SURVIVAL PATTERNS OF PATIENTS ENROLLED INTO ISLAND HOSPICE SERVICE PALLIATIVE CARE PROGRAMME

Submitted By

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In Partial Fulfillment of MSc. Clinical Epidemiology

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March 2011

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to my family, friends, colleagues and the Island Hospice Service team for their support in this project. My profound gratitude also goes to my supervisor, Professor S. Rusakaniko for his expert and professional guidance in this study.

ABSTRACT

Introduction and Background: Palliative care services aim to attain the best quality of life of patients. However, the lack of information on the survival of patients under palliative care has resulted in the implementation and assessment of care models being focused on reach without much consideration of the quality of care and the quality of life of patients in the context of survival. Amongst the few studies undertaken elsewhere, the target groups and settings to which the findings are inferable to are distinct to the Zimbabwean scenario. This study's main aim was, therefore, to determine the survival of patients after enrolment into Island Hospice Service (IHS), a Zimbabwean palliative care programme established as the first hospice in Africa.

Methodology: The study took the form of a Retrospective Cohort Design with data obtained from a computerized database at IHS. A total of 597 patients enrolled in the programme between 01/01/06 and 31/12/07 were included in the study and were retrospectively followed up with respect to mortality from their respective dates of enrolment to the study end-date of 31/12/08. Observations were censored on the study end-date and date of transfer or relocation.

Results: This study found that the overall median survival of patients referred to the IHS palliative care programme is 419 days. This estimate is considerably higher than that found from other previous studies which range from 11 to 54 days. Patients diagnosed with HIV only were noted to have longer survival compared to those with Cancer only as well as those with both HIV and Cancer. The median survival estimates for patients with Cancer only and those with both Cancer and HIV were observed to be 84 days and 113 days respectively whilst that for those with HIV only was indeterminate. Some statistically significant differences in survival were also observed for study factors such as gender, age, source of referral and functional status but with variations under the specific disease groups.

Conclusion: Patients enrolled in the IHS programme generally live longer relative to other palliative care programmes. The survival patterns of these patients are influenced by several factors, key among them being the disease status and functional status on enrolment. The study identified the need to incorporate survival data in care planning and modelling. Providing some awareness of the IHS Palliative Care programme to health professionals is also recommended as a possible strategy to improve the timing of referrals. This study also presents an opportunity for further epidemiological inquiry that may contribute to the organisation's cancer prevention efforts.

LIST OF ABBREVIATIONS

AIDS	Acquired Immuno Deficiency Syndrome
ART	Antiretroviral Therapy
CDC	Centres for Disease Control
CI	Confidence Interval
CV	Censoring Variable
DIC	Days in Care
EPR	Eligible Participants Register
IHS	Island Hospice Service
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immune Virus
HR	Hazard Ratio
JREC	Joint Research Ethics Committee
MoHCW	Ministry of Health and Child Welfare
MRCZ	Medical Research Council of Zimbabwe
OI	Opportunistic Infection
PCU	Palliative Care Unit
PCP	Pneumocystis Pneumonia
PGL	Persistent Generalized Lymphadenopathy
PIS	Patient Information Sheet
PLWHA	People Living with HIV and AIDS
SPR	Study Participants Register
WHO	World Health Organisation

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1. INTRODUCTION AND BACKGROUND

1.1 Introduction

HIV and AIDS has presented one of the most devastating health challenges facing mankind in modern history. The problem is more pronounced in resource poor and underdeveloped countries. Globally, there are an estimated 33.3 million people who are HIV infected with at least 67% of this global burden living in sub-Saharan Africa[1].

In Zimbabwe, the first AIDS case was reported in 1983 and since then the epidemic has spread rapidly throughout rural and urban areas. The prevalence of HIV infection among adults in Zimbabwe is currently estimated at 13.7%[3], a 10.9% drop from the Ministry of Health and Child Welfare and Centre for Disease Control (MoHCW/CDC) 2003 estimate of 24.6%. Though such a decline is commendable, the prevalence rate is still regarded as high and still points to a higher incidence or infection rate within the population. There were over 1000 reported deaths from AIDS each week and an estimated 1 025, 472 children (age 0 – 14 years) were orphaned at the end of 2008[3]. The severity of the epidemic has also been compounded by the already existing cancer burden in Africa in general and the notable increased incidence of HIV related cancers in the country[4].

In the backdrop of an overburdened health care system, largely attributed to the pressure of the AIDS pandemic, the deteriorating economic situation and the loss of trained staff to other countries; the burden of care of the terminally ill, particularly those with HIV, has inevitably shifted to the family unit and the community. Governmental and non-governmental organisations have adopted and implemented various innovative mitigatory and preventive measures to try and lessen the impact of the HIV and AIDS pandemic in Zimbabwe. Numerous home-based care groups were established as a result of society's response to the challenge of caring for the sick at home.

The World Health Organisation (WHO) defines home based care as "*a programme that through regular visits, offers health care services to support the care process in the home environment of the person with HIV infection. Home visits may be the only service provided or be part of an integrated programme which offers the patient and his/her family services in the home, hospital or community."* [WHO, 1993]

Over the years, there has also been a growing realisation and acknowledgement that chronically ill patients and families need respite, reassurance and psychological support. The care provided therefore requires a holistic approach which encompasses the provision of comprehensive physical, material, psychological, social and spiritual care and support, explicitly focusing on the patients and the families concerned.

Palliative Care is defined as: *" A holistic approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual"* [W.H.O definition]

The principal aim of palliative care services is therefore to achieve the best quality of life for patients with a life threatening illness through the management and control of pain, symptoms, and emotional, psychosocial and spiritual needs. The need for the service in Zimbabwe has been ever-increasing since the first African hospice and palliative care programme was initiated in the country by Island Hospice Service in 1979. WHO estimates that 1 in every 60 Zimbabwean is in need of palliative care[5]. The government and other organisations have since embarked on mainstreaming palliative care into HBC programmes and the national health professionals' curriculum. However, very few organisations with special focus on palliative care have been established in the country and hence a scale-up of palliative care services in the country and region as a whole is ever more crucial.

As highlighted in the WHO palliative care definition, early identification and ultimately the timing of referral amongst other factors is of paramount importance in the process of effective palliative care delivery. However, previous studies have been drawn to the general conclusion that timing of referral to palliative care service is late in the progression of disease and illness of the patient consequently compromising the attainment of the best possible quality of life of patients. This study investigates the survival of patients with life threatening illnesses enrolled in Island Hospice Service' (IHS) palliative home based care programme with the aim of establishing an understanding of the survival patterns of this group as well as identifying possible factors associated with their survival.

1.2 Background to Island Hospice Service (IHS)

IHS comprises of a multidisciplinary team of nurses, social workers and medical doctors that provides direct care (palliative home-based care) in the community and capacity building through training of community volunteers, health professionals and other individuals. Patients enrolled in IHS' direct care programme are diagnosed with Cancer and/or HIV/AIDS with the main sources of referral including health professionals, public health institutions, community or relatives/family. The organization has, at any point in time, at least 800 patients registered under active direct care service, of which at least 60% would be HIV infected. The enrolment criteria is not restricted to the dying or those of poor functional status only but also allows for enrolment of those who are ambulatory or intermittently sick but with a diagnosis of a life threatening illness such as Cancer and HIV/AIDS. The IHS team provides care and support at its offices and through home visits and community outreach clinics to attend to these patients. The HIS programme does not have an in-patient unit with beds for admission.

1.3 Statement of the Problem

The models of care, implementation and assessment of impact of palliative care interventions globally and Zimbabwe in particular take very little cognisance of the survival of palliative care patients. This is largely owing to the paucity of information on the survival patterns of this group of patients.

The strategies that IHS has adopted to meet the increasing need for palliative care services in Zimbabwe have largely been driven by the need to meet demand in terms of numbers. No consideration has been placed on the duration of survival of these patients under care by the organisation. One of the unintended consequences of the strategies has been a drastic decline in the number of direct nurse/patient contacts over specified periods. The average nurse/patient contacts have declined from the standard 16 contacts/quarter to 1-2 contacts/quarter over the past couple of years. As palliative care services aim to attain the best quality of life of patients, a programming concern that arises from the prevailing and current scenario is whether the time spent in care is adequate for the attainment of this goal. The above problem is compounded by the growing global realization that most patients are referred to palliative care services rather late in their illnesses.

In addition, the quality of life of patients as measured in palliative care impact assessment is embedded on the relief of pain/symptoms; psychological, emotional and spiritual wellbeing without consideration of survival. This could largely be attributed to the continued allegiance to the historical perspective and context of palliative care which primarily focused on dying patients and was firmly rooted in one of its principles – "Neither hastens nor postpones death". However, palliative care has evolved to become a broader concept that addresses the needs of both dying and non-dying patients particularly in the advent of life prolonging Anti-Retroviral (ARV) medications for the HIV positive.

The lack of survival data of palliative care patients denies both clinicians and programmers of the opportunity to design effective models of care that take survival into consideration as well as to adequately assess the effectiveness of palliative care interventions.

2.0 LITERATURE REVIEW

2.1 Palliative Care

2.1.1 Background to Palliative Care

The root word for palliation in Latin, "palliare", means to cloak or shield. At a simple level we can imagine that palliation protects people from the ravages of illness[13]. Palliative care is a concept that has evolved from hospice care, a term that was first applied to specialised care for dying patients in 1967 by Dame Cecily Saunders, the founder of the first modern hospice – St Christopher's Hospice in London. Her experiences as a nurse, social worker and physician led her into establishing the initiative that aimed at addressing the patient neglect as well as their unnecessary suffering due to symptoms and lack of attention. Due to their perceived benefits, early hospices were established from 1975 and they became sanctuaries for the dying which provided end-of life care. As hospice care was narrowly focused on the dying, a broader concept that would build on the hospice movement and address the needs of both the dying and non-dying was imperative and hence the evolution of palliative care.

Palliative Care is a medical specialty focused on the relief of pain and other symptoms of life threatening illnesses. More specifically, WHO defines Palliative Care as "*" A holistic approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual"*

The goal is to prevent and ease suffering and to offer patients and their families the best possible quality of life. Palliative Care is appropriate at any point in a life threatening illness and is not dependent on prognosis. The principles of Palliative Care are:

- Provides relief from pain and other distressing symptoms
- Integrates the psychosocial and spiritual aspects of patient care
- Offers support systems to help patients to live as actively as possible until death
- Offers support systems to help the family cope during the patient's illness and in bereavement

- Uses team approach to address the needs of patients and their families including bereavement counseling, if indicated.
- Will enhance quality of life and may positively influence the course of illness
- Affirms life and regards dying as a normal process; Provides a series of interventions that intend neither to shorten nor to prolong life
- Neither hastens nor postpones death
- Is applicable in the course of illness in conjunction with therapies that are intended to prolong life and includes those investigations needed to better understand and manage distressing clinical complications.

Worldwide, palliative care practice has generally become widespread and has evolved in its approaches over the years. Though variations in the target groups, settings for care provision and the clinical approaches have been noted; focus on the patient and family and its key domains of pain and symptom management, psychological, spiritual and emotional support remain central in practice. In the developed world, palliative care provision is both at institutional level (national and private organisations) and community level (home care) whilst for the developing countries this specialized practice is mainly mainstreamed in home based care programmes. The main target group for palliative care has predominantly been cancer patients since its formative years to date and this is mainly so in the developed countries. However, with the advent of HIV and AIDS and its severity in the developing countries, particularly in Africa, a significant number of patients enrolled into palliative care programmes are HIV and AIDS patients.

2.1.2 Cancer

Cancer is a general term for a group of diseases characterized by the disorder of growth at cellular level. The abnormal cells can spread to areas far from the site of origin to form metastases. Cancer is a life threatening condition.

A tumour is an abnormal mass of tissue, or an abnormal growth of cells, more than the body requires. There are benign (harmless) tumours and malignant tumours which are referred to as cancers. Whilst benign tumours do not spread, cancer spreads into the surrounding tissues, nearby areas and through the blood and lymph system to other organs or bones. When a cancer

spreads to another part of the body it is called a secondary cancer or metastases whilst its point of origin is known as the primary cancer. Cancers generally fall into the following groups:

1. Carcinoma: Cancer of the skin or the linings of organs: skin, breast, lungs, bowel or uterus
2. Sarcoma: Cancer of bones or muscles
3. Leukaemia: Cancer of blood cells

Cancer can be diagnosed by X-rays, Scans (which include ultra sound scan, CAT scan and MRI Scan), blood tests, examination or biopsy. The conventional approaches in cancer treatment are surgery, radiotherapy and chemotherapy.

Cancer patients suffer from chronic pain and symptoms compounded by psychosocial and emotional challenges associated with any life threatening illness. The pain and symptoms experienced by cancer patients has been distinct in negatively impacting the quality of life of patients and their families.

Although, for Western countries, long-term survival rates for many types of cancers have substantially improved in past decades because of advances in early detection and treatment, Africa is still experiencing very high cancer mortality rates and short survival times. This has largely been attributed to late detections as most cancers have been noted to present at an advance stage.

2.1.3 HIV and AIDS

Acquired Immuno Deficiency Syndrome (AIDS), is an incurable condition in which the human body loses the ability to fight infections because the immune system has been weakened by HIV (Human Immuno Virus) emerged as a devastating epidemic in the 1980s. Since then, HIV has spread widely throughout the world with Sub Saharan Africa, especially Southern Africa, being the hardest hit. HIV prevalence rates and AIDS related deaths have continued to be high in this region. In the absence of a cure for HIV, more and more AIDS related deaths have been reported worldwide.

AIDS is the final stage of HIV infection when the virus has seriously weakened the body' defence against infection and/or disease. HIV is mainly transmitted through sexual intercourse, direct blood-blood contact (e.g. sharing of needles) and from mother to baby. It has been established that the progression from HIV infection to AIDS is both complex and variable. However, the ability of the human body's immune system to fight the virus for a long period of time has generally led to a relative longer period of survival amongst people infected with HIV. The WHO in 2002 developed a four-phase clinical staging system to describe HIV progression in adults and adolescents shown below: Asymptomatic HIV has been noted to last from less than one year of infection to 10-15 years or more whilst HIV/AIDS related illness (symptomatic) could last months to years before the final development of AIDS.

