



## School of Health Systems & Public Health



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### Trends & Associations of HIV-related admission and mortality proportions in Princess Marina Hospital, Gaborone from 2000-2006

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A Dissertation by

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**Declaration**

“The work contained in this dissertation (protocol development, data collection supervision, data analysis and dissertation write-up) were completed by myself between November 2013 and September 2014. It is original work except where due reference is made and neither has been nor will it be submitted for the award of the degree at any other University. Any part of this dissertation does not relate to any work previously done in connection with another qualification or award. The work of others used in any form in this dissertation were cited and indicated in the list of reference section.

Signed: \_\_\_\_\_  \_\_\_\_\_

Dr. Mooketsi Molefi

Date: \_\_\_\_\_ 10 \_\_\_\_\_ FEBRUARY \_\_\_\_\_ 2015 \_\_\_\_\_

## **Trends & Associations of HIV-related admission and mortality proportion in Princess Marina Hospital, Gaborone from 2000- 2006**

### **Abstract**

**Background.** Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome (HIV/AIDS) has been recognised in Botswana for the last two decades, however, facility-based trends and associations of Hospital admissions and mortality proportions due to HIV/AIDS and determinant factors, have not been studied in settings such as Princess Marina Hospital. .

**Objective.** The aim of this study was to analyse the HIV-related admission and mortality proportions at Princess Marina Hospital in the years 2000, 2003 and 2006, compare and establish the trends

**Methods.** Patient records for the years 2000, 2003 and 2006 were reviewed. Cases were identified by documented HIV status or evidence of clinical immunosuppression by having any of the conditions listed in section B20-B24 of the International Classification of Diseases (ICD 10 B20-B24). HIV-related admissions, HIV-related mortality proportions and HIV- Case fatality Rates were calculated for each of the specified periods. Chi-square test for linear trend in STATA was used. A Log binomial regression method was used to identify important risk factors for HIV-associated mortality and admission.

**Results.** A total of (N= 24 541) records were reviewed for the years 2000-2006. The HIV-admission proportions (HIV related admission/Total admissions) were 0.101(988/9748), 0.112(868/7745) and 0.123(754/6148) admissions for the years 2000, 2003 and 2006, respectively. The HIV mortality proportions (HIV-related mortality/Total mortality) were 0.381(289/759), 0.474(309/652) and 0.371(252/680) deaths for the years 2000, 2003 and 2006, respectively. The HIV-Case Fatality Rates (HIV-admission/HIV-related mortality) were 29.2% (289/988), 35.6% (309/868) and 33.4% (252/754) for the years 2000, 2003 and 2006, respectively. Chi-square test for linear trend in STATA was only statistically significant for HIV-related admissions ( $p < 0.05$ ). The log binomial regression model indicated that the relative risks of both HIV-related admission and death were lower in females (aRR 0.54 CI 0.32,0.93) and (aRR 0.53 CI 0.34,0.86), but increased in the age-group 14-49 years (aRR 2.08 CI 1.07,4.04) and (aRR 1.21 CI 1.12,3.94), respectively.

**Conclusion.** The proportion of HIV-related admissions has increased, HIV related deaths and the HIV-Case Fatality Rate were notable since 2000-2006. Moreover, there was a linear trend in the proportion of HIV-related admission but none evident in HIV-related deaths and HIV-Case Fatality Rate. Female gender and age group 14-49 years were the two most important determinants for both HIV-related admissions and deaths. Future research focusing on recent trends and determinants of both HIV-related admissions and deaths are required.

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Figure 1.....Boxplot of age distribution among patients from 2000, 2003 & 2006

Figure 2.....Boxplot of CD4 distribution from year 2000-2006

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**Abbreviations**


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UB	University of Botswana
PMH	Princess Marina Hospital
HIV	Human Immune-deficiency Virus
AIDS	Acquired Immunodeficiency Disease
NACA	National AIDS coordinating Agency
IDSR	Integrated Disease Surveillance and Response
ART	Antiretroviral Therapy
CFR	Case fatality rate
ANC	Antenatal care
SES	Socioeconomic status
TB	Tuberculosis
ID	identity
STD	Sexually transmitted diseases
ELISA	Enzyme-linked Immunosorbent assay
TDF	Tenofovir
3TC	Lamivudine
FTC	Emtricitabine
EFV	Efavirenz
NVP	Niverapine
AZT	Zidovudine
DDI	Didanosine
LPV	Lopinavir
D4T	Stavudine
H	Isonizid
R	Rifampicin
Z	Pyrazinamide
E	Ethambutol



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## OPERATIONAL CASE DEFINITIONS

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1. HIV/AIDS patient: any patient recorded by the physician as having HIV/AIDS based on International Code of Diseases (ICD) 10 (B20-B24)
2. HIV-related mortality: any case of death recorded by the physician as caused by HIV/AIDS or clinical immunosuppression consistent with ICD 10(B.20-24), excluding any death from suicide, drug overdose or accident of an HIV patient
3. HIV-related admission: any case of admission recorded by the physician as linked to HIV/AIDS or clinical immunosuppression consistent with ICD 10(B.20-24), excluding admissions for delivery, elective surgeries and any other unrelated condition.
4. HIV infection: any positive result from rapid HIV tests on an over 18 months; any reactive specimen on parallel ELISA testing or Rapid testing is considered HIV antibody positive and is diagnostic of HIV infection
5. CD4: CD4 level
6. VL : patient viral load
7. Non HIV patient: any patient hospitalized for a condition other than HIV
8. ART: anti-retroviral treatment
9. ART-MASA-beneficiary (ART-MB): HIV patient eligible for MASA free ART , care and follow up
10. ART-Private beneficiary (ART-PB): HIV patient eligible for free ART, care and follow up from private insurance
11. ART-MASA and Private-beneficiary (ART-MB-PB): HIV patient eligible for free ART, care and follow up from both MASA and private insurance
12. ART-non-beneficiary: HIV patient non-eligible for free ART, care and follow up from both MASA and Private insurance
13. Proportion of HIV-related admission: the number of HIV hospitalization cases by the total number of hospitalization in a given year,
14. Proportion of HIV-related mortality: the number of HIV related deaths over the total number of deaths from all cases in a given year ,

