starts to decrease. This could be owing to high HIV prevalence among females in Swaziland (Swaziland Ministry of Health, 2014:15).

4.3.12 Association between cervical abnormalities and risk factors

Bivariate logistic regression was used to establish relationship between cervical cancer and each explanatory variable using chi-square.

Table 4.9: Association between cervical abnormalities and risk factors

Risk factor	OR	Chi2	P-Value	95 per cent CI
Young and Old	0.96	0.21	0.22	0.89 - 1.02
Urban and Rural	0.97	0.08	0.78	0.78 - 1.20
Region and No region	0.99	0.02	0.90	0.88 - 1.11
Married and unmarried	1.23	4.36	0.04	1.01 -1.49
Early sexual debut and Delayed sexual debut	0.72	8.47	0.00	0.58 - 0.90
Few number of lifetime partners and Many number of lifetime partners	1.07	1.03	0.31	0.94 - 1.21
Smoking and Not smoking	1.64	3.98	0.08	0.94 - 2.84
Drink alcohol and Not drink alcohol	0.93	0.11	0.76	0.60 - 1.45
History of STIs and No history of STIs	1.22	2.54	0.11	0.96- 1.55
HIV positive and HIV negative	2.11	51.01	0.00	1.61 - 2.75
On antiretroviral therapy and On no antiretroviral therapy	2.09	28.42	0.00	1.60- 2.72
Early menstruation and Late menstruation	0.84	2.56	0.18	0.65 - 1.08
History of cervical cancer and No history of cervical cancer	1.01	0.08	0.94	0.68 - 1.51

Table 4.9 demonstrates that patients that were married were 1.23 times (CI: 1.01 - 1.49) likely to have cervical abnormalities than unmarried patients. HIV positive patients were 2.11 times (CI: 1.61 - 2.75) likely to have cervical abnormalities than HIV negative patients. Patients on antiretroviral therapy were 2.09 times (CI: 1.60- 2.72) likely to have cervical abnormalities than those not on ART. Patients who delayed sexual debut were 0.72 times (0.58 - 0.90) likely to have cervical abnormalities than those who had an early sexual debut. According to Baussano, Diaz, Tully, Muñozc, de Sanjosé, Bosch and Franceschi (2017: 104), early age at first sexual intercourse has been associated with an increased risk of high HPV infection, a sexually transmitted infection, that in susceptible women virtually all cases of invasive cervical cancer.

4.4 OVERVIEW OF RESEARCH FINDINGS

The study results revealed that the overall prevalence of cervical cytology test results was 24.9%. This is in line with assertion by Swaziland Ministry of Health (2016:12) that the country is not sparred from the burden related to cervical cancer among women. It is the first most common malignancy in women accounting for 31% of all female cancers. The prevalence of cervical cytology could be more since it was reported that about one in every five women aged 30-49 years had ever had a screening test for cervical cancer (Swaziland Ministry of Health, 2014:15). About 13.3% cases screened positive for cervical abnormalities using VIA, while 15.1 % screened positive for cervical abnormalities from the Pap test.

A number of studies have identified risk factors associated with cervical abnormalities. However, this study indicates that being married, being HIV positive, age at sexual debut and being on ART were associated with cervical abnormalities. Marriage is expected to be a protective factor for cervical abnormalities; however, being married increased the odds (OR=1.23, p= 0.04). Delaying sexual intercourse at a young age minimises the chances of cervical abnormalities (OR=0.72, p=0.00). Bahmanyar et al. (2012:443) corroborate this in the PATRICIA trial that there was a significant association between several behavioural risk factors and infection with cervical cancer. Women who are HIV positive are at particular risk of progression to invasive cervical cancer. The study established that being HIV positive (OR=2.11, p= 0.00) and on ART (OR=2.09, p= 0.00) was associated with cervical abnormalities. According to The Lancet (2017:856), lowered immune system can be caused by immune suppression from corticosteroid medications, organ transplantation, treatments for other types of cancer, or from HIV and AIDS. Risk factors including number of lifetime partners, smoking, history of STIs and history of cervical cancer had higher odds of cervical abnormalities, but were not significant.

4.5 CONCLUSION

This chapter focused on analysis, presentation and description of main research findings of the study. These results were introduced by the presentation and discussion of the characteristics of the respondents. Bivariate and multivariate logistic regression were used to establish relationship between cervical cancer and each

explanatory variable. The next chapter will discuss these findings and conclusions and make recommendations based on them.

