FACTORS AFFECTING BREAST, CERVICAL AND PROSTATE CANCER TREATMENT OUTCOMES IN ZAMBIA

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APPROVAL

This dissertation by **Francis Dien Mwansa** has been approved as partial fulfilment of the requirements for the award of the Degree of Master of Science in Field Epidemiology (By Research) by the University of Zambia.

Examiner1_____Signature_____Date_____

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Examiner3:_____Signature:_____Date:_____

Chairperson

Board of

Examiners:_____Signature:_____Date:_____

Supervisor: Dr. Gershom Chongwe **Signature:**  **Date:**16th April, 2019

ABSTRACT

Cervical, breast and prostate cancers represent 51% cancer mortality and morbidity in Zambia. This study aimed to show their prevalence, incidence trends, describe associated typical patient socio-demographic characteristics and survival factors using the Zambia National Cancer Registry (ZNCR) data collected during January 1st 2008 - December 31st 2015.

We conducted secondary ZNCR data incidence and mortality analyses of by province for these cancers. Data were cleaned using Excel and Epi Info Version 7.2.1.0. Analysis was done in Stata-13 for socio-demographic, treatment and survival factors. We determined annual incidence rates, from the mid-year (2011) onwards; and overall incidence using the mid-year population. Chi tests for trend and independence were used.

Of 10,765 cervical, breast and prostate cancer records analysed, there was an increase in incidence ($p<0.001$) and death rates during 2008 - 2015.

Most breast cancer patients (56.9%) were aged between 30-54years, 56% were married, 64.3% lived in Lusaka, Eastern and Copperbelt provinces and were commonly treated by chemotherapy (32.9%) and surgery (32.2%). Highest breast cancer case fatality (CFR) and crude death rates (CDR) per 100,000 population were in Lusaka (32.9% and 82) and Eastern (18.9% and 107) respectively. For instance, controlling for marital status a positive HIV status reduced the odds of survival by 40%.

Most cervical cancer patients (61.5%) were aged between 30-54years, 53.1% married, 57.9% lived in Copperbelt, Eastern and Lusaka provinces and were commonly treated by Chemotherapy (37.3%) and Radiotherapy (31.8%). Highest CFRs were in Lusaka (35.9%) and Eastern (14.3%) and lowest (2%) in Muchinga provinces, but Copperbelt province had the lowest CDR at 210/100,000 people. Controlling for marital status, HIV status and age, Radiotherapy increased the odds of survival by 70%.

Most prostate cancer patients were aged between 60-84years, 54% were married and were commonly treated by Chemotherapy (34.1%) and surgery (29.6%). Lusaka (43%) and Eastern (13.1%) provinces had highest prostate cancer CFRs and a CDR of 310/100,00 population. Controlling for age, surgery, chemotherapy, radiotherapy and province of birth, being married increased the odds of surviving from prostate cancer 7.5 times.

Breast and cervical cancers in Zambia mainly affected those younger than 55years while prostate mainly affected those older than 60 years and increased with age. Age, surgery, marital status and province of residence appear to have a major effect on morbidity and survival. Early screening programmes can help address these cancers.

Key words: breast cancer, cervical cancer, prostate cancer, Zambia

DECLARATION

I, **Francis Dien Mwansa**, affirm that this work is entirely my own, except where the words or ideas of other writers are specifically acknowledged according to accepted citation conventions. This dissertation has not been submitted for any other course at the University of Zambia or any other institution. I have revised, edited and proofread this dissertation incorporating as advised and taught the information from my supervisors, programme coordinators and mentors.

By submitting this dissertation to the University of Zambia for the Degree of Master of Public Health by Research programme, I further attest that it has not been submitted to another university in part or in whole for the award of another programme.

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NHRA Approval Date: 5th September 2017

Signature_____ **Date**_____

Francis Dien Mwansa

DEDICATION

I dedicate this:

To all those who walked by my side along this journey, knowingly or otherwise whereby I hope, at last, to qualify as an Epidemiologist;

To all those who have known doubt and perplexity during the process of learning and practicing the art and science of Epidemiology, as I have and hope to continue doing all my life;

To my wife and children who filled the happier parts of the times spent between new insights and paragraphs, lending their attention to a mind lost in numbers and their potential meaning;

And to my God, my help in times past and present

My hope for years to come

My comfort when my comprehension appear(ed) to be finite

My refuge when all appear to fail.

GLOSSARY OF ACRONYMS

AAR	Adjusted Age Rate
AOR	Adjusted Odds Ratio
CDC	Centres for Disease Control and Prevention
CDH	Cancer Diseases Hospital
CDR	Crude Death Rate
CFR	Case Fatality Rate
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
IQR	Interquartile Range
KS	Kaposi Sarcoma
PHO	Provincial Health Office
UTH	University Teaching Hospital
WHO	World Health Organisation
ZNCR	Zambia National Cancer Registry

Chapter 1: INTRODUCTION

1.1 Background of the Study

The World Health Organization (WHO 2015a) described cancer as a leading cause of death and accounted for 7.6 million deaths (around 13% of all deaths) in 2008. The Centers for Disease Control and Prevention (CDC 2015) breaks down the latest (2012) available global information on cancer as follows: 14.1 million as new cancer cases diagnosed, 8.2 million as people who died from cancer and 32.6 million as those who were five-year cancer survivors (people who are alive five years after being diagnosed with cancer). The latest available information on the burden of cancers in Africa (Jemal et al. 2012) is that in 2008, the continent had 715,000 new cancer cases and 542 cancer deaths.

Cancers are a spectrum of disorders that affect every population in the world (Republic of Zambia Ministry of Health 2014). Cancer is further described as a disease caused by an uncontrolled division of abnormal cells in a part of the body. Cancer is increasingly recognised as a critical public health problem in Africa in general and Zambia in particular. While communicable diseases continue to burden African populations, it is becoming clear that non-communicable diseases also require the attention of those whose goal it is to ensure the health of Africans (Abratt & Vorobiof 2003; Jemal et al. 2012; Jemal et al. 1999; Parham et al. 2014).

Despite collecting cancer data since 1977, the typical cervical, breast or prostate cancer patient has not been characterised. A lot of information was therefore obtained and kept at the Zambia national cancer registry (ZNCR). We could only find one paper that set out to discuss the distribution of the cancers in Zambia. This review has therefore provided descriptive characteristics of cervical, breast and prostate cancer patients and other measures of occurrence of these diseases in Zambia. It has further provided disease determinants for the three cancers as well as provide some information on the outcomes per treatment mode.

1.2 Statement of the Problem

The first problem is that the ZNCR collects data which is barely used to inform national policies meant to address cancers. Secondly, despite being host to a huge data base, the typical cancers have not been well characterised in Zambia. Thirdly, without being peer reviewed, and feedback obtained from stakeholders, the ZNCR may not make required changes so as to collect information which stakeholders require. Fourthly, information on the mortality and morbidity trends of breast, cervical and prostate cancer in Zambia is not readily available for a country with a cancer registry. Lastly, the commonest treatment modes for these three cancers in Zambia are not on record to influence planning both in the long and short term.

The ZNCR data is expected to be systematically collected, stored, analysed and applied for the institution to fulfill its meaningful existence. The absence of analysis on the outcomes of a given disease, a given treatment option and duration of treatment gives little room for improvement and direction of that improvement. The absence of data on such outcome analysis represents a lost opportunity to make desired improvements to both the management of cancer in general and plan appropriately.

The Zambia Cancer Index (Cancer Index 2017) lists thirty (30) other papers discussing cancer-related issues in Zambia but none used ZNCR data let alone characterised cervical, breast and prostate cancer patients in Zambia as per recommendation by the International Cancer Benchmarking Partnership (International Cancer Benchmarking Partnership 2014). In the first study to investigate the international cancer survival disparities with the aim of informing health policy to raise standards and reduce inequalities in survival, the ICBP (Coleman et al. 2011) noticed persistent regional and international differences in survival. This further warranted need to have the ZNCR data studied so as to avoid application of foreign data to handle local problems.

The latest annual report from the national cancer registry (Republic of Zambia Ministry of Health 2014) indicated 3,181 new cancer cases 65.3% of them distributed as follows:

- 1,082 new cervix uteri cases
- 463 new Kaposi Sarcoma cases
- 358 new prostate cases, and
- 174 new breast cancer cases.

Kaposi Sarcoma (KS) is very prevalent in Zambia but the Zambia National Cancer Registry (ZNCR) has a lot of missing information on it. In addition, most of the Kaposi Sarcoma is HIV related and ZNCR the does not collect information on HIV treatment. Because of this KS was not considered in this work. The burden of the other three cancers as reported for 2013 was 51% of all cancers.

Cancer in Zambia has received much attention in recent years due to its high mortality, which has very high, detrimental and important economic effects. Cancers are widely distributed in Zambia (Zyaambo et al. 2013) and addressing them needs the participation of all stakeholders as highlighted in the national cancer control strategic plan (Republic of Zambia Ministry of Health 2017).

Zambia offers three forms of treatment for cancer in surgery, radiotherapy and chemotherapy. While surgical and chemotherapy treatments are the most widely used, radiotherapy is much restricted to the only cancer diseases hospital (CDH) which offers full oncology treatment services (African Cancer Registry Network 2015; Republic of Zambia Ministry of Health 2013). It is important to know the distribution and application of these treatment modes to patients.

1.3 Justification

Outcome analysis of the ZNCR data should reflect “real-world” experience with cancer management in Zambia based on diverse patient population, surgeon and hospital settings, potential earlier safety signals in management of cancer patients and a large number of cases with long-term follow-up. Because registry data was useful for establishing benchmarks against which to compare specific designs, outcome analysis would provide such a bench-mark for future analysis

Continued collecting of data without adequately analysing it had a number of disadvantages, including but not limited to making the process lose the motivation of collecting quality data, risking missing timely action opportunities had the data been analysed before and risking leaving the cancer registry data too bulky and complex so as not to be very beneficial and meaningful in future (analysis).

This study was justified in that it was meant to:

- help bridge the knowledge gap about cervical, breast and prostate cancers in Zambia;
- provide clinical and administrative practitioners with 'real-world' experience on the cervical, breast and prostate cancer in Zambia;
- provide cervical, breast and prostate cancer benchmarks in Zambia;
- help yield the true benefits of the cancer registry investment; and
- provide the basis for possible review of the cancer registry variables.

1.4 Research Objectives

1.4.1 General Objective

The main objective of this research was to determine the factors that affected the outcome of prostate, breast and cervical cancer treatment from the Zambia national cancer registry data from January 1, 2008 to December 31, 2015.

1.4.2 Specific Objectives

To help attain this, the three sub-objectives below will help:

1. To outline the demographic and clinical characteristics of prostate, breast and cervical cancer patients in Zambia;
2. To compare initial treatment outcomes of surgery, radiotherapy, chemotherapy/hormonal therapy and other treatment methods for each of breast, cervical and prostate cancers in Zambia; and
3. To identify demographic and clinical factors associated with poor treatment outcomes of breast, cervical and prostate cancer in Zambia.

Chapter 2: LITERATURE REVIEW

2.1 Review of Literature

The cancer registry is an essential part of any rational programme of cancer control (Anazawa, Miyata, and Gotoh 2015; Gotoh et al. 2016). Whereas the medical system assumes that existence of a cancer registry may sort out a lot of problems to do with data collection, access and usage, this is seldom the case as most cancer registries world over were relatively new and standard operating procedures were in their infancy (Silva 1999). Because cancer registry information was often the best secondary data a developing country like Zambia has, it was important to ascertain the significance of this data on the practice of all aspects of cancer management by analysing the data. To address this aim, this paper reviewed the information that already existed to determine the factors associated with cancer treatment outcomes in Zambia.

Analysis of data from the Zambia cancer registry had focused on the distribution of the cancer diseases (Zyaambo et al. 2013). The areas of factors associated with outcomes of treatment appear to have not been explored except for outcomes of cervical cancer screening and some paediatric cancers (Slone et al. 2014). There is no record of work on the treatment outcomes for cervical, breast and prostate cancer in Zambia. Equally, extensive search in the neighbouring countries revealed similar outcome, no record of research in that line.

From other regions of the world, some work on outcomes of localised prostate cancer following conservative management (Lu-yao et al., 2009) has been done but yet still little on treatment outcomes in the clinical trial setting. There was general agreement that because of the lack of results from randomised clinical trials comparing the efficacy of aggressive therapies with that of more conservative therapies for clinically localised prostate cancer, for instance, men and their physicians may select treatments based on other criteria. The closest was an examination of the association of socio-demographic and clinical characteristics with four management options: radical prostatectomy, radiation therapy, hormonal therapy, and watchful waiting (Harlan et al. 2001). To appreciate the factors that affect treatment outcomes of prostate cancer treatment (like cervical and breast cancer), we must examine, in detail, the different

methodologies that have been used to investigate this topic and analyse the data from the national cancer registry to make the results more applicable to Zambia and the sub-Saharan region.

There was also little known about breast cancer in Zambia in terms of factors affecting outcomes of the disease and its treatment. A similar picture exists in sub-Saharan Africa. However, it was a known fact, for instance, that African-American women had had a lower incidence of breast cancer, yet higher mortality rate from breast cancer compared with White-American women.

African-American women also have had a higher risk for early-onset, high-grade, node-positive, and hormone receptor-negative disease (Fregene and Newman 2005). While this paper may not give such detail, it should be able to discuss to some detail the paradoxical finding by Fregene and Newman of low incidence of breast cancer in women of sub-Saharan Africa.

Cervical cancer research on the other hand, in Zambia and the rest of the region, had lately been very informative albeit focusing on preventive interventions. Much of the work had also focused on HIV patients (Parham 2002; Parham et al. 2009) until recently with the expansion of the screening programme as demonstrated by (Pfaendler et al. 2008) in the implementation of the Loop electrosurgical excision procedure (LEEP) Zambia.

With currently no national-level data that map women's cancer control services in the country of Zambia (African center of excellence for women's cancer control 2015), characterising a breast or cervical cancer patient has therefore been restricted to extrapolations from foreign data and limited interpolations from individual hospital data. The proposed work herein is expected to give a 'real-world' national picture.