- 15.HIV case fatality rate: number of HIV related deaths over the number of patients hospitalized for HIV in a given year times 100%
- 16.MASA: A Setswana word meaning “a new dawn”
- 17.MASA intervention program: National antiretroviral program
- 18.Patients with lower socio economic status (LSES): patients admitted at PMH general ward.
- 19.Patients with higher socio-economic status (HSES): Patients admitted at PMH private ward

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## 2.0 LITERATURE REVIEW

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Botswana has been reported as one of the countries with highest HIV prevalence and HIV-related mortality rate in Sub-Saharan Africa <sup>(1-3)</sup>. With the advent of national ART-intervention program providing free access to antiretroviral drugs and care to HIV-positive Botswana through the MASA program, a tremendous improvement has been achieved on HIV/AIDS health indicators<sup>(4)</sup>. Reportedly, HIV/AIDS prevalence has dropped from 40% in 1996 from ante natal clinic (ANC) surveillance to about 23.9% of adult prevalence in 2007 <sup>(5)</sup> and similarly the prevalence of HIV in the age groups 15-19 and 20-24 dropped from 24.7% to 13.2% and 38.7% to 24.1% between 2001 and 2009, respectively<sup>(6)</sup>. HIV-related deaths are also said to have decreased in the same time period. How both these indicators dropped at the same time period still remains unclear, for the following reasons: (i) ART does not stop HIV transmission in the population completely, (ii) other population groups e.g. non-citizens, still do not have free access to ART yet they form about 5-10% of Botswana population<sup>(7)</sup> and share with everyone in the country social activities including sexual activity which is the main mode of HIV transmission in Sub-Saharan Africa<sup>(8)</sup>, so it may not be profitable to exclude such groups from comprehensive HIV/AIDS programmes design. More importantly is the fact that ART is known to improve the quality of life of HIV patients<sup>(9)</sup> and to prolong their life expectancy<sup>(10, 11)</sup>, which clearly indicates that the severity of outcomes associated with HIV infection, being hospital admission, HIV mortality and Case Fatality Rate are useful as measure of the impact HIV has had in the Botswana population.

HIV/AIDS as a serious conditions, has led to increased need for patient hospitalization due to severity of the illness, thus has increased the patient density in health facilities <sup>(12, 13)</sup>. Traditionally, the care involved with HIV/AIDS patients required special attention. The management protocol, treatment nor trained personnel to recognize and deal with HIV related conditions, were not available in Botswana. In addition, the problems were accentuated by the

acute shortage of medical staff across the country <sup>(3, 14)</sup>. This resulted in higher facilities offering HIV/AIDS care such as Princess Marina experiencing exceptionally high proportion of admission and mortality. The advent of ART and other programmes, however, have changed the profile admission and mortality as reported by others. How these indicators have changed over time in some resource limited settings such as Princess Marina Hospital is yet to be known.

Literature on the trends of HIV associated admissions and mortality is scarce. Several studies around the globe report a high burden of high related admissions and deaths in their health facilities and a marked decline after the introduction of ART intervention programmes <sup>(8, 15-17)</sup>. Most studies regionally have not adequately reported on this, as they report only on one aspect of the problem, the situation before ART intervention or after <sup>(18-20)</sup>. Trends are important to study as they can highlight changes that have taken place, their magnitude, and allow comparison between time periods as well as projections for the future, which are all important to policy makers, healthcare workers and healthcare providers<sup>(21)</sup>.

Socioeconomic, demographic and biologic factors are an important consideration to study over time as these have been found to predict admission and mortality related to HIV <sup>(22-25)</sup>. Biological markers such as CD4 cell count, among others, have been found to be important predictors of admission and mortality <sup>(26, 27)</sup>. Income on its own may be more intimately associated with health challenges than other factors such as educational status and occupation which in addition to income contribute to the socio-economic designation of the individual.

Trends in the occurrence of AIDS defining illnesses depend on several factors including the prevalence of the infectious agent in the population or amongst the at-risk group, the CD4 levels at which an opportunistic disease occurs, and the various incubation periods of each opportunistic disease causing agent <sup>(28, 29)</sup>. Therefore, risk factors associated with high/low rates of HIV hospital admission and mortality at the height of the epidemic and after the

implementation of programmes such as the MASA, also needed to be highlighted periodically as evidence for policy making and resource orientation in order to alleviate unnecessary HIV related hospital admissions and mortality.

In most resource limited settings it is often difficult to utilize hospital records as source of data to infer to population statistics but Botswana's situation is different. Using ANC as proxy indicator where more than 97% of ANC is provided by skilled labor, it is suggestive that access to primary health care facilities is high. In addition, about 98% of deaths take place in hospitals<sup>(30)</sup> then by studying In-hospital admission rates related to HIV/AIDS, Case fatality rates from HIV and overall mortality attributable to HIV/AIDS as indicators of HIV disease severity, we were able to generalize the findings to the rest of Botswana.

Therefore our primary concern when implementing ART intervention program was to look at the severity of outcomes associated with HIV infection. Since the MASA-ART program started : (i) what proportion of HIV patients were still being admitted to hospital for HIV-related conditions per year; (ii) what proportion of all hospital admissions/ deaths per year are attributed to HIV-associated conditions, are the types of questions that one should ask when addressing HIV situation in Botswana. It may be too soon to look at HIV prevalence as an indicator for MASA-ART program effectiveness. This is because if the program was successful in averting the severity of HIV-disease there would be more people living with HIV but less HIV related hospital admission and mortality. It is surprising that 12 years after the beginning of MASA-ART intervention program in Botswana, changes on the severity of outcomes associated with HIV infection still unknown; yet this is the most needed piece of information to make sure that we are moving in the right direction.

