Estimating the current trend and future incidence of top five cancers in Kampala, Uganda: Kaposi sarcoma, cervical, breast, prostate and Non-Hodgkin's lymphoma

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ABSTRACT

Estimating the current trend and future incidence of top five cancers in Kampala, Uganda: Kaposi sarcoma, cervical, breast, prostate and Non-Hodgkin's lymphoma.

Background. Predicting the future cancer burden is essential for planning and evaluating cancer control and prevention programmes. The aim of this study is to evaluate the current trend and predict cancer incidences of the top five cancers in Uganda: Kaposi sarcoma (KS), cervical, breast, prostate, and Non-Hodgkin's lymphoma (NHL).

Methods. Cancer registry data were obtained from the population-based Kampala cancer registry (KCR), and population data were acquired from the Uganda Bureau of statistics office (UBOS). We analyzed the current trends (2000-2014) and future predictions (2015-2029) of incidence by cancer type. Two prediction methods were applied: first, we fitted the age-period-cohort model using Nordpred R-package. Second, we extrapolated results of the recent trend from joinpoint model to estimate future incidence with the assumption that the coefficient estimates will remain constant in the future. Incidence rates were standardized using the standard world population and expressed as per 100,000 persons. We also assessed if the changes in number of cases are influenced by changes in risk of cancer or changes in population.

Results. The number of breast, cervical, and prostate cancer incidence cases is forecasted to increase by 65%, 22% and 45% respectively from 2010 to 2029. Incidences of KS and NHL are, on the other hand, anticipated to decrease in both genders. The age-standardized-rates (ASRs) are expected to decrease from 30.3 to 6.1 for KS and from 7.3 to 2.4 for NHL. The reduction in the number of cases from 2010 to 2029 is predominantly attributed to the change in cancer risks. These patterns are expected to remain unchanged in the next decade.

Conclusion. Cancer burden of breast, cervical and prostate is expected to increase in the next decade whereas the burden of KS and NHL is decreasing in Uganda. Future research should be directed towards strategies to control the growing burden in these cancers.

Keywords. Current trend, Future Incidence, Kaposi sarcoma, cervical, breast, prostate, Non-Hodgkin's lymphoma, Uganda

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Introduction

1.1 Background

Cancer incidence and mortality are growing expeditiously in the whole world. According to GLOBOCAN 2018, 18.1 million new cases and 9.6 million cancer deaths were estimated to have occurred globally. [1] The cancer burden increased from 14 million incidence and 8.2 million mortality cases that were estimated in 2012.[2] The worldwide cancer burden is predicted to rise to nearly 22 million incidence and 13 million deaths by 2030 with the largest burden on low- and middle-income countries (LMICs) due to rapidly growing populations, aging and adopted lifestyle behaviors that increase cancer risk.[3]

Rapid growth of cancer incidence and high mortality have also been observed in Sub-Saharan Africa (SSA) and hence cancer has emerged as one of the biggest public health burden in this region. Infection related cancers such as Kaposi sarcoma and cervical cancer are the most prevalent cancers in SSA. According to the review and synthetic analysis study that was conducted in 2008, 32.7% of the cancers in SSA are attributed to infections compared to 16.1% of the entire world. [4] The burden of cancer is also increasing because of other risk factors such as; aging and growth of the population as well as increased prevalence of risk factors associated with economic transition, including smoking, obesity, physical inactivity, and reproductive behaviors.[3]

The biggest challenge in SSA is lack of comprehensive data on the burden and trends of cancer incidence to inform policies, strategies and interventions in Sub-Saharan Africa, mostly because of absence of accurate and valid systems of cancer surveillance (notably cancer registries, given the absence of comprehensive vital registration)

1.2 Literature review

1.2.1 Cancer statistics in Uganda

Uganda has a growing burden of cancer just like most countries all over the world. The available literature demonstrates increasing incidence of cancer in both males and females. Cancer incidence trends studies that have been conducted using data from Kampala Cancer Registry (KCR), showed great increase in the number of new cases and Age Standardized Rates (ASRs) of all the cancers.

Among males, ASRs (per 100,000) for all cancer sites increased from 54 in 1960s to 149 in 1990s and then 212 in 2010 with prostate and Kaposi sarcoma as the leading cancers. The ASRs of prostate cancer increased from 25.7 in the 1990s to 58 per 100,000 persons in 2010 with the annual percentage change (APC) of 5.2%. Kaposi sarcoma, however, showed the decreasing trend with the ASRs falling from 39.7 to 29.3 with the APC of -2.1%.

Among females, the overall ASRs increased from 73 in the 1960s to 146 in

1990s and 202 in 2010. Cervical and breast cancers were the most frequent in women with the ASRs rising from 38.1 and 18.0 in the 1990s to 50.2 and 31.2 in 2010 with annual percentage changes of 1.8 and 3.7 respectively. [5,6,7] Overall, according to the recent report published in 2013 using the Kampala cancer registry data recorded from 1991 to 2010, the top five cancers were KS, cervical, breast, NHL and prostate.[7]

1.2.2 Cancer statistics in other sub-Saharan African countries

There is very limited information available regarding the incidence of cancer in sub-Saharan Africa. However some few countries have tried to study the trends in incidence at different points of time.

A trends study on the incidence of cancer that was conducted in the same period (1991 to 2010) in Zimbabwe that is located in the South Eastern part of Africa exhibited similar trends where breast and cervical cancers were the most malignancies among women as they significantly increased by 4.9% and 3.3% annually respectively. Prostate cancer increased by 6.4% annually and by 2004, it had become the most common cancer among men in Zimbabwe like in Uganda. Kaposi sarcoma and Non-Hodgkin's Lymphoma also showed declining trends in the entire period among both males and females.[8]

In a 5 year cross sectional study (2004 to 2008) that was conducted in Nairobi Cancer registry, a population based cancer registry in Kenya which neighbors

Uganda on the right, Prostate cancer was the most common cancer in men (ASRs 40.6 per 100,000) while breast cancer was the most common among women (ASRs 51.7 per 100,000). Cervical cancer was ranked the second most common cancer among women in Nairobi with an ASR of 46.1 per 100,000, somewhat lower than those of other registries in the East African region. The rate of Kaposi sarcoma was relatively low during the period (men 3.6/100,000; women 2.0/100,000) compared to other regions in East Africa.[9]

Another trends study in the incidence of cancer was conducted in the rural Eastern Cape Province; South Africa, 1998–2012. Unlike other SSA countries, cancer of the esophagus was the most commonly diagnosed cancer in males and second in females during the 15 year period, however, it showed decreasing trends among both genders. The ASRs (per 100,000) declined from 32.4 in 1998 to 23.2 in 2012 among males and from 20.6 to 14.5 among females. Prostate cancer was the second among males with ASRs increasing by more than 50% as they rose from 4.1 to 9.9 per 100,000 men. In women, cancer of the cervix uteri was the most common malignancy, with significant increase in incidence during the same period from 22.1 to 29.0. The incidence of breast cancer increased by 61%, although the absolute rate was low (12.2/100,000) in 2012.[10] KS showed a dramatic increase in incidence in both sexes (3.5-fold in men, 11-fold in women), a trend relatively different to what was observed in Kampala, Uganda and Harare, Zimbabwe. [7,8,10]

In Nigeria, located in West Africa, they analyzed cancer incidence data obtained from 2 population based cancer registries, the Ibadan Population Based Cancer Registry (IPBCR) and the Abuja Population Based Cancer Registry (APBCR) covering a 2 year period 2009–2010 (ABCR). The average age of diagnosis for all cancers for Ibadan and Abuja were 51.1 and 49.9 years in men and 49.1 and 45.4 years in women respectively. Breast and cervical cancers were the most common cancers among women and prostate cancer among men in both registries. Breast cancer ASRs (per 100,000) at the IBCR was 52.0 per and 64.6 in ABCR. Cervical cancer ASRs at the IBCR was 36.0 and 30.3 at the ABCR and for prostate cancer, the rates were 17.4 and 25.9 respectively. Both registries recorded very few cases of KS, 40 in Abuja (25 in men and 15 in women) and 19 in Ibadan (12 in men and 7 in women) [11] KS ASRs in men were relatively low (1.34 in Abuja and 2.81 in Ibadan) compared to other SSA countries like in Harare Zimbabwe, the rates were 47.2 per 100,000 and 39.3 per 100,000 in Kampala, Uganda in 2001.[12]

Cesaltina Lorenzoni also examined the trends in Cancer Incidence in Maputo, Mozambique from 1991 to 2008.[13] Like other SSA countries, this study found a rise in cancer in both sexes particularly cancers associated with western lifestyles (prostate and breast) and also infection related cancers (uterine cervix, liver and Kaposi sarcoma). In males, the most common cancers were Prostate, Kaposi sarcoma and the liver of which prostate showed the most dramatic increase over the whole study period (AAPC + 11.3; 95% CI: 9.7-13.0) .

Among females, the most frequent cancers were cervix (AAPC + 4.7%; 95% CI: 3.4 to 6), breast (AAPC + 6.5% 95% CI: 4.3 to 8.7) and KS (AAPC +15.4%; 95% CI: 11.1 to 19.6).[13]

1.2.3 Significance of Prediction of cancer incidence

There is limited literature on the prediction of cancer incidence in Sub-Sahara African countries. Most information of cancer prediction is from developed countries. Prediction estimates of cancer burden have very significant implications for any country, they can help to anticipate future resources needed, evaluate primary prevention strategies and inform research. Future planning is an integral part of cancer control programmes. [14]

Predicting future incident cases can help health planners and policy makers to anticipate the resources needed to screen, diagnose, and treat patients newly diagnosed with cancer while providing ongoing care to cancer survivors. [15]

Cancer predictions can also help the control and prevention team to target and evaluate prevention strategies by forecasting the cancer burden under various exposures to etiologic factors (e.g. diet, physical activity, tobacco use and infections).

Cancer predictions can also alert researchers about the impact of changes in population risk before the full extent of the cancer burden manifests and thus suggest the need for new and enhanced prevention strategies or areas of etiologic research. [16]

Prediction of cancer incidence can also be used as a benchmark in evaluating the impact of some prevention interventions. For example, a comparison between the current incidence rate of cervical cancer and its future rate might be helpful to assess the effectiveness of cervical cancer control and screening program.[17]

1.3 Research Questions

1. What was the incidence and trend in incidence of Kaposi sarcoma, cervical, breast, prostate and Non-Hodgkin's lymphoma cancers in Uganda from 2000 – 2014.
2. Is the current incidence and trend of top five cancers in Uganda similar to other Sub-Saharan African countries?
3. How will the future incidence of Kaposi sarcoma, cervical, breast, prostate and Non-Hodgkin's lymphoma cancers be by 2029 in Uganda?
4. Is the change in cancer incidence due to the changes in the cancer risks or due to demographic changes during both observed and predicted periods?

1.4 Study objectives

1.4.1 Primary objective

The main objective of this study is to estimate the current trend and future incidence of top five cancers in Kampala, Uganda: Kaposi sarcoma, cervical, breast, prostate and Non-Hodgkin's lymphoma.

1.4.2 Secondary objectives

1. To compare the incidence and trend in incidence of top five cancers in Uganda and other sub-Sahara African countries.

2. To assess if the change in cancer incidence is due to the changes in the cancer risks or due to demographic changes during both observed and predicted periods.

2. Methods and Data Source

2.1 Study design

This is a retrospective and cross sectional study

2.2 Data source

Data was obtained from Kampala Cancer Registry (KCR), a population based registry situated in the Department of Pathology, Makerere University College of Health Sciences, Kampala, Uganda.

2.2.1 History of the Kampala cancer registry

KCR is one of the longest standing cancer registries on the African continent established in 1954 with the aim of obtaining information on cancer occurrence in the population of Kyadondo County situated in Kampala. It`s active operations were greatly affected by the political turmoil after 1971 and so it stopped working in 1980. Its activities were later resumed in 1989 and has continued to function since then. This long period of operation of KCR provides a unique opportunity to study temporal trends in cancer patterns in an African setting, the fact that there have been marked social changes in the population in the last 50 years in Africa.

Case finding is conducted by active search for newly diagnosed cases identified from the records of pathology laboratories and hospitals (public and private) in the region and from the Hospice care centers. Cancer diagnoses are coded for topography and morphology according to the International Classification of Diseases for Oncology and entered into a database managed with the CanReg software a computer program designed by the Unit of Descriptive Epidemiology of the international Agency for Research on cancer.[6,7]

2.2.2 Kampala Cancer Registry coverage

Kampala cancer registry covers the area of Kyadondo County which comprises Kampala, the capital city of Uganda and its neighboring urban and semi-urban areas. Kyadondo County lies on the equator at a longitude of approximately 340 East and covers an area of 1,914 square kilometers which is relatively small compared to the whole country that covers about 236,040 square kilometers.[18]

Figure1. Map of the area covered by KCR

Source: http://www.afcrn.org/images/stories/image003-300px.jpg

Map of (left) Uganda, showing the location of KCR and (right) Kampala and Kyadondo County, the area covered by the registry.

