ANTIRETROVIRAL (ART) AND PREVENTION OF MOTHER –TO- CHILD TRANSMISSION (PMTCT) THERAPIES ADHERENCE IN GREATER GABORONE, BOTSWANA: A MIXED METHODS HEALTH GEOGRAPHIC STUDY

By

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ABSTRACT

ANTIRETROVIRAL (ART) AND PREVENTION OF MOTHER –TO- CHILD TRANSMISSION (PMTCT) THERAPIES ADHERENCE IN GREATER GABORONE, BOTSWANA:
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Botswana is among the highest HIV/AIDS epidemic burden bearing countries in the world. While treatment for HIV was introduced in Botswana in 2002, the uptake and adherence of the antiretroviral (ART) and Prevention of Mother-to-Child Transmission (PMTCT) therapies are still relatively low. The goal of this research is to provide recommendations on how to improve adherence to ART and PMTCT treatment regimens for adult men and women, and pregnant women and new mothers living with HIV in Botswana. With improved ART adherence, there is high potential for a reduction in new HIV infections as a result of suppressed viral load. This reduction will contribute to the global goal of the UNAIDS (United Nations AIDS) "Treat All Program" to eliminate new HIV infections by 2030. ART adherence is measured in two ways (a) biological (serum CD4 count and viral load) and (b) using a composite score of biological and behavior, including reporting missed dosages. With this in mind, this study will examine three dimensions of ART non-adherence in a sampled population of HIV infected adult men (n=239) and women (n=419), including pregnant women or new mothers (n=67) attending 21 ART clinics in Greater Gaborone. First, ART adherence was investigated at the individual-level to assess and evaluate differences by gender, age and geography. Second, PMTCT was investigated at the individual-level to identify challenges to adherence during pregnancy and early motherhood. Third, the climate of Botswana is hot, arid and dry and this study therefore, investigate the impacts of weather extremes on adherence behavior. The findings from this study show that men have lower adherence to ART than women; and men 30+years are at the highest risk of transmitting HIV infection. Lower adherence in men 30-40 years may in part, be explained by taking other drugs for co-conditions in addition to ARVs. With increasing age, lower

adherence among men 50+ years is largely explained by single marital status and the need to seek other companions for support later in life. Second, among pregnant women and mothers, a majority cohabit with HIV infected men (n=45) and many (n=22) do not know their partner's HIV status. Post-partum, many women do not disclose their own HIV status until later in their infant's first year of life, in part because mother's are processing their own HIV status as trust is evolving in the relationship. Not knowing a partner's HIV status and/or not disclosing one's own HIV status, do not significantly lead to poor adherence and increased the risk of HIV transmission, however, declining trends in CD4 counts are observed, suggestive that there are difficulties adhering to ART for both partner and mother post-partum. Third, high ambient temperature is an important barrier to monthly clinic visits for both men and women living in urban, peri-urban and rural areas; and water rationing is a significant risk factor for non-adherence in rural areas. Being turned away by the clinic because of no water availability, is another important barrier for women including, pregnant and post-partum mothers and men living with HIV in Greater Gaborone. The findings from these three studies recommend (a) targeting men 30+ years living with HIV for medical and social support to ensure high ART adherence, to reduce HIV transmission; (b) provide additional social services for women and their partners, during pregnancy and post-partum to enhance trust associated with HIV disclosure, to ensure high ART adherence; and (c) increase public health messaging about how to overcome environmental barriers to ART adherence, especially on extremely hot days and days of water rationing, while also ensuring water availability in all ART clinics. These recommendations may be extended beyond Botswana, to other sub-Saharan African countries to optimize ART treatment success and the elimination of HIV transmission over the next decade.

This dissertation is dedicated to the memories of professors Florence Margai (1962-2015) and Michael Bernard Kwesi Darkoh (1940-2016). Although you were my inspiration to pursue my doctoral degree, you were unable to see my graduation. This is for you.

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CHAPTER 1: ANTIRETROVIRAL (ART) AND PREVENTION OF MOTHER -TO -CHILD TRANSMISSION (PMTCT) THERAPIES ADHERENCE IN GREATER GABORONE, BOTSWANA: A MIXED METHODS HEALTH GEOGRAPHIC STUDY

1.0. INTRODUCTION

In the early 1970s, the first cases of human immunodeficiency virus [HIV] and Acquired immunodeficiency syndrome [AIDS] were reported in Kinshasa, Democratic Republic of Congo (DRC). The speculation was that HIV was brought upon by a traveler from Cameroon via river transport into the DRC [Joint United Nations Programme on HIV and AIDS] (UNAIDS), 2012). A decade later, the incidence of HIV skyrocketed in DRC's neighboring country of Uganda, while rapidly diffusing across countries in East Africa. The primary factors underlying the early diffusion of HIV were widespread rural-to-rural and rural-to-urban labor migration, the low social-status of women, the high-ratio of men to women in the cities and the availability of sex workers (Pepin, 2011; UNAIDS 2013). In the mid-1980s in East Africa, sex workers testing positive for HIV reached 36.7%; and disturbingly, when seroprevalence studies were conducted among pregnant women, HIV prevalence was 8.6% (Maticka-Tyndale, 2012). HIV epidemics however, were not observed in West African countries, such as Cameroon and Gabon where HIV was known to originate, probably because of the long distances and difficult travel between cities, which limited sexual networks such as those that fueled the spread of HIV in East Africa (UNAIDS, 2013).

In the late-1980s, there was a third shift in HIV diffusion, this time to countries in Southern Africa, including Botswana, Malawi, Zambia and Zimbabwe, where HIV epidemics were emerging (World Health Organization [WHO], 2011). Factors contributing to the southern diffusion of HIV included the in-migration of truck drivers' delivery goods into and across the region, high levels of unemployment and labor migration, such as miners to South Africa and other migrants, as well as soldiers (Renton, 2006; Reiners & Watkins, 2010) and finally, the culture of polygynous relationships and multiple concurrent partners increased local transmission (Levinsohn, 2011; Hanson, 2008; Mathers et al., 2008). In Southern

Africa, the sexual networks initiated by men were generally accepted, and even encouraged in some cultures. Women were more vulnerable to infection if sex was unprotected due to potential of tear and blood entry into her body. While condom use was the most effective mode of HIV transmission prevention, women were not able to insist on condom use by their male partners because of the subservient role of women, when making decisions in culture. Men dominated the sexual relationship and as a result, women could not always practice 'safe sex', even when they knew of the risks involved—a difficult cultural practice in terms of limiting HIV transmission, that continues to be observed today. The HIV epicenter of adult HIV prevalence in the world today is in Southern Africa, specifically the four neighboring countries: Eswatini (27.4 per 100 adults), Lesotho (23.8), Botswana (22.8) and South Africa (18.8) (UNAIDS, 2018).

In 2015 UNAIDS established the 90-90-90 "Treat All Strategy" to be achieved by 2030, where 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive antiretroviral therapy (ART) and 90% of all people receiving ART will experience viral suppression (UNAIDS, 2017) thereby, eliminating HIV transmission. Of the four countries with the highest HIV prevalence, Eswatini and Botswana have met their 90-90-90 programmatic goals (UNAIDS, 2019); however, both countries continue to have a substantial number of new infections and AIDS-related deaths. In 2018, Eswatini reported n=7,800 (incidence rate, 8.62 per 100 population) and Botswana n=8,500 (incidence rate, 4.36) new HIV infections. To assess if these new HIV cases are contributing to growing or shrinking HIV trends, the Incidence Prevalence Ratio (IPR) is used, with an IPR < 0.03 indicating the HIV epidemic is expected to decline (UNAIDS, 2019). In 2018 Eswatini, the IPR = 0.037 and Botswana, IPR = 0.022 suggestive that both countries can expect a decline in their HIV epidemics, with Botswana expected to decline slightly faster than Eswatini. Another indicator, the Incidence Mortality Ratio (IMR) identifies a point at which HIV related health care costs diminish, with an IMR < 1.0 (in a scenario of low mortality) indicating a decline in the HIV population, thereby, the ability to reduce the costs of ART

services. In Eswatini, the IMR = 3.25 (case-fatality rate = 11.4 deaths per 1,000 HIV infected individuals) and Botswana, IMR = 1.77 (case-fatality rate = 12.97). The case-fatality rates for Eswatini and Botswana are higher than that of South Africa (9.22) but lower than that of Lesotho (17.9), suggestive of the need to maintain health care costs that fund the "Treat All Program" into the near future. Excluding South Africa because of its high population, Botswana has the highest number of people living with HIV (n=370,000), which may be a reflection of surveillance and reaching its 90-90-90 targets. However, Botswana continues to have a high number of new infections and a relatively high number of AIDS–related deaths. For these reasons, Botswana is an extremely important country to study HIV beyond "Treat All Program" success; specifically, the population(s) that continue to transmit and acquire new infections, and the reasons behind this transmission—most importantly, ART treatment adherence. The findings from these investigations will help to build upon the country's "Treat All Program", to further reduce HIV transmission and AIDS-related deaths, while also promoting longer life expectancy and quality of life in Botswana.

First, more discussion is provided on the structural and physical drivers of the HIV epidemic in Southern Africa, while also providing a more in-depth understanding of those structures and physical drivers in Botswana.

1.1. SOCIO-DEMOGRAPHIC DRIVERS OF HIV IN SOUTHERN AFRICA

1.1.1. Culture

It has been documented widely in the literature that intergenerational sex and cultural roots are major drivers of the persistence of HIV particularly when Southern Africa became the AIDS belt (endemic) (Leclerc-Madlala 2008; MacPhail and Campbell 2001; Hunter 2007; Auerbach et al., 2011 and Yeboah 2007). Leclerc Madlala (2008) divides this concept of intergenerational sex in two ways: age disparate – i.e., men who are five years older than their female partners and intergenerational –i.e., men ten years older than their female partners. Throughout Southern Africa and Botswana, high HIV incidence have

been found among older men and young women. This is explained by the practices of intergenerational sex, where men with higher disposal incomes buy sex from younger women. In most cases these acts are not considered prostitution, because sometimes these relationships last months or longer. In the Botswana context, older men tend to have higher disposal incomes because they have established job experience, hence higher incomes and some men have investments such as cattle (described below), which are also a sign of wealth in this region. In these relationships, condom negotiation for young women is very rare because older men demand respect from women of younger age (Malema, 2012). Leclerc-Madlala (2008) argues that unlike in the literature that proposes women are driven into intergenerational sex because of poverty (Dow and Essex, 2010; Muula, 2008; Keetile, 2014; UNFPA, 2017; Pascoe et al., 2015). Leclerc-Madlala (2008) also indicates that "some girls wanted luxurious things such as cellphones and cars", which lead to believe that some women are not drawn into these acts because of lack of basic needs (Nkosana and Rosenthal, 2007). The young women, because of the cultural attitudes, beliefs and practices embedded in them –i.e., that the man is a provider, tend to be either in school or unemployed because they have reliable sources of income (Smith, 2002). There is also the tendency to blame the government for everything in Botswana (Malema, 2012). When graduates cannot find jobs, the government has to find paid internships for them. This in turn perpetuates the "give and take" situation where the people are the receivers of the government, in the same way as women are receivers in intergenerational sex (Cullen, 2006). Other studies from Zimbabwe which have marriage patterns comparable with many other parts of the region, found young married women with partners, who were 16 or more years older, were at three times greater risk of HIV infection than those with partners 0–15 years older than themselves (Schaefer et al., 2017).