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### **3.0 STUDY AIM**

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To determine the trends and associations of HIV-admission and mortality proportions in Princess Marina Hospital from 2000-2006 at 3 year intervals

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### **3.1 STUDY OBJECTIVES**

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1. To determine the proportion of HIV-related deaths and admissions for years: 2006, 2003 and 2000 and establish trends
2. To estimate HIV CFR for years: 2006, 2003, 2000 and establish trends
3. To investigate factors [i.e., CD4+ cell count, viral load, age, sex, SES, neighborhood of residence, nationality] associated with the risk of hospital admission for AIDS and with HIV-hospital mortality in order to compare and identify the most important predictor(s) over time

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### **4.0 METHODOLOGY**

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#### **4.1 Study Design**

The study was a cross-sectional retrospective review of all medical records of patients admitted to Princess Marina Hospital from 2000, 2003 and 2006.

#### **4.2 Study subjects**

All patients admitted to Princess Marina hospital for the years 2000, 2003 and 2006

#### **4.3 Setting**

The study was conducted in Princess Marina Hospital which is the highest of the public health facilities in Botswana. PMH is a 500-bed hospital offering comprehensive HIV/ AIDS care to patients from all over Botswana. A large number of patients with HIV related conditions are admitted and treated by medical teams led by specialists/consultants.

#### **4.4 Data collection**

Sources of data were mainly patient files stored at the records department for years 2006, 2003 and 2000.

A data collecting tool was developed in collaboration with the Ministry of Health and the University of Botswana, Public Health Medicine Unit . The instrument had been revised by the University of Botswana Public Health Unit and by other partners. The last amendments however, were not made until the instrument was pre tested. The drafted instrument was in English and no attempt was made for its translation into Setswana since no contact was made with participants nor surrogates.

The instrument is presented in the appendix 1; it is easy and self-explanatory. The tool is made of two types of forms, one administrative part and 3 Data Collection Forms (DCF): the Administrative section matched preset study codes to the patient's name. The first section of the Data Collection Form( DCF A) bearing the preset codes as the identifier now, collected demographic data; Date of birth, Age, sex, Residence, citizenship status( citizen of Botswana or not), and the Socio-economic category. The second section of the form (DCFB), collected information on HIV status, date of admission and discharge, final/discharge diagnoses, discharge mode and the cause of death where applicable. The third section, DCF C collected HIV information; Anti-retroviral therapy status, CD4 cell count, Viral Load, type of beneficiary when on ART and the regimen. Responses were coded as outlined in the DCF keys, to minimize variability, for ease of data entry and analysis.

The tool was pre-tested on 112 patients' records in Ramotswa, a hospital near Gaborone caring for similar clientele but of smaller bed capacity. Necessary amendments were made in the data collecting tool immediately after the pre-testing to ensure appropriateness for the data to be collected. The final draft was adopted and finalized for use.

#### **4.5 Sample size**

An exhaustive sample size of year data for 2000, 2003 and 2006 was carried out.

#### **Inclusion & Exclusion criteria**

Records of every patient admitted to PMH during the selected time periods were included in the study. Patients who died or were discharged after less than 24 hours of being admitted were excluded. Records of patients brought in for death certification were excluded.

#### 4.6 Study Outline

From each inpatient, the following data items [See data collecting tool: appendix # 1] were collected by enumerator: patient's name matched to a preset study code, date of birth, Gender( coded) , citizenship( coded) , Date of Admission , Final diagnosi(es) [diagnosis 1, 2] as coded as by the international classification of diseases code 10( ICD – 10); CD4 level and viral load at the admission, whether or not patient stayed in a private ward, date of discharge from the hospital, whether patient was discharged alive or dead, whether patient was transferred to another facility; whether s/he escaped from hospital. All PMH inpatients admitted at the general ward will be recorded as of lower socioeconomic status (LSES), while those admitted at PMH private ward were recorded as of higher socioeconomic status (HSES).

Patients admitted twice or more times with the same condition within the same year were counted as single case for that year. Aside from data obtained from hospital records, no contact was made with respondents or surrogates to obtain additional information on patients.

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#### 4.6 ETHICS

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In this study, no human biological material was used nor contact with the respondents. The study was limited to collection and analysis of data from hospital records, no contact was made with respondents or surrogates to obtain additional information. The unique study ID was used to protect the identity of the participant. A log file matching the study ID to the name of the participant was kept safe and confidential. The data collected was kept with extreme confidence within the research team and used solely for research purpose. No respondent name's name appears in any of our reports or any peer reviewed paper to be born from these data.



Ethical approval was sought from the University of Botswana's Institutional Review Board (UB- IRB), Botswana MoH and the University of Pretoria's Ethics Board (189/2014)

Permission to access data collection at PMH as well as patient's files, electronic medical and mortuary records was sought from these facility management teams; copies of the study protocol were provided to them any questions were addressed.

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## 5.0 DATA PROCESSING AND ANALYSIS

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Data was processed and analysed using STATA (Statacorp. 2012 *Stata Statistical software: Release 12*. College Station, TX: StataCorp LP)).

Summary statistics for count data such as Age, CD4 cell count were presented in tables. Also frequency distributions of gender, socioeconomic status and citizenship were summarized in tables, per year

Years 2000, 2003 and 2006 will be computed as continuous variables in the models and its p-values interpreted as p-value for trend as suggested by Vittinghof <sup>(31)</sup>

A Log binomial regression methods was used to investigate factors important for predicting risk for admission or death since the outcomes were not rare Associations of (i) Hospital admission HIV/AIDS, (ii) HIV/AIDS-Hospital mortality, with patients' characteristics [i.e., CD4 count, citizenship, age, sex, SES] were investigated using two log binomial regression sub-models: (i) with HIV-related admission (yes or no) and (ii) HIV-related death( yes/no) as dependent variables.

The following variables were investigated as correlates of outcome variables to compute for Risk Ratios(RR) and their 95% confidence intervals: inpatient age, sex, CD4 number, viral load, SES, whether or not ART-beneficiary, year of hospitalization (2000 to 2006) All variables significant in the main effects models, as well as those suspected to have different relationships with the outcome variable depending on the third factor, will be investigated in a series

of interactions; only the models that explained the highest proportion of variability of the outcome was be presented; the level of significance was set at  $P < 0.05$ .