2.3 Study Population

2.3.1 Population data

The population data of the observed (2000-2014) and predicted (2015-2029) periods was obtained from the Uganda Bureau of Statistics (UBOS), which provided the estimates by gender and 5-year age groups. Population censuses were conducted in 1991, 2002 and 2014, so the intercensal and predicted population estimates were done using a log-linear function assuming constant rates of change within age-sex groups.

Uganda`s population increased from 17.4 million in 1991 to 24.2 in 2002 and then 34.9 in 2014. Kyadondo county population contributes almost 15% of the country`s population and it has grown by over 10-fold, from 47,000 in 1959 to 774,000 in 1991, 1.21 million in 2002 and over 2.64 million in 2014 mainly due to progressive urbanization.[18]

Kyadondo County population is predicted to increase by more than 50% by 2029 with the predominantly young population of people aged 0-30 years and very few aged 50 years and above as shown in Figure 1.

The population of Kyadondo consists mainly of the Baganda ethnic group (50%) and other ethnic groups from Uganda (30%). The other 20% is made up of immigrants from neighboring countries, and small numbers of Asians (especially from India) and European.

Table 1. Kyadondo county population distribution from 2000 to 2030

	2000		2014		2020		2030	
Sex	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
0-4	114,308	115,792	188,698	183,325	191,404	188,768	225,910	221,974
5-9	94,202	100,407	165,767	167,562	170,814	175,271	206,050	210,232
10-14	86,405	104,854	140,662	168,583	150,784	181,170	181,603	217,727
15-19	86,480	119,061	134,000	183,178	144,931	200,487	173,338	240,378
20-24	96,940	115,926	158,772	218,674	165,063	223,937	196,713	273,301
25-29	85,955	85,430	140,438	158,550	145,754	161,442	173,492	195,966
30-34	62,274	51,234	103,742	95,567	107,794	96,636	128,963	117,139
35-39	38,029	32,820	63,502	62,548	65,314	63,228	77,873	76,975
40-44	25,471	22,259	49,965	46,979	48,897	45,954	59,174	56,394
45-49	15,318	13,310	29,234	27,519	28,139	26,796	33,635	32,696
50-54	10,940	10,566	20,519	21,094	19,548	19,992	23,166	23,966
55-59	5,754	5,452	10,957	11,164	10,583	10,774	12,663	13,074
60-64	5,022	6,281	9,429	11,199	8,989	10,918	10,674	12,912
65-69	2,879	3,297	5,397	6,096	5,149	6,041	6,109	7,253
70-74	2,295	3,619	4,368	6,721	4,080	6,522	4,820	7,772
75+	4,022	5,723	8,185	12,598	7,829	11,890	9,471	14,519
Total	**736,292**	**796031**	**1,233,635**	**1,381,359**	**1,275,071**	**1,429,827**	**1,523,654**	**1,722,277**

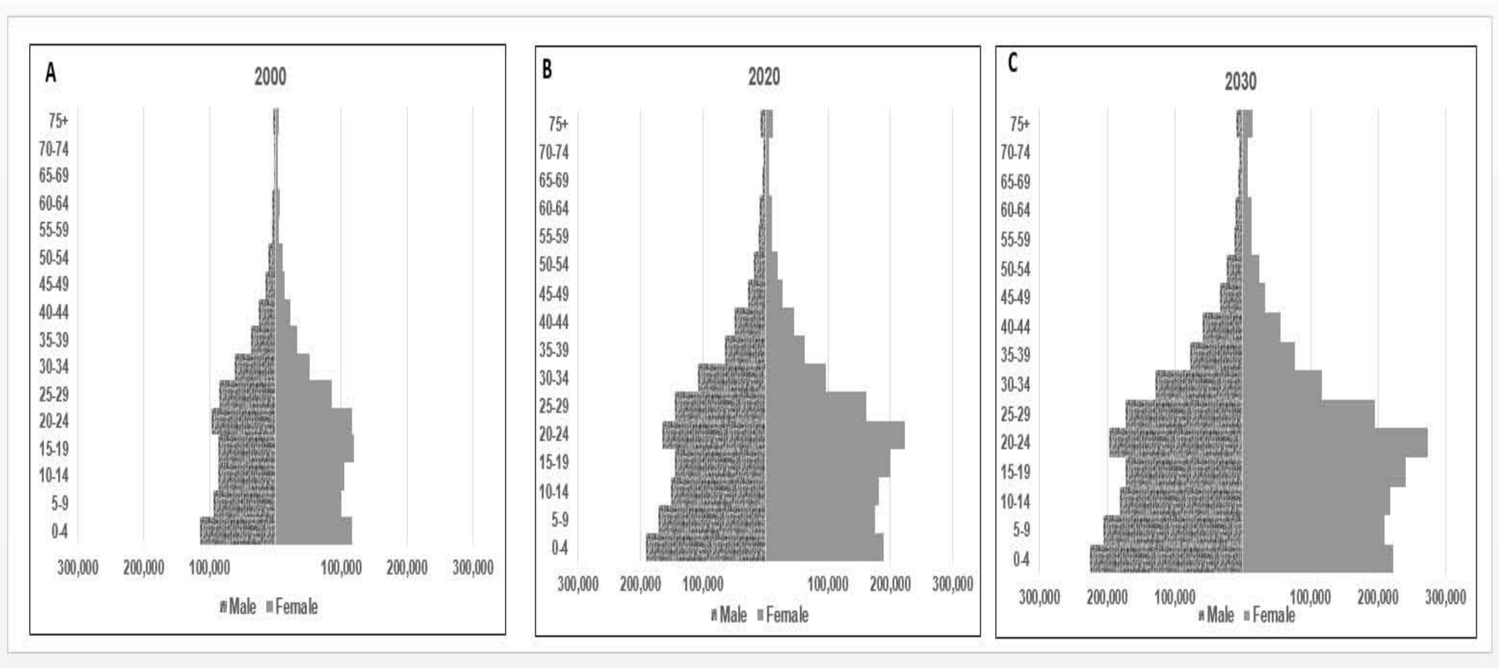


Figure 2: Kyadondo county population pyramids by age groups and gender

2.3.2 Incident cases

Cancer Cases were selected from the KCR database according to the International Classification of diseases for Oncology (ICD-O-3) by World Health Organization. Kaposi sarcoma, cervical, breast, prostate and Non-Hodgkin's lymphoma cancers are defined as C46, C53, C50, C61 and C83 respectively. [19]

We obtained data of the new cases that were registered in the 15 year period, from 2000 to 2014. The important variables that were considered for analysis included; Age, sex, date of diagnosis, ICD-O-3, basis of diagnosis.

A total 11,851 cases were registered but we however excluded 62 cases of males with breast cancer.

Table 2. Summary of cases of top five cancers registered at the Kampala cancer registry, 2000-2014

Year	C50.Breast*	C53.Cervical	C61.Prostate	C46.KS	C83.NHL
2000	76	161	62	291	53
2001	74	125	49	290	59
2002	56	140	53	278	86
2003	86	130	55	283	105
2004	108	152	68	358	107
2005	92	188	64	353	101
2006	107	215	104	310	114
2007	109	215	83	378	115
2008	117	181	77	343	119
2009	108	191	97	395	93
2010	146	198	104	284	93
2011	124	234	107	256	81
2012	164	286	140	305	88
2013	161	227	117	312	83
2014	134	206	93	210	62
Total	**1,662**	**2,849**	**1,273**	**4,646**	**1,359**

Abbreviations: KS-Kaposi sarcoma, NHL-Non Hodgkin's Lymphoma

Breast-Female breast cancer*

2.3.3 World Standard Population

We used the standard world population (WHO 2000-2025) for age-standardization.[19] In our analysis, to be consistent with census population data provided by the National Bureau of Statistics, we categorized the population into sixteen five-year age groups from 0-4 to 75+.

Table 3. WHO World Standard Population Distribution (%), based on world average population between 2000-2025

Age Group	World standard population (%)
0-4	8.86
5-9	8.69
10-14	8.60
15-19	8.47
20-24	8.22
25-29	7.93
30-34	7.61
35-39	7.15
40-44	6.59
45-49	6.04
50-54	5.37
55-59	4.55
60-64	3.72
65-69	2.96
70-74	2.21
75+	3.06
Total	**100.00**

Source: WHO Age Standardized rates, 2001[20]

2.4 Statistical analysis

2.4.1 Descriptive statistics

Descriptive statistics were analyzed using Stata version 14 (StataCorp LP, College Station, TX) software. Demographic characteristics and clinical factors were summarized using frequencies and percentages for categorical variables. Mean and standard deviations (SD) for continuous variables such as age were stratified by cancer types.

2.4.2 Trend analysis for the observed period (2000-2014) using joinpoint

Cancer rates were calculated as cases per 100,000 people and age-adjusted to the standard population using Joinpoint Regression Analysis program provided by the Surveillance Research Program of the US National Cancer Institute. (Version 4.7.0.0, https://surveillance.cancer.gov/joinpoint/).

Annual number of cancer incidence cases and population data were used as inputs into the program. The Joinpoint regression then was performed by the software to identify the "joinpoint", where the linear slope of the incidence trend changes significantly. Crude rates (CRs), age-standardized-rates (ASRs), Annual Percentage Change (APC) and the average annual percentage change (AAPC) in the whole studied period were calculated and presented together with their 95% confidence intervals. The Joinpoint program selected the best fitting piecewise continuous log-linear model.

In this model, the standardized rates are measured on a logarithm scale and change linearly with calendar years over specific intervals where the slopes of the trend remains constant.[21]

Crude rates (CRs) are the number of cases occurring in a specified population, usually expressed as the number of cases per 100,000 population at risk.

Crude rate= $\frac{Count}{Population}$ x 100,000

Age-adjusted rates (ASRs) are the weighted average of crude rates, where the crude rates are calculated for different age groups and the weights are the proportions of persons in the corresponding age groups of a standard population.

ASRs for an age group comprised of the ages x through y is calculated using the following formula.

$$ASR_{x\text{-}y} = \sum_{i=x}^{y} [(\frac{counti}{Popi}) \text{ x } 100{,}000 \text{ x } (\frac{stdpopi}{\sum_{j=x}^{y} stdpopj})]$$

Count: number of cases in the i^{th} age group

Pop_i: relevant population for the same age group

$Stdpop_i$: standard population for the same age group.

Permutation test was performed to determine the minimum number of points, called "joinpoints", necessary to fit the data. The joinpoint regression model then identifies "joinpoints", where the linear slope of the trend changes significantly, and the annual rates of change in each trend segment.[22]

The joinpoint regression model for the observations, (X_1, Y_1) where $X_1 \leq \ldots\ldots\ldots \leq Xn$ without loss of generality, may be written as;

$$\boldsymbol{E}[\boldsymbol{y}/\boldsymbol{x}] = \boldsymbol{\beta_0} + \boldsymbol{\beta_1 x} + \delta_1(\boldsymbol{x} - \boldsymbol{\tau_1})^+ + \cdots + \boldsymbol{\delta_k}(\boldsymbol{x} - \boldsymbol{\tau_k})^+ + \varepsilon$$

Where the $\boldsymbol{\tau_k}$`s are the unknown joinpoints

Annual Percentage change (APC) is one way to characterize trends in cancer rates over time. The output estimates the APC when the input file tab is $\ln(y) = xb$. The cancer rates are assumed to change at a constant percentage of the previous year**.** Rates that change at a constant percentage every year change linearly on a log scale and therefore, the APC for a series of data is estimated with the following regression model; $\log(R_y)$ =b_0+b_1y where $\log(R_y)$ is the natural log of the rate in year y.

The APC from year y to year y+1 =$[\frac{R_{y+1-R_y}}{R_y}]$ x 100

= $\frac{(e^{bo+b1(y+1)} - e^{bo+b1(y)})}{e^{bo+b1(y)}}$ x 100

=$e^{b1} - 1)\ x\ 100$

Average Annual Percent Change (AAPC) is a summary measure of the trend over a pre-specified fixed interval. It allows us to use a single number to describe the average APCs over a period of multiple years. It is valid even if the joinpoint model indicates that there were changes in trends during those years.

AAPC is computed as a weighted average of the APCs from the joinpoint model, with the weights equal to the length of the APC interval.