CHAPTER 5

CONCLUSIONS AND RECOMMENDATIONS

5.1 INTRODUCTION

Chapter 4 focused on analysis, presentation and description of main research findings of the study. This chapter presents the conclusions and recommendations of the study. The purpose of the study was to explore and describe factors associated with cervical cancer among women of reproductive age between 15 and 49 years in Swaziland. Focus was on the conclusions of the research in relation to the research questions asked and specifically the problem statement. Limitations of the study are limited to generalizability of the findings.

5.2 RESEARCH DESIGN AND METHOD

A chi-square test was used to establish associations between the outcome variables and explanatory variables. Having cervical cancer or not was used as an outcome variable, while explanatory variables included socio-demographic, reproductive, behavioural ad clinical variables. All explanatory variables were coded as categorical variables in order to use bivariate logistic and multivariate regression methods. Bivariate logistic regression was used to establish relationship between cervical cancer and each explanatory variable using chi square.

5.3 SUMMARY AND INTERPRETATION OF THE RESEARCH FINDINGS

5.3.1 Distribution of socio-demographic factors

The median age of the patients was 32 years. The distribution of number of patients screened for cervical abnormalities at age group of 16-19 years was lower than other age groups. Nevertheless, it rose steadily, and with a pick at age group of 30-34 years then started declining in the following age group of 35-39 years. The majority of the patients came from Hhohho Region while the minority came from Shiselweni Region. The majority were either single or married.

5.3.2 Distribution of reproductive factors

The majority of the patients had children that were less or equals to three while a few patients had less than three children.

5.3.3 Distribution of behavioural factors

The majority of patients had their sexual debut between the age group 10 to 19 years, while three indicated that they never had sex in their lives. The majority (51%) of patients indicated that they had two or less partners in their lifetime. About two patients indicated that their number of lifetime partners ranged from 21 to 23. Patients were asked about smoking habits; 94.2% indicated that they do not smoke. About 10.7% of the patients indicated that they take alcohol. About 26.3% had history of STIs.

5.3.4 Distribution of clinical factors

About 60.4% patients were HIV negative while 33.6% were HIV positive. About 20.8% indicated to be on antiretroviral therapy, while 18.9% had missing antiretroviral therapy status. About 62.4% of the patients had their first menstruation at 10 to 14 years. About 10.5% indicated that they had a history of cervical cancer.

5.3.5 Cervical cancer screening using Visual Inspection

About one in ten patients screened positive while seven in ten screened negative for cervical abnormalities using the VIA method. Others had missing results.

5.3.6 Cervical cytology screening

The majority (82.4%) screened negative while 15.1 % screened positive for cervical abnormalities from the Pap test. Among those that screened positive, a higher percentage (7.9%) showed high grade squamous intraepithelial lesions. A few cases of patients (0.1%) had cancer.

5.3.7 Association between age group and Bethesda results

The age group 30 to 34 years had more cases of both LSIL and HSIL as compared to the other age groups. Cancer cases picked in the age group 25 to 29 years and age group 40 to 44 years with one cases in each. More cases of AGC were shown in the age group 40 to 44 years, while more cases of ACUS were established in the age group 25 to 29 years.

5.3.8 Association between age and visual inspection results

Among the patients screened positive for cervicitis, the majority (68) were contributed by age group 30 to 34 years, while age 16 to 19 years contributed the least number of cases (4). The one case diagnosed with genital warts came from age group 20 to 24 years.

5.3.9 Prevalence of cervical abnormalities

The study results revealed that the overall prevalence of cervical cytology test results was 24.9%.

5.3.10 Association between Age and overall cervical test results

The number of patients screened for cervical abnormalities at age group of 16-19 years was lower than all other age groups. The highest number of cervical abnormalities were recorded at age group of 30-34 years.

5.3.11 Association between cervical abnormalities and risk factors

The combination of marital status, HIV status, ART status, age at sexual debut have been identified as factors associated with cervical abnormalities. Patients that were married were 1.23 times (CI: 1.01 -1.49) likely to have cervical abnormalities than unmarried patients. HIV positive patients were 2.11 times (CI: 1.61 - 2.75) likely to have cervical abnormalities than HIV negative patients. Patients on antiretroviral therapy were 2.09 times (CI: 1.60- 2.72) likely to have cervical abnormalities than those not on ART. Patients who delayed sexual debut were 0.72 times (0.58 - 0.90) likely to have cervical abnormalities than those who had an early sexual debut.