Table 1: HIV Progression

HIV Progression in Adults and Adolescents
1. Asymptomatic or PGL
2. Symptomatic with infections such as herpes zoster, minor skin problems and slight weight loss but no impairment of normal activity
3. Symptomatic with OIs severe enough to keep the person in bed up to half the day during the previous month
4. AIDS, with wasting, chronic diarrhea and fever, PCP and other life threatening conditions such as and keeping the person in bed up to half the day during the previous month

The treatment and medical care of HIV in patients ranges from prevention and treatment of opportunistic infections (OIs) to Anti Retroviral Therapy (ART) which specifically targets the virus itself. Opportunistic infections (OIs) are common causes of death in HIV-infected patients and ART has proved lowered the incidence of OIs for those who have access.

The effectiveness of highly active antiretroviral therapy (HAART) against the human immunodeficiency virus (HIV) has been a medical success story. A Denmark study conducted by Nicolai Lohnse et al in 2007 established that Many HIV-infected persons with access to antiretroviral therapy have a near-normal life expectancy, but mortality among them is still higher than that in the general population. This study also noted that despite the improvements in antiretroviral therapy, lifestyle factors were a potentially significant factor in the excess mortality among HIV patients, which appears to be only partially attributable to immunodeficiency. Other previous studies have also shown that HIV progression is also influenced by a web of other factors encompassing social, psychological, spiritual and emotional aspects hence the

appropriateness of the holistic approach to care, particularly palliative care, which have been effective in complementing conventional approaches in the management of opportunistic infections.

2.2 A Brief Theoretical Background to Survival Analysis

Studies that are aimed at investigating the survival of patients make use of survival analysis techniques in order to establish patterns as well as to be able to compare findings with other related studies. The outcome variable of interest in survival analysis is time until an event occurs. This time variable is also known as survival time as it gives the time that an individual has "survived" from a particular starting time (e.g., time initiated the treatment) to a particular endpoint of interest (e.g., recovery or death). In the case of this study, this would be the time of enrolment into the programme to the time of death. Survival time can thus be days, weeks, months and years from the beginning of follow-up until the event occurs.

It is also common that some study participants may withdraw or will be lost to follow-up during the observation period as well as that they may not experienced the event of interest by the study end date. Some information about the individuals' survival times would be available but not the exact survival times and as such, the investigator would only know as much about their survival time to that point of loss to follow-up, withdrawal or study end. In this case, these observations are said to be censored.

The main summary statistic used in describing survival data is known as the Median Survival Time. The basic interpretation of this statistic is that we would expect half (50%) of the population under study to survive beyond this survival time. The measure therefore provides a sound platform for planning, resource allocation and development of appropriate models of care.

In order to obtain a comprehensive picture of survival patterns, techniques used include the Log Rank Test which is a particularly useful tool in comparing the survival experiences of two groups of individuals, for example in comparing the survival patterns of males and females in a population. Survival data can also be modeled using various regression models. The proportional hazards model is a regression model used when investigating or controlling for several variables

in survival data. It is one of the most general of regression models as it is not reliant on assumptions based on the shape or nature of an underlying survival distribution.
A more comprehensive outline of the Survival Analysis Theoretical Framework is attached as Appendix 1.

2.3 Survival of Patients in a Palliative Care Setting

A number of studies aimed at investigating the survival of patients after enrolment in palliative care programmes have been undertaken in different countries. These studies have mainly focused on cohorts of terminal ill cancer patients receiving care from either community based palliative care units (specialists providing care at home) or hospital based units and inpatient units. The majority of these studies have shown a median survival time of 11 to 38 days. In Australia for instance, the majority of published studies that have looked at survival in palliative care settings looked at terminal cancer patients in inpatient settings and found a median survival of only 14 to 15 days. However, one particular study investigating the survival after enrollment in an Australian Palliative Care programme (home care setting) looked at 1138 terminal cancer patients and established a median survival of 54 days, with 9.3% of patients dying within 7 days and 17% living longer than six months. The median percentage of time spent on the programme since diagnosis was found to be 17%.

A multicentre prospective cohort study involving 94% of the 62 PCUs in Italy established a median survival of 37.9 days and 14.3% of the patients died within 7 days whilst 27% and 15.3% lived longer than 90 days and 180 days respectively. Participants in this study were terminal cancer patients drawn from community based palliative care units (Home PCUs), Mixed PCUs (collaboration between public hospital ward (oncology unit) and charity institution) and Hospice Units (institution). The home care units were the most common. Median survival was noted to vary significantly with gender, type of cancer, type of PCU and source of referral. For instance, males were observed to have a lower median survival (34 days) as compared to females (41 days). Median survival was significantly ($p=0.049$) lower for hospice patients (22.5 days), compared to Home PCUs (35 days) or by Mixed PCUs (42 days). Other multicenter studies have observed median times ranging from 25 to 35 days.

One of the main factors attributed to the low survival amongst palliative care patients in these studies has been that of late referrals. A pictorial representation of the stage of introduction of palliative care in most developing countries by Figure 1 below shows that referrals are made when curative approaches and management of OIs are no longer useful. Based on these observations and previous studies, there has been great advocacy for the adoption of a 'mixed management model', shown by Figure 2 which involves the simultaneous management of both curative/disease modifying and palliative measures.

Figure 1: Palliative Care in the Developing World: Current for HIV/AIDS Patients

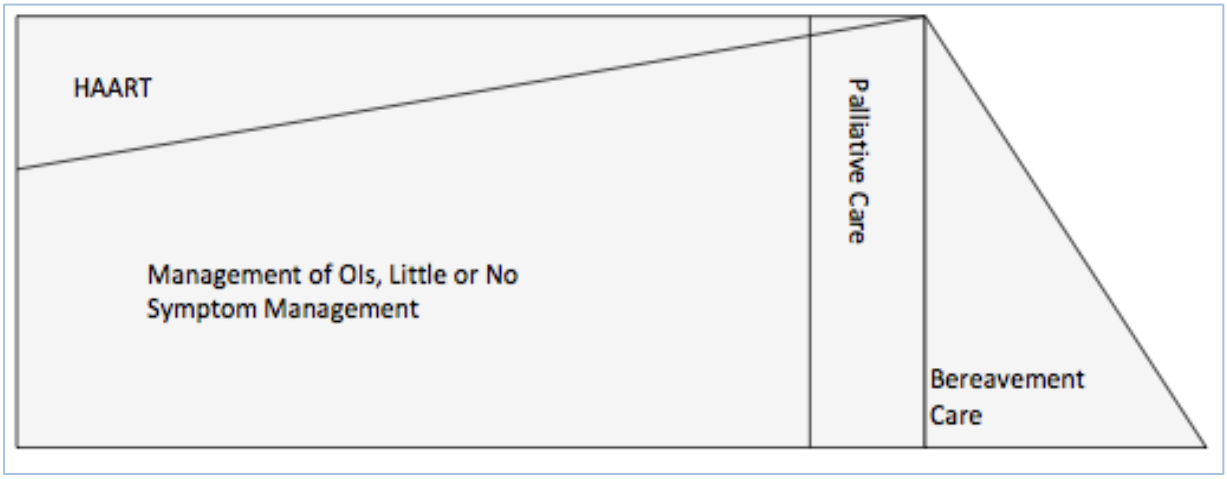
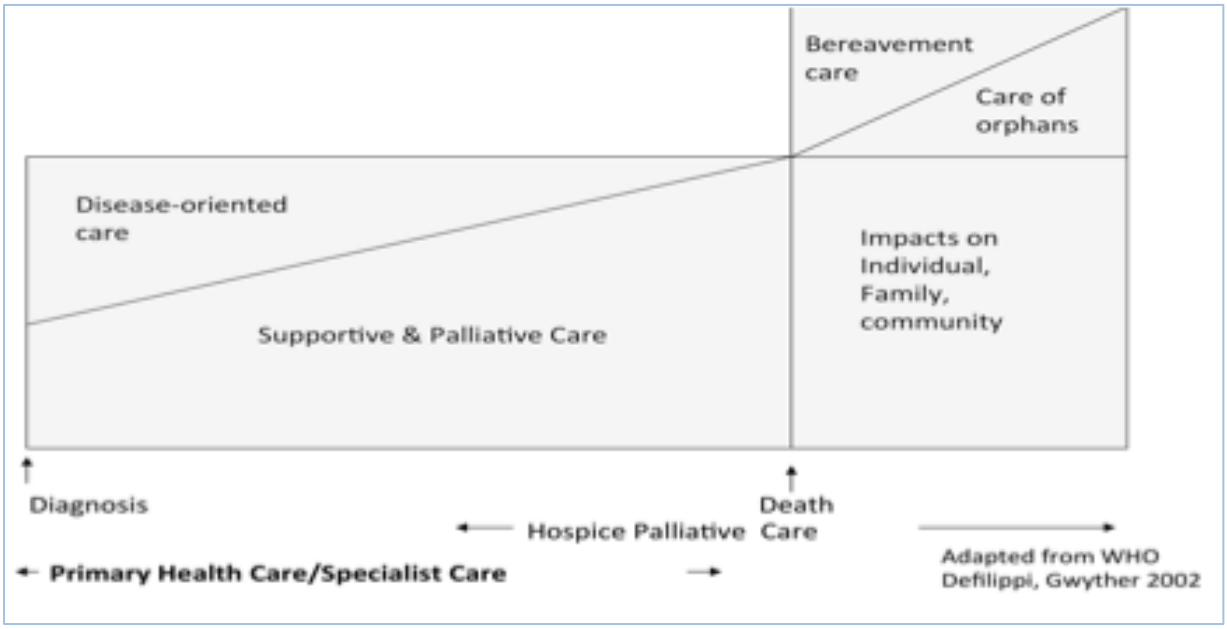


Figure 2: Ideal: "Mixed Management Model"



The knowledge of the importance and the practice of early referral are also likely to vary amongst referring institutions and health practitioners and as such, an understanding of the associations between the patients' sources of referral and the survival patterns is therefore instrumental in targeting for palliative care advocacy.

2.4 Justification of the Study

Some studies have been previously undertaken to determine the survival of patients after enrolment into a palliative care programmes. However, none have been conducted in Zimbabwe or the Region. Whilst these previous studies undoubtedly present value to evidence based clinical practice, the target groups and settings to which the previous findings are inferable are distinct to the Zimbabwean scenario. Patients included in these studies were predominantly cancer patients whilst, in contrast, the majority of palliative care patients in Zimbabwe are HIV infected.

The need for a wider dissemination of palliative care services has been widely acknowledged in the country and the region at large. However, whilst evidence based approaches are imperative in this drive, both the quantity and quality of clinical research in palliative care has not fully developed. Island Hospice Service is the largest direct palliative care provider in Zimbabwe and is regarded as Africa's Centre of Excellence in palliative care. However, minimal research and specifically none in the area of survival has been undertaken at this centre or the region. Evaluations have been restricted to the continuous assessment of the quality of care in the domains of pain/symptom relief and psychosocial wellbeing as well as compliance to programmatic work-plans without much consideration of the survival of palliative care patients.

Previous studies have also established associations between survival time of terminally ill patients and other factors such as age, gender, source of referral and diagnosis amongst others. For instance, the majority of cancers in Africa are noted to present at an advanced stage. It is therefore worthwhile to undertake a comparative analysis of the survival patterns of patients with cancer to those with HIV and AIDS or those with HIV related cancers in order to enhance clinical approaches in service delivery.

An understanding of the determinants of survival and the quality of life of patients is therefore critical in the planning of clinical trials or other research in palliative care as well as for epidemiological needs assessments. This study will also look at the extent of appreciation by stakeholders of timely referrals of patients in a developing world setting. A comprehensive understanding of the associations between survival and possible determinant factors is essential in enhancing the effectiveness of clinical practice and palliative care service delivery in general.

2.5 Research Question

What survival pattern/distribution is exhibited by terminally ill patients after enrollment into Island Hospice Service Palliative Care Programme?

2.6 Aims and Objectives of the Study

2.6.1 Aims

The aims of this study are to:

1. To determine the survival patterns of patients after enrolment into IHS' Palliative Care Programme
2. To assess the associations between demographic and clinical factors such as age, gender, disease, source of referral and functional status on assessment with survival.

2.6.2 Objectives

The objectives of the study are:

1. To determine the median length of survival of patients after enrolment in IHS palliative care programme.
2. To assess the associations between disease (HIV+ only, Cancer only, HIV+ and Cancer) and survival of patients after enrolment into the programme.
3. To assess the associations between age, gender, source of referral and functional status (assessment) on survival.

3.0 METHODOLOGY

3.1 Study Design

The study took the form of a Retrospective Cohort Study Design. Data was obtained retrospectively from a computerized database at Island Hospice Service. A patient is enrolled into the programme when he/she has been diagnosed (test or clinically by presenting symptoms according to WHO standards) with a life threatening illness primarily HIV and AIDS and Cancer (see Section 1.2)

Demographic and clinical data including age, gender, referral source, diagnosis and functional status of all patients is recorded in this database on assessment and enrolment into the palliative care programme. The source of data for the Database is the Patient Information Sheet (PIS)[1] which is the assessment and registration form used on enrolment into the programme. The database is updated on an ongoing basis with further clinical data during the patients' clinical course. A detailed description of the database and the data collection and processing system is provided as Appendix 3.

Patients were included in the study if they were enrolled in the programme between 01 January 2006 and 31 December 2007 and these were retrospectively followed up with respect to mortality from their respective dates of enrolment until 31 December 2008 thus giving a minimum follow-up period of 12 months. Observations were censored on the study end date (31 December 2008) and on the date of transfer or relocation from the programme. Patients who were alive after the end of follow-up period were verified through clinical records showing further contact.

3.2 Location of the Study

This study was located in Harare. All patients enrolled into the IHS programme are drawn from Greater Harare including Chitungwiza and Norton.

3.3 Study and Outcome Factors

The primary outcome factor was the survival status of patients (Died or Alive) whilst the secondary outcome factor was the length of survival of patients after enrolment into the programme.