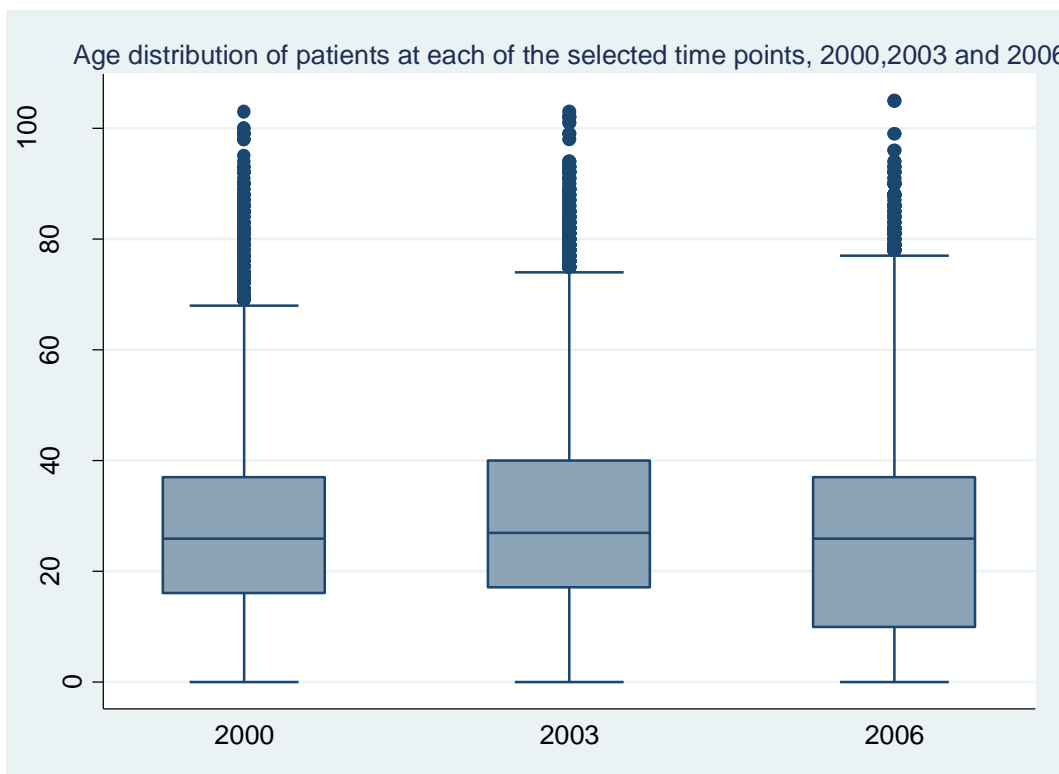
**6.0 RESULTS**

**Table 1** Summary of the age distribution of participants records reviewed from 2000-2006

File-year	Variable (n)	Median, IQR (yrs)
	Age	
2000	9671	26,21
2003	8186	27,23
2006	6134	26,27

The median age of participants enrolled in the years 2000, 2003 and 2006 were 26, 27 and 26 years, respectively

**Figure 1** Age distribution among patients' records from 2000, 2003 and 2006



**Table 2** Summary of the basic demographic characteristics of patients whose records were reviewed from 2000-2006

Variable	2000 n (%)	2003 n (%)	2006 n (%)
<b>Sex</b>			
Male	4023(41.27)	3679(43.84)	2394(38.91)
Female	5598(57.43)	4497(53.59)	3734(60.70)
Missing	127(1.3)	214(2.55)	124(0.39)
<b>Citizenship status</b>			
Citizen of Botswana	9475(96.77)	7980(95.11)	5126(82.62)
Non-citizen	305(3.12)	326(3.89)	234(3.77)
Not documented	11(0.11)	84(1.00)	844(13.46)
<b>SES</b>			
Low SES	9179(99.27)	8319(99.15)	6300(99.46)
High SES	62(0.63)	68(0.81)	22(0.35)
Indeterminate	9(0.01)	3(0.03)	12(0.19)

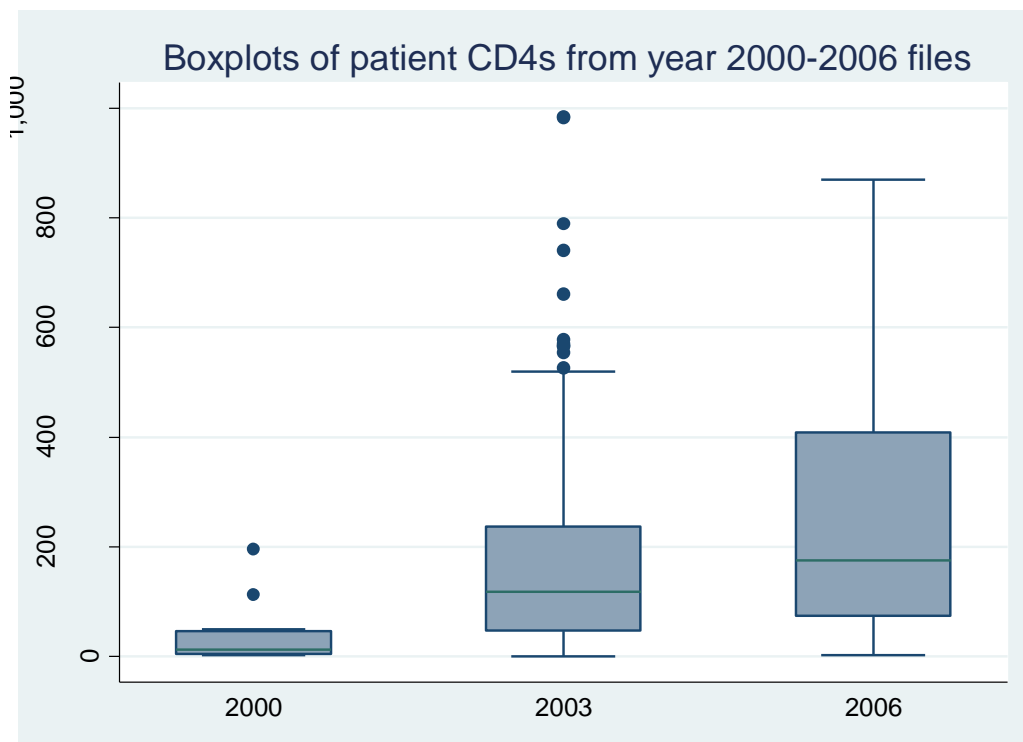
Basic demographic characteristics of participants such as age, citizenship status, socio-economic status etc., were also studied. Across the three years studied, the majority were females with 57.43%, 53.59% and 60.70% majority for 2000, 2003 and 2006, respectively. Up to about 97% of participants enrolled were citizens of Botswana, with only up to about 4% as non-citizens of Botswana. Regarding the socio-economic status, the majority were of low socio-economic status, >99% across the three years.