Culture embedded in terms of social roles and wealth place a significant role in shaping the geographic patterns of HIV prevalence (Kandala et al., 2012). Mining towns and military camps are the landscapes of HIV in Botswana. It is in these places where HIV prevalence is as high as 43.0% (National AIDS Coordinating

Agency [NACA], 2015). In these mining towns, because of their remoteness, men tend to live by themselves, perhaps only checking on their families once a month. These men are also paid higher salaries because they have extra benefits such as housing allowance, and scarce skill and remote area allowance, and with this income and far from their families are willing to participate in sex with young women who are willing to travel to these places. As the case of Botswana, Corno and Walque (2012) found that in Lesotho and Eswatini, women married to miners were more likely to engage in extra-marital sex during their husbands' absence. Additionally, miners were less likely to use condoms, especially during extra-marital relationships (Corno and Walque, 2012).

1.1.2. Behaviors

Alcohol abuse is another driving factor for HIV in Botswana because there is no age drinking limit (Keetile, 2014). Young women who could be younger than 18 years, have access to bars where they can meet older men who will buy them drinks and later lead to unsafe sex because of the impaired ability to negotiate safe measures. The legal age for purchase and consumption of alcohol in Eswatini is 18 years (WHO, 2014). Even though the legal age limit is 18, young adults (less than legal age) still have access to alcohol and substance abuse in Eswatini. Use of alcohol and drugs appears most common in high school students and out-of-school youth. The latter who reported drinking alcohol, 58.9% do so daily or weekly (Swaziland Ministry of Sports, Culture, and Youth Affairs Report, 2015). As mentioned above in the case of Botswana, drinking impairs one's ability to negotiate safer sex measures. Status disclosure is a huge problem among HIV-infected pregnant women (as will be investigated in-depth in Chapter 3 of this dissertation). There are various reasons why many pregnant and new mothers do not disclose to their partners and families. In South Africa, 21.3% (n=80) of healthcare workers thought that HIV-infected individuals should not have children; 53.8% thought HIV-infected individuals were having too many children; and 46.3% thought that social grants were an incentive for HIV-infected women to have children (Mnyani and McIntyre, 2013). Some women were afraid of telling partners because they were accused of bringing the virus home (Visser

et al., 2008; Makin, 2010). In Botswana, most mothers were scared to disclose to families because they were afraid to be questioned about their lack of breastfeeding (Clark, 2006).

1.1.3. Poverty

It is also evident however, that one cannot fight HIV without also addressing poverty, socioeconomic inequality and the broader issues of economic development (Avalos et al., 2016). Poverty interplays a major role in sexual-risk vulnerability, and reluctance of people to seek protection from HIV as well as medical attention. Young women are often unemployed in Botswana, particularly after they finish their college education. The country' s rate of unemployment has dropped from 19.9% in 2011 to 17.6% in 2016 (IMF, 2016). However, unemployment for the youth aged between 18-35 years is estimated at 25.1% and among university degree holders at 11.4% (Statistics Botswana, 2016). As regards to gender comparison, the female unemployment rate is higher (19.1%) than that of their male counterparts (16.3%) (Statistics Botswana, 2016). The Botswana Multi Topic Household Survey of 2015/16 survey estimated youth aged between 15 and 35 years' unemployment at 25.2%, with female unemployment higher at 26.9% compared to 23.6% for males. Unemployment can drive young women to risky behaviors of transactional sex. The "Botswana Pilot Incidence Report of 2015" predicted that by 2016, the women who are less than 25 years and never married would account for the 55.0% of all the new HIV infections, while men of the same age ranges, as well as women older than 25 years would account for about a quarter of HIV incidence (Botswana Pilot Incidence Report, 2015). Unemployment in neighboring countries is very common particularly in Lesotho, where not only women are involved but young men who turn to being herd boys taking care of other people 's cattle. Herd boys are among the most disadvantaged young people in Lesotho. Poverty drives these young people to take up herding livestock as a full-time occupation, meaning many are deprived of formal education and lack access to health services, including HIV prevention, treatment and care (Lesotho Ministry of Health, 2015).

1.2. WEATHER AND CLIMATE IN BOTSWANA

Botswana is located in the subtropical high-pressure belt of the Southern Hemisphere in the interior of Southern Africa and away from oceanic influences (Kenabatho, 2016). There are 17 synoptic stations in Botswana, distributed in strategic places across the country, which record weather parameters (temperature, wind, humidity, pressure and rainfall). In addition, there are about 500 rainfall stations in the country that measure and record rainfall only. All the stations recorded warmer maximum temperatures for the period of 2015, than in the previous year 2014 (Statistics Botswana, 2016). The highest mean monthly maximum temperature of the period (April to September) was 34.9C for Shakawe (North) in September 2015, while the lowest was 21.2 C for Tsabong (Kgalagadi District) in June 2015 (Statistics Botswana, 2016). Precipitation patterns are highly variable, temperatures are consistently high and water resources are very scarce (Kenabatho, 2016). Drought is therefore, a recurring element of Botswana's climate (Government of Botswana, 2002). Drought is the most frequent natural hazard in Botswana; one in four years being a drought year.

As climate change increases the chances of droughts and dry spells in Southern Africa, the complex relationship between food security and HIV/AIDS can make matters worse for disaster management in two ways. First, the nutritional requirements of people living with HIV/AIDS are higher: up to 15.0% greater for protein and 50.0% greater for energy (Piwoz and Preble, 2000). Secondly, HIV/AIDS amplifies the effect of drought on nutrition (Mason et al., 2005). This creates a vicious circle: inability to provide adequate nutrition in times of drought weakens the immune system and increases susceptibility to opportunistic infections, such as tuberculosis, which in turn undermine the overall nutritional status of people experiencing this depravity in Botswana. In Botswana, it is believed that culture and climate/weather play important roles in HIV transmission and this research will further investigate these roles in Chapter 4 of this dissertation. The spatial variation of water availability in Botswana can increase the chances of HIV transmission among the northern (wet and rainy) and southern (hot and dry) regions

of the country. This mismatch can provide for a circular migration where those in the south who have limited water resources move to the northern part of the country, increasing the risk of HIV transmission. Once people have HIV it is important that they adhere to treatment regimes. The relationship between water scarcity, scorching temperatures and low treatment adherence is complex and may operate in several ways, including missing clinic appointments because of embarrassment by not being able to bathe, longer walk-times for water collection and missed appointments, scorching temperatures and unable to walk to the clinic, especially if the person is severely immune-compromised or pregnant or a new mother, conditions of which are highly vulnerable because walking becomes impossible in scorching temperatures. In poor remote areas, where air conditioning in health facilities is a luxury becomes an inhibiting factor of adherence among the vulnerable poor. Since the adoption of Millennium Development Goals [MDGs], especially the right to human health, there has been a steady increase in the provision of antiretroviral (ARV) therapy in Botswana and other affected regions around the world. Unfortunately, despite intense publicity campaigns to expand the global use of ARVs, a gap remains between the governmental roll out efforts (coverage) and those who actually have access or receive the medications. In particular, there are concerns with loss to follow-up rates, which have steadily increased among adults (NACA, 2015). There are also high treatment failure rates for adults (an increase in first line adult failure rate from less than 6.0% recorded in 2012, to over 10.0% in 2013) due to the challenges of adherence to counselling and monitoring (NACA, 2015). The ART coverage is also compromised by the low testing rate of 63.7% (according to Botswana AIDS Impact Survey [BAIS] IV of 2013) of the population aged 15- 49 years, who in the 12 months preceding the survey had a HIV test and received results (NACA, 2015). Adherence to ART is important for sustained HIV suppression, improved health and longevity and importantly from a public health perspective, reduced risk of drug resistance (Chesney, 2006; WHO, 2003). No research to my knowledge, has focused on how climate/weather extremes in Botswana, impacts ART and Prevention of Mother- to- Child Transmission [PMTCT] treatment adherence.

1.3. PURPOSE OF STUDY

The purpose of this research is to assess ART adherence levels in population(s) at risk of HIV transmission and to provide recommendations on how to improve adherence to ART and PMTCT treatment regimens for adult men and women, and pregnant women and new mothers living with HIV in Botswana. ART is a lifelong commitment whereas, the person should adhere completely in order to achieve viral suppression. A reduced viral load decreases significantly the risk to transmit new HIV infections. With this in mind, this study will examine three dimensions of ART and PMTCT non-adherence for people living with HIV in urban, peri-urban and rural areas of Botswana: To investigate the relationships between ART and PMTCT non-adherence and immunodeficiency at the individual-level, and socioeconomic, cultural and environmental factors, including health care services at the contextual-level; and to investigate the role of high ambient temperatures and water scarcity and rationing on ART and PMTCT adherence, for people living with HIV in Botswana.

The format of this dissertation will begin with a description of the biology of HIV, the states of HIV disease, routine diagnostic tests and ART and PMTCT treatment protocols. I will then discuss the status of and concerns around adherence to ART and PMTCT adherence to justify the need for this study. Following this Background Section, I will present in more detail the objectives that will be implemented to meet the goal of this research. Each objective will be presented in the format of a peer-reviewed paper, that will include the theory and conceptual framework, data and methods proposed for these studies and the results and conclusions. The final chapter of this dissertation will be a summary of the overall findings from these three investigations, and their policy and programmatic impacts. Finally, recommendations for future research to monitor ART and PMTCT adherence that will build upon the “Treat All Program” in Botswana, is provided.

1.4. BACKGROUND

1.4.1. Biology of HIV

Diseases are interruptions or disorders in body functions, systems or organs (Williams and Williams, 2005; Merrill, 2011). They can either be infectious or non–infectious, and the infectious diseases can be further classified as emerging and re-emerging diseases (ERIDs) (Margai, 2010; Merrill, 2011). Emerging infectious diseases are illnesses that have newly appeared among people or that have existed but are increasing in incidence and geographical space (Morse, 1995; Margai, 2010). HIV was appropriately classified as an emerging infectious disease that evolved into a pandemic epidemic following its discovery in the early 1980s. Today HIV is considered endemic due to its persistence in populations throughout the world, and most prominently in Southern Africa.

