FACTORS CONTRIBUTING TO MORTALITY AMONG HIV INFECTED PEOPLE ON ISONIAZID PREVENTIVE THERAPY (IPT) IN BOTSWANA

by

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DE CL A R A T I O N

I declare that FACTORS CONTRIBUTING TO MORTALITY AMONG HIV INFECTED PEOPLE ON ISONIAZID PREVENTIVE THERAPY (IPT) IN BOTSWANA is my own work and that all the sources I have used or quoted have been indicated and acknowledged by means of complete references and that this work has not been submitted before for any other degree at any institution.

16 February 2013

Mavis Neo Bengtsson

Date
ABSTRACT

The purpose of the study was to describe factors contributing to mortality among HIV-infected people on Isoniazid Preventive Therapy (IPT) in Botswana. A quantitative, explorative, descriptive study was used and 80 records of deceased IPT respondents were reviewed through the use of a checklist.

The demographic factors, baseline physical examination, hospitalisation and drug history were taken into consideration. Out of the deceased patients, 75% were female. The major findings showed that 100% (N=80), the most highly indicated causes of death were gastroenteritis (18.75%), cryptococcal meningitis (17.5%) and pneumonia (16.25%). Of the patients (28.75%) who died before completing the six months of IPT, the causes of death were gastroenteritis (21.7%), symptoms and signs of bacterial pneumonia (17.4%), cryptococcal meningitis (13%), Pulmonary Tuberculosis (PTB) (13%), septicaemia (13%), and murder (13%). It has been recommended that there should be reorganisation of services of care for HIV-infected persons, such as provision of Cotrimoxazole Prophylaxis Therapy (CPT) and Antiretroviral Therapy (ART) to ensure holistic approach care. The future study should include HIV-infected children on IPT using the same or modified objectives. The conclusion drawn was that disintegrated interventions of IPT, CPT and ART and lack of holistic care for PLHIV lead to opportunistic infections that caused mortality on patients on IPT.

KEY CONCEPTS

HIV/AIDS, Isoniazid Preventive Therapy (IPT), mortality, demographic factors, baseline physical examination, hospitalisation, drug history.
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Chapter 1
Orientation to the study

1.1 INTRODUCTION

Mycobacterium tuberculosis (TB) remains one of the leading causes of morbidity and mortality globally (Zumla, Mwaba, Huggett, Kapata, Chanda & Grange 2009:197). The World Health Organization (WHO) estimated that in 2008 there were 11.1 million prevalent cases of tuberculosis (WHO 2009b:5). This included some 9.4 million people who had contracted the disease that same year, of which 1.4 million were new cases of TB that occurred in people living with human immunodeficiency virus (PLHIV) (WHO 2009b:5).

In 2006 TB killed an estimated 1.7 million people, including 230 857 who were Human Immunodeficiency Virus (HIV)-positive (WHO 2008b:393). About 639 000 people (83 per 100 000) died of TB in sub-Saharan Africa in 2006 (WHO 2008b:393). A study done in Thailand by Cain, Anekthananon, Burapat, Akksilp, Mankhatitham, Srinak, Nateniyom, Sattayawuthipong, Tasaneeyapa and Varma (2009:260) found that the most common causes of death were TB (27%), HIV-associated causes other than TB (35%), and a condition not related to TB or HIV (15%). The study further indicated that hospitalisation at enrolment was strongly associated with increased risk of death caused by TB, but not death due to other causes, which further suggests that delay in TB diagnosis may be partially responsible (Cain et al 2009:262).

One cohort study in West Africa identified the two key causes of severe morbidity as TB and invasive bacterial infections (Moh, Danel, Messou, Ouassa, Gabillard, Anzian, Abo, Salamon, Bissagnene, Seyler, Eholié & Anglaret 2007:2489). This was after the study had revealed that other independent risk factors for mortality and/or severe morbidity were, at baseline: high viral load, advanced clinical stage, past history of tuberculosis, low BMI, low haemoglobin and low CD4 cell count; and during follow-up: low CD4 cell count and persistently detectable viral load (Moh et al 2007:2489).
Botswana has one of the world’s highest HIV infection rates, at 17.6% (Botswana CSO 2009:3), and also has the highest burden of TB per capita, with a TB notification rate of 470 per 100,000 of population (Botswana MoH 2009:5). Even though a high notification rate could be positive, signifying a good notification process, the Ministry of Health (2010:4) indicated that there had been increased total relapse cases of 8.5% in 2008, compared with the 5.9% in 2007. The re-treatment of TB cases also increased to 11.4% in 2008, compared with 5.9% in 2007 (Botswana MoH 2010:4). Of the 9,645 TB cases reported in 2008, 88% were new infections (Botswana MoH 2010:4).

IPT regimen used in Botswana is 300 mg Isoniazid daily for 6 months. Isoniazid (INH) is known for its effectiveness (92%) in reducing TB (Samandari, Agizew, Nyirenda, Tedla, Sibanda, Shang, Mosimaneotsile, Motsamai, Bozeman, Davis, Talbot, Moeti, Moffat, Kilmarx, Castro & Wells 2011:10). The above study showed that some patients on IPT became sick, hospitalised and dead.

It was for this reason that the researcher decided to identify all records of deceased HIV-infected people who had used Isoniazid Preventive Therapy (IPT) from 2005 to 2008 in Botswana. The researcher selected all the records in the IPT register of patients that had fallen sick and died, and used them as the basis for the study. No sampling was done; rather a census was taken, because of the manageable total number of 80 records. All the available records were investigated in order to analyse and describe the causes of mortality of HIV-infected people on IPT. Determining and exploring the actual causes of death might help in identifying effective interventions.

1.2 BACKGROUND INFORMATION ABOUT THE RESEARCH PROBLEM

Botswana is one of the resource-limited countries in sub-Saharan Africa and has a population of 1.8 million. According to the Botswana AIDS Impact Survey III (BAIS III) (Botswana CSO 2009:3) an estimated 17.6% of Batswana (people of Botswana) were now living with HIV and AIDS, making Botswana one of the countries worst affected by HIV in the world. Since the beginning of records in 1990, the TB notification rate began to rise along with the emergence of HIV (Botswana MoH 2007:11). As a result, Botswana also has one of the world’s highest burdens of TB per capita (Botswana MoH 2009:5).
In view of the high TB rates, Botswana rolled out its IPT programme in 2001. IPT regimen used in Botswana is 300 mg daily for 6 months. Between 2001 and April 2007, the IPT Programme in Botswana had registered 75 235 HIV-infected people. Of these, 73 263 (97%) were determined to be eligible for IPT because they were HIV-infected, had clear TB symptom screening and clear chest X-rays. Of those determined to be eligible, 543 declined IPT, 863 were later excluded and 963 did not start IPT. The reasons were pregnancy, active TB and death (Motsamai 2008:14).

Eligible clients who started IPT were a total of 71 541, and 35% (25 075) of these were documented as having completed a full course of therapy (defined as 6 or 9 visits). Approximately 59% (43 313) of eligible patients who began IPT did not complete a full course of therapy. Although the reason for 70% of the group’s not completing therapy was unknown, among this group 180 patients developed active TB, and 683 patients died (cause unknown) (Motsamai 2008:14).

Despite the confirmed efficacy of IPT, concerns about the durability of protection, toxicity, drug resistance and adherence have limited its uptake (Golub, Saracen, Cavalcante, Pachelo, Moulton, King, Efron, Moore, Chaisson & Durovi 2007:1441–1442). The protection offered by IPT to those infected with HIV may depend on a number of factors, including the degree of immune suppression of the individual, duration of IPT, adherence to and potency of the regimen, as well as the general risk of re-infection in that setting (Woldehanna & Volmink 2004:10).

While much attention has been given to morbidity and mortality of HIV-infected people; little attention has been given to this phenomenon in HIV-infected people using IPT. A clinical trial was conducted in Botswana between 2004 and 2009, to determine if continuous use of IPT was better than 6 months’ use. The results of the study indicated that continuous use of IPT reduced TB incidence by 43% as compared with 6 months of IPT use, and was 92% effective in reducing TB on tuberculin-skin-test positive patients, as evidenced by Samandari, Agizew et al (2011:8). The conclusion was that continuous IPT use among the HIV-infected was superior to 6 months use of IPT (Samandari, Agizew et al 2011:10). However, although continuous use of IPT reduced TB by 43%, there were some participants in that study who took IPT and yet died, or were hospitalised. The current study therefore investigated records of HIV-infected people
who were on IPT and died, in order to determine the causes of mortality and to explore the factors that contributed to their mortality.

1.3 RESEARCH PROBLEM

The gap identified in the literature review was the inadequate evidence of studies conducted in Botswana or elsewhere in Africa determining the causes of morbidity and mortality of HIV-infected people on IPT. This gap in research evidence, together with the challenges found when offering IPT in Botswana, as earlier indicated by Motsamai (2008:14), and the results of the report by Samandari, Agizew et al (2011) led the researcher to investigate factors contributing to mortality among HIV-infected people on IPT.

The IPT programme evaluation done in Botswana in 2008 also indicated that at the initial screening, the evaluation of patients was often incomplete, as physical examinations were not conducted routinely. In most cases physical examination was not performed and symptom screening was minimal. Health workers reported that clients collected their Isoniazid refills from the pharmacy without seeing a doctor or nurse (Botswana MoH 2008:14). No data could be found regarding whether these clients were simply being overlooked and were presenting at other parts of the healthcare sector, or were defaulting (Botswana MoH 2008:14). The researcher therefore was led to investigate what contributed to the mortality of HIV-infected people while on IPT.

1.4 RESEARCH PURPOSE

The purpose of the study was to explore the factors that contributed to mortality in HIV-infected people on IPT.

1.4.1 Research objectives

The objectives of the study were to

- determine the causes of mortality among HIV-infected people on IPT
- explore the factors that contributed to mortality among HIV-infected people on IPT
1.5 SIGNIFICANCE OF THE STUDY

The benefit of this study would be to develop strategies to improve the quality of care and to reduce mortality of HIV-infected people on IPT. This could assist in future recommendations and interventions to prevent further illnesses and deaths among HIV-infected people and those on IPT.

The study could be significant for medical and laboratory technologists and nursing and pharmaceutical professionals. They could ensure that HIV-infected patients were comprehensively screened for TB before enrolling on an IPT programme, and were meticulously monitored for the duration of the IPT programme.

1.6 DEFINITIONS OF KEY CONCEPTS

Both conceptual and operational definitions are important. A conceptual definition presents the abstract or theoretical meaning of the concepts being studied. Even straightforward terms need to be conceptually defined by researchers. This is necessary because quantitative researchers must indicate how the variable will be observed and measured in the study (Polit & Beck 2008:59).

An operational definition of a concept specifies the operations that the researchers must perform to collect and measure the required information. Operational definitions should be congruent with conceptual definitions (Polit & Beck 2008:59).

1.6.1 Operational and conceptual definitions

1.6.2 Hospitalisation

This refers to admission to a particular hospital, based on the severity of the disease (Gordis 2004:39). For the purpose of this study, hospitalisation is based on documented records of admission of HIV-infected people on IPT in any medical centre for any illness.
1.6.3 Isoniazid Preventive Therapy (IPT)

This refers here to the patient taking Isoniazid 300 mg daily for 6–9 months as prophylaxis for TB, according to the national programme of a country (Botswana MOH 2008:7). For the purpose of this study, IPT being taken was based on documented records of the patient concerned having taken Isoniazid 300 mg daily for between 0 and 6 months.

1.6.4 Mortality

Expressing mortality in quantitative terms can pinpoint differences in the risk of dying from a disease between people in different geographic areas and subgroups in a population (Gordis 2004:48). For the purpose of this study only, mortality is any death documented on the records of HIV-infected persons who were on IPT, which occurred any time from 0-6 months, regardless of the cause.

1.6.5 Risk factors

These refer to aspects of personal habits or environmental exposure that are associated with an increased probability of the occurrence of a disease (Bonita, Beaglehole & Kjellstrom 2006:32). For the purpose of the study, risk factors are any threats documented in the records, which can either cause illness or death.

1.6.6 Patients

A patient is a person who is under medical care or treatment (http://www.medterms.com). For the purpose of this study, patients refer to those clients who were HIV-infected and were taking IPT and are deceased.

1.7 META-THEORETICAL PARADIGM

Quantitative research describes and examines relationships and determines causality among variables. It incorporates logistic, deductive reasoning, as the researcher examines particulars to make generalisations about a phenomenon (Burns & Grove 2009:23).
The focus is concise and reductionist. Reductionism involves breaking the whole into parts so that the parts can be examined. The quantitative approach to scientific inquiry emerged from a branch of philosophy called “logical positivism”, which operates according to strict rules of logic, truth, laws, axioms and predictions. Quantitative researchers hold the position that truth is absolute and there is a single reality that can be defined by careful measurement. To find the truth as a quantitative researcher, the researcher must be completely objective, meaning that values, feelings and personal perceptions cannot enter into the measurements of reality (Burns & Grove 2009:22). An explorative and descriptive study was done, which means there was no manipulation of variables, and it was ensured that there was no bias during the process.