Traditionally, researchers in disease outcomes have aimed to focus on one disease in their analyses of treatment outcomes, and is the case in most papers herein referenced. However, such a narrow focus may not fully explain how the same treatment modalities such as surgery for diseases (cancers) differ across disease. Because such use of the same treatment method is common in the management of

cancers, understanding its effects enables greater knowledge of procedure itself (D'Amico et al. 2002). Therefore, instead of intentionally avoiding the science of comparing outcome of a procedure across disease, they should be explored in their own right. This paper therefore proposes a look at cervical, breast and prostate cancer in that light.

While the above studies provide valuable information regarding the known aspects of the treatment outcomes of the three cancers largely outside sub-Saharan Africa, caution needs to be exercised before applying these results to sub-Saharan Africa and specifically Zambia. It should not be assumed that the results obtained from studies using small cohorts are applicable to the general public especially that most of the cited studies were urban-based to the exclusion of the rural areas with unappreciated burden. Similarly, an outcome of an intervention on one cancer may not give enough information to apply it on another. Therefore, cancer registry data with a bigger span and diversity was hoped to provide this information.

Limitations on the referenced papers as regards their generalisability to the Zambia population existed. A major limitation of the research on breast cancer in sub-Saharan Africa (Fregene and Newman 2005) was that it attributed low incidence of breast cancer largely to protective reproductive history, including late menarche, early menopause, high parity with prolonged breastfeeding, irregular menses, and fewer ovulatory cycles. This picture may only be true in a fraction of the region as the picture has changed over the past decade and the incidence has been rising (Kantelhardt et al. 2015).

The radical prostatectomy versus radiation therapy study (Harlan et al. 2001) and the one on factors associated with initial therapy for clinically localised prostate cancer (Lu-yao et al. 2009), though done outside Zambia (sub-Saharan Africa), provides credible insights to look for in the data provided by the cancer registry in discussing common treatment methods as recorded by the cancer registry.

Studies cited above on cervical cancer focus on preventive interventions (and outcomes) and, looking at characterising cervical, breast and prostate cancer patients and disease treatment outcomes for cervical cancer in Zambia would be new.

Most research involving the cancer treatment interventions sought to identify the comparison of one intervention to another, and therefore the assumption was made that discussion of other possible factors, often discussed as confounders, was irrelevant and the better intervention was usually adopted. It may therefore be advantageous to also investigate the factors that affect primary treatment outcome without comparing a new treatment intervention with another but merely looking at the outcomes of the different diseases using the available interventions. However, few studies have used this methodology, and those that have discussed one disease as opposed to multiple. Therefore, future studies on factors may have to cross the disease barrier as this would be helpful to better understand the factors particularly those that are crosscutting being separated from those that are disease specific.

While the treatment methods of cancers were a well-established phenomenon, 'what remains in dispute is 'the better treatment outcome per disease in sub-Saharan Africa'. Associated factors are therefore also less clear. While some factors such as race have been studied in the United States of America and seem to indicate that racial and ethnic minorities and medically underserved groups are more likely to develop cancer and die from it than the general U.S. population (Coughlin and Ekwueme 2009; Shavers 2002), less was known about sub-Saharan Africa (Abratt and Vorobiof 2003), and Zambia in particular. There was however little known about whether this racial and social difference, for instance, affected the response to these known treatment methods. Therefore, in order to understand why surgery/radiation/chemo-therapy outcomes differed across all three cancers, and which in this environment was a better treatment mode and speculate why if it differed from what prevailed in other regions, we needed to study the factors together from the same data source.

A number of factors are known to affect (any) cancer treatment outcomes, which are related to the treatment modality, patient and/or provider. Those accounting commonly for poor outcome include extremes of age (Hartmann et al. 2015), economic environment (Ginsburg et al. 2017; Muwonge et al. 2016; Slone et al. 2014), being non-Hispanic (Jones 2015; Shavers 2002), being HIV positive (Parham et al. 2010), late detection (Greenwald, Sondik, and Young 1986; Muwonge et al. 2016; Rahaei et al. 2015; Sankaranarayanan et al. 2010), risk factor prevalence (Hortobagyi et al. 2005;

Jemal et al. 1999) and treatment choice (Kingham et al. 2013) amongst others. Factors specific to a disease such as HPV vaccination status in the case of cervical cancer, being black as in the case of prostate cancer and reproductive factors that increase the risk of breast cancer such as long menstrual history, nulliparity, recent use of post-menopausal hormone therapy or oral contraceptives, and late age at first birth as discussed by (Jemal et al. 1999; Mohite, Pratinidhi, and Mohite 2015) may not be discussed as the ZNCR may not have collected data on this or to that detail.

HIV infection discussed by (The World Bank 2006; De Vuyst et al. 2013) as one of the major factors in determining the outcome of treatment (as well as disease progression) would be discussed to the extent that the ZNCR collects information on the HIV status of the notified cases.

Given the pivotal role of a cancer registry particularly in research (International Agency for Reseach on Cancer 1991; Silva 1999), the output in terms of research papers from the ZNCR which has been in existence since 1977 is low. It may be that registry data was difficult to work with as local works on cancer such as (Asombang et al. 2014) were derived from hospital departmental gastric cancer research database. This could be because of the quality of data which most researchers have questioned as far back as 1994 (Teppo, Pukkala, and Lehtonen 1994). Until the ZNCR is subjected to this kind of scrutiny and the like of which was done on its Norwegian counterpart (Larsen et al. 2009), it would be difficult to justify the lack of activity in this regard. Given the differences observed within European countries, the results from the ZNCR were expected to differ from the global picture. However, the factors were likely to be the same only differing in terms of extent.

Generally in Africa, as noticed by (Finocchario-Kessler et al. 2016), treatment of diseases (cervical cancer, for instance) with effective medicine was one the severely under-researched areas and so literature on factors affecting treatment outcomes was also little.

2.2 Theoretical Background

No theoretical or conceptual framework was found during this review to help facilitate this discussion. Frameworks around prevention health-seeking behaviour however did exist.

(Chapa 2016) gave a nice narrative of experienced range of factors that affect cancer treatment outcomes. Understanding this would be better done in a structured manner. This made Andersen's Behaviour Model of Health Services relevant to the work contained herein. In the works, in 1974, Ronald Andersen, outlined a health behaviour model that addressed the patient's demographic profile, variables that could affect outcomes, and the patient's perceived need. He called them predisposing, enabling and need variables, respectively and demonstrated below (Figure 2.1).

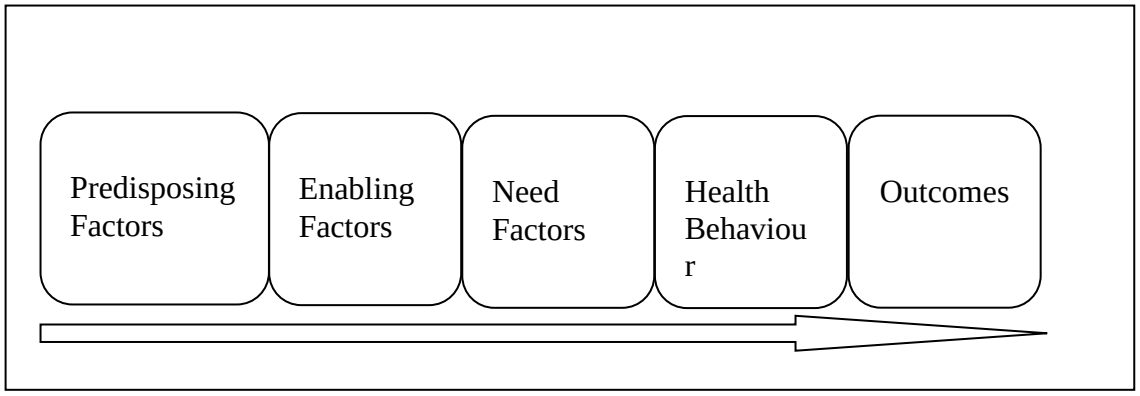

Figure 2.1 Anderson Model of Health Services Utilisation

To further understand this model and apply it appropriately, a systematic review on its use done by (Babitsch, Gohl, and von Lengerke 2012), particularly in variable terms of categorisation proved useful.

Figure 2.1 describes four factors which ultimately have a contribution towards the health outcomes. These include:

• *Individual predisposing factors:* These included the demographic characteristics such as age, sex, education, occupation and ethnicity.
• *Enabling factors:* These include financing (income and wealth) and organisational factors source of care, transportation, travel time and waiting time). These are considered to serve as conditions enabling services utilization.

• *Need factors:* This exists at two levels. There's the need for health services (i.e., how people view and experience their own general health, functional state and illness symptoms) and evaluated need (i.e., professional assessments and objective measurements of patients' health status and need for medical care).

• *Health behaviour:* The above sets of three factors determines the behaviour of the patient, to seek health care or not and to what extent.

• All these put together determine the health outcome, in this case the outcome of cancer treatment. The ZNCR only provided information on some of the predisposing and need factors. This means that we were unable to fully apply the model especially that we could not get additional information from the patients.

Chapter 3: METHODOLOGY

3.1 Study Design, Setting and Population

This was a cross sectional study that reviewed secondary data of all patients of prostate, breast and cervical cancer notified between January 1, 2008 and December 31st, 2015 in the ZNCR who received cancer therapy. To calculate the seven-year prevalence, 2011 is the midpoint in the period under review and that year's population was taken as the country's crude population for the period under review. In 2011, as estimated from 2010 census of population and housing (Central Statistical Office Zambia 2012), Zambia had 13,718,722 people. As the ZNCR collected data from across the country, the Zambian population was considered the study population.

Until 2015, the registry was receiving cancer notification forms from hospitals all over Zambia (population about 13 million in 2010), and entering the data into a CanReg-4 database. In 2015, there are staff in each Provincial Health Office (PHO) that are responsible for data entry for their province with support from Clinical Care Specialists. The national cancer registry gets information from CDH too. The main source of information is the computerised register of cancer cases seen in the hospital (system based on Microsoft Access database). The national cancer registry used files exported from this system. Three files have to be merged (Patient, Clinical information, treatment information).

By mid 2017 when the data used herein was obtained from the registry, the ZNCR staff had just completed recording data on all cases diagnosed or treated in Lusaka district (no matter where their place of residence), with the aim of having a complete coverage of the district population which would complete cleaned and transferred (from CanReg3 to CanReg5) data for the years under review. Such levels of data completeness may not be generalized to the whole country but this analysis assumed adequate representation countrywide.

3.2 Sample Size

Assumptions as guided by (Sullivan, Dean, and Mir 2017) on the web-based 'openepi.com', were made to determine the sample size as follows: A national population of over one million, an anticipated percentage frequency (proportion) of 50%, an absolute precision of 5% and a design effect of 1.0 for a random sample. According to (Zyaambo et al. 2013) the most reported cancer in Zambia was cervical cancer at 48.5% prevalence. As 50% would give the highest possible sample size and was close to the reported prevalence, it was used in the calculation. This was so done as to be certain the total entries in the census were not insufficient so as not to be useful. The result was as presented in Table 1.

From Table 1, at 95% confidence level, a sample size of 165 was needed from the ZNCR for each of prostate, cervical and breast cancers. This notwithstanding, a census of all patients of prostate, breast and cervical cancer notified between January 1, 2008 and December 31st, 2015 in the ZNCR who received initial cancer therapy, was included in the study. The attached (Appendix 1) data collection tool was used to extract data from the database.

Table 3.1 was informed by the following assumptions: Population size (for finite population correction factor or fpc)(*N*) of greater than 1000000, a hypothesized % frequency of outcome factor in the population (*p*) of 50%+/-5, confidence limits as % of 100(absolute +/- %)(*d*) of 5% and a design effect (for cluster surveys-*DEFF*) of 1.

Table 3. 1 Sample size for frequency in a population

Sample Size (n) for Various Confidence Levels	
Confidence Level (%)	**Sample Size**
95%	**384***
80%	165
90%	271
97%	471
99%	664
99.9%	1082
99.99%	1512
Equation	
Sample size $\boldsymbol{n = [DEFF*Np(1-p)]/ [(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)]}$ *Required sample size	

3.3 Data Extraction, Analysis and Outcomes of interest

Secondary data from the ZNCR was used for this study and so was imported into Epi Info Version 7.2.1.0 then Microsoft Excel 2010 for data cleaning and finally into Stata 13.0 for analysis. Descriptive statistics per disease were provided around the treatment outcome of remission or no remission. These include frequencies and proportions presented in distribution tables and/or graphs.

For continuous variable data presentation, medians and interquartile ranges (IQR) were used and compared using the Two-sample Wilcoxon Rank-Sum (Mann-Whitney) Test as they were not normally distributed. Categorical variables were presented as numbers and percentages. Chi squared test was used to test and evaluate the difference between the categorical variables. Particularly, we compared patient demographic and comorbidity characteristics by treatment approach using Chi square testing. Principal analyses included comparison of treatment mode across diseases. Because of the constituent differences amongst provinces, the crude cancer mortality rates were calculated at presented at per 100,000 population rates.

Univariable logistic regression analyses according to independent variables associated with place (of residence), cancer staging, age, sex, ethnic group, occupation, HIV status, and type of primary treatment were done.

Multivariable analyses on the main risk factors were run. Given the dichotomous nature of the dependent variable (dead or alive), logistic regression was used beginning with unadjusted odds ratios before analysing with the significant predictors in an appropriate model to provide more information on potential confounders and effect modifiers. Potential confounders include age, sex, treatment type and disease staging, while potential effect modifiers include type of treatment and disease staging. Adjusted odd ratios (AOR) together with their 95% confidence intervals were reported.

