DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

SCHOOL OF MEDICINE UNIVERSITY OF NAIROBI

FOUR YEAR TREND AND FOLLOW UP OF WOMEN AGED MORE THAN 15 YEARS WITH REPRODUCTIVE TRACT CANCERS IN KENYATTA NATIONAL HOSPITAL (2008-2011).

INVESTIGATOR

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H58/64581/2013

A research dissertation, submitted to the University of Nairobi, Department of Obstetrics and Gynaecology in partial fulfillment for the requirements, for the award of Masters of Medicine (M.MED) in Obstetrics and Gynecology.

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ACKNOWLEDGEMENT:

My supervisors: Prof. SBO.OJWANG, Dr ROSE JEPCHUMBA KOSGEI and DR P.OMINDA OKEMWA, for their immense guidance, support and patience through this process.

Staff and colleagues: Department of Obstetrics and Gynaecology, University of Nairobi.

To staff and patients of KNH,

Statistician: Mr. David Ndegwa Gathara

My family, friends and well wishers.

THANK YOU.

DEDICATION:

To all present and future researchers in gyn-oncology.

LIST OF ABBREVIATIONS

AIDS: Acquired Immunodeficiency syndrome

FIGO STAGE: International Federation of Gynecology and Obstetrics staging

GBD: Global Burden of Disease

GLOBOCAN: project whose aim was to provide contemporary estimates of the incidence, mortality and the prevalence from major types of cancer at national level for 184 countries of the world.

HPV: Human Papilloma Virus

HIV: Human Immunodeficiency Virus

IARC: International Agency for Research on Cancer, the specialized cancer agency of World Health Organization

IJC: International Journal of Cancer

KNH: Kenyatta National Teaching and Referral Hospital

LFU: Lost to follow up

MDG's: Millennium development goals

NCD's: Non-communicable diseases

NHIF: National Hospital Insurance Fund

SEER Program: Surveillance, Epidemiology and End Results program

UON: University of Nairobi

WHO: World Health Organization

OPERATIONAL DEFINATIONS

1. Trends: a pattern of gradual change in a condition or a general tendency of a series of data pointing to move in a certain direction over time, represented by a line or a curve on a graph.
2. Lost to follow-up: refers to incomplete ascertainment of the primary outcome for the study participants.
3. Female reproductive tract cancers as defined by the International Classification of disease (ICD 10), include cancer of the ovary, fallopian tubes, uterus, cervix, vagina, vulva, skin overlying the female genital organs and choriocarcinoma.

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ABSTRACT

Background: Female reproductive tract malignancies involve the ovary, fallopian tubes, uterus corpus, choriocarcinoma, cervix, vagina, vulva and skin overlying the genital. In a study done in Kenyatta National Hospital in 2009, on ovarian cancer showed a survival of 50% at 2years from diagnosis and 20% at 5years(6).Sub Saharan Africa disproportionately bears the burden of female genital tract cancers of up to 35% of all female cancers compared to 13% in North America(15) and 12% in Canada (20).
Design: A four year observational descriptive study.
Objective: To determine the trend and follow-up of women with reproductive tract cancers among women aged more than 15years in Kenyatta National Hospital over four year duration, 2008 - 2011.
Setting: Kenyatta National Hospital.
Methods: Three hundred and ninety three women with reproductive tract cancer patients on follow up at KNH from January 1st 2008 to December 31st 2011 histology reports formed the study population. Their respective case records were retrieved and analyzed for any prognostic factors that influenced follow up at two and four years. The proportion and trends over the years were also determined.
Results: Three hundred and ninety three (393) patients' case records were analyzed, of which 38% of the female cancers were of the reproductive tract. Among the reproductive tract cancers, cervical cancers accounted for 70.2%, uterine cancers10.4%, ovarian cancers 8.7% and vulva cancers at 8.4% respectively. Only 3% of the patients were followed up beyond 5years, with 86.5% followed up to 2years, 10.4% were followed up to 5years. On the prognostic factors associated with prompt and long duration of follow up were; irregular menses and contraceptive use.
Conclusion: Reproductive tract cancers comprised 38% of all the cancers. There was a rising trend on the reproductive tract cancer cases over the study duration. Cervical cancer accounted for 70% of all the reproductive tract cancers with the premalignant lesions having a direct relation on the cervical cancer diagnosis. Majority of the patients were followed up to 2years i.e. 86.5% and only 3% beyond 5years Prognostic factors associated with longer duration of follow up were having an insurance cover (NHIF), been married and irregular menses. This mainly catered for the financial implication, social support and more contact with the health care worker for the irregular menses respectively.
Recommendations: Enrollment to NHIF, accessible patient support for the cancer patients and increased advocacy on screening by the health care workers.

1: INTRODUCTION AND BACKGROUND

Female reproductive tract cancers as defined by the International Classification of disease (ICD 10), include cancer of the ovary, fallopian tubes, uterus, cervix, vagina, vulva, skin overlying the female genital organs and choriocarcinoma. The common clinical prognostic factors for female gynecological cancers are well studied. They include International Federation of Gynecology and Obstetrics (FIGO) stage, histology type, histological grade, lymph node status and age at diagnosis. Race has been shown to be prognostic only for cancer of the endometrium, ovary and vulva(1). However each of the gynecologic cancers has their unique, pathogenesis, risk factors, natural progression and prognostic factors. The various female reproductive cancers will hereby be discussed subsequently.

Ovarian Cancer

Ovarian cancer accounts for 6.3% of all cancers in women globally. At Kenyatta National Hospital, ovarian cancer represents about 20-25% of all gynecological cancers. More than 80%of primary ovarian cancers are epithelial in origin. Other types include germ cell, sex cord stromal and mixed cell types. The risk factors include nulliparity, history of breast or colon cancer among first degree relative's, uninterrupted and long periods of ovulatory cycles. Protective factors are multiparity, oral contraceptive use, and anovulatory disorders. Median age is 60-64 years and there is no reliable screening test available. Symptoms are non specific and include abdominal discomfort, upper abdominal fullness, early satiety, dyspepsia, fatigue, urinary frequency and dyspnea are deemed suspicious(2,4).

The pathogenesis of ovarian cancer is linked to events that disrupt the integrity of the ovarian capsule predisposing to tumor genesis. Hereditary factors account for 5-10% of all cases and mutation of the tumour suppressor genes BRCA1 and BRCA2 is common. Molecular biology of the non familial epithelial ovarian cancer typically involves activation of oncogenes ERBB2 and c-*fms.* Epithelial ovarian cancers do not have well defined premalignant lesions. Mucinous cancers of the ovary frequently show point mutations of the K-*ras* oncogene. On examination most patients will have a pelvic mass, which can be bilateral, solid or fixed mass with associated ascites or nodular cul-de-sac. Adjuvant therapy with platinum based chemotherapy and cytoreductive surgery improves survival. The five year survival for stage I, II, III and IV is 65-89%, 64-79%,29-49% and 13% respectively(2,5).

In a study done in Kenyatta National Hospital in 2009, epithelial tumors were the commonest (86%) and the least being sex cord tumors (1%). At the time of diagnosis 9%, 7%, 18% and 30% of the patients were at stage I, II, III and IV respectively. Management used was chemotherapy (46%), surgery (18%) and a combination of both (13%). Radiotherapy was rarely used alone or in combination. Survival at 2years from diagnosis was 50% and at 5years was 20% (6).

In a study that analyzed ovarian cancer for 15 years (1973-1987) in North America, the five year survival rate was higher than Kenya. For cancer of the ovary stage I, II, III and IV is 87.8%, 64.2%, 30.4% and 18.0% respectively. In the study, the main prognostic factor was found to be the histological subtype with mucinous cystadenocarcinoma

having a better prognosis than serous tumors'. Presence of malignant ascites was found to be a worse prognostic factor(1).

Fallopian tube cancer

Primary carcinoma of the fallopian tube is rarest and comprise only 0.14-1.8% of female genital malignancies(4). It is mostly unilateral (80%). Secondary carcinoma (metastatic) is common (90%), the primary sites are from ovary, uterus, breast or gastrointestinal tract(6).

The etiology of primary fallopian tube carcinoma remains unclear(3). The risk factors include infertility, chronic tubal inflammation, endometriosis, nulliparity, smoking and genetic predisposition. The classic Latzko's triad of abdominal mass, intermittent profuse watery discharge (hydrops tubaeprofluens) and vaginal bleeding is considered pathognomonic for tubal carcinoma(4).

There is no screening available for fallopian tube malignancy. Imaging though not a screening tool can be used to raise a high index of suspicion. A sausage shaped mass or multilobular mass with a cog wheel appearance on ultrasound, or low impedance vascular flow within the solid components on ultrasound with colour doppler might lead to a suspicion of tubal malignancy. Ultrasound guided/laparoscopy is recommended and biopsy is confirmatory. Magnetic resonance imaging is better for detecting tumor infiltration of extra tubal organs. Treatment is cytoreduction and chemotherapy.

Endometrial cancer

Endometrial cancer is a common gynecological malignancy. Prevalence in Kenya unknown but hospital based data show that for every 30 cases of cervical cancer there is one for endometrial cancer. The life time risk for developing endometrial cancer is about 2%(3). The single most important and best defined risk factor for adenocarcinoma of the uterus is unopposed elevated estrogen levels in menopausal women. In Sub Saharan Africa where hormonal replacement therapy is rarely practiced, obesity is the predominant risk factor for unopposed elevated estrogen in menopausal women. Adipose tissue has active aromatase enzymes thus adrenal androgens are rapidly converted to oestrogens within the adipose tissue of obese individuals. The elevated circulating estrogens cause hyperplastic growth of the endometrium. Other risk factors include chronic anovulation, low parity, nulliparity, early menarche, late menopause, and use of tamoxifen, diabetes mellitus, race with blacks getting more affected and history of breast or ovarian cancer. Use of combined oral contraceptive pill is a known protective factor(1,3,4,7,8).

Endometrial cancer does not have a screening modality for its precancerous lesions. However, postmenopausal bleeding is the predominant symptom (75%) that should warrant investigation for endometrial cancer. Fractional endometrial curettage is used to diagnose and determine extent of the lesion. The mainstay of treatment is total abdominal hysterectomy and bilateral salpingo-oophorectomy with or without radiation of the vaginal vault. In advanced disease stage and surgically high risk patient's radiotherapy is used for treatment. For the recurrent metastatic lesions chemotherapy is

the treatment of choice(3,4)

Cervical Cancer

Cervical cancer whose etiology is Human papillomavirus (HPV) is the second most common cancer among women worldwide. The incidence of cervical cancer in Kenya is estimated to be 2,454 women per year with the annual number of deaths estimated at 1,676 women. The incidence of cervical cancer is projected to rise to 4,261 resulting in 2,955 deaths in 2025(4,9,10). A 10 year (1981-1990) analysis of Kenyan hospital data indicate that cancer of the cervix accounted for 8-20% of all cancer cases and 70-80%of all genital tract cancers. In North America in a 15 year analysis (1973-1987), the five year survival rate was 97, 54.9, 40.5 and 12.4% for FIGO stage I, II, III and IV(1,8).