HIV is a retrovirus that occurs as two types: HIV-1 and HIV-2 (described below). Both types are transmitted through direct contact with HIV-infected body fluids, including blood transfusion, sexual contact, mother-to-child transmission during pregnancy, delivery and breast milk, and sharing needles contaminated with HIV. When HIV enters the body, the virus attaches itself to dendritic cells, usually found near the mouth, upper gastrointestinal tract, vagina and rectum (Centers for Disease Control and Prevention (CDC), 2015). The virus can infect many cells in the body, including brain cells but it mainly targets the T-lymphocytes or cluster of differentiation 4 [CD4] cells also referred to as helper cells. Unlike other viruses for which there are successful vaccines, HIV quickly integrates itself into the deoxyribonucleic acid [DNA] of the host cell, where, in some cells, it remains latent and essentially invisible to the immune system (Chun et al., 1998). Because latency is established very early -i.e. within days to weeks after infection, the window period in which HIV remains vulnerable to eradication through immune responses is very short (Chun et al., 1998). Once latency is established, it has not yet been possible to eradicate the virus, even in patients receiving highly active antiretroviral therapy (HAART) for extended periods of time (Chun et al., 1998). Instead treatment will be ongoing to reduce the viral load of a person over their life span with HIV.

HIV-1 is more common worldwide and in this study, the focus is on HIV-1, thus HIV herein refers to HIV-1. HIV-2 is found mostly in West Africa. HIV-2 is less easily transmitted than is HIV-1 (Pepin, 2011). The lower infectivity of HIV-2 is likely related to lower ribonucleic acid [RNA] levels. In addition, HIV-2 infection is characterized by higher CD4 cell counts and lower viral load. While HIV-2 can be transmitted from an infected mother to her child, the rate of transmission is lower than with HIV-1. Overall, without intervention 0-4% of breastfed infants become infected with HIV-2 if the mother is infected compared to more than 25.0% of transmission if the mother is infected with HIV-1. Furthermore, HIV-2 infection generally takes longer to progress to symptomatic and has a lower mortality rate than HIV-1 infection. There are rare instances where a person may be infected with both HIV-1 and HIV-2 (CDC, 2008).

1.4.2. Stages of HIV Disease

There are three stages in HIV infection. The acute HIV Infection is the first stage where within two to four weeks of being infected, a person, but not all, will develop "flu-like" symptoms because the virus is replicating at high amounts (UNAIDS, 2015). During this acute stage, an infected person is at risk of transmitting the virus because of the high viral load (Dow and Essex, 2010). With no AVR treatment, the infection moves to the second stage called, clinical latency (CDC, 2015). At this, stage, the virus is being produced at low levels and the person may appear asymptomatic for an average of 10 years. At this time, the CD4 count will begin to decline, while the viral load increases to the final stage known as AIDS (Acquired Immunodeficiency Syndrome). During this final stage, the immune system is damaged and the body becomes vulnerable to an array of opportunistic infections, most importantly but not limited to pneumonia and cancers (WHO, 2015).

1.4.3. Diagnostic Tests for HIV

The CD4 count is the number of CD4 T-lymphocyte cells in the blood, while the CD4 cells are the type of white blood cells that assist the immune system to fight infection (CDC, 2015). Viral load refers to the number of copies of HIV-1 RNA per milliliter of plasma in the blood and is measured using polymerase

chain reaction (PCR) testing (Mellors et al., 2007; CDC, 2008). This test can also be used to check the person's response to ART therapy. The CD4 count in a healthy immune system ranges from 500 to 1600 cells/mm3). When HIV actively multiplies, it infects and kills CD4 cells falling below 200 cells/mm3 with AIDS (WHO, 2015).

Generally, as the CD4 count decreases, the viral load increases, shortly after the person becomes infected with HIV. Although HIV ultimately resides within cells, the plasma measurement is an accurate reflection of the burden of infection and the magnitude of viral replication (Schacker et al., 1998). It is used to assess the risk of disease progression and can help guide initiation of therapy. The range of detectable virus differs somewhat with each test, but the lowest level of detection generally is 20-75 copies/ml (Egger et al., 2000). A viral load below this "undetectable" level indicates the inability of the test to detect HIV in the plasma, but does that there is an absence of HIV from the body (Hogg et al., 2001). The highest levels of detection of the viral load assays typically are between 500,000 copies/mL and 750,000 copies/mL (Palella et al., 2003). Viral loads higher than these levels are reported, for example, as >500,000 copies/ml. A high viral load leads to a higher transmission risk and can be a sign of more severe disease progression. People in this stage who are not on ARVs can survive an average of one to three years (UNAIDS, 2015). In Botswana, to my knowledge, the laboratory diagnostic limit is 400 copies/ml meaning that anything below 400 is considered suppressed viral load.

1.4.4. Treatment for HIV in Botswana

First and second line ART regimens for new non-pregnant adult/adolescent patients included taking about three pills a day that were: tenofovir (TDF) + femtricitabine (FTC) (or 3TC) + efavirenz (EFV) or nevirapine (NVP), according to the woman's reproductive potential, while the second line included: zidovudine (AZT) + 3TC + LPV/r (MoH, 2008). This was an era where the CD4 count threshold was <250 copies/ml. Prior to 2012, Botswana provided ART to all adults with CD4 counts ≤ 350 cells /µL. (MoHW Botswana, 2012). After 2012, a fixed dose combination of Atripla –combination of tenofovir (TDF) TDF/emtricitabine (FTC)

or 3TC/ efavirenz (EFV) was implemented for all patients regardless of their CD4 count and/or reproductive status (MoHW Botswana, 2015). Atripla is one pill that contains these three medications, given daily with a low toxicity level.

1.4.5. PMTCT Treatment

HIV positive women on ART who are considering to become pregnant minimize the risk of a negative pregnancy outcome, and it is recommended that the following conditions are met prior to becoming pregnant (i) viral load suppression of less than 400 copies/mL (ii) CD4 count above 200 cell/µL and (iii) stable on ART for no less than 2 years. In 2008, Botswana treatment guidelines recommended that tenofovir (TDF) should be avoided in pregnancy, and zidovudine (AZT)-based ART used instead. If AZT cannot be used, for instance due to anemia, then stavudine (d4T) should be used instead, but after delivery, d4T should be changed to TDF (MoH, 2008). In 2012, If her CD4 was less than 350 she will be initiated on ART for her own health benefit. But if the CD4 is above 350 she will be taking ART for prophylaxis reason to transmission risks to the infant. In 2014, in accordance to Botswana 's national Vision 2016 Policy's pillar of having an AIDS free generation, Triple ART Prophylaxis (TAP) was provided to all pregnant women living with HIV (MoHW, 2015). In 2016, recommendations were that all HIV positive ART naïve pregnant women be placed on ART for themselves and their baby's welfare (PMTCT) as soon as possible. In addition, it is recommended that during labor, all HIV positive women regardless of their ART regimens, should receive supplemental AZT (zidovudine) 300 mg every three hours not to exceed 1,500 mg (MoHW, 2016).

1.4.6. ARV Uptake and Adherence in Botswana

Botswana was one of the first countries to take advantage of the MDG Goal's initiative to offer free ARV therapy to all infected citizens. Importantly, Botswana has a second higher percentage of HIV infected people taking ART (84.6%), (Free ART launched in 2002) compared to Eswatini (86.0%) (2003), Lesotho (74.0%) (2004) and South Africa (61.0%) (2004) (UNAIDS, 2018). However, the country continues to be

challenged by the epidemic despite an intensive and aggressive HIV/AIDS prevention campaign (NACA, 2012). In 2000, Botswana went into a public–private partnership with the African Comprehensive HIV/AIDS Partnerships (ACHAP), a non-governmental organization formed by the Bill & Melinda Gates Foundation and The Merck Company Foundation/Merck & Co., Inc. to make ARV therapy free and universal (MOH 2005; Bene and Darkoh, 2014; Farahani et al., 2013). As part of this partnership, both Bill and Melinda Gates and the Merck Company Foundation contributed US$50 million each, while Merck & Co., Inc., pledged to donate two types of ARV medicines free of charge for the duration of the partnership (MOH, 2005). 'Masa programme', which is the brand name for the national ARV programme (Bene and Darkoh, 2014). The name of the national ARV Programme, 'Masa', which means 'new Dawn' in Setswana, 'signifies the hope to live longer, healthier lives by providing them with time to nurture their families and build a future for the nation' (Government of Botswana, 2006:3).

In order to sustain this programme, there are HIV policies in place that spearhead the financial allocation towards HIV prevention in Botswana. The latest financial year of 2016, saw only 10.0% of the financial resources going towards HIV prevention while 73.0% went to PMTCT (Avalos et al., 2016). The government of Botswana is the major sponsor for all HIV/AIDS programs today in the country at 64.4% (this was 2.4% of the total government spending in 2015) (MoHW, 2016). Bilateral and multilateral donors were second at 31.0% while the private sector contributed 4.6% towards funding HIV/AIDS programs in Botswana (Avalos et al., 2016). In June 2016, Botswana launched a "Treat All" Strategy where all people living with HIV regardless of their CD4 count were enrolled. While local programs were underway, the CD4 350 was still in place. For a 15-year period of 2015-2030, adopting a comprehensive "Treat All" Strategy, Botswana hopes to become one of the first countries in the world to achieve HIV epidemiological control by 2020 (MoHW, 2016). To track patients people living with HIV for ART and monitor the progress as well as the effectiveness of the programme, the government of Botswana supported by the United States President's Emergency Plan for AIDS Relief (PEPFAR) established a monitoring and evaluation unit within the national

ART programme in the Department of HIV/AIDS Prevention and Care in the Ministry of Health (Farahani et al., 2013). The electronic patient tracking and outcome monitoring captures individual level patient data and the system is able to generate facility level reports that assist in both clinic management and patients care (Farahani et al., 2013).