[1] Appendix 2: Patient Information Sheet

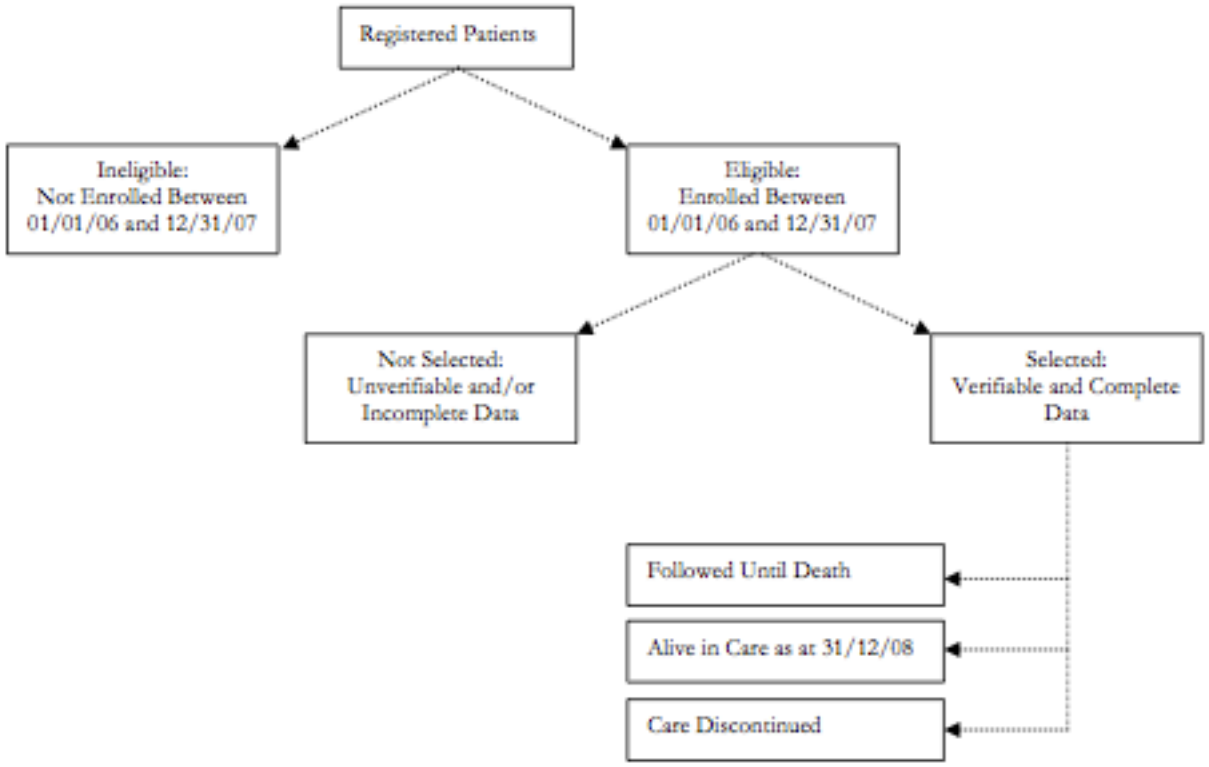
The Study factors were:

- Diagnosis (HIV& AIDS, Cancer, HIV& AIDS and Cancer), Stage of Disease, Type of Cancer, ART Status
- Age Group (Less than 20 years, 20-39, 40-59 and 60+ years),
- Gender (Male, Female)
- Referral Source
- Functional Status on Assessment
-

3.4 Inclusion and Exclusion Criteria

All new patients enrolled into IHS' palliative care programme between 01 January 2006 and 31 December 2007 were included in the study. Patients with missing data on date of admission, date of death (if died), diagnosis and date of transfer (if transferred) were excluded from the study.

Figure 3: Flowchart of the Study



3.5 Sampling and Sample Size

The study targeted **ALL** new patients enrolled into the programme between 01 January 2006 and 31 December 2007 and regarded these as eligible. However, not all eligible patients were selected into the study as some patients had incomplete and unverifiable data. A total of 1420 patients were registered in the IHS Main Database at the time of the study. However, based on the inclusion criteria, only 605 patients were eligible to participate as they were enrolled into the programme during the period starting 01 January 2006 up to the 31st December 2007. Of these, 8 patients had incomplete and unverifiable data relating to either their enrolment date or their end date of follow-up (date of death, transfer or end of study follow-up) hence they were excluded resulting in 597 patients participating in the study.

3.6 Data Management

3.6.1 Data Extraction

The completeness and quality of data was critical in this study. A review of the PIS, the primary source of data for the database, revealed that some of the study variables were not adequately captured by the tool. For instance, there was no section that specifically asked for the patient's stage of disease on assessment as well as the date of transfer. This information was however included in the detailed qualitative patient notes and transfer registers which did not form part of the database. This information was therefore extracted from the notes and Unique Identifiers for each patient were used to update the database records using the extracted information. The following table provides a brief outline of the state of data and the action taken.

Table 2: Data Extraction

Variable	Completeness State of Data	Action Taken	Source of Data
Outcome Measurement			
Date First Seen	Partial	Extraction, Verification	Dbase, PIS Records, IAS
Date of Death	Partial	Extraction, Verification	Dbase, PIS Records, IAS
Date of Transfer	Unavailable	Extraction	PIS Records, IAS, DNR
Measurement of Study Factors			
Age	Partial, Ungrouped	Extraction, Verification	Dbase, PIS Records, IAS
Gender	Partial	Extraction, Verification	Dbase, PIS Records, IAS
Diagnosis	Partial, Ungrouped	Extraction, Verification	Dbase, PIS Records, IAS
Stage of Disease	Unavailable	Extraction	Dbase, PIS Records, IAS
Type of Cancer	Partial, Ungrouped	Extraction, Verification	Dbase, PIS Records, IAS
ART Status	Partial	Extraction, Verification	Dbase, PIS Records, IAS
Source of Referral	Partial	Extraction, Verification	Dbase, PIS Records, IAS
Functional Status	Partial	Extraction, Verification	Dbase, PIS Records, IAS

A systematic approach was employed to ensure data completeness and accuracy. The following steps were undertaken in the data extraction:

i) **Creation of an Eligible Participants Register: -** The IHS Patient Database was created in Epi Info using an MS Access platform. Using the field "Date First Seen", all patients enrolled into the programme between 01/01/06 and 31/12/07 were selected and listed. These records were exported to Microsoft Excel to create a spreadsheet register with all the details of eligible participants.

ii) Data Extraction Tools, Sources and Process: -. Based on the register, a Data Extraction Form[2] containing fields for Date First Seen, Date of Transfer, Date of Death, Diagnosis, Stage of Disease, ART Status, Functional Status, Source of Referral, Age and Gender of each Participant referenced by a Unique Identifier was developed. This tool was used to extract missing data from hard copy records stored in an Indexed Archival System (IAS) and Death/Transfer Notification Register (DNR) available at IHS.. The records were also used for verification of entries to ensure accuracy. The extraction and verifications of patients' deaths, dates of deaths, live patients under care and dates of transfers/relocations was not only conducted through the IAS and DNR but also through face-face interviews with clinical nurses who work with the patients on a day to day basis and who made reference to their patient records. A verification checklist column on the Data Extraction Form was useful in ensuring that each record and requisite variables had been cross checked.

3.6.2 Data Entry

Extracted data was entered into the Eligible Participants Register Database. Cleaning was done using frequency tabulations of variables and observation as this helped in the examination for completeness. All records without complete and verifiable data on Date of Enrolment, Date of Death and Date of Transfer were excluded from the study or analysis at this stage.

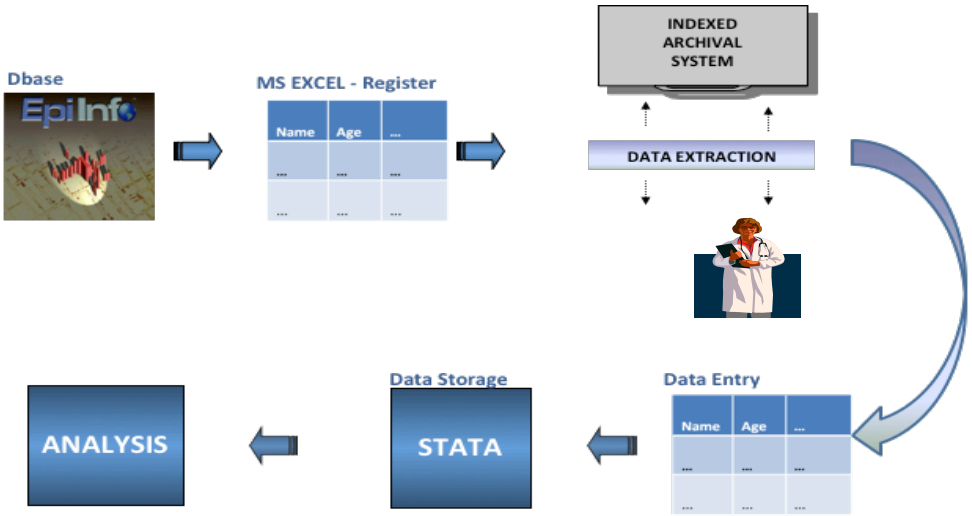
3.6.3 Data Safety

This stage of the data management primarily looked at storage and protection of confidential information. The updated Eligible Participants' Register (EPR) was electronically saved separately under a different file name called Study Participants Register (SPR). This register did not contain the names of study participants but made use of a unique identifier, in this case the

[2] Appendix 4: Data Extraction Form

reference number allocated to each patient on enrolment into the programme. This served to protect the patients' confidentiality. The EPR was saved on disk and stored safely and separately from the SPR. The SPR file was then exported to STATA version 10 and saved under a similar name in preparation for data analysis. All disks with the data for the study were backed up and stored separately and securely. The data management process can be summarized by the flow chart below.

Fig 4: Data Management Process Flow to Analysis



3.7 Data Analysis

Data was analyzed using the statistical analysis package STATA Version 9. The process of analyzing the data followed a series of steps aimed at addressing the objectives of the study.

Step 1: *Outline the socio-demographic and medical characteristics of study participants.*

Step 2: *Determine the primary outcome of participants in the study.*

Step 3: *Determine the median survival time of patients*

Step 4: *Assess the associations of study factors using the Log Rank Test*

Step 5: *Model survival data using the Cox Proportional Hazards Model*

3.7.1 Generating Survival Data

Since the objective of collecting and processing patient data on an ongoing basis was not for the purposes of this current study, there was need to align the form and structure of the data to suit the analysis requirements for survival data. The following steps will be followed.

i. Generating the Time Variable:

The date of enrolment into the programme is recorded for each new patient on enrolment in the database under the variable name Date First Seen (DFS). The date of death is also recorded in the database for each patient who has died under care. These two dates were used to compute the days in care (DIC) for each patient who had died. Similarly the DIC for those patients who were alive or had transferred was computed using the DFS and the respective censoring dates, either the date of study end (31/12/08) or transfer dates. Censored observations were then coded. Under the Censoring Variable (CV), the failures (deaths) were coded zero while censored observations were coded 1. The following table shows the process used in generating the time variable and coding the censoring variable.

Example: Generating the Time Variable DIC and Censoring Variable CV

Ref Number	Date First Seen	Date of Death	Censoring Date	DIC Computation	DIC	Censoring Variable	CV
P126	03/06/06	13/03/07	N/A	= C1-B1	272	= IF(C1="Missing",1,0)	0
P230	12/7/2007	Missing	31/12/08	= D2-B2	390	= IF(C2="Missing",1,0)	1
P100	11/5/2006	Missing	13/12/06*	= D3-B3	38	= IF(C3="Missing",1,0)	1
P002	1/2/2006	3/6/2006	N/A	= C4-B4	63	= IF(C4="Missing",1,0)	0
P315	3/3/2007	22/03/07	N/A	= C5-B5	19	= IF(C5="Missing",1,0)	0

*** = Date of Transfer**

ii. Grouping Ungrouped Data

Some of the variables included in the data set were in continuous variable form but were required as categorical data at analysis stage. For instance, the age of patients is computed as an absolute figure from the date of birth during enrolment but the analysis required an assessment of the survival distributions of age groups. As such, some computations were done for specific variables in order to group them and further code them prior to the analysis. An example of the process undertaken in MS Excel is shown below.

Example: Grouping and Coding: Variable Age

Age	Command Syntax	Age Group – Coded
15	= IF(OR(A2<18,17<A2<40),1,2)+IF(A2>39,1)	1
27	= IF(OR(A3<18,17<A3<40),1,2)+IF(A3>39,1)	2
22	= IF(OR(A4<18,17<A4<40),1,2)+IF(A4>39,1)	2
65	.	3
77	.	3
56	.	3
33	.	2
13	= IF(OR(A10<18,17<A10<40),1,2)+IF(A10>39,1)	1

Age Groups: 1 = 0-18 Years; 2 = 19-40 Years and 3 = Above 40 Years

iii. Data Coding

As highlighted in previous sections, categorical data for both outcomes and study factors were coded. A Data Coding Manual[3] was used as a reference tool in data entry and analysis.

iv. Completeness of Data

The completeness of the data was analyzed and is presented in the table below.

Table 3: Completeness of Data

	Before Data Extraction		After Data Extraction	
Variable	Response	% Complete	Response	% Complete
Age	594	99.5	594	99.5
Gender	597	100.0	597	100.0
Diagnosis	515	86.3	578	96.8
Stage of Disease	92	15.4	242	40.5
ART Status	222	65.9	337	100.0
Source of Referral	520	87.1	549	92.0
Functional Status	451	75.5	473	79.2

3.7.2 Statistical Data Analysis

The analysis conducted in this study made use of the following data analysis plan to meet its objectives.