The risk factors are early age at first coitus, multiple partners, high parity, smoking, sexually transmitted diseases and immunosupression mostly from HIV. Cervical cancer has a well defined natural history with a long period of precancerous stage; cervical intraepithelial neoplasia (CIN). This has made cervical cancer one of the gynecological cancers with robust screening modalities (11). Despite, availability of a robust screening modality for cervical cancer, screening in Kenya remains opportunistic(12). National Cervical Cancer Prevention Program Strategic Plan 2012-2015 in Kenya indicate that only 3.2%of women aged 18-69 years have been screened for cancer of the cervix(9,13,14).

HPV is the primary cause of 99.7% of all cervical cancers .Globally about 70% of all cases of cervical cancer are caused by HPV types 16 and 18. Infection with one or more of the 15 high risk oncogenic types leads to invasive cervical cancer after 10-20 years. The pathogenesis of the HPV is linked to its replication cycle that effectively evades immunological detection by the host. The virus infects the primitive keratinocytes in the basal layers of squamous epithelia. Integration and replication of the HPV DNA occurs independent of the host cell cycle via its genes E1/E2 and E6/E7 respectively. Viral proteins synthesis and assembly occurs in the proliferative compartment of the epithelia, the gene involved L1/L2. Shedding of HPV periodically in large amounts facilitates transmission to naïve individuals. Over expression of E6/E7 is capable of interfering with important tumour suppressor protein in the host cell leading to cervical dysplasia (13,15)

Cervical cancer symptoms include vaginal discharge, abnormal bleeding, postcoital bleeding, pelvic pain and pelvic mass. The histological types are mainly squamous cell cancer (90%) and adenocarcinoma (10%). Treatment options depend on staging. Radical trachelectomy is an option for women who desire future childbearing and are stagedIA1- IB1<2cm diameter, with a five year survival of 98%. Radical hysterectomy is an option for stage Ib, IIa with a five year survival of 90%. Radiation therapy which is either external beam or intracavitary radium can be used for any stage with a five year survival rate of 90%for stage I (1,8,16).

HIV infection has been shown to be one of the predisposing factors to cervical cancer (10,13). This is particularly important in the Kenyan setting where there is still a high HIV prevalence rate of 6%(17). HIV infection predisposes women to multiple oncogenic

HPV subtypes, leads to persistent HPV infections and leads to a faster progression of CIN to invasive cancer, thus shortening the natural history of cervical cancer drastically(14). A study done on same day colposcopic examination and loop electrosurgical excision procedure (LEEP) at Kenyatta National Hospital, showed similar results for Pap smear cytology, colposcopic and LEEP histology among HIV infected, uninfected and unknown HIV status women(14).

Vaginal Cancer

Primary carcinoma of the vagina is rare and most vaginal cancers are metastatic. The commonest site is in the upper third of the posterior wall, however for choriocarcinoma or endometrial carcinoma metastases are in the lower third of the anterior wall or vault. The median age is 55years. Squamous cell carcinoma accounts for 90% of the cases with a five year survival rate of 40-45%. Clear cell adenocarcinoma is seen in adolescent girls who have had history of intrauterine exposure to diethylstilboestrol. Radiation is the primary mode of treatment but surgery is the treatment of choice for upper vaginal low stage tumor in younger patients. The literature did not yield any studies done specifically in Kenya on Vaginal cancers (3,4). In North America, a 15 year analysis (1973-1987)the five year survival was 64.2% 52.5%,35.9% and 18.3% for stage I, II, II and IV respectively(1,8).

Vulval cancer

Cancer of the vulvar comprises 5%of malignancies of the female genital tract. It's the fourth most common gynecologic malignancy after uterine, ovarian, and cervical. It occurs commonly in postmenopausal women, with median age of 60 years. Other risk factors include vulvar dystrophy, HPV, cigarette smoking, immunodeficiency syndromes and race with European ancestry more predisposed (1,3,4,7). Symptoms are non specific and include pruritus, vulvar bleeding and discharge. Clinical manifestation is unifocal vulvar plaque, ulcer and a mass. Diagnosis of gross lesions is done histologically to determine diagnosis and depth of stromal invasion. If no gross lesion is visible but clinical suspicion is high, colposcopic vulvar examination using 3-5%acetic acid is indicated.

Histology types include; squamous cell (90%), melanoma (5%), basal cell carcinoma (2%), sarcoma (1%) and extramammary Paget's disease (1%). In management of vulvar cancer, surgery is designed to achieve negative margins thus consideration is dependent on the size of the lesion. Chemo-radiation is indicated for advanced stage III &IV. Prognosis of vulval carcinoma depends on HPV positive younger patients tend to have a better prognosis(4).

The five year survival rate was 90.6%, 76%, 62.1% and 38% for stage I, II, III and IV respectively. The survival for the whites was 73.4% and non whites had a less risk of 0.91% with survival of 75.6%(1,5,8)

Choriocarcinoma

Choriocarcinoma is a highly malignant tumor arising from the chorionic epithelium. Choriocarcinoma consist of sheets of anaplastic cytotrophoblast and syncytiotrophoblast without chorionic villi. The hyperplastic trophoblastic column of cells invade the muscle thus evidence of haemorrhage and muscle necrosis. The commonest site of metastases is lung, followed by anterior vaginal wall, brain and liver. Ovarian choriocarcinoma (non-gestational) may also be associated with malignant teratoma or dysgerminoma. Non gestational choriocarcinoma are usually resistant to chemotherapy and radiotherapy thus fatal.

The symptoms include persistent ill health, irregular or brisk vaginal bleeding, continued amenorrhea whereas others are due to metastatic lesions to the various organs. Chemotherapy is the mainstay of treatment curing 85%of patients with non-metastatic choriocarcinoma. Primary surgery has a limited role in management and only decreases the number of courses of chemotherapy. Radiotherapy is indicated in patients with brain and liver metastases. Choriocarcinoma has a good prognosis with a 85% five year survival rate (1,3,15).

2: LITERATURE REVIEW

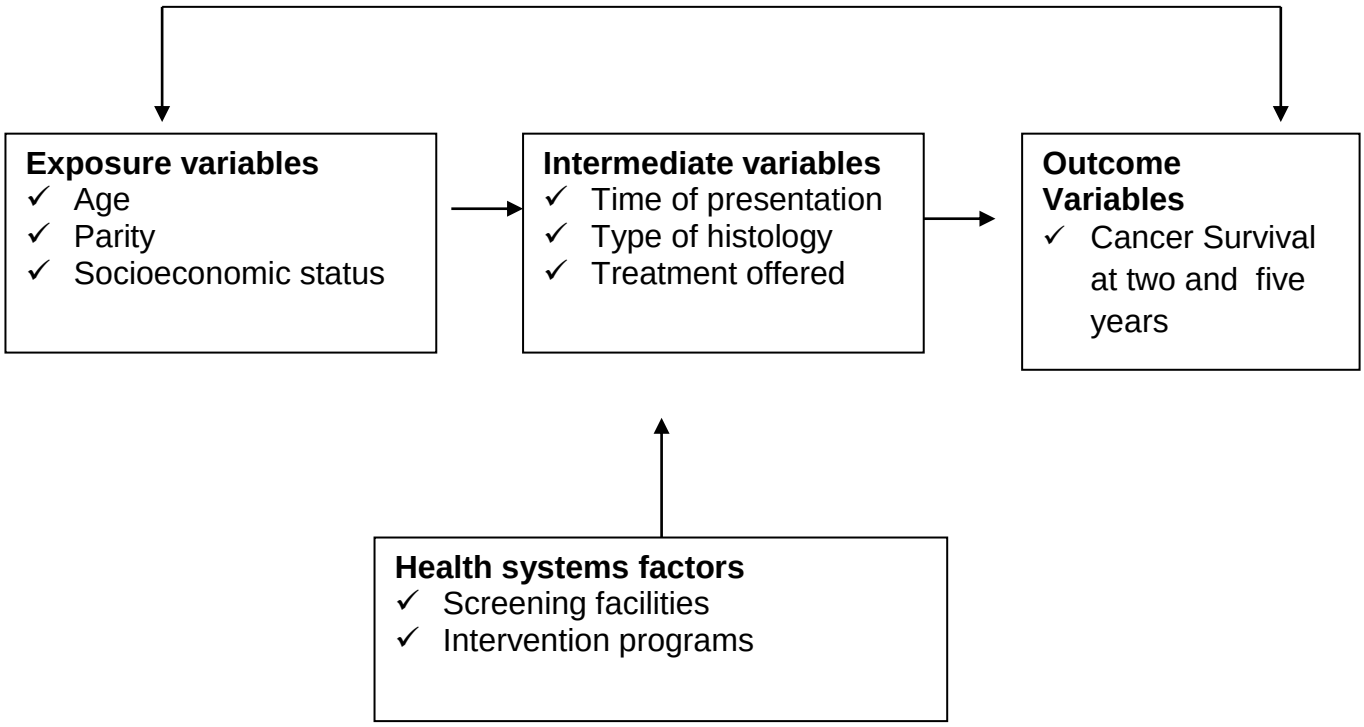
In Kenya, cancer ranks as the third cause of morbidity and mortality after infectious and cardiovascular disease. Cancer accounts for 7% of the total national mortality each year. It is estimated that the annual incidence of cancer is about 28,000 new cases with an annual mortality of 22,000 cases. Over 60% of those affected are below 70 years while the risk of getting cancer before 75years of age is 14% and the risk of dying of it is estimated at 12%(9).

World cancer Report 2014(18),estimates the global all cancer incident rates as about 14.1 million cases per year. This is expected to rise to 22 million annually within the next two decades. In the same period cancer deaths were predicted to rise from an estimated 8.2 million annually to 13 million. The comprehensive global cancer statistics from the International Agency for Research on cancer (IARC) indicate that globally gynecological cancers account for 19% (969,000/5.1 million) estimated new cancer cases (19). Unfortunately, Sub Saharan Africa disproportionately bears the burden of female genital tract cancers of up to 35% of all female cancers compared to 13% in North America(15) and 12% in Canada (20). This discrepancy may be attributed to organized systematic cancer screening and intervention programs in developed countries(20) compared to few and mainly opportunistic screening among the developing countries(13). In addition, management of invasive cancers still remains a challenge and limited to few referral centers(2).

In 2012,Globocan estimates for Kenya's new cases for cervical, endometrial and ovarian cancers were 4802, 643 and 748 respectively, an upward trend in comparison to the 2008 survey that showed 2454,319 and 719 respectively(19).This increase may be attributed to increased awareness and availability of modern diagnostic equipments(18).In 2012 mortality estimates for cervical, endometrial and ovarian cancer were 2451, 211 and 538 respectively. These were higher than the 2008 mortality estimates for the same which were 1676,107 and 542 respectively (19). The increase in mortality may be attributed to the late presentation of the patients and detection of the disease process at advanced stages(2). Of all the genital cancers, cervical cancer takes the lead in Sub Saharan Africa, and has been showing an upward trend over the years. A study in Botswana (2006-2009), showed that cancer of the cervix constituted 80.6% of all genital cancers, followed by endometrial, vulval and ovarian cancer 10.0%, 4.5% and 3.4% respectively (7).