$AAPC = \{\exp(\frac{\sum w_i b_i}{\sum wi}) - 1\}$ x 100

Where; b_i : Slope coefficient for each segment in the desired rage of years

w_i : length of each segment in the range of years

2.4.3 Prediction of cancer incidence

To predict cancer incidence from 2015 to 2029, we used two methods. First, we applied the Age-period-cohort model using Nordpred R-package. Second, we extrapolated results of the recent trend from a joinpoint model to estimate future incidence until 2029.

Cancer incidence prediction using Nordpred R-package

Nordpred R-package is an age-period-cohort model that was developed by the cancer registry of Norway. This model is one of the most widely used method in long-term estimations of cancer incidence. There are three components, also called three effects in this model: age (time of disease onset), period (year of disease onset) and birth cohort (birth date of case).

In the age-period-cohort model, different link functions were taken into account in order to estimate the future incidence;

In this study, we used: the Poisson regression model with a log-link function and the power-link model. However, in previous publications, for better predictions, Moller et al. recommended using the power-link function instead of the log-link function to level off the exponential growth.[23] Therefore, we presented results obtained from the power-link function as main results and described results from log-link function in some few tables to compare the outcomes.

The Poisson regression with power-link function is expressed as below:

$$\boldsymbol{R_{ap}} = (\boldsymbol{A_a} + \boldsymbol{D} \times \boldsymbol{p} + \boldsymbol{P_p} + \boldsymbol{C_c})^{\boldsymbol{5}}$$

R_{ap}: Incidence rate in the age group (a) and in the period (p).

A_a: Age component of the age group (a)

D: common drift parameter

P_p: Non-linear period component of the period (p)

C_c: Non-linear cohort component of the cohort (c).

The drift parameter in the model is used to determine the average trend. To consider the effects of current data gradually decrease with time, the drift parameters of the first, second and third 5-year periods were reduced by 0%, 25% and 50% respectively. In case the observed rates show significant sharp curvatures, the predictions based on the recent periods is more accurate than the entire periods. If the observed incidence show significantly sharp curvature, data from the last 10 years was used to predict the drift component. Otherwise, the average trend of the entire observation period was used for prediction.

We therefore aggregated data into three 5-year periods (2000-2004 ,2005-2009, 2010-2014) for the observed period and three 5-year periods (2015-2019, 2020-2024 and 2025-2029) for the predicted period. Age was grouped into sixteen 5-year age groups (from 0-4 to 75+). The lowest age limits of the model were determined by ensuring that starting age group has some cases in the observed periods of each cancer site. We started with 20-24 age group for breast and cervical cancers, 34-39 age group for prostate cancer and 0-4 for the other cancer sites. [23,24,25]

Cancer incidence prediction using Joinpoint.

We also applied Joinpoint prediction method in this study. In this approach, cancer incidence prediction through 2029 were calculated by extrapolating results from the trend analysis using joinpoint regression described above. To obtain the predicted rates of period 2015-2029, we extrapolated the intercepts and the slope coefficients from the most recent trend segment identified by the joinpoint model. The underlying assumption of this method is that the slope coefficients will remain constant through 2029.[26]

2.4.4 Determining if the change in incidence is due to the changes in the cancer risk or due to the population change

We calculated the percentage change in cancer incidence counts over the last observed period (2010-2014) and the last prediction period (2025-2029). This percentage change was then apportioned into the contribution from change in cancer risk and the contribution from change in population structure (size and age of population).The percentage change due to the change in risk of each cancer site was computed by subtracting the number of cases that would result from multiplying the current crude rates by the forecasted population estimates from the predicted number of cases. The percentage change due to change in population was calculated by subtracting the observed number of cases from the incidence cases that would result by multiplying the current crude rate and the forecasted population estimates. These values help to determine whether changes in incidence are due to the effect of cancer risk or due to population change.[17,24]

2.5 Ethical consideration

We applied for a study "waiver of exemption" conducted using the public non-identification secondary data provided by the Kampala Cancer registry, Uganda. We obtained the IRB approval to conduct this study using the KCR data from Makerere University, School of Health Sciences Institutional Review Board and Ethics committee (MAK-SHS-IRB).

This study was also conducted after getting approval by the National Cancer Center IRB (NCC2019-0189).

The registry data provided had serial numbers, it therefore cannot be tracked back by use of personal identification number. Therefore personal information is not at risk of being exposed. Since we used secondary data, we did not use consent forms to obtain data from the participants.

3.0 Results

3.1.1 Basic statistics of the five cancers from 2000 to 2014: Breast, cervical, Prostate, Kaposi sarcoma and Non-Hodgkin's Lymphoma

For five cancer types included in this study, a total of 11,789 cases were registered in Kampala cancer registry from 2000 to 2014.

Kaposi sarcoma was the most incident cancer in the 15 years with 4,646 cases of which 55.8 % were males. More than 90% were adults aged 15 years and above. Histology of the primary tumor was the most basis of diagnosis. (Table 3)

Cervical cancer was the second most incident cancer among both sexes and the first among females. A total of 2,849 cases were registered from 2000 to 2014 of which 60.1% were women in their premenopausal stage (<50 years). Histology of primary tumor (54.7%) was the most basis of diagnosis used followed by clinical only and Squamous cell carcinoma was the most incident cervical cancer histological type. (Table 4)

For breast cancer, 1,662 cases were registered in the 15 years and it was the second most incident cancer among women. Of those, 58.7% were in the pre-menopausal stage (<50 years). The number cases increased annually since 2000 but they were slightly lower in 2014. It is probably because some 2014 cases were not yet registered by the time we obtained the data from the registry. Most cases recorded had histology of the primary tumor (52%) as the basis of diagnosis. Infiltrating duct carcinoma and adenocarcinoma, NOS are the most incident breast cancer subtypes and neoplasm malignant as the most common subtype based on the basis of diagnosis as clinical only.

(Table 5)

Table 4. Kaposi sarcoma basic statistics of the cases, Kyadondo County (2000-2014)

Total = 4,646

Variable	Value	Frequency	%
Age (Years)	Mean/SD (34.8/16.6)		
	<15	326	7.02
	>15	4,320	92.98
Gender	Females	2052	44.17
	Males	2594	55.83
Status	Alive	1739	47.71
	Dead	537	14.73
	Unknown	1369	37.56
Basis of diagnosis	Histology of primary	3281	70.6
	Clinical only	1233	26.5
	Death Certificate Only	122	2.6
	Cytology	8	0.2
	Surgery	2	0.1

Table 5. Cervical cancer Basic statistics of the cases, Kyadondo County (2000-2014)

Total = 2,849

Variable	Value	Frequency	%
Age (Years)	Mean/SD (47.9/15.5)		
	Pre-menopausal (<50)	1,711	60.06
	Post-menopausal (≥50)	1,138	39.94
Status	Alive	1,322	46.4
	Dead	343	12.0
	Unknown	1184	41.6
Basis of diagnosis	Histology of primary tumor	1,558	54.69
	Clinical only	1,221	42.86
	Death Certificate Only	46	1.61
	Surgery/Autopsy	20	0.7
	Others	4	0.15
Histological Subtype	Squamous cell carcinoma	1,382	48.51
	Carcinoma	92	3.23
	Adenocarcinoma	80	2.81
	Other	1,295	45.45

Table 6: Female Breast cancer Basic statistics of the cases, Kyadondo County (2000-2014)

Total = 1,662

Variable	Value	Frequency	%
Age (Years)	Mean/SD (47.9/15.6)		
	Pre-menopausal (<50)	975	58.7
	Post-menopausal (≥50)	687	41.3
Status	Alive	778	49.7
	Dead	311	19.3
	Unknown	319	31.0
Basis of diagnosis	Histology of primary tumor	873	52.5
	Clinical only	693	41.7
	Cytology	54	3.2
	Death Certificate Only	37	2.2
	Surgery/Autopsy	4	0.2
	Histology of metastases	1	0.1
Histological subtype	Neoplasm, malignant	776	46.7
	Infiltrating duct carcinoma	381	22.9
	Adenocarcinoma, NOS	248	14.9
	Others	257	15.5

Prostate cancer was the second most incident cancer among males after KS with 1273 cases registered in the 15 year period. Only 3% of these cases were observed among men aged less than 50 years meaning it mostly affects elderly men aged 50 years and above. The average age was 71 years. Clinical only was the most used basis of diagnosis (51.5%). (Table 6)

NHL was the fifth registered cancer with 1359 cases. Unlike other four cancers, many cases were observed in children aged 15 years and below (41.1%) and the average age was 26.7. More cases were among males that contributed about 55.6%. The number of cases tremendously increased from 2003 to 2008 and later gradually reduced.

Table 7. Prostate cancer basic statistics of the cases, Kyadondo County (2000-2014)

Total=1,273

Variable	Value	Frequency	%
Age (Years)	Mean/SD (70.5/11.6)		
	<50	41	3.2
	≥ 50	1,232	96.8
Status	Alive	505	48.9
	Dead	289	28.0
	Unknown	239	23.1
Basis of diagnosis	Clinical only	656	51.5
	Histology of primary history	587	46.1
	Death Certificate only	21	1.7
	Other	9	0.7

Table 8. NHL Basic statistics of the cases, Kyadondo County (2000-2014)

Total =1,359

Variable	Value	Frequency	%
Age (Years)	Mean/SD (26.7/21.1)		
	<15	558	41.1
	≥15	801	58.9
Gender	Females	604	44.4
	Males	755	55.6
Status	Alive	442	40.0
	Dead	296	26.8
	Unknown	368	33.3
Basis of diagnosis	Histology of primary tumor	755	55.6
	clinical	490	36.1
	DCO	50	3.7
	cytology	43	3.2
	laboratory	11	0.8
	Other	10	0.7

3.1.2 Current trends of cancer incidence (2000-2014)

Observed Crude rates

Of the five cancers, only prostate and breast cancers showed increasing trends. Breast cancer significantly increased from 8.9 to 11.7 (APC=1.9, 95% CI, 0.2 to 3.7), Prostate cancer from 8.4 to 9.3. Cervical cancer slightly decreased with the APC of - 0.3. KS and NHL showed decreasing trends in that period. KS rates first slightly decreased from 2000 to 2009 (APC=-1.1) but later dramatically decreased up to 2014 (APC=-11.4) with significant AAPC of -4.9% (95% CI, -8.0, -1.7) from 2000 to 2014.

NHL on the other hand exhibited fluctuating rates, it first increased from 2000 to 2003, slightly decreased from 2003 to 2008 and later drastically up to 2014 (AAPC=1.6, 95%CI, -1.6 to -5.6) . (Figure 3)

Observed Age standardized rates

In terms of ASRs, prostate greatly increased from 45.5 to 53.1 while breast cancer slightly increased from 31.3 to 33.1 per 100,000. Conversely, cervical, KS and NHL cancers displayed decreasing trends. The cervical cancer ASRs marginally decreased from 56.4 to 52.9 per 100,000 women. KS rates for both males and females markedly decreased from 47.0 to 12.8 with the significant APC of -5.8% (95% CI, -8.1 to -3.6). NHL showed both increasing and decreasing trends in the entire observed period as rates first increased from 6.3 in 2006 to 9.0 in 2006 and later significantly declined to 3.6 in 2014. (AAPC = -1.8, 95% CI, -6.1 to 2.6). (Figure 4)