[3] **Appendix 5: Data Coding Manual**

Table 4: Data Analysis Plan

Analysis Plan			
Output	**Main Variable (s)**	**Type of Analysis/Method Used**	**Main Summary Statistic**
Socio-demographic characteristics of participants	Age Group, Gender, Diagnosis, Stage of Disease, Type of Cancer, Functional Status, Source of Ref.	Descriptive Statistics - Frequency Tables	Count (n); Percent (%)
Patient outcomes (primary) determined	Outcome Status (Alive, Dead)	Descriptive Statistics - Frequency Tables; Cross tabulations with Study Factors	Count (n); Percent (%)
Secondary Outcome - Median Survival of cohort determined	Time Variable (Days in Care - DIC)	Kaplan-Meier Product Limit Method	Median Survival Time
Associations between study factors and survival pattern determined	DIC, Age Group, Gender, Diagnosis, Stage of Disease, Type of Cancer, Functional Status, Source of Ref.	Kaplan-Meier Product Limit Method stratified according to study type, Log Rank Test	Median Survival Times, p-values evaluated
Survival data is modeled	DIC, Age Group, Gender, Diagnosis, Stage of Disease, Type of Cancer, Functional Status, Source of Ref.	Regression Analysis of survival data using the Cox Proportional Hazards Model	Hazard Ratios, 95% Confidence Intervals evaluated

3.8 Ethical Considerations

This study was undertaken with the approval of the Joint Research Ethics Committee (JREC). The following are some of the specific ethical considerations made in undertaking this study:

- Confidentiality: All patients had a unique reference number and patient information was treated with confidentiality.
- Patients and families will benefit from evidence based clinical practice and improved quality of care.
- Potential Harm: Possible stigma may arise due to an established association between short lengths of survival and specific conditions identified and enrolment into a palliative care unit. The association of specific conditions with " End of Life"

4.0 RESULTS

This study was aimed at assessing the survival patterns of patients under the IHS Palliative Care programme. A total of 1420 patients were registered in the IHS Main Database. However, based on the inclusion criteria, only 605 patients were eligible to participate as they were enrolled into the programme during the period starting 01 January 2006 up to the 31st December 2007. Of these, 8 patients had incomplete and unverifiable data relating to either their enrolment date or their end date of follow-up (date of death, transfer or end of study follow-up) hence they were excluded. These findings are therefore based on 597 participants, giving a response rate of 98.7%.

4.1 Characteristics of Study Participants

The majority (64.2%) of the participants were females. The age of participants ranged from 1 to 105 years and a median age of 45 years (Q1=33, Q2=61) was observed. Participants aged between 40 and 59 years constituted the majority (33%) of the cohort. Table 5 below shows the age and gender distribution of the participants in this study.

Table 5: Demographic Characteristics of Patients

	n	(%)
Age Group	**n=594**	
Below 20 years	75	12.6
20-39 years	159	26.8
40-59 years	196	33.0
60+ years	164	27.6
Gender	**n=597**	
Male	214	35.8
Female	383	64.2

Fifty six and a half percent (56.5%) of the participants were HIV positive. Those who had a primary diagnosis of HIV only, however, constituted 42.9% of the cohort whilst those with Cancer only and both HIV and Cancer as the primary diagnosis represented 41.7% and 15.4% respectively as shown in Fig 5 below.

Fig 5: Distribution of Participants by Diagnosis

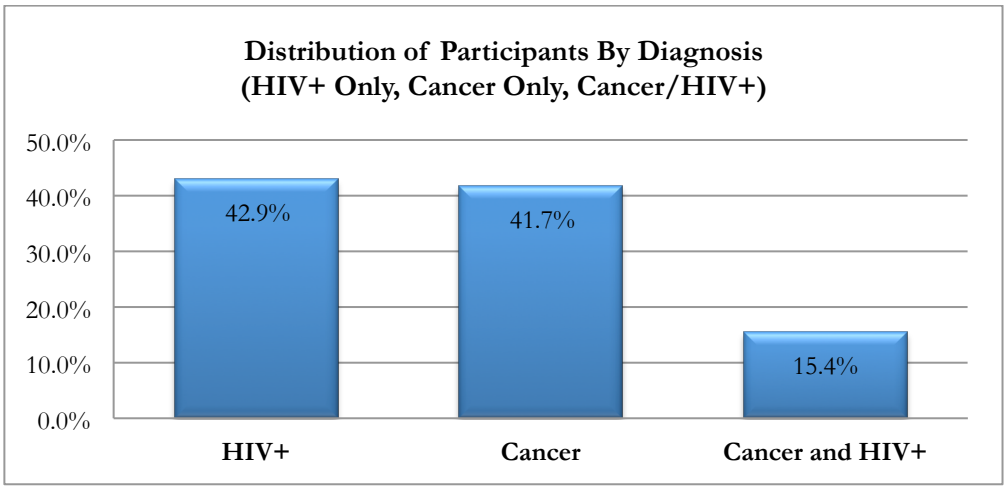


Table 6 below shows that 26.7% of those who were HIV infected were on ART.

Table 6: Distribution of HIV+ Patients by ART Status

	n=337	(%)
ART Status		
Not On ART	247	73.3
On ART	90	26.7

The most common cancers amongst those presenting with cancer were observed to fall under the broad classes of Digestive/Gastrointestinal (24.8%), Gynecologic (13.9%) and Genitourinary (13.9%) as shown in Table 7 below.

Table 7: Distribution of Cancer Patients by Type of Cancer

	n	(%)
Type of Cancer (Broad Classification by Body Region)	**n=330**	
Blood	12	3.6
Bone	10	3.0
Brain	3	0.9
Breast	41	12.4
Digestive/Gastrointestinal	82	24.8
Endocrine	3	0.9
Eye	3	0.9
Genitourinary	46	13.9
Gynecologic	46	13.9
Head and Neck	9	2.7
Respiratory	21	6.4
Skin	26	7.9
Unknown Primary Cancer (UPC)	28	8.5

The most common sources of referral to the IHS programme were observed to be Specialist Doctors (55%) and Community Caregivers (30.8%). Patients who were fully active on enrolment constituted the greatest proportion (39.8%) of this cohort whilst 14.6% were bedridden.

Table 8: Distribution of Patients by Source of Referral and Functional Status

	n	(%)
Source of Referral	**n=549**	
Specialist Doctor	302	55.0
General Practitioner	57	10.4
Institutional	9	1.6
Self	12	2.2
Community Caregivers	169	30.8
Functional Status	**n=473**	
Fully Active	188	39.8
Restricted	113	23.9
Ambulatory	33	7.0
Limited Self Care	70	14.8
Bedridden	69	14.6

4.2 Survival Outcomes and Associations with Study Factors

4.2.1 The Outcome Status of Patients as at Study End Date

As previously noted, the primary outcome in this study is the Outcome Status of patients. A total of 326 patients, 54.6% of the cohort, died within the follow-up period which ranged from a minimum of 12 months to 36 months. Two hundred and seventy one observations were censored by the end of the follow-up period, 31 December 2008. Of these, 266 patients were still alive at end of follow-up whilst 5 participants had their care discontinued due to transfer or relocation during the course of follow-up. Table 9 below provides a summary of the primary outcome analysis.

Table 9: Patient Outcomes

	N	(%)
Followed Until Death	326	54.6
Care Discontinued Due to Transfer/Relocation	5	0 8
Alive as at 31/12/08	266	44.6

Table 10 below presents findings obtained through cross-tabulations between the study factors and the outcomes (Died or Alive as at study end date).

Table 10: Demographic and Background Characteristics by Outcome

			Died n (Row %)		Alive as at 31/12/2009 n (Row %)		Pearson's Chi Square (χ^2) Test: p-value
Age Group		**n=589**					P<0.001
	Below 20 years	75(100%)	15	(20.0)	60	(80.0)	
	20-39 years	156(100%)	65	(41.7)	91	(58.3)	
	40-59 years	195(100%)	103	(52.8)	92	(47.2)	
	60+ years	163(100%)	141	(86.5)	22	(13.5)	
Gender		**n=592**					P=0.001
	Male	213(100%)	139	(65.3)	74	(34.7)	
	Female	379(100%)	187	(49.3)	192	(50.7)	
Diagnosis		**n=574**					P<0.001
	HIV+	247(100%)	48	(19.4)	199	(80.6)	
	Cancer	239(100%)	209	(87.4)	30	(12.6)	
	Cancer + HIV+	88(100%)	66	(75.0)	22	(25.0)	
ART Status		**n=336**					P=0.590
	On ART	90(100%)	34	(37.8)	56	(62.2)	
	Not On ART	246(100%)	81	(32.9)	165	(67.1)	
Source of Referral		**n=544**					P<0.001
	Specialist Doctor	300(100%)	255	(85.0)	45	(15.0)	
	General Practitioner	56(100%)	24	(42.9)	32	(57.1)	
	Institutional	9(100%)	4	(44.4)	5	(55.6)	
	Self	12(100%)	3	(25.0)	9	(75.0)	
	Community Caregivers	167(100%)	22	(13.2)	145	(86.8)	
Function Status		**n=469**					P<0.001
	Fully Active	186(100%)	35	(18.8)	151	(81.2)	
	Restricted	112(100%)	61	(54.5)	51	(45.5)	
	Ambulatory	33(100%)	22	(66.7)	11	(33.3)	
	Limited Self Care	70(100%)	55	(78.6)	15	(21.4)	
	Bedridden	68(100%)	61	(89.7)	7	(10.3)	

The results show that the proportion of patients who were alive as at the end of the study period decreases with the age group from 80% of patients aged below 20 years to 13.5% for those aged 60 years and above. Although the proportion of those who survived and those who died is somehow similar for females, the majority (65.3%) of males died during the follow-up period. The majority (80.6%) of patients diagnosed with HIV were alive by the end of the study whilst the opposite was observed for those with both HIV and Cancer and those with Cancer as only 25% and 12.6% of patients falling in these groups survived. The proportion of patients who died during the follow-up period was higher amongst those referred by Specialist Doctors (85%) as

compared to those referred by either self or other individuals with those referred by community caregivers having the least proportion of 13.2%. Bedridden patients had the highest proportion (89.7%) of patients who died during follow-up.

In addition to the relative frequencies corresponding to each of the subgroups, associations between these and the outcome were determined using Pearson's Chi-square test for association. Based on the frequencies and p-values obtained, it was observed that ART Status was the only variable without an association with the primary outcome. More specifically, the p-value of $0.590 > 0.05$ implies that there is no association between outcome and ART Status for those who are HIV infected. The findings show that there is a statistically significant association ($p<0.001$) between diagnosis and the primary outcome. This implies that the patterns of survival differ between those with HIV only, Cancer only and those co-infected with Cancer and HIV with the latter having the least survival followed by Cancer only and HIV only.

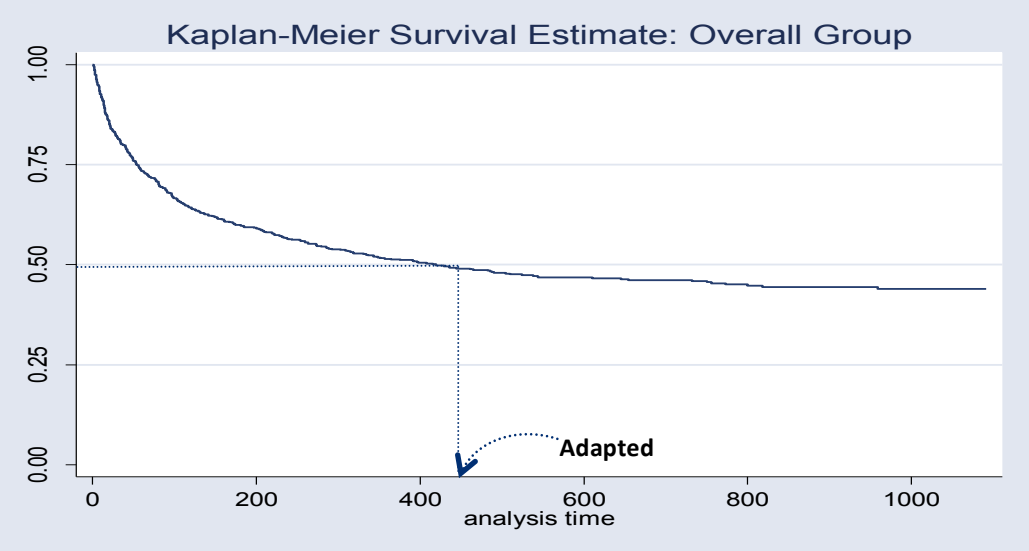
4.3 The Median Survival – The Kaplan-Meier Product Limit Method

Using the Kaplan-Meier Product Limit Method, the survival distribution of the cohort was plotted. The probability of survival was estimated and a Median Survival Time of 419 days for the cohort was found as shown in Table 11 and by the Kaplan-Meier Survival Curve in Fig 6 below.

Table 11: Overall Median Survival Estimate

	n	Median Survival Time (Days)
Overall	597	419

Fig 6: Kaplan-Meier Survival Curve for 597 Patients Enrolled into IHS Palliative Care Programme

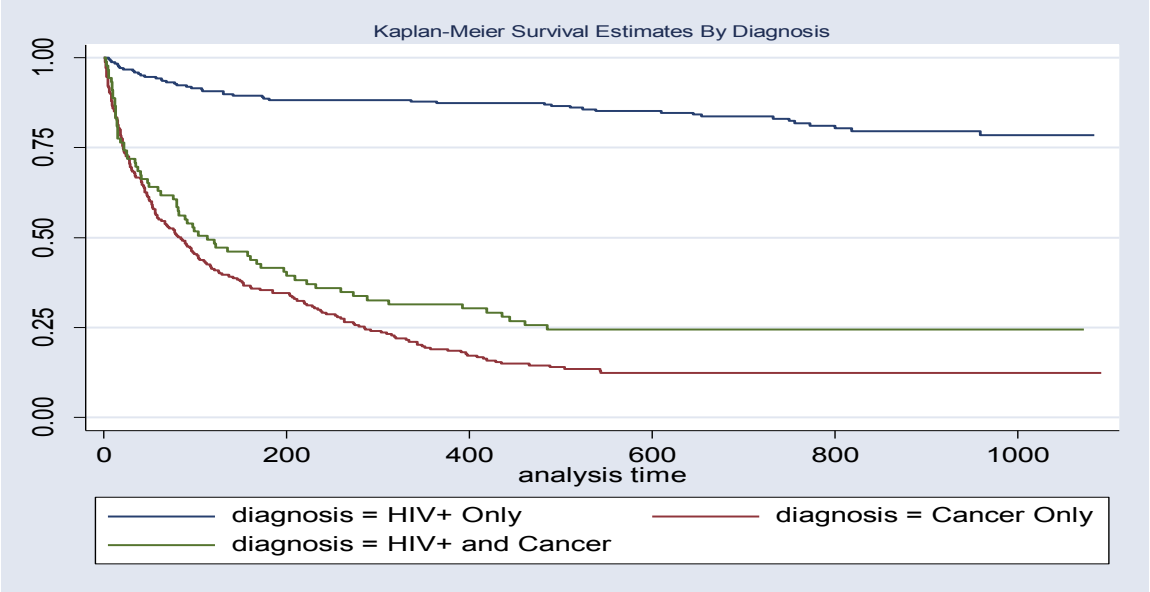


The median survival time illustrated above is the one that represents the whole cohort. Based on this estimate, we therefore expect 50% of a cohort of patients enrolled into IHS palliative care programme to survive beyond 419 days from the day of enrolment into the programme.