CONCEPTUAL FRAMEWORK

Figure 1: Conceptual Framework



Conceptual Framework Narrative

Reproductive tract malignancies are a major cause of morbidity and mortality among women. In analysis of the various prognostic factors it will aid in policy formulation, guidelines and subsequent management. The two and five year survival rate for the same will call in for individualized care among the populations in an attempt to avert the catastrophic outcome.

JUSTIFICATION

Cancer incidence remains a global problem, with the developing countries bearing the highest burden in morbidity and mortality. More than half of the cancers in 2012 occurred in low resource countries with an extrapolated further increase by 2025. Despite this huge burden, there is a paucity of data for the female reproductive tract cancers in these settings. This is exemplified by a lack of national cancer registries. For instance, Kenya does not have a robust cancer registry. What is available are hospital based data that are largely paper based. Data is significant in quantifying disease pattern, risk factors and prognosis for use by policy makers.

In Kenya, data from hospital based registries indicate that, cancer of the cervix accounts for 70-80% of all cancers of the female reproductive tract, and 8-20% of all cancer cases for the period 1981-1990. The Nairobi cancer registry records 10-15 new cases of cervical cancer in Nairobi each week.

Critiques of the millennium development goals (MDG'S) attribute omission of the non-communicable diseases (NCD'S) including cancers, in the almost completed 2015 development agenda to a lack of data. The post 2015 sustainable development agenda re-emphasized to avert the current burden in low & medium resource countries; thanks to some data on cancers in the last 15 years. Despite this improvement on data over that last 15 years, resource limited settings including Kenya still lags behind.

This study seeks to determine the trend and follow up of women aged more than 15 years with reproductive tract cancers in KNH over four years duration 2008 -2011. Results from this study will offer baseline data to better understand female reproductive tract cancers in our setting. Results from this study will be useful for strengthening and development of policy and guidelines for gynecologic cancers. Results can be compared to other similar settings.

RESEARCH QUESTION

What are the trend and follow up of women aged more than 15years with reproductive tract cancers in Kenyatta National Hospital? (2008-2011).

BROAD OBJECTIVE

To determine the trend and follow up of women aged more than 15years with reproductive tract cancers in Kenyatta National Hospital over four year duration, 2008 – 2011.

SPECIFIC OBJECTIVE

Among women aged more than 15years with cancers in Kenyatta National Hospital to determine the:

1. Proportion of cancers contributed by reproductive tract malignancies.
2. Trends of reproductive tract malignancies.
3. Two and four year follow up of women with reproductive tract cancers.
4. Prognostic factors associated with duration of follow up for reproductive tract cancers.

3: STUDY METHODOLODY

Study Design

This was an observational descriptive study. The trend and follow up of women aged more than 15years with reproductive tract cancers in Kenyatta National Hospital; over four year duration 2008 -2011 were analyzed using their case records. Analysis of all women with cancers was undertaken to determine the proportion of cancers contributed by reproductive tract malignancies, the two and four year follow-up, the trend over the four years and the prognostic factors associated with duration of follow-up.

Study Site and setting

The study was carried out at KNH Pathology Laboratory, University of Nairobi (UON), Anatomic Pathology Department and Kenyatta National Hospital Records Department, Reproductive Health Department, Nuclear medicine department and KNH Palliative care unit. The KNH Pathology Department is situated within the university complex. It is integrated with the UON core functions of training and research. It also carries out a wide range of advanced immunotyping of tissues. For complicated cases consultative discussions among experts including teleconferencing with Ohio State University among other collaborating partners is done. The personnel work harmoniously to achieve the mission and vision of excellence, quality care for the patients and forensics'. The specimens are received on weekdays and majority, over 90% are from KNH. On receipt at the laboratory they are accorded a laboratory number for referencing and registration. As per the laid out standards operating procedures, tissue preparation, reporting and storage is done. The KNH Health Records Department collects the reports for filling in patients' case records for definitive clinical management by the clinical team. A copy of

the report is archived in the UON Pathology Department museum. In a year, the KNH Pathology Department reports approximately 6,000 female specimens, out of which 30% comprise of reproductive health cancers.

Kenyatta Records Department has a centralized filling system that is largely paper based. Terminal digit filling system is used solely for the purpose of convenience and large numbers. Each service delivery point within KNH has a designated Records Officer/unit. Each client /patient is accorded a unique number at the initial service point and forms a reference for that particular patient within the hospital for all services and subsequent hospital visits. Outpatient/day visit case record files are returned to the central office at the close of the day for coding as per International Classification of Disease 10 and International Classification of Procedure in medicine. Indexing is subsequently done electronically. The health information personnel maintain a daily bed return for the inpatients; this captures any transfer in or out and discharges. Discharges include the deceased, alive and absconder. On receipt of the patients' case records at the Records Department, signing is done for purposes of accountability, indexing and coding. Most of the patients/clients seen are from within East Africa, however referrals for specialized services span all over the African Nations. The files are retrieved a week prior to the client/patient next appointment/admission. The statistical unit is mandated with the task of availing the data for planning and research.

The KNH Reproductive Health Department offers a wide range of specialized services in obstetrics and gynecology. The services are offered from various service points. The Department has a designated unit at the Accident and Emergency Department that is covered around the clock by a sitting Registrar. The Registrar triages the patients for ward admission, clinic follow up or treat-and-discharge. All cold gynecologic oncology patients are followed up at the Gyn-Oncology clinics on Fridays. Acute patients are admitted to ward 1D. The scheduled elective gynecology patients are admitted in ward 1B for surgical intervention and chemotherapy. Radiotherapy services are centralized at the Nuclear Medicine Department.

A multidisciplinary approach to care is used in managing the Gyn-oncology patients. The team includes: Palliative Care Unit, Renal Unit, Radiology Department, and Nutrition Department among others.

Study Population

Histology reports of all female patients ≥15years who had histologically confirmed diagnosis of any cancer dating 1st January 2008 –31st December 2011 at UON Pathology Department museum.

Inclusion Criteria

1) Case records of women aged more than 15years with reproductive tract cancers.

Exclusion criteria

1) Case records that cannot be retrieved in the Kenyatta National Hospital Records Department.
2) Case records retrieved but with missing data outcome i.e. no entry or exit date.
3) Histology findings made from autopsy specimens.
4) Patients with indeterminate sex as indicated on the histology request form

Sample Size and Sampling procedure

The sample size was determined by using a statistical formula as used by Fisher et al 2003. A previous study in KNH reported two and five year survival rates at 50% and 20% respectively(2). In this study the 2 and 5 year survival rate were used as surrogates for 2 and 4 year follow up rates. Hence, the two year survival rate was used for sample size estimation because it would give the largest sample size on follow up; the following formula was used;

$$\mathbf{n} = \frac{\mathbf{z^2} \times \mathbf{p(1-p)}}{\mathbf{d^2}}$$

n=required sample size

z= confidence level at 95% (standard value of 1.96)

p =proportion of women surviving at 2 years (50%).

d = margin of error at 5% (standard value of 0.05).

$$\mathbf{n} = \frac{1.96^2 \times 0.5\ (1-0.5)}{0.05^2} = 384$$

Given that the KNH Pathology Laboratory reports about 6000 female specimens, the sample size formula after correction for a definite population for less than 10 000 is

Cs=n x N/N+n

Cs=the corrected sample size

N=the total number of women with reproductive cancers (6000)

n=the calculated sample size from Fishers et al 2003 before correction

384 x 6000/6000+384=360.9

Minimum sample size is therefore taken **361**

Similar studies undertaken in KNH have shown a record retrieval rate of 80% and availability of outcome in 85% of the records(2). Therefore the above sample size was inflated to determine the number of case records to retrieve from the records department.

Inflate for retrieval rate =361 x 100/80 = 451

Inflate for missing outcome = 451 x 100/85 = 530

Therefore 530 female reproductive cancers were identified from UON Pathology Department Museum and case records retrieved from KNH records.

Study Procedures

Recruitment of study participants started at the UON Pathology Department Museum register. All records of women aged $\geq$ 15 years with histology for all cancers were retrieved from this register. At this stage, age, histology, patient identification number

and the date biopsy specimen was received was collected for one thousand and eighty six women with reproductive tract cancer records. One thousand seven hundred and sixty five women with non reproductive tract cancers were excluded from the study at this point after doing their respective cancer counts using the 1CD 10 classification of disease. Using the patient identification number, Five hundred and thirty case records for women with reproductive tract cancers were to be retrieved from the KNH Records Department. However, Four hundred and twenty nine case records were retrieved accounting for 80% file retrieval rate. Three hundred and ninety three case records had complete data for analysis thus data outcome rate was 90% slightly higher than previous studies done in KNH that had 85%.

The date when the biopsy specimen was received in the KNH Pathology Laboratory was the entry point for this study. For patients whose vital data was not available, the last date of clinical review was considered the date of lost-to-follow up (LFU). One hundred and one case records that did not have an entry or exit date were excluded from the study due to missing outcome data. No verbal autopsy was carried out because of the retrospective nature of the study and choice of doing passive data collection rather than active.

The recruitment process is summarized in figure 2.

Recruitment into the study

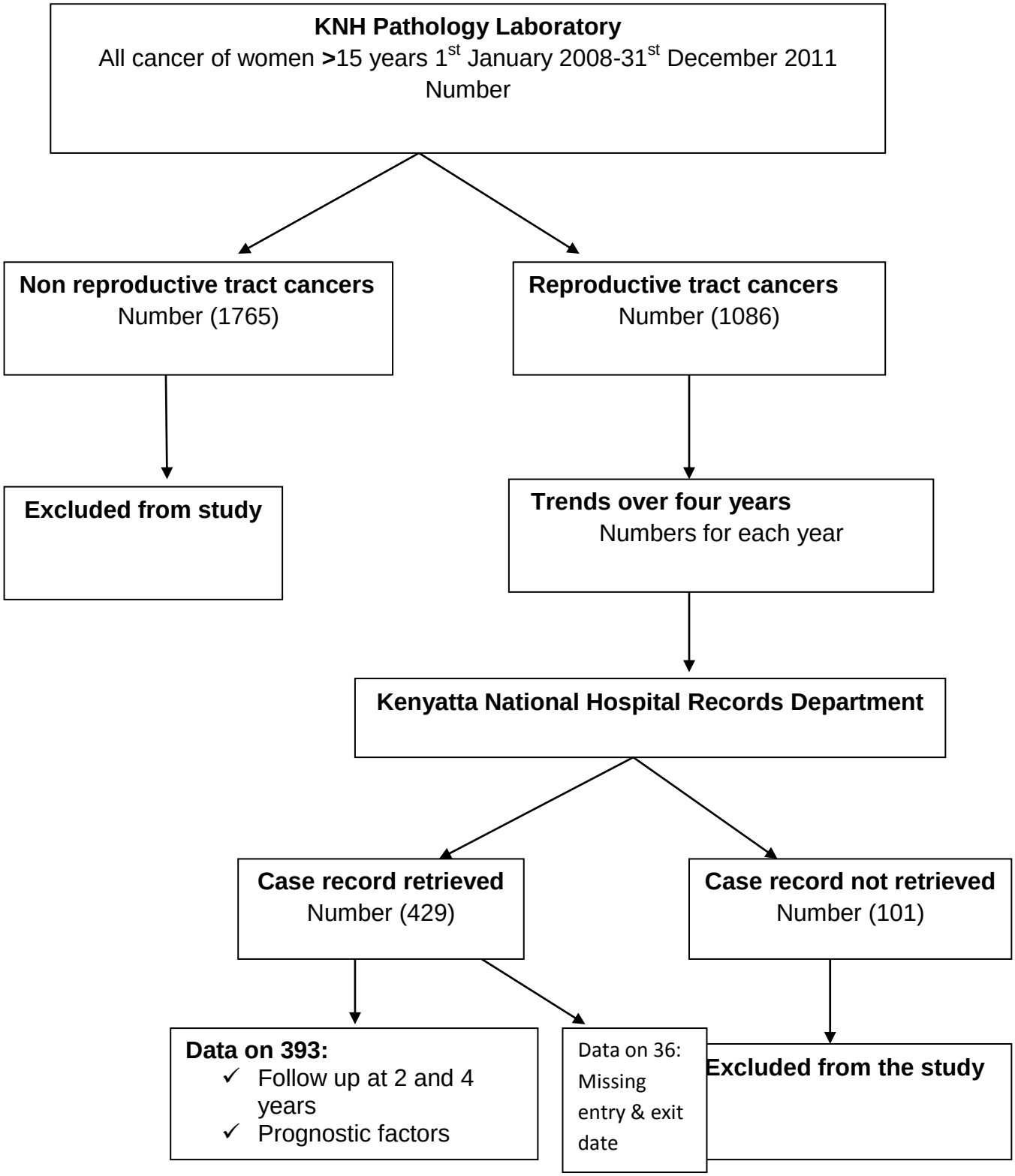
Five hundred and thirty women with reproductive tract cancers were identified from the UON Pathology Department Museum register from a total of one thousand and eighty