**Table 3** HIV status of patients whose records were reviewed from 2000-2006

Variable	2000 n(%)	2003 n(%)	2006 n(%)
HIV status			
Positive	403(4.12)	974(11.61)	998(16.08)
Negative	143(1.46)	489(5.83)	1288(20.75)
Unknown	9245(94.42)	6927(82.56)	3920(63.17)

Concerning the HIV-status of patients, the majority did not know their HIV-status; the worst year being the year 2000 (94.42%) and year 2006 with the lowest figure of 63.17%. Only 4.12% of participants were documented as HIV-positive, while only 1.46% were documented HIV-negative.

**Figure 2** Boxplot of patients CD4 distribution for the years 2000-2006



**Table 4** Median CD4 & IQR, ART status and most frequent regimen (2000-2006)

Variable	2000	2003	2006
CD4 (n)	9	144	220
Median, IQR	12,41.5	118,191	175.5,335
<b>On ART?</b>			
Yes	101(25.06)	357(36.65)	434(43.49)
No	147(36.48)	357(36.65)	458(45.89)
Unknown	155(38.46)	260(26.70)	106(10.62)
<b>Common ART used</b>			
TDF-based			
AZT-based			
D4T-based	99(98.02)	286(80.11)	322(74.10)
DDI-based			

Of the patients that tested HIV-positive, their median CD4 counts were 12, 118 and 175.5 cells per ml, for the years 2000, 2003 and 2006, respectively. Only 25.06%, 36.65% and 43.49% of participants were on some form of ART in 2000, 2003 and 2006 respectively. Majority of those that were on ART, AZT-based regimen was the commonest regimen used.

**Table 5** The proportion of HIV-related admissions and linear trend test for 2000-2006 data

File-year	Total admissions N	HIV-related admissions (n)	Proportion	p-value†
2000	9748	988	0.101	
2003	7745	868	0.112	0.00
2006	6148	754	0.123	

† Chi-square for linear trend p-value using Patrick Royston's test (ptrend)

The proportions of HIV-related admissions were 0.101, 0.112 and 0.123 in the years 2000, 2003 and 2006, respectively. Moreover, this was statistically significant for linear trend using the ptrend test in STATA.

**Table 6** The proportion of HIV-related deaths and linear trend test for 2000-2006 data

File-year	Total deaths N	HIV-related deaths (n)	Ratio (n/N)/1000 deaths	p-value†
2000	759	289	381	
2003	652	309	474	0.55
2006	680	252	371	

† Chi-square for linear trend p-value using Patrick Royston's test (ptrend)

Regarding proportions of HIV-related deaths, they were 0.381, 0.474 and 0.371 in the years 2000, 2003 and 2006, respectively. Test for linear trend was not statistically significant using ptrend in STATA.

**Table 7** HIV-Case Fatality Rate and linear trend in PMH from 2000-2006

File-year	Total admissions N	HIV- N	HIV-related deaths (n)	HIV-Case Fatality Rate (%)	p-value†
2000	988		289	29.25	0.09
2003	868		309	36.00	
2006	754		252	33.42	

† Chi-square for linear trend p-value using Patrick Royston's test (ptrend)

The resultant HIV-Case Fatality Rate in PMH ranged from 29.25% to 36%, with the year 2003 being the worst. The test for linear trend was not statistically significant.

**Table 8** Crude Bivariate analysis of independent variables predicting HIV-death from 2000-2006, (Log binomial regression)

Variable (n)	RR	SE	p-value	CI
<b>Sex</b>				
Female	0.94	0.07	0.389	0.81-1.09
male	1			
<b>Age(yrs)</b>				
0-13	0.78	0.15	0.214	0.54-1.15
14-49	1.83	0.23	<0.001	1.42-2.35*
>50	1			
<b>Citizenship</b>				
Non-citizen	0.79	0.19	0.327	0.49-1.27
Citizen	1			
<b>HIV</b>				
Unknown	0.24	0.04	<0.001	0.17-0.33*
Positive	1			
<b>ART</b>				
No	1.33	0.10	<0.001	1.15-1.53*
Yes	1			
<b>MASABeneficiary</b>				
Non-beneficiary	1.27	0.10	0.002	1.10-1.48*
Beneficiary	1			



In the bivariate model the risk of HIV-related admission is lower in the HIV-unknown status (RR 0.24 CI 0.17-0.33) while Age group 14-49 years, non-ART use and non-beneficiary were significant risk factors for HIV-related admissions (RR 1.83 CI 1.42,2.35), (RR 1.33 CI 1.15-1.53) and (RR 1.27 CI 1.10-1.48), respectively.