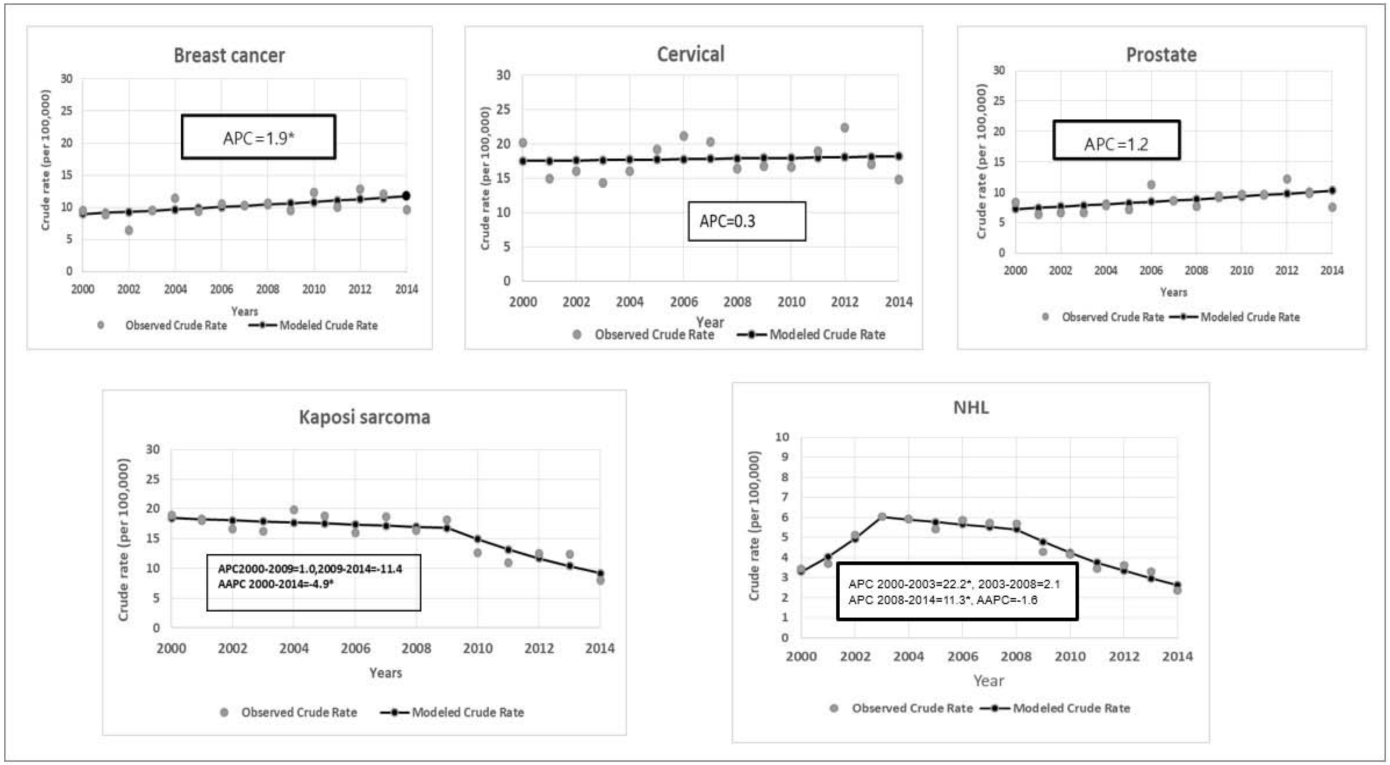


Figure 3. Crude rates in the observed period (2000-2014) by cancer site, Kyadondo County

* *Significant Annual Percentage Change and Average annual Percentage change*

Crude rates were obtained using joinpoint software

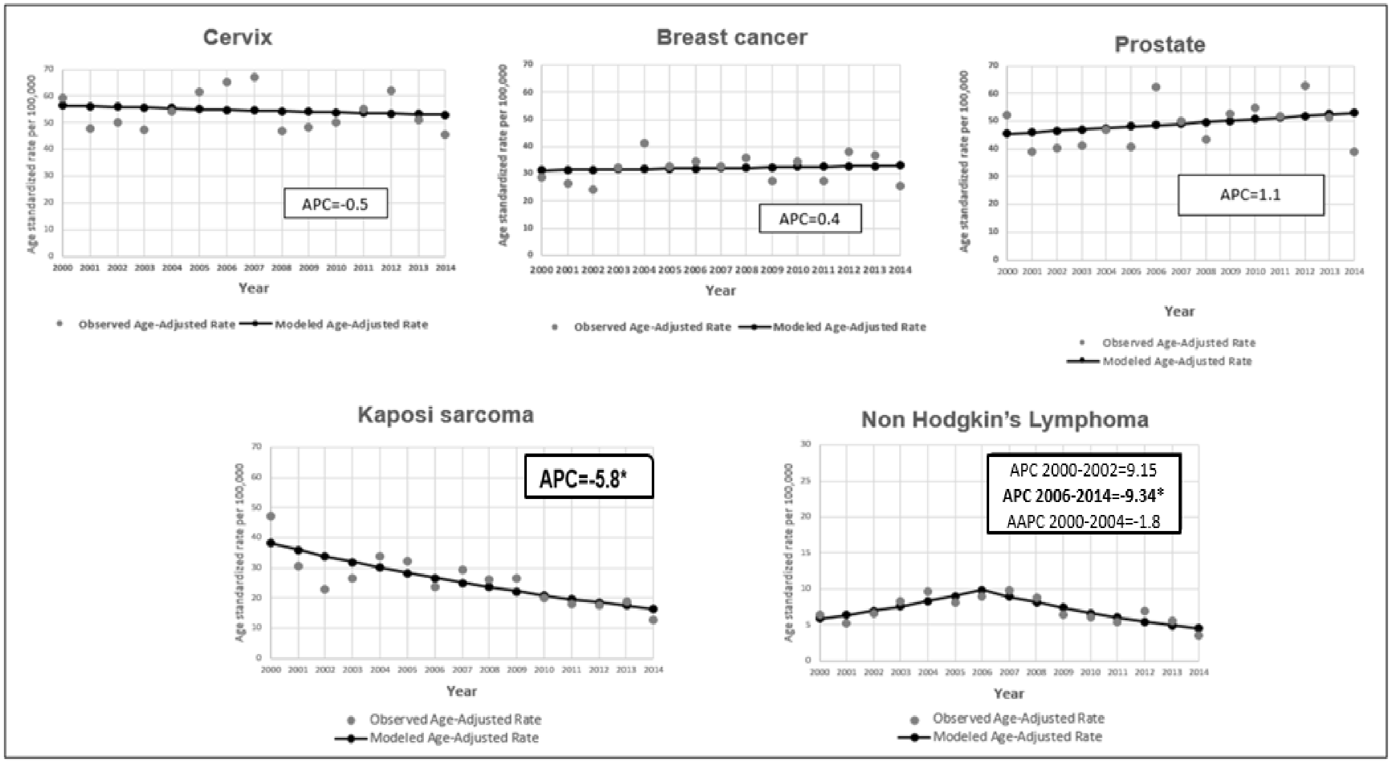


Figure 4. Age standardized incidence rates in the observed period (2000-2014) by cancer site, Kyadondo County

** Significant Annual Percentage Change and Average annual Percentage change ASRs were obtained using joinpoint software*

3.2 Prediction of cancer incidence up to 2029

3.2.1 Observed and Predicted Crude and ASRs

Generally, breast and prostate cancers ASRs and crude rates are predicted to continue increasing in the next decade while those of cervical cancer, KS and NHL are expected to decrease in the future following the same trends exhibited in the observed period.

The highest crude rates were observed in males with KS (20.7 per 100,000) in the first observed period of 2000-2004 but the highest rates are expected to be in women with cervical cancer in the future starting from 2010 up to 2029 with the rates of 17.2 per 100,000 in the period of 2025-2029. In terms of ASRs, the highest rates were observed in cervical cancer (51.9 per 100,000) in 2000-2004 but in the future prostate cancer will take the lead.

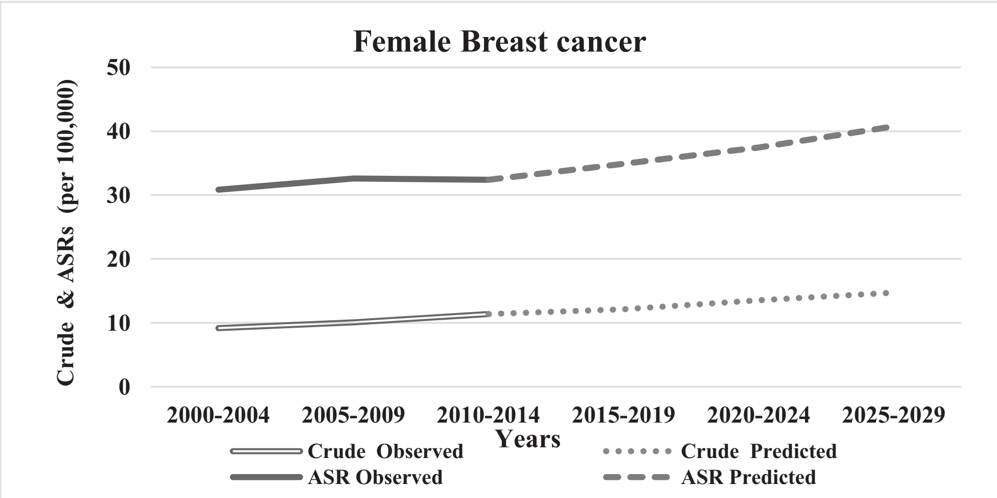
Breast cancer crude rates gradually increased from 9.2 in 2000-2004 to 14.7 in 2025-2029 and ASRs from 30.9 to 40.8 in 2025-2029 in each 100,000 women. (Figure 5)

Cervical cancer crude rates first increased from 16.3 (2000-2004) to 18.7 (2005-2009) and later steadily reduced across all periods to 17.2 (2025-2029). ASRs also first increased from 51.9 (2000-2004) to 57.9 (2005-2009) and later fell to 52.9 in last observed period (2010-2014) and the rates are expected to remain stable up to 2029. (Figure 6)

Prostate cancer exhibited increasing trends in both crude and ASRs however the crude rates were so low compared to the ASRs. The dramatic change was observed in the ASRs that are expected to increase from 44.9 (2000-2004) to 64.3(2025-2029) in each 100,000 men while crude rates are expected to slightly increase 7.2 to 11.3 in both periods. (Figure 7)

KS showed significant decrease in both crude and ASRs in both genders as seen in the observed period. More rates were seen in males compared to females. Crude rates are anticipated to fall from 20.7(2000-2004) to 5.2 (2025-2029) in males and from 15.6 to 3.1 in females and the ASRs from 36.5 to 8.6 in males and 24.7 to 4.5 in women respectively. (Figure 8 & 9)

Of all the five cancers, NHL had the lowest rates that were less than 10 in both the observed and predicted periods. Like KS, more rates were among men compared to women but are predicted to become equal in the future. (Figure 10 & 11)



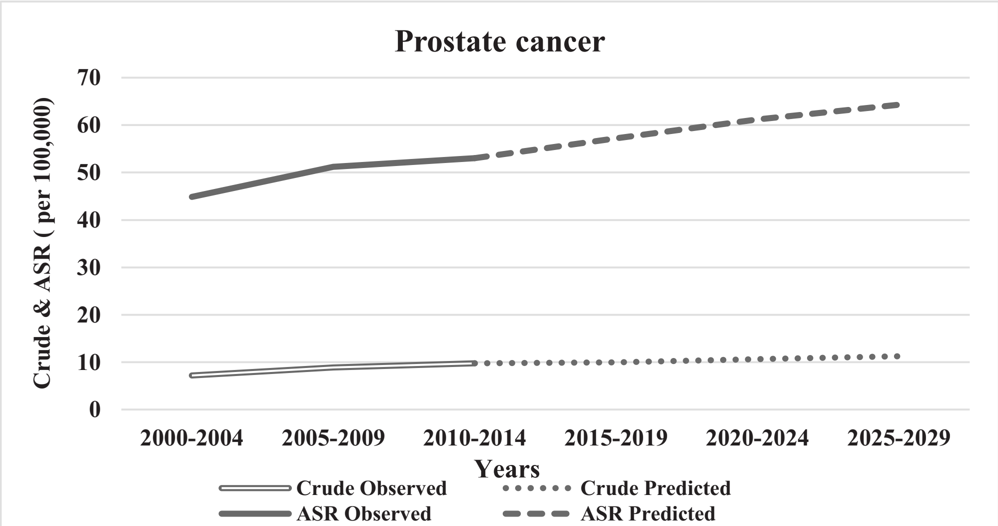


Figure 5. Breast cancer Crude and ASRs for both observed and predicted periods, Kyadondo County (2000-2029)

Crude and ASRs were obtained using Nordpred R- package

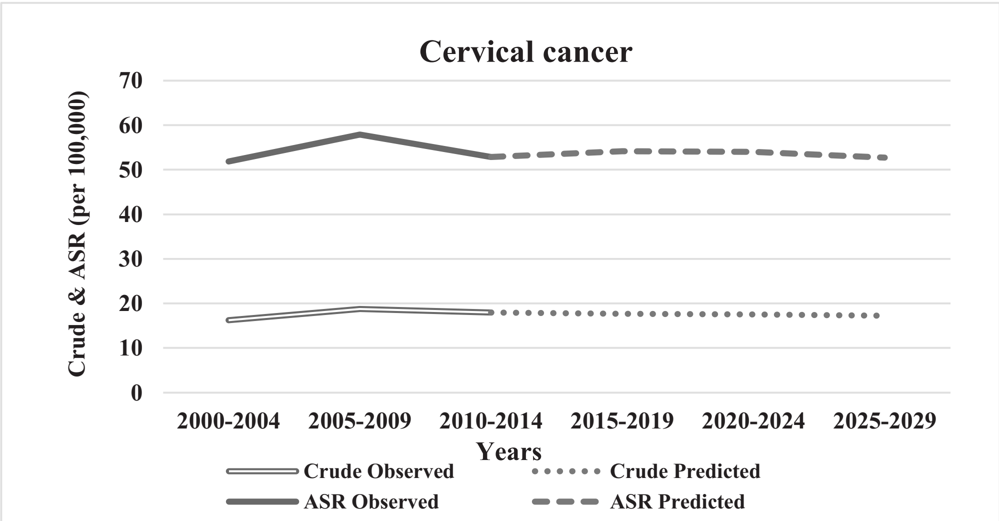


Figure 6. Cervical cancer Crude and ASRs for both observed and predicted periods, Kyadondo County (2000-2029)