Although the ART program has done well since inception, there are concerns with loss to follow-up rates which have steadily increased among adults. Among the challenges encountered with growing numbers has been less time for one-on-one counselling of patients and intensive follow up through community channels for those who fail to honor clinic appointments (MoHW, 2017). There were also high treatment failure rates for adults (an increase in first line adult failure rate from less than 6.0% recorded in 2012 to over 10.0% in 2013) due to the challenges of adherence to counselling and monitoring (NACA, 2015). Adherence on ART is important for sustained HIV suppression, improved health and reduced risk of drug resistance (Chesney, 2006; WHO, 2003). Patients on ARVs are able to maintain consistent adherence levels that can result in viral suppression, increased CD4 counts and improved quality of life and survival. On the other hand, poor adherence from the initial and periodic lapses in adherence may lead to emergence of drug resistance and loss of future treatment options (Thompson et al., 2012). Adherence drug resistance is not the only cause of treatment failure. The natural history of HIV infection is very unpredictable and people respond to treatment regimes in different ways (O'Brien et al., 2000; WHO, 2006). If people are sharing ARVs or skipping their daily dosage regimes (sub-optimal adherence) their immune system becomes compromised and this can lead to drug-resistance and treatment failure (WHO, 2006). A patient's adherence to ART is influenced by number of factors including prescribed regimen, patient-provider relationship, patients' social situation and clinical condition (Schneider et al., 2004). It is also vital that each patient receives and fully understands information about HIV disease and the goals of the therapy. The aim of ART involves achieving and maintaining viral suppression; decreasing HIV related mortality and preventing sexual transmission. However, education alone is not enough to assure high

levels of adherence because non-adherence is often a consequence of behavioral, structural and psychosocial barriers (Halkitis et al., 2005). Patients must also be positively motivated when initiated to maintain therapy.

1.4.7. PMTCT Uptake and Adherence in Botswana

Despite the availability of effective interventions, most children were infected through vertical transmission in Southern Africa (Drobac et al., 2008). Without any intervention, about 30% of babies born to HIV infected mothers will be infected (Drobac et al., 2008). In 2007, a third of pregnant women were living with HIV and almost all of them were receiving antenatal care and delivery in a health facility in Botswana (MOH, 2008). PMTCT services were introduced in Botswana in 1999, but by 2003, the program uptake was still only at 30.0%. There was an evident dramatic increase of 55.0% in 2007 and mother to child transmission dropped to under 4.0% (Drobac et al., 2008). In 2014, in accordance to Botswana 's national Vision 2016 Policy's pillar of having an AIDS free generation, Triple ART Prophylaxis (TAP) was provided to all pregnant women living with HIV (MoHW, 2015). Due to this, mother to child transmission rates are expected to fall below 1.0% every year (MoHW, 2015). The risk of mother-to-child transmission can be significantly reduced by providing antiretroviral medicine (as lifelong therapy (ARV) or as prophylaxis) for the mother during pregnancy, labor and delivery, with antiretroviral prophylaxis for the infant, and antiretroviral drug to the mother or child during breastfeeding (if breastfeeding), and use of safe delivery practices and safer infant feeding (Drobac et al., 2008).

By the year 2014, the PMTCT programme was available in all the 634 health facilities that provide maternal child health services in Botswana (MoHW, 2015). The percentage of pregnant women who were tested for HIV and received their results (during pregnancy, during labor and delivery, and during the post-partum period, including those with previously known HIV status) was 94.3% in 2014, a decrease of 5.0% for 2013. However, male involvement remained low at 18.0% in 2014 a slight increase from 11.0% in 2011. In 2016, the number increased to 97.0% of new antenatal care (ANC) attendees who underwent an HIV

test. Of these, 26.0% of women who delivered during this 2.0% (n=51) also took both ZDV and NVP, while 869 (30.0%) were on Triple ART Prophylaxis (TAP), giving an uptake of 95.0% in 2016. In 2017, women testing remained at 97.0%, HIV positive number slightly decreased to 25.0% (n=3,171 of 12, 512), male testing increased to 21.0%, PMTCT uptake remained at 95.0% and 96.0% of infants born to HIV positive women were started on nevirapine [NVP] (MoHW, 2017).

Although, the PMTCT program has done very well in Botswana, there are some challenges that need to be addressed in order to eliminate the vertical HIV infections. Challenges include low testing (46.0%) for children from six weeks to two months as reported in BAIS IV of 2013 due to poor turnaround times at the level of the laboratory (BAIS IV, 2013) as well as low male partner testing (21.0%) in 2017 (MoHW, 2017). PMTCT is a comprehensive therapy which means that other than the drugs provided for the woman, there is prophylaxis for HIV exposed children, periodic HIV testing to monitor the baby as well as partner testing and counselling. While the percentage of these babies who will ultimately receive their results improves over time, the purpose of early infant diagnosis and subsequently early treatment is lost for those who do not receive their results in time. Most of the health departments in Botswana also tend to work separately to achieve the same goal of HIV elimination in newborns. This is indicated by the poor integration of services such as routine HIV testing, ART, Tuberculosis (TB) and Sexual Reproductive Health (SRH) (NACA, 2015).

Finally, in relation to ARV non-adherence to expand on the discussion above, people living with HIV were more likely to miss their hospital due to high temperatures and rare heavy rainfalls particularly in poorer ones who rely on walking. Rare heavy rains (and the fact that they are usually accompanied by lightning) in Botswana usually impact the network services as well as the availability of electricity. Health workers rely on electricity to store patients results on computers and fridges that store blood results. If there is no electricity available, usually the work of the day stops, patients are sent home without their results and this can discourage them even them further. There are few public health facilities that have reliable power

back up. High temperatures as much as heavy rainfall, impact ART access and adherence negatively. People living with HIV particularly with low CD4 counts, pregnant women and new mothers are highly vulnerable because walking makes it impossible in scotching temperatures. In poorer areas such as rural areas, where air conditioning in health facilities is a luxury becomes even a promoting factor to non-adherence among the vulnerable poor.

1.4.8. Gaps in the Literature

Unlike many African countries, where government programs have not been aggressive, the government of Botswana is working extremely hard to combat HIV/AIDS. HIV prevention methods and messages are everywhere, and news about the epidemic are the daily bread of newspapers, radio and television (Epstein and Ashburn, 2004). Free condoms are found in every corner of the country in remote clinics, bars and schools. Botswana was the first African country to offer ARVs to its citizens in 2002. Despite these efforts, the HIV epidemic in Botswana continues to be high. According to Green (2004), Botswana like many African governments relies on western donors who spend a lot of money on promoting condoms, but put little emphasis on advising people to be faithful to their sexual partners (Green, 2004). Botswana is known historically as a culture of seasonal migrants where both men and women often spent time away from their homes and may be involved in long term relationships with different people in different places. Cattle in Botswana are valuable as they are the traditional form of wealth and are kept in remote cattle posts. Only boys and men are responsible for taking care of them, this means that from time to time, they leave their partners behind to check on them. It is common in the country that most people do not use condoms regularly, but only with commercial sex workers and casual partners locally known as “small houses”. In long term relationships, most people use the condoms in the early settings encounters but later abandon them as a gesture of trust. These are the risky relationships because one partner can be committed in another relation with someone else. Hesselberg and Iversen (2011) term the basic cause of the HIV epidemic as multilocal nature of families and partners. In recent years, urban labor migration has

become so common in the country where people move away from rural areas in search of jobs. This rural-urban circulation particularly of young men play a significant role of widespread sexual connectivity which is a major risk of HIV (Hesselberg and Iversen, 2011). The relationship between HIV and climate is a complex one because vulnerability is involved. Vulnerability (Drimie and Casale, 2009; Chambers, 1989; Chambers, 1992) has two aspects which are external (stresses that people are subjected to) and internal (their capacity to cope with those stressors).

While previous studies have begun to document the drivers of HIV in Botswana (Bene and Darkoh, 2012 and 2014; Bene, 2014), including the increase in uptake of ART in peri-villages, however, the variation in HIV prevalence, ART/PMTCT uptake and adherence at the local level in Botswana is unknown. Examining the rate of adherence (which entails whether the patients are following the medical instructions) is a key piece of this study. Boonstra and colleagues (2002) categorizes adherence into two: full or acceptable adherence. The former means that the clients are taking their pills/drugs without any failure, while the latter means patients take their drugs, but they sometimes miss the doses for a variety of reasons and circumstances. How well patients adhere to the ARVs is influenced by many factors, including the doctor-patient relationship, acceptability, family support, religion, climate parameters such as ambient temperatures and water scarcity as well as the availability of food. The goals of the therapy are to increase CD4 count and reduce the viral load, therefore adherence is important. Studies have shown that ART/PMTCT can play an important role in preventing HIV transmission (Beaten et al., 2011; Sheth et al., 2009, Graham et al., 2007). Lower levels and decreased concentration of HIV have been seen on patients' genital secretions that are on ART therapy (CDC, 2015). Research have illustrated that increased use of ARVs also lead to reduced rates of new HIV diagnoses; HIV transmission is now considered low when an individual's viral load is below 400 copies/ml (CDC, 2009). Assessment of the factors inhibiting full adherence can assist health providers in addressing potential barriers to adherence. Little is known on the relationship between environmental factors such as high temperatures, water rationing and ART in Africa

as well as Botswana. The study results will fill an existing gap in the literature on climate and ART/PMTCT uptake. Also, in an era where treatment is used as prevention, more investigation is important to understand HIV disease progression as there are cases of patients who enrolled later in the ART program. This study will contribute to this important epidemiological transition of HIV life course. The Ministry of Health and Wellness [MoHW] in Botswana will benefit from these results and recommendations on how to address the disparities and adherence in the ART/PMTCT uptake. The study also serves as a useful reference for other regions as well as contributes to the emerging literature on climate and ART/PMTCT adherence, especially in the African context.

1.5. STUDY GOAL

The goal of this research is to provide recommendations on how to improve adherence to ART and PMTCT treatment regimens for adult men and women, and pregnant women and new mothers living with HIV in Botswana. With this in mind, this study will examine three dimensions of ART and PMTCT non-adherence for adults living with HIV in urban, peri-villages and rural areas of Botswana:

1.5.1. Objective 1

To investigate the life-course of HIV infected women and men from HIV diagnosis to newly-initiated ART and subsequent barriers to ART adherence in Greater Gaborone, Botswana.

1.5.1.1. Research Questions

RQ1: In terms of life course, what is the length of time between HIV diagnosis and ARV initiation?

RQ2: What are the levels of ART non-adherence for adult women and men living with HIV and do these levels vary by age, and other socio-demographic characteristics?

RQ3: How does length of time between HIV diagnosis and ARV initiation impact ART non-adherence?

1.5.2. Objective 2

To investigate barriers to PMTCT adherence and their potential impact(s) on immunodeficiency (as a reflection on HIV transmission) for pregnant women and new mothers in Greater Gaborone, Botswana.

1.5.2.1. Research Questions

RQ1: What is the level of ART non-adherence for pregnant and post-partum women (mothers) and all other women?