**Table 9** Crude Bivariate analysis of independent variables predicting HIV-admission from 2000-2006, (Log binomial regression)

Variable (n)	RR	SE	p-value	CI
<b>Sex</b>				
Female	0.96	0.07	0.614	0.83-1.12
male	1			
<b>Age(yrs)</b>				
0-13	0.85	0.17	0.410	0.58-1.25
14-49	1.86	0.25	<0.001	1.43.-2.41*.
>50	1			
<b>Citizenship</b>				
Non-citizen	0.88	0.20	0.594	0.56-1.39
Citizen	1			
<b>HIV</b>				
Unknown	0.20	0.04	<0.001	0.13-0.29*
Positive	1			
<b>ART</b>				
No	1			
Yes	1.40	0.10	<0.001	1.22-1.60*
<b>MASABeneficiary</b>				
Beneficiary	1			
Non-ben	1.37	0.10	<0.001	1.19-1.58*

Of the factors investigated in this bivariate model, unknown HIV status reduced the risk of HIV-related admission (RR 0.20 CI 0.13-0.29) while age-group 14-49 years, non-ART use and non-beneficiary status increased the risk of admission for HIV (RR 1.86 CI 1.43-2.41), (RR 1.40 CI 1.22-1.60) and(

RR 1.37 CI1.19-1.58). The other factors investigated were not statistically significant.

**Table 10** Dependent variable: HIV-related admissions (N=2610)

**Sub Model A**

Independent variables	Proportion	Unadjusted		Adjusted	
		RR	95%CI	RR	95%CI
Year :2000	0.40	1		1	
2003	0.34	0.96	0.79-1.17	0.96	0.42-2.19
2006	0.26	0.75	0.60-0.94*	0.78	0.55-0.97*
Fileyear				0.95	0.91-0.97‡
Sex: Male	0.49	1		1	
Female	0.51	0.96	0.83-1.12	0.54	0.32-0.93*
Age: >50	0.19	1		1	
0-13	0.22	0.85	0.58-1.12	0.72	0.32-1.61
14-49	0.59	1.86	1.43-2.41*	2.08	1.07-4.04*
Citizenship:					
Non-citizen	0.04	0.88	0.56-1.39	omitted	
Citizen	0.96	1			
HIV: Positive					
Unknown	0.44	1		1	
	0.56	0.20		1.21	0.87-1.62
ART use:					
Yes	0.19	1		1	
No	0.81	1.40	1.22-1.60	1.25	0.32-4.90
MASA-Beneficiary					
Yes	0.83	1		1	
No	0.17	1.37	1.19-1.58	2.66	0.60-11.69

‡=Adjusted p-value for trend over time (p=0.04)

In the final model predicting factors associated with HIV-admission (sub-model A), the risk of HIV-related admission reduced in the year 2006 (aRR 0.78 CI 0.55-0.97) compared to 2000. The risk of HIV-related admission were statistically and significantly reduced if you were female (aRR 0.54 CI

0.32,0.93) but increased for those belonged to the 14-49 year age-group (aRR 2.08 CI 1.07,4.04).

**Table 13 Dependent variable: HIV-related death (N=469)**

**Sub Model B**

		Unadjusted		Adjusted	
Independent variables	Proportion	RR	95%CI	RR	95%CI
<b>Year</b> :2000	0.15	1		1	
2003	0.48	1.85	0.53-6.42	1.19	0.53-2.64
2006	0.37	1.45	0.41-5.17	0.33	0.29-1.36
<b>Fileyear</b>				0.96	0.91-0.98
<b>Sex:</b> Male	0.53	1		1	
Female	0.47	0.94	0.81-1.09	0.50	0.34-0.86*
<b>Age:</b> >50	0.20	1		1	
0-13	0.60	0.78	0.54-1.15	0.64	0.29-1.36
14-49	0.20	1.83	1.42-2.35	2.10	1.12-3.94*
<b>Citizenship:</b> Non-citizen	0.04	0.41	0.05-3.52	omitted	
Citizen	0.96	1			
<b>HIV:</b> Positive	0.66	1		1	
Unknown	0.34	0.29	0.11-0.75*	0.30	0.22-1.11
<b>ART use:</b> Yes	0.75	1		1	
No	0.25	2.82	0.32-25.49	1.76	0.41-7.51
<b>MASABeneficiary</b> Yes					
No	0.22	1		1	
	0.78	0.17	0.01-1.81	1.11	0.24-5.11

‡=Adjusted p-value for trend over time ( p=0.04)

In sub-model B, where factors associated with HIV-death were investigated, the risk of HIV-related death reduced were lower in females compared to their male counterparts (aRR 0.53 CI 0.34, 0.86). The risk of HIV-related death, were however increased in the age-group 14-49 years (aRR 1.21 CI 1.12, 3.94) when compared to the > 50 years age-group. The other factors were not statistically significant while citizenship variable lacked variability.

Factors CD4 count, SES and citizenship were not included in the final model as they lacked statistical significance to be included in the final models perhaps owing to the small sample size.

Age, sex, ART use and MASA beneficiary status were investigated for effect modification by developing interaction terms but no effect modification was evident in the relationship between admission for an HIV related illness and the risk of hospital admission or death.

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## 7.0 DISCUSSION

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Trends and associations of HIV-admission and mortality in Princess Marina Hospital from year 2000, 2003 and 2006 have now been studied and are known.

From the data gathered, the basic demographic characteristics in table 1 describe a relatively young population of patients being investigated (median age under 30), which would be typical of a developing country <sup>(32)</sup>. Furthermore, each year and overall the majority of patients admitted to PMH were females which is a finding consistent other studies <sup>(33, 34)</sup>. An overwhelming majority of patients that were admitted to the facility were citizens of Botswana, however, there was a notable increment in the numbers of non-citizens in 2003 and 2006 perhaps owing to the country's economic and political attractiveness regionally. Being a public facility, it was noted that a great majority of patients that were admitted were of low socio-economic category as per our classification across the three years analysed.