Crude and ASRs were obtained using Nordpred R- package

Figure 7. Prostate cancer Crude and ASRs for both observed and predicted periods, Kyadondo County (2000-2029)

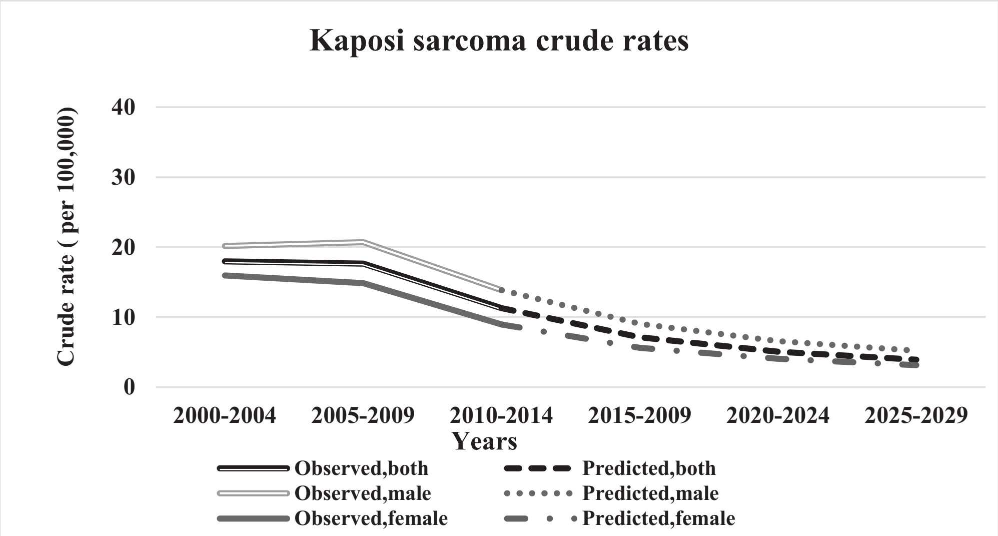


Figure 8. KS Crude rates by gender for both observed and predicted periods, Kyadondo County (2000-2029)

Crude and ASRs were obtained using Nordpred R- package

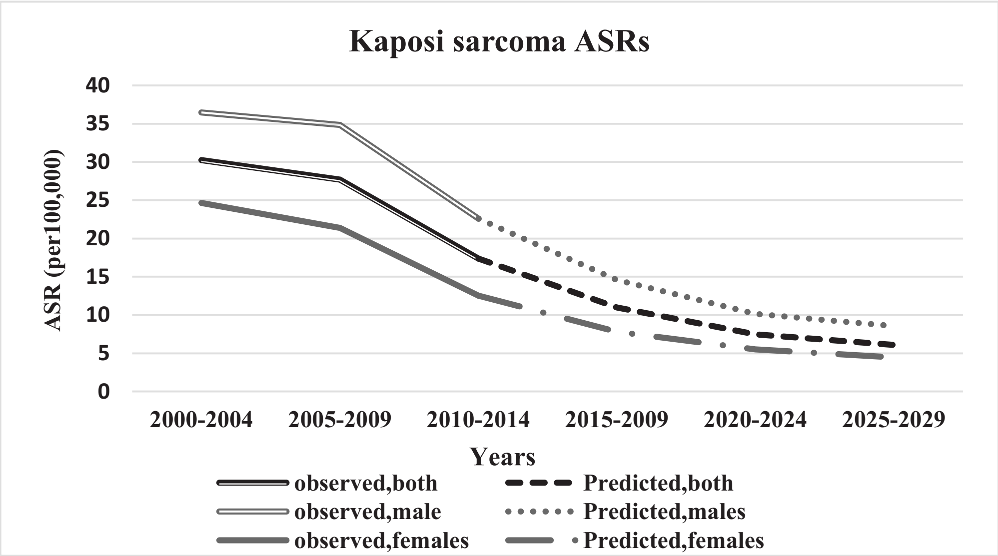


Figure 9. KS ASRs by gender for both observed and predicted periods, Kyadondo County (2000-2029)

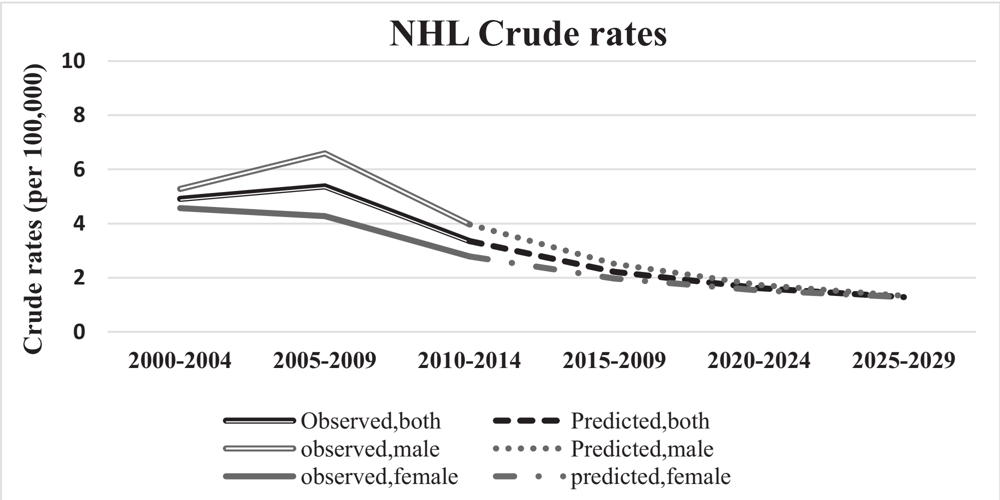


Figure 10. NHL cancer Crude rates by gender for both observed and predicted periods, Kyadondo County (2000-2029)

Crude and ASRs were obtained using Nordpred R- package

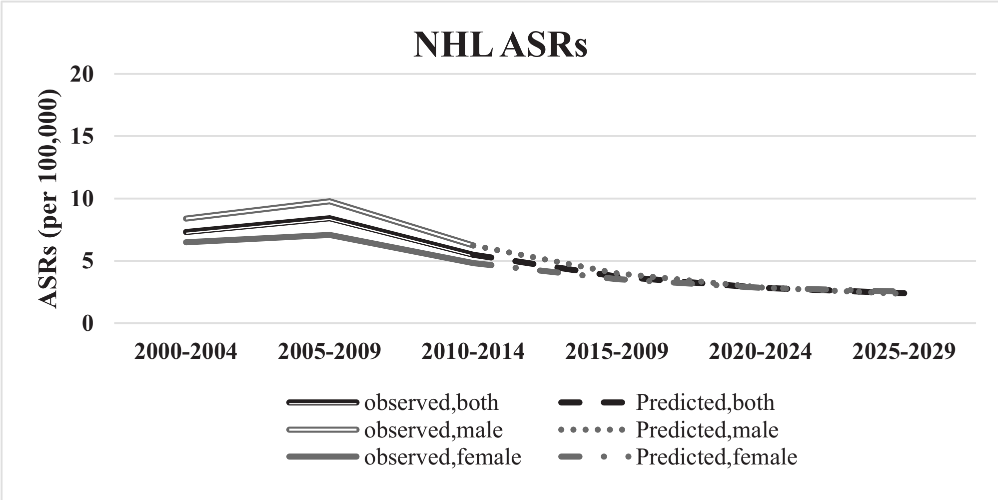


Figure 11. NHL ASRs by gender for both observed and predicted periods, Kyadondo County (2000-2029)

Crude and ASRs were obtained using Nordpred R- package

Table 9.Crude rates in the observed and predicted periods by cancer site, using three approaches.

Cancer type	Model	2000-2004	2005-2009	2010-2014	2015-2019	2020-2024	2025-2029
Breast	Power-link	9.2	10.1	11.4	12.1	13.5	14.7
	log-link	9.2	10.1	11.4	12.7	14.9	15.1
	Joinpoint [a]	9.2	10.1	11.4	12.4	13.7	15.0
Cervical	Power-link	16.3	18.7	18.0	17.7	17.5	17.2
	log-link	16.3	18.7	18.0	17.6	17.3	16.9
	Joinpoint [a]	16.3	18.8	18.1	18.4	18.6	18.9
Prostate	Power-link	7.2	8.9	9.8	10.0	10.7	11.3
	log-link	7.2	8.9	9.8	10.2	11.2	12.3
	Joinpoint [a]	7.2	8.9	9.8	11.1	12.6	14.2
KS - Both	Power-link	18.0	17.6	11.3	7.3	5.3	4.1
	log-link	18.0	17.6	11.3	7.1	5.0	3.9
	Joinpoint [a]	18.0	17.6	11.3	6.5	3.6	1.9
NHL - Both	Power-link	4.9	5.4	3.4	2.2	1.6	1.3
	log-link	4.9	5.4	3.4	2.3	1.8	1.4
	Joinpoint [a]	4.9	5.4	3.4	1.9	1.0	0.6

Abbreviations: KS, Kaposi sarcoma; NHL, Non-Hodgkin's lymphoma. Crude rates were obtained using the age-period-cohort models (power and log link functions) and extrapolation of Joinpoint regression results.
[a]Average crude rates for the 5 year periods

Table 10. ASRs in the observed and predicted periods by cancer site, using three approaches.

Cancer type	Model	2000-2004	2005-2009	2010-2014	2015-2019	2020-2024	2025-2029
Female Breast	Power-link	31.1	32.8	32.5	34.9	37.6	40.8
	log-link	31.1	32.8	32.5	35.5	38.1	41.9
	Joinpoint [a]	30.6	32.7	32.5	33.5	34.1	34.8
Cervical	Power-link	51.9	57.9	52.9	54.1	53.9	52.5
	log-link	51.9	57.9	52.9	54.1	54.0	52.7
	Joinpoint [a]	51.8	57.9	52.8	52.3	51.1	50.0
Prostate	Power-link	44.9	51.2	53.0	57.2	61.2	64.3
	log-link	44.9	51.2	53.0	58.4	63.8	65.2
	Joinpoint [a]	43.9	49.9	52.0	54.9	58.0	61.3
KS - Both	Power-link	30.3	27.7	17.4	11.2	7.9	6.6
	log-link	30.3	27.7	17.4	11.0	7.5	6.1
	Joinpoint	32.2	27.6	17.4	13.8	10.2	7.6
NHL - Both	Power-link	7.3	8.4	5.5	3.8	2.8	2.4
	log-link	7.3	8.4	5.5	3.7	2.8	2.4
	Joinpoint [a]	7.2	8.4	5.5	3.4	2.1	1.3

Abbreviations: KS, Kaposi sarcoma; NHL, Non-Hodgkin's lymphoma.
Crude rates were obtained using the age-period-cohort models (power and log link functions) and extrapolation of Joinpoint regression results.
[a]*Average Age standardized rates for the 5 year period*

3.2.2 Changes in incidence due to risk and population changes

Change in the number of cases between the last five years of the observed period (2010-2014) and the last five years of the predicted period (2025-2019) was described in (table 11). For each cancer site, we presented the overall percentage changes in the number of cases and the proportions of change attributable to changes in the risk and population (age structure and size).