RQ2: How does marital status vary for partners with HIV and/or mothers who do not disclose their own HIV status?

RQ3: From their perspectives, what are the reasons for non-disclosure among pregnant and post-partum women (mothers)?

1.5.3. Objective 3

To investigate the role of environmental factors (high temperatures and water scarcity and rationing) on ART and PMTCT non-adherence, for adults living with HIV in Greater Gaborone, Botswana.

1.5.3.1. Research Questions

RQ1: Do environmental factors such as heat, water scarcity and rationing impact ART adherence for women and men living with HIV?

RQ2: Do environmental variables such as heat, water scarcity and rationing impact ART clinic attendance?

RQ3: Are environmental factors barrier(s) to PMTCT adherence for mothers in particular?

The first study (Objective 1) is outlined in Chapter 2; followed by the second and third studies (Objectives 2 and 3) in Chapters 3 and 4.

CHAPTER 2: Antiretroviral Therapy (ART) Adherence among HIV Infected Adults: A Health Geographic Study in Greater Gaborone, Botswana

2.0. INTRODUCTION

In 2018, an estimated 36.4 million (range, 31.4 to 42.3) people worldwide were infected with the Human Immunodeficiency Virus (HIV), prevalence rate = 0.8 per 100 population (United Nations Joint Programme on AIDS (UNAIDS), 2019). Of these, approximately 1.7 million (range 1.4 to 2.3) were new HIV infections, incidence rate = 0.39 per 1,000 population (UNAIDS 2019). Worldwide, a majority of new infections occurred in the United Nation's region of East and Southern Africa, n=800,000 (incidence rate, 3.2 per 1,000 population) (UNAIDS, 2019). In 2015, the World Health Organization (WHO) implemented the "Treat All Program", a 90–90–90 target treatment strategy for 2030, whereby 90% of people living with HIV know their HIV status, 90% of people who know their HIV-positive status receive antiretroviral treatment (ART) (also referred to as ART uptake) and 90% of people on ART achieve a suppressed or non-detectable HIV viral load (UNAIDS, 2019). The premise of the program is, as ART uptake increases, the viral load of people living with HIV will decrease, thereby reducing person-to-person transmission and the elimination of new HIV infections. In East and Southern Africa, there are approximately 20.6 million people living with HIV. Of these, n=13,764,070 (68.0%) people receive ART, and 58.0% of those on ART have a suppressed viral load (UNAIDS, 2019). These findings demonstrate substantial progress toward achieving the "Treat All Program" goals in East and Southern Africa; and additional focused efforts are warranted.

Within the East and Southern Africa region, are four countries with the highest adult (15-49 years) HIV prevalence in the world (2018)—Eswatini, n=210,000 (rate, 27.3 per 100), Lesotho, n=340,000 (23.6), Botswana, n=370,000 (20.3) and South Africa, n=7.7 million (20.4) (UNAIDS, 2019). Of these, South Africa has the greatest number of people living with HIV followed by Botswana. Eswatini introduced free antiretroviral drugs (ARVs) in 2003, thereafter South Africa and Lesotho initiated treatment in 2004 (WHO,

2005). Botswana was the first African country to provide free ARVs in 2002, yet remains one of the countries most affected by HIV in the world (UNAIDS, 2019); and is therefore, the focus of this study.

HIV originated in Botswana in 1980. Although ARVs were free after 2002, employees of the mining industry and their family members, and people with other positions of higher income were most likely to receive HIV treatment. In 2010, the WHO introduced the CD4 blood count to ascertain among those HIV infected, who should receive ART. It was recommended that HIV infected persons with a CD4 count of 350cells/mm^3 or less receive access to ART (WHO, 2013). In 2013, those guidelines were increased to CD4 count of 500 cells/mm^3 or less to ensure a greater number of HIV infected people receive treatment (WHO, 2013; 2016). In 2012, Botswana adopted the 2010 recommendation of CD4 count of 350 cells/mm^3 or less as a guide by which to offer ART but did not adopt the subsequent 2013 guidelines (BIAS IV, 2013). Instead in 2016, Botswana implemented the "Treat All Program" to include universal access to ART regardless of the CD4 count (UNAIDS, 2017). In June 2016, this program was officially launched and while some ART facilities are still using the CD4 count 350 criteria, the roll-out of universal access to ART continues. Recently the viral load was added in conjunction with the CD4 count to evaluate treatment effectiveness.

According to the UNAIDS (2018) Botswana is on target to achieve its "Treat All Program" goals with an estimated 91.0% of people with HIV who know their HIV status, 92.0% of those who know their HIV positive status, receive ARVs and of those taking ARVs, over 95.0% have achieved viral suppression (UNAIDS, 2019). Despite this success, in 2018 there were n=8,500 new HIV infections in Botswana. Importantly, these new infections varied by gender and age with females disproportionally affected (n=4,500) compared to men (n=3,700). Adolescent and young adult females were twice as likely as males to acquire a new HIV infection. In contrast, adult men (25-49 years) were 1.5 times more likely than adult women to be newly diagnosed with HIV. Furthermore, approximately, 25.0% of new infections were late diagnoses (CD4 count < 200 cells/mm^2) (UNAIDS, 2019). There is a need therefore, to further understand

treatment and the life-course of HIV infected women and men in Botswana. Finally, in 2017, only n=849 adults 15+ years were newly-initiated on ART (UNAIDS, 2019), which may account for less than 10.0% of new HIV infections that year (UNAIDS, 2019). To reduce viral load and ultimately eliminate HIV transmission among newly infected adolescents, young adults and adult women and men, and people currently living with HIV, it will be important to ensure ART access and optimize ARV adherence.

2.1. GOAL OF THE STUDY

The goal of this research is to investigate the life-course of HIV infected women and men from HIV diagnosis to newly-initiated ART and subsequent barriers to ART adherence. A survey was conducted during the winter in Botswana (May to August, 2016) among a sample of adult (n=667) women (n=428) and men (n=239) living with HIV, and also enrolled in ART treatment at 21 government clinics, in urban, peri-urban and rural areas of Greater Gaborone. The findings from this study are used to inform the "Treat All" programmatic goals in Botswana.

2.2. BACKGROUND

2.2.1. HIV Life-Course

There are three stages of HIV infection (CDC, 2019) Stage 1 or acute HIV infection occurs within two to four weeks following exposure. People may experience flu-like symptoms as their viral load increases, and at this stage they are very contagious. Stage 2 or clinical latency stage, is when HIV infection becomes chronic, reproducing at lower levels. People are asymptomatic for up to a decade, during which time HIV transmission can still occur. If ART is initiated early in Stage 2 people living with HIV may lead productive lives, and often die of common chronic diseases. However, if people are not started on ART or poorly adhere to ARV treatment, the progression of disease may occur more rapidly as evidence by dropping CD4 count or increase in viral load. Under these conditions, people living with HIV may acquire opportunistic infections, and move into Stage 3 also referred to as AIDS (Acquired Immunodeficiency Syndrome). Without ARVs, people living with AIDS may survive about three years. An AIDS diagnosis is made when

their CD4 count drops below 200 cells/mm^2 or if they develop opportunistic infections including cancers, such as Kaposi's sarcoma and lymphoma, tuberculosis and pneumonia. Late initiation of ARVs or late HIV diagnosis occurs when the CD4 count drops below 200 cells/mm^2 (UNAIDS, 2019), generally during the later period of Stage 2 or Stage 3 of HIV infection. Adherence to ARVs across the life-course of people living with HIV, is therefore paramount for individual's life longevity and prolonged survival, in addition to the elimination of HIV transmission—a public health priority.

2.2.2. ART Adherence

Adherence is defined as "the extent to which patients follow the medication instructions prescribed" (Haynes et al., 2005) and the "medication must be appropriately prescribed, filled, initiated, continued, and taken as intended and failure at one or more of these junctures will have consequences for patients' health" (Rand 1993). The WHO adapted these definitions of long-term adherence to include "the extent to which a person's behavior–taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" (WHO, 2003).

Adherence is expressed quantitatively as "the number of people who routinely take their ARV medications divided by all people prescribed treatment" (WHO, 2006), which in practicality is a difficult measure and hence, there is no gold standard for adherence measurement. ARV adherence in a population is thus, generally estimated using indirect measures (DiMatteo, 2004) including pill counts, pharmacy refill records, electronic drug monitors, self-reporting tools—questionnaires and visual analogue scales and biomonitoring measurements (Golin et al., 2002; Paterson et al., 2000; Bangsberg et al., 2000; WHO, 2006). These indirect methods of monitoring adherence are briefly described below followed by studies demonstrating their successes and failures.

Pill Count: is a measure of adherence calculated by counting the remaining doses, assuming the remaining pills in excess represent missed doses (Golin et al., 2002; Bangsberg et al., 2000; NcNabb et al., 2001). Pill

counting is commonly conducted in clinics or unannounced home visits and is relatively easy to implement with cooperative patients.

Pharmacy Refill Records: ARVs are generally prescribed following each month's clinic visit, thus if a refill is not obtained, it is assumed that the patient is not taking their medication (Turner, 2002; Steiner and Prochazka, 1997; Maher et al., 1999). Studies (Hogg et al., 2002; Low-Beer et al., 2000; Wood et al., 2002) have shown that pharmacy refill measures that can be used in the evaluation of viral suppression, ARV resistance, and progression to AIDS and death). When n=291 young adults on ARVs were studied in Gaborone, and the main outcome measure was treatment failure (defined as two consecutive HIV viral load measurements ≥400 copies/mL during 24-months of follow-up) (Genn et al., 2018). Pharmacy refill non-adherence was defined as two consecutive refill adherence measurements <95.0% during the same period. Authors found that 53 (18.0%) experienced treatment failure and 128 (44.0%) had refill non-adherence (Genn et al., 2018).

Pill counts and pharmacy refill measures are often used together to measure ART adherence. A study in Gaborone (Ndubuka and Ehlers, 2011) sought to understand whether pill counts and pharmacy refill records could predict immunological and viral responses, through increased CD4 cell count and suppressed viral load, for patients taking ARVs. Pill counts were calculated by dividing the number of pills actually taken by the total number of prescribed ARV pills expected to be taken over a 30-day period and expressed as a percentage (Ndubuka and Ehlers, 2011). The remaining pills in excess of what was expected were considered as missed doses on a monthly basis. To calculate pharmacy refill, exact dates when ARVs were collected from the pharmacy were compared with the expected refill dates and the exact number of days of being late for pharmacy refills was recorded (Ndubuka and Ehlers, 2011). Adherence was defined as a composite adherence rate equal to or higher than 95% while levels of adherence 94.9% and lower were considered non-adherent. The mean adherence rates were 95.9% for the pharmacy refill and

96.4% for the pill count, providing a mean composite adherence rate of 96.2% (Ndubuka and Ehlers, 2011). Patients who were ART adherent, as measured by consistent pharmacy refills for greater than four months, were significantly more likely to achieve viral load suppression and benefit immunologically, than were less-adherent patients (Ndubuka and Ehlers, 2011). Pharmacy refills and pill counts adherence measurements were shown to be reliable methodologies (Ndubuka and Ehlers, 2011) by which to monitor ARV adherence.