5.4 CONCLUSIONS

Results from the study imply that the combination of marital status, HIV status, ART status, age at sexual debut have been identified as factors associated with cervical abnormalities. Therefore, more attention is needed to consider or even address some of these factors when designing sexual reproductive services, especially cervical cancer screening.

5.5 RECOMMENDATIONS

Based on the findings of the study, the following recommendations are made:

- In response to cervical cancer being leading among female cancers and also increasing cases, there is a need to strengthen cervical cancer screening and prevention to become an essential part of a comprehensive sexual and reproductive health services for women.
- HIV services should be integrated into the Gynaecology Department in order to improve early diagnosis and cervical abnormalities treatment outcomes. The screening programme needs to be evaluated.
- The age group 30-34 has the highest number of cases with cervical abnormalities. Therefore, there should be a targeted study focusing on why the high cases using qualitative methods.
- Future research should be rolled out to public health units especially in rural areas for more access and coverage.
- Special programmatic needs on cervical cancer prevention are required considering that the country has about 13% of women with cervical abnormalities.

5.6 CONTRIBUTIONS OF THE STUDY

Because of the retrospective nature of the study, the researcher was able to establish the magnitude and factors associated with cervical abnormalities, therefore providing evidence to help plan cervical cancer screening coverage. The results will also serve as evidence for the development of a national cervical cancer screening policy and also strengthening the cancer registry in Swaziland.

5.7 LIMITATIONS OF THE STUDY

This study made use of secondary data and the general limitation was using variables that exist. The objectives were therefore streamlined according to the information available, despite wanting a detailed analysis for completeness. A significant number of records on HIV and ART status were missing owing to the lack of offer of HIV services in the Gynaecology Department. The study is limited to cervical cases in Mbabane Government Hospital and those diagnosed from January 2014 through to December 2014 only. The study was limited to extraction of patients' data without an

interaction with them. The researcher could not determine the sample size as the study sample size was dependent on the aggregated data available in the data warehouse.

5.8 CONCLUDING REMARKS

In order to meet the Sustainable Development Goals for sexual reproductive health, it is vital that the cervical cancer be further minimised by advancing cervical cancer screening services for women in Swaziland.