All analyses were adjusted for the *a priori* confounders of treatment complexity using a data driven, stepwise approach. Based on the Wald test from logistic regression, p-value cut-off point was set at 0.20 as more traditional levels such as 0.05 often fail to identify important variables (Bendel and Afifi 1977; Bursac et al. 2008; Costanza and Afifi 1979) Covariates assessed as potential confounders included the binary variables of sex,

HIV status (unknown status was considered as missing data) and marital status. Confounding was defined as a 10% change in the estimated effect with addition of a variable to the logistic regression model. Marital status for breast cancer and surgery for cervical and prostate cancers) were determined to be confounders and so our final multivariable models was adjusted for marital status and surgical complexity, respectively. Backward stepwise logistic regression was used and model diagnostics was done using Akaike's information criterion and Bayesian information criterion.

Survival from each of the cancers was the main outcome. The Anderson Model of Health Services Utilisation (Chapa 2016) was used to categorise factors affecting initial cancer treatment outcome from the variables obtained in the registry. Outcomes were categorised as dead or alive as opposed to remission or no remission. Deaths were further looked at separately to determine first the relationship to the disease of diagnosis and later by logistic regression the factors associated with death.

3.4 Selection Criteria

3.4.1 Inclusion Criteria

The study included all patients notified with breast, cervical and prostate cancer to the ZNCR between 1st January 2008 and 31st December 2015. Both patients with primary breast, cervical and prostate cancers in any combination at initial diagnosis were all included. There was no restriction on age in terms of inclusion, only suspicious ages were followed up and clarified. This was summarised in Figure 3.1.

3.4.2 Exclusion Criteria

As shown in Figure 3.1, patients with missing outcome status were excluded. Also, those who did not receive at least one form of treatment or reported as such were excluded from the study. Missing and questionable data elements for the same patient were considered for possible inclusion upon review for consistency. For instance, for a patient diagnosed with prostate cancer but born in 2016, the first step was to seek clarity from the entry form, then the reporting province and finally the district. If not clarified, then the entry was excluded. For patient record with intact personal details but missing any other data element, the same follow up was done and included if other elements are okay. A few examples of patients entered as male with cervical cancer and

could not be clarified from the source district were excluded. Most were clarified. Of the personal details, age and sex were considered the most important without which the patient record was removed in totality from the analysis if those could not be clarified as suggested above.

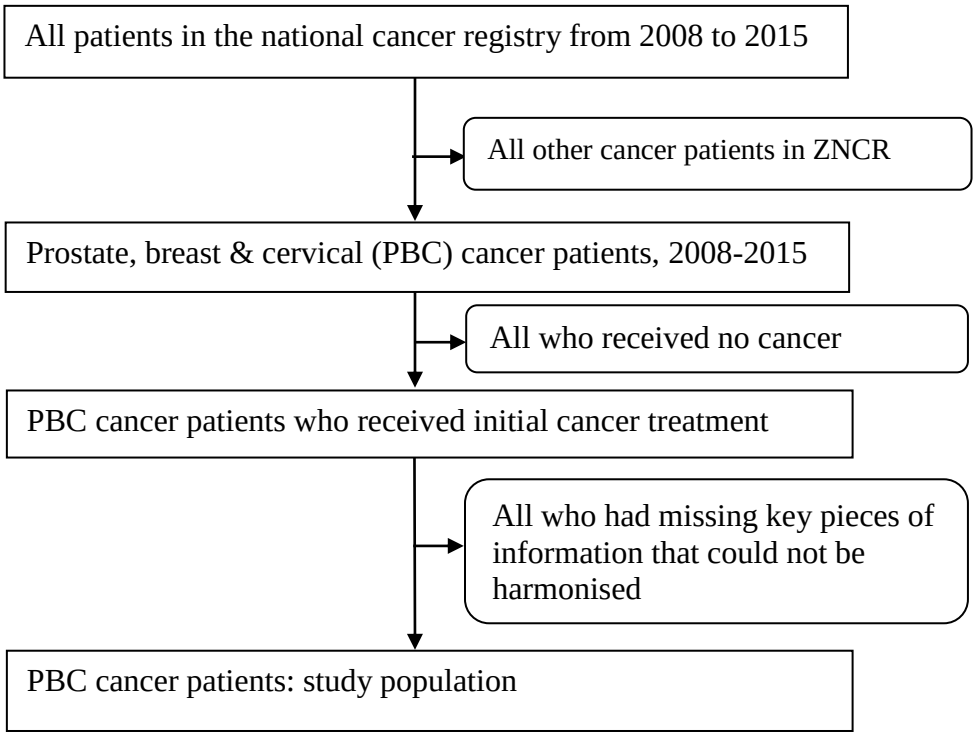

Figure 3. 1 Flow chart of participation in the study (adapted from (Mulrooney et al. 2009)

3.5 Ethical issues

The study considered ethical issues and challenges around secondary data, data confidentiality and security (Tripathy 2013) accordingly. Anonymisation of the data was done by coding at entering because the ZNCR has identifying information. The data was then kept as encrypted files in computers for the principal researcher and the supervisors. Applications for approval of the study protocol were sought and obtained from the National Health Research Authority and ERES Converge IRB (Ref. No. 2017-Jun-032).

3.6 Limitations of the Study

We would have loved to present incidence rates rather than incidence counts but the absence of critical information such as death date made it difficult to have person years

and hence the incidence rates. The ZNCR provides an opportunity for a rolling study but continued absence of the person-time information makes that difficult.

The absence of key dates from the registry meant that duration of treatment, duration of illness, date of death, etc which have a huge bearing on the outcome, meant that survival studies could not be done. This work initially sought to analyse an optimal duration of treatment that had a preferred impact on desired outcomes but the absence of key dates in the registry made this impossible to do.

The fact that there is uncertainty on ZNCR's completeness and may not be as extensively covered as Lusaka district may be, means that the findings may not be viewed as very representative of the national picture. However, this work took and harmonised as much complete data as possible and not necessarily the most recently obtained.

No cost estimates for any intervention were done in this review, it is hoped that the information shared here will provide planners and clinicians the ability to estimate the cost of each of the treatment and the total cost of managing specific cancers including how many of the annual cases can adequately be managed within the resources available.

One of the expected outcomes of this review was to give a 'real-world' national picture of the three cancers but this was limited by the limited variables in the registry. Variables such as HPV vaccination status in the case of cervical cancer, race as in the case of prostate cancer and reproductive factors that increase the risk of breast cancer such as long menstrual history, nulliparity, recent and prolonged use of post-menopausal hormone therapy or oral contraceptives, and late age at first birth as discussed by (Jemal et al. 1999; Mohite et al. 2015) were not discussed as the ZNCR does not collect data on this or to that detail.

ZNCR could not address all the factors identified from the Andersen Model of Health Services Utilisation and so the linkage was incomplete in the discussion.

The assignment of treatments to patients was not randomly done to the extent that would make the ZNCR a randomised experiment rather than an observational study,

and so we could not apply the word “causes" rather than just “is associated with" to any statistically significant result.

Lack of exchangeability, that any two groups were comparable, for instance, that every other determinant amongst those who died is the same as those who survived, left room for confounding. Some of the confounders were not collected in the ZNCR and so could not be controlled for.

Surgery may explain some good outcome in one of the cancers but ‘other treatments’ do not rule out effect modification. Other treatments were a huge block but details of these did not exist in the ZNCR.

Chapter 4: RESULTS

4.1 Population Description

We analysed a total of 10,653 breast, cervical and prostate patient records notified to the ZNCR over an eight year period (January 2008 to December 2015) and the summary distribution is included in Table 4.1. The distribution was such that 1,476 were breast cancer patients, 7,374 were cervical cancer patients and 1,803 prostate cancer patients. For each of these diseases, the following were studied; Age, Sex, HIV status, Dead-or-Alive Status, Marital Status, Home Address, Birth Place, Age Category and Cancer Site. These are summarised in Table 4.1. Age has been broken down in the WHO standard 5 year age groups with the lowest category across all three cancers ranging from the minimum to 29 years. The age range was from 14 years to 99 years. The median age for all was 51 (IQR: 40-65) years (alive and dead). The table also shows a summary for all three cancers the counts of the outcome of interest, survivors, and the total (of the dead and alive) as the last column. Where possible, a column percentage in each category (variable) is reported.

Of the total of 10,653 patients analysed in this study of these three cancers 1,848 were males and 8,805 were females. Of the 9,510 survivors, 1,531 were males while 7,979 were females. This meant that 1,143 died in the period under study of breast, cervical and prostate cancers.

Only HIV positive patients are reported; the difference between this and that reported in the last column of totals representing the numbers for the dead who had HIV. The difference (7,929) between this (1,581) and the total number of survivors (9,510) was the count for those where were HIV negative. Similarly, those reported as being on ART in the second column for all three cancers is for those where were alive in the study period. The difference () between this (1,481) and those reported as having HIV in the same column (1,581) represented those who were not on ART (100).

Those reported as unmarried/unknown included those who had never been married before, those were divorced, widows and widowers, those on separation and those who whose marital status was unknown.

Table 4.1 Demographic characteristics and descriptive statistics of breast, cervical and prostate cancer patients in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (N = 10,653).

Cancer	**All Three Cancers (Breast, cervical and prostate)**	
Status	**Alive**	**Alive & Dead (% of total)**
No. of patients	9510	10,653
Age (years)	n(%)	n(%)
Min-29	515(5.4)	549 (5.1)
30-34	746(7.84)	834 (7.75)
35-39	1024(10.8)	1139 (10.58)
40-44	1155(12.2)	1300 (12.08)
45-49	1023(10.7)	1134 (10.53)
50-54	1028(10.8)	1154 (10.72)
55-59	796(8.4)	902 (8.38)
60-64	758(8.0)	843 (7.83)
65-69	739(7.8)	859 (7.98)
70-74	675(7.1)	799 (7.42)
75-79	387(4.1)	452 (4.2)
80-84	291(3.1)	350 (3.25)
85-89	90(1.0)	119 (1.11)
90-Max	283(3.0)	331 (3.07)
Median (IQR)	51 (40-65)	51 (40-65)
Range	14-99	14-99
Sex (Male/Female)	1531/7979	1848/8805
Treatment	n(%)	n(%)
Surgery	2885(14.3)	3575(15.5)
Chemotherapy	7167(35.6)	8294(36.1)
Radiotherapy	5028(25.0)	5567(24.2)
Palliative Care	142(0.7)	155(0.7)
Hormonal Therapy	269(1.3)	285(1.2)
Other Treatment	4623(23.0)	5121(22.3)
	n(%)	n(%)
HIV Status Positive **HIV Status Negative**	1581(16.62) 8029(84.43)	1785(16.76) 9868(92.63)
On ART	1,481	1,673
Marital Status	n(%)	n(%)
Married	5344(56.2)	5880 (53.6)
Un-(married/known)	4166(43.8)	5087(46.4)

Table 4.2 below shows the overall summaries of where the patients were born as well as where they were living at the time of being attended to. Most (3.047,541and 3,588) of the patients (alive, dead and in total respectively) were living in Lusaka province during the period under study. Copperbelt and Eastern provinces had the second and third largest residents with breast, cervical or prostate cancers. A similar picture is seen when the study looked at where these patients were born from, showing Lusaka province leading with 20.1% (4,414) and followed by Eastern province with 13.5% (2,970) and Copperbelt province with 9.0% (1,974) of the total number of patients attended to during the period under study.

Table 4.2 Geographic characteristics and statistics of breast, cervical and prostate cancer patients in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (N = 10,653).

Cancer	**All Three Cancers**	
Status	**Alive**	**Total (% of total)**
Provincial Home Address	count(col%)	count(col%)
Central	927(9.7)	1054(11.1)
Copperbelt	1257(13.2)	1395(14.7)
Eastern	1142(12.0)	1353(14.2)
Luapula	392(4.1)	471(5.0)
Lusaka	3047(32.0)	3588(37.7)
Muchinga	182(1.9)	212(2.2)
North-western	408(4.3)	472(5.0)
Northern	655(6.9)	724(7.6)
Southern	887(9.3)	995(10.5)
Western	526(5.5)	609(6.4)
Unknown	87(0.9)	94(1.0)
Province of Birth		
Central	601(6.3)	1434(6.5)
Copperbelt	907(9.5)	1974(9.0)
Eastern	1231(12.9)	2970(13.5)
Luapula	338(3.6)	870(4.0)
Lusaka	1937(20.4)	4414(20.1)
Muchinga	143(1.5)	364(1.7)
North-western	311(3.3)	740(3.4)
Northern	702(7.4)	1628(7.4)
Southern	892(9.4)	1996(9.1)
Western	424(4.5)	1028(4.7)
Unknown	2024(21.3)	4516(20.6)

4.2 Breast Cancer Prevalence

We reviewed 1,476 breast cancer records that were notified and registered into the ZNCR from 2008-2015 as shown in Tables 4.3. Of these, 45 were male while 1,431 were female. Breast cancer case fatality rate (CFR) was 9.7% in a 3:140 male to females ratio. The median age for breast cancer was 49 (IQR: 38-61) years old with an age range of 14 to 99 years. Majority of the breast cancer surgery (75%) was given to those aged between 30 and 64. Most breast cancer patients (56%) were married. Over the same period, 189 of these breast cancer patients were HIV positive with 92.6% of them on the highly active antiretroviral therapy (HAART). The commonest treatment methods were by chemotherapy (32.9%), surgery (32.2%) and other non-surgical, non-chemotherapy, non-therapy, non-hormonal and non-palliative methods (23.5%).