Electronic Drug Monitors: The Medication Event Monitoring System (MEMS) uses a computer chip embedded in a specially designed pill-bottle cap to record the time and duration of each bottle opening. MEMS adherence is calculated by dividing the number of observed bottle openings, by the number of expected doses over the study period (NcNabb et al., 2001; Arnsten et al., 2001). Wisepill, a wireless pill container transmits a cellular signal when opened. In their study, Haberer and colleagues (2010) found that when adherence levels were measured by Wisepill, compared with unannounced pill counts, self-reports, and HIV RNA (Haberer et al., 2010), real-time adherence monitoring was found to be feasible for resource-limited settings and may detect sub-optimal adherence prior to viral rebound (Haberer et al., 2010).

Self-Reporting Tools: Self-reporting based on four-day recall appears to be the best indicator to monitor the viral load (Ferradini et al., 2006). Four-day recall adherence measures the number of tablets taken correctly as a proportion of those prescribed (Ferradini et al., 2006). Another self-reporting tool is the visual analogue scale, -i.e., the percentage of patients taking at least 95% of their tablets correctly. Both methods have been shown to aide both program and public health evaluation (Ferradini et al., 2006).

Ferradini et al. (2006) found the average population adherence rate to be 85.0% but only 60.0% achieved the optimal the adherence rate (Ferradini et al., 2006). The authors concluded that having both self-reporting tools are ideal to verify the results (Ferradini et al., 2006). Nance and colleagues (2016) validated

what authors in Malawi proposed of using both measures in a study for reliability (Ferradini et al., 2006; Nance et al., 2016). Other studies (Arnsten et al.,2001; Paterson et al., 2000; Golin et al., 2002)) have found that a single low, untimed antiretroviral drug level was sensitive in identifying those with very poor adherence (<60.0%), but therapeutic drug levels were not necessarily indicative of good adherence (Liechty et al., 2004). Plasma concentrations are limited by their ability to detect only recent adherence behavior (Machtinger and Bangsberg, 2006.)

Biological Markers: Biological markers include plasma concentrations of ARVs (Machtinger and Bangsberg, 2006). Plasma concentrations of a protease inhibitor is a class of ARVs that block protease (an HIV enzyme) to prevent new (immature) HIV from becoming a mature virus, that can infect other CD4 cells (Dandache et al., 2007). Biological markers are significantly associated with adherence behavior. Furthermore, low concentrations of antiretroviral drugs also may be caused by factors other than adherence, such as malabsorption, drug interactions, and individual metabolic differences (Machtinger and Bangsberg, 2006.) Other studies have been conducted where antiretroviral concentrations in hair samples were evaluated as a marker for antiretroviral exposure and, less directly, long-term adherence (Bernard et al., 2002; Gandhi and Greenblatt, 2002).

An ART adherence rate of at least 95.0% will prevent treatment failure and/or drug-resistance (Chesney et al., 2000; Rabound et al., 2011). Poor adherence to ARVs will not fully suppress viral replication (Rabound et al., 2011) which in turn may mutate making the drugs no longer effective (Center for Disease Control [CDC], 2017). If resistance occurs, different medications are used ones to target the virus (CDC, 2017). Resistance is especially difficult to manage in resource-limited settings, where there are fewer choices for ARV medicines (CDC, 2017). This is particularly true for African countries, already burdened with high HIV prevalence, low staff personnel, budget cuts and insufficient of ARV supply. ARV adherence is thus, critical to reduce viral load and the elimination of HIV transmission. People living with HIV who

have a low viral load also have a stronger immune system, fewer illnesses, and can lead a healthier life, thereby, improving overall population health.

2.2.3. Barriers to ARV Adherence

Studies that investigate barriers to ART adherence generally fall into three areas: patient-centered barriers, social-structural barriers, and service-centered barriers.

Patient-Centered Barriers include age greater than 35 years and single (Peltzer et al., 2011) and divorced (Birbeck et al., 2011) marital status, low education (Charurat et al., 2010; Peltzer et al., 2011; Birbeck et al., 2011), low health literacy, inadequate knowledge about HIV, its treatment and how to interpret laboratory results, forgetting or being too busy, being away from home, or a change in daily routine, side-effects to the ARVs (Birbeck et al., 2011), alcohol abuse, depression or other illness, and the use of other medicines (Kip et al., 2009) and lack of interest or desire to take a "drug holiday" (Chesney, 2000). Studies have indicated that patients with chronic co-morbidities, such as diabetes and hypertension take their ARVs only about 70.0% of the time (Hashmi, 2007 (77% adherence); Martin, 2005 (69.8%); Brown, 2011 (75%); Charurat et al., 2010 (70.4%)). Generally, ARV adherence is better in urban compared to rural areas (Peltzer et al., 2011).

Social-Structural Barriers include non-disclosure of HIV status and stigmas (Weiser et al., 2003; Birbeck et al., 2011), low levels of social support (Yang et al., 2018), high-unemployment (Charurat et al., 2010), food insecurity, religious rituals such as fasting and poverty (Bezabhe et al., 2014). Stigmas surrounding HIV are particularly important. Weiser et al. (2003) found in Gaborone and Francistown clinics (n=3), Botswana that 69.0% of patients kept their HIV status a secret from families and 94.0% from their community; and 32.0% of patients feared that they could lose their job if their HIV status was known, and 15.0% reported that stigma interfered with the ability to adhere to medication. Another study by Thupayagale-Tshweneagae (2010) in urban Botswana found that young adults would keep silent about

their HIV status, but sought treatment for other conditions (such as flu) to avoid being stigmatized. Furthermore, young adults were concerned with begging forced to reveal their HIV status when pregnant, divorced or assaulted to further avoid being stigmatized.

Service-Centered Barriers to non-adherence, include lack of transport and travelling costs, longer travel to the clinic, health workers' inability to conduct home visits and to contact defaulters, limited clinic operational hours, waiting times at clinics, nurses' attitudes and knowledge, poor laboratory services including, delays in getting HIV testing results and insufficient supply of medications (Bezabhe et al., 2014; Birbeck et al., 2011; Kip et al., 2009; Halkitis et al., 2005; Stirratt et al., 2006; Carr and Gramling, 2004). In contrast, ARV adherence increased if people living with HIV lived < 2 hours from the clinic (Charurat et al., 2010), when provider-patient spoke the same language, when patient education and counselling were provided and dose-frequency was simplified (Orrell et al., 2003; Bezabhe et al., 2014).

While patient-related and service-centered barriers are more tangible to address, there are virtually no offered solutions other than education to *social-structural barriers* to improve ART adherence and will therefore, be a focus in this study.

2.3. THEORETICAL PERSPECTIVE

This study adopts the Theory of Planned Behavior (TPB) within a framework of Intergenerational Relationships. Intergenerational relationships are termed as "relations between men and women, where there is a 10-year or more age disparity between partners" (Leclerc-Madlala, 2008). Intergenerational relationships on its own is not a theory, but gender ideology particularly in Africa. It is well suited under the framework of the Theory of Planned Behavior (TPB). TPB is a psychological conceptual framework that explains human action (Ajzen, 2001). The theory was derived from the theory of reasoned action (Fishbein and Ajzen, 1975) that assumed that most human social behavior can be predicted from intentions alone (Ajzen, 2001). The new addition here is the component of perceived behavioral control, which is people's perception of the ease or difficulty of performing the behavior of interest (Ajzen, 1991;

2002). Theory of planned behavior explains that human behavior is guided by (a) beliefs about likely consequences and attributes of behavior (behavioral beliefs), (b) normative expectation of other people (normative beliefs) and the (c) presence of factors that may further or inhibit performance of the behavior (control beliefs) (Ajzen, 2002). A central factor in the theory is the individual's intention to perform a certain behavior (Ajzen, 1991). "Intentions are assumed to indicate the motivational factors that influence a behavior that is, they illustrate how hard people are willing to try, and how much of an effort they are planning to exert in order to perform a behavior (Ajzen, 1991; pg. 181)." Attitudes towards the behavior show the degree to which a person has favorable or unfavorable evaluation of behavior at the moment while the subjective norm refers to the perceived pressure of the performance (or not) of the behavior at hand (Ajzen, 1991). Attitudes can be internalized (self-stigmatization) or external. In a qualitative study (n=32) conducted in Gaborone, Botswana, participants who had accepted their HIV status described having developed a new perception of 'self', where they embraced the new image of 'self' with the virus. These individuals were able to have better ARV adherence compared to those who were in denial (Nam et al., 2008). Subjective norms are a product of the normative expectations of other meaningful people towards a particular behavior and the motivation to comply with the opinions of others (Jewkes, Levin and Penn-Kekana, 2003). Stigma surrounding HIV and ART is still prevalent in Botswana where HIV is thought to be contracted through promiscuous behavior. HIV/AIDS has many Setswana derogatory names such as (segajaja, 'the scourge' or malwetsi a dikobo, 'Disease of the blanket') because it is linked to unacceptable moral behavior, which gives reason for judgement of an individual by family or community (Nam et al., 2008; Heald, 2005).

Lastly, perceived behavioral control is determined by an individual's beliefs whether there are inhibitors to their control over the behavior and the perceived power the individual feels to remove these barriers (Ajzen, 1991). Cross generation relationships align with the second arm of TPB (subjective norms), in the sense that the age-disparity between partners is a constraining factor the younger partner to negotiate

safer sex (Leclerc-Madlala, 2008; Jewkes, Levin and Penn-Kekana, 2003). This means that young women might be obliged to have unprotected sex with older men because it is a norm/culture to do so in their society or it could be motivated by the fact that due to poverty and age differences, the young women 's voice might be dim when it comes to safe sexual encounters.

2.4. STUDY DESIGN

This study utilized an observational, cross-sectional, population-based survey study design. Face-to-face interviews were conducted among n=667 adults living with HIV and attending 21 HIV clinics in the Greater Gaborone area. The questionnaire design consisted of closed and open questions, reflecting on retrospective recall of events, as well as current knowledge, attitudes and beliefs and behavioral practices. The sampling methodology to include participants is further described below.