4.3.1 Disease Specific Survival Patterns

The survival of the cohort was analyzed across the 3 disease groups i.e. HIV+ only, Cancer only as well as both HIV+ and Cancer. Differences were noted in the survival times of participants according to their diagnosis. Patients with HIV-only live longer than those with either Cancer or those with both Cancer and HIV. The median survival of HIV+ patients was indeterminate implying that more than 50% of patients in that group lived beyond the follow-up period of at least 12 months (365 days). On the contrary, we expect to remain with 50% of a cohort of patients with Cancer-only after only 84 days of follow-up. The median survival time for those with both HIV and Cancer was slightly higher at 113 days. The difference in the survivor curves for the diagnoses was observed to be statistically significant ($p<0.001$). Fig 7 below presents the survivor curves according to diagnoses.

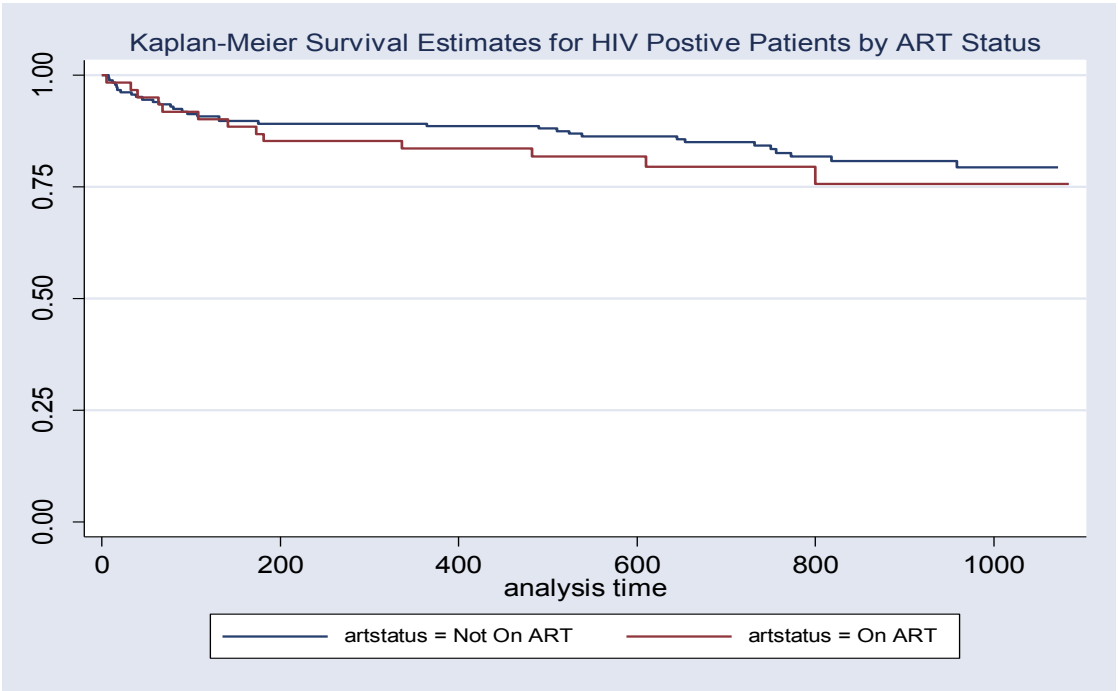
Fig 7: Survival Estimates by Diagnosis



4.3.1.1 Survival and ART Status amongst HIV+ Patients

The median survival times for HIV infected patients on ART and those not on ART are both indeterminate as shown in Fig 8 and their respective survivor functions are not statistically significantly different (p=0.424, Log-rank test for equality of survivor functions).

Fig 8: Survival Estimates By ART Status: HIV+ Patients Only



4.3.1.2 Survival and Cancer Types

The median survival times obtained suggest that patients with Cancer of the Blood (429 days) and those with Cancer of the Head and Neck (243) have better survival amongst the patients diagnosed with Cancer only. The test for the equality of survivor functions also shows that there is adequate evidence to suggest that the survivor functions according to cancer types are different. A p-value of 0.04 was obtained. Patients with the least survival amongst those with Cancer only were observed to be those with cancer of the Bone (16 days), Brain (41), Digestive/Gastrointestinal (50 days) and Endocrine (53 days).

Table 12: Survival Estimates by Cancer Types

Type of Cancer (Broad Classification by Body Region)	n=241	Median Survival Time Days	Log-Rank Test
Blood	7	429	
Bone	10	16	
Brain	2	41	
Breast	33	160	
Digestive/Gastrointestinal	69	50	
Endocrine	3	53	
Eye	2	89	
Genitourinary	37	96	
Gynecologic	33	80	
Head and Neck	7	243	
Respiratory	17	71	
Skin	1	-	
Unknown Primary Cancer (UPC)	20	103	**p=0.04**

The survivor functions of specific cancer types within some of the sub-classes were observed to be statistically significantly different with p= 0.000. Patients diagnosed with Cancer of Gall Bladder, Liver and Hepatoma had the shortest survival times amongst those with Digestive/Gastrointestinal Cancers with estimates of 19, 24 and 35 days respectively as shown in Fig 9 below.

Fig 9: Vertical Presentation of Median Survival Estimates: Digestive/Gastrointestinal Cancers

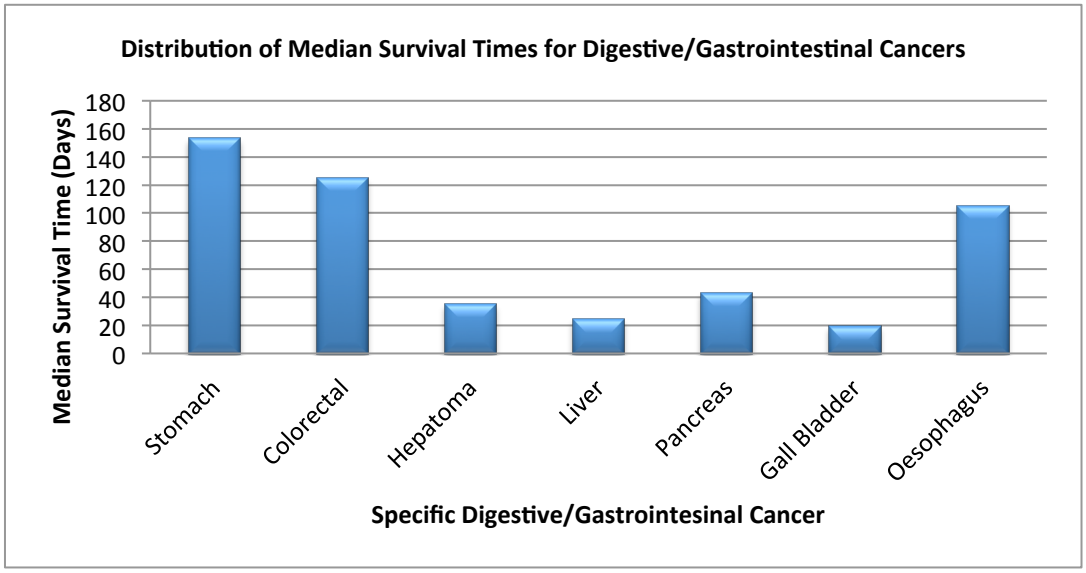


Table 13 gives the survival times for specific cancers under Gynecologic and Genitourinary classes**.**

Table 13: Medium Survival Times for Genitourinary and Gynecologic Cancers

		Median Survival Time (Days)	Log Rank Test p-value
Genitourinary	**n=37**		**p= 0.082**
Kidney	3	109	
Prostate	29	126	
Bladder	5	45	
Gynecology	**n=32**		**p= 0.675**
Cervix	27	80	
Ovary	4	23	
Uterus	1	-	

Patients with Respiratory, Digestive/Gastrointestinal and Blood cancers were observed to have the shortest survival times of 8, 22 and 22 days respectively amongst those with both HIV and Cancer as shown in Table 14 below.

Table 14: Median Survival Times by Cancer Types for Patients with Both HIV and Cancer

Type of Cancer (Broad Classification by Body Region)	n=89	Median Survival Time Days	Log-Rank Test
Blood	5	22	
Brain	1	-	
Breast	8	80	
Digestive/Gastrointestinal	13	22	

Eye	1	-	
Genitourinary	9	82	
Gynecologic	13	172	
Head and Neck	2	-	
Respiratory	4	8	
Skin	25	259	
Unknown Primary Cancer (UPC)	8	122	**p<0.001**

The survivor functions were observed to be statistically significantly different with $p < 0.001$ obtained from the log rank test for the equality of survivor functions.

4.3.1.3 Survival and Stage of Disease

Data on the stage of disease for patients with HIV only was observed to be incomplete and inadequate to facilitate meaningful survival analysis. Although data for those with Cancer and both diseases was also incomplete, the following survival estimates were obtained.

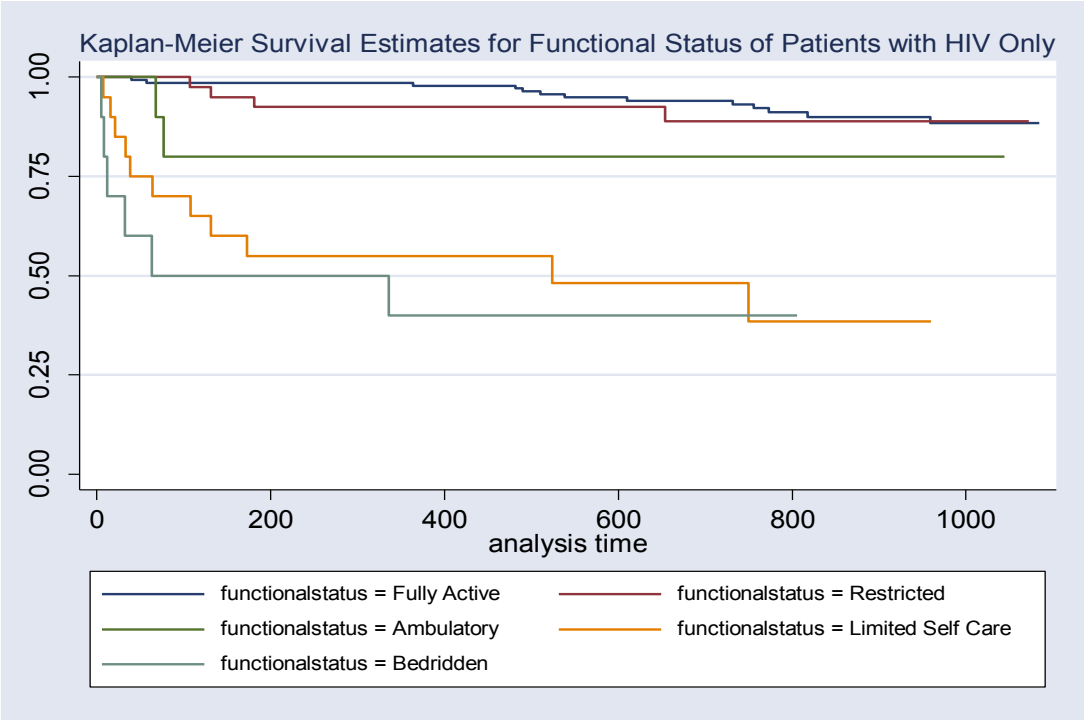
Table 15: Survival and Stage of Disease

	n	**Median Survival Time Days**	**Log-Rank Test**
Cancer	**n=153**		**p=0.906**
Stage I	1	-	
Stage III	3	105	
Stage IV	149	71	
HIV+ and Cancer	**n=40**		**p=0.414**
Stage I	1	-	
Stage III	3	40	
Stage IV	36	80	

The median survival estimates suggest that Stage IV Cancer patients have a relatively shorter survival of 71 days whilst those with both HIV and Cancer and are in Stage IV are expected to live longer than the Stage III counterparts. The survivor functions according to the disease stage were however not statistically significantly different with p-values greater than 0.05 as highlighted in Table 15 above.

Survival analysis stratified by functional status of patients on enrolment was conducted with the survivor functions corresponding to each status graphically displayed below.

Fig 10: Survival and Functional Status for Patients with HIV Only



Patients with HIV only and whose functional state fell in the last two stages of the functional performance scale, Bedridden and Limited Self Care, had survival estimates of 63 days and 524 days respectively whilst the rest had indeterminate median survival estimates. The survivor functions were observed to be statistically significantly different with $p<0.001$.

Similarly, statistically significant differences were observed in the survival of patients according to their functional status for those with Cancer only and those with both HIV and Cancer. Patients who are either bedridden or have limited self care on enrolment have a relatively shorter survival as shown by Table 16 below.

Table 16: Survival and Functional Status of Patient on Enrolment

	n	Median Survival Time Days	Log-Rank Test
Cancer	**n=165**		**p<0.001**
Fully Active	29	161	
Restricted	48	60	
Ambulatory	15	271	
Limited Self Care	30	84	
Bedridden	43	19	
HIV+ and Cancer	**n=75**		**p<0.001**
Fully Active	9	-	

Restricted	24	259
Ambulatory	8	97
Limited Self Care	20	81
Bedridden	14	22

4.3.2 Survival and Demographic Characteristics

4.3.2.1 Survival and Gender

The median survival times for males and females with HIV only were indeterminate and their survivor functions were not statistically significantly different (p=0.827). Similarly, differences between the survival of males and females diagnosed with Cancer only were not statistically significant (p=0.165). Their median survival times of 89 days and 84 days respectively were also noted to be reflective of the median survival time of 84 days for the combined group of patients with cancer only. The survival patterns of males and females with both HIV and Cancer were, however, observed to be statistically significantly different (0.018) with the males having a considerably lower median survival of 81 days as compared to that of their female counterparts of 209 days. Table 17 below provides a summary of these findings.