six for the four year duration. To ensure representation of the various reproductive cancers probability proportional to size sampling strategy was used with the more cancers contributing more cases compared to the rare cancers. A sampling frame for each of the reproductive cancers was created and using a random numbers generation table, the required sample was retrieved for each of the cancers. For this study, the missing file was replaced by the next unit number for uniformity. This was undertaken to minimize the possible effect of missing data bias on the findings.

Study personnel

The Principal Investigator was responsible for collection of the data and the day to day running of the study.

FIGURE 2: RECRUITMENT PROCESS



Data Variables

Outcome and exposure variables with their sources will be described according to the specific objectives as shown in table 1.

Table 1: Outcome and exposure variables with their sources of data according to objective

Objective	Outcome variables	Exposure variables	Sources of data
1) The proportion of cancers contributed by reproductive tract malignancies.	✓ The proportion of reproductive tract cancers.	✓ Number of all cancers in women ≥ 15 years. ✓ Number of reproductive tract cancers.	✓ UON Pathology Department Museum registers.
2) The trend of reproductive tract malignancies.	✓ Trends over four years (2008-2011).	✓ Numbers per year for: ovary, fallopian tube, endometrial, cervical, vaginal, vulva and choriocarcinoma.	✓ UON Pathology Department Museum registers.
3) The two and four year follow up of women with reproductive tract cancers.	✓ Two and four year follow up of reproductive tract cancers.	✓ Date when biopsy specimen was received. ✓ Date of death or lost-to-follow up (LFU).	✓ UON Pathology Department Museum registers. ✓ Patient's case record. ✓ KNH Palliative Unit.
4) The prognostic factors associated with duration of follow up.	✓ Duration of follow up.	✓ Characteristics: education, age, parity, occupation, marital status, religion, residence, home village, referred from, NHIF contribution. ✓ FIGO staging. ✓ Histological type and grade. ✓ Lymph node status. ✓ Management: chemotherapy, surgery, radiotherapy or a combination.	✓ UON Pathology Department Museum registers. ✓ Patient's case record at KNH Records Department. ✓ Nuclear Medicine department (Radiotherapy).

Data Collection and Management

Data collection was done with the aid of a data abstraction form (appendix 1). Each eligible patient record had a separate data abstraction form completed by the Principal Investigator. For purposes of case record retrieval, patient unique identifying number was used to retrieve case records from the KNH Records Department. To maintain confidentiality a study number was assigned henceforth.

At the end of each data collection day, verification for missing data was done. Data from the abstraction form was entered into an Access database that was pass word protected.

Data Analysis Methods

Descriptive analysis was undertaken and missing data quantified. Proportions were reported for categorical data while mean and standard deviation was reported for continuous variables. The proportions of reproductive cancers were reported as the number of reproductive cancers among all female cancers archived at the UON Pathology Department Museum. Trend in reproductive cancers were presented as counts registered over the study period stratified into annual quarters. Therefore for objective 1 and 2 descriptive analysis was undertaken as outlined above.

For objective 3 and 4 inferential statistics was undertaken with the outcome of interest for this study being 2 and 4 year follow up from date of diagnosis. Women lost to follow up were censored at the time in point when they last had contact with a health care

provider in any of the designated unit for multi disciplinary management.

Inferential statistics were used to determine the association between 2 and 4 year follow up and explanatory variables using a *chi-square* test for categorical variables and a student t-test for continuous variables.

Poisson regression analysis was used to determine the magnitude and direction of effect for association between explanatory variables and duration of follow up. A multivariable model to determine factors that predict follow up for reproductive cancers was built as a final step.

Ethical Considerations

The proposal was presented for approval to the Kenyatta National Hospital/ University of Nairobi Ethics & Research Committee (KNH/UON-ERC).The study commenced after approval by KNH/UON-ERC and permission granted by KNH Pathology Laboratory, UON Pathology Department, KNH Records Department, KNH Reproductive Health Department, Nuclear Medicine Department and KNH Palliative Care Unit.

There were minimal risks foreseen with this study because of its retrospective nature. Confidentiality was maintained at all times. No patient identifiers were analyzed. All research data was kept by the Principal Investigator in a lockable cupboard and all electronic data were pass word protected.

No patients, relatives or guardians were interviewed for this study, hence no informed consent required.

Limitation

One hundred and thirty seven case records could not be included in the study because they were either missing in the records department or had no entry and exit dates and hence inappropriate for the study. At the same time some of the case records used in this study missed data for some of the variables. To mitigate the possible effect of these limitations, random sampling was used to replace the missing and or inappropriate case records. Furthermore the case records analyzed were increased by 9%.

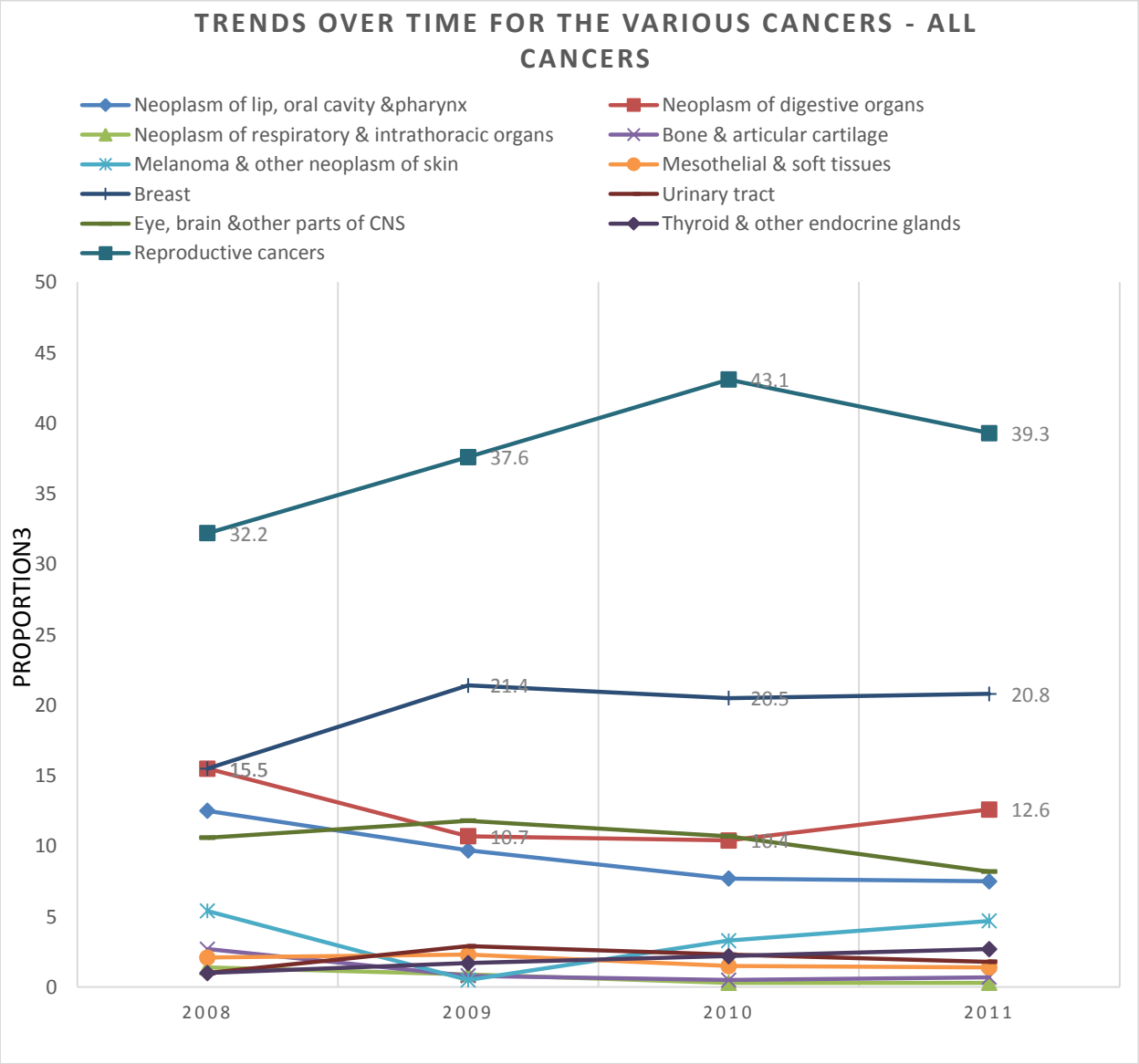
4: RESULTS

The mean age for the 393 study subjects whose case records were analyzed was 50 years (SD 15 years), with a median (IQR) =47(39 - 60) years and range of 25 - 94 years (table2).

Table 2: Socio-demographic characteristics of women aged more than 15 years with reproductive tract cancers in KNH, 2008- 2011.N=393		
Variable		**n(%)**
Marital status	Single Married Divorced/separated Widow Unknown	58(14.8) 252(64.1) 15(3.8) 61(15.5) 7(1.8)
Religion	Christian Muslim Others Not indicated	379(96.4) 9(2.3) 1(0.3) 4(1.0)
Occupation	Employed Self-employment Unemployed Not indicated	50(12.7) 115(29.3) 213(54.2) 15(3.8)
Education level	None/nursery Primary Secondary College Unknown	72(18.3) 176(44.8) 71(18.1) 25(6.4) 49(12.5)
NHIF	Yes No Not indicated	264(67.2) 108(27.5) 21(5.3)
Referred from	KNH Other within Nairobi Other outside Nairobi Unknown	17(4.3) 76(19.3) 287(73.0) 13(3.3)

Of the 393 study subject with reproductive tract malignancy, majority of the respondents were married 64% as shown in table 2. A slightly larger proportion of 67.2% had an NHIF insurance cover. Most of the respondents were referred from outside Nairobi 73%.