1.7.1 Assumption underlying the study

The following assumption served as a starting point for this study:

- Certain risk factors contribute to mortality among HIV-infected people on IPT

1.8 RESEARCH DESIGN

The research design was a retrospective, quantitative, explorative, descriptive design. Quantitative research is a formal, objective, systematic process to describe and test relationships and to examine cause and effect interactions among variables (Burns & Grove 2005:747). Descriptive research provides an accurate portrayal or account of statistics of a particular individual, situation or group. Descriptive studies offer researchers a way to: (1) discover new meaning; (2) describe what exists; and (3) determine the frequency with which something occurs, and categorise the information. Descriptive studies are usually conducted when little is known about a phenomenon; they provide the basis for the conduct of correlational, quasi-experimental and experimental studies (Burns & Grove 2009:25). Exploratory research is designed to increase knowledge of the field of the study. For example, pilot or preliminary studies are often conducted before a larger study to test a methodology or provide an estimate of an effect size (Burns & Grove 2005:357).

There was an exploration and description of variables that existed (such as age, cluster determinant 4 for lymphocyte cells (CD4), body-mass index (BMI), tuberculin skin test (TST), highly-active antiretroviral therapy (HAART), Cotrimoxazole prophylaxis therapy
(CPT), and gender), to determine the frequency with which a variable occurred, categorise information and compare the variables under study without manipulating these variables. There was no control over the independent variables, namely risk factors. There was no interference with cause and effects of the variables, meaning that the researcher did not implement anything in the study to achieve the outcome, unlike in an experimental study, where there is manipulation of the variables to achieve the expected outcome. The results were described according to the findings.

1.9 RESEARCH METHODS

1.9.1 Population and sample

The population under study consisted of all HIV-infected people who were on IPT and had documented records of their hospitalisation and death. To be included, the records had to indicate that the patients were on their first to sixth month of IPT in January 2005 to December 2008. This was a period when IPT was given under close monitoring in two sites in Botswana. The patients were reviewed on a monthly basis by the nurses or could come to the hospital at any time they were not feeling well. Patients were only allowed to come to the same clinic until completion of their prophylaxis. The reason for choosing the indicated time frame was that it would also provide a good sample size for the analysis.

A list of all records for sampling consisted of records of patients who had taken IPT with some notes of admission or some notes of death, such as death certificate or documented verbal autopsy report (documented verbal history about the illness that led to the death of the individual, collected by health personnel from a relative or a caregiver). No sampling was done; rather a census was used because of the manageable sampling frame of 80 records. The researcher studied all the available records of HIV-infected people who took IPT, were hospitalised and died while on IPT.

1.9.2 Procedure of data collection

The existing de-identified data contained in the records at Botswana and United States of America Centre for Disease Control and Prevention (Botusa) was used. A checklist was used to extract data from all the available 80 records. Questions included were
identification (ID), age, gender, educational level, employment, facility used, weight, height, temperature, CD4 count, TST reading, illnesses, hospitalisations, reasons for hospitalisation, if the patient used ART or CPT, and causes of death. The researcher completed all the 80 checklists in two weeks' time. After completion of data collection, the data was entered into the computer on an Excel spreadsheet.

1.9.3 Data analysis

According to Burns and Grove (2009:44), data analysis is the process used by the researcher to reduce, organise, and give meaning to the data collected. This is done to make the results or findings easier for the reader to grasp, and also provides a way of enabling the research question to be answered in the light of the study findings of Holland and Rees (2010:61).

The study was explorative and descriptive by nature; hence descriptive statistics were used. Descriptive statistics include frequency tables and measures of central tendency such as mean, median, mode, variability: variance, standard deviation and range on ratio continuous variable. These were used to summarise each extracted response from all the records. Variables that the researcher analysed included: age group, CD4 counts, use of HAART, BMI, gender, TST result, and CPT. Ranges and variance of age, CD4 count, BMI and TST were also calculated. Explorative analysis was also applied wherever possible. This included summarising data using statistical charts – pie charts, bar graphs for nominal variables and histograms for continuous variables. The Statistical Package for Social Sciences (SPSS) was used for the analysis of the collected data.

1.10 VALIDITY AND RELIABILITY

Validity is a measure of the truth or accuracy of a claim, an important concern throughout the research process (Burns & Grove 2005:755). Validity of the design is the strength of a design to produce accurate results, which is determined by examining statistical conclusions, internal validity, construct validity and external validity (Burns & Grove 2005:754). Validity of an instrument determines the extent to which the instrument actually reflects the abstract construct being examined (Burns & Grove 2005:755).
Internal validity is the extent to which the effects detected in the study are a true reflection of reality, rather than the results of extraneous variables (Burns & Grove 2005:215).

1.10.1 Internal validity

Internal validity in this study is the extent to which factors contributing to mortality among HIV-infected people on IPT are a true reflection of reality, rather than being due to the effects of extraneous or chance variables that are not necessarily related to factors contributing to mortality among HIV-infected people on IPT.

1.10.2 External validity

External validity is concerned with the extent to which the study findings can be generalised beyond the sample used with the study (Burns & Grove 2005:219).

In this study the efforts to enhance external validity were through use of a census, which made it more representative, and there was comparison of findings with previous studies found in the literature. No sampling error was possible as a census was used. External validity of this study may, however, have been compromised by the fact that some of the records were incomplete.

1.10.3 Reliability

Reliability means dependability in a general sense, but in research it specifically means the degree to which random error is absent from a particular measurement procedure; consistency and repeatability of measurements results that use a particular measurement procedure (Stommel & Wills 2004:440).

Since the researcher was using records of the deceased patients’ reliability in the sense of dependability and trustworthiness was dependent upon the health personnel who had previously carried out the tests on the patients, whether they were qualified and were using reliable equipment, so that the researcher could depend on the results of the tests, such as CD4, temperature, height and weight.
1.11 ETHICAL CONSIDERATIONS

1.11.1 Permission to conduct research

The application for ethical clearance with the Higher Degrees Committee of the Department of Health Studies at the University of South Africa (Unisa), had been granted (see Annexure 1). Letters asking for permission to conduct the study were submitted (see Annexure 2). For the approvals for ethical clearance with the Ministry of Health, Botswana Health Research and Development Committee (HRDC) (see Annexure 3). Permission was granted for the use of records in Botusa (see Annexure 4).

1.11.2 Confidentiality and anonymity

There was respect for privacy and confidentiality and there was no misuse of records. Records and checklist were anonymous, as there were no names and the records were coded.

1.11.3 Scientific honesty

Scientific honesty in this record was maintained by ensuring proper referencing and by listing all scientific sources at the end. The researcher was competent to conduct the research, as the researcher had passed theoretical Masters in Public Health (MPH) modules on health measurements and research methodology in 2009. In addition, the researcher was being guided by two supervisors who are qualified lecturers and experienced researchers from Unisa.

The Director of Botusa did not find it necessary for the researcher to request a waiver because records used had no names of the patients and records could not be traced to a specific patient as the records were coded. There were no risks involved to the patients as the patients were no longer living, and data was retrieved from the records without any intervention.
1.12 SCOPE AND LIMITATIONS OF THE STUDY

Records studied on mortality of HIV-infected people on IPT were taken in two sites of Gaborone and Francistown which provided IPT. Possibilities exist that patients who died at other sites might have had different contributory factors to mortality.

1.13 STRUCTURE OF THE DISSERTATION

The dissertation comprises the following five chapters:

- Chapter 1: introductory information, gives an overview of the background to the research problem, the research objectives and the definition of concepts used in the study.
- Chapter 2 is the literature review and discusses the scientific sources reviewed for the study.
- Chapter 3 covers the research methodology and discusses the research design, the methodology used for data collection, the analysis and the ethical principles considered for the study.
- Chapter 4 presents and discuses the analysis of data and the research findings.
- Chapter 5 includes conclusions and recommendations drawn from the research findings.
- The final part of the report will consist of the annexures and will include references and the research checklist.

1.14 CONCLUSION

The chapter introduced the entire study. The chapter highlighted the background information to the research problem, which was that deaths occurred to some people living with HIV and were on IPT. The study aims and objectives were covered. The purpose of the study was to explore the factors associated with mortality in HIV-infected people on IPT and the risk factors associated with such mortality. Definitions of key concepts were specified in this chapter. The chapter concluded by outlining the content of the following chapters. The next chapter addresses the literature review on contributory factors to mortality in HIV-infected people on IPT.
Chapter 2

Literature review

2.1 INTRODUCTION

This chapter discusses the current knowledge on causes of mortality in HIV-infected people using IPT and identifies literature gaps supporting the choice of the topic for this study. The background of the problem and purpose of the study have already been discussed in the previous chapter.

A literature review is conducted to generate a picture of what is known about a particular situation and the knowledge gaps that exist in it. It refers to those sources that are pertinent or highly important in providing the in-depth knowledge needed to study a selected problem (Burns & Grove 2005:37).

In this study, the researcher found out from the review to what extent the literature showed that although INH had been found to be most effective in the prevention of tuberculosis, some HIV-infected patients on this treatment still became sick and some died.

2.2 PURPOSE OF THE LITERATURE REVIEW

The purpose of the literature review was to gain more understanding on causes of mortality on HIV-infected people using IPT. The review also helped the researcher to:

- refine the research problem and background information to the problem
- acquaint the researcher with current knowledge on causes of mortality on HIV-infected people using IPT and identify literature gaps supporting the choice of the topic
- identify relevant concepts to be included in the research
- identify and refine the study methodology and process
- develop the data collection instrument (Burns & Grove 2005:93)
2.3 SCOPE OF LITERATURE REVIEW

Although Botswana is one of the resource-limited settings in southern Africa, the literature review included both theoretical and empirical sources. Primary sources were mostly used to develop the report. Journal articles, research methodology and theoretical textbooks were used.

2.3.1 Theoretical sources

A variety of types of theoretical source were used for the study. These can generally be grouped into research methodology sources and conceptual theoretical sources. Sources on research theory, research methodology and theoretical conceptual reviewed for this study included mainly textbooks.

2.4 LITERATURE REVIEWED ON MORTALITY IN HIV-INFECTED PEOPLE AND IPT

2.4.1 Global perspectives on TB and HIV

In total, approximately 1.7 million people died of TB in 2009. The number of TB deaths per 100 000 population among HIV-negative people, plus the estimated number of TB deaths among HIV-infected people, equates to a best estimate of 26 deaths per 100 000 population (WHO 2010a:7). There were an estimated 14 million prevalent cases of TB in 2009 (WHO 2010a:7). Over 95% of TB infections are in the developing countries, where TB remains a dominant cause of morbidity and mortality (Heymann 2008:643).

In some sub-Saharan areas where 10–15% of adults are co-infected with both AIDS and TB, annual TB disease rates have increased fivefold to tenfold from the start of HIV/AIDS in the 1980s and today (Heymann 2008:646). Salaam-Blyther (2008:3) found that in countries with high HIV/AIDS prevalence, HIV/TB co-infection poses a significant health challenge. TB was the second most frequent cause of morbidity (38%) in West Africa, and its incidence remains high in TB-high-burden countries even with the use of ART.
Also, TB was the third major cause of in-programme deaths in South Africa; although in rural Malawi it was not found to be a risk factor for high early mortality in patients on ART (Abdulrazaq 2009:148). In Swaziland, 75% of TB patients were HIV-infected. South Africa, with 0.7% of the world’s population and the highest number of HIV-infected people, had 28% of all HIV/TB co-infection cases (Salaam-Blyther 2008:3).

2.4.2 HIV and TB in Botswana

Botswana has one of the world’s highest HIV infection rates, at 17.6% (Botswana CSO 2009:3), and also has the highest burden of TB per capita, with a TB notification rate of 470 per 100 000 population (Botswana MoH 2009:5). Even though this high notification rate could be positive, signifying a good notification process, the Ministry of Health (2010:4) indicated that there had been an increase of 8.5% in total relapse cases in 2008, compared with the 5.9% in 2007. The re-treatment of TB cases also increased to 11.4% in 2008, compared with 5.9% in 2007. Of the 9 645 TB cases reported in 2008, 88% were new infections (Botswana MoH 2010:4).

In addition to early diagnosis and effective treatment of infectious cases of PTB, other important strategies to prevent and control TB are vaccination of children with Bacillus Calmette Guerin (BCG) and treatment of persons with latent tuberculosis infection (LTBI), who are at high risk of developing active disease. Botswana rolled out its IPT programme in 2001 (Motsamai 2008:14). The results reported by Samandari, Agizew et al (2011:8) indicated that continuous IPT use was 92% effective in reducing TB incidence in people who were TST positive.

2.4.3 Tuberculosis transmission

Exposure to tubercle bacilli occurs from the airborne aerosolised droplet nuclei that measure 1-5 microns in diameter, and are produced by persons with pulmonary tuberculosis during forceful expiration efforts (cough, sneezing or singing) (Heymann 2008:645). The droplet nuclei are then inhaled by contact into pulmonary alveoli, and the Mycobacteria tuberculosis are ingested by alveolar macrophages, initiating new infection (Heymann 2008:645). Latent tuberculosis infection (LTBI) occurs when individuals infected with Mycobacterium tuberculosis carry the organism in a latent state, which is characterised by slowed or intermittent metabolism and replication below the level
necessary to produce clinical illness. The risk of reactivation of latent infection is low in healthy individuals, but is greatly increased in individuals with immuno-suppression, most notably that due to HIV infection (Churchyard, Scano, Grant & Chaisson 2007:52).