Table 4.3 Demographic characteristics and descriptive statistics of breast cancer patients in the Zambia National Cancer Registry from January 1st 2008 to December 31st 2015 (n = 1,476)

Cancer	**Breast cancer**			
Status	**Alive**	**Dead**	**Total**	**P value[a]**
No. of patients	1333	143	1476	0.499
Age (years)	n(%)	n(%)	n(%)	
Min-29	103(7.7)	12(8.4)	115(7.8)	0.013
30-34	117(8.8)	12(8.4)	129(8.7)	0.909
35-39	142(10.7)	16(11.2)	158(10.7)	0.671
40-44	174(13.1)	25(17.5)	199(13.5)	0.160
45-49	157(11.8)	12(8.4)	169(11.4)	0.372
50-54	168(12.6)	18(12.6)	186(12.6)	0.679
55-59	102(7.7)	17(11.9)	119(8.1)	0.262
60-64	116(8.7)	5(3.5)	121(8.2)	0.031
65-69	96(7.2)	8(5.6)	104(7.0)	0.074
70-74	78(5.9)	8(5.6)	86(5.8)	0.150
75-79	32(2.4)	5(3.5)	37(2.5)	0.957
80-84	25(1.9)	3(2.1)	28(1.9)	0.494
85-89	5(0.4)	1(0.7)	6(0.4)	0.676
90-Max	18(1.4)	1(0.7)	19(1.3)	0.446
Median (IQR)	49 (38-61)	48 (37-58)	49 (38-61)	
Range	14-99	14-99	14-99	
Sex (Male/Female)	42/1291	3/140	45/1431	0.486
Treatment	n(%)	n(%)	n(%)	
Surgery	1049(31.7)	119(36.4)	1168(32.2)	0.946
Chemotherapy	1079(32.7)	116(35.5)	1195(32.9)	0.930
Radiotherapy	360(10.9)	23(7.0)	383(10.5)	0.147
Palliative Care	23(0.7)	3(0.9)	26(0.7)	0.340
Hormonal Therapy	6(0.2)	0(0.0)	6(0.2)	0.494
Other Treatment	787(23.8)	66(20.2)	853(23.5)	0.772
	count	count	count	
HIV Status Positive	167	22	189	0.016
On ART	153	22	175	0.006
Marital Status	n(%)	n(%)	n(%)	0.001
Married	765(57.4)	61(42.7)	826(56.0)	
Un-(married/known)	568(42.6)	82(57.3)	650(44.0)	

[a]Pearson chi2 comparing those who survived to those who died

Table 4.4 show the geographic distribution (by province) by birth and residence of the breast cancer patients in the period under study. During this period, a combined 64.3% lived in Lusaka, Eastern and Copperbelt provinces, while 48.8% of the patients were born in these same three provinces.

Table 4.4 Geographic characteristics and descriptive statistics of breast cancer patients in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (n = 1,476)

Cancer	**Breast cancer**			
Status	**Alive**	**Dead**	**Total**	**P value[a]**
Provincial Home Address	n(%)	n(%)	n(%)	
Central	91(6.8)	6(4.2)	97(6.6)	0.215
Copperbelt	221(16.6)	10(7.0)	231(15.7)	0.010
Eastern	128(9.6)	27(18.9)	155(10.5)	0.078
Luapula	42(3.2)	6(4.2)	48(3.3)	1.000
Lusaka	516(38.7)	47(32.9)	563(38.1)	**0.006**
Muchinga	31(2.3)	3(2.1)	34(2.3)	0.628
North-western	41(3.1)	5(3.5)	46(3.1)	0.936
Northern	77(5.8)	11(7.7)	88(6.0)	0.123
Southern	115(8.6)	12(8.4)	127(8.6)	0.827
Western	60(4.5)	14(9.8)	74(5.0)	**0.031**
Unknown	11(0.8)	2(1.4)	13(0.9)	
Province of Birth				
Central	87(6.5)	10(7.0)	97(6.6)	0.318
Copperbelt	182(13.7)	7(4.9)	189(12.8)	**0.036**
Eastern	158(11.9)	33(23.1)	191(12.9)	0.141
Luapula	44(3.3)	6(4.2)	50(3.4)	0.356
Lusaka	315(23.6)	26(18.2)	341(23.1)	0.158
Muchinga	29(2.2)	2(1.4)	31(2.1)	0.087
North-western	31(2.3)	5(3.5)	36(2.4)	0.736
Northern	103(7.7)	13(9.1)	116(7.9)	0.922
Southern	129(9.7)	13(9.1)	142(9.6)	0.869
Western	58(4.4)	12(8.4)	70(4.7)	0.531
Unknown	197(14.8)	16(11.2)	213(14.4)	0.684

[a]Pearson chi2 comparing those who survived to those who died

There was however no statistical difference by Pearson Chi squared test (at 5% Alpha Level) in terms of outcome (dead or alive) by province of residence across the country except for Lusaka and Western provinces. Similarly, except for Copperbelt province, there was difference by Pearson Chi squared test (at 5% Alpha Level) in terms of outcome (dead or alive) by province of birth across the country.

Table 4.5 shows that the age-adjusted breast cancer incidence rate was 19.4 per 100,000 population in Zambia.

Table 4.5 Age-adjusted breast cancer rate in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (n = 1,476)

Age	**Count**	**Population**	**Crude Rate (per 100,000)**	**WHO Standard Age Population Distribution**	**Age-adjusted Rate (per 100,000)**
Min-29**	115	10,255,705	1.12	0.5838	
30-34	129	861,791	14.97	0.0715	
35-39	158	700,400	11522.56	0.0659	
40-44	199	496,313	40.10	0.0604	
45-49	169	382,117	44.23	0.0537	
50-54	186	296,017	62.83	0.0455	
55-59	119	201,849	58.95	0.0372	
60-64	121	167,964	72.04	0.0296	
65-69	104	126,860	81.98	0.0221	
70-74	86	93,962	91.53	0.0152	
75-79	37	64,166	57.66	0.0091	
80-Max*	53	71,578	74.05	0.0063	
All Ages	1476	13,718,722	10.76		**19.39**

*For purposes of comparison, the age group 80-Max is an aggregate of the age groups 80-84, 85-89, 90-94, 94-99 and 100+

**For purposes of comparison, the age group Min-29 is an aggregate of the age groups 0-4, 5-9, 10-14, 15-19, 20-24 and 25-29

Table 4.6 Crude breast cancer mortality rates (Per 100,000 population) by birth province by age in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (n = 1,476)

Zambia	Central	Copperbelt	Eastern	Luapula	Lusaka	Muchinga	N.Western[±]	Northern	Southern	Western
Prov. Rate*	30.48	21.98	106.56	29.00	81.97	5.01	57.44	63.91	43.60	73.31
Min-29	0.20	0.00	0.00	0.13	0.17	0.18	0.18	0.12	0.00	0.00
30-34	0.00	0.72	4.22	0.00	1.06	0.00	0.00	1.57	3.01	1.88
35-39	0.00	0.89	5.02	0.00	1.36	0.00	0.00	5.50	2.52	2.36
40-44	6.26	2.48	8.77	0.00	4.25	0.00	7.82	5.00	5.40	9.53
45-49	5.38	1.58	6.56	3.29	1.57	4.84	0.00	0.00	2.36	3.92
50-54	3.39	0.00	16.99	4.11	13.21	0.00	6.74	3.93	0.00	0.00
55-59	4.95	0.00	12.30	12.04	10.00	0.00	0.00	11.61	9.68	19.62
60-64	0.00	3.59	8.81	0.00	4.60	0.00	0.00	0.00	0.00	7.18
65-69	0.00	0.00	11.11	9.43	7.00	0.00	0.00	8.33	7.26	18.07
70-74	10.31	0.00	14.07	0.00	10.62	0.00	18.35	11.31	0.00	0.00
75-79	0.00	0.00	10.16	0.00	0.00	0.00	24.37	16.54	13.35	0.00
80+	0.00	12.73	8.54	0.00	28.12	0.00	0.00	0.00	0.00	10.75

(Those with Unknown birth province were excluded)

*Prov. rate referred to provincial rate. [±]N.Western refers to North western province

As shown in Table 4.6, at 106.6 per 100,000, Copperbelt province had the highest crude mortality rate, followed by Lusaka (82/100,000), Northern (63.9/100,000) and North-western (57.4/100,000) respectively. Highest breast cancer case fatality (CFR, 32.9%) and crude death rates (CDR, 82 per 100,000 population) were in Lusaka followed by Eastern with CFR at 18.9% and CDR 107 per 100,000 population.

In absolute terms, the number of breast cancer patients had increased from 146 in 2008 to 222 in 2014, with Lusaka, Copperbelt, Eastern, Southern and Northern provinces the major contributors of up to 66.5% of the burden. The rate of diagnosis of new breast cancer patients (Figure 4.1) showed an upward trend for all provinces except for Lusaka province whose rate has been on the downward trend in the period under study. The diagnosis trend for the Copperbelt province is upwards doubling within the period under study.

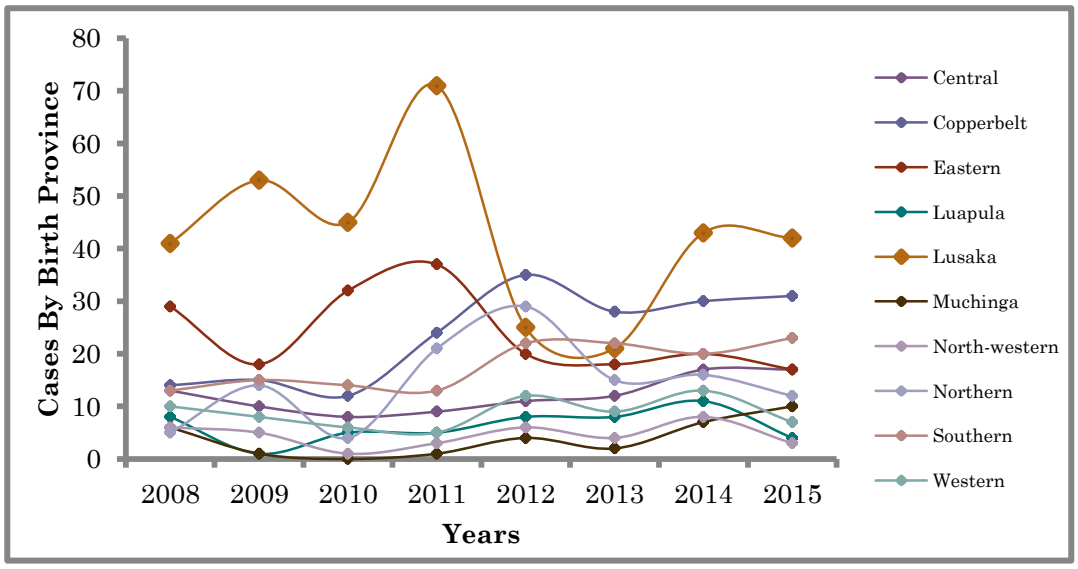

Figure 4. 1 Trends of breast cancer diagnosis by birth province in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (n = 1,476)

Table 4.7 Breast cancer treatment outcome by birth province in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (No. = 1,476)

	Surgery			**Radiotherapy**			**Chemotherapy**			**Hormonal**			**Palliative Therapy**			**On ARVs**			**Other Therapy**		
Province	**Alive**	**Dead**	**Total (Col%)**	**Alive**	**Dead**	**Total (Col%)**	**Alive**	**Dead**	**Total (Col%)**	**Alive**	**Dead**	**Total (Col%)**	**Alive**	**Dead**	**Total**	**Alive**	**Dead**	**Total (Col%)**	**Alive**	**Dead**	Total
Central	76	8	84(7.19)	25	2	27(7.05)	78	9	87(7.36)	0	0	0(0.00)	1	0	1(8.00)	12	2	14(8.00)	32	0	32(4.11)
Copperbelt	144	7	151(12.93)	58	2	60(15.67)	157	7	164(13.87)	2	0	2(33.33)	4	0	4(15.38)	34	2	36(20.57)	97	0	97(12.45)
Eastern	135	30	165(14.13)	52	5	57(14.88)	144	28	172(14.55)	1	0	1(16.67)	1	1	2(7.69)	9	6	15(8.57)	70	0	70(8.99)
Luapula	42	6	48(4.11)	14	1	15(3.92)	40	5	45(3.81)	0	0	0(0.00)	1	0	1(3.85)	2	0	2(1.140	15	0	15(1.93)
Lusaka	275	24	299(25.60)	99	4	103(26.89)	286	25	311(26.31)	3	0	3(50.00)	4	0	4(15.38)	48	5	53(30.29)	232	0	232(29.78)
Muchinga	25	2	27(2.31)	6	0	6(1.57)	25	2	27(2.28)	0	0	0(0.00)	0	0	0(0.00)	7	1	8(4.57)	14	0	14(1.80)
N.Western	25	5	30(2.57)	6	1	7(1.83)	27	4	31(2.62)	0	0	0(0.00)	0	1	1(3.85)	2	0	2(1.14)	12	0	12(1.54)
Northern	83	11	94(8.05)	33	3	36(9.40)	84	13	97(8.21)	0	0	0(0.00)	7	0	7(26.92)	12	1	13(7.43)	59	0	59(7.57)
Southern	111	10	121(10.36)	35	3	38(9.92)	121	10	131(11.08)	0	0	0(0.00)	1	1	2(7.690	11	1	12(6.86)	55	0	55(7.06)
Western	49	10	59(5.05)	11	2	13(3.39)	49	7	56(4.74)	0	0	0(0.00)	1	0	1(3.850	6	1	7(4.00)	27	0	27(3.47)
Unknown	84	6	90(7.71)	21	0	21(5.48)	55	6	61(5.16)	0	0	0(0.00)	3	0	3(11.54)	10	3	13(7.43)	166	0	166(21.31)
Zambia	1049	119	1168	360	23	383	1066	116	1182	6	0	6	23	3	26	153	22	175	779	0	779
Overall %	90%	10%		94%	6%		90%	10%		100%	0%		88%	12%		87%	13%		100%		

Table 4.7 shows that the commonest primary treatment modes for breast cancer were surgery, radiotherapy and chemotherapy. All of hormonal, palliative therapy was given as adjuvant therapy. Similarly, Antiretroviral therapy (ARVs) and other therapies were given as adjuvant to the primary treatment. Most surgical intervention occurred in Lusaka (25.60%) followed by Eastern province (14.13%), Copperbelt province (12.93%) and Southern province (10.36%), with the rest done (36.98%) in the remaining 6 provinces of Zambia. The trend per province for radiotherapy, chemotherapy and hormonal therapy (respectively) were very similar to that of rates of surgical intervention. Majority of the breast cancer surgery (75%) was given to those aged between 30 and 64.