Table 17: Survival and Gender

Diagnosis/Disease	Gender	Median Survival Time (Days)	Log-rank Test for Equality of Survivor Functions
HIV+ Only	Males	Indeterminate	p=0.827
	Female	Indeterminate	
Cancer Only	Males	81	p=0.167
	Female	84	
Both HIV and Cancer	Males	81	p=0.018
	Female	209	

There is a generally fair distribution of gender across the cancer types as shown in Table 18 below.

Table 18: Distribution of Cancer Types by Gender

	Gender		
Type of Cancer	Males	Females	Total
Blood	3	2	5
Brain	1	0	1
Breast	0	8	8
Digestive/Gastrointestinal	7	6	13
Eye	0	1	1
Genitourinary	9	0	9
Gynecologic	0	13	13
Head and Neck	0	2	2
Respiratory	2	2	4

Skin	14	11	25
UPC	3	5	8
Total	**39**	**50**	**89**

The difference in the survival functions of males and females was assessed across functional status in order to control for any potential confounding effect. A statistically significant difference (p=0.000) in the survivor functions was noted as shown in Table 19 below.

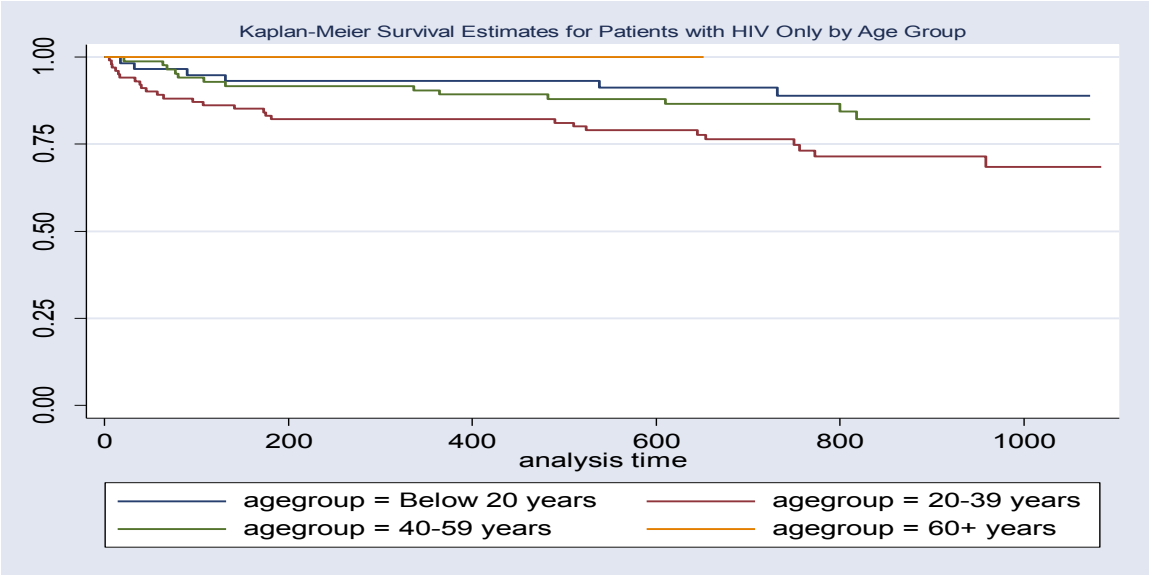
Table 19: Median Survival of Estimates by Gender across Functional Status

	Median Survival (Days)		
Functional Status	**Males**	**Females**	**Stratified Log-Rank Test for Equality of Survivor Functions**
Fully Active	-	-	P<0.001
Restricted	197	259	
Ambulatory	13	209	
Limited Self Care	34	80	
Bedridden	15	37	

4.3.2.2 Survival and Age

The median survival times for HIV+ patients for all the age groups were indeterminate. However, differences between the survivor functions were statistically significant (p=0.035). Fig 11 below illustrates the differences and indeterminate nature of the survivor curves. Notably, the illustration suggests that HIV+ patients aged 20-39 years have a shorter survival span followed by those in the 40-59 years age group.

Fig 11: Survival Estimates for Patients with HIV Only By Age Group



Considering those with Cancer only, the results suggested that patients in the 20-39 years survive longer than those in the other age groups with a median survival time of 292 days. However, the differences observed were not statistically significant (p=0.118). Survival estimates across the age groups for those with both HIV and Cancer were also not statistically significantly different as shown in Table 20 below.

Table 20: Survival and Age

Diagnosis/Disease	Age	Median Survival Time (Days)	Log-rank Test for Equality of Survivor Functions
Cancer Only	Below 20 years	16	p=0.118
	20-39 years	292	
	40-59 years	60	
	60+ years	71	
Both HIV and Cancer	Below 20 years	122	p=0.179
	20-39 years	222	
	40-59 years	157	
	60+ years	80	

4.3.3 Survival and Referral Source

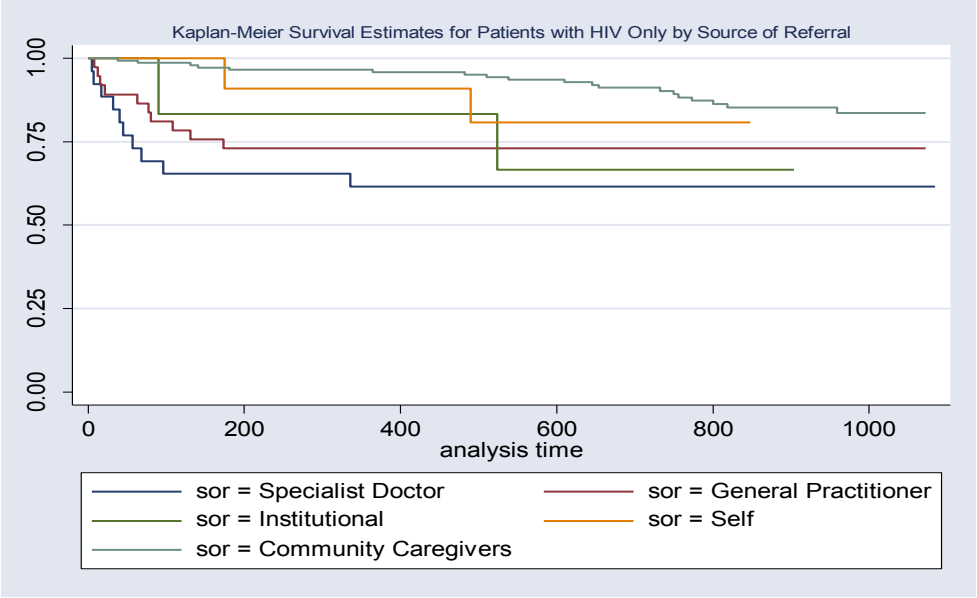
The majority (55%) of the patients in this cohort were referred to IHS by a specialist doctor. Of these, 71% were patients with Cancer only. Table 21 is a cross tabulation of patient diagnosis and the source of referral.

Table 21: Cross-tabulation of Diagnosis and Source of Referral

	Source of Referral				
Diagnosis	**Specialist Doctor**	**General Practitioner**	**Institutional**	**Self**	**Community Caregiver**
HIV+ Only	27	37	6	11	146
Cancer	214	8	0	1	7
HIV+ and Cancer	60	12	3	0	8

The median survival estimates for patients diagnosed with HIV only for each of the different referral sources were observed to be indeterminate. However, using the log rank test, their survivor functions were observed to be statistically significantly different with patients referred by the Specialist Doctors graphically depicted as relatively having shorter survival whilst those referred by the community surviving the longest as shown in Fig 12.

Fig 12: Survival Estimates by Source of Referral for Patients Diagnosed with HIV Only



The survivor functions corresponding to the different sources of referral for patients diagnosed with Cancer only and those with both Cancer and HIV were statistically significantly different. In both cases, patients referred by a Specialist Doctor had the lowest median survival times whilst those referred by the community caregivers exhibited the longest survival with their median survival estimates being indeterminate. Table 22 provides the summary estimates.

Table 22: Survival and Source of Referral for Patients with Cancer, Both HIV and Cancer

Diagnosis/Disease	Source of Referral	Median Survival Time (Days)	Log-rank Test for Equality of Survivor Functions
Cancer Only	Specialist	78	**p<0.001**
	General Practitioner	45	
	Self	-	
	Caregiver	-	
Both HIV and Cancer	Specialist	91	**p=0.015**
	General Practitioner	122	
	Institutional	209	
	Caregiver	-	

4.4 Modeling Survival Data – The Cox Proportional Hazards Model

Survival data was modeled using the Cox Proportional Hazards Model whose function represents the risk of dying in a very short time interval after a given time *t*. It provides the risk of dying at a particular specified time. Hazard Ratios respective to each study factor and the corresponding p-values and 95% confidence intervals are shown in the Tables 23, 24 and 25 below.

Table 23: Modeling Survival Data - Cox Regression: Patients with HIV Only

	Hazard Ratio	P-value	[95% Conf. Interval]
Gender	1.31	0.480	0.62; 2.75
Age Group	0.95	0.845	0.60; 1.52
ART Status	1.00	0.992	0.47; 2.13
Functional Status	2.09	<0.001	1.68; 2.62

Table 24: Modeling Survival Data - Cox Regression: Patients with Cancer Only

	Hazard Ratio	P-value	[95% Conf. Interval]
Gender	0.74	0.211	0.46; 1.19
Age Group	1.35	0.106	0.94; 1.94
Broad Cancer Type	0.96	0.217	0.89; 1.02
Specific Cancer Type	0.98	0.020	0.96; 1.00
Functional Status	1.29	0.001	1.12; 1.50
Stage	1.00	0.553	0.55; 1.82

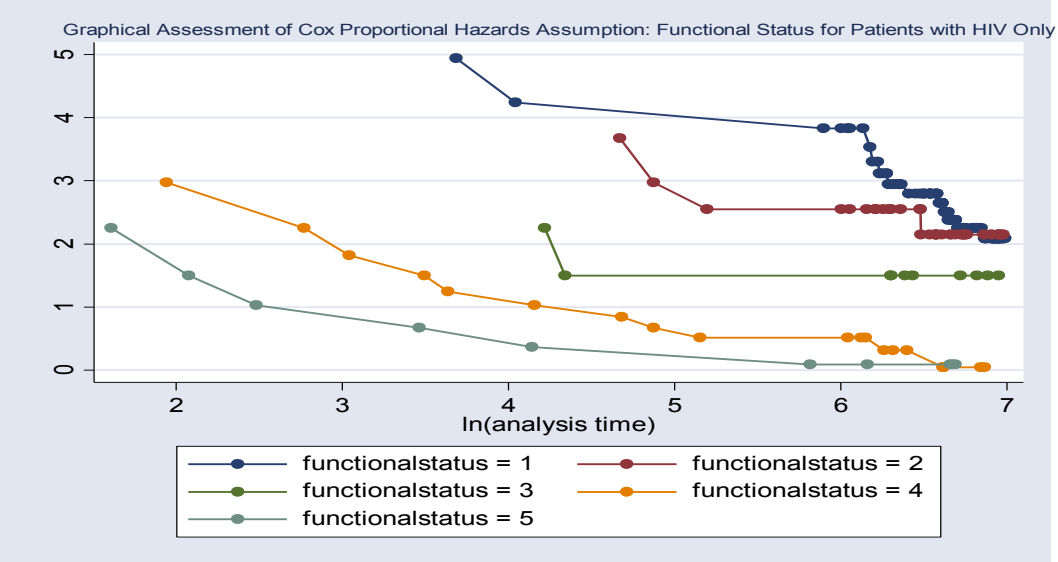
Table 25: Modeling Survival Data - Cox Regression: Patients with Both HIV and Cancer

	Hazard Ratio	P-value	[95% Conf. Interval]
Gender	0.66	0.348	0.27; 1.58
Age Group	1.13	0.731	0.57; 2.24
Broad Cancer Type	0.99	0.836	0.85; 1.14
Specific Cancer Type	0.98	0.420	0.94; 1.02
Functional Status	1.81	0.001	1.26; 2.57
Stage	0.63	0.291	0.27; 1.48

The functional status of clients was observed to be the only significant predictor of survival for patients with HIV only as well as for those with Cancer only or both HIV and Cancer. In all cases, the higher one is on the functional performance scale, i.e. towards limited self care and bedridden status, the higher the risk of dying. The corresponding p-values were less than 0.05 and the corresponding 95% confidence intervals did not include a 1. Although a p-value of $0.02 < 0.05$ was obtained for the variable Specific Cancer Type for patients with Cancer only, the 95% confidence interval included a 1. For all the other variables, the p-values were observed to be greater than 0.05 and had 95% CIs which included a 1 implying that the risk of dying in a short time interval after a given time t is not influenced by the type of cancer for those patients with cancer only.

The underlying assumption of proportionality for the Cox Proportional Hazards Model was not satisfied for all the three diagnosis. In all cases, the plot of the Log Hazard Ratio Function (LHRF) showed that the hazard functions were not proportional as the plots were not constant over time. A plot of the variable Functional Status would show the functions converging, crossing and diverging contrary to the expected linearity as shown in Fig 13 below.

Fig 13: Graphical Assessment of the Proportional Hazards Assumption



5.0 Discussion

This study found that the overall median survival of patients referred to the IHS palliative care programme was 419 days. This median survival time is considerably longer than that found from other previous studies looking at the survival patterns after enrolment in palliative care programmes which range from 11 to 54 days [7-9]. These differences could be attributed to a number of factors which include the disease specific and demographic characteristics of participants, the stage of illness on enrolment as well as the models of care.

Participants in the referenced studies mainly suffered from cancer, heart diseases and other terminal illnesses. This study, however, looked at patients presenting with mainly HIV and Cancer related illnesses. Considering the differences in the manifestation, progression and management of diseases in general, and particularly with HIV, it is practical to expect different survival patterns due to the inclusion of HIV patients in this study. Patients diagnosed with HIV only were noted to have longer survival compared to those with Cancer only as well as those with both HIV and Cancer.