2.4.4 HIV Transmission

Sexual transmission of HIV (the most common route of infection) is when the virus initially enters individually by infecting resting CD4+ cells, activated CD4+ T-cells, resident macrophages, dendritic cells, or mucosal cells lining the rectal or cervico vaginal cavity (Levy 2007:325). Many individuals develop symptoms after 10 years, in which their CD4+ cell count has dropped below 350 and the viral load increases substantially (due to HIV rising too high in the blood and lymph nodes) and there is reduction in antiviral CD8+ cells. The virus (often with the X4 phenotype) has properties associated with virulence in the host that include the cellular host range, rapid kinetics of replication and CD4+ cell cytopathicity (increase in cell killing) (Levy 2007:327).

2.4.5 Background of IPT

Isoniazid (INH) Preventive Therapy, or IPT, refers to the use of Isoniazid tablets or suspension to treat patients who are infected with TB but do not have active TB disease, the condition known as LTBI (WHO 2011:1). For these patients, a six- to nine-month course of INH monotherapy significantly reduces the risk of progression from LTBI to active TB. Because HIV fuels the TB epidemic in countries with high HIV prevalence, providing IPT for people living with HIV (PLHIV) not only reduces the individual patient’s risk but also helps to mitigate TB transmission to others. WHO recommends the use of IPT in areas with high HIV prevalence (WHO 2011:2). In view of the high TB rates, Botswana rolled out its IPT programme in 2001, and uses a six-month course of INH monotherapy. Despite the confirmed efficacy of IPT, concerns about the durability of protection, toxicity, drug resistance and adherence have limited the uptake of the treatment (Golub et al 2007:1441-1442). The protection offered by IPT to those HIV-infected may depend on a number of factors, including the degree of immune suppression of the individual, duration of IPT, and adherence to and potency of the regimen, as well as the general risk of re-infection in that setting (Woldehanna & Volmink 2004:10).
Wallis, Doherty, Onyebujo, Vahedi, Laang, Olesen, Parida and Zumla (2009:162) have indicated that despite the availability of this inexpensive, effective, and reasonably well-tolerated therapy, tuberculosis continues to be a major global health problem. While Martinson, Barnes, Moulton, Msandiwa, Hausler, Ram, McIntyre, Gray and Chaisson (2011:12) specify that IPT has the potential to save millions of lives and contribute importantly to TB control in HIV high-burden regions, tuberculosis is still the most common opportunistic infection and the leading cause of death in HIV-infected people, especially in Africa, where tuberculosis rates have increased sharply in the past two decades.

A study done by Cohen, Lipsitch, Walensky and Murray (2006:7042), among other conclusions, projected the effects of IPT Intervention on HIV. They stated that effective IPT would avert a major cause of death among HIV-infected people in high TB-burden settings. These researchers used simulations that showed reductions in HIV-related deaths during the first few years after initiation of IPT programmes. However, they pointed out that, because the average lifespan of HIV-infected people was extended under IPT, HIV prevalence would increase, and HIV-infected people would have more time to transmit HIV to others. This process would lead to an increase in later HIV-related deaths as a result of delayed early mortality and increased transmission opportunity.

### 2.4.6 HIV and TB co-infection

The two diseases represent a deadly combination, since they are more destructive together than either disease alone. Other key facts about HIV/AIDS-TB co-infection are that TB is harder to diagnose, progresses faster, is almost always fatal if undiagnosed or left untreated, and kills up to half of all AIDS patients worldwide (Salaam-Blyther 2008:3). People with HIV/AIDS are up to 50 times more likely to develop TB in a given year than HIV-negative people; and about 90% of HIV-infected people living with HIV/AIDS die within four to twelve months of contracting TB if they are not treated for TB (Salaam-Blyther 2008:3). Heymann (2008:645) concurs that for adults co-infected with HIV and latent TB, the lifetime risk of developing active TB disease rises from an estimated 10% to up to 50%. In southern Africa the sero-prevalence of TB may be as high as 70–80% (Heymann 2008:643).
2.5 CAUSES OF MORTALITY IN HIV-INFECTED PEOPLE

One study showed that there were long diagnostic delays in urban African settings. The median total delay was eight and a quarter weeks; 24% of the patients had delays of more than 14 weeks, and half of this delay was due to the delay by the health system (Sendagire, Schim van der Loeff, Mubiru, Konde-Lule & Cobelens 2010:6). Many patients start treatment late, with a history of AIDS-defining illnesses and low CD4 cell counts; leading causes of death include tuberculosis, acute sepsis, Cryptococcal meningitis, malignancies, and wasting syndrome (Brinkhof, Boulle, Weigel, Messou, Mathers, Orrell, Dabis, Pascoe & Egger 2009:8).

Another study done by Bailey, Roper, Huayta, Trejos, López Alarcón and Moore (2011:209) also indicated clear opportunities missed for the diagnosis of tuberculosis, resulting in a delay in treatment for patients and the continued spread of Mycobacterium tuberculosis in the community. Sendagire et al (2010:6) reported that in Kampala over 90% of the patients had consulted one or more health-care providers before the final diagnosis was made, with a median of four visits per patient. This suggested that there were many missed opportunities for TB diagnosis in the health system in Kampala.

However, the increased risk of dying in HIV-infected people with TB disease may be due to HIV-related conditions rather than TB (Straetemans, Bierrenbach, Nagelkerke, Glaziou & Van der Werf 2010:5). Straetemans et al (2010:5) add that in five studies assessing cause of mortality and including HIV-infected people initiating TB treatment, the percentage of HIV-infected TB patients dying from TB during TB treatment varied from 16% to 46% of the total number of deaths of HIV-infected people during TB treatment. They point out that this means that in more than half of the HIV-infected TB patients, TB was not the main cause of death; other main causes of death included pneumonia, gastrointestinal disease, wasting syndrome, Kaposi’s sarcoma, meningitis, (other) opportunistic infections and toxic epidermal necrolysis (Straetemans et al 2010:5-6).

An observational cohort study done by Zhou, Elliott, Li, Lim, Kiertiburanakul, Kumarasamy, Merati, Pujar, Chen, Phanuphak, Vonthanak, Sirisanthana, Sungkanuparp, Lee, Kamarulzaman, Oka, Zhang, Tau and Ditangco (2009:4) found out that factors associated with overall mortality were: patients being aged more than 40
years, having lower CD4 counts and not receiving antiretrovirals. On the other hand, increased risks of TB morbidity and mortality were substance use, tobacco smoking and alcohol use (Heymann 2008:646). Mortality risk also increased when TB or any other AIDS-defining Illness was diagnosed during follow-up, and mortality was greatest in patients with multiple AIDS-defining illnesses other than TB, and patients with both TB and at least one other AIDS-defining illness (Zhou et al 2009:4).

A study done by Churchyard et al (2007:52) indicated that overall, TB preventive therapy is not associated with a reduction in mortality. However, among individuals with positive TST results, there is a 20% reduction in mortality. Of note is that TB-preventive therapy using Isoniazid/Rifampicin (INH/RIF) was associated with a significant 31% reduction in mortality in two trials. Mortality was reduced by 26% with the use of INH alone among individuals with positive TST results (Churchyard et al 2007:52). Moore, Liechty, Ekwaru, Were, Mwima, Solberg, Rutherford and Mermin (2007:719) found a mortality rate of 26% among patients in Uganda who received a diagnosis of TB within three months after starting ART, but they also reported high mortality rates among other patients with AIDS and active TB.

Koenig, Riviere, Leger, Joseph, Severe, Parker, Collins, Lee, Pape and Fitzgerald (2009:830) reported similar findings that patients with AIDS who received a diagnosis of TB during the first three months after ART initiation had a mortality rate of 27%, which was three times higher than that among other patients with AIDS and TB. One study in Thailand indicated in the results that receiving Cotrimoxazole was no longer significantly associated with reduced mortality (Akksilp, Karnkawinpong, Wattanaamornkiat, Viriyakitja, Mon Kongdee, Sitti, Rienthong, Siraprapasiri, Wells, Tappero & Varma 2007:1004).

Mills, Cohen and Colijn (2011:1517) found that local network structures could induce high levels of repeated re-infection that might undermine the projected effectiveness of IPT. Such incidence could be linked to factors like overcrowding and shebeens (informal bar) locations. Increase in TB could be due to a number of factors, including immigration from high-incidence areas, HIV infection, deteriorated socio-economic conditions among the poorest segments of the population, besides the dismantling of TB control services (Heymann 2008:643). Morbidity and mortality are also high among the adult males,
impoverished, disadvantaged and minority populations and are usually higher in urban areas (Heymann 2008:643).

Although some HIV-infected people starting ART in sub-Saharan Africa experienced mortality rates that were comparable with those experienced by other patients with a chronic condition, early mortality in adults starting ART continues to be high in sub-Saharan Africa (Brinkhof et al 2009:8). Reducing mortality in PLHIV will require intensive collaboration between HIV and TB programmes to ensure prompt HIV testing and initiation of life-saving treatment (Varma, Sriprapa Nateniyom, Somsak, Akksilp, Mankatittham, Sirinak, Sattayawuthipong, Burapat, Kittikraisak, Monkongdee, Cain, Wells & Tappero 2009:8).

2.6 CONCLUSION

The literature was reviewed to gain more understanding on the causes of mortality in HIV-infected people using IPT. Various sources were accessed to find the literature information related to this study. The global perspectives of TB and HIV, HIV and TB in Botswana, tuberculosis transmission, HIV transmission, the background of IPT and causes of mortality in HIV-infected people were discussed. The next chapter will discuss research design and methods.
Chapter 3
Research design and method

3.1 INTRODUCTION

The previous chapter focused on the literature which was reviewed to gain more understanding of factors contributing to mortality in HIV-infected people using IPT. The current chapter covers the study design, study population and sample, data collection method and instrument, ethical considerations, validity and reliability, and data analysis plans.

The research design used to study the factors contributing to mortality among HIV-infected people on IPT was a retrospective, quantitative, explorative, descriptive design. The researcher had control over the choice of the research problem, research methodology and variables to be studied. Data was collected through the use of a structured data collection instrument in the form of a checklist.

3.2 RESEARCH SETTING

The research setting refers to where the data was collected. The study took place in Gaborone; the records used were from two sites in Francistown and Gaborone. All these 80 records were archived safely in offices of Botusa in Gaborone. Gaborone is the capital city of Botswana in the southern part of the country, whereas Francistown is the second-largest city in Botswana on the northern part of the country. Gaborone is 169 km² and has a population of 227 333, while Francistown is 79 km² with a population of 100 079, according to the Central Statistics Office of Botswana (Botswana CSO 2011).

3.3 STUDY DESIGN

The research design used was a retrospective, quantitative, descriptive design. Quantitative research is used to denote research designs and methods that yield
numerical data and are based on a positivist philosophy; analysis is usually based on statistical methods (Gerrish & Lacey 2010:531).

Quantitative research emphasises measurement; the research describes and examines relationships and determines causality among variables, or describes what is known through this measurement (Holland & Rees 2010:290). It incorporates logistic, deductive reasoning, as the researcher examines particulars to make generalisations about the universe (Burns & Grove 2009:23). According to Gerrish and Lacey (2010:134), qualitative research is a broad umbrella term for research that uses methods that collect evidence that can be transferred into numerical data and are based on a positive position.

A quantitative approach was used to study the factors contributing to mortality among HIV-infected people on Isoniazid Preventive Therapy. The quantitative approach to scientific inquiry emerged from a branch of philosophy called “logical positivism”, which operates according to strict rules of logic, truth, laws, axioms and predictions (Burns & Grove 2009:22).

3.3.1 Retrospective study

A retrospective study is one where the data already exists at the start of the study and the researcher gathers the data from the past through experiences, or records (Holland & Rees 2010:291). The data was gathered from existing records of those (HIV-infected persons?) who had taken IPT between January 2005 and December 2008 and whose death was documented during this period of taking IPT or afterwards but within the period covered by the records.

3.3.2 Descriptive studies

Descriptive studies offer researchers a way to discover new meaning, describe what exists, determine the frequency with which something occurs and categorise information (Burns & Grove 2009:25). Descriptive research provides an accurate portrayal or account of statistics, of a particular individual, situation or group (Burns & Grove 2009:25). Descriptive studies are usually conducted when little is known about a phenomenon and they provide the basis for the conduct of correlational, quasi-
experimental and experimental studies (Burns & Grove 2009:25). Descriptive research is the research that has its main objective, the accurate portrayal of the characteristics of persons, situations or groups, and or the frequency with which certain phenomena occur (Polit & Beck 2008:752).