4.3 Factors Affecting Breast Cancer Survival

In trying to understand how survival related to each of the treatment interventions, the Fisher's exact test was used. It showed an association ($p<0.001$) among the treatment interventions and the main outcome variable (survival over the period under study). It also showed an association between marital status and survival. The same was true when dead was used as an outcome. We, however, could not show if there was any statistically significant difference in the mean age at diagnosis between those who died of the disease and those who survived in the period under study from the Two-sample Wilcoxon Rank-Sum (Mann-Whitney) Test, $p = 0.8900$.

As can be seen on Table 4.8, on univariable analysis, Palliative care, Chemotherapy, Radiotherapy, Surgery and Sex were not associated with survival at 0.2 alpha level. While all other variables caused a 10% change in the estimated effect with addition of such variables to the logistic regression model (confounding), surgery and sex had no such effect. They were however maintained in the main model *a priori* and within 0.2 alpha level. At any p value, the confidence interval appeared to include the null value but at bivariate analysis binary variables excluded the null value. For instance, controlling for marital status a positive HIV status reduced the odds of survival by 40%.

Controlling for place of birth, place of residence, age and ART, radiotherapy increased the odds of survival 3.11 times. Controlling for place of birth, place of residence, age, ART and radiotherapy treatment, the odds of survival were paradoxically reduced by 98% amongst those who received palliative care.

Table 4.8 Unadjusted and adjusted analysis of independent variables to breast cancer survival in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (n = 1,333)

Factors		Cancer Survivors (n=1,333)	Unadjusted	Adjusted	
Age (years)		n(%)	Odds ratio	Odds ratios	CI* (95%)
	Min-29	103(7.7)	Ref.	Ref.	N/A
	30-59	860(64.7)	1.01	2.50	0.58 - 10.70
	60-79	322(24.2)	1.23	2.95	0.57 - 15.35
	80-Max	48(3.7)	0.87	1.00	N/A
Treatment	Radiotherapy	360(10.9)	1.45	**3.11**	**1.02 - 9.49**
	Palliative Care	23(0.7)	0.54	**0.02**	**0.00 - 0.41**
On ART	Negative	1166	Ref.	1.00	N/A
	Positive	167	0.59	0.35	0.10 - 1.21
Provincial	Central	91(6.8)	Ref.	1.00	N/A
Home	Copperbelt	221(16.6)	1.39	1.00	N/A
Address	Eastern	128(9.6)	**0.38**	6.63	0.15 - 286.01
	Luapula	42(3.2)	0.62	1.00	N/A
	Lusaka	516(38.7)	0.93	5.11	0.41 - 62.93
	Muchinga	31(2.3)	0.91	1.00	N/A
	North-western	41(3.1)	0.60	1.00	N/A
	Northern	77(5.8)	0.62	3.86	0.01 - 156.80
	Southern	115(8.6)	0.84	1.00	N/A
	Western	60(4.5)	**0.35**	1.00	N/A
	Unknown	11(0.8)	**0.16**	1.00	N/A
Province of	Central	87(6.5)	Ref.	1.00	N/A
Birth	Copperbelt	182(13.7)	**3.14**	1.00	N/A
	Eastern	158(11.9)	**0.62**	10.93	0.48 - 250.38
	Luapula	44(3.3)	1.01	1.00	N/A
	Lusaka	315(23.6)	**1.61**	16.37	0.93 - 287.13
	Muchinga	29(2.2)	2.00	1.00	N/A
	North-western	31(2.3)	0.61	1.00	N/A
	Northern	103(7.7)	1.09	6.77	0.34 - 135.36
	Southern	129(9.7)	1.37	11.87	0.37 - 376.88
	Western	58(4.4)	0.62	1.00	N/A
	Unknown	197(14.8)	1.13	1.00	N/A

* Confidence Interval

4.4 Cervical Cancer Prevalence

Between 2008 and 2014, the ZNCR recorded 7,374 cervical cancer patients with 686 of these dying within the same period, giving a 9.3% case fatality. Table 4.9 shows that this study reviewed all the 7.374 cervical cancer records that were notified and registered into the ZNCR from 2008-2015. The youngest patient was 18 years old while the oldest was 99 years old. The mean age for cervical cancer patients was 47 (IQR: 38-58) years. The majority (61.5%) of the patients were aged between 30 and 54 years old.

Most cervical cancer patients (56%) were married. Over the same period under review, of the 1,493 HIV positive cervical cancer patients, 94.8% of them were on the highly active antiretroviral therapy (HAART). The commonest treatment methods were by chemotherapy (32.9%), surgery (32.2%) and other (non-surgical, non-chemotherapy, non-therapy, non-hormonal and non-palliative methods accounted for 23.5%.

There was a statistically significant difference between survivors and those died across selected age categories such as under 30 years, between 40 and 44 and above 55 years of age (except for the age group (85-89). Table 4.9 also demonstrates that the most commonly offered treatment (69.1%) treatments were chemotherapy and radiotherapy, by absolute counts. Other treatments (non-surgery, non-chemotherapy, non-palliative care and non-ART) accounted for 21.9% of treatments.

Over this period, 1,493 representing 20.2% (95% Confidence Level: 19.3-21.2) of the cervical cancer patients were HIV positive out of which 94.8% (1,415) were on ART with a statistically significant difference between those who survived and those who died. Most (4,081 representing 53.1%) were married while the unmarried (3,607) were either divorced, widowed, never married or of an unknown status and there was no statistical difference between survivors and those died in terms of marital status.

Table 4.9 Demographic characteristics and descriptive statistics of cervical cancer patients in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (n = 7,374)

Cancer	**Cervical Cancer**			
Variable	**Alive**	**Dead**	**Total (Alive+Dead)**	**P value[a]**
No. of patients	6688	686	7374	**0.002**
Age (years)	n(%)	n(%)	n(%)	
Min-29	412(6.2)	19(2.8)	431(5.8)	**0.013**
30-34	627(9.4)	67(9.8)	694(9.4)	0.860
35-39	881(13.2)	87(12.7)	968(13.1)	0.507
40-44	972(14.5)	100(14.6)	1072(14.5)	**0.167**
45-49	837(12.5)	85(12.4)	922(12.5)	0.428
50-54	792(11.8)	93(13.6)	885(12.0)	0.964
55-59	591(8.8)	69(10.1)	660(9.0)	**0.203**
60-64	477(7.1)	44(6.4)	521(7.1)	**0.207**
65-69	378(5.7)	54(7.9)	432(5.9)	0.505
70-74	274(4.1)	31(4.5)	305(4.1)	**0.007**
75-79	146(2.2)	11(1.6)	157(2.1)	**0.002**
80-84	95(1.4)	11(1.6)	106(1.4)	**0.099**
85-89	14(0.2)	5(0.7)	19(0.3)	0.772
90-Max	192(2.9)	10(1.5)	202(2.7)	**<0.001**
Median (IQR)	47 (38-58)	49 (39-59)	47 (38-58)	
Range	18-99	20-99	18-99	
Treatment	n(%)	n(%)	n(%)	
Surgery	959(7.0)	317(16.3)	1276(8.2)	0.360
Chemotherapy	5028(36.9)	769(39.6)	5797(37.3)	0.798
Radiotherapy	4447(32.7)	502(25.9)	4949(31.8)	0.542
Palliative Care	108(0.8)	8(0.4)	116(0.7)	0.489
Hormonal Therapy	10(0.1)	2(0.1)	12(0.1)	**0.192**
Other Treatment	3057(22.5)	343(17.7)	3400(21.9)	**0.096**
	count	count	count	
HIV Status Positive	1320	173	1493	**<0.001**
On ART	1250	165	1415	**<0.001**
Marital Status	n(%)	n(%)	n(%)	**<0.001**
Married	3711(55.5)	370(37.0)	4081(53.1)	
Un-(married/known)	2977(44.5)	630(63.0)	3607(46.9)	

[a]Pearson chi2 comparing those who survived to those who died

Table 4.10 discusses the outcomes depending on where the patient was born and where they lived at the time of being attended to. Majority (43.9%) of cervical cancer patients were born in three provinces (namely, Lusaka, Copperbelt and Eastern provinces). The majority (57.9%) also lived in these three provinces during the period under study. There was also a statistical difference between survivors and those who died living in Central, Copperbelt, Eastern, Luapula and Lusaka, and between survivors and those who died born in Copperbelt, Eastern, Luapula and Lusaka.

Table 4.10 Geographic characteristics and descriptive statistics of cervical cancer patients in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (n = 7,374)

Cancer	**Cervical Cancer**			
Status	**Alive**	**Dead**	**Total (Alive+Dead)**	**P value[a]**
Provincial Home Address	n(%)	n(%)	n(%)	
Central	690(10.3)	94(9.4)	784(10.2)	**0.109**
Copperbelt	893(13.4)	110(11.0)	1003(13.0)	**0.192**
Eastern	893(13.4)	143(14.3)	1036(13.5)	**<0.001**
Luapula	295(4.4)	50(5.0)	345(4.5)	**<0.001**
Lusaka	2058(30.8)	359(35.9)	2417(31.4)	**<0.001**
Muchinga	121(1.8)	20(2.0)	141(1.8)	0.344
North-western	251(3.8)	43(4.3)	294(3.8)	0.479
Northern	454(6.8)	48(4.8)	502(6.5)	0.436
Southern	638(9.5)	75(7.5)	713(9.3)	0.053
Western	340(5.1)	54(5.4)	394(5.1)	0.239
Unknown	55(0.8)	4(0.4)	59(0.8)	0.518
Province of Birth				
Central	419(6.3)	84(8.4)	503(6.5)	0.463
Copperbelt	633(9.5)	64(6.4)	697(9.1)	**0.173**
Eastern	940(14.1)	165(16.5)	1105(14.4)	**<0.001**
Luapula	250(3.7)	61(6.1)	311(4.0)	**<0.001**
Lusaka	1389(20.8)	182(18.2)	1571(20.4)	**<0.001**
Muchinga	91(1.4)	27(2.7)	118(1.5)	0.610
North-western	187(2.8)	38(3.8)	225(2.9)	0.262
Northern	452(6.8)	78(7.8)	530(6.9)	0.743
Southern	622(9.3)	73(7.3)	695(9.0)	**0.121**
Western	278(4.2)	61(6.1)	339(4.4)	0.382
Unknown	1427(21.3)	167(16.7)	1594(20.7)	**0.172**

[a]Pearson chi2 comparing those who survived to those who died

The median age for cervical cancer was 47 (IQR: 38-58) years old with an age range of 18 to 99 years. Table 4.11 shows the age-adjusted cervical cancer incidence rate nationwide. This was 190.3 per 100,000 population, derived as shown through WHO standard population distributions.

Table 4.11 Age-adjusted cervical cancer rates in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (No. = 7,374)

Age	**Count**	**Population**	**Crude Rate (per 100,000)**	**WHO Standard Population Distribution**	**Age-Adjusted Rate (per 100,000)**
Min-29	431	5,210,185	8.27	0.5838	
30-34	694	432,217	160.57	0.0715	
35-39	968	336,172	287.95	0.0659	
40-44	1072	233,825	458.46	0.0604	
45-49	922	188,484	489.17	0.0537	
50-54	885	152,001	582.23	0.0455	
55-59	660	101,775	648.49	0.0372	
60-64	521	89,262	583.68	0.0296	
65-69	432	68,615	629.60	0.0221	
70-74	305	50,288	606.51	0.0152	
75-79	157	32,283	486.32	0.0091	
80-Max	327	36,816	888.20	0.0063	
All Ages	7047	6,895,107	102.20		**190.29**

Table 4.12 discusses the crude cervical cancer mortality rates (Per 100,000 population) by birth province by age Highest CFRs were in Lusaka (35.9%) and Eastern (14.3%) and lowest (2%) in Muchinga provinces. The highest CDRs, per 100,000 people, were in Lusaka (726), Eastern (674), Northern (410), Southern (407), Northwestern (390) and Western (384) provinces and lowest in Muchinga (248) and Copperbelt (210) provinces.

Table 4.12 Crude cervical cancer mortality rates (Per 100,000 population) by birth province by age in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (n = 7,374)

Zambia	**Central**	**Copperbelt**	**Eastern**	**Luapula**	**Lusaka**	**Muchinga**	**±N.Western**	**Northern**	**Southern**	**Western**
Prov. Rate	**534.23**	**210.00**	**673.50**	**282.17**	**726.17**	**247.77**	**389.54**	**410.32**	**407.47**	**383.64**
Min-29	0.19	0.12	0.65	0.52	0.34	0.00	0.00	0.91	0.16	0.00
30-34	12.48	8.83	16.77	6.55	13.07	9.50	9.26	22.02	5.84	28.19
35-39	34.49	17.13	25.70	20.29	27.30	17.34	5.88	26.33	12.78	13.48
40-44	35.67	26.99	54.17	32.97	47.13	0.00	15.87	57.70	28.96	36.57
45-49	27.24	29.08	56.87	13.49	40.92	19.37	30.04	55.66	32.21	42.99
50-54	72.39	38.63	97.56	24.66	66.94	24.65	117.63	23.81	40.81	56.53
55-59	49.54	5.73	102.67	35.22	96.46	56.17	0.00	70.11	74.14	57.82
60-64	55.80	45.79	38.37	26.09	66.08	36.74	0.00	62.92	21.13	36.02
65-69	58.24	21.83	95.10	70.95	140.53	22.58	25.46	46.15	75.03	30.94
70-74	41.14	15.87	71.80	51.43	81.35	61.41	0.00	44.70	47.52	39.79
75-79	90.25	0.00	37.22	0.00	0.00	0.00	99.40	0.00	47.97	0.00
80+	56.79	0.00	76.63	0.00	146.06	0.00	85.98	0.00	20.91	41.30

(Those with Unknown birth province were excluded)

±N.Western refers to North western province

Table 4.13 Cervical cancer treatment outcome by birth province in the ZNCR between January 1st 2008 and December 31st 2014 (n = 7,274)