We expect notable decreases in the number of cases of KS and NHL in both males and females mostly due to the change in their risk factors. Overall, KS is expected to decrease by 56% in both genders (-83% due to the risk change and 27% due to the population change), NHL by 52% (-78% due to the risk change and 27% due to the population)

Breast, prostate and cervical cancers cases are on the other hand expected to increase. The highest changes are expected to be in breast (65%) and prostate (45%). The increase in the incidence of two cancers is mostly due to the increase in their risk factors. Cervical cancer cases are also anticipated to increase by 22% in the next decade and the change is expected to mostly be due to increase in the women population. Cervical risks are forecasted to reduce by 5% in the future. (Table 8)

Table 11. Observed and predicted incidence rates and number of cases by cancer site, Kyadondo County

Cancer type	Observed (2010-2014)			Predicted (2025-2029)				Percentage changes (%)		
	Population[a]	Cases[b]	Crude rate[c]	Population[d]	Crude rate[e]	Predicted cases[f]	Expected cases[g]	Overall[h]	Due to risk change[i]	Due to population change[j]
Breast	6405169	729	11.38	8172708	14.71	1202	930	65	37	28
Cervix	6405169	1151	17.97	8172708	17.22	1407	1469	22	-5	28
Prostate	5745816	561	9.76	7245398	11.26	816	707	45	19	26
KS - Both	12150984	1367	11.25	15418106	3.91	603	1735	-56	-83	27
KS - Male	5745816	794	13.82	7245398	5.2	377	1001	-53	-79	26
KS - Female	6405169	573	8.95	8172708	3.11	254	731	-56	-83	28
NHL - Both	12150984	407	3.35	15418106	1.28	197	517	-52	-78	27
NHL - Male	5745816	228	3.97	7245398	1.33	96	288	-58	-84	26
NHL - Female	6405169	179	2.79	8172708	1.28	105	228	-42	-69	27

Abbreviations: KS, Kaposi sarcoma; NHL, Non-Hodgkin's lymphoma

[a]Observed Population, [b]Number of cases, [c]Observed crude rate from 2000-2004

[d]Predicted population, [e]Predicted crude rate from 2025-2029

*[f]Predicted cases = (d*e)/100,000*

*[g]Expected cases= (c*d)/100,000*

*[h]Overall percent change in the predicted cases (2025–2029) vs. observed cases (2010–2014) =(f-b)/b*100*

*[i]Percentage change in the predicted cases due to changes in the risk= (f-g)/b*100*

*[j]Percentage change in the predicted cases due to the population changes =(g-b)/b*10*

3.2.3 The age-specific rates in the observed (2000-2014) and predicted periods (2015-2029) by cancer site

Figure 12 shows the age specific incidence rates by cancer site and the patterns were similar in both observed and predicted periods in all the five cancers.

For breast and cervical cancers, the rates gradually increased from young women aged 25-29 and were at the peak among those aged 50-70 years. Prostate cancer started at the older age group of 55-59 and the rates steeply increased as age increased and were at the peak among men aged 70-74. KS and NHL showed fluctuations in all age groups but higher rates were observed in older age groups and the rates are anticipated to decrease by 2029. Unlike other cancer types, NHL had some cases in children aged 15 years and below.

3.2.4 The age-specific number of cases in the observed (2000-2014) and predicted periods (2015-2029) by cancer site

The number of cases in each age group differ by cancer type as shown in (tables 9-14).

For breast and cervical, in both the observed and predicted periods cases are expected to increase across all age groups and they are more among women aged 30 to 65.

In prostate cancer, more cases were observed among men aged 60 and above and the number of cases are expected to continually increase in the future across all age groups.

The incidence of KS and NHL showed markedly decreasing trend along the study periods in both genders and in all age groups. For KS more cases were observed among people aged 30 to 45 and children less than 15 years among those with NHL.

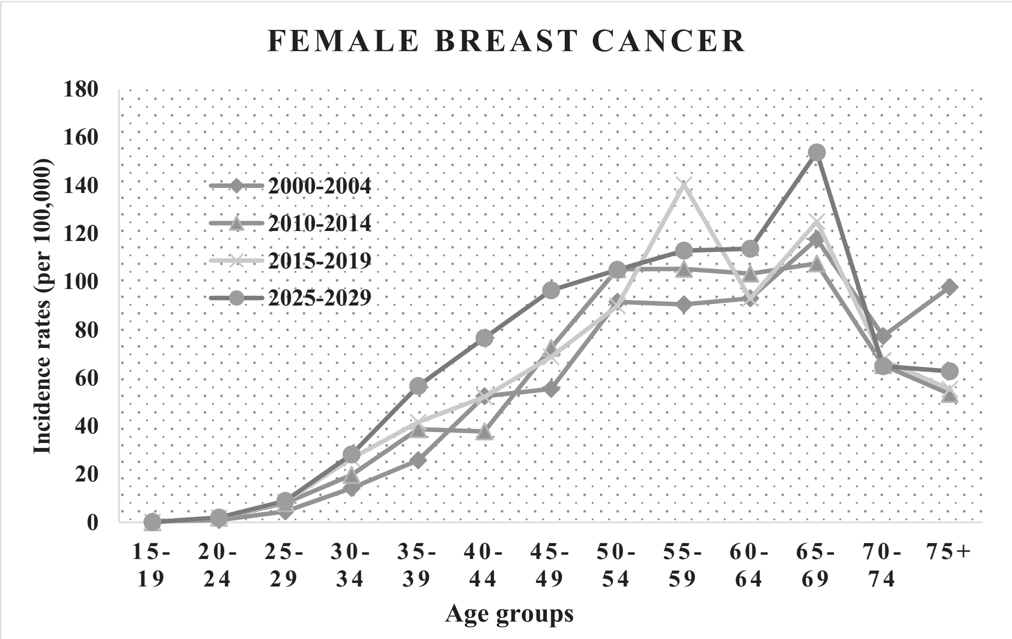


Figure 12. Breast cancer Age-specific incidence rates in the observed (2000-2014) and predicted periods (2015-2029), Kyadondo County

Age specific incidence rates were obtained using Nordpred R- package

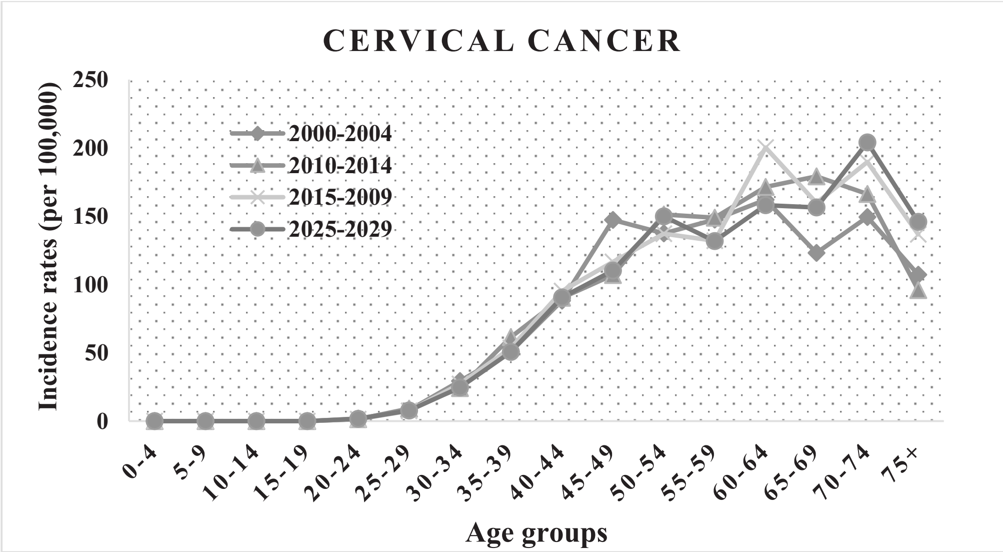


Figure 13. Cervical cancer Age-specific incidence rates in the observed (2000-2014) and predicted periods (2015-2029), Kyadondo County

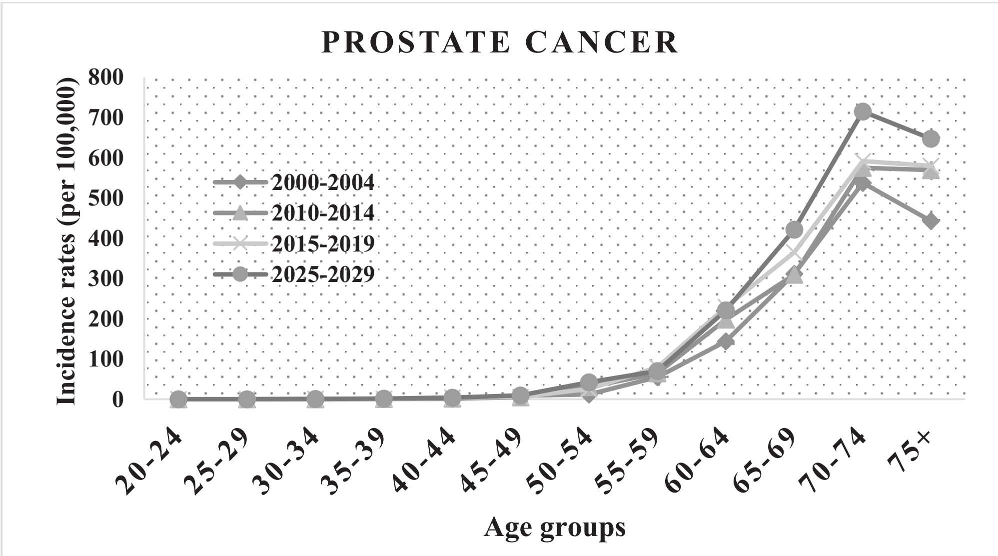


Figure 14. Prostate cancer Age-specific incidence rates in the observed (2000-2014) and predicted periods (2015-2029), Kyadondo County

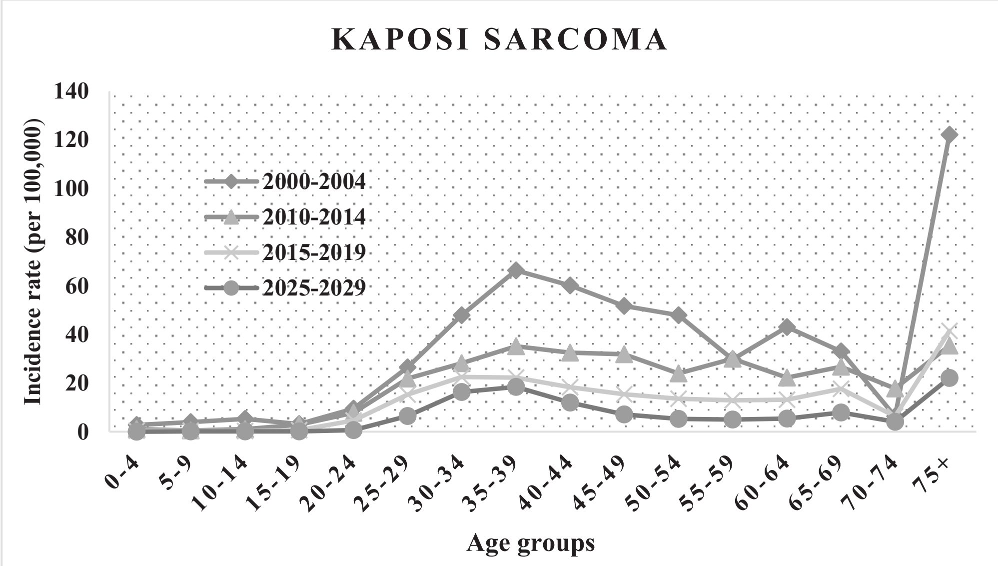


Figure 15. KS Age-specific incidence rates in the observed (2000-2014) and predicted periods (2015-2029), Kyadondo County

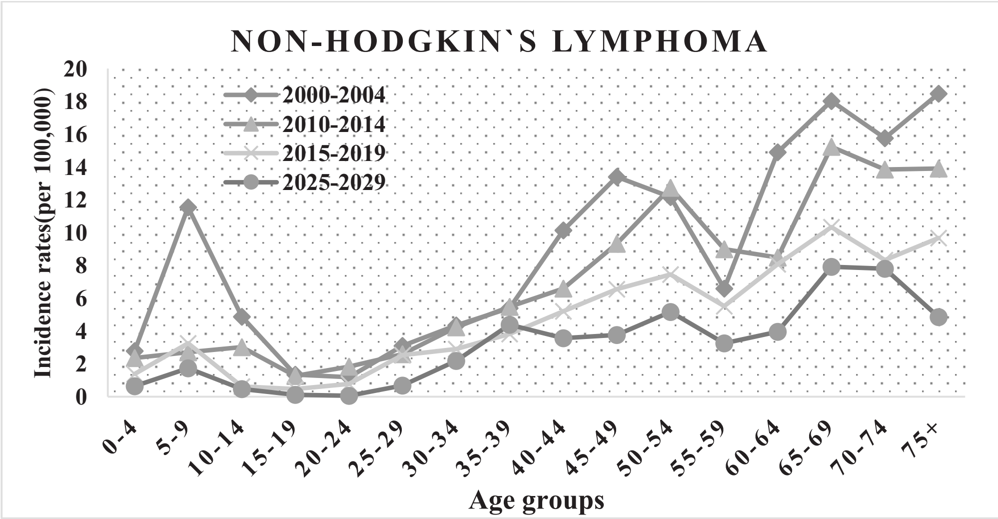


Figure 16. NHL Age-specific incidence rates in the observed (2000-2014) and predicted periods (2015-2029), Kyadondo County