There has not been any research done in Botswana on the factors contributing to mortality among HIV-infected people on Isoniazid preventive therapy. HIV-infected people on IPT may still die despite being on IPT. The records of 80 HIV-infected patients who had taken IPT and had died were studied to explore the contributory factors to their mortality. The purpose of this descriptive study was therefore to describe and document aspects of a situation as it naturally occurred in a given population and categorise them.

3.4 RESEARCH METHODS

Polit and Beck (2012:741) define research methods as the techniques used to structure a study and to gather and analyse information relevant to the question in a systematic fashion.

3.4.1 Population

The study population is the people, things or events the researcher wants to say something about (Holland & Rees 2010:54). Burns and Grove (2005:342) indicate that in some studies the entire population is the target of the study. Many of these studies use data available in large databases, such as census data or other government-maintained databases. The epidemiologists often use entire populations for their large database studies. Burns and Grove (2005:342) add that in other studies, the entire population of interest in the study is very small and well defined. In this case the study population included all 80 records of men and women who were HIV-infected and were on IPT in the period January 2005 to December 2008 in two sites in Gaborone and Francistown, Botswana, which had documented records of death. The records were safely archived in Botusa, Gaborone.
3.4.1.1 Eligibility criteria

The eligibility criteria for this study were records of all deceased men and women who had been infected with HIV and were available in Gaborone. The reason for involving the entire population was that it was of manageable size and a suitable size for a dissertation of limited scope.

3.4.2 Data collection

3.4.2.1 Data collection approach and method

Data collection for the study was through the use of structured questions in the checklist to extract data from all the 80 records. The advantage of using a checklist for extraction of data in all the records was that the researcher used exactly the same set of questions and in the same sequence. This increased objectivity of the collected data.

The advantage of the data collection approach selected was that the data collector was experienced in data collection and familiar with health personnel. The other advantage of using a checklist to collect data in this study was that it required less time and energy to administer and that it was less costly.

3.4.2.2 Development and testing of the data collection instrument

In order to collect the needed data or information in the study, the researcher had to develop a measuring instrument to be used to extract data from all the 80 records, to ensure uniformity and consistency. The questions that were formulated were guided by the objectives of the study. The research instrument, the checklist, was developed specifically for this study. The development of the checklist was based on the literature review.

The design of the checklist took time and effort and it was drafted a number of times in consultation with the supervisors of the study at the University of South Africa (Unisa), who critically reviewed and verified the interpretation of the questions in the checklist before it was finalised. The checklist was also evaluated by experts of Unisa, Department of Health Studies, Higher Degrees Committee before they gave their consent to the researcher to carry on with the study.
3.4.2.2.1 Pre-testing of the data collection instrument

The checklist was pre-tested once on five records which did not belong to the population under study. The reasons for this pre-test were to test whether the instrument would elicit responses required to achieve the research objectives; to test whether wording of questions was clear; and to test whether the content of the instrument was relevant and adequate.

Since the researcher was using the entire population from Botusa, the records used for the pre-testing were from Princess Marina Hospital in Gaborone, as they were not part of the study population. These records were of HIV-infected patients who had been admitted to this hospital, were on IPT and had died. The researcher requested permission from the hospital superintendent to use five records from their facility for pre-testing. Permission was granted by the Hospital Ethics Committee (see Annexure 5). More options were then added to the checklist for repeated hospitalisations. The final data collection instrument (checklist) was submitted to the supervisors for approval (see Annexure 6). This helped to improve the checklist.

3.4.2.3 Characteristics of the data collection instrument

The checklist had a total of 36 items which were divided into the following five sections:

- The first section covered demographic data, and included 5 items.
- The second section had 6 items on the baseline physical examination.
- The third section had 11 items on hospitalisation, and the section was duplicated four times to allow for those who were hospitalised more than once.
- The fourth section had 11 items on drug history.
- The fifth section had 4 items on the death.

3.4.2.4 Data collection process

The researcher secured the date for data collection from the Associate Director for the TB/HIV Division, who then communicated with the data manager to facilitate access to the records. The existing de-identified data contained in the records at Botusa was used.
The researcher personally completed the checklist to extract data from all the available 80 records. The sections covered questions on inherent ID, age, sex, educational level, employment, facility used, weight, height, temperature, CD4 count, TST reading, illnesses, hospitalisations, reasons for hospitalisation, if the patient was using ART or CPT, and causes of death. Data collection was completed within two week. Upon completion of data collection, the data was entered into the computer on an Excel spreadsheet.

3.5 DATA ANALYSIS

According to Burns and Grove (2009:44), data analysis is the process used by the researcher to reduce, organise, and give meaning to the data collected. This is done to make the results or findings easier for the reader to grasp, and also provides a way of enabling the research question to be answered in the light of the study findings (Holland & Rees 2010:61). According to Gerrish and Lacey (2010:24), validity concerns the extent to which the research measures what it purports to measure without bias or distortion.

The study was explorative and descriptive by nature; hence descriptive statistics were used. Descriptive statistics include frequency tables and measures of central tendency such as mean, median, mode, variability: variance, standard deviation and range of ratio continuous variables. These were used to summarise each extracted response from all the records. Variables that were analysed included: age group, CD4 counts, use of HAART, BMI, gender, TST result, and CPT. Ranges and variance of age, CD4 count, BMI and TST were also calculated. Explorative analysis was also applied. This included summarising data using statistical charts – pie charts, bar graphs for nominal variables and histograms for continuous variables.

The data analyses focused on answering or addressing the study objectives. In order to determine the causes of mortality among patients, the researcher focused on finding the modal causes of mortality. Hence frequency tables were used to analyse the corresponding variable. In order to explore the risk factors for mortality among patients on IPT, patients were grouped into two distinct groups – those who had died within the six months of IPT administration and those who had died afterwards. For future reading, the group of the deceased patients who had died before the six months of IPT ended
would be called “the dead”, while the other group would be called “the survivors”. This was done so that for each factor considered, the relative risk (or risk ratio) would be calculated and interpreted accordingly. Relative risk (RR) is the ratio of the risk of disease for those with the risk factor to the risk of disease for those without the risk factor (Woodward 2005:117). If the RR is greater than 1, then the factor under consideration increases the risk of the disease, and when it is less than 1, it reduces the risk. Note that with reference to this study, the “disease” here is considered to be death within the six-month period of IPT.

In order to compute the relative risk (RR) of a given factor, the following 2 × 2 table was constructed for each corresponding risk factor:

<table>
<thead>
<tr>
<th>Risk factor status</th>
<th>Survival status during 6 mths of IPT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Died</td>
<td>Survived</td>
</tr>
<tr>
<td>Exposed</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Not exposed</td>
<td>c</td>
<td>d</td>
</tr>
<tr>
<td>Total</td>
<td>a + c</td>
<td>b + d</td>
</tr>
</tbody>
</table>

Since the whole population was considered for analysis, the RR for each factor was taken as a population parameter; therefore there was no need to find confidence interval estimates. It should be noted that this kind of analysis consists of only nominal variables with only two outcomes. For the continuous variables, only explorative analysis would be used to compare the two groups. In particular, box plots would be used to compare the population means of the continuous variables for the two groups.

The SPSS statistical package was used for the analysis of the collected data and analysis was done with the help of a statistician.

3.6 VALIDITY AND REABILITY

Validity is the measure of the truth or accuracy of a claim, an important concern throughout the research process (Burns & Grove 2005:755). Validity of the design is the strength of the design to produce accurate results, which is determined by examining
statistical conclusions, internal validity, construct validity and external validity (Burns & Grove 2005:754). Validity of an instrument determines the extent to which the instrument actually reflects the abstract construct being examined (Burns & Grove 2005:755). According to Gerrish and Lacey (2010:24), validity concerns the extent to which the research measures what it purports to measure without bias or distortion.

3.6.1 Internal validity

Face validity refers to the extent to which a method appears to measure what it is intended to measure (Peat, Mellis & Xuan 2002:106). The checklist was constructed so that it could measure the attributes to be studied, which were the factors contributing to mortality of HIV-infected people on IPT. In ensuring face validity, the checklist was subjectively assessed for presentation and the relevance of the questions. The checklist was evaluated by experts in research (Unisa supervisors). The researcher had ethical approval, had conducted a literature review and had guidance from the experienced supervisors from Unisa.

Content validity refers to the extent to which questionnaire items cover the research area of interest (Peat et al 2002:106). The checklist was an appropriate method for collecting the data. Items in the checklist adequately covered the domain under investigation.

Internal validity refers to the extent to which the study methods are reliable (Peat et al 2002:105). Pre-testing of the checklist prior to data collection was done in order to enhance its validity. As previously described, pre-testing of the data collection instrument was done on five records with similar characteristics to those of the population. This was done to assess the flow of questions, whether they were technically sound, appropriateness of categorisation of variables and relevance of the items to the title and study objectives. The pre-test proved that the instrument used in the research study was satisfactory, the categorisation of variables was appropriate and relevant to the research title and could therefore be found valid. A population or census was used for study. Since the study was retrospective, the researcher blocked some possible extraneous variables by measuring or including them (such as the demographic characteristics of the deceased patients).
3.6.2 External validity

External validity is about the generalisability of causal inferences and this is a critical concern for research that yields evidence for evidence-based nursing practice (Polit & Beck 2012:237). Peat et al (2002:105) also define external validity as the extent to which the study results can be applied to a wider population.

In this study external validity was enhanced through selecting the records of all the patients to be studied. There was no possibility of a sampling error as all the records were selected and sampling was not used. The records used were from two sites in Francistown and Gaborone. As only records were used, dropout or attrition of the sample, which could have affected the power of the study, did not occur and this also made it statistically significant.

3.6.3 Reliability

Reliability in a general sense is dependability. Specifically in research, it means the degree to which random error is absent from a particular measurement procedure, and consistency and repeatability of measurements results that use a particular measurement procedure (Stommel & Wills 2004:440). Since records were used, reliability in the sense of dependability and trustworthiness was dependent upon the checklist, as it covered the domain of the investigation and it was used for the 80 records under study.

3.7 ETHICAL CONSIDERATIONS

Holland and Rees (2010:288) define ethics as the code of practice followed by the researcher to ensure the protection of individuals involved in a study. This relates to such principles as doing good and avoiding harm; protecting the human rights of the individual, including the decisions about taking part in the study under informed consent; treating everyone fairly; protecting the identity of those involved in studies and gaining approval from an ethics committee set up to protect the individuals’ human rights and safety and control the actions of researchers (Holland & Rees 2010:288). In this case every record had an opportunity to be in the study. The records were de-identified and
were coded; therefore, it was not possible for the researcher to trace them back to the original patient. The Ethical Committee for Unisa and the Ministry of Health in Botswana approved the study. Botusa approved the use of its de-identified records.

3.7.1 Permission to conduct research

Ethical clearance by the Higher Degrees Committee of the Department of Health Studies, Unisa, was granted (see Annexure 1). The researcher was granted permission to conduct the study by the Botswana Ministry of Health Research Development Committee (Institutional Review Board) (see Annexure 3). Permission for the use of the records in Botusa was given by principal investigator (see Annexure 4). The permission was sought from Botusa and not from families of the deceased because the records had been de-identified and could not be traced back to the owners. Permission for the use of five records for pre-testing the checklist in Princess Marina Hospital was granted by the Hospital Ethics Committee (see Annexure 5).

3.7.2 Confidentiality and anonymity

Privacy and confidentiality were respected and there was no misuse of records. Records and checklists were anonymous as they were coded. Originals or copies of death certificates were not inserted in the records; the information from the certificates had been transcribed in the records by the nurses at that time. The researcher was committed to maintaining confidentiality and anonymity.

For the pre-test a waiver was requested and was granted by the Princess Marina Hospital Ethics Committee. There were no risks involved to the patients because the researcher was dealing with de-identified records.

3.8 CONCLUSION

The research design used was a retrospective, quantitative, explorative, descriptive design to determine factors contributing to mortality among HIV-infected people on IPT. Because of the manageable size of the records, there was no sampling. All the 80 records of patients who were HIV-infected, had been on IPT and had died were studied. The entire population was involved in the study. Data was collected through the use of a
checklist. Descriptive statistical analysis was done on raw data. The researcher complied with ethical principles. The next chapter will deal with presentation and analysis of data.
Chapter 4
Presentation and analysis of data

4.1 INTRODUCTION

Chapter 3 described and discussed the research design and method in detail. This chapter focuses on implementing the data-analysis methods discussed in the previous chapter. These are mainly exploratory analysis, descriptive statistics and analysis of relative risk for a given risk factor. In this chapter, the research results are presented and interpreted from the spreadsheet. The data analyses were carried out using a statistical package called SPSS version 13.0, with the help of a statistician.

The main aim of this data analysis was to answer the two research objectives, which were to

- determine the causes of mortality among HIV-infected patients on IPT
- explore the factors that contributed to mortality among the HIV-infected people on IPT

4.2 ANALYSIS AND INTERPRETATION OF DATA

The analysed data are presented below, according to the checklist sections. Tables and graphs have been used, together with summary statistics.