	Surgery			**Radiotherapy**			**Chemotherapy**			**Hormonal**			**Palliative Therapy**			**On ARVs**			Other Therapy		
	A*	D**	Total(%)	A*	D**	Total(%)	A*	D**	Total(%)	A*	D**	Total(%)	A*	D**	Total(%)	A*	D**	Total(%)	A*	D**	Total
Central	51	24	75(5.82)	344	57	401(8.10)	365	77	442(7.62)	0	1	1(8.33)	6	0	6(5.17)	111	16	127(8.98)	141	19	160(4.70)
Copperbelt	113	15	128(9.93)	468	48	516(10.43)	529	55	584(10.07)	2	0	2(16.67)	24	2	26(22.41)	204	25	229(16.18)	330	24	354(10.41)
Eastern	137	63	200(15.52)	744	98	842(17.01)	840	150	990(17.08)	1	0	1(8.33)	13	2	15(6.03)	173	24	197(13.92)	313	31	344(10.11)
Luapula	35	29	64(4.97)	185	28	213(4.3)	207	54	261(4.50)	0	0	0(0.00)	6	1	7(11.21)	46	4	50(3.53)	112	16	128(3.76)
Lusaka	147	66	213(16.52)	1215	103	1318(26.63)	1311	163	1474(25.43)	2	0	2(16.67)	12	1	13(0.86)	305	41	346(24.45)	293	36	329(9.67)
Muchinga	10	7	17(1.32)	71	16	87(1.76)	76	22	98(1.69)	0	0	0(0.00)	1	0	1(4.31)	13	3	16(1.13)	42	6	48(1.41)
N.Western	22	14	36(2.79)	108	21	129(2.61)	168	33	201(3.47)	0	0	0(0.00)	5	0	5(15.52)	21	2	23(1.63)	95	9	104(3.06)
Northern	67	20	87(6.75)	328	45	373(7.54)	376	64	440(7.59)	0	0	0(0.00)	17	1	18(15.52)	90	13	103(7.28)	201	20	221(6.50)
Southern	88	34	122(9.46)	489	39	528(10.67)	546	64	610(10.52)	1	0	1(8.33)	14	1	15(12.93)	129	14	143(10.11)	228	23	251(7.38)
Western	50	17	67(5.20)	215	36	251(5.07)	239	49	288(4.97)	1	0	1(8.33)	3	0	3(2.59)	56	14	70(4.95)	126	20	146(4.29)
Unknown	239	41	280(21.72)	280	11	291(5.88)	371	38	409(7.06)	3	1	4(33.33)	7	0	7(6.03)	102	9	111(7.84)	1176	141	1317(38.71)
Zambia	959	330	1289	4447	502	4949	5028	769	5797	10	2	12	108	8	116	1250	165	1415	3057	345	3402
Zambia %	74%	26%		90%	10%		87%	13%		83%	17%		93%	7%		88%	12%		90%	10%	

*A = Alive, **D = Dead; All percentages are column percentages

As shown in table 4.13, the commonest primary treatment modes reflected were surgery, radiotherapy and chemotherapy. All of hormonal, palliative therapy was given as adjuvant therapy. Similarly, Antiretroviral therapy (ARVs) and other therapies were given as adjuvant to the primary treatment. Most radiotherapy and chemotherapy interventions occurred in Lusaka (26.63% and 25.43%, respectively) followed by Eastern province (17.01% and 17.08%, respectively), Southern province (10.67% and 10.52%, respectively) and Copperbelt province (10.43% and 10.07%, respectively). Although surgery was not the main treatment intervention over the period in Zambia, Lusaka (16.52%), Eastern (15.52%), Copperbelt (9.93%) and Southern (9.43%) provinces were the main providers of surgical treatment of cervical cancer.

In absolute terms, the number of cervical cancer patients had increased from 772 in 2008 to 1,042 in 2014, with Lusaka, Copperbelt, Eastern, Southern, Northern and Central provinces the major contributors of up to 66.61% of the burden. The rate of diagnosis of new cervical cancer patients showed an upward trend for all provinces except for Lusaka and to smaller extent Eastern provinces whose rates have been on the downward trend between the period under review (Figure 4.2).

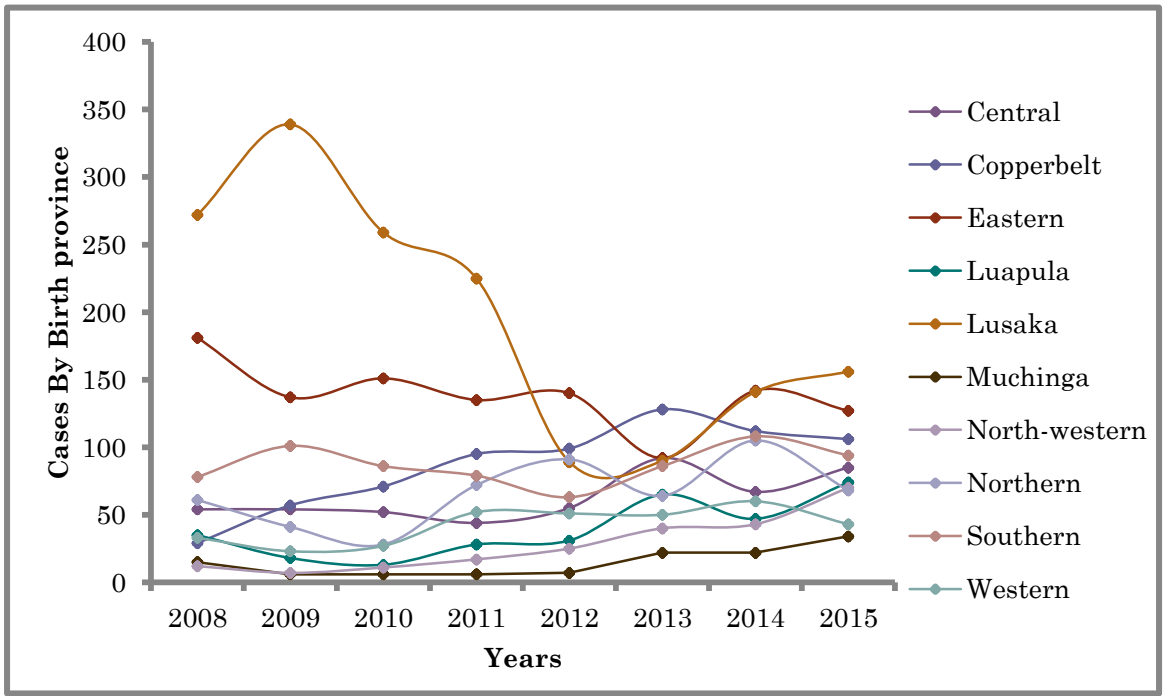

Figure 4. 2 Trends of cervical cancer diagnosis by birth province in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (n = 7,374)

4.5 Factors Affecting Cervical Cancer Survival

In an effort to determine any association between treatment interventions, HIV status and marital status, and the main outcome variable (survival over the period under study), we used the Fisher's exact test. At $p<0.001$ we determined that there was an association between survival of those with cervical cancer and the aforementioned factors. There was sufficient evidence of a statistical difference in the mean age at diagnosis between those who died of the disease and those who survived in the period under study through the Two-sample Wilcoxon Rank-Sum (Mann-Whitney) Test, $p < 0.001$

Nearly all variables were significant at univariable analysis at 0.2 alpha level. Only variables that caused at least a 10% change in the estimated effect with addition of such variables to the logistic regression model (confounding) and/or were statistically significant at univariable analysis were included in the final model. Chemotherapy, Hormonal therapy and all variables that perfectly predicted the outcome were dropped from the model. Controlling for marital status, HIV status and age, Radiotherapy increased the odds of survival by 69%. And controlling for marital status, treatment by radiotherapy and age, being HIV positive reduced the odds of survival by 58%. Controlling for age, HIV status and treatment by radiotherapy, being married increased the odds of survival by 31%. These findings are summarised in Table 4.14.

Table 4.14 Unadjusted and adjusted analysis of independent variables to cervical cancer survival in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (n = 6,688)

Factors		**Cancer Survivors (n= 6,688)**	**Unadjusted**	**Adjusted**	
		n(%)	**Odds ratios**	**Odds ratios**	**Confidence Interval (95%)**
Age (years)	Min-29	412(6.2)	Ref.	Ref.	Ref.
	30-34	627(9.4)	**0.43**	0.51	0.24 - 1.08
	35-39	881(13.2)	**0.46**	**0.40**	0.20 - 0.82
	40-44	972(14.5)	**0.42**	0.49	0.24 - 1.03
	45-49	837(12.5)	**0.44**	**0.41**	0.20 - 0.86
	50-54	792(11.8)	**0.37**	**0.34**	0.16 - 0.71
	55-59	591(8.8)	**0.34**	**0.33**	0.15 - 0.71
	60-64	477(7.1)	**0.32**	0.59	0.25 - 1.41
	65-69	378(5.7)	**0.17**	**0.40**	0 .17 - 0.93
	70-74	274(4.1)	**0.12**	**0.33**	0.14 - 0.81
	75-79	146(2.2)	**0.12**	0.36	0.12 - 1.06
	80-84	95(1.4)	**0.09**	**0.30**	0.10 - 0.97
	85-89	14(0.2)	**0.03**	**0.10**	0.02 - 0.45
	90-Max	192(2.9)	**0.22**	2.43	0.30 -19.66
Treatment	Radiotherapy	5028	**1.09**	**1.69**	**1.01 – 2.84**
HIV Status	Negative	5368	Ref.	Ref.	Ref.
	Positive	1320	**0.56**	**0.42**	**0.33 – 0.54**
Marital	Un-(married/known)	2977	Ref.	Ref.	Ref.
Status	Married	3711	**2.18**	**1.31**	**1.01 - 1.69**
	Unknown	1427(21.3)	**1.45**	0.91	0.14 - 6.08

4.6 Prostate Cancer Prevalence

Table 4.15 shows a record of 1,803 prostate cancer patients notified to the ZNCR during the period under study of which 314 had died within the same period, giving a 17.4% case fatality. Most prostate cancer patients (61.5%) were aged between 60-84years, with 54.0% of them married. The median age for prostate cancer was 71.5 (IQR: 65-78) years old with an age range of 32 to 99 years.

Of the 83 HIV positive prostate cancer patients 5 were on the highly active antiretroviral therapy (HAART). The commonest treatments modes were chemotherapy (34.1%), surgery (29.6%) and other non-surgical, non-chemotherapy, non-therapy, non-hormonal and non-palliative methods (21.9%).

Table 4.15 further shows that there was statistically a significant difference between the numbers of those who died and those who survived in the ages older than 59 (except for 85-89). And in terms of treatment here was a statistically significant difference between the numbers of those who died and those who survived within those that received each of surgery, chemotherapy, palliative care and other treatments (non-radiotherapy, non-ART).

Table 4.15 Demographic characteristics and descriptive statistics of prostate cancer patients in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (n = 1,803)

Cancer	**Prostate Cancer**			
Status	**Alive**	**Dead**	**Total (Alive+Dead)**	**P value[a]**
No. of patients	1489	314	1803	
Age (years)	n(%)	n(%)	n(%)	0.368
Min-29	0(0)	0(0)	0(0)	-
30-34	2(0.1)	0(0)	2(0.1)	0.645
35-39	1(0.1)	1(0.3)	2(0.1)	**0.046**
40-44	9(0.6)	1(0.3)	10(0.6)	0.986
45-49	29(1.9)	3(1.0)	32(1.8)	0.925
50-54	68(4.6)	10(3.2)	78(4.3)	0.495
55-59	103(6.9)	15(4.8)	118(6.5)	0.592
60-64	165(11.1)	30(9.6)	195(10.8)	**0.001**
65-69	265(17.8)	51(16.2)	316(17.5)	**0.057**
70-74	323(21.7)	75(23)	398(22.1)	<**0.001**
75-79	209(14.0)	46(14.6)	255(14.1)	**0.003**
80-84	171(11.5)	38(12.1)	209(11.6)	**0.051**
85-89	71(4.8)	22(7.0)	93(5.2)	0.971
90-Max	73(4.9)	22(7)	95(5.3)	<**0.001**
Median (IQR)	71 (64-78)	72 (66-80)	71.5 (65-78)	
Range	32-99	39-99	32-99	
Surgery	877(27.4)	254(41.3)	1131(29.6)	<**0.001**
Chemotherapy	1060(33.1)	242(39.3)	1302(34.1)	**0.028**
Radiotherapy	221(6.9)	14(2.3)	235(6.2)	0.919
Palliative Care	11(0.3)	2(0.3)	13(0.3)	**0.094**
Hormonal Therapy	253(7.9)	14(2.3)	267(7.0)	-
Other Treatment	779(24.3)	89(14.5)	868(22.7)	**0.003**
HIV Status Positive	94(91.3)	9(8.7)	103	0.723
On ART	78(94.0)	5(6.0)	83	0.372
Married	868(58.3)	105(33.4)	973(54.0)	
Un-(married/known)	621(41.7)	209(66.6)	830(46.0)	

[a]Pearson chi2 comparing those who survived to those who died

Table 4.16 show that most (61.2%) of the prostate cancer patients lived in Central, Copperbelt, Eastern, Lusaka and Southern provinces. Also, most of these patients (45.1%) were born in Lusaka, Eastern, Northern and Southern provinces with an additional 25% of them having been born in unidentified provinces.

Nearly 27% of patient records had no information on place of birth. Highest CFRs were in Lusaka (35.9%) and Eastern (14.3%) and lowest (2%) in Muchinga provinces.