It is prudent for one to possibly attribute the longer survival of HIV patients in this study to the dynamics and natural progression of the disease itself, early referral as well as to consider the uptake of the life prolonging ART as a possible confounder. The chi-square tests of association between ART Status and the outcome of death was, however, not significant ($p=0.590$). This is further augmented by the survival estimates which show that the median survival times for HIV infected patients on ART and those not on ART are both indeterminate as shown by Fig 8 and that their respective survivor functions are not statistically significantly different ($p=0.424$, log-rank test for equality of survivor functions). If ART was indeed confounding factor, one would therefore expect lower median survival estimates for the HIV infected but not on ART as ART would have prolonged survival for those on the therapy and the increased the median survival estimated. In addition to this, the survival curve for those on ART was observed to be below the survival curve for those not on ART hence suggesting that those who are not on ART live longer than those on ART. Whilst the efficacy of ART is in this case somewhat challenged graphically, it is vital that the non significance ($p=0.424$) of the differences in the survivor functions be

emphasized. This anomaly, if significant, would have possibly pointed to the assertion that the HIV infected patients in the programme are probably initiated on ART rather late in their illness and when the disease has progressed to the advanced stages for there is sound evidence of the efficacy of ART as a life prolonging medication in existing literature [14].
The median survival of 84 days for the Cancer patients, though still higher, is relatively closer to that obtained on the other studies whose populations and samples were predominantly comprised of cancer patients.

This study also provides evidence that overally; patients with both HIV and Cancer live relatively longer in the programme compared to those with Cancer only. A review of the findings show that this is consistent for some of the types of cancers such as the Gynecologic cancers with those having both HIV and Cancer having a median survival of 172 days compared to those with Cancer only whose median survival was estimated at 80 days. However, the opposite is true for Digestive/Gastrointestinal, Blood cancers and Respiratory as very low median survival times of 22, 22 and 8 days respectively were observed for those with both HIV and Cancer. Literature [17] generally provides evidence that HIV infected patients have a high risk of developing certain cancers, such as Kaposi Sarcoma, non-Hodgkin lymphoma, and cervical cancer. For those with HIV, these cancers are often referred to as "AIDS-defining conditions," suggesting that they signify the development of AIDS. Over the past years, Digestive and Gynecologic cancers such as Liver, Colorectal and Cervical cancers have also been noted to be highly prevalent amongst the HIV infected, particularly in Sub-Saharan Africa [17]. The shorter survival observed in this study could, therefore, very well be attributed to the progression of the disease itself. It is interesting to note that amongst those with both HIV and Cancer, those diagnosed with Skin and Gynecologic cancers had substantially high median survival estimates of 259 and 172 days respectively. The most common sub-group of cancer (28%) amongst those with both HIV and Cancer is Skin cancer which is mainly constituted with Kaposi Sarcoma. Gynecologic cancers, which make up 15% of the same group, are largely comprised of cervical cancers in this study.

In principle, the IHS Palliative Care Programme embraces the concept of initiating palliative care from diagnosis. Other Palliative care programmes particularly those in the referenced studies, on the other hand, only cater for terminally ill patients i.e. end-of life care. This is a very critical

aspect in that it is logical to expect patients on end-of-life care to live for a relatively shorter period than a cohort with a combination of both terminally or non-terminally ill patients. Patients presenting with poor functional status and were exhibiting advanced stages of their diseases generally had lower survival estimates in this study whilst patients who were fully active on enrolment exhibited higher survival. Patients who were bedridden on enrolment had a median survival estimate of 63 days, relatively close to those obtained in the referenced studies looking at end of life care. Looking at the other end of the functional performance scale, the median survival time for patients who were fully active on enrolment was indeterminate for HIV+ only and Cancer/HIV+ patients whilst for those with Cancer only it was estimated at 161 days. The closeness of the median survival of the bedridden participants to that of other studies may very well be linked to the high likelihood of these patients having been in the terminal stages of their illnesses, a predominant characteristic of participants in other studies.

The differences in the survival according to stage of disease were, nonetheless, not significant for Cancer and Cancer/HIV+ patients. Although the median survival estimates for both groups stratified by Stage of Disease suggest that patients at Stage IV on enrolment have relatively shorter survival than their overall group estimates, there is insufficient evidence to suggest that the survival functions of the different stages are significantly different ($p=0.906$ and $p=0.414$ respectively). Whilst this may be contradictory, as one would expect a high likelihood of the Stage IV patients to be Bedridden or having Limited Self Care, the non-significance could have arisen from the incompleteness of the stage data, resulting in a sample size which may have not been adequate to facilitate the detection of significant differences in the survival functions.

Closely related to the above discussion is the aspect of the model of care used in the IHS Programme in comparison to those implemented elsewhere. The palliative care programmes in the referenced studies are predominantly in-patient units although two have a combination of both in-patient and out-patient units. The IHS palliative care programme is a community based programme in which patients are attended to in their homes. The effect of this is evidenced by the stratified analysis based on referral sources. Whilst the main source of referral, like in other studies, were the health professionals (55%), community caregivers also contributed a significantly high proportion (30.8%) of referrals to the IHS programme due to its community

and home based care approach. Patients referred by community caregivers were, for all diagnoses, exhibiting higher survival rates as compared to those referred by the specialist and general health practitioners. This could be attributed to an improved targeting and case identification system at community level due to the cadre of trained caregivers. On the other hand, patients with life threatening illnesses such as Cancer and HIV are traditionally discharged from the public health institutions for home care when the disease has advanced and are no longer responsive to curative treatment as well as when they are exhibiting a poor functional status. The low median survival estimates exhibited by patients referred by the health professionals could nevertheless be reflective of the health professionals' understanding of palliative care which has historically been regarded as end-of-life care. This therefore results in the health professionals only referring patients when they are in their end stages of life and are being discharged from the public health system. There is consequently a great need for advocacy on the benefits of early initiation of palliative care services targeting health professionals and institutions.

Differences in the survival patterns of males and females were only significant for patients with both HIV and Cancer. Females with both HIV and Cancer survive longer than their male counterparts with median survival estimates of 209 and 81 days respectively ($p=0.018$; Log-rank test for equality of survivor functions). The differences could be attributed to the types of cancers and the functional status of the patients as these variables were both found to be associated with the survival of patients with HIV and Cancer. Using Pearson's Chi-square Test for Association, a statistically significant association between Gender and Type of Cancer was observed ($p<0.001$). Although amongst the Cancer/HIV+ patients there is a generally fair distribution of gender within those cancers with low median survival estimates (Respiratory, Digestive and Blood), the differences in the median survival estimates for the gender related cancers, Genitourinary and Gynecologic, of 82 and 172 days respectively is striking and could have influenced the difference across the gender strata for this group. The results also indicate that although it is consistent that survival is shorter with poor functional status on enrolment for both males and females who have HIV and Cancer, the estimates for males are significantly lower than those for the females ($p<0.001$) suggesting that the differences in survival across gender is, however, not necessarily due to the functional status of the patients.

Age was noted to have no significant influence on the survival of Cancer and Cancer/HIV+ patients. On the other hand, differences across age groups for patients with HIV were statistically significantly different (p=0.035) despite their median survival estimates being indeterminate. Patients aged between 20-39 years have shorter survival than the other age groups. Patients aged 60 years and above survive the longest. The results are consistent with national and regional statistics which reflect adults aged 20-39 years being the most impacted by HIV and AIDS in terms of prevalence and AIDS related mortality [3, 10].

Despite the associations observed at the various levels, the functional status of patients on enrolment was identified as the only variable with some predictive capability on the survival of patients after enrolment. Patients who are either bedridden or have limited self care on enrolment have a significantly higher risk of dying in a relatively short period of time. The underlying assumption of proportionality was however not satisfied by the model. Observed differences could therefore be as a result of natural changes in the hazard over time.

5.1 Study Limitations

The main limitation of this study was embedded in its design. Being retrospective in nature implied that the data used was secondary and therefore, although the overall quality of the data was satisfactory, there were some deficiencies in its completeness due to missing data. As highlighted in Table 3 of the methodology section, the overall completeness rate of data was 76% before extraction, after which it increased to 87%. The latter, despite the improvement, still points to gaps in the data quality.

The paucity of data on Stage of Disease resulted in the analysis being restricted to patients with either Cancer Only or both HIV and Cancer. The process of extracting the data also presented possible bias arising from the misclassification of the stages as it relied on extracting qualitative information from records and aligning to standard stage characteristics. Generally, the incompleteness of data may have also had effect on the ability of a particular analysis to detect small differences as the sample size would have been reduced for that particular variable being analyzed.

There may have also been some observer bias in detecting inconsistencies or errors in the records of patients who did not die during the follow-up period as death was a primary outcome of interest. This therefore could have affected the accuracy of the data.

5.2 Conclusion and Recommendations

In summary, this study found that patients enrolled into IHS Palliative Care programme have a median survival time of 419 days. The estimate obtained is substantially higher than that found in literature but this is largely due to the differences in disease specific and demographic characteristics of participants as well as the models of care implemented by the IHS programme in relation to those from which other studies are based.

Patients who have HIV only live longer than those with both HIV and Cancer as well as those with Cancer only. An association between gender and survival was only observed for patients with both HIV and Cancer in which females were noted to live longer than the males. Age is significantly associated with survival but only for patients with HIV only although the median survival estimates remained indeterminate for all age groups. Patients who are bedridden on enrolment have shorter survival compared those with better functional status. This was also observed to be the only significant variable on modeling. However, the main underlying assumption for the Cox Proportional Hazards Model was not satisfied by the data. The findings of this study need to be interpreted with consideration of the quality of data, which may have had some deficiencies in the completeness and possible inaccuracies arising from probable bias.

Nevertheless, it is essential that a review of the programme be done in light of the study's key findings. A structured model of care planning that takes cognisance of the differences of the survival patterns of patients should be established. There is need for improved awareness and sensitization of IHS Palliative Care model, targeting the health professionals in order to ensure improved timing of referral.

It is also of the essence that a review of the IHS Programme's data collection and processing system be conducted with the aim of improving the completeness and accuracy of data. Specific areas requiring attention in this regard include:

- Review of the Patient Information Sheet (PIS) in order to standardize the fields and recording of variables such as Diagnosis and Stage of Disease using nationally and/or internationally recognized standards
- Training of the health professionals on the recording of the PIS with a focus on the completeness and accuracy
- Enhancing the database check codes in order to minimize data entry errors
- Refresher training of officers on the use and management of the Beneficiary Database

This study also presents an opportunity for further inquiry. A critical programming question that may need investigation is whether a structured model care plan based on survival data as earlier recommended would be more effective in improving the quality of life of patients. The high prevalence of some cancers such as digestive/gastrointestinal cancers amongst patients referred to the service warrants further epidemiological inquiry, taking into account other known risk factors, as this would also provide an essential and sound evidence base for cancer prevention efforts by the organization.

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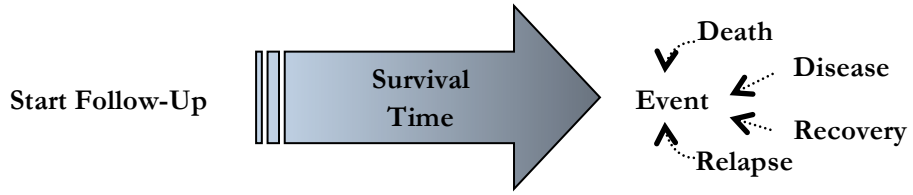
APPENDICES

APPENDIX 1: SURVIVAL ANALYSIS – A CONCEPTUAL FRAMEWORK

1.1 Background

Survival analysis is a collection of statistical data analysis techniques for which the outcome variable of interest is time until an event occurs. The time variable is also known as survival time as it gives the time that an individual has "survived" from a particular starting time (e.g., time initiated the treatment) to a particular endpoint of interest (e.g., recovery or death). Survival time can thus be days, weeks, months and years from the beginning of follow-up until the event occurs. An event, also known as failure, can refer to disease incidence, death, recovery from disease/injury, relapse from remission or any other particular endpoint of interest that may occur to an individual. Failure may also be a positive event such as is the case in the attainment of certain functional abilities after treatment or surgery.

Figure 1.3: Survival Analysis Model



1.2.1 Censoring

A common feature in survival data is that for some individuals, we may have some information about individual survival time but do not have the exact survival time. Complete survival time may not be available as some patients may still be alive or in remission at the end of a follow-up period. Those observations which contain partial information on their survival times are known as Censored Observations. Censored observations may also arise when individuals are lost to follow-up after a study period. In general, censored observations arise whenever the dependent variable of interest represents the time to an endpoint of interest, and the duration of the study is limited in time. Censoring mainly occurs when:

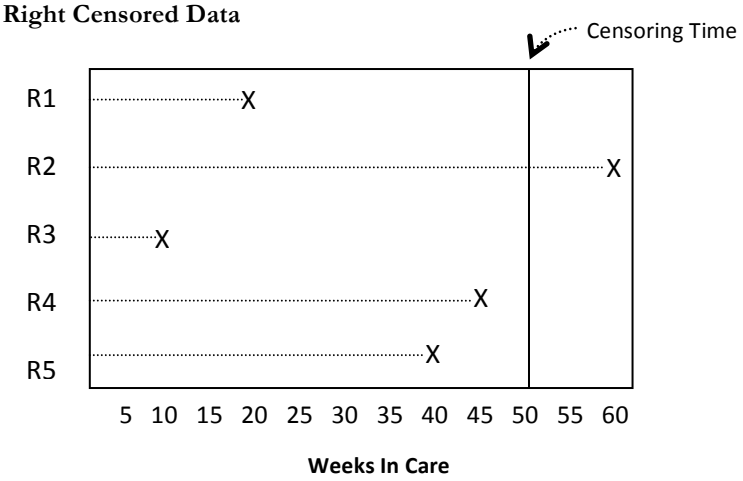
1. Individual **withdraws** from a study because of some specific reason or death (i.e. if death is not the outcome of interest.
2. Individual is **lost to follow-up** during the study period.
3. **Study ends** before individual experiences the event/endpoint of interest.