4.2.1 Demographic features of the patients

Item 1.1 Gender of the patients (N=80)

The table below (Table 4.1) shows the gender distribution of the patients. Out of the 80 patients considered, most of the records (75% n=60) belonged to females, while only a quarter of them were males. In a study by Setlhare, Forcheh and Gabaitiri (2009:225), based in Botswana, it was found that AIDS is the leading contributor to mortality among females (9.1%) and the third leading contributor among males (7.0%).
Table 4.1  Gender of the patients (N=80)

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>Female</td>
<td>60</td>
<td>75</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>100</td>
</tr>
</tbody>
</table>

Item 1.2  Age of the patients (N=80)

The diagram below (Figure 4.1) shows the age distribution of the patients. The majority of the patients, at 75% (n=60) were between 25 and 44 years (categories of 25 to 29, 30 to 34, 35 to 39 and 40 to 44 years categories). Only a small number of patients were over 50 years (6%, n=5).

![Age of the patients (N = 80)](image)

**Figure 4.1  Age of the patients (N=80)**

Table 4.2 below gives the summary statistics for the age of patients. From the table below, 75% (n=60) of the patients were found to be less than 41 years, with the minimum age being 20 years. The median was about 35 years, which is almost the average age (35) of the patients.
Table 4.2 Summary statistics of the age of the patients (N=80)

<table>
<thead>
<tr>
<th>Min</th>
<th>1st Quartile</th>
<th>Median</th>
<th>3rd Quartile</th>
<th>Max</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>30</td>
<td>35</td>
<td>41</td>
<td>60</td>
<td>35</td>
</tr>
</tbody>
</table>

Item 1.3 Education level of the patients (N=80)

The records indicated that 90% of the patients had some formal education: that is, they had at least gone through primary education. The education level differed from “never been to school” to “tertiary education”. There were 10% (n=8) who had never attended school. The bulk had attended up to secondary education: 51% (n=41), followed by those who had only primary education: 34% (n=27). Those who reached tertiary education were 5% (n=4) (Figure 4.2). A study done by Munseri, Talbot, Mtei and Fordham von Reyn (2008:1040) demonstrated that education above secondary level was associated with a higher rate of IPT completion. This is an expected finding, as education is often associated with better understanding and comprehension of instructions and therefore better adherence.

![Education level of the patients (N = 80)](image)

**Figure 4.2 Education levels of the patients (N=80)**

Item 1.4 Employment status of the patients (N=80)

Records indicate that most of the patients were employed: 76% (n=61). There were only 24% (n=19) of the patients who were unemployed (Figure 4.3). There was no record of the type of employment. There was no data indicating the source of income for those that were not working.
Item 1.5 Place or facility used by patients (N=80)

All the records: 100% (N=80) were in Gaborone. Gaborone was used as the site for research because it was the place where all the records were archived. Of the 80 records, a total of 72% (n=58) were from Gaborone and 28% (n=22) were from Francistown (Figure 4.4). The study done by Munseri et al (2008:1040) found that distance from the clinic, limited education and lack of family support increased the risk of IPT cessation; thus they were associated with premature IPT cessation.
4.2.2 Section B – Baseline physical examination

Item 2.1 Baseline height of the patients (N=80)

The data on height was collected in order to calculate body mass index (BMI). Table 4.3 below shows that there were 25% \( n=20 \) patients in each height category of 155 to 159 cm and 165 to 169 cm.

<table>
<thead>
<tr>
<th>Height (cm)</th>
<th>( n )</th>
<th>Percent (%)</th>
<th>Cumulative frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>150-154</td>
<td>6</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>155-159</td>
<td>20</td>
<td>25</td>
<td>33</td>
</tr>
<tr>
<td>160-164</td>
<td>13</td>
<td>16</td>
<td>49</td>
</tr>
<tr>
<td>165-169</td>
<td>20</td>
<td>25</td>
<td>74</td>
</tr>
<tr>
<td>170-174</td>
<td>9</td>
<td>11</td>
<td>85</td>
</tr>
<tr>
<td>175-179</td>
<td>8</td>
<td>10</td>
<td>95</td>
</tr>
<tr>
<td>180-184</td>
<td>3</td>
<td>4</td>
<td>99</td>
</tr>
<tr>
<td>185-189</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>100</td>
<td>-</td>
</tr>
</tbody>
</table>

Item 2.2 Baseline weight of the patients (N=80)

Figure 4.5 below shows that the weight of the patients ranged from 30 kg to 109.9 kg. The weight range of 50–59.9 kg was the highest: 31% \( n=25 \). This weight range was followed by 40–49.9 kg: 26% \( n=21 \). Only 1% \( n=1 \) weighed less than 39.9 kg and 1% \( n=1 \) over 100 kg.
Item 2.2.1 Baseline BMI of patients \((N=80)\)

BMI is a ratio of weight to height squared. It is used for estimating human body fat based on an individual's weight and height. The BMI of the whole group \((N=80)\) patients ranged from 13.1 to 36.2; this meant that the range was from underweight to obese. The analysis showed that a large number of patients: 55\% \((n=44)\) had a normal BMI of 18.5–24.9. Those with a BMI showing under weight (low BMI of <18.5) were 26\% \((n=21)\). The number with a BMI showing overweight and obese (for category BMI of 25 to 29.9 and >30) was 19\% \((n=15)\) (Figure 4.6).

![Baseline BMI of patients \((N=80)\)](image)

**Figure 4.6 Baseline BMI of patients \((N=80)\)**

Item 2.3 Baseline body temperature of patients \((N=80)\)

The records indicated that the temperature was checked through the auxiliary route and with degrees in Celsius units (Figure 4.7).

![Baseline body temperature of the patients \((n=76)\)](image)

**Figure 4.7 Baseline body temperature of the patients \((n=76)\)**
There were 5% \((n=4)\) patients whose baseline temperature had not been recorded; hence they were excluded from analysis. Figure 4.7 shows that the records indicated that 89% \((n=68)\) of the patients’ temperatures during baseline investigation for IPT enrolment were normal, that is 35.5 to 37.2°C. Those with hypothermia (>35.5°C) were 8% \((n=6)\). Fever is one of the WHO recommended TB screening symptom. Records showed that if the patient presented with fever during initial IPT investigations, that patient was not placed on IPT immediately but rather investigated further for active TB.

**Item 2.4 Baseline CD4 count of patients \((n=71)\)**

Among the records considered, 11.25% \((n=9)\) of the patients had their baseline CD4 counts missing and therefore these records could not be included for analysis. As shown in Figure 4.8, most patients: 78.87% \((n=56)\) had CD4 counts that were below 400 (categories of 0 to 99, 100 to 199, 200 to 299 and 300 to 399). Those with a CD4 count of 500-599 and of 600-699 were each 4.23% \((n=3)\). There was no record that indicated a CD4 count of 700-899. Only 1.40% \((n=1)\) had a CD4 count of 900-999.

![Baseline CD4 count of the patients \((n=71)\)](image)

For those patients with complete data, the records indicated that their corresponding CD4 count ranged from 18.7 to 907, with a mean of 268.2. Figure 4.9 shows the corresponding box plot comparing the ‘dead’ and ‘survivors’ baseline CD4 counts. The plot shows that the mean CD4 count of the survivors is much higher than the mean of those who died within the IPT administration period – the ‘dead’. Hence one can
conclude that the higher the CD4 count one has during enrolment in IPT, the more likely one is to be able to complete IPT.

**Figure 4.9**  *Box plot of the baseline CD4 count comparing those who died before the end of the IPT and those who survived IPT and only died later on (n=71)*

**Item 2.5 Baseline TST of patients (N=80)**

The TST during the initial investigation for IPT enrolment ranged from 0 mm to 22 mm. The records indicated that the TST was positive when it was more than 5 mm. Those that were 0 mm–5 mm were regarded as having negative TST. Figure 4.10 shows that most of the patients: 80% (n=64) had a negative TST at an initial investigation. Of the patients with a negative TST there were 69% (n=55) with a non-reactive (0 mm) TST. Those with a TST above 5 mm (positive) were 20% (n=16).
Figure 4.10 Baseline TST of the patients (N=80)

Table 4.4 below enumerates those who died within the six months of IPT administration against their TST results. Applying the 2 x 2 table as explained in Chapter 3, section 3.5 to Table 4.4, the relative risk of those who tested positive to those who tested negative is 0.182. Thus testing positive on a TST reduces the risk of dying within the IPT administration period. Therefore the government or relevant stakeholders should work hard in ensuring that they greatly reduce the number of false negatives in order to save lives.

Table 4.4 TST results and survival status of patients during the six months' duration of IPT administration (N=80)

<table>
<thead>
<tr>
<th>TST result</th>
<th>Survival status during six 6mths of IPT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Died</td>
<td>Survived</td>
</tr>
<tr>
<td>Positive</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>Negative</td>
<td>22</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>57</td>
</tr>
</tbody>
</table>

4.2.3 Section C – Hospitalisation

Item 3.1 Self-reported illnesses in IPT patients (n=47) in the 6 months of taking IPT

From the records considered, 41.25% (n=33) of the deceased patients did not have any self-reported illness within the months of taking IPT, and therefore could not be included for analysis.
Table 4.5 shows that there were 47 patients who reported signs and symptoms of a variety of diseases. The leading self-reported illnesses were gastroenteritis and common cold/influenza: 19.15% \((n=9)\) each. These were followed by pneumonia/PTB: 14.89% \((n=7)\). The least self-reported illnesses were herpes zoster and hepatitis, both at 2.13% \((n=1)\).

**Table 4.5  Self-reported illnesses in IPT patients \((n=47)\) in the six months of taking IPT**

<table>
<thead>
<tr>
<th>Self-reported illnesses</th>
<th>Frequency</th>
<th>Relative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common cold/influenza</td>
<td>9</td>
<td>19.15</td>
</tr>
<tr>
<td>Pneumonia/PTB</td>
<td>7</td>
<td>14.89</td>
</tr>
<tr>
<td>Generalised body pains &amp; weakness</td>
<td>4</td>
<td>8.51</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>9</td>
<td>19.15</td>
</tr>
<tr>
<td>Meningitis</td>
<td>3</td>
<td>6.38</td>
</tr>
<tr>
<td>Oral Candidiasis</td>
<td>3</td>
<td>6.38</td>
</tr>
<tr>
<td>Cancer (cervix / lung)</td>
<td>3</td>
<td>6.38</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>2</td>
<td>4.26</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>1</td>
<td>2.13</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>1</td>
<td>2.13</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>10.64</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

**Item 3.2  Number of hospitalisations in the six months of taking IPT \((N=80)\)**

Most of the patients (85%) had no hospitalisation during the six-month period of IPT administration. There were only 15% \((n=12)\) patients hospitalised.

**Item 3.3  Reason(s) for hospitalisation \((n=12)\)**

There were 12 patients that were hospitalised for various reasons. Out of these \((n=12)\) patients, 25% \((n=3)\) were hospitalised because of signs and symptoms of gastroenteritis. There were 16.7% \((n=2)\) hospitalised because of vaginal bleeding; 8.3% \((n=1)\) because of signs and symptoms of hepatitis; and 8.3% \((n=1)\) hospitalised with symptoms of meningitis. There were 25% \((n=3)\) hospitalised due to signs and symptoms of pneumonia/ pulmonary tuberculosis; 8.3% \((n=1)\) was hospitalised due to seizures, and 8.3% \((n=1)\) was hospitalised due to oral candidiasis.
Item 3.3.1 Diagnosis during hospitalisation \((n=12)\)

Table 4.6 shows that of the patients hospitalised \((n=12)\), 25\% \((n=3)\) were diagnosed with gastroenteritis, followed by 16.67\% \((n=2)\) diagnosed with bacterial pneumonia and decubitus pneumonia and sepsis. There were 16.67\% \((n=2)\) diagnosed with pulmonary TB.

<table>
<thead>
<tr>
<th>Hospitalisation diagnosis</th>
<th>Frequency</th>
<th>Relative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia &amp; decubitus pneumonia &amp; sepsis</td>
<td>2</td>
<td>16.67</td>
</tr>
<tr>
<td>Abortion</td>
<td>1</td>
<td>8.33</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>3</td>
<td>25.00</td>
</tr>
<tr>
<td>Cryptococcal Meningitis</td>
<td>1</td>
<td>8.33</td>
</tr>
<tr>
<td>PTB</td>
<td>2</td>
<td>16.67</td>
</tr>
<tr>
<td>Cancer (cervix/lung)</td>
<td>1</td>
<td>8.33</td>
</tr>
<tr>
<td>Mental disorder/psychosis with seizures</td>
<td>1</td>
<td>8.33</td>
</tr>
<tr>
<td>Intracranial space occupying lesion</td>
<td>1</td>
<td>8.33</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

Item 3.3.2 Current CD4 count at the time of hospitalisation \((n=12)\)

The CD4 count of hospitalised patients \((n=12)\) ranged from 37–513. Of these patients, those with a CD4 count below 500 were 83.33\% \((n=10)\), and 16.67\% \((n=2)\) had a CD4 of 500–599. None of the hospitalised patients had a CD4 count of 600 or above.