Table 4.16 Geographic characteristics and descriptive statistics of prostate cancer patients in the Zambia National Cancer Registry between January 1 2008 and December 31st 2014 (n = 1,803)

Cancer	**Prostate Cancer**			
Status	**Alive**	**Dead**	**Total (Alive+Dead)**	**P-value**
Provincial Home Address	n(%)	n(%)	n(%)	
Central	146(9.8)	27(8.6)	173(9.6)	0.004
Copperbelt	143(9.6)	18(5.7)	161(8.9)	0.238
Eastern	121(8.1)	41(13.1)	162(9.0)	<0.001
Luapula	55(3.7)	23(7.3)	78(4.3)	<0.001
Lusaka	473(31.8)	135(43.0)	608(33.7)	<0.001
Muchinga	30(2.0)	7(2.2)	37(2.1)	0.101
North-western	116(7.8)	16(5.1)	132(7.3)	0.479
Northern	124(8.3)	10(3.2)	134(7.4)	0.709
Southern	134(9.0)	21(6.7)	155(8.6)	0.028
Western	126(8.5)	15(4.8)	141(7.8)	0.730
Unknown	21(1.4)	1(0.3)	22(1.2)	0.677
Province of Birth				
Central	95(6.4)	22(7.0)	117(6.5)	0.067
Copperbelt	92(6.2)	9(2.9)	101(5.6)	0.499
Eastern	133(8.9)	56(17.8)	189(10.5)	<0.001
Luapula	44(3.0)	30(9.6)	74(4.1)	<0.001
Lusaka	233(15.6)	62(19.7)	295(16.4)	<0.001
Muchinga	23(1.5)	10(3.2)	33(1.8)	0.022
North-western	93(6.2)	16(5.1)	109(6.0)	0.331
Northern	147(9.9)	21(6.7)	168(9.3)	0.639
Southern	141(9.5)	20(6.4)	161(8.9)	0.075
Western	88(5.9)	17(5.4)	105(5.8)	0.624
Unknown	400(26.9)	51(16.2)	451(25.0)	0.062

[a]Pearson chi2 comparing those who survived to those who died

Using the WHO standard population distribution, Table 4.17 demonstrates calculation of the prostate cancer crude death rate for Zambia during the period under study. The population estimate for the year midpoint of the period under study (2011) was used here. Table 4.17 shows that the age-adjusted prostate cancer incidence rate nationwide was 56 per 100,000 population.

Table 4.17 Age-adjusted prostate cancer rates in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (n = 1,803)

Age	Count	Population	Crude Rate (per 100,000)	WHO Standard Population Distribution	Age-Adjusted Rate (per 100,000)
Min-29	0	5,045,520	0	0.5838	
30-34	2	429,574	0.47	0.0715	
35-39	2	364,228	0.55	0.0659	
40-44	10	262,488	3.81	0.0604	
45-49	32	193,633	16.53	0.0537	
50-54	78	144,016	54.16	0.0455	
55-59	118	100,074	117.91	0.0372	
60-64	195	78,702	247.77	0.0296	
65-69	316	58,245	542.54	0.0221	
70-74	398	43,674	911.30	0.0152	
75-79	255	31,883	799.80	0.0091	
80-Max	397	34,762	1142.05	0.0063	
All Ages	1803	6,786,799	26.57		**55.69**

From Table 4.18, it is clear that the highest CDRs, per 100,000 people, were in Lusaka (1,384), Eastern (901), Luapula (855), Southern (407) and Northwestern (628) and lowest in Copperbelt (126) provinces. As variations exist within provinces, it was essential to show these differences particularly by age. Central, Copperbelt, Eastern, Luapula, Lusaka and Western provinces start reporting prostate cancer patients as early as the beginning of the sixth decade of life (50-60 years) whereas the rest start in the next decade.

Table 4.18 Crude prostate cancer mortality rates (Per 100,000 population) by birth province by age in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (n = 1,803)

Zambia	**Central**	**C/belt**	**Eastern**	**Luapula**	**Lusaka**	**Muchinga**	**N.W**	**Northern**	**Southern**	**Western**
Prov. Rate	**474.44**	**125.57**	**900.96**	**854.56**	**1,384.28**	**310.44**	**628.03**	**453.77**	**429.15**	**385.71**
Min-29	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
30-34	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
35-39	0.00	0.00	0.00	0.00	0.00	5.62	0.00	0.00	0.00	0.00
40-44	0.00	0.00	0.00	0.00	1.86	0.00	0.00	0.00	0.00	0.00
45-49	0.00	0.00	0.00	0.00	2.90	0.00	9.94	0.00	0.00	0.00
50-54	6.98	3.97	5.93	8.22	4.35	0.00	0.00	15.56	0.00	10.63
55-59	0.00	5.21	17.06	24.71	12.91	38.45	0.00	0.00	10.14	30.12
60-64	35.92	0.00	31.05	75.36	62.81	0.00	49.88	29.49	40.40	0.00
65-69	47.82	20.37	160.30	60.34	125.65	28.09	64.72	72.61	69.32	43.47
70-74	41.33	45.66	273.13	191.10	422.13	67.48	117.28	91.64	114.92	149.85
75-79	84.72	0.00	201.30	194.02	219.06	0.00	191.20	118.76	90.36	61.98
80+	257.67	50.37	212.19	300.82	532.62	170.79	195.01	125.71	104.00	89.67

(Those with Unknown birth province were excluded; C/belt = Copperbelt province and N.W = North Western Province)

Table 4.19 Prostate cancer treatment outcome by birth province in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (n = 1,803)

	Surgery			**Radiotherapy**			**Chemotherapy**			**Palliative Therapy**			**On ARVs**			**Other Therapy**		
	Alive	Dead	Total	Alive	Dead	Total	Alive	Dead	Total	Alive	Dead	Total	Alive	Dead	Total	Alive	Dead	Total
Central	68	20	88(7.78)	18	2	20(8.51)	80	18	98	2	0	2(15.38)	6	0	6(7.23)	0	1	1(1.12)
Copperbelt	56	7	63(5.57)	20	1	21(8.94)	68	6	74	1	0	1(7.69)	5	0	5(6.02)	0	3	3(3.37)
Eastern	106	54	160(14.15)	21	3	24(10.21)	118	50	168	3	1	4(30.77)	8	2	10(12.05)	0	8	8(8.99)
Luapula	31	27	58(5.13)	6	2	8(3.4)	33	26	59	0	1	1(7.69)	2	0	2(2.41)	0	7	7(7.87)
Lusaka	194	57	251(22.19)	34	2	36(15.32)	215	58	273	0	0	0(0.00)	29	0	29(34.94)	0	9	9(10.11)
Muchinga	10	7	17(1.5)	4	0	4(1.7)	19	7	26	0	0	0(0.00)	0	0	0(0.00)	0	3	3(3.37)
North-western	39	14	53(4.69)	14	1	15(6.38)	83	13	96	0	0	0(0.00)	2	0	2(2.41)	0	4	4(4.49)
Northern	78	18	96(8.49)	26	2	28(11.91)	112	18	130	2	0	2(15.38)	9	0	9(10.84)	0	5	5(5.62)
Southern	80	17	97(8.58)	34	0	34(14.47)	118	17	135	0	0	0(0.00)	7	1	8(9.64)	0	3	3(3.37)
Western	56	15	71(6.28)	18	1	19(8.09)	73	12	85	2	0	2(15.38)	5	1	6(7.23)	0	7	7(7.87)
Unknown	159	18	177(15.65)	26	0	26(11.06)	141	17	158	1	0	1(7.69)	5	1	6(7.23)	0	39	39(43.82)
Totals	877	254	**1131**	221	14	**235**	1060	242	**1302**	11	2	**13**	78	5	**83**	0	89	**89**

NB: No patient was recorded as having received hormonal therapy for prostate cancer

Of the treatment modes shown in Table 4.19, the commonest primary treatment modes were surgery, radiotherapy and chemotherapy. All of palliative therapy was given as adjuvant therapy. Similarly, Antiretroviral therapy (ARVs) and other therapies were given as adjuvant to the primary treatment. Most surgery and chemotherapy interventions occurred in Lusaka (22.19% and 20.97%, respectively) followed by Eastern province (14.15% and 12.90%, respectively).

In absolute terms, the number of prostate cancer patients had increased from 102 in 2008 to 301 in 2014, with Lusaka, Copperbelt, Eastern, Southern, Northern provinces the major contributors of up to 61.2% of the burden. Figure 4.3 shows that the rate of diagnosis of new prostate cancer patients showed an upward trend countrywide between the period under review. While the rest of the country's trends are steadier, there was a sharp drop in notifications between 2012 and 2013 for Lusaka provinces and sharp rise for Northern province in 2014.

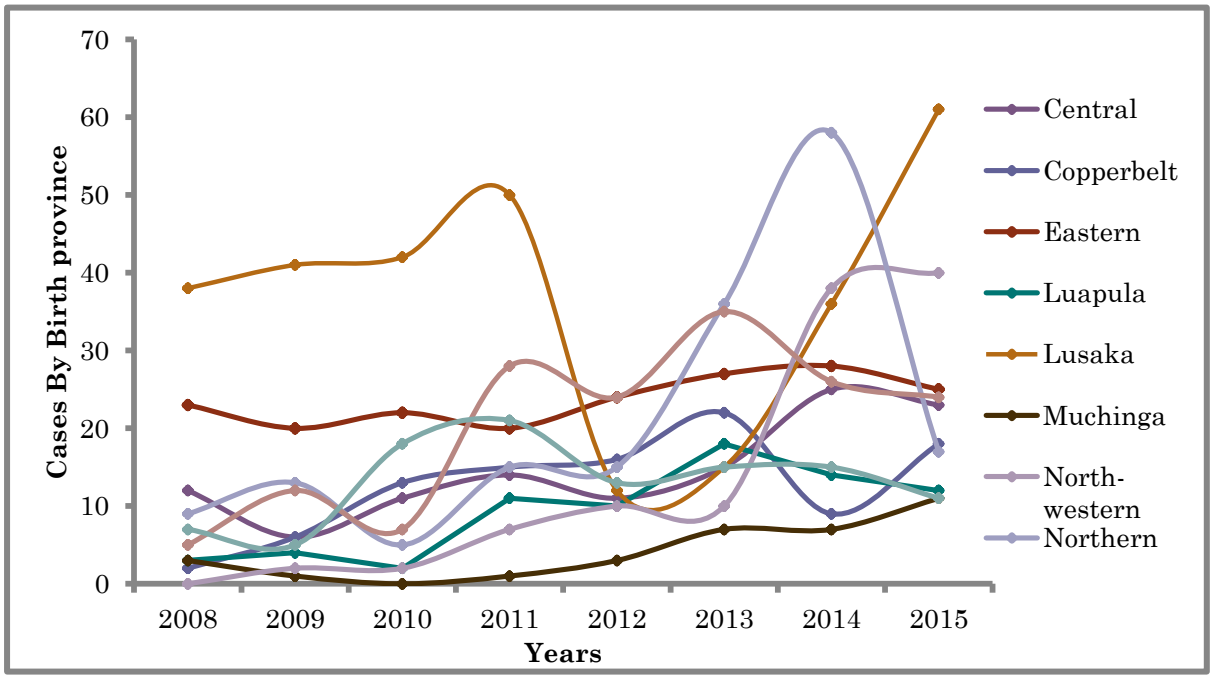

Figure 4.3 Trends of prostate cancer diagnosis by birth province in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2014 (No. = 1,803)

4.7 Factors Affecting Prostate Cancer Survival

This study used a Fisher's exact test (p = 0.197) to determine whether there was an association between the treatment interventions and the main outcome variable (death or survival over the period under study) in those with prostate cancer. The study also showed that there was a statistically significant difference in the mean age at diagnosis between those who died of the disease and those who survived in the period under through the Two-sample Wilcoxon Rank-Sum (Mann-Whitney) Test, p = 0.0018.

At univariable analysis, being aged older that 80, undergoing surgery and being born in Eastern and Luapula provinces (relative to being born in Central province) reduced survival odds from prostate cancer while being born on the Copperbelt increased survival odds by 2.3 times.

Controlling for age, surgery, chemotherapy, radiotherapy and province of birth, being married increased the odds of surviving from prostate cancer 7.5 times. Undergoing chemotherapy also increased survival odds 3.6 times, controlling for age, marital status, surgery, radiotherapy and province of birth but as the confidence interval include a null value and so this could have been due to chance (Table 4.20).

Table 4.20 Unadjusted and adjusted analysis of independent variables to prostate cancer survival in the Zambia National Cancer Registry between January 1st 2008 and December 31st 2015 (n = 1,489)

Factors		Cancer Survivors (n= 1,489)	Unadjusted	Adjusted	
		n(%)	Odds ratio	Odds ratio	Confidence Interval (95%)
Age (years)	Min-29	0(0/~)	N/A	N/A	N/A
	30-59	212(14.2)	Ref.	Ref.	N/A
	60-79	962(64.6)	0.71	0.42	0.05 - 3.65
	80-Max	315(21.2)	**0.54**	1.62	0.11 - 22.55
Treatment	Surgery	877(27.4)	**0.18**	0.28	0.06 - 1.35
	Chemotherapy	1060(33.1)	0.45	3.56	0.68 - 18.72
	Radiotherapy	221(6.9)	1.31	2.51	0.67 - 9.44
Marital Status	Un-(married/known)	621	Ref.	Ref.	N/A
	Married	868	2.82	**7.48**	**2.16 - 25.84**
Province of	Central	95(6.4)	Ref.	Ref.	
Birth	Copperbelt	92(6.2)	**2.32**	2.09	0 .10 - 43.59
	Eastern	133(8.9)	**0.57**	0.94	0.10 - 8.50
	Luapula	44(3.0)	**0.37**	0.33	0.03 - 4.02
	Lusaka	233(15.6)	0.93	0.67	0.08 - 5.80
	Muchinga	23(1.5)	0.58	**0.01**	**0.00 - 0 .84**
	North-western	93(6.2)	1.47	0.81	0.08 - 8.42
	Northern	147(9.9)	1.69	2.76	0.17 - 44.51
	Southern	141(9.5)	1.70	8.43	0.54 - 130.70
	Western	88(5.9)	1.24	1.00	N/A
	Unknown	400(26.9)	1.63	11.75	0.71 - 194.83

Chapter 5: DISCUSSION

The main objective of this research was to determine the factors that affected the outcome of prostate, breast and cervical cancer treatment from the Zambia national cancer registry data from January 1, 2008 to December 31, 2015. The first step in assessing these factors was done through an attempting to demographically and clinically characterise prostate, breast and cervical cancer patients in Zambia. Each cancer has been discussed to some detail.