Figure 3: Proportion of cancers contributed by reproductive tract malignancies among women aged more than 15 years in Kenyatta National Hospital, 2008- 2011



As illustrated in Figure 3, reproductive tract cancers accounted for approximately 38% and took a lead among the various cancers diagnosed on the women aged more than 15years.

Figure 4: Trend of reproductive tract malignancies among women aged more than 15 years in Kenyatta National Hospital, 2008- 2011

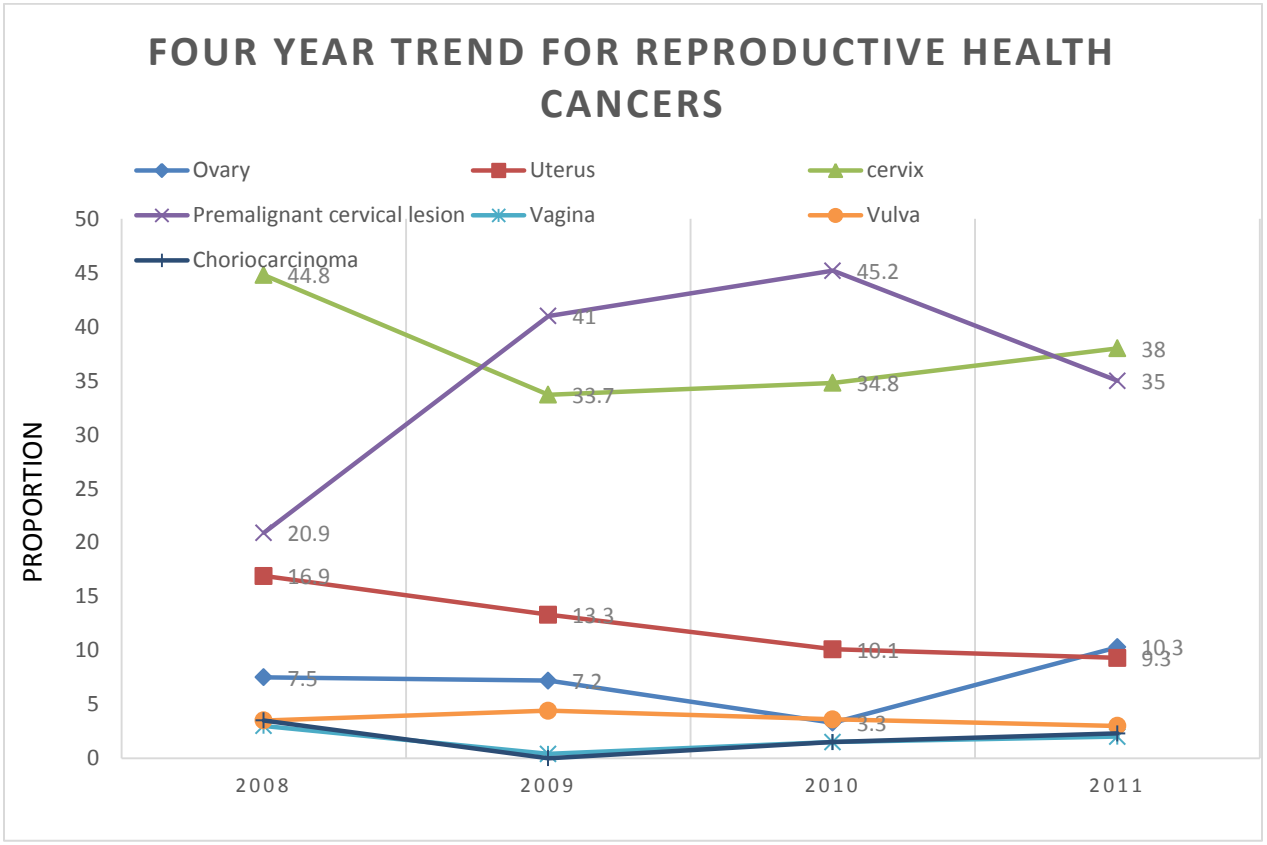
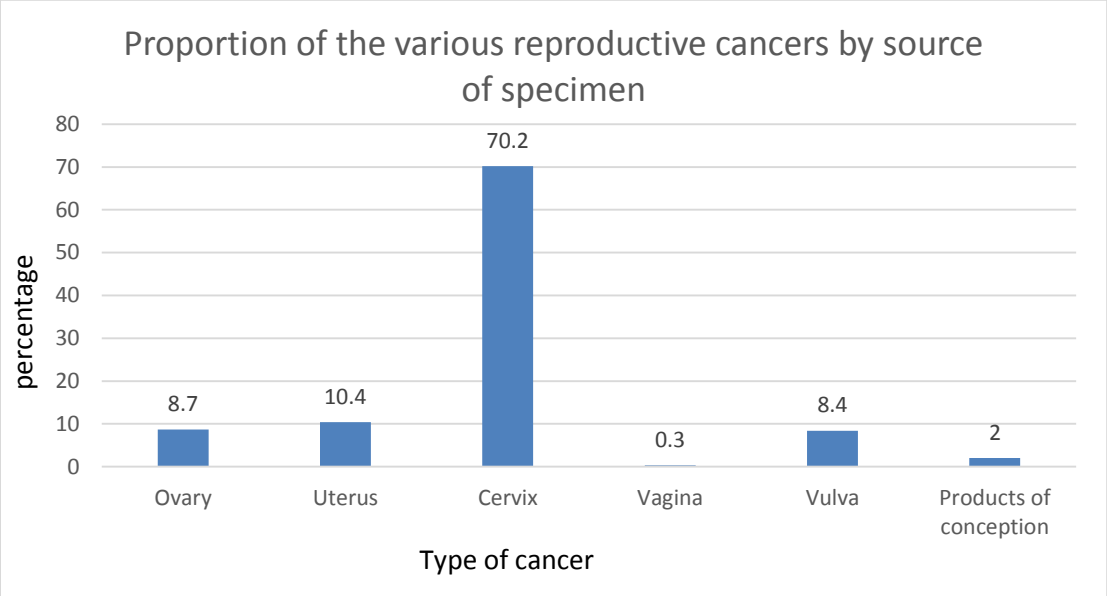


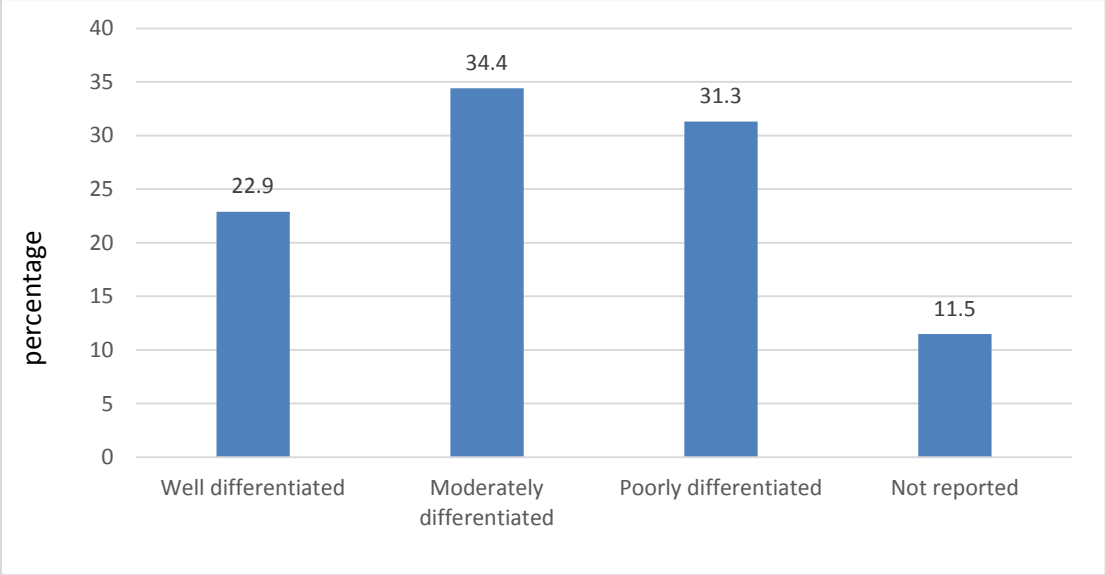
Figure 4 depicts a rising trend for diagnosis of premalignant cervical lesions for the period 2008 to 2010 and the reverse for cervical cancer. In 2011 a drop in diagnosis of premalignant lesions is noted and a subsequent increase in cervical cancer. A downward trend is observed for the uterine cancers whereas vulva cancers remain static. Cancers of the ovary show a slow rise towards the end of the study.

Figure 5: Proportion of the various female reproductive tract cancers among women aged more than 15 years in Kenyatta National Hospital, (N=393)



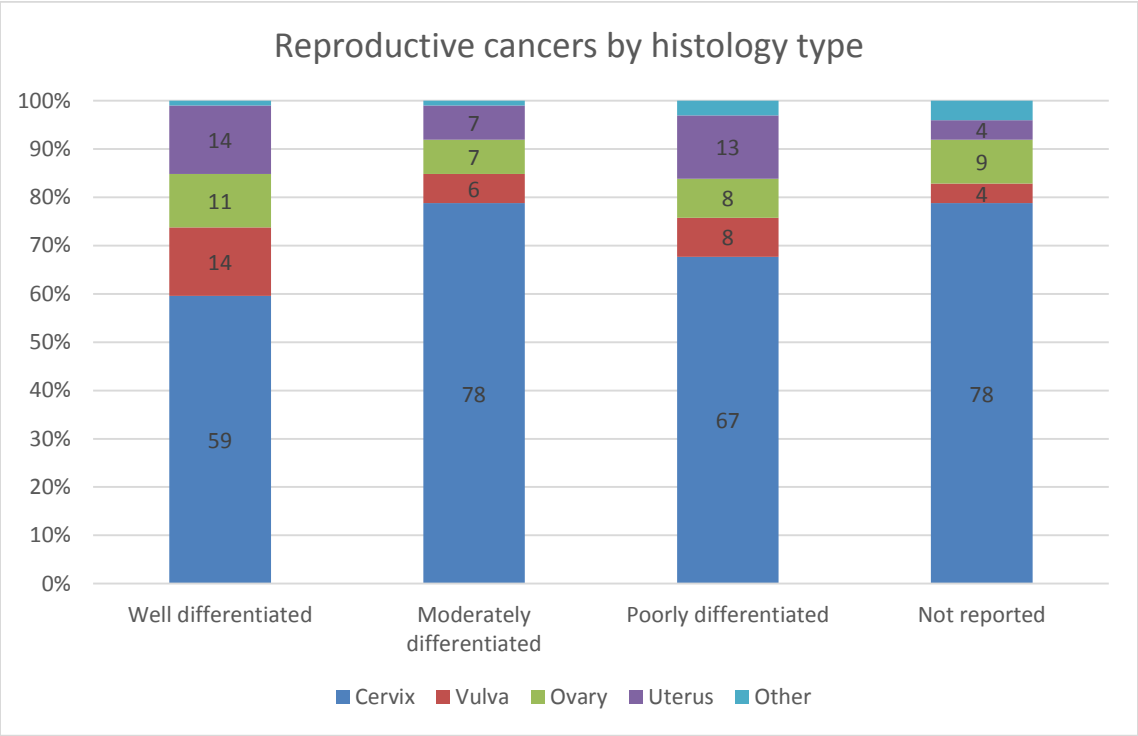
Of the reproductive tract cancers, cancer of the cervix comprised the majority 70.2% while cancers from products of conception and cancer of the vagina being the least reported at 2% and 0.3% respectively in Figure 5.