Item 3.3.3 Weight at the time of being hospitalised \((n=12)\)

The weight of the patients \((n=12)\) hospitalised ranged from 37.1 to 80.7 kg. Of these 12 patients, 33.33\% \((n=4)\) were below 50 kg. The patients weighing 50–69.9 kg (categories of 50–59.9 and 60–69.9 kg) were 41.67\% \((n=5)\). There were 16.67\% \((n=2)\) patients weighing 70–79.9 kg and only 8.33\% \((n=1)\) had a weight of 80–89.9 kg. There was no patient with the weight of 90 kg and above.
Figure 4.11 shows the BMI for the hospitalised patients \((n=12)\), which ranged from 12.1–30.1. The hospitalised patients that had an underweight BMI were 33% \((n=4)\). Patients with normal BMI were 50% \((n=6)\).

![BMI during hospitalisation (n=12)](image)

**Figure 4.11 BMI when hospitalised (n=12)**

**Item 3.3.4 Temperature on hospital admission \((n=7)\)**

Of the 12 hospitalised patients, there were 25% \((n=3)\) whose body temperature was not recorded, and hence they were not included for analysis. The admission temperature for the remaining hospitalised patients, 58.33% of 12 \((n=7)\), ranged from 35.7 to 39.6°C. There were 88.89% \((n=8)\) admitted with a normal temperature of 35.6–37.2°C. Only 11.11% \((n=1)\) had a temperature of 39.6°C.

**Item 3.3.5 Type and results of chest X-ray (CXR) done when hospitalised \((n=12)\)**

Of those hospitalised \((n=12)\), there were only 16.67% \((n=2)\), whose records indicated that they were X-rayed, therefore the remaining ten patients were excluded from analysis. Both the patients had chest X-rays. One of the chest X-rays was regarded as abnormal, while the other chest X-ray was normal.

**4.2.3.1 Second hospitalisation (re-admission) \((n=1)\)**

Only one patient (8.33%) out of the \(n=12\) had a second hospital admission. This was a readmission for the patient diagnosed with cervical cancer.
4.2.4 Section D – Drug history

Item 4.1 ART used during the six months of taking IPT (N=80)

There were 37.5% (n=30) of the patients using ART and these were all on first-line drug treatment. There were 62.5% (n=50) patients that did not use ART. Of the 50 patients not using ART, 23.75% (n=19) patients were eligible for ART but not using it. There were 10% (n=8) patients not on ART whose initial CD4 cell count was not recorded (missing).

ART is a treatment for people infected with HIV. The standard treatment (often called HAART) consists of a combination of at least three antiretroviral drugs that suppress HIV replication. Therefore it is considered a risk for a person with HIV not to be enrolled in ART. This is why, as depicted in Table 4.7 below, non-use of ART is taken as being risk exposed. Table 4.7 provides a summary of the deceased patients against the use of ART. The computed relative risk is 2.70, implying that not taking ART while on IPT increases the risk of dying within the six months of IPT administration. The results also show that 19 out of the 23 deceased patients who died before the end of IPT were not on ART.

Table 4.7 ART and survival status of patients within the six months’ duration of IPT administration (N=80)

<table>
<thead>
<tr>
<th>Use of ART</th>
<th>Survival status during six months of IPT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Died</td>
<td>Survived</td>
</tr>
<tr>
<td>No</td>
<td>19</td>
<td>31</td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>26</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>57</td>
</tr>
</tbody>
</table>

Item 4.2 Completion rate of Isoniazid in six months (N=80)

Table 4.8 shows that the total number of 80 (N=80) patients used Isoniazid. But from the N=80 that were on Isoniazid, 71.25% (n=57) completed six months of Isoniazid, and 28.75% (n=23) were on Isoniazid for less than six months because of death within the period. The patients died from various causes before they could complete their six months of IPT.
A study done in Tanzania to determine the acceptability, compliance and side effects of Isoniazid (INH) prophylaxis against tuberculosis among HIV-infected police officers in Dar es Salaam indicated that 34.4% did not complete the six months of IPT (Bakari, Moshi, Aris, Chale, Josiah, Magao, Pallangyo, Mugusi, Sandstrom, Biberfeld, Mhalu and Pallangyo (2000:495). Another study in Brazil showed that IPT completion was higher among HIV-infected patients receiving HAART (87%) than those not yet receiving HAART (79%, \( P < 0.01 \)) (Durovni, Cavalcante, Saraceni, Vellozo, Israel, King, Cohn, Efron, Pacheco, Moulton, Chaisson & Golub 2010:1).

**Table 4.8 Completion rate of Isoniazid in six months (\(N=80\))**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Completed IPT (n=57(71%))</th>
<th>Did not complete IPT (n=23) (29%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>(n=14) 25%</td>
<td>(n=6) 26%</td>
</tr>
<tr>
<td>Female</td>
<td>(n=43) 75%</td>
<td>(n=17) 74%</td>
</tr>
</tbody>
</table>

**Item 4.2.1 Prescribed number of Isoniazid tablets in a day (\(N=80\))**

The records showed that two doses of 300 mg and 400 mg were used. The records indicate that there were 56 patients (70%) who took 4 tablets (400 mg) of INH a day, while 30% \((n=24)\) took 3 tablets (300 mg) of INH per day. The amount of tablets was determined by the body weight of the individual. Those taking the 300 mg of INH tablets per day had a weight of less than 50 kg. Those with a weight of 50 kg and above took 400 mg per day. However, the records from January 2006 indicate that every patient was switched to a standard dose of 300 mg per day, regardless of their weight. This was according to the amended Botswana IPT national guidelines. INH and pyridoxine were supplied on a monthly basis and there was a monthly health review with each patient.

**Item 4.3 Reported alcohol intake during the course of IPT (\(N=80\))**

Of the 80 patients \((N=80)\), 17.5\% \((n=14)\) patients were consuming alcohol, though the type of alcohol or the extent of alcohol intake was not indicated. There were 82.5\% \((n=66)\) patients not using alcohol during the six months of taking IPT.
Alcohol intake during IPT was also considered as one of the factors that could contribute to mortality among HIV-infected people on IPT. The results have vindicated this argument. From Table 4.9 below, the computed relative risk is 2.48. Thus alcohol intake during IPT increases the risk of death before the end of IPT programme. In addition, it should be realised from Table 4.9 that more than half (8 out of 14) of those who consumed alcohol while still on IPT died before they could finish the therapy.

Table 4.9 Alcohol intake and survival status of patients during the six months’ duration of IPT administration (N=80)

<table>
<thead>
<tr>
<th>Use of alcohol</th>
<th>Survival status during six months of IPT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Died</td>
<td>Survived</td>
</tr>
<tr>
<td>Yes</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>No</td>
<td>15</td>
<td>51</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>57</td>
</tr>
</tbody>
</table>

Item 4.4 Use of Cotrimoxazole Preventive Therapy (CPT) during the six months of taking IPT (N=80)

Cotrimoxazole is a prophylaxis which is used for the prevention of bacterial infections that cause gastroenteritis and pneumonia. The records indicated that out of the 80 patients, only 10% (n=8) used CPT, 57.5% (n=46) did not use CPT, while for 32.5% (n=26) it was not recorded whether they ever used CPT or not. Records indicated that co-trimoxazole for prophylaxis was provided through the government programme to patients with CD4 lymphocyte counts below 200.

Item 4.4.1 Length of time Cotrimoxazole Preventive Therapy (CPT) used (N=80)

Cotrimoxazole was to be used as prophylaxis for any patient whose CD4 count was less than 200 for the period until CD4 count reached 200. By the sixth month of IPT use, there were 38.75% (n=31) eligible for CPT, but only 26% (n=8) of the 31 patients eligible used CPT. Of the 8 patients that used CPT; 50% (n=4) used it for one month, 25% (n=2) used it for two months, while 12.5% (n=1) used it for seven months. There
was only one patient (12.5%) that used it for eleven months. Reasons for discontinuation were not indicated.

**Item 4.5  Drugs used during the course of IPT (N=80)**

The entire 80 patients were taking pyridoxine 25 mg tablets every month. It was indicated that the pyridoxine was taken every day together with Isoniazid tablets. Most of the records (72.5%: n=58) had missing information on other medicine taken during the six months of the IPT. There were 2.5% (n=2) patients with some medications indicated, which were multivitamins, Ibuprofen, amitriptyline and thiazide. The antiretroviral medications, however, were well indicated in the records.

**Item 4.6  Liver function test done before the initiation of IPT (n=79)**

A liver function test was done on patients before they were started on IPT. There were 98.75% (n=79) records which indicated that a liver function test was done during the initial investigations, before initiating the IPT; only 1.25% (n=1) had missing data on this. The entire number tested (n=79) had normal liver-function test results.

**Item 4.7  Chest X-ray for initiation of IPT**

The records showed that a chest X-ray was the requirement before enrolment into IPT. This was to ensure that individuals were not given IPT when they had active PTB. The entire 80 patients had a chest X-ray done during the initial investigation. Out of the N=80, only 8.75% (n=7) patients had abnormal chest X-ray results. None of the abnormal chest X-rays was conclusive of tuberculosis.

Table 4.10 enumerates those who died within the six months of IPT administration against their chest X-ray results. In total, there were 8.75% (n=7) cases of abnormal chest x-rays among the deceased patients. The risk of dying within the six months of IPT if one had an abnormal chest X-ray was 3 out of 7. This is an almost 50-50 chance of succeeding through the use of IPT.
Table 4.10  Chest X-ray results and survival status of patients during the six months’ duration of IPT administration (N=80)

<table>
<thead>
<tr>
<th>Chest X-ray</th>
<th>Survival status during 6 months of IPT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Died</td>
<td>Survived</td>
</tr>
<tr>
<td>Abnormal</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Normal</td>
<td>20</td>
<td>53</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>57</td>
</tr>
</tbody>
</table>

The computed relative risk was found to be 3.65. This result implies that an abnormal chest X-ray greatly increases the risk of dying within the IPT administration period. Therefore those who have abnormal chest X-rays should be given a great deal of care.

4.2.5  Section E – Death

Item 5.1  Time of death of the patients (N=80)

There were 80 patients on IPT. Some successfully completed the six months’ IPT and died afterwards, whilst some died within the six months of IPT. There were 28.75% (n=23) patients that died before they could complete six months of Isoniazid preventive therapy, while 71.25% (n=57) died after they had completed their six months of Isoniazid preventive therapy. The patients that died after six months of IPT died between one and 29 months after the completion of treatment.

Item 5.1.1  Cause of death of the patients (N=80)

One of the main objectives of this research project was to determine the causes of death among the deceased IPT patients. From the 80 records, there were over 32 different causes of death, with 14 patients (17.5%) having had two or more causes of death as indicated in Table 4.11.
Table 4.11  The distribution of the causes of the death among the 80 deceased patients.
(Note that the relative frequency was computed using $N=80$ because ‘cause of death’ is a multiple-response variable)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Frequency</th>
<th>Relative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>14</td>
<td>17.50</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>13</td>
<td>16.25</td>
</tr>
<tr>
<td>Cardiac diseases</td>
<td>5</td>
<td>6.25</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>15</td>
<td>18.75</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>3</td>
<td>3.75</td>
</tr>
<tr>
<td>Cancer (cervix / lung)</td>
<td>7</td>
<td>8.75</td>
</tr>
<tr>
<td>Sepsis / septicaemia</td>
<td>10</td>
<td>12.50</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3</td>
<td>3.75</td>
</tr>
<tr>
<td>Haemorrhagic</td>
<td>3</td>
<td>3.75</td>
</tr>
<tr>
<td>PTB</td>
<td>9</td>
<td>11.25</td>
</tr>
<tr>
<td>Kidney problems</td>
<td>3</td>
<td>3.75</td>
</tr>
<tr>
<td>Murder</td>
<td>3</td>
<td>3.75</td>
</tr>
<tr>
<td>Other (related to AIDS)</td>
<td>6</td>
<td>7.50</td>
</tr>
<tr>
<td>Other (unrelated to AIDS)</td>
<td>4</td>
<td>5.00</td>
</tr>
</tbody>
</table>

Of the 14 patients with multiple causes of death, only 2 died while still on IPT. Table 4.11 shows a frequency table for different causes of death among the patients. The leading causes of death were gastroenteritis, meningitis and pneumonia, causing deaths of 18.75%, 17.5% and 16.25% of the patients respectively. These were followed by sepsis/septicaemia and PTB, with a relative frequency of 12.55% and 11.25% respectively. Other causes such as cardiac disease, hepatic failure, cancer (cervix/lung), hypertension, and haemorrhagic and kidney problems accounted for the deaths of less than 9% of the patients. There were some other causes of death which had an incidence of two or one, which were grouped together as ‘others’.