For the first time, a description of typical breast, cervical and prostate cancer patients has been provided in keeping with the recommendations of the global cancer benchmarking watchdog (Anazawa et al. 2015; International Cancer Benchmarking Partnership 2014).

This study further managed to highlight areas in the cancer registry variables which would need review such as the so many cancer staging types being used for the same cancer.

The study also highlighted the factors (of those collected by the ZNCR) that contribute to outcomes of treatment of each of the cancers, limitations notwithstanding. The study further highlights the need to combine the registry findings, given their contribution towards explaining the outcomes after multivariable analysis, with results obtained from a clinically set similar study.

5.1 Prevalence of Breast, Cervical and Prostate Cancers

Breast cancer appears to be disease mainly for those Zambians in the third to fifth decade of life. Of these, the disease appears to be more prevalent in the Southern, Eastern and midlands parts of the country. The volumes of diagnoses were also higher in these places and increasing. Surgery is often the primary means of treating breast cancer the radiotherapy and/or chemotherapy is used as adjuvant therapy (Nounou et al. 2015). More and effective use of radiotherapy may have to do with potential late presentation but most likely due limited availability of surgical services in provinces and hence patients get referred at a stage where radiotherapy is preferred as it shrinks the tumors.

This practice appeared to be supported by the increased the odds of survival 3.11 times by treating with radiotherapy controlling for place of birth, place of residence, age and ART.

The early presentation of breast cancer patients was consistent with many other studies in the region (Amir et al. 2001; Anyanwu 2008; Fregene and Newman 2005). In the eastern and southern African region, the median age for breast cancer is very similar to the findings in the ZNCR as the case is demonstrated in the Tanzanian Cancer registry (Amir et al. 2000). In the latter, the median age reduced at the peak of the HIV pandemic. This may not be a feature in the Zambia scenario given the high number of HIV positive breast cancer patients on antiretroviral treatment.

5.2 Breast, Cervical and Prostate Cancer Treatment Outcomes

The second objective was to compare treatment outcomes across surgery, radiotherapy, chemotherapy/hormonal therapy and other cancer treatment methods. In the Zambian set-up, it was clear that surgery and chemotherapy were the main means of treatment. Our review did show that most Zambians (75%) got the preferred treatment mode (surgery) with the peak incidence. What this review could not tell however was what type of surgery and if this was timely as most patients in the region present very late. Like many places in the region, radiotherapy does not match up to the surgery and chemotherapy probably due to poor access to radiation facilities in Africa (Vanderpuye et al. 2017).

5.3 Breast and Cervical Cancers' Regional distribution

Typically therefore, a breast cancer from Zambia was born and raised in eastern, southern and midlands parts of Zambia, was married, was HIV negative (if positive was on HAART) and was likely to be treated by surgery and/or chemotherapy. Lusaka and Eastern provinces of Zambia boasted of having the largest numbers of women with cervical cancer by birth and residence and also the highest mortality rates (age-adjusted and absolute) from cervical cancer. The same findings were noted in the only published review of the ZNCR by (Zyaambo et al. 2013).

The finding that the median age for an HIV positive patient with cervical cancer in the ZNCR was 47 (IQR: 38-58) years was different from the finding by (Kapambwe et al. 2016) which put the median age at 35 years for the HIV seropositive, and median age at 40 years for the HIV seronegative.

Similarly, the finding that Zambia's (age-adjusted) 190 cases per 100,000 of the general population cervical cancer rate was nearly four times higher than the reported 50 cases per 100,000 population (Jemal et al. 2012) would need further studying. The differences may require further studies to be understood.

With only one centre providing specialised (radiotherapy and chemotherapy) cancer treatment in Zambia, one would expect surgery to be the leading form of treatment given that everyone of the ten provinces have at least one general hospital where such services would be given. The cervical cancer case fatality (9.3%) and the limited use of surgery as an intervention suggests late presentation and poor access to health services. This would be in agreement with the reports by (Kingham et al. 2013). Lusaka and Eastern provinces offered the highest numbers of the chemotherapy and radiotherapy services, which agreed with the numbers and mortality seen in these provinces.

5.4 HIV and Cervical Cancer

Cervical cancer tended to have a face of HIV and this was why its screening had for a long time been associated with the HIV programme. The prevalence of 20.2% (95% Confidence Level: 19.3-21.2) of the cancer amongst HIV positives was not very far from the 14.9% reported in the Zambia population based impact assessment (ZAMPHIA) of 2015 (Republic of Zambia Ministry of Health et al. 2015). That the ZAMPHIA reported figure is outside the 95% confidence interval for our calculated 20.2% indicates a statistically significant difference between the two. Typically then, a cervical cancer patient in Zambia would most likely be less than 50 years old, if HIV positive then likely on HAART, more likely to have been born and be living in Lusaka and/or Eastern provinces (than any other part of the country), likely married and would more likely be treated with either chemotherapy or radiotherapy as opposed to surgery or hormonal therapy.

Early screening programmes can help address cervical cancer. The screening programme may have to consider populations younger than the ages of high prevalence. For instance, the Zambian screening programme for cervical cancer begins at 25 years of age but nearly 10% of those aged 30 to 34 years would have had full-blown invasive cervical cancer.

5.5 Prostate Cancer a Geriatric Illness

Prostate cancer is unique characteristically compared to breast and cervical cancers. While the country's life expectancy at birth stood at 58 years (WHO 2015b), prostate cancer's incidence peaks after that. This means that the disease should be rare in poor Zambians who normally do not live beyond the life expectancy at birth. This could explain the lower incidence of the disease in the most rural of provinces and also the highest crude death rates as seen in Luapula, Eastern and North Western provinces of Zambia.

As the case may be for all cancers in places where screening programmes were not strong, as the case may be for most rural Zambia, treatment for prostate cancer may be limited by late presentation, advanced disease, and a scarcity of urologists, pathologists, radiotherapy options, and androgen-deprivation therapies (Kingham et al. 2013). Surgery and chemotherapy were the commonest treatment modes, suggesting that potentially late presentation may not be such a big problem.

Typically, a prostate cancer patient in Zambia more likely will be over 60 years old, living anywhere in the country, likely to die much earlier if living further from Lusaka province, mostly likely to live longer if married and less likely to live older than without it.

5.6 Need for Special Breast, Cervical Prostate Cancer Focus

Specific factors peculiar to Lusaka and Eastern provinces ought to be studied to have meaningful lessons obtained from the high cancer incidence rates and treatments in these two provinces. Surgery, chemotherapy and radiotherapy were the commonest

treatment means across all three cancers, and clearly where earlier presentation was evident by age distribution, surgery was more likely to be used.

This review further highlights the significance of maintaining a complete data set in the registry to highlight meaningful inferences. It further adds to the body of evidence on the burden of these three diseases. So far, whether the patient died or survived appeared to be the most reliable and measurable outcome from the ZNCR although incidence and treatment outcome would be possible if dates were better captured in the registry.

Potential confounders and effect modifiers such as disease staging and proximity to the national cancer diseases hospital could not be further assessed due to limited data from the registry. Given that the age distribution differs by province adjusted age rates were used throughout.

It is curious to see such a large drop in incidence of all cancers in 2013 and 2014 especially for Lusaka province across all three diseases. This may not be a true decrease in incidence, but potentially being caused by some artifact in surveillance. The possibility of records from these years being lost or surveillance lapsed was followed up but this could not be verified.

Chapter 6: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusions

Breast and cervical cancers in Zambia mainly affected those younger than 55 years while prostate cancer mainly affected those older than 60 years and increased with age. Age, surgery, marital status and province of birth and residence appear to have a major effect on morbidity and survival. Early screening programmes can help address these cancers. These screening programmes may have to consider populations younger than the ages of high prevalence. This means that the Ministry of Health and partners will need to relook at the age at which screening (where recommended) is done.

The ZNCR provides and opportunity for a rolling study but continued absence of the person-time information makes that difficult. This meant that the paradoxical finding by Fregene and Newman of low incidence of breast cancer in women of sub-Saharan Africa could not be explored. Further, studies in a more clinical setting are required to supplement the epidemiological findings to be derived from the ZNCR.

6.2 Recommendations: Implicit and Explicit Learning

The ZNCR need to consider the following recommendations strongly:

i. Re-evaluate current policy around breast and cervical cancer screening and health promotion programmes in the country
ii. Re-engineer the cancer registry database to ensure relevant dates are captured.
iii. Need to have further research done on treatment outcomes in the clinical trial setting
iv. ZNCR to harmonise the staging for each cancer and avoid different notations of the same
v. The “other” forms of treatment which were listed in the registry ought to be described a bit more granular too

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APPENDICES

Appendix 1: CANCER OUTCOMES DATA COLLECTION TOOL

PATIENT DETAILS

1. Name of patient	2. Date of birth	3. Gender	M	F

4. Nationality	5. Ethnic group	6. Contact No.

7. Permanent Usual Address	8. Occupation	9. HIV status*	+ve	-ve
		If unknown		

*Indicate N/A if unknown

SORCE OF INFORMATION – HOSPITAL OR CLINICAL DETAILS

10. Notification time

First	
Second	
Third	
>Third	

11. Facility where patient seen

12. Date seen

13. Hospital responsible for subsequent follow up and treatment

TUMOUR

14. Date of diagnosis	15. Primary site	16. Histological/Clinical diagnosis

17. Basis of diagnosis	18. Clinical staging	19. Patient's present status

20. Date of last contact/death	21. Cause of death

TREATMENT

22. Surgery		23. Radiotherapy		24. Chemotherapy/hormonal therapy	
Yes		Yes		Yes	
No		No		No	

25. Palliative care		26. Other treatment		Unknown treatment	
Yes		Yes		Yes	
No		No		No	

Appendix 2: ETHICAL APPROVAL

ERES CONVERGE

33 Joseph Mwilwa Road
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I.R.B. No. 00005948
F.W.A. No. 00011697

3rd August, 2017

Ref. No. 2017-Jun-032

The Principal Investigator
Dr. Francis Dien Mwansa
Zambia Field Epidemiology Resident
C/o Ministry of Health Headquarters
LUSAKA.

Dear Dr. Mwansa,

RE: AN ANALYSIS OF FACTORS THAT AFFECT CERVICAL, BREAST AND PROSTRATE CANCER TREATMENT OUTCOMES 6 MONTHS AFTER INITIAL TREATMENT IN ZAMBIA – A RETROSPECTIVE COHORT STUDY.

Reference is made to your resubmission dated 1st August, 2017. The IRB resolved to approve this study and your participation as Principal Investigator for a period of one year.

Review Type	**Ordinary**	Approval No. **2017-Jun-032**
Approval and Expiry Date	Approval Date: 2nd August, 2017	Expiry Date: 1st August, 2018
Protocol Version and Date	Version-Nil	1st August, 2018
Information Sheet, Consent Forms and Dates	• N/A	1st August, 2018
Consent form ID and Date	Version-Nil	1st August, 2018
Recruitment Materials	Nil	1st August, 2018
Other Study Documents	Checklist.	1st August, 2018
Number of participants approved for study	384	1st August, 2018

Specific conditions will apply to this approval. As Principal Investigator it is your responsibility to ensure that the contents of this letter are adhered to. If these are not adhered to, the approval may be suspended. Should the study be suspended, study sponsors and other regulatory authorities will be informed.

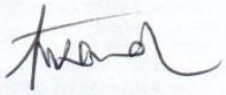
Conditions of Approval

- No participant may be involved in any study procedure prior to the study approval or after the expiration date.
- All unanticipated or Serious Adverse Events (SAEs) must be reported to the IRB within 5 days.
- All protocol modifications must be IRB approved prior to implementation unless they are intended to reduce risk (but must still be reported for approval). Modifications will include any change of investigator/s or site address.
- All protocol deviations must be reported to the IRB within 5 working days.
- All recruitment materials must be approved by the IRB prior to being used.
- Principal investigators are responsible for initiating Continuing Review proceedings. Documents must be received by the IRB at least 30 days before the expiry date. This is for the purpose of facilitating the review process. Any documents received less than 30 days before expiry will be labelled "late submissions" and will incur a penalty.
- Every 6 (six) months a progress report form supplied by ERES IRB must be filled in and submitted to us.
- ERES Converge IRB does not "stamp" approval letters, consent forms or study documents unless requested for in writing. This is because the approval letter clearly indicates the documents approved by the IRB as well as other elements and conditions of approval.

Should you have any questions regarding anything indicated in this letter, please do not hesitate to get in touch with us at the above indicated address.

On behalf of ERES Converge IRB, we would like to wish you all the success as you carry out your study.

Yours faithfully,
ERES CONVERGE IRB



Prof. E. Munalula-Nkandu
BSc (Hons), MSc, MA Bioethics, PgD R/Ethics, PhD
CHAIRPERSON

Appendix 3: ZAMBIA NATIONAL HEALTH RESEARCH AUTHORITY APPROVAL

THE NATIONAL HEALTH RESEARCH AUTHORITY
C/O Ministry of Health
Haile Selaisse Avenue,
Ndeke House
P.O. Box 30205
LUSAKA

MH/101/23/10/1

5 September 2017

Dr. Francis Dien Mwansa

Zambia Field Epidemiology Resident

C/O Ministry of Health Headquarters

LUSAKA

Re: Request for Authority to Conduct Research

The National Health Research Authority is in receipt of your request for authority to conduct research titled **"An analysis of factors that affect cervical, breast, and prostate cancer treatment outcomes 6 months after initial treatment in Zambia."**

I wish to inform you that following submission of your request to the Authority, our review of the same and in view of the ethical clearance, this study has been **approved** on condition that:

1. The relevant Provincial and District Medical Officers where the study is being conducted are fully appraised;
2. Progress updates are provided to NHRA quarterly from the date of commencement of the study;
3. The final study report is cleared by the NHRA before any publication or dissemination within or outside the country;
4. After clearance for publication or dissemination by the NHRA, the final study report is shared with all relevant Provincial and District Directors of Health where the study was being conducted, University leadership, and all key respondents.

Yours sincerely,

Sandra Chilengi-Sakala
For/Director
National Health Research Authority