2.5. DATA AND METHODS

2.5.1. Study Area

This study took place in the Greater Gaborone area, which includes the capital city of Gaborone city (as its own district) and three surrounding districts, South East, Kgatleng and Kweneng East within which urban, peri-urban and rural areas were available for study. According to the last national census in 2011, the city of Gaborone had a population of n=231,592, while the larger metropolitan area had about one-half million (n=421,907) people (Botswana Census, 2011). The prevalence of HIV in Gaborone in 2013, was 17.0 per 100 population (estimated HIV n=49,016); South East, 16.6 (n=35,443); Kgatleng, 19.9 (n=30,858) and Kweneng East, 21.5 (n=61,384). Using these HIV estimates to calculate ART uptake in 2017, Gaborone and South East districts had the highest uptake, 68.0% (n=33,332 people receiving ARVs) compared to Kgatleng, 35.7% (n=11,028) and Kweneng East, 43.4% (n=26,587) (Kelepile and Grady, 2019 in review). While ART uptake will not be a focus of this study, further understanding ART adherence among people living with HIV is needed in this high HIV prevalence area of Botswana.

2.5.2. Primary Data Collection

The data for this study were generated primarily from a survey (quantitative) administered to adult women and men who are living with HIV and enrolled on ART (face to face interview), at the study area. This survey was conducted during winter in Botswana of 2016 (May to August). A sample of adults (n=667) men (n=239) and women (n=428) living with HIV, who were enrolled in ART treatment at 21 government clinics, in urban, peri-urban and rural areas (in Greater Gaborone) were interviewed. These patients were required to attend the clinic every month, and it is at this visits where, they collect their ARV drug and have doctor consultation. Biological data such as CD4 count, viral load, date initiated on ART, weight and height were collected from the patients' medical cards. Patients were required to bring their medical file each time they visit their ART facility. Only the latest readings were taken as the patients take new readings at least three times a year. The inclusion criteria were age 18 years and older and HIV positive, attending the clinic for ART. The questionnaires were administered to participants in Setswana (national) and English (official) languages. The use of Setswana language (local) was useful in this study because patients and staff understood it better than English. All participants were asked to sign an informed consent before partaking in the study to obtain their permission to participate. The principal researcher and four research assistants administered the questionnaires. The principal researcher took a training with the Michigan State University [MSU] IRB, while the principal researcher with materials trained the research assistants who were all Botswana locals, which were directly obtained from the MSU IRB (#x15-1269e). All the assistants were fluent in both the languages. The complete survey is provided in Appendix A.

Ethics Overview: The survey took place in the urban, peri -urban and rural areas of Botswana from May until August 2016. Given the sensitivity of this research, an approval from the Institutional Review Board (IRB) was secured from both Michigan State University, and the Ministry of Health and Wellness in Botswana (see Appendices A and B) prior to administering the survey. After satisfying the requirements

of the MoHW IRB requirements, to obtain access to the different clinics, separate IRBs were sought from the District Health Management Teams [DHMTs] in Botswana. MOHW provides primary health care services through DHMTs, which are responsible for running a network of health facilities; hospitals, clinics, health posts and mobile stops as well as community based preventative and promoting services (MoHW, 2018).

2.5.3. Sampling Methodology

2.5.3.1. Districts selection (n=4)

The selected study area has a high HIV prevalence, high number of HIV positive patients as well as high number of ART clinics attending to patients receiving ARVs. Purposive sampling as conducted –i.e., of non-probability sample in which "the principal researcher deliberately selects specific elements or subjects for inclusion in a study in order to ensure that the elements will have certain characteristics relevant to the study (Palinkas et al., 2016). The study covered Gaborone (urban), South East (peri-urban), Kgatleng and Kweneng East (both rural) areas, which were within day driving distance to the principal researcher 's residence; and had all the identified characteristics based on geography and HIV prevalence. To calculate the number of clinics needed, the national prevalence (22.0%) was used since the study did not consider districts as rigid boundaries.

2.5.3.2. Clinics selection (n=21)

There were 84 ART health facilities in the study area, 22 in Gaborone (17.0 HIV prevalence), 6 in South East (16.6% HIV prevalence), 26 in Kgatleng (19.9 HIV prevalence) and 30 in Kweneng East (21.5 HIV prevalence). Using the national prevalence (0.22*84 clinics), 18 clinics were recommended. To account for over and under sampling of facilities, the number was increased to 21 clinics. The clinics were then purposively selected based on the proximity to the principal researcher's location. From the urban area of Gaborone, five clinics [Broadhurst Traditional, Bontleng, Phase 2, Old Naledi and Village] were selected. Among these urban clinics, three clinics (Broadhurst, Bontleng and Old Naledi) are located in low-income

neighborhoods. Old Naledi is mainly a squatter settlement in the outskirts of Gaborone characterized by small businesses and relatively high population density. This neighborhood is also close to Gaborone dam which is the city is major source of water, so minor fishing is evident as well as less dry landscapes. Five peri-urban [Nkoyaphiri, Mafitlhakgosi, Mmopane, Mogoditshane and Tlokweng Main] are located in the peri-urban villages close to Gaborone. Due to the growing population of Gaborone, most people commute and reside in these peri villages. Due to high densities of people, clinics in these areas, are usually located around residential neighborhoods which means are closer to people's homes. There are also decent tarred roads close to the peri-urban clinics. The eleven rural clinics [Makakatlela, Siga, Phuthadikobo, Bokaa, Kopong, Gabane, Morwa, Mochudi1, Kgosing, Lentsweletau and Taung] usually had limited tarred roads and people use dirt roads to reach to these facilities.

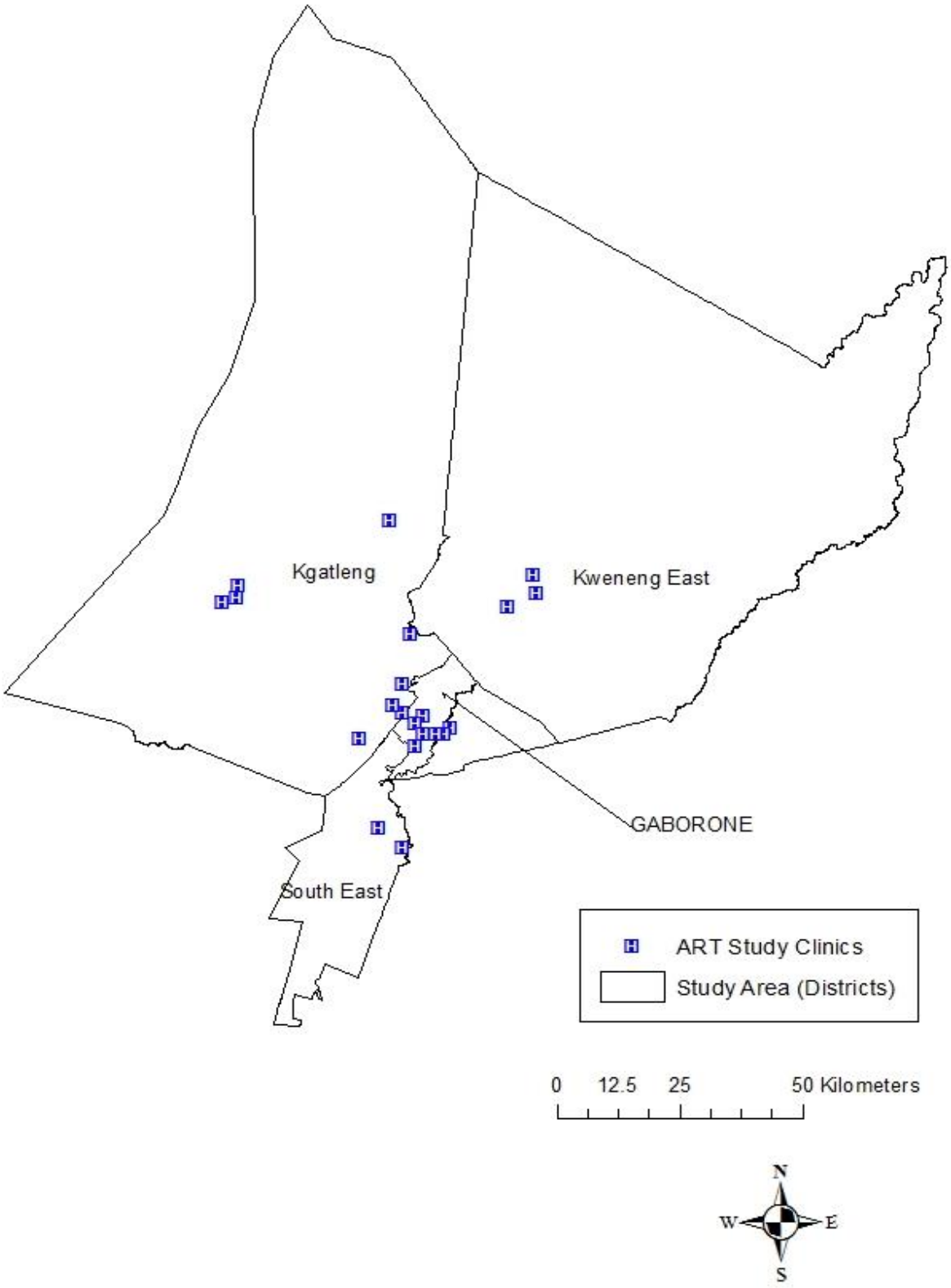


Figure 1: Map of Study Area Showing ART Health Facilities and Districts in Greater Gaborone, Botswana.

The second stage involved selection of adult men and women in the chosen districts (Equation 1.1). The sample size for the participants was calculated using the formula below: The formula was adopted from a national stigma associated with HIV/AIDS survey conducted in 2014 (Botswana Stigma Index Survey Report, 2014).

$N= (t^2pq)/ (d^2)$ [Equation 1.1]

Where;

n = minimum sample size required

t = z value of confidence level desired (95% confidence level)

p = estimated prevalence in target population (the national adult prevalence rate of 22%).

d = precision. The higher the precision desired the larger the sample size will be. 0.05 (5%) is the most common d value.

q = 1-p. Assuming 95% confidence and a precision of 0.05

Formula: Equation 1.1

N= $(1.96^2)*0.22*(1-0.22))/ (0.05^2)$ = 263.6. Design effect = 263.6 x 2 = 527.2

= **527** would be the minimum sample size required for adult men and women living with HIV and receiving ARVs in the study area, and to strengthen results and stable rates, this number was increased to 667 based on the extra availability of the patients at each clinic after reaching the targeted n=30 per clinic. To give the number of patients per clinic, the power to reject the null hypothesis was assessed in Open Epi Software (Dean, Sullivan, and Soe, 2013). The power of a statistical test is the probability that the test will correctly identify a false null hypothesis (Kar and Ramalingam, 2013). The power was set at 80% meaning that the study will be able to detect a true effect of the non-adherence 80% of times assuming that false negative results will occur only 20% of times. Failure to reject the null hypothesis when it is false is called type II error, so the higher the power of the study, the greater will be the required sample size (Kar and Ramalingam, 2013). The districts (n=4) where people came from in urban, peri-urban and rural areas)

were known with all the 21 clinics. Thus the minimum required population of n=527 patients was used, and input 80% reject power required for each clinic, result came as 30. Even though 30 was the minimum, some clinics were oversampled. The clinics were geocoded in Google Earth to produce a KMZ file, which was later converted to a geographic shape file in ArcGIS 10.5 (ESRI, 2018).