With reference to the year 2002 marking the beginning of the National ART-roll out in Botswana<sup>(35)</sup>, the majority of patients were not tested for HIV in the pre-ART era. e.g year 2000 resulting in a high proportion of HIV unknown status and a high burden of HIV related opportunistic infections. As management of these conditions was challenging due to little known about the diseases, patients died. However, the numbers improved significantly after the year 2000 to about 90% of people who knew their HIV-status by the end 2006. These efforts may be attributed to amongst others, the accelerated MASA ART programme roll-out, the aggressive health education and HIV-awareness campaigns that were on-going at that time<sup>(35)</sup>. Before 2000, it is evident that a few individuals had access to ART even before the commencement of MASA but the number soared after the drugs were made available to all eligible nationally. Both in the pre and post-ART era, the commonest class of drugs used was AZT-based therapy

The proportion of patients with being admitted to PMH with HIV-associated conditions was notable even by 2000 through to 2006. With each of the time

point, an HIV-related admission proportion exceeding 10% of the overall admissions. This is a significant proportion to the admission number given the challenges of staff, facilities and management of the condition at these times. The proportion of patients presenting with HIV associated conditions was ever increasing at from 2000 with a positive linear trend.. This is not surprising as this coincides with a time when HIV was rampant in Botswana <sup>(35)</sup> but also there was a drive for people to test and know their HIV status from 2003 through routine HIV testing as opposed to Voluntary Counselling and Testing( VCT<sup>(36, 37)</sup>. Of the deaths that occurred in the years 2000, 2003 and 2006, HIV-related proportion of around 35% is significantly high showing how ravaging the disease was in those times. There was however no linear trend picked in the proportion of HIV-deaths from 2000 to 2006. This may have been due to the mixed effects of more people testing, improved diagnosis of HIV-related conditions by healthcare workers, programme interventions etc.. As an estimate of HIV-severity on PMH wards, the HIV-Case Fatality Rate was calculated and ranged from about 29% to 36%, with 2003 being the worst even higher than reported in some studies regionally<sup>(38)</sup> The linear trend was not statistically significant here probably too due to the mixed effects of the same factors mentioned above..

In the final adjusted sub-models presented to investigate possible factors associated with HIV-related admission and HIV-related death, it was shown that female gender and unknown HIV were protective factors while the age-group 14-49 years was a significant risk factor for both HIV-related admission and death. This is consistent with findings from other studies showing that the most affected are the youth presented in the age group category <sup>(39)</sup> with consequent admission to hospital and death.

It was not surprising that patients with unknown HIV-status were less likely to be admitted to hospital or die from HIV, perhaps because those days doctors based their diagnoses on clinical signs without performing any HIV tests, which might have underestimated the magnitude of HIV related admission and mortality within this specific group.

## **STUDY LIMITATIONS**

There are several limitations to be acknowledged in this study. Since there was no universally accepted definition of HIV-related admission and/or death,

fairly precise case definitions had to be constructed with the help from previous studies<sup>(40, 41)</sup>. This was a huge challenge since there is no universally accepted definition of an HIV related event. In addition plus an appreciation of the fact that a great majority of patients seen in the pre-ART era would probably not have known their HIV status<sup>(42)</sup>, a broader HIV associated event definition had to be adopted hence the modified case definition to include opportunistic infections likely to be AIDS defining.

The results showed an increasing proportion of patients admitted with HIV associated conditions over time. This may have been influenced by other extraneous factors such as changes in the HIV prevalence over time such that as more people test, the prevalence goes up and as such more HIV related conditions would be seen in health facilities.

Fifty three records representing 0.2%( 23 from 2000, 13 in 2003 and 17 in 2006) were excluded from the analyses due to missing data, mainly the outcome of admission . The risk of admission and or death in patients with missing data could not be ascertained.

The use of hospital data in developing country settings where not every sick person attends hospital; and burials often occur without the knowledge of the cause of death could have led to an underestimation of outcomes, however we established that most deaths in Botswana, generally occurred in a health facility<sup>(30)</sup>. The quality of the data was generally acceptable, as each medical file was covered in a protective hardcover sheath, and under lock and key. A few of these however had torn covers and it was difficult to ascertain the integrity of the information within. Nevertheless, data that are regularly generated in hospitals have been effectively used for epidemiological purposes as they are inexpensive and readily available<sup>(43)</sup>. In developing countries like Botswana where health data are often lacking, hospital data can provide good evidence for planning and policy/decision making if they are properly collected and processed<sup>(43)</sup>. In this work, we meticulously addressed these issues through increased daily supervision throughout data collection( Appendix III).Patients with some missing data or whose data could not be matched between different sources within the same hospital were excluded from the study. Also excluded from the study patients, were patients with

no/unclear diagnostic records. Also the fact that 98% deaths in Botswana occur in hospital can only contribute to increase validity of findings from this study.

Funding was a major constraint as funds were limited to support mainly the research assistants' stipends and at various time points the data collection had to be interrupted while funds were being sought, which prolonged the data collection period.

A significant length of time was spent on searching for relevant year medical files at times which consumed our study time and funding. Better storage, accessibility and availability of files would have been quicker and perhaps allowed more comprehensive data retrieval. .

In summary, from 2000-2006, there was linear trend of increasing in HIV-related admission ratios, whilst none was evident in HIV-related deaths ratio and the HIV-Case Fatality Rate. Female gender reduced the risk of HIV-related admission and death, while the risk of both HIV-related admission and death increased in the age-group 14-49 years



# *Appendix 1*

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**Trends and associations of HIV related admission and mortality ratios in Princess Marina Hospital between 2000 and 2006**

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## *Study training Manual for data collectors*

*Version 1.0*

*Developed by Dr. M. Molefi & Dr. J.G. Tshikuka*

# Introduction

## Contents

The tool has two main parts, an administrative form (AF) and data collection form (DCF). A complete form composed of an AF and DCFs( A,B & C) and twenty(20) entries or records of patients were inserted. AF was stored away separately in a lockable place and only recalled if needed to an authorized personnel.