Figure 6: Histological differentiation of the female reproductive tract cancers among women aged more than 15 years in Kenyatta National Hospital, (n=393)



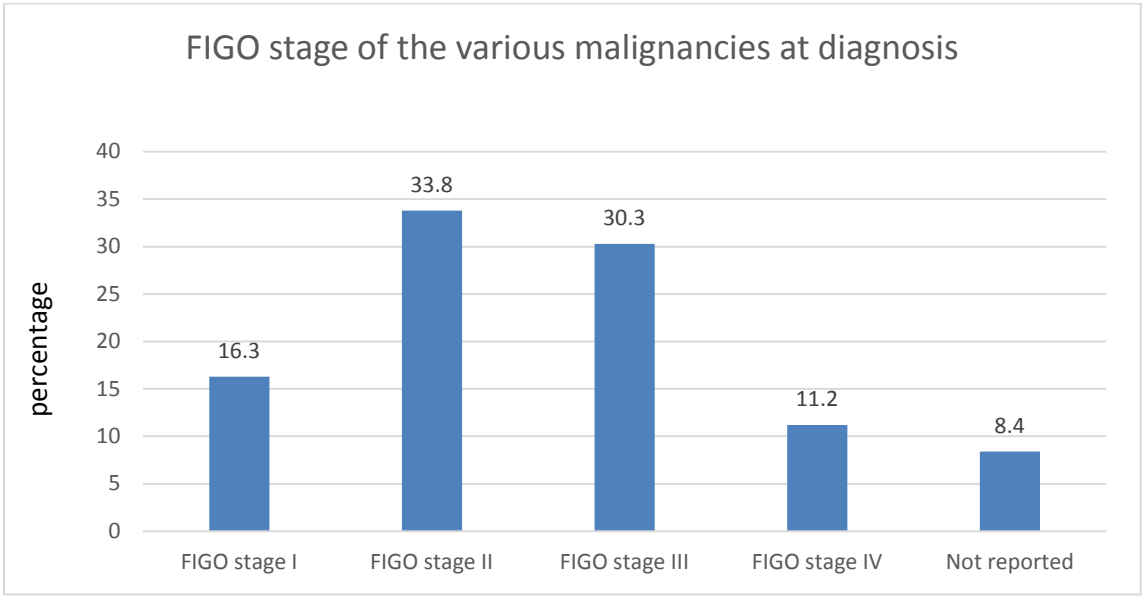
Most of the specimens reported were moderately or poorly differentiated at 34.4% and 31.3% respectively shown in Figure 6.

Figure 6b: Histological differentiation as per the specific female reproductive tract cancers among women aged more than 15 years in Kenyatta National Hospital.



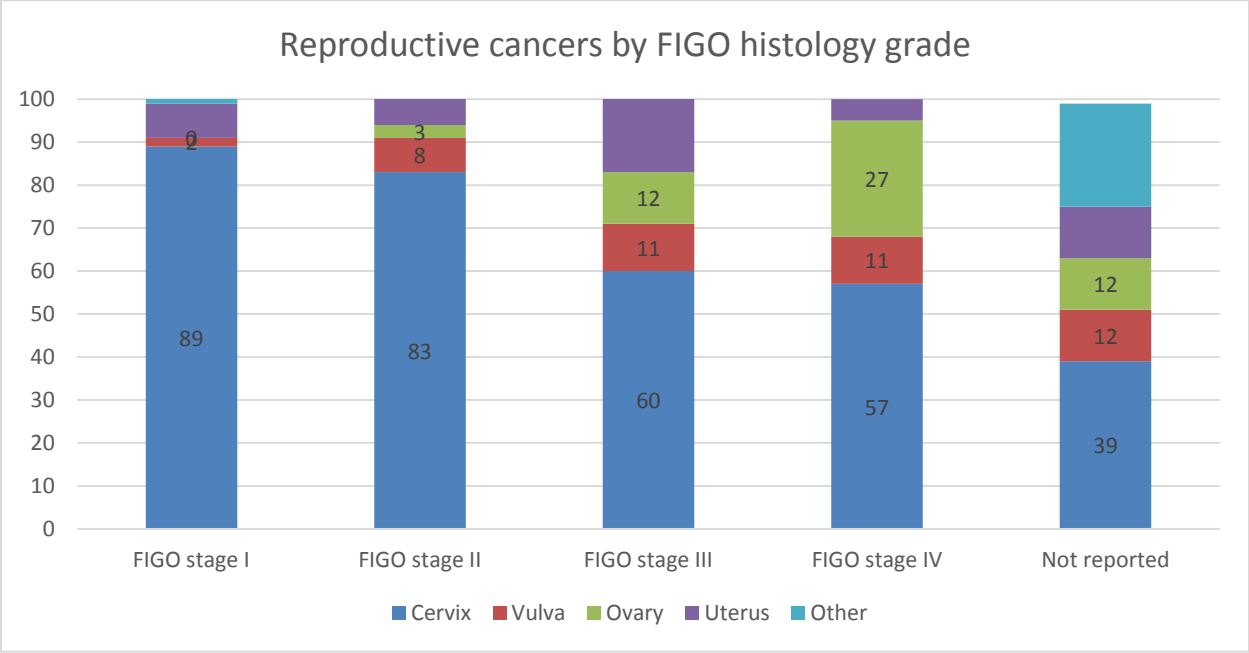
A further analysis as per the specific cancer type is as shown above with cancer of the cervix forming the larger portion among all levels of differentiation

Figure 7: FIGO stage at diagnosis for the female reproductive tract cancers among women aged more than 15 years in Kenyatta National Hospital, 2008-2011.



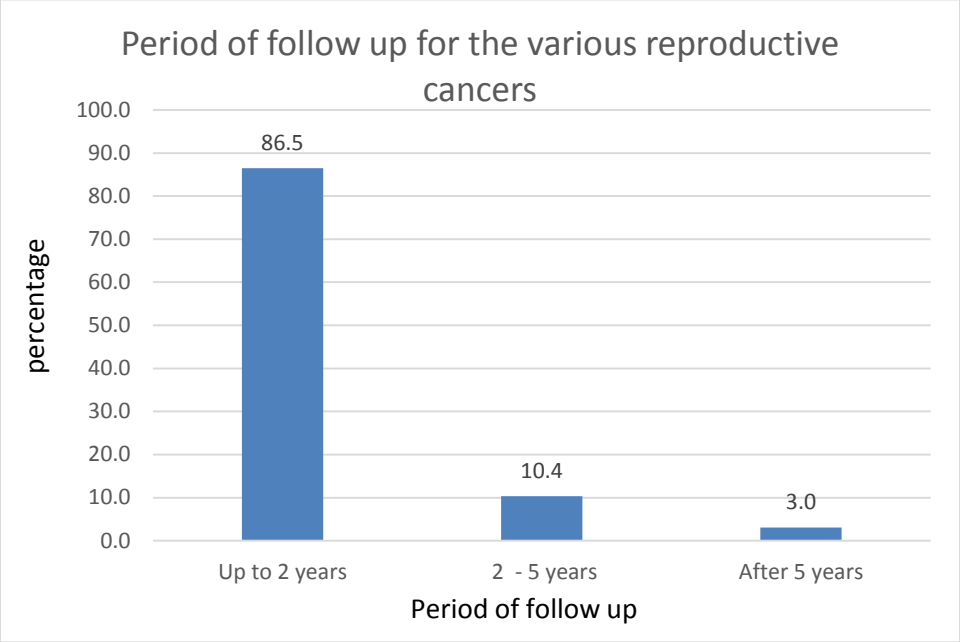
Majority of the respondents were either at FIGO stage II or FIGO stage III, 33.8% and 31.3% respectively (figure 7)

Figure 7b: FIGO stage at diagnosis for the specific female reproductive tract cancers among women aged more than 15 years in Kenyatta National Hospital.



Majority of the Cancer of the cervix was FIGO stage 1 & II; 89% and 83% respectively, cancer of the ovary was mainly diagnosed at FIGO Stage IV at 27%

Figure 8: Duration of follow up for the various female reproductive tract cancers among women aged more than 15 years in Kenyatta National Hospital, 2008-2011.



As shown in Figure 8, only 3% of the respondents were followed up within KNH for more than 5 years. However, the majority 86% was followed up for up to 2 years from the time of diagnosis.

Table 3: Bivariate analysis for associations of demographic factors with lost to follow up at 2 years among women aged more than 15 years in Kenyatta National Hospital, 2008- 2011

		Loss to follow up		OR	95% CI		P Value
		before 2 years N=340 n%)	After 2 years N=53 n(%)				
Marital status	Single	56(16.5)	2(3.8)	Ref			
	Married	210(61.8)	42(79.2)	0.18	0.04	0.76	0.02
	Divorced/separated	14(4.1)	1(1.9)	0.50	0.04	5.92	0.582
	Widow	54(15.9)	7(13.2)	0.28	0.05	1.39	0.118
	Unknown	6(1.8)	1(1.9)	0.21	0.02	2.73	0.235
Religion	Christian	328(96.5)	51(96.2)	Ref			
	Muslim	8(2.4)	1(1.9)	1.24	0.15	10.15	0.839
	Others	1(0.3)	0(0.0)	-----	-----	-----	-------
	Not indicated	3(0.9)	1(1.9)	0.47	0.05	4.57	0.513
Occupation	Employed	38(11.2)	12(22.6)	Ref			
	Self-employment	105(30.9)	10(18.9)	3.32	1.32	8.30	0.01
	Unemployed	184(54.1)	29(54.7)	2.00	0.94	4.28	0.072
	Not indicated	13(3.8)	2(3.8)	2.05	0.40	10.41	0.385
Education level	None/nursery	65(19.1)	7(13.2)	Ref			
	Primary	158(46.5)	18(34.0)	0.95	0.38	2.37	0.905
	Secondary	55(16.2)	16(30.2)	0.37	0.14	0.96	0.042
	College	19(5.6)	6(11.3)	0.34	0.10	1.14	0.08
	Unknown	43(12.6)	6(11.3)	0.77	0.24	2.45	0.661
	Not indicated	7 (2.0)	3 (5.7)				
NHIF	No	240(70.6)	24(45.3)	Ref			
	Yes	82(24.1)	26(49.1)	0.32	0.17	0.58	<0.001
	Not indicated	18(5.3)	3(5.7)	0.60	0.16	2.18	0.438
Referred from	KNH	15(4.4)	2(3.8)	Ref			
	Other within Nairobi	62(18.2)	14(26.4)	0.59	0.12	2.88	0.515
	Other outside Nairobi	255(75.0)	32(60.4)	1.06	0.23	4.86	0.938
	Unknown	8(2.4)	5(9.4)	0.21	0.03	1.36	0.102

Overall, of the demographic factors, having a NHIF insurance cover, marital status, secondary education level were significantly associated with less loss to follow up at 2 years. Respondents with a NHIF insurance cover had significantly decreased risk of loss to follow up (LFU) within 2 years by 0.32 times (95% CI 0.17 – 0.38; P value 0.001) when compared to respondents without a NHIF insurance cover.