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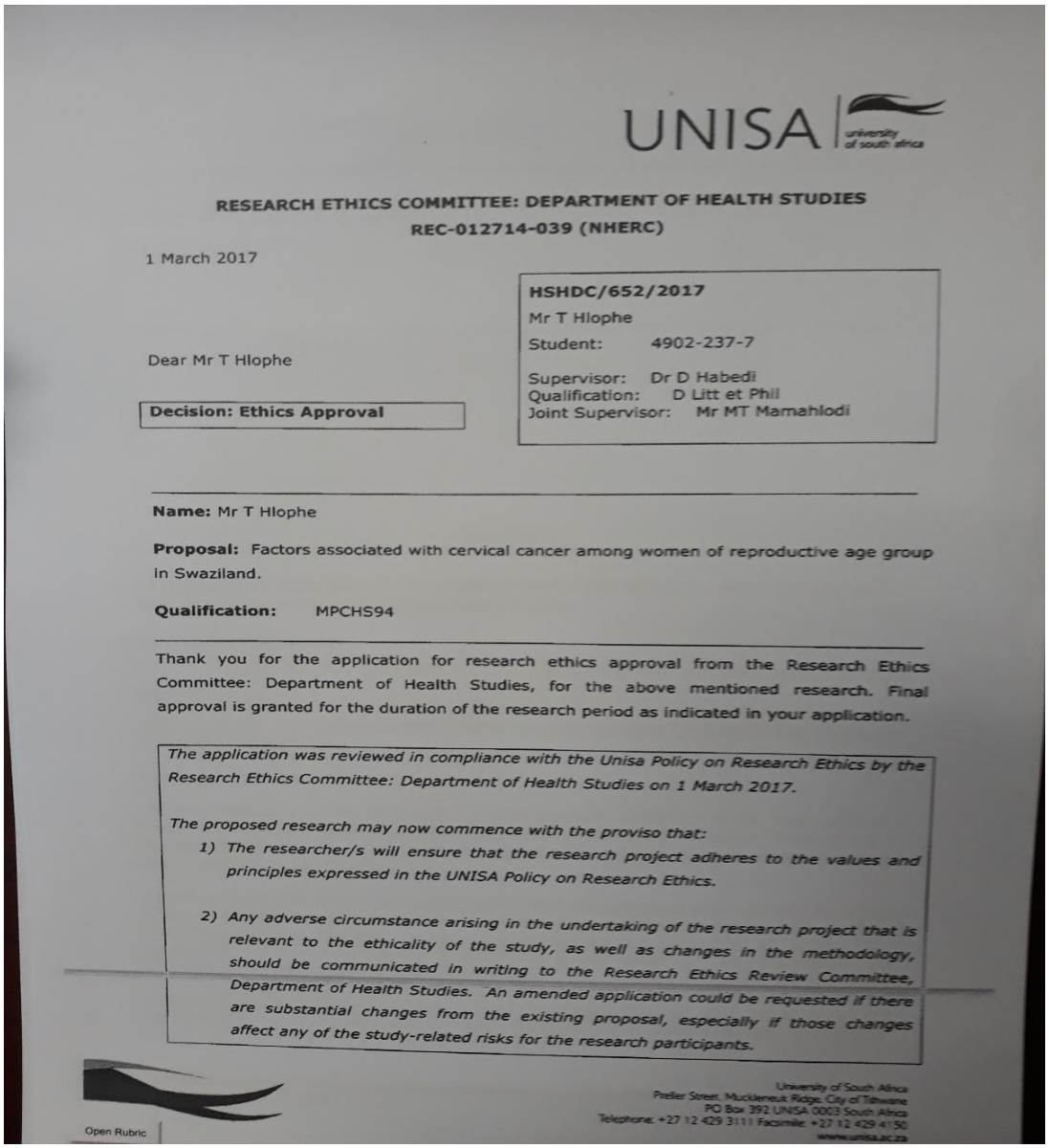
7. LIST OF ANNEXURES

Annexe A: Approval from the University



UNISA university of south africa

RESEARCH ETHICS COMMITTEE: DEPARTMENT OF HEALTH STUDIES
REC-012714-039 (NHERC)

1 March 2017

HSHDC/652/2017
Mr T Hlophe
Student: 4902-237-7

Supervisor: Dr D Habedi
Qualification: D Litt et Phil
Joint Supervisor: Mr MT Mamahlodi

Dear Mr T Hlophe

Decision: Ethics Approval

Name: Mr T Hlophe

Proposal: Factors associated with cervical cancer among women of reproductive age group in Swaziland.

Qualification: MPCHS94

Thank you for the application for research ethics approval from the Research Ethics Committee: Department of Health Studies, for the above mentioned research. Final approval is granted for the duration of the research period as indicated in your application.

The application was reviewed in compliance with the Unisa Policy on Research Ethics by the Research Ethics Committee: Department of Health Studies on 1 March 2017.

The proposed research may now commence with the proviso that:

1) *The researcher/s will ensure that the research project adheres to the values and principles expressed in the UNISA Policy on Research Ethics.*

2) *Any adverse circumstance arising in the undertaking of the research project that is relevant to the ethicality of the study, as well as changes in the methodology, should be communicated in writing to the Research Ethics Review Committee, Department of Health Studies. An amended application could be requested if there are substantial changes from the existing proposal, especially if those changes affect any of the study-related risks for the research participants.*

Open Rubric

University of South Africa
Preller Street, Muckleneuk Ridge, City of Tshwane
PO Box 392 UNISA 0003 South Africa
Telephone: +27 12 429 3111 Facsimile: +27 12 429 4150

Annexe B: Letter seeking consent from the Department of Health in Swaziland

APPLICATION FORM FOR ETHICAL REVIEW OF RESEARCH PROTOCOLS

All Applicants who seek to submit research proposals for ethics review and clearance are required to complete and submit this application form. Applicants are expected to provide all required information. Applicants are also expected ensure that all required documents have been attached. Review will only be initiated after all required documents have been received. Where clarification is needed, applicants are encouraged to contact the review board secretariat on tel. no (00268) 2404 0865/ (00268) 24044905