Page 1.....	AF
Page 2.....	DCF A
Page 3.....	DCF B
Page 4.....	DCF C

Page 1

PILOT

LOG SHEET FORM

DATE: \_\_/\_\_/2014

DATA COLLECTOR CODE:

#	Surname, Name	Preset code
1		xBW72
2		xCT53
3		xDW99
4		xFZ83
5		xGZ88
6		xJD34
7		xKB25
8		xKX26

Page 2

PILOT

version 1.0

Site: x

DATE: \_\_/\_\_/2014

DATA

COLLECTOR CODE:

DCF A

Demographics									
#	code	File Year	Logged	DOB	Age	Sex	Residence (Address)	Citizenstatus	SEScat
1	xBW72								
2	xCT53								
3	xDW99								
4	xFZ83								
5	xGZ88								
6	xJD34								
7	xKB25								

Page 3

version 1.0

Site: 1

DATE: \_\_/\_\_/2014

DATA COLLECTOR CODE:

DCF B

CLIN INFO						
#	DOA	HIV status	Final/discharge diagnosis	Discharge date	Dischargemode	Mode=4, State cause
1						
2						
3						
4						
5						
6						
7						

Page 4

version 1.0

Site: 1

DATE: \_\_/\_\_/2014

DATA COLLECTOR CODE:

DCF C

Hiv1					
#	On ART	CD4	Virallload	beneficiary	Current regimen
1					
2					
3					
4					
5					
6					

# KEY

## DCF A ( Page 2)

Logged=name assigned unique study code

Yes 1

No 0

D.O.B =date of birth

Format=DD/MM/YYYY

Sex

Male=1

Female=2

Citizen status

Citizen of Botswana=1

Non-citizen=0

Indeterminate=2

S.E.S cat=Socio-economic category

All Lenmed-Bokamoso, GPH and PMH private ward= High =1

All Government ordinary ward=0

## DCF B (Page 3)

D.O.A=date of admission

Format=DD/MM/YYYY

HIV status Code

Positive 1

Negative 0

Unknown 9

Final/discharge diagnoses

List any two causes documented

NB: Even without HIV documentation, some patients may have UNEXPLAINED O.I.s listed in ICD-coding, Kindly note these e.g. B21.0

Unknown diagnosis=9

Discharge date                      Format=DD/MM/YYYY

Mode   Code

Home   1

Absconded                      2

Transfer out                      3

Death                              4

Not documented   9

If not 4,

Code=5

Cause of death not documented=9

**DCF C ( Page 4)**



**NB: Patients with more than 1 month ART relapse shall be assessed as not on ART**

**Patients with less than 1 month relapse shall be deemed/treated as onART**

**Patients on AZT prophylaxis shall be considered on HAART**

On ART=On antiretroviral therapy?

Yes= 1

No= 0

Unknown 9

For Yes=1

Participant	ART benefit	Description	codes
-------------	-------------	-------------	-------

ALL Private hospital patients, and PMH private ward		CitizenPublic private partnership	
1			

Non-citizen	Fully private(out-of-pocket payment)	2	
-------------	--------------------------------------	---	--

All PMH patients except Private ward patients		CitizenMASA program beneficiary	3
-----------------------------------------------	--	---------------------------------	---

Non-citizen	Non-beneficiary		4
-------------	-----------------	--	---

Insufficient data to categorize=5

Not applicable=6

CD4 = CD4 documentation just before admission/on admission/documentated currently

No CD4 documented , put asterik \*

Viral load= Viral load just before admission/on admission/documentated currently

No VL documented, put asterik \*

Current regime= the ART regime the patient is on currently

TDF-based= 1

AZT-based= 2

D4T-based= 3

DDI-based= 4

Not on any regimen= 9

Other=5

Not specified=6

# *APPENDIX II*

## ICD 10 coding (B20-B24)

- B20.0**        **HIV disease resulting in mycobacterial infection**
- HIV disease resulting in tuberculosis**
- B20.1**        **HIV disease resulting in other bacterial infections**
- B20.2**        **HIV disease resulting in cytomegaloviral disease**
- B20.3**        **HIV disease resulting in other viral infections**
- B20.4**        **HIV disease resulting in candidiasis**
- B20.5**        **HIV disease resulting in other mycoses**
- B20.6**        **HIV disease resulting in *Pneumocystis carinii* pneumonia**
- B20.7**        **HIV disease resulting in multiple infections**
- B20.8**        **HIV disease resulting in other infectious and parasitic diseases**
- B20.9**        **HIV disease resulting in unspecified infectious or parasitic disease**
- HIV disease resulting in infection NOS**
- B21**         **Human immunodeficiency virus [HIV] disease resulting in malignant neoplasms**
- B21.0**        **HIV disease resulting in Kaposi's sarcoma**

- B21.1 HIV disease resulting in Burkitt's lymphoma**
- B21.2 HIV disease resulting in other types of non-Hodgkin's lymphoma**
- B21.3 HIV disease resulting in other malignant neoplasms of lymphoid, haematopoietic and related tissue**
- B21.7 HIV disease resulting in multiple malignant neoplasms**
- B21.8 HIV disease resulting in other malignant neoplasms**
- B21.9 HIV disease resulting in unspecified malignant neoplasm**
- 
- B22 Human immunodeficiency virus [HIV] disease resulting in other specified diseases**
- B22.0 HIV disease resulting in encephalopathy**
- HIV dementia**
- B22.1 HIV disease resulting in lymphoid interstitial pneumonitis**
- B22.2 HIV disease resulting in wasting syndrome**
- HIV disease resulting in failure to thrive**
- Slim disease**
- B22.7 HIV disease resulting in multiple diseases classified elsewhere**
- Note: For use of this category, reference should be made to the morbidity or mortality coding rules and guidelines in Volume 2.**
- 
- B23 Human immunodeficiency virus [HIV] disease resulting in other conditions**

**B23.0 Acute HIV infection syndrome**

**B23.1 HIV disease resulting in (persistent) generalized lymphadenopathy**

**B23.2 HIV disease resulting in haematological and immunological abnormalities, not elsewhere classified**

**B23.8 HIV disease resulting in other specified conditions**

**B24 Unspecified human immunodeficiency virus [HIV] disease**

**Acquired immunodeficiency syndrome [AIDS] NOS**

**AIDS-related complex [ARC] NOS**

# *APPENDIX III*

Pre-testing in BLH, Ramotswa



Records Department and Data collection in PMH, Gaborone







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