Compared with respondents who were single, respondents who were married had a significantly decreased risk of loss to follow up within 2 years (OR 0.18; 95% CI 0.04 – 0.76; p value 0.020). Similarly, Compared with respondents who had no education respondents who had secondary education had a significantly decreased risk to LFU within 2years OR 0.37, 95% CI 0.14-0.96; p value 0.042.This is summarized in table 3 comprehensively.

Table 4: Bivariate analysis for associations of the various risk factors with LFU at 2 years among women aged more than 15 years in Kenyatta National Hospital, 2008- 2011

		Loss to follow up		OR	95% CI		P –Value
		before 2 years n=340	After 2 years n=53				
Irregular menses	No	260(76.5)	34(64.2)	Ref			
	Yes	33(9.7)	15(28.3)	0.29	0.14	0.58	0.001
	Not indicated	47(13.8)	4(7.5)	1.54	0.52	4.53	0.436
Menopause	No	190(55.9)	31(58.5)	Ref			
	Yes	133(39.1)	19(35.8)	1.14	0.62	2.11	0.671
	Not indicated	17(5.0)	3(5.7)	0.92	0.26	3.34	0.905
Contraception	No	208(61.2)	26(49.1)	Ref			
	Yes	108(31.8)	26(49.1)	0.52	0.29	0.94	0.03
	Not indicated	24(7.1)	1(1.9)	3.00	0.39	23.11	0.292
Family history of malignancy	No	313(92.1)	49(92.5)	Ref			
	Yes	8(2.4)	3(5.7)	0.42	0.11	1.63	0.208
	Not indicated	19(5.6)	1(1.9)	2.97	0.39	22.72	0.293
History of smoking or alcohol use	No	299(87.9)	50(94.3)	Ref			
	Yes	22(6.5)	3(5.7)	1.23	0.35	4.25	0.748
	Not indicated	19(5.6)	0(0.0)	1.00	1.00	1.00	
Number of sex partners	One partner	189(55.6)	22(41.5)	Ref			
	Two partners	54(15.9)	14(26.4)	0.45	0.22	0.94	0.033
	> 3 partners	47(13.8)	8(15.1)	0.68	0.29	1.63	0.392
	Not indicated	50(14.7)	9(17.0)	0.65	0.28	1.49	0.307
Coitache	Mean (SD)	17(3.3)	18 (4.4)	1.08	0.99	1.17	0.070

As shown in table 4, history of irregular menses and use of contraceptives were significantly associated with less loss to follow up at 2 years. With respondents who had no history of irregular menses as the reference group, respondents with irregular menses had a significantly decreased risk of being LFU at 2 years by 0.29 times (95% CI 0.14 – 0.58; p value 0.001). A history of previous contraceptive use was significantly associated with a decreased risk of 0.52 times (95% CI 0.29 – 0.94; p value 0.030) when compared to respondents who had no history of contraceptive use. Mean age for

coitache was 17 years in this study 54 study participants(15.9%) had multiple partners with OR 0.45(95%CI 0.22-0.94; p value 0.033). None of the other risk factors were significantly associated with LFU at 2 years.

Table 5: Bivariate analysis for associations of co-morbidities with lost to follow up at 2 years among women aged more than 15 years in Kenyatta National Hospital, 2008- 2011

		Loss to follow up		OR	95% CI		P Value
		before 2 years n=340	After 2 years n=53				
Diabetes mellitus	No Yes	328(96.5) 12(3.5)	51(96.2) 2(3.8)	Ref 0.93	0.20	4.29	0.929
Hypertension	No Yes	305(89.7) 35(10.3)	45(84.9) 8(15.1)	Ref 0.65	0.28	1.48	0.301
HIV	No Yes	287(84.4) 53(15.6)	42(79.2) 11(20.8)	Ref 0.71	0.34	1.46	0.345
STDs	No Yes	335(98.5) 5(1.5)	52(98.1) 1(1.9)	Ref 0.78	0.09	6.78	0.819
PID	No Yes	337(99.1) 3(0.9)	52(98.1) 1(1.9)	Ref 0.46	0.05	4.53	0.508
Endometriosis	No Yes	339(99.7) 1(0.3)	53(100.0) 0(0.0)	Ref 1.00	1.00	1.00	
None/Not indicated	No Yes	139(40.9) 201(59.1)	23(43.4) 30(56.6)	Ref 1.11	0.62	1.99	0.73

Co-morbidities did not influence the duration of follow up as depicted in table 5 the association were not statistically significant.

Table 6: Bivariate analysis for associations of type on management and LFU at 2 years among women aged more than 15 years in Kenyatta National Hospital, 2008- 2011							
		Loss to follow up		OR	95% CI		P Value
		before 2 years n=340	After 2 years n=53				
Chemotherapy	No Yes	279(82.1) 61(17.9)	44(83.0) 9(17.0)	Ref 1.07	0.50	2.31	0.865
Surgery	No Yes	227(66.8) 113(33.2)	28(52.8) 25(47.2)	Ref 0.56	0.31	1.00	0.05
Radiotherapy	No Yes	179(52.6) 161(47.4)	37(69.8) 16(30.2)	Ref 2.08	1.11	3.88	0.021
surgery and chemotherapy	No Yes	332(97.6) 8(2.4)	50(94.3) 3(5.7)	Ref 0.40	0.10	1.56	0.189
surgery and radiotherapy	No Yes	314(92.4) 26(7.6)	48(90.6) 5(9.4)	Ref 0.79	0.29	2.17	0.654
Surgery, chemotherapy, radiotherapy	No Yes	331(97.4) 9(2.6)	49(92.5) 4(7.5)	Ref 0.33	0.10	1.12	0.076
Not indicated	No Yes	319(93.8) 21(6.2)	52(98.1) 1(1.9)	Ref 3.42	0.45	26.00	0.234

None of the various types of management for the cancers were significantly associated with the LFU at 2 years; this is outlined in Table 6.

Table 7: Multivariable model for predictors of loss to follow up at 2 years among women aged more than 15 years with reproductive tract cancers in Kenyatta National Hospital, 2008- 2011

		OR	95% CI		P Value	LRT
NHIF	No	Ref				
	Yes	0.32	0.17	0.61	0.001	0.016
	Not indicated	0.58	0.15	2.27	0.432	
Irregular menses	No	Ref				
	Yes	0.22	0.10	0.48	<0.001	
	Not indicated	1.50	0.48	4.66	0.481	
Marital status	Single	Ref				
	Married	0.14	0.03	0.62	0.01	
	Divorced/separated	0.54	0.04	6.90	0.635	
	Widow	0.19	0.03	1.01	0.051	
	Unknown	0.12	0.01	1.67	0.114	

LRT: Likelihood ratio test

The significant predictors (LRT 0.016) of loss to follow up at 2 years were having an insurance cover, history of irregular menses and being married with all these factors having a decreased risk for loss to follow up respectively shown in table 7.

5: DISCUSSION

Reproductive tract malignancies constituted 38% of all female cancers taking a lead among the various cancers diagnosed on the women aged more than 15years. This has been the trend in the last decade which prompts for more concerted efforts in halting the untoward effect of the disease. With the increasing numbers of new cancers and the morbidity associated it has become a Global challenge and worse off for sub Saharan Africa(4).

Among the reproductive tract malignancies, cervical cancer tops' the list followed by uterine, ovarian and vulval. The same scenario is seen in a relatively similar study in Botswana(7). The trend depicted for the premalignant cervical lesions and cervical cancer are of a more direct relationship i.e. with increased diagnosis for the premalignant lesion the later decreases. This may be due to a clear, well outlined protocol for screening and intervention available at the point of care. A previous study done on same day colposcopic examination and loop electrosurgical excision procedure showed minimal overtreatment and no delay for treatment of cervical intraepithelial neoplasia in KNH, Kenya(14).

Cancer follow up and survival is the main indicator of outcome of cancer health services or treatment, and an important component in evaluating cancer control strategies. Challenges of lost to follow up are common in low or medium resource countries due to deficiencies in health infrastructure and recording of health statistics among others. . In this study we sought to estimate the follow up rate at 2 and 4 years. Majority of the patients' were followed up to 2years i.e. 86.5%, 10.4% up to 5years and only 3% were

followed up after 5years. In depth inferential analysis of bivariate associations, insurance status (NHIF), secondary education level, marital status (married), irregular menses, and contraceptive use were significantly associated with loss to follow up at 2years.

This compares with other study findings that the socioeconomic, demographic and disease related factors largely determine the compliance to treatment and follow up(3). In my study a multivariable association done identified possession of an insurance cover by NHIF, marital status (married) and irregular menses to have more statistical significant associations with decreased risk to LFU at 2years.Patterns of long-term follow up care for patients treated for cancer are not well characterized. However, lifelong follow up is frequently recommended though the perceived risk of recurrence, late long term effects and risk of second cancer are low and could be varied as per the cancer type.

In a study at a Major Cancer Hospital in South India on factors associated with LFU/drop-outs of cervical cancer patients (2006-2007), among a total of 784 patients; drop-out rates 94(12%) were associated with disease related factors i.e., higher chances of drop out among higher stages and ischaemic heart disease (21). Patients in the LFU group 690(34%) were affected mainly by socioeconomic, demographic and disease related (SEDD) factors. Older patients, widowed/divorced/separated/unmarried, middle school education, poorer performance status and in higher stages were likely to be LFU(21). The LFU for the study was 34% in comparison to my study it was nearly

half i.e. 86.5% at two years, though I combined the entire spectrum of reproductive tract cancers. Similarly, cervical cancer accounted for two thirds (70%) of the reproductive cancers thus some correlation in terms of the magnitude of the disease in both settings. This triggers an alarm on need to retain patients on care with individualized comprehensive plan of management.

Studies on survivorship are few; in a USA study to determine the proportion of cancer survivors that are LFU at 5years after diagnosis, treatment, and the characteristics of those who do not continue survivorship, of the 183 cancer patients who were known to be alive at five years, 92 (50.3%) were LFU and 50% (46/92) of this LFU group were LFU within 1 year of diagnosis. Follow-up was not significantly associated with age (p=0.48), insurance status (p=0.29) and race (p=0.06). In the retrospective study of 183 patients who were treated with chemotherapy only 49.7% continued with follow up at their treatment center. This depicts the scenario in the developed countries where insurance status has no major impact on the ability to access health care.

In my study most patients with NHIF insurance cover were less likely to be LFU before 2years with NHIF catering for most of the essential services i.e. surgery, chemotherapy and radiotherapy in the main referral hospital, KNH. However, due to the increasing numbers, accessibility and prompt delivery of the treatment modalities was greatly hampered. In the developing countries health care financing has a great input in survival for cancer patients due to the required costly investigations and treatment(9). Distance from clinical care facility increases the likelihood of not honoring a follow-up

appointment. As observed in this study majority of the patients were referred from outside Nairobi.