<table>
<tr><td colspan="8">Title of study: Factors associated with cervical cancer among women of reproductive age group in Swaziland</td></tr>
<tr><td colspan="2">Scope of study</td><td>International</td><td colspan="2">National</td><td colspan="2">Sub-national</td></tr>
<tr><td colspan="2">(Tick appropriate box)</td><td></td><td colspan="2">✓</td><td colspan="2"></td></tr>
<tr><td colspan="2">Name of Funder</td><td colspan="6"></td></tr>
<tr><td colspan="3">Study budget in Lilangeni</td><td colspan="5">SZL</td></tr>
<tr><td colspan="3">Names collaborating partners (where applicable)</td><td colspan="5">University of South Africa,</td></tr>
<tr><td colspan="2">Study category (Tick appropriate box)</td><td></td><td colspan="2">Study type (Tick appropriate box)</td><td></td><td colspan="2">Study duration in months</td></tr>
<tr><td>Quantitative</td><td>✓</td><td></td><td>Behavioural</td><td></td><td></td><td colspan="2" rowspan="3">12</td></tr>
<tr><td>Qualitative</td><td></td><td></td><td>Clinical</td><td>✓</td><td></td></tr>
<tr><td colspan="2"></td><td></td><td>Epidemiological</td><td></td><td></td></tr>
<tr><td colspan="3">Name of Principal Investigator</td><td colspan="5">Thabo Hlophe</td></tr>
<tr><td colspan="2">Contact Details Of Principal investigator</td><td colspan="2">Cell Phone
+268 7618 2047</td><td>Fax</td><td colspan="2">Email
thabo.hlophe@gmail.com</td></tr>
</table>

APPLICATION CHECKLIST

Tick appropriate box against documents which have been included where applicable

Ref.	Document	Tick
1	Completed application form	✓
2	Cover letter	
3	Evidence of administrative permission to conduct the research by involved institutions/sites (where applicable)	✓
4	Detailed current resume or curriculum vitae of Principal Investigator/s including Principal investigators declaration	✓
5	Summary resume or biography for other investigator(s)	✓
6	Evidence of approval/rejection by other Ethics Committees, including comments and requested alterations to the protocol, where appropriate.	✓
7	Research protocol (see outline in Annex 1)	✓
8	Questionnaires and interview guides (with back-translated versions where applicable)	N/A
9	Case report forms (CRFs), abstraction forms and other data collection tools	✓
10	Participant/subjects Information Statement(s) (where applicable)	N/A
	Informed consent form(s) including photographic and electronic media consent statements.	N/A
11	Advertisements relevant to the study (where applicable)	N/A
12	Source of funding and detailed budget breakdown including material and incentives to participants if applicable	
14	Notification form for adverse effects/events.	N/A
15	Proof of payment	✓
16	Proof of insurance cover for research subjects in clinical trials or where applicable	N/A

Annexe C: Letter of approval: Department of Health in Swaziland

Research Protocol clearance certificate

Type of review	Expedited	X		Full Board			
Name of Organization	STUDENT						
Title of study	FACTORSASSOCIATED WITH CERVICAL CANCER AMONG WOMEN OF REPRODUCTIVE AGE GROUP IN SWAZILAND						
Protocol version	1.0						
Nature of protocol	New	x		Amendment			
List of study sites	MBABANE GOVERNMENT HOSPITAL						
Name of Principal Investigator	THABO HLOPHE						
Names of Co- Investigators	N/A						
Names of steering committee members in the case of clinical trials	N/A						
Names of Data and Safety Committee members in the case of clinical trials	N/A						
Level of risk (Tick appropriate box)	Minimal			High			
	X						
Clearance status (Tick appropriate box)	Approved	X		Disapproved			
Clearance validity period	Start date	13/04/2017		End date	13/04/2018		
Signature of Chairperson							
Date of signing	13/04/2017						
Secretariat Contact Details	Name of contact officers	Ms Simangele Masilela					
	Email address	kaluamasi@gmail.com					
	Telephone no.	(00268) 24040865/24044905					