1.2.1.1 Right and Left Censoring

Although censoring may arise in various forms, a basic distinction lies between left and right censoring. An observation is said to be right censored if all that is known about *T*, the time of occurrence of some event, is

greater than some valueC_T, the endpoint of observation. The censoring time C_T is often fixed and the number of individuals failing is a random variable. Left censoring, on the other hand is when all that is known is that the individual has experienced the event before the start of the study. Right censoring is far more common in both the social and natural sciences.

Figure 1.4 **Right Censored Data**



1.2.1.2 Type I, Type II and Random Censoring

Type I censoring refers to when follow-up is terminated at a point in time. It therefore means that the censoring time is fixed and is under the control of the investigator. In Type II censoring, observation is terminated after a specified number of events have occurred. Random censoring occurs when the termination of observation is not under the control of the investigator. This type of censoring also occurs when you have a single termination time but entry times vary randomly amongst individuals. While standard approaches in survival analysis do not distinguish between Type I, Type II and Random Censoring; a basic requirement is that random sampling should be *noninformative*. That is, an individual who is censored at time C_T should be representative of all other individuals with the same explanatory variables who survive up to the timeC_T.

1.2.2 The Survival Function

An underlying assumption in survival analysis is that survival times are a result of some random process. The survival time *T* for an individual is therefore a random variable which follows a probability distribution. The probability distribution of a random variable can be represented by the Cumulative Distribution Function c.d.f which gives us, for a variable *T*, the probability that the variable will be less than or equal to a given value *t*. The c.d.f is given by $F(t) = P(T \leq t)$

In survival analysis, we are interested in establishing the probability that an individual survives beyond a given time *t*. The distribution of survival times can thus be represented by the survival function:

$$S(t) = P(T > t) = 1 - F(t)$$

The survivor function is pivotal in survival analysis as essential summary information on survival data may be availed through obtaining survival probabilities for different values of *t*. The survival curve is a graphical plot of $S(t) vs\ t$ and it shows us, for each time plotted on the X axis, the proportion of individuals surviving as at that point. A theoretical representation of a survivor function as it ranges from 0 to ∞ (infinity) exhibits a smooth survival curve in contrast to the step function graphs obtained in practice as shown below.

Figure 1.5 Theoretical S(t)

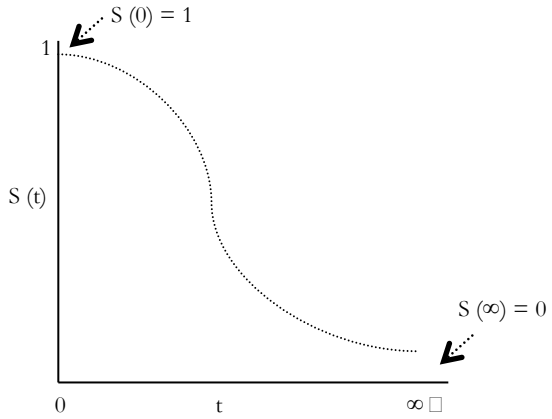
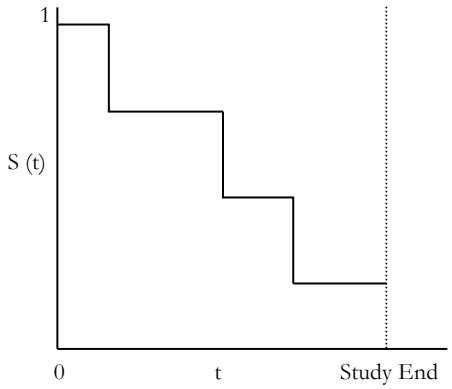


Figure 1.6 S(t) in Practice



The probability of surviving at any point in time can easily be drawn from a survival curve. This leads us to an important summary statistic that is widely used in describing survival distributions:-

The Median Survival Time: This is the survival time at which the cumulative survival function is equal to 0.5. The general interpretation is that we expect that 50% of the population will survive beyond that time corresponding to the survival probability of 0.5. The 25th and 75th percentiles of the cumulative survival function can also be determined likewise.

1.2.3 The Hazard Function

The hazard function at time *t* is defined as the risk of dying in a very short interval of time after time *t* given that one is alive at time *t*. (MCE 504 S9). The hazard function, denoted by *h(t),* is given by the formula:

$$h(t) = \lim_{\Delta t \to 0} \frac{P(t \leq \Delta t | T \geq t)}{\Delta t}$$

The hazard function is also sometimes referred to as the conditional failure rate as it computes the number of failures per time units in the respective interval respective to the number of surviving cases at the mid-point

of the interval. The numerator is a conditional probability whilst the denominator Δt denotes a small change in time. It is therefore a probability per unit time hence it being regarded as a rate.

3.2.4 Estimating Survival Functions from Samples with Censored Observations

3.2.4.1 The Kaplan Meier (Product Limit) Method: Ungrouped Data

The survival function can be estimated directly from continuous failure or survival times. If for *n* individuals with provided survival times and *r* of these being larger than a specified time *t*, then the probability of surviving more than *t* units is given by *r/n*.

$$S(t) = P(T > t) = {}^{r}/_{n}$$

In view of censored observations, the product limit estimator, first proposed by Kaplan Meier in 1958, takes into consideration the censored status of an observation through a constant that either assumes *1* if an observation is uncensored (complete), and *0* if it is censored in the estimator:

$$S(t) = \prod_{j=1}^{t} [(n-j)/(n-j+1)]^{\sigma_j}$$

Where n is the total number of observations, $\prod$ is the product of all observations less than or equal to t and σ_j is a constant that assumes 1 if the j^{th} observation is uncensored and 0 if is censored.

The Kaplan Meier estimate of the survival function is a step function (similar to Fig 1.6 above) with each step down depicting the occurrence of at least one death. The median and other percentile survival times can obtained from the Kaplan Meier Survival Curve. In the event that the survival curve always exceeds the corresponding survival probability of 0.5 then the median survival time cannot be determined.

3.2.5 Comparing Survival Curves

3.2.5.1 The Log Rank Test

The Log Rank Test is a very useful tool in comparing the survival experience of two groups of individuals. The test is robust in detecting differences between survival curves when the mortality rate in one group is consistently higher than that of the second group. The statistic used for comparing the two groups is:

$$X^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2}$$

O_1 and O_2 are the observed numbers of deaths in the two groups whilst E_1 and E_2 are the corresponding expected numbers of deaths. X^2 follows a chi-squared distribution with 1 degree of freedom if the null hypothesis is true. The decision rule in this test is such that: If $X^2 > X^2_{Tabulated}$ we reject Ho and conclude that there is a statistically significant difference in survival between the groups. A stratified log rank test can also be done to control for potential confounders. The log rank test makes use of the Mantel-Haenszel Test Statistic to accumulate the observed number of failures at each time to the expected number of failures given that the survival distributions of the groups being compared are identical.

3.2.5.2 Cox Proportional Hazards Model

The proportional hazards model is a regression model used when investigating or controlling for several variables in survival data. It is one of the most general of regression models as it is not reliant on assumptions based on the shape or nature of an underlying survival distribution. The model is based on modeling the hazard function $h(t)$. It assumes that the underlying hazard rate (rather than survival time) is a function of the independent variables. The model with p explanatory variables is given by:

$$h_i(t) = h_0(\mathrm{t})e^{(\beta_1 X_{i1} + \beta_2 X_{i2} + \beta_3 X_{i3} + \ldots\ldots \beta_p X_{ip})}$$

Where $h_0(\mathrm{t})$ is the baseline hazard, the hazard for the respective individual when all independent variable values are equal to zero, and $h_i(\mathrm{t})$ represents the hazard function for subject *i*.

APPENDIX 2: PATIENT INFORMATION SHEET

PATIENT BACKGROUND INFORMATION **REF NO:** _____

SURNAME:_____**FIRST NAME(S)** _____

I.D No: _____ **ADDRESS:** _____**TEL**_____

PATIENT D.O.B:_____/_____/_____ **AGE**_____ **SEX:** _____**MARITAL STATUS:**_____

(Married, Divorced, Single, Widowed, Child)

OCCUPATIONAL STATUS:_____**HEAD OF HOUSEHOLD**_____

(Formal, Informal, Unemployed, School Going, Tertiary) **(e.g., patient, wife, husband, aunt, children, grandparents)**

RELIGION:_____**HOUSEHOLD FAMILY SIZE**_____

(e.g., Christian, Moslem, Rastafarian, African Tradition, none)

NUMBER OF CHILDREN IN HOUSEHOLD:_____**NUMBER OF ORPHANS IN HOUSEHOLD:**_____

NAME OF PRIMARY CAREGIVER_____**AGE OF PRIMARY CAREGIVER:**_____

NEXT OF KIN:_____**ADDRESS:**_____**TEL:**_____

REFERRAL DATE_____/_____/_____ **FIRST SEEN:**_____/____/_____

NURSE(s):_____
S/WORKER:_____

PATIENT BRIEF CONFIDENTIAL MEDICAL HISTORY

REFERRING DOCTOR:_____**TEL:**_____**GP:**_____**TEL:**_____

SPECIALIST:_____**TEL:**_____**MED. AID:**_____**MA NO:**_____

MEMBER'S

NAME:_____**EMPLOYER:**_____

DIAGNOSIS:_____

_____ ☐ ☐

REASON FOR REFERRAL:_____**HIV TEST DONE? NO** **YES**

IF YES, WHEN? _____HIV STATUS ☐ (+) ☐ (-) ☐

n/t ☐ ☐ ☐

IF (+), IS THE PATIENT ON ART? YES NO N/A

PATIENT ON PROPHYLACTIC TREATMENT? YES ☐ NO ☐

PATIENT ATTENDING O.I CLINIC? YES ☐ NO ☐

PATIENT'S FUNCTIONAL STATUS ON DAY OF ASSESSMENT (*Please Circle the Appropriate*):
1) Fully Active 2) Restricted 3) Ambulatory 4) Limited Self Care 5) Bedridden

IF BEDRIDDEN, FOR HOW LONG?_____

ALLERGIES:_____
_____

DATE CASE REGISTERED _____/_____/_____ SIGNED (M&E):……

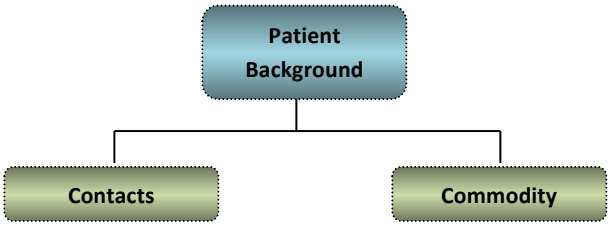
DATE CASE CLOSED _____/_____/_____ REASON

(Nurse)_____

D.O.D: ____/_____/_____PLACE OF DEATH_____DAYS IN CARE_____

Description of IHS Beneficiary Database and Data Collection & Processing Flow

The IHS Database uses the Epidemiology Informatics (EPI INFO) software and operates on a Microsoft Access Platform. The database is relational with 1 Parent View (Patient Background and Medical Information) and 3 Child Views (Contacts, Commodity Distribution) as shown by the diagram below.



The Parent View which is the main source of information for this study stores patient information which falls into the following categories:

1. Patient Background Information
   - Identification including Unique Reference Number
   - Socio-demographic data
   - Referral Date, Date First Seen
   - Nurse Attending and Assigned Social Worker
2. Patient Brief Medical History
   - Referral Source and Reason for Referral
   - Doctor/Physician
   - Diagnosis
   - Treatment (IHS or other)

Data for the Parent View is sourced from the Patient Information Sheet (PIS) which is the assessment and registration form used on enrolment into the programme. The IHS Standard Operating Procedures (SOPs) of the Data Collection and Processing System stipulates the following with regards to the PIS and Beneficiary Database.

- The responsible nurse shall forward the PIS to the M&E Department for entry into the Beneficiary Database within 72 hours of assessment.
- The M&E Department shall return all entered PIS Forms to the responsible nurse with a "Processed" stamp on each within 48 hours.
- All Patient Deaths shall be notified to the M&E Department through the PIS clearly with the Date of Death and Place of Death clearly written.
- The M&E Department shall enter the DODs and PODs, close file, sign accordingly and store in the Indexed Archival System within 48 hours of notification.

The Contacts Database, which is a Child View of the Parent View, shall be updated monthly using the Nurses Contacts Form. Similarly, the Commodity Distribution Database is, on a monthly basis updated on the type and quantity of commodity (e.g. 2 Bars of Soap, 2 Pair of Latex Gloves) distributed to each respective beneficiary. The Unique Identifiers are programmed for auto-search to facilitate easy update of the database with regards to additional Background or Child View information during the course of care.

SURVIVAL PATTERNS OF PATIENTS ENROLLED INTO IHS PALLIATIVE CARE PROGRAMME
DATA CODING MANUAL

OUTCOME

1. OUTCOME STATUS

1=Died
2=Alive
3=Transferred/Relocated

2. CENSORING VARIABLE = CV

1=Censored
0=Not Censored

3. TIME VARIABLE = Days in Care (DIC)

STUDY FACTORS

1. GENDER

1=Male
2=Female

2. AGE GROUP

1= Below 20 years
2= 20-39 years
3= 40-59 years
4= 60+ years

3. DISEASE

DIAGNOSIS

1= HIV and AIDS
2= Cancer
3= HIV and AIDS + Cancer

Type of Cancer (Broad Classification by Body Region)

1 = Blood
2 = Bone
3 = Brain
4 = Breast
5 = Digestive/Gastrointestinal
6 = Endocrine
7 = Eye
8 = Genitourinary
9 = Gynecologic
10 = Head and Neck
11 = Respiratory
12 = Skin
13 = Unknown Primary Cancer (UPC)

Stage of Disease (Specified)

1=Stage I
2=Stage II
3=Stage III
4=Stage IV

ART STATUS
1=On ART
2=Not On ART

4. FUNCTIONAL STATUS ON ENROLMENT
1= Bedridden
2= Ambulatory
3= Fully Active
4= Restricted
5= Limited Self Care

5. REFERRAL SOURCE
1= Specialist Doctor
2= General Practitioner
3= Health Institution
4= Community
5= Self