The impact of cancer extends beyond the physical effects of the disease and requires support during diagnosis, treatment and follow-up after treatment. This may likely explain the less likelihood of married patients to be LFU at 2years. Education level increased compliance and understanding of the disease condition and subsequent management thereof. This emphasizes the need for awareness campaigns on the established, available and accessible screening programs(13).

History of irregular menses and use of contraceptive placed the patients on a decreased risk of being LFU at 2years. This may be due to frequent contact with the health care provider(6). Subsequently, these visits can be used as an opportunity for advocacy on best health practices more especially on the primary preventive measures for the reproductive cancers(3).

Majority of the patients presented at FIGO stage II and III(2) however, 8.4% had no documentation on the stage. On the histological differentiation majority were moderately to poorly differentiated. The mode of management had no statistical significance because it may not have been the ideal upon diagnosis but rather on basis of availability due to, long waiting list and limited intervention equipments/personnel.

The use of data available only from KNH limits the use of the findings because it may not be a representative of the whole population. Thus the estimated LFU rates may be biased. However, this study forms a baseline for the current state of care and offers

action points for improvement and policy formulation and guidelines. In my study an assumption is made; that the analyzed cancers were the primary tumour and not metastatic nor recurrent.

CONCLUSION

Majority of the female cancers were of reproductive tract comprising 38% slightly above a third of all the cancers. Cervical cancer accounted for 70% i.e. two thirds of all the reproductive tract cancers. The remaining third were shared among the rest with the top three being; cancer of the uterus (10.4%), ovary (8.7%), vulva (8.4%) respectively. The observed rise in cases of cancers requires further studies to confirm whether it was a real occurrence or incidental finding. On the follow up of the patients at KNH only 3% of the patients were followed up for more than 5 years, majority of the patients were followed up to 2years i.e. 80%. Among the factors that were associated with longer duration of follow up were, secondary education level, marital status, insuarance cover (NHIF), irregular menses and contraceptive use. However on the multivariable analysis only marital status, NHIF and marital status had statistical significance.

RECOMENDATIONS

1. Promote uptake of NHIF cover for the whole population and for those without during diagnosis to be facilitated by the health care worker on first contact during registration. Follow up with persistent text reminders through next of kin & patients cell phone numbers prior to next appointment by the records department.
2. Re-initiate advocacy on primary prevention programs and campaigns to be done by the public health nurse in conjunction with the experts i.e. Reproductive Health Specialists. Brief health education and issuance of pamphlets prior to consultation by the specialist at the point of care.
3. Emphasize counseling of patient on the disease and identification of the crucial need of support either from family or friends. This is to be done at the patients support centre with an input of the mental health department.
4. Develop and implement clear guidelines/protocols on treatment and follow up of patients. Guidelines to be developed by the reproductive health specialist under the leadership of the gyn-oncologist. This will help optimize the impact of the visits with the health care provider and offer guidance on subsequent management.
5. Promote linkage with the peripheral facilities on continued care and support. This is to be coordinated at the KNH referral office by the nurse in-charge and his/her team.

6: TIMELINES

Table 6.1: Timelines											
Activity		**2015**									
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
Proposal Development											
Ethical approval and											
Seeking for funding											
Data collection											
Data analysis											
Report writing and											
Presentation of results											
Final Dissertation											

REFERENCES:

1. Kosary CL. FIGO stage, histology, histologic grade, age and race as prognostic factors in determining survival for cancers of the female gynecological system: an analysis of 1973-87 SEER cases of cancers of the endometrium, cervix, ovary, vulva, and vagina. Semin Surg Oncol. 1994;10(1 994):31–46.

2. Cheserem EJ, Kihara A, Kosgei RJ, Gathara D, Gichuhi S. Ovarian cancer in Kenyatta National Hospital in Kenya : Characteristics and management *. 2013;2013(February):165–71.

3. Ministry of Public Health and Sanitation & Ministry of Medical Services. National Reproductive Health Strategy 2009-2015. 2009;(August):1–80.

4. Services H. NCD Burden of Disease. 2013;

5. Sant M, Aareleid T, Berrino F, Bielska Lasota M, Carli PM, Faivre J, et al. EUROCARE-3: survival of cancer patients diagnosed 1990-94--results and commentary. Ann Oncol. 2003;14 Suppl 5:v61–118.

6. Walraven G, Scherf C, West B, Ekpo G, Paine K, Coleman R, et al. The burden of reproductive-organ disease in rural women in The Gambia, West Africa. Lancet. 2001;357:1161–7.

7. Tanko MN, Kayembe MA, Cainelli F, Vento S. Malignant Tumours of the Genital Tract among Batswana Women. Ghana Medical Journal. 2012. p. 142–6.

8. Howlader N, Noone A-M, Krapcho M, Garshell J, Miller D, Altekruse S, et al. SEER Cancer Statistics Review, 1975-2011. Natl Cancer Inst. 2014;

9. Gok M of H. National Cervical Cancer Prevention Program. 2012;(January 2012):1–38.

10. Parkin DM, Bray F. Chapter 2: The burden of HPV-related cancers. Vaccine. 2006;24.

11. Denny L, Adewole I, Anorlu R, Dreyer G, Moodley M, Smith T, et al. Human papillomavirus prevalence and type distribution in invasive cervical cancer in sub-Saharan Africa. Int J Cancer [Internet]. 2014;134(6):1389–98. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23929250

12. Ojwang SB;, Waweru MM;, Kingondu CS;, Karanja JG;, Kamau RK; WWARP of the CCDS at the D of O and GL. 2007. No Title. Rev Pap Cerv Cytol diagnosis Serv Dep Obstet Gynaecol Lab. 2007;

13. Cacx kenya EAMJ.pdf.

14. Muruka K, Nelly MR, Gichuhi W, Anne-beatrice K, Eunice CJ, Rose KJ. Same day colposcopic examination and loop electrosurgical excision procedure (LEEP) presents minimal overtreatment and averts delay in treatment of cervical intraepithelial neoplasia in Kenyatta National Hospital ,. 2013;2013(May):313–8.

15. Yakasai I a., Ugwa E a., Otubu J. Gynecological malignancies in Aminu Kano Teaching Hospital Kano: A 3 year review. Niger J Clin Pract. 2013;16(1):63–6.

16. Disability-Adjusted Life Years for Breast and Reproductive System Cancers in Cuban Women of Childbearing Age. 2014;16(3).

17. B PROFOJWANGSHADRACK, OTIENO DRODAWAFRANCISXAVIER. "Gichangi P, Estambale B, Mwayo J, Rogo K, Ojwang SBO, Opiyo A, Termmerman M.Knowledge and Practice about cervical cancer and papsmear testing among patients at Kenyatta National Hospital, Nairobi, Kenya. S. 2003. No Title.

18. Release P. Global battle against cancer won't be won with treatment alone--effective prevention measures urgently needed to prevent cancer crisis. Cent Eur J Public Health. 2014;22(February):3–4.

19. Release P. Latest world cancer statistics Global cancer burden rises to 14 . 1 million new cases in 2012 : Marked increase in breast cancers must be addressed. Int Agency Res Cancer, World Heal Organ [Internet]. 2013;(December):2012–4. Available from: http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223_E.pdf

20. Navaneelan T. Health at a Glance Trends in the incidence and mortality of female reproductive system cancers. 2015;(82).

21. Paul M1, George PS MA, Information A, • 1Stony Brook University, School of Medicine, NY U. No Title.

APPENDICES

Appendix 1: Data abstraction form

UON ANATOMIC PATHOLOGY LABORATORY

Patient case record number Study number:

Laboratory number

Date specimen received month/day/year

Date of pathology report

ICD code Diagnosis

AGE (month/day/year)

SPECIMEN

( ) Ovary

( ) Fallopian tube

( ) Uterus

( ) Cervix

( ) Vagina

( ) Vulva

( ) Products of conception (placenta)

PATHOLOGY REPORT

- ✓ ***Histology type***

( ) Well differentiated

( ) Moderately differentiated

( ) Poorly differentiated

- ✓ ***Histology grade***

( ) Grade I

( ) Grade II

( ) Grade III

- ✓ FIGO stage I, II, III,IV
- ✓ Lymph node status

( ) Lymph node involvement

( ) No lymph node involvement

Kenyatta National Health Records Department

Patient personal details

Marital status

( ) Single

( ) Married

( ) Separated/divorced

( ) Widowed

( ) Unknown

Religion

( ) Christian

( ) Hindu

( ) Muslim

( ) Others

Occupation

( ) Employed

( ) Self employed

( ) Unemployed

( ) Not indicated

Patient residence

( ) Residence

( ) Home village

Referred from

( ) KNH

( ) Other within Nairobi

( ) Other outside Nairobi

( ) Unknown

Education level

( ) None/nursery

( ) Primary

( ) Secondary

( ) College

( ) Unknown

NHIF registered

( ) Yes

( ) No

Physician records

- ✓ Parity
    - ( ) 1
    - ( ) 2 to 3
    - ( ) 4 to 5
    - ( ) 5 plus
    - ( ) Not indicated
- ✓ Age at menarche
- ✓ Irregular menses (chronic anovulation) yes/no
- ✓ Menopause yes/no
- ✓ Coitache yes/no
- ✓ No of sexual partners
- ✓ Contraception yes/no
- ✓ Family history of malignancy yes/no
- ✓ History of smoking or alcohol use yes/no
- ✓ Co morbidities (DM,HTN,HIV,STD'S,PID,ENDOMETRIOSIS)

Management

- ( ) Chemotherapy
- ( ) Surgery
- ( ) Radiotherapy
- ( ) Surgery and chemotherapy
- ( ) Surgery and radiotherapy
- ( ) Surgery, chemotherapy, radiotherapy

( ) Not indicated

Body mass index (BMI)

Date of death

Date of last appointment seen

Appendix 2: KNH/UON-ERC Approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES

POBOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300 Ext 44355

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http:.!/www.erc.uonbi.ac.ke
Facebook: https:llwww.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https:lltwitter.com/UONKNH_ERC

KEI'JYATTA NATIONAL HOSPITAL
POBOX 20723 Code 00202

Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP,Nairobi

Ref: KNH-ERC/A/334

31st July 2015

Dr.Racheal Muruga Kinyanjui
Dept. of *Obs/Gynae*
School of Medicine
University of Nairobi

Dear Dr. Muruga

Research proposal- Trends and Survival of Reproductive Tract cancers of women aged more than 15 years in Kenyatta National Hospital over four years (2006·2009) *{P298/05/2015}*

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and approved your above proposal. The approval periods are 31st July 2015 - 30th July 2016.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be usee.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERe before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. *(Attach a comprehensive progress report to support the renewaD.*
D Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study.
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website http;jlwww.erc.uonbi.ac.ke

Protect to discover

~L.....,.~--

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SECRETARY, KNH/UON.ERC

c.c. The Principal, College of Health Sciences, UoN The Deputy Director CS, KNH
The Chair, KNH/UoN-ERC
The Dean, School of Medicine, UoN
The Chairman, Dept. of Obs/Gynae,UoN
Supervisors: Prof. S.B.O. Ojwang, Dr.Rose Jepchumba Kosgei