The ‘others’ group of causes of death was further divided into two groups: those that were related to HIV/AIDS and those that were not. The deaths unrelated to HIV/AIDS were recorded as having been due to road accidents and suicide, while the other group (HIV/AIDS related deaths) were recorded as due to anaemia, mental disorder, herpes, asphyxiation, and choking.
Table 4.12  Distribution of causes of death for the patients who died within the IPT administration period \((n=23)\)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Frequency</th>
<th>Relative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>3</td>
<td>13.0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4</td>
<td>17.4</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>5</td>
<td>21.7</td>
</tr>
<tr>
<td>Cancer (cervix / lung)</td>
<td>1</td>
<td>4.4</td>
</tr>
<tr>
<td>Sepsis / septicaemia</td>
<td>3</td>
<td>13.0</td>
</tr>
<tr>
<td>PTB</td>
<td>3</td>
<td>13.0</td>
</tr>
<tr>
<td>Murder</td>
<td>3</td>
<td>13.0</td>
</tr>
<tr>
<td>Other (unrelated to AIDS)</td>
<td>1</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Table 4.12 indicates that gastroenteritis, pneumonia and ‘other’ (unrelated to AIDS) were the leading causes of death for those who died before the end of the IPT period. Gastroenteritis affected 21.7% of the patients; pneumonia and ‘other’ (unrelated to AIDS) each affected about 17.4% of the patients.

Item 5.2  CD4 count at the time of death \((n=23)\)

Due to the fact that 22% \((n=5)\) of the 23 patients who died during the IPT period had an unrecorded CD4 cell count, their records were excluded from analysis. The remaining 18 that died before they could complete their six months’ administration of IPT, 61% had a CD4 cell count of less than 200 cells/µL, while 29% of patients had a CD4 count of 200 and above (Table 4.13).

Table 4.13  CD4 count at the time of death \((n=18)\)

<table>
<thead>
<tr>
<th>CD4 count (cells/µL)</th>
<th>n</th>
<th>Percent (%)</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-99</td>
<td>5</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>100-199</td>
<td>6</td>
<td>33</td>
<td>61</td>
</tr>
<tr>
<td>200-299</td>
<td>2</td>
<td>11</td>
<td>72</td>
</tr>
<tr>
<td>300-399</td>
<td>4</td>
<td>22</td>
<td>94</td>
</tr>
<tr>
<td>400-499</td>
<td>0</td>
<td>0</td>
<td>94</td>
</tr>
<tr>
<td>500-599</td>
<td>0</td>
<td>0</td>
<td>94</td>
</tr>
<tr>
<td>600-699</td>
<td>1</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>≥700</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>100</td>
<td>-</td>
</tr>
</tbody>
</table>
Item 5.3 Drugs used at the time of death

The entire population (\(N=80; 100\%\)), was given a daily dose of 25 mg of pyridoxine for the six months of taking Isoniazid. The limiting factor to researching this question was that most of the records did not indicate the drugs that were being used at the time of death other than antiretroviral therapy, Isoniazid and pyridoxine. Of the patients, 37.5% \((n=30)\) were indicated to have been taking ART at the time of death.

4.3 CONCLUSION

This chapter discussed the analysis and interpretation of data. The analysis was based on the full 80 patients. The analysis was conducted with the help of a statistical software program, and results of the analysis were presented according to the checklist items.

The results from the analysis of data on patients’ demographic data, baseline physical examination, hospitalisation, drug history, death and factors contributing to mortality among HIV-infected people on Isoniazid preventive therapy (IPT) were discussed in this chapter with illustrative tables and figures. The next chapter will discuss the study findings in line with the study objectives, the recommendations drawn from the findings and the study limitations.
Chapter 5
Discussion, limitations and recommendations

5.1 INTRODUCTION

The previous chapter covered the analysis, presentation and the description of the research findings of data collected from records of 80 patients. This chapter will discuss the study findings in line with the study objectives, the recommendations drawn from the findings and the study limitations.

5.2 SUMMARY OF THE RESEARCH FINDINGS

5.2.1 Demographic data

5.2.1.1 Gender of the patients (N=80)

The findings revealed that the majority of patients: 75% (n=60) were females. These were findings from Botswana’s two major towns. According to the Botswana AIDS Impact Survey (Botswana CSO 2009:1), the HIV prevalence rate for females was 20.4% compared with 14.2% for that of males. The HIV incidence rate also shows gender disparity, in that females showed a higher incidence than males. The AIDS Survey showed that urban areas had an HIV prevalence rate of 19.1% compared with 17.1% from rural areas (Botswana CSO 2009:1).

Parker (2011:5) argues that the higher prevalence is because women are more vulnerable to HIV, since often they are subjected to gender violence and use condoms irregularly. Parker (2011:5) goes on to state that women’s vulnerability to HIV infection in Botswana is directly related to an interplay of factors, where immediate needs and consumer-related wants in a context of poverty, unemployment or low income flow into transactional and inter-generational sexual relationships; where high partner turnover and concurrent sexual partnerships have become the norm.
The position of women in society is one of the drivers of the AIDS epidemic. Because women generally tend to possess little power over their own bodies, they are put at risk of HIV infection by a combination of the social acceptance of male partners having more than one sexual relationship, inability to negotiate condom use and sexual exploitation (NACA 2012:19). Since women’s HIV prevalence is high, and studies indicate the vulnerability of women’s inability to negotiate condom use, this means there is increased susceptibility to repeated infection, which in turn compromises the immune system of an individual and as a result leads to opportunistic infections and death.

5.2.1.2 Age of the patients (N=80)

Findings revealed that 48% (n=39) of the patients were aged between 30 and 39 years. The sentinel survey done in Botswana in 2011 supports this, as it showed that HIV prevalence increases gradually with age; HIV prevalence was higher in the age group of 35–39 years by 52.3% (Botswana MoH 2011:30). The BAIS III survey (Botswana CSO 2009) shows a similar age distribution of HIV prevalence. HIV prevalence increases sharply with age, peaking between the ages of 30 to 45 years, and gradually declines with age (Botswana CSO 2009:1).

Parker (2011:12) indicates that the HIV prevalence age for Botswana young people aged 15 to 29 years is 8.6% in males and 18.3% in females. More women are infected with HIV at an early age, and as they grow they face more social and economic challenges of unemployment, not being well paid and not married. They tend to engage in risky behaviour of having multiple partners, inconsistent condom use and alcohol use. These in turn debilitate their immune system, as they expose them to re-infections.

5.2.1.3 Education level of the patients (N=80)

The records indicated that 90% of the patients had some formal education; that is, they at least went through primary education. A study done by Bernabé-Ortiz (2008:104) on factors associated with survival of patients with tuberculosis in Lima, Peru, indicated that among this population commencing treatment for tuberculosis, body mass index and HIV infection were associated with an increased risk of death; in contrast, a higher education level was associated with improving survival.
5.2.1.4 Employment of the patients (N=80)

The findings showed that the majority: 76% (n=61) of the patients were employed. The type of employment was not stated. There was no data indicating the source of income for those that were not working, and even for those who were working, their extra source of income was not indicated in the records. Parker (2011:23) indicates that people with low incomes, especially women, are more vulnerable and are at risk of poor nutrition, which affects the immune system, and are at risk of abuse. One can affirm the evident effects of abuse because 3.75% (n=3) of the patients in this study (all females) were killed by their partners, though the reasons for the murder were not stated.

The study done by Parker (2011:23) points out that women seeking work or who have low-income work are particularly vulnerable, as they may be exposed to rape, exploitation by police and other officials, exploitation by taxi drivers or being drawn into transactional sex or sex work to secure shelter or money. There are also some jobs such as working in prisons or the medical laboratory or hospital, especially in isolation wards, that can expose one to communicable diseases like tuberculosis, pneumoconiosis and others. The above factors expose individuals infected with HIV to re-infection, which in turn raises the viral load and increases the chances of opportunistic infections and mortality.

5.2.2 Physical examination of the patients (N=80)

Records showed that all 100% (N=80) of the patients underwent thorough investigations such as checking of temperature, CXR, TST and TB symptom screening before being commenced on IPT. This was done to avoid giving IPT to patients with active TB. Records showed that those with a cough during initial assessment were investigated further for active TB, and if they were free from active TB, they were enrolled for IPT. When active TB is not ruled out and the patient receives Isoniazid as monotherapy, such a patient can develop mono resistance to INH. Reddy, Brady, Gilman, Coronel, Navincopa, Ticona, Chavez, Sánchez, Rojas, Solari, Valencia, Pinedo, Benites, Friedland and Moore (2010:2) state that it is very important that before individuals are commenced on IPT, thorough investigation be carried out to rule out active TB. Samandari, Bishai, Luteijn, Mosimaneotsile, Motsumai, Postma and Hubben (2011:1107) reported that adding chest X-ray (CXR) to a “Symptom” policy would
reduce new Isoniazid resistance (INH-R) and multi drug resistance tuberculosis (MDR TB) cases.

5.2.2.1 BMI among the patients (N=80)

The findings revealed that only 26% (n=21) of the 80 patients had BMI suggestive of being underweight. Most of the patients: 74% (n=59) had a BMI of normal to obese (combination of normal, overweight and obese). Although the findings revealed that 74% (n=59) of the 80 patients in this study had normal to obese BMI, it is interesting that Hanrahan, Golub, Mohapi, Tshabangu, Modisenyane, Chaisson, Gray, McIntyre and Neil (2010:6) found that persons with obese and overweight BMI have a significantly decreased risk of both mortality and TB, whereas those with underweight BMI have an increased risk of mortality. WHO (2008a:36) indicates that multiple studies have established that malnourished adults with HIV are at an elevated and progressive risk of HIV disease progression and mortality as BMI decreases, especially below 18.5. WHO recommends providing supplementary feeding for mild-to-moderately malnourished adults (BMI<18.5), regardless of HIV status (WHO 2008a:36).

5.2.2.2 TST among the patients (N=80)

The findings revealed that 80% (n=64) of the patients had a negative TST. A negative TST means that one does not have latent Mycobacterium tuberculosis. Samandari. Agizew et al (2011:9) indicated that there was no observable benefit of IPT to HIV-infected people not infected by Mycobacterium tuberculosis. Bachhuber and Gross (2009:1040) showed that the results from their simulated meta-analyses indicated a likely mortality benefit of IPT in purified protein derivative (PPD) -positive individuals. The other study done by Durovni et al (2010:2) emphasised the strong effect on HIV-infected patients with a positive tuberculin skin test (TST) (64% reduction) compared with those with a negative or unknown TST (14% reduction in both). Golub, Pronyk, Mohapi, Thsabangu, Moshabela, Struthers, Gray, McIntyre, Chaisson and Martinson (2009:6) reported that many of the patients in their study received IPT because of a positive TST, and this may have increased the effectiveness of IPT more than might be seen in clinical settings in which skin testing was not performed. Mills et al (2011:1517) found that local network structure for HIV and TB can induce high levels of repeated re-infection that may undermine the projected effectiveness of IPT.
**5.2.2.3 CD4 of the patients (N=80)**

The findings revealed that 63.38% (n=45) of the patients had a CD4 count ranging between 0 and 299 (a combination of 0–99, 100–199 and 200–299). Lodwick, Sabin, Porter, Ledergerber, Van Sighem, Cozzi-Leprí, Khaykin, Mocroft, Jacobson, De Wit, Obel, Castagna, Wasmuth, Gill, Klein, Gange, Riera, Mussini, Gutierrez, Touloumi, Carrièri, Guest, Brockmeyer and Phillips (2010:5) suggest that people with HIV who have not taken ART and have a CD4 count above 350 have a raised risk of death compared with the general uninfected population, although this increased risk seems to be of modest magnitude. Having a higher CD4 count does not exclude one from the risk of dying; individuals who are HIV-infected and on IPT, regardless of the level of the CD4 cell count, need regular monitoring for other opportunistic infections, as they increase the risk of dying.

Holmes, Wood, Badri, Zilber, Wang, Maartens, Zheng, Lu, Freedberg and Losina (2006:466) indicated in their research in South Africa that the incidence of all opportunistic infections (OIs) increased significantly at a lower CD4 cell count; the most frequently diagnosed opportunistic infections when the cell count is less than 200 included TB, oral and oesophageal candidiasis, chronic diarrhoea, and wasting syndrome.

In this study, the median CD4 cell count at IPT initiation was 229 and the interquartile range (IQR) was 18.7–907. Of the 18 patients who died before completing six months’ administration of IPT; 61.11% (n=11) had a CD4 cell count of less than 200. The mean of the CD4 cell count of those that died before completion of the six months’ IPT was 177.1 and the mean CD4 cell count of those that died after six months of IPT was 268.2.

**5.2.2.4 CXR and TB symptomatic screening among the patients (N=80)**

The findings showed that 100% (N=80) of the patients did have a chest X-ray prior to IPT; there were only 9% (n=7) chest X-rays that were abnormal, but not suggestive of TB. Reddy et al. (2010:2) indicate that Isoniazid alone is an appropriate treatment for latent TB infection (LTBI), but inadvertent Isoniazid monotherapy for active TB is ineffective and leads to drug resistance. Therefore, the pathway to commencing IPT
must reliably exclude active TB. Churchyard, Fielding, Lewis, Chihota, Hanifa and Grant (2010:26) concur that chest radiography in addition to symptom screening substantially increases the proportion of infectious TB cases detected and should be included as part of TB screening if available, particularly in settings of high TB prevalence.

5.2.3 Hospitalisation of the patients (N=80)

5.2.3.1 Self-reported illnesses of the patients (n=47)

Of the 47 patients with some self-reported illnesses, 19.15% (n=9) reported signs and symptoms of gastroenteritis; those who reported signs and symptoms of common cold/influenza were also 19.15% (n=9). The second most reported signs and symptoms were for pneumonia/PTB illnesses, at 14.89% (n=7).