MINISTRY OF HEALTH
13 APR 2017
HEALTH RESEARCH REVIEW BOARD
SWAZILAND

Annexe D: Assessment of data collection instrument

SWAZILAND CANCER REGISTRY
CANCER ABSTRACT FORM
Tel: 24043064/24049988

SNCR

FACILITY CODE ☐☐☐☐☐☐ REGION CODE ☐☐☐☐

1. ☐ NEW CASE ☐ FOLLOW UP

2. STUDY ID Number ☐☐☐☐☐☐☐☐☐☐☐ 3. Marital Status (1Single/2not single) ☐

4. Contact number(patient) ☐☐☐☐☐☐☐☐ 5. Alternative contact (NoK) ☐☐☐☐☐☐☐☐

6. Age ☐☐☐ 7. Date of birth d d m m y y y y 8. Sex [1=male 2=female 9=unknown] ☐

10. Race (Black= 1 , White=2, Asian= 3, Colored=4,Other=9) ☐ 11. Religion (christianity, muslim, Hindu, other) .....

12. Education level ..... 13. Occupation .....

B. Risk Factors/ Other Diseases

Previous Cancer Diagnosis

14. Was cancer disgnosed previously other than the current (1 - Yes, 2 - No, 9 - Unknown) ☐
If Yes, Date of diagnosis d d m m y y y y
Site/Topography C ☐☐.☐ Histology/Morphology ☐☐☐☐/☐

15. Smoking (1 - Yes, 2 - No, 9 - Unknown) ☐ 16. Alcohol (1 - Yes, 2 - No, 9 - Unknown) ☐
If Yes, No. of cigars per day ☐☐ 17. History of contraceptives
18. History of CA 19. Serology
20. HIV Status (1 - Negative, 2 Positive, 0 - Unknown) ☐ If Positive, is patient on ART (1 - Yes, 2 - No, 9 - Unknown)
If on ART, ART number ☐☐☐☐☐☐☐☐☐☐ 21. History of STIs ☐
22.Time started on ART 23. Sexual Onset (year) ☐ 24. Menarche ☐
25. Family history of cancer (1 - Yes, 2 - No, 9 - Unknown) 26.Number of Lifetime partners ☐ 27.PAP result
28. # of lifetime partners 29.VIA result ☐ 30.CRYO ☐
Other Diseases .....

C. TUMOUR

31. Duration of Symptoms ☐☐ days ☐☐ months ☐☐ years

32. Basis of diagnosis (0 death cert only, 1 clinical only, 2 clinical/ultrasound, 3 biochem Immuno test, 4 cytology/haematology ☐
5 Histology of metastasis, 6 Histology of primary, 7 unknown)

33. Primary site of the tumors .....C ☐☐ ☐

34. Laterality ☐ Rt ☐ Lt ☐ Bil ☐ Unk ☐ N/A

35. Histology ..... M ☐☐☐☐

36. Behaviour ☐
0-Benign
1-uncertain
2-in situ
3-Malignant

37. Grade ☐
1- well-diff
2 - moderately diff
3- undiffrrentiated/ Anaplastic
4- T-cell
5- poorly diff
6-b-cell
7- Null cell
8- Killer cell
9- unknown

38.Stage ☐
0-In situ
1- stage 1
2- stage 2
3- stage 3
4- stage 4
9- unknown

T .....
N .....
M .....

D.TREATMENT

39. FIRST COURSE OF TREATMENT: [1=NO; 2=YES;9=UNKNOWN] ☐

Surgery	☐	Date d d m m y y y y	Radiotherapy	☐	Date d d m m y y y
Chemotherapy	☐	Date d d m m y y y y	Hormone therapy	☐	Date d d m m y y y
Immunotherapy	☐	Date d d m m y y y y	Other	☐	Date d d m m y y y

Remarks if any .....

Form completed by: ..... Date d d m m y y y y Signed .....

Data entered by: ..... Date d d m m y y y y Signed .....

Checked by: ..... Date d d m m y y y y Signed .....

Annexure E: Editing certificate

EDITING AND PROOFREADING CERTIFICATE

7542 Galangal Street
Lotus Gardens
Pretoria
0008

10 November 2018

TO WHOM IT MAY CONCERN

This certificate serves to confirm that I have edited and proofread Mr TT Hlophe's dissertation entitled, **"Factors associated with cervical cancer among women of reproductive age group in Swaziland".**

I found the work easy and intriguing to read. Much of my editing basically dealt with obstructionist technical aspects of language, which could have otherwise compromised smooth reading as well as the sense of the information being conveyed. I hope that the work will be found to be of an acceptable standard. I am a member of Professional Editors' Guild.

Hereunder are my particulars:

Jack Chokwe (Mr)

Contact numbers: 072 214 5489

jackchokwe@gmail.com

Professional EDITORS Guild