Age specific incidence rates were obtained using Nordpred R- package

Table 12. Cervical cancer Age specific number of cases for both the observed and predicted periods, Kyadondo County (2000-2029)

Age group	2000-2004	2005-2009	2010-2014	2015-2019*	2020-2024*	2025-2029*
20-24	13	14	15	16	19	22
25-29	38	54	67	57	66	74
30-34	83	109	106	124	123	137
35-39	93	132	176	158	185	184
40-44	111	153	192	204	209	241
45-49	109	113	133	146	169	171
50-54	78	131	144	129	151	171
55-59	44	58	75	67	70	82
60-64	54	77	88	103	95	97
65-69	22	32	50	45	59	54
70-74	29	39	51	58	59	75
75+	34	78	54	76	99	100
Total	**708**	**990**	**1151**	**1184**	**1305**	**1407**

Table 13: Female Breast cancer Age specific number of cases for both the observed and predicted periods, Kyadondo County (2000-2029)

Age group	2000-2004	2005-2009	2010-2014	2015-2019*	2020-2024*	2025-2029*
15-19	2	1	0	1	1	1
20-24	6	13	18	20	22	25
25-29	21	29	58	64	73	82
30-34	40	47	86	120	140	156
35-39	47	60	111	123	180	206
40-44	66	76	80	111	143	204
45-49	41	83	90	86	120	149
50-54	52	49	100	84	89	119
55-59	27	41	53	71	67	70
60-64	31	42	53	48	76	70
65-69	21	26	30	36	34	53
70-74	15	24	20	21	26	24
75+	31	42	30	31	34	43
Total	**400**	**533**	**729**	**814**	**1005**	**1202**

Table 14. Prostate cancer Age specific number of cases for both the observed and predicted periods, Kyadondo County (2000-2029)

Age group	2000-2004	2005-2009	2010-2014	2015-2019*	2020-2024*	2025-2029*
30-34	2	3	2	3	4	5
35-39	1	1	3	3	4	5
40-44	1	4	4	10	9	11
45-49	7	6	6	8	18	16
50-54	7	19	28	23	25	46
55-59	17	27	32	40	41	42
60-64	39	60	85	97	111	112
65-69	48	61	76	89	111	123
70-74	66	82	114	114	137	164
75+	99	161	211	213	246	290
Total	**287**	**424**	**561**	**599**	**705**	**815**

Table 15. Kaposi sarcoma Age specific number of cases for both the observed and predicted periods-Males, Kyadondo County (2000-2029)

Age group	2000-2004	2005-2009	2010-2014	2015-2019*	2020-2024*	2025-2029*
0-4	23	23	13	5	2	1
5-9	26	36	5	4	2	1
10-14	35	32	6	2	1	1
15-19	14	22	17	3	0	0
20-24	37	64	49	23	8	2
25-29	108	162	157	117	77	41
30-34	148	188	152	134	124	97
35-39	145	173	139	104	107	113
40-44	101	105	102	61	54	64
45-49	46	57	46	27	20	20
50-54	43	37	35	18	14	12
55-59	14	17	19	9	6	5
60-64	21	12	15	7	5	4
65-69	8	15	10	6	4	3
70-74	2	10	4	2	2	1
75+	35	41	25	23	11	12
Total	**806**	**994**	**794**	**543**	**435**	**377**

**Predicted age specific cases obtained using Nordpred R- package*

Table 16. Kaposi sarcoma Age specific number of cases for both the observed and predicted periods-Females, Kyadondo County (2000-2029)

Age group	2000-2004	2005-2009	2010-2014	2015-2019	2020-2024	2025-2029
0-4	11	9	6	2	1	0
5-9	16	23	4	3	1	1
10-14	20	28	10	3	2	1
15-19	21	23	26	9	2	2
20-24	74	89	87	65	37	16
25-29	140	156	145	102	100	71
30-34	150	188	108	86	79	88
35-39	113	105	66	36	31	32
40-44	59	71	41	21	12	12
45-49	35	31	36	12	7	4
50-54	12	17	10	6	2	1
55-59	4	7	11	4	3	1
60-64	5	7	6	6	3	2
65-69	3	2	4	3	3	2
70-74	0	2	5	2	2	3
75+	31	27	8	16	14	17
Total	**694**	**785**	**573**	**376**	**300**	**254**

Table 17. NHL Age specific number of cases for both the observed and predicted periods-Males, Kyadondo County (2000-2029)

Age group	2000-2004	2005-2009	2010-2014	2015-2009	2020-2024	2025-2029
0-4	17	25	25	13	8	6
5-9	58	73	31	36	25	20
10-14	37	33	26	7	9	7
15-19	7	22	12	4	1	2
20-24	8	14	18	6	3	1
25-29	10	17	18	18	8	4
30-34	11	22	16	12	16	8
35-39	10	31	13	11	10	16
40-44	12	26	18	11	10	11
45-49	14	15	15	12	8	8

50-54	5	13	16	9	8	6
55-59	4	6	4	3	3	3
60-64	4	5	3	3	2	2
65-69	4	5	5	2	2	2
70-74	2	3	4	2	1	1
75+	8	6	4	3	2	1
Total	**211**	**316**	**228**	**151**	**115**	**96**

Table 18. NHL Age specific number of cases for both the observed and predicted periods-Females, Kyadondo County (2000-2029)

Age group	2000-2004	2005-2009	2010-2014	2015-2009	2020-2024	2025-2029
0-4	17	25	16	12	11	10
5-9	65	49	11	17	15	14
10-14	14	18	18	4	4	4
15-19	8	14	7	5	2	2
20-24	6	7	14	9	5	2
25-29	19	12	18	20	17	10
30-34	16	22	23	17	22	20
35-39	11	21	19	12	12	17
40-44	15	12	11	11	8	8
45-49	7	9	9	5	5	4
50-54	9	12	8	5	4	5
55-59	0	2	5	2	1	1
60-64	5	3	5	5	4	2
65-69	2	5	3	3	3	3
70-74	3	8	3	2	3	4
75+	2	7	9	6	3	5
Total	**199**	**226**	**179**	**134**	**119**	**110**

**Predicted age specific cases obtained using Nordpred R- package*

3.3 Comparison of age standardized rates in Uganda and other Sub-Saharan African countries

Since there is limited literature on patterns of cancer in SSA, we compared the age standardized incidence rates of the top five cancers in Uganda (cervical, breast, prostate , KS and NHL) with three countries (Zimbabwe, Mozambique and South Africa) that are in the same region to examine if they have similar trends based on previous publications. Generally, the trends in the incidence of these cancers were relatively similar in these countries. (Table 15)

The trends study in the incidence of cancer in Harare Zimbabwe was conducted in the same period as that of Kampala, Uganda (1991-2010). In that period, breast and prostate cancers particularly showed marked increases in ASRs in both countries; by 3.7% and 5.2% annually to 6.4% and 4.9% respectively). There was also an increase in cervical cancer however the APC was somewhat lower in Uganda (1.8%) compared to 3.3% of Zimbabwe. In both countries, the incidence of KS increased to a maximum around 1998-2000 and then declined after that in all age groups. Unlike this study where NHL is showing decreasing trends in both genders, it exhibited increasing trends in both countries in the past years.

The trends study in the incidence of cancer that was conducted in Maputo, Mozambique (1991-2008) also showed an increase in ASRs of cervical, breast and prostate cancers by 4.7%, 6.5% and 11.3% respectively. NHL also increased by 6.4% in males and 9.0% in females. Unlike in Uganda and Zimbabwe where KS

ASRs decreased, the rates in Mozambique increased by 11.2% in males and 15.4% in females.

We also compared with the incidence trends (1998-2012) in South Africa using data obtained from the East Cape Province PBCR that covers an area that is entirely rural. The study author however did not compute the annual Percentage Changes like other countries, he instead calculated the Standard errors of the ASRs, and of the ratio of the ASRs in pairs of time period, the standardized rate ratio (SRR). In terms of ASRs, Kaposi sarcoma showed dramatic increase in incidence in both sexes a trend different from other SSA that show declining trends. It increased by 3.5-fold in men, from 1.7 (1998-2002) to 5.8 (2008-2012) and by 11-fold in women from 0.3 (1998-2002) to 3.5 (2008-2012) although the rates are relatively low compared to SSA countries. Other dramatic increases were observed in prostate cancer that increased by more than 50% in incidence (SRR 2.43, 95% CI 1.33-1.95). Breast and cervical cancers also exhibited increasing trends in the entire study period. NHL was not reported in this study as it was not among the most eight incident cancers that were considered.

Table 19. Comparison of age standardized rates in Uganda and other Sub-Saharan African countries

Author	Country	Study period		Age standardized Incidence rates –Females				Age standardized rates – Males			
			Cancer type	**2000-2004**	**2005-2009**	**2010-2014**	**APC (95%CI)**	**2000-2004**	**2005-2009**	**2010-2014**	**APC (95%CI)**
Current study	**Uganda**	**2000-2014**	KS	24.4	21.3	12.5	-8.1(-10.8:-5.4)	36.1	34.5	22.5	-4.3(-6.5:-1.9)
			Cervical	51.8	57.9	52.8	-0.5(-2.2:1.4)				
			Breast	30.6	32.7	32.5	0.4(-1.8:2.6)				
			Prostate					43.9	49.9	52.0	1.1(-1.1
			NHL	6.4	7.1	4.8	-3.1(-6.6:0.6)	8.3	9.7	6.2	-3.0(-7.0:1.2)
Wabinga. R[7]	**Uganda**	**1991-2010**	**Cancer type**	**1991-1995**	**2001-2005**	**2006-2010**	**APC (95%CI)**	**1991-1995**	**2001-2005**	**2006-2010**	**APC (95%CI)**
			KS	18.2	21.5	16.1	-0.3(-1.8:1.2)	39.7	28.9	29.3	-2.1(-0.8:3.3)
			Cervical	38.1	48.9	50.2	1.8(0.3:3.4)				
			Breast	18.0	29.6	31.2	3.7(2.3:5.5)				
			Prostate					25.7	38.8	58.0	5.2(3.0:7.3)
			NHL	2.1	6.3	6.4	7.0(3.0:10.9)	3.9	8.1	9.0	5.4(3.3:7.5)
Chokunonga.E[8]	**Zimbabwe**	**1991-2010**	KS	15.0	27.5	19.2		42.2	48.6	28.5	
			Cervical	62.1	78.7	103.8	3.3(2.0:4.6)				
			Breast	20.9	30.3	46.8	4.9(2.9:6.9)				
			Prostate					30.1	58.5	73.3	6.4(5.1:7.7)
			NHL	4.6	9.2	12.4	6.9(4.4:9.3)	5.1	9.9	12.7	6.7(4.1:9.3)

Cesaltina L[13]	**Mozambique**	**1991-2008**	**Cancer type**	**199-1996**	**1997-2002**	**2003-2008**	**APC (95%CI)**	**1991-1996**	**1997-2002**	**2003-2008**	**APC (95% CI)**
			KS	1.6	4.9	12.0	15.4(11:20)	5.6	12.1	25.0	11.2(8.6:14)
			Cervical	34.3	43.3	62.0	4.7(3.4:6.0)				
			Breast	13.7	12.8	26.2	6.5(4.3:8.7)				
			Prostate					17.4	28.2	61.7	11.3(9.7:13)
			NHL	2.1	2.8	6.0	9.0(4:14)	3.8	3.9	7.7	6.4(2.3:10.5)
Ntuthu I. M [10]	**South Africa**	**1998-2012**	**Cancer type**	**1998-2002**	**2003-2007**	**2008-2012**	**SRR (95% CI)**	**1998-2002**	**2003-2007**	**2008-2012**	**SRR (95% CI)**
			KS	0.3	1.4	3.5	10.7(5.8:19.7)	1.7	3.2	5.8	3.5(2.2:5.4)
			Cervical	22.1	24.6	29.0	1.3(1.2:1.5)				
			Breast	7.6	7.5	12.2	1.6(1.3:2.0)				
			Prostate					4.4	6.3	9.9	2.4(1.9:3.2)

Abbreviations: APC - Annual Percentage Change; SRR- Standard Rate Ratio

ASRs were obtained from literature review

4.0 Discussion

4.1 General findings

This study explored the most up to date cancer trends and to our knowledge, is the first to predict the future trends up to 2029 of the incidence of most common cancers in Uganda. Our findings predict an upward trend in the incidence of cervical, breast and prostate cancers and a decreasing trend in the HIV/AIDS related cancers, KS and NHL, in Kyadondo County in the next decade. We compared results from three different approaches: age-period-cohort model with power-link function, age-period-cohort model with log-link function, and extrapolation of Joinpoint regression. Three different models applied for prediction provided consistent results hence demonstrating the robustness of our study findings.