There were 25% (n=12) of the 47 patients hospitalised. Of those hospitalised, 8.3% (n=1) died before completion of the six months’ IPT. None of the patients were hospitalised at the time of their enrolment. The study done by Cain et al (2009:262) indicates that hospitalisation at enrolment was strongly associated with increased risk of death caused by TB, but not death due to other causes, which further suggests that delay in TB diagnosis may be partly responsible.

5.2.4 Drug history of patients (N=80)

5.2.4.1 CPT of patients (N=80)

The findings demonstrated low use of CPT among patients. There were 10% (n=8) that used CPT, but among these eight patients there was no sound monitoring of CPT. There was inconsistent use of CPT, ranging from 1 month to 11 months. Reasons for discontinuation were not indicated, despite the fact that 75% (n=6) of the patients still had a CD4 cell count of below 200 after termination of CPT. Of the 25% (n=20) who qualified for CPT at the time of enrolment, only 40% (n=8) took CPT. This is most probably due to poor monitoring and evaluation integration and weak patient referral tracking. The records showed that patients were asked each time they came for their IPT review if they were on Cotrimoxazole. Records did not indicate reasons for those
who were no longer taking Cotrimoxazole. There was no indication of those that had a CD4 count of less than 200 being referred for CPT.

The study findings indicated that the leading causes of death compared with other illnesses were gastroenteritis: 18.75% \((n=15)\); Cryptococcal meningitis: 17.5% \((n=14)\) and pneumonia: 16.25% \((n=13)\). Date, Vitoria, Granich, Banda, Fox and Gilks (2010:256) have provided evidence that despite the effectiveness of CPT in reducing morbidity and mortality, nationwide implementation seems to be impeded by the lack of consistent supplies of CPT and lack of monitoring of the implementation of CPT. Lawn and Wood (2011:1386) indicate that careful screening and prophylaxis for co-infections is also important, because multiple pathologies appear to be the rule rather than the exception in HIV-infected patients.

According to the study done by Holmes et al (2006:468), the results suggested a large potential health gain from maximisation of preventive therapies, especially early Isoniazid preventive therapy, and Cotrimoxazole in patients with 200 CD4 or less, and prophylaxis against Cryptococcal disease with 50 CD4 or less.

### 5.2.4.2 Alcohol intake of patients \((N=80)\)

Of the 80 patients, 17.5% \((n=14)\) were indicated to have been consuming alcohol. Those with inconsistent use of alcohol were regarded as consuming alcohol; the type of alcohol or the extent of alcohol intake was not indicated. The records indicated that 82.5% \((n=66)\) of the deceased patients were not using alcohol during the six months of taking IPT. Parker (2011:22) holds that patients who consume alcohol have a higher chance of being non-adherent to the drugs they are being provided with than others who do not take alcohol. Parker (2011:22) indicates that women who drink stand a higher chance of being sexually abused by their male counterparts who drink.

According to Parker (2011:22), alcohol consumption is associated with sexual risk and vulnerability to HIV infection. He goes on to say that drinking higher quantities of alcohol (binge drinking) is more strongly associated with risk than frequency of drinking. Males are more likely to engage in higher risk behaviour following drinking, whereas risk to women is related to alcohol consumption by a partner (Parker 2011:22). Alcohol causes liver damage, which in turn can lead to death or can interfere with the drugs that have
been ordered for the patient. The records showed that of the 14 patients that consumed alcohol, 42.86% (n=6) died before they could complete six months of IPT. The reasons for death were indicated as murder, RTA, Cryptococcal meningitis, Kaposi sarcoma (KS) of the lungs, vomiting and pneumonia.

5.2.4.3 **ART among patients (N=80)**

Records indicated that of the 80 patients, 37.5% (n=30) were on ART. Of the 62.5% (n=50) not using ART, the records indicated that 38% (n=19) patients were eligible for ART but were not using it. Reasons for not taking antiretrovirals were not stated.

Lawn, Harries, Anglarete, Myer and Wood (2008:1905) found that early death rates threaten the credibility of ART delivery among communities accessing such therapy and among health workers who are responsible for providing this care. Although many factors are likely to contribute to this mortality, an overriding issue is that patients typically present for ART once they have developed advanced symptomatic disease (Lawn et al 2008:1905). When the disease is advanced, mortality is more likely.

Lawn and Wood (2011:1386) highlight the need for effective prevention of TB by using Isoniazid preventive therapy and ART as complementary strategies. NACA (2012:45) states that the challenge is still those whose CD4 cell count qualifies them for ART enrolment but who do not want to enrol for ART. This was also seen in the current study findings, in that 38% (n=19) of the deceased patients were eligible for ART but were not on ART.

Charalambous, Grant, Innes, Hoffmann, Dowdeswell, Pienaar, Fielding and Churchyard (2010:S12) have indicated that the risk of death after starting ART remains high until the CD4 cell count increases, and additional interventions are therefore urgently needed to reduce the risk of death among ART initiators. These data from the treatment cohort suggest that individuals starting ART may have a substantial reduction in mortality if IPT is given concurrently.

Durovni et al's (2010:8) results showed that among a patient population that was predominantly receiving HAART, adverse events were not a major concern, but they state that of course patients should continue to be monitored for adverse events while
receiving IPT. In their study, there were 2.5\% (n=2) with hepatic failure which was suspected to have been induced by INH; both were females aged 41 years and 32 years respectively and neither had reported alcohol intake; their liver function test were normal on the initial examination.

In the current study, the findings showed that all 37.5\% (n=30) patients on ART were on first-line treatment. None of them was either on second- or third-line treatment. NACA (2012:45) reports that the antiretroviral programme in Botswana has sustained a high treatment adherence rate (estimated at over 90\%), and the rate of progression from first- to second-line treatment remains low, with over 90\% of patients still on first-line treatment even after 10 years of the programme’s existence. Such low rates of migration to second-line treatment are a reflection of high adherence rates.

Golub et al (2009:6) showed that IPT given prior to HAART significantly reduced tuberculosis risk in HIV-infected patients in South Africa whose tuberculosis risk was extremely high. Whereas HAART alone also reduced tuberculosis risk in that population, the combination of both interventions was considerably more effective. In the current study findings it showed that there were 14.89\% (n=7) that died of possible PTB/pneumonia and 38\% not on ART yet were eligible.

5.2.5 Cause of death of the patients in this study (N=80)

Despite the fact that the deceased patients were on IPT, there were various documented causes of death. The 41.25\% (n=33) of the patients did not have any of the self-reported illnesses reported within the months of taking IPT. This shows that patients often move around with life-threatening illnesses that they do not report to the health workers, despite visiting the clinics every month. Among all the 80 patients, there were over 32 different illnesses that led to death, and most of the patients had two or more illnesses as the cause of death.

The most often indicated cause of death was gastroenteritis (n=15; 18.75\% of the patients), Cryptococcal meningitis was the cause of death of 17.5\% (n=14) patients, possible pneumonia of 16.25\% (n=13), and sepsis/septicaemia of 12.5\% (n=10). One can therefore confidently state that TB was not among the three leading causes of death.
Date et al (2010:256) indicate that patients diagnosed with relatively early HIV infection are often lost to clinical care, only to re-enter the medical care system later, when their disease is advanced. Date et al (2010:256) add that national HIV programmes should focus on improving long-term HIV care for people living with HIV by providing CPT and IPT, because both treatments can prevent opportunistic infections among people living with HIV and improve their quality of life. Setlhare et al (2009:224) in Botswana found in their study that when infants were included, pneumonia was by far the leading cause of deaths among both males (11.0%) and females (13.6%).

In the current study, there were 28.75% ($n=23$) of the patients that did not complete six months of IPT. Death before completion of treatment was due to: septicaemia: 13.0% ($n=3$), gastroenteritis: 21.7% ($n=5$), Cryptococcal meningitis: 13.0% ($n=3$), symptoms and signs of bacterial pneumonia: 17.4% ($n=4$), pulmonary tuberculosis: 13.0% ($n=3$), Murder:13.0% ($n=3$): RTA (hit by speeding police car): 4.4% ($n=1$) and Kaposi’s sarcoma of the lungs: 4.4% ($n=1$).

The study done in Thailand by Cain et al (2009:260) found that the most common causes of death were TB: 27%, HIV-associated deaths other than TB: 35%, and a condition not related to TB or HIV: 15%.

Lawn, Myer, Harling, Orrell, Bekker and Wood (2006:775) assessed a South African community-based ART programme, and found that mortality in the first four months of ART (‘early deaths’), and mortality after four months of ART (‘late deaths’) was independent of baseline immune status but was strongly associated with the response to ART, as reflected by the absolute blood CD4 cell count and viral load at 4 months. As such, the late mortality rate reflected therapeutic success, including drug regimen efficacy and tolerability as well as patient adherence to treatment (Lawn et al 2006:775).

In the current study, findings showed that the cause of death that occurred more frequently than others was gastroenteritis; the second most common cause of death was Cryptococcal meningitis, and pneumonia was the third most common cause of death. Of the 28.75% ($n=23$) patients who died before completing the six months of IPT because of death, the leading cause of death was gastroenteritis, the second was pneumonia and the third was Cryptococcal meningitis.
5.3 RECOMMENDATIONS

Based on the above findings, the following recommendations can be made in order to reduce factors contributing to mortality in HIV-infected people on IPT.

5.3.1 Practice (HIV and TB care at ARV and general clinics)

The findings show that four most common causes of death among the patients were gastroenteritis, pneumonia, Cryptococcal meningitis and tuberculosis. Nurses and doctors should monitor whether the patients do take the Cotrimoxazole regularly. They should keep registers of patients on Cotrimoxazole which can be regularly monitored and evaluated in order to enhance good adherence, which in turn reduces mortality. Intensive TB case finding through TB screening should be done at the ARV clinics, and patients without active TB could be commenced on IPT. IPT and Cotrimoxazole registers could be monitored at the ARV clinics.

5.3.2 Health management

Pneumonia and gastroenteritis were among the four most common causes of mortality; despite this only a small percentage of the 80 patients, 10% (n=8) were on Cotrimoxazole prophylaxis, and these patients discontinued Cotrimoxazole prophylaxis despite their CD4 count still being below 200. Health managers need to be vigilant with this and work together on a regular basis with medical officers and nurses to assess the reasons contributing to inadequate utilisation of CPT on HIV-infected patients on IPT, and give the required assistance. This could be done through regular planned meetings and evaluation of records.

5.3.3 Policies and procedures

Records showed inadequate monitoring and evaluation of CPT of patients. Indicators that measure CPT and IPT prescription should be included in systems to monitor patients with HIV.

The findings also revealed that 78% (n=63) of the patients had a negative TST. Negative TST means one does not have latent Mycobacterium tuberculosis. HIV
programmes should focus on improving long-term HIV care for people infected with HIV, by providing CPT and IPT in order to record progress in implementation. This effort requires a package of activities including training, advocacy and reorganisation of services so that HIV-infected patients will not need to travel to multiple clinics to initiate IPT.

5.3.4 Health education

The results suggest that increased health education efforts must be continued regularly by all health professional in their clinical practice. Intensive CPT and IPT education programmes should be implemented if not yet available, and improved if they are already in place. HIV-infected persons need to be made aware of the importance of CPT and IPT services.

5.3.5 Health research

It is recommended that a wider scope of this study should be developed, as the current study captured only a small portion of HIV/AIDS-infected patients in Botswana. This future study should include HIV/AIDS infected children on IPT using the same or modified objectives.

5.4 SCOPE AND LIMITATIONS OF THE STUDY

Records studied on mortality of HIV-infected people on IPT were taken in two sites of Gaborone and Francistown which provided IPT. Possibilities exist that patients who died at other sites might have had different contributory factors to mortality.

There was missing information in some records on the use of CPT; therefore, it was not possible to analyse the data to see if it is a risk to use or not to use CPT.

Because existing records were the source of information for this research, the results may not reflect recent progress at various facilities in the implementation of these policies.
5.5 CONCLUSION

TB being lower down as the cause of death for PLHIV on IPT shows the benefit of IPT. The leading cause of death was gastroenteritis, pneumonia and Cryptococcal meningitis and this necessitate for service integration. Understanding the local epidemiology, as well as understanding risks and the service needs of the PLHIV served are essential components of developing appropriate, comprehensive services and thereby enhancing quality, public health impact. Service Integration provides persons with seamless comprehensive services from multiple programs without repeated registration procedures, waiting periods, or other administrative barriers. Not only is services integration needed for HIV and TB, additional prevention service integration for gastroenteritis, pneumonia and Cryptococcal meningitis should be considered a priority as they are leading causes of mortality. This will eliminate missed opportunities and hence maximise the survival and health benefit for PLHIV.
LIST OF SOURCES


Botswana CSO see Botswana. Central Statistics Office.


Botswana MOH see Botswana. Ministry of Health.


NACA see National AIDS Coordinating Agency, Botswana.


WHO see World Health Organization.