We chose to study the current trend and the future incidence of KS, cervical, breast, prostate and NHL because according to the available literature, they are the most incident cancers and are currently the biggest public health burden in Uganda. They therefore require urgent action to reduce their growing burden.

The increasing burden of cancer cases and other chronic diseases in low and middle income countries is mostly attributed to demographic changes in terms of population growth and aging[27] which is not the case in Uganda according to this study.

The tremendous change in the incidence of top cancers in Uganda is mostly attributed to the change in their risk factors. The most known risk factors in Uganda are;

increased prevalence of obesity, smoking, harmful use of alcohol, physical inactivity and decreasing infections.[6]

4.1.2 Comparison of cancer incidence in Uganda and other Sub-Saharan African countries

There are few cancer trend data reported in sub-Saharan Africa notably due to the scarcity of population based cancer registries. We therefore compared the trends in ASRs of cancer incidence in Uganda with only three SSA countries; Zimbabwe[8], Mozambique[13] and South Africa[10] that had relatively long trends study periods in cancer incidence available with published data. We were unfortunately not able to compare the future ASRs because we were not able to find information regarding prediction of cancer incidence in these particular countries.

In general, these countries had relatively similar trends in cancer incidence in previous years. Increasing trends in ASRs were observed in the cancers of the breast, cervical and prostate. Different trends were mostly observed in KS where it had decreasing ASRs in Uganda and Zimbabwe and increasing trends in Mozambique and South Africa.

NHL exhibited increase in ASRs in all the countries, a trend different from this study where the rates are currently decreasing in Uganda and are expected to continue decreasing in the future.

4.2 Breast cancer incidence trends and the associated factors

Breast cancer exhibited exponential growths in the number of cases and ASRs and is predicted to contribute greatly to the cancer burden in Uganda in the near future. Its incidence rates are lower in developing countries than in developed countries but are growing faster in developing countries. According to the trends study on the global burden of cancer from 1990 to 2013, breast cancer ASRs increased by 46% in developing countries and by only 8% in developed countries [28] In the previous trends study conducted in Kampala, Uganda from 1991 to 2010, breast cancer increased by 3.7% annually, and the increase was attributed to the increase in its risk factors. Similar trends were observed in other sub-Saharan African countries, such as Zimbabwe[8], Nigeria[11] and Kenya [9] .

There is scantiness of studies that have examined risk factors that have accelerated the increase of breast cancer incidence in Ugandan women, and few that have been conducted in other sub-Saharan African countries are limited to some reproductive and anthropometric variables.[29] As well, little information is known about the Population attributable fractions (PAFs) of different risk factors to the growing burden of breast cancer in SSA. However, some studies have been conducted assessing the global PAFs of certain risk factors by some researchers.

In 2017, Jonathan Pearson-Stuttard and his collogues [30], estimated the worldwide cancer incidence attributable to diabetes and high Body Mass Index (BMI) as individual breast cancer risk factors by country and sex using GLOBOCAN statistics on estimated cancer incidence in 2012.[31] They found that diabetes and BMI contribute 2.2% and 6.9% respectively of all the breast cancer cases globally.[28] In 2015, Delphine Praud estimated the global cancer incidence attributable to alcohol consumption and his findings were that 7.3% (PAF) of all breast cancer cases are attributable to alcohol drinking.[32]

According to our knowledge, no studies have been conducted to estimate the breast cancer PAFs due to specific risk factors in SSA. However some case control studies have been conducted to examine the association of breast cancer with some factors. For example a study that was conducted at a national referral hospital in Kampala, Uganda found some associations between high breast density and breast cancer.[33] Another study done in the same hospital in 2012, found some associations among postmenopausal women using combined oral contraceptive and breastfeeding seemed to be associated with reduced odds of breast cancer.[34] In a hospital based case-control study conducted in South Africa also found significant increases in breast cancer risk among women that used either oral or injectable contraceptives over a long period of time.[35] In a Nigerian study, breast cancer was estimated to have increased by 7% due to early age at menarche, 15% due to reduced parity and 15% because of short breastfeeding period.[36] Augustin and his colleagues examined behavioral risk factors of breast cancer in Bangui, Central Africa and found associations with illiteracy, positive family history of cancer, radiation exposure, fresh fish, groundnut, soybean, alcohol, habit of keeping money in bras, overweight and obesity.[37]

Breast cancer increase in Uganda is also due to the increase in awareness, increased efforts in screening and early detection. Screening is mostly opportunistic in nature and the Uganda cancer institute has put in more efforts by sending health workers to different regions for out reaches so that all people get a chance of being screened. Screening methods have improved from self-exam, to ultra sound and then mammography. Increase of activism of survivorship where survivors willingly teach other women and increased funding from various cancer societies and organizations have also boosted early detection and good outcomes. Moreover, the highest age specific incidence rates from our study were observed among women in their postmenopausal ages. It is therefore possible that the increase is related to declines in fertility or increase in body weight although no studies have been done to prove this according to our knowledge.[6,38]

4.3 Prostate cancer incidence trends and the associated factors

Prostate cancer also showed increasing trends and is predicted to have the highest ASRs in Uganda in the next decade. Like breast cancer, its incidence rates are lower in developing countries than in developed countries and growing greatly than the former. According to the trends study on the global burden of cancer from 1990 to 2013 prostate cancer exhibited the steepest increase in the as the ASRs increased by 135% in developing countries and by 63% in developed countries.[28]

The growing burden of prostate cancer in Uganda was observed in the previous 20 years (1991 to 2010) trends study where it's ASRs increased by 5.2% annually and in

2010, it was the most common cancer among men in Uganda and had one of the highest rates observed in Africa[7,31]. In this study prostate cancer has exhibited increasing trends in both ASRs and crude rates and is predicted to have the highest incidence in the near future.

According to Wabinga and Donald Maxwell Parkin, the increase in the prostate cancer incidence in the previous years was mostly attributed to increase in awareness, readiness to perform prostatectomy for urinary symptoms in old men, and histological examination of operative biopsies and they highlighted that screening was probably not one of the contributing factors.[7] However, Uganda has now adapted the use of prostate specific antigen in screening, which detects indolent prostate cancer cases that may not otherwise have been detected in one's lifetime hence screening could have contributed greatly to the increase of prostate cancer cases in the recent years.[39,40] Recent studies that have been conducted in Europe and United States predict that 23% to 42% of prostate cancer cases could be due to over diagnosis through PSA testing.[41,42]. Increase in life expectancy is also one of the contributing factors to the increased incidence of prostate cancer. For instance, Life expectancy in males rose from 48.8 in 2002 to 62.2 in 2014.[43]

4.4 Cervical cancer incidence trends and the associated factors

Cancer of the cervix uteri has been the most common cancer in Ugandan women since 1950s.[44] Over the 15-year observed period in this study, ASRs decreased by -0.5% annually from 2000 to 2014, a trend relatively similar to what was estimated by the

Institute for Health Metrics and Evaluation in the period of 1990–2010 in Uganda. The ASRs are predicted to continue decreasing in the future [45] However, the number of cervical cancer cases are predicated to increase in the next decade and approximately 30% of this growth is due to the increase the women population.

According to the global burden of cancers attributable to infections in 2012, 100% (PAF) of cervical cancer cases are attributable to Human Papilloma Virus (HPV)[46,47]. Like other cancers there is no available literature on the cervical cancer PAFs in SSA.

The risk of cervical cancer in Kampala, Uganda, as elsewhere, is mostly due to HPV [48] and HIV infection has also been proved to be positively associated with cervical cancer risk.[49,50,51] The decreasing trend in the ASRs of cervical cancer has been accelerated by the Ugandan government putting in more efforts to fight the HPV. This has been achieved through increased awareness, screening which is mostly opportunistic in nature. The government introduced the nationwide HPV vaccination in 2014.[52] The Ministry of Health has tried to ensure that it increases on the coverage of HPV vaccine among young adolescents through various strategies[53] including school-based programmes.[54] Different programmes offering screening for precancerous lesions of cervical cancer using visual inspection with acetic acid, colposcopy, Pap smear and preventive treat by cryotherapy have been operating since 2006, they may have contributed to the reducing its incidence .[55]

4.5 KS & NHL incidence trends and the associated factors

KS and NHL are the well-known AIDS-defining cancers that have shown consistent decrease in the era of antiretroviral therapy that reduces the risk of both cancers among individuals with HIV[56] . 100% and 74·1% (PAFs) of the KS and NHL cases respectively are attributable to infections according to the synthetic analysis was conducted in assessing the global burden of cancers attributable to infections in 2012[46]

The tremendous decrease in the incidence of both cancers has been observed in this study and their change is mostly attributed to the decrease in their risk factors. For both the observed and predicted periods, the number of KS cases and ASRs are more in males compared to females. The number of cases are forecasted to decrease by over 50% in both genders. NHL ASRs increased from 2000 to 2006 and later started gradually decreasing and tending to diminish in the future. The tremendous decrease in the incidence of these cancers could be due to the consistent decrease in the prevalence of HIV infection. For example, an HIV sentinel surveillance conducted among pregnant women seeking antenatal screening showed a continued decline in HIV rates in many hospital across Uganda and the decrease was mostly marked in young women.[57]

Its decline has been attributed to HIV/AIDS prevention programmes including increased availability and uptake of antiretroviral therapy (ART) and prevention of mother to-child transmission and sexual behaviour[58,59]. The ART coverage among adults in Uganda increased from 43% in 2006 to 62% in 2010.[60] The increasing availability of ART in has not only led to the dramatic decrease in the incidence of these cancers, but has also significantly improved the overall survival and quality of life for patients. Similar outcomes have been observed in other SSA countries such as Zimbabwe, South Africa[58,61]

5.0 Study strengths and limitations

This study was, to our knowledge, the first to predict the future incidence trends of the top five cancers in Uganda. Our findings were analyzed using age-period-cohort model from Nordpred package that was developed by Harald Fekjær and Bjørn Møller at the Cancer Registry of Norway. This approach is one of the most popular methods for long-term prediction of cancer incidence and it has been tested in several studies. [17,23,25,62]

Several methods were applied for cancer prediction and provided similar results hence indicating the strength of our study findings.

Another strength of this study is that we used data from the long standing cancer registry (KCR) that is considered to have good quality data. Its data has thus been published in successive volumes of Cancer Incidence in Five continents (CI5) in volumes VII, VIII, IX and X by IARC. [63] Data from this registry is always used to represent the cancer incidence of the entire country since it is the only cancer registry, however more regional registries should be established since different regions may have different risk factors.

The first limitation of this study is that the age- period-cohort model we used assumes that the past trends will continue in the future which may not be true in some cases. Further, predictions are likely to be more accurate in the short term than in longer periods of time, as trends are likely to change over time. In the future, a sensitivity study is recommended to check the robustness of this study findings.

Second, our prediction models did not anticipate changes in major risk factors attributable to the changes in each cancer type. In future, different modelling approaches, which attempt to explicitly assess risk factor changes for cancers where large breakthroughs in prevention and early detection are expected, would be a useful complement to this current work. In addition to that, there is limited information regarding cancer attributable risk factors in Uganda and SSA at large in the published literature which is the main reason why we did not quantify the effect of changes in known risk factors on incidence of these cancers over time. More researches assessing cancer risk factors need be conducted as this information is vital for cancer control and prevention.

The third limitation is that the data had a lot of missing variables regarding staging so we were not able to study the stages of each cancer site yet staging is very important for several reasons; it helps doctors in planning treatment, estimating a person`s prognosis and knowing the cancer stage also helps in determining the clinical trials that may be suitable for treatment options of a patient. So, the cancer registry staff should endeavor to complete all the missing variables for good quality data.

6.0 Conclusion

Cancer burden in breast, cervical and prostate cancers is expected to increase in the next decade whereas the burden of KS and NHL is decreasing. This information will be useful for the government of Uganda in planning the allocation of future cancer services.

To address the expected impact of cancers with increasing incidence on the Ugandan health care system, several additional interventions should be planned to increase on the number of professionals in the field of oncology, invest in cancer research and put in place infrastructure needed to deliver cancer care.

Cancer prevention measures should also implemented for example the national screening programmes. Screening is currently opportunistic hence many people are not able receive the services. More researches should be conducted to quantify the effect of changes in known risk factors on the increasing incidence of breast, cervical and prostate cancers in Uganda.

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