Following the selection of clinics and participants, systematic random sampling was employed to select the patients at their respective clinics. Every second patient to enter the door was selected until the minimum required sample of n=30 patients per clinic was reached. Participants were visited daily at their respective ART facilities in the study area. The health personnel and the researchers briefed the ART patients on the purpose of the study during morning health talks, before the interviews took place in interview rooms.

2.5.3.3. Reliability and Validity of Data Collected

For reliability purposes, all the patients were visited at their respective clinics at the same time (from 7:30 am until 2:00pm). In addition to the principal researcher, four experienced research assistants assisted with the data collection. These assistants were locals who were trained on IRB requirements and fluent in Setswana language (as described above). The principal researcher and assistants attempted to make the patients comfortable in order to open-up about their treatment adherence behaviors, without the fear of judgment. The data were coded by the principal researcher to remove the bias which could be incurred if all the assistants coded the data. Pope et al (2002) asserts that "a clear account of the data collection and analysis is important because it allows readers to judge evidence and interpretations presented".

2.5.4. Non-Adherence Definition

Adherence in this research is defined by three variables (1) patient's CD4 count >= 350 copies/mL [CD4_REC], (2) taking the pills as instructed by the doctor (100% dosage) [ARVPrescribe] and (3) having missed a (one) dosage sometimes [MissDose] (95% or at least missed 1 pill a month). If all of these

variables were satisfied, the patient was considered to be “Adherent” (code 0), but if one or more of these criteria were not met, then the patient was considered “Non-Adherent” (code 1) to their ART treatment regime. In this study, the dependent variable in subsequent statistical models was “Non-Adherence”.

The explanatory (independent) variables to predict Non-Adherence, were coded as sex (female=1, male=0); age groups— (base, 30-39 years=0, and 18-24=1, 25-29=1, 35-39=1, 45-49=1, 50+=1; Body Mass Index (BMI) height and weight from which to calculate their body mass index (BMI) as an indicator of overall nutritional status. They were also asked the year diagnosed with HIV (HIV_Year) and the year ARVs were initiated (ARV_Cat). These variables were studied using continuous annual measures, and categories as follows: The first patient reported being diagnosed in Botswana was in 1985 [Category 1: 1982-1985]; the universal free ARV drugs were introduced in Botswana in 2002 [Category 2: 2002-2016]. Any illness/condition [llness], this variable was coded as 1, and 0 for no illness. To understand the side effects of ARVs, the question on how they felt after taking ARVs [ARVFeel], was asked, and if one felt no side effects after a dose, the response was coded as a 0. Anyinfo (any information provided-open ended). This question provided for the richness of the discussion points that they researcher may have overlooked. All the continuous variables were assessed to check for distribution and normality through histograms and correlation techniques. The variable ‘viral Load’- which is the amount of virus in a patient’s body was skewed with many outliers, so patients with high numbers (<7000 copies m/L) were removed. Further the variable ‘SexPartner’-which the number of partners that one had over the past year, had a couple of extreme values such as 16 partners in 12 months, so two patients were removed, leaving the n=658 in the analysis.

2.5.5. Descriptive Methods

The dependent and independent variables were examined for their frequencies and cross tabulations. Histograms were evaluated for the continuous variables. These descriptive analyses, were also used to check if all the assumptions of regression analyses were being met. To assess the HIV life-course of

individuals, the stage of life at time of HIV diagnosis was estimated by taking their age in 2016 (age at interview) (Y axis) minus their year of reported HIV diagnosis (X axis). The range in numbers of years post HIV diagnosis, that ARVs were initiated, are provided in each x, y cell using low and high estimates for each age group.

2.5.6. Analytical Methods

Individual-level regression analyses were estimated in this study. However, imbalanced data was a limitation for many analyzes, thus population-level analyses were implement as described herein. Imbalanced datasets can significantly affect the performance of the classifiers as the working model will be biased towards the majority class to minimize the overall error term (Estabrooks, 2000; Dubey et al., 2014). The imbalanced data problem occurs when the explanatory variables are unevenly distributed among different classes. In the case of binary classification, the number of observations in one class is significantly greater than that of the other (Zheng et al., 2004). In this study, the data were frequently imbalanced. For instance, there were almost twice the number of females (n=419) sampled as there were men (n=239). Another example was the classes observed within the variable age, with 30-39 years for women having the highest frequency (n=148) compared to the same class for men (n=60). Another example of imbalance was seen with the unemployment variable, where 172 women were unemployed compared to (n=47) of men. To address imbalanced data, this study utilized the Least Squares (LS)-means procedure to estimate the marginal totals of population parameters in SAS 9.4 (SAS Institute Inc., 2002-2012, Cary, NC, USA). The linear functions were defined by population marginal means of the corresponding means for balanced data (Cai, 2014). When performing an LS-means procedure with logistic regression in SAS, it produces a diffogram, and odds ratios with 95% confidence intervals. In a diffogram, each line segment corresponded to one pairwise difference between LS-means. A line segment centered at the LS-means in a pair and had both a vertical and a horizontal line that indicated values and

levels that corresponded to the pair. The length of the line segment reflected the projected width of a confidence interval for the difference (Cai, 2014).

2.6. RESULTS

2.6.1. Life Course of People Living with HIV and ART-Initiation Post-HIV Diagnosis

The life-course of patient's living with HIV often showed long periods of time between HIV diagnosis and ART initiation. Although it is unclear if these same patients received late HIV diagnoses, a summary of findings stratified by women and men is provided below.

2.6.1.1. Women

Using the low age-group estimates (Table 1), there was no woman born with HIV. However, there were women diagnosed with HIV across the life-course, including the life stages of infancy (n=1), childhood (n=47), young adult (n=127), adult (n=120), mid-early adult (n=71), mid-late adult (n=38), older adulthood (n=14) and oldest adult (n=1). Using the high age-group estimates (Table 2) women's age of HIV diagnosis shifted to slightly higher age groups as expected. There were no women born with HIV, nor diagnosed in infancy. HIV diagnoses occurred in childhood (n=8), young adult (n=47), adult (n=103), mid-early adult (n=139), mid-late adult (n=73), older adult (n=37) and oldest adult (n=14). In general, women diagnosed with HIV across the life-course began ARV treatment during Stage 2 of the disease, with a few individual women with late diagnoses –i.e., late Stage 2 or possibly Stage 3.

Table 1. HIV Diagnoses Across the Life Course by Current Age and Low Estimate[1] of Years ARV Initiated Post-HIV Diagnosis—Sample of Women (n=419) Living with HIV in Greater Gaborone, Botswana, 2016.

	HIV Diagnoses Across the Life Course									
				Young		Mid-Early	Mid-Late	Older	Oldest	
Life Stage	Birth	Infant	Childhood	Adult	Adult	Adult	Adult	Adult	Adult	Total
Women	< 1 Year	1 Year	1-5 Years	18-24 Years	25-30 Years	31-39 Years	40-49 Years	50-59 Years	60+ Years	Years
Age in 2016 (n)										
18-24 Years	--	--	17	4	--	--	--	--	--	21
-ARV Mean Years (range)	--	--	4(0-10)	0(0)	--	--	--	--	--	1(0-14)
25-30 Years	--	1	16	47	6	--	--	--	--	70
-ARV Mean Years (range)	--	16(16)	6(0-12)	2(0-6)	0(0)	--	--	--	--	2(0-9)
31-39 Years	--	--	13	70	63	2	--	--	--	148
-ARV Mean Years (range)	--	--	6(0-13)	7(0-13)	3(0-6)	0(0)	--	--	--	3(0-15)
40-49 Years	--	--	1	6	50	64	3	--	--	124
-ARV Mean Years (range)	--	--	5(5)	10(3-16)	8(0-14)	4(0-9)	0(0)	--	--	2(0-18)
50-59 Years	--	--	--	--	1	5	34	1	--	41
-ARV Mean Years (range)	--	--	--	--	14(14)	10(6-12)	4(0-9)	0(0)		1(0-8)
60+ Years	--	--	--	--	--	--	1	13	1	15
-ARV Mean Years (range)	--	--	--	--	--	--	11(11)	5(0-10)	0(0)	2(0-7)
Low Estimate (N)	0	1	47	127	120	71	38	14	1	419

[1] Estimates based on low-age range.

Table 2. HIV Diagnoses Across the Life Course by Current Age and High Estimate[1] of Years ARV Initiated Post-HIV Diagnosis—Sample of Women (n=419) Living with HIV in Greater Gaborone, Botswana, 2016.

	HIV Diagnoses Across the Life Course									
				Young		Mid-Early	Mid-Late	Older	Oldest	
Life Stage	Birth	Infant	Childhood	Adult	Adult	Adult	Adult	Adult	Adult	Total
Women	< 1 Year	1 Year	1-5 Years	18-24 Years	25-30 Years	31-39 Years	40-49 Years	50-59 Years	60+ Years	Years
Age in 2016 (n)										
18-24 Years	--	--	6	15	--	--	--	--	--	21
-ARV Mean Years (range)	--	--	7(0-10)	2(0-5)	--	--	--	--	--	3(0-10)
25-30 Years	--	--	2	23	45	--	--	--	--	70
-ARV Mean Years (range)	--	--	19(11-26)	5(0-12)	2(0-5)	--	--	--	--	3(0-26)
31-39 Years	--	--	--	9	56	82	--	--	--	148
-ARV Mean Years (range)	--	--	--	6(1-12)	9(0-16)	3(0-8)	--	--	--	4(0-13)
40-49 Years	--	--	--	--	1	56	67	--	--	124
-ARV Mean Years (range)	--	--	--	--	14(14)	9(0-16)	4(0-9)	--	--	6(0-16)
50-59 Years	--	--	--	--	--	1	6	34	--	41
-ARV Mean Years (range)	--	--	--	--	--	14(14)	10(6-12)	3(0-9)		5(0-14)
60+ Years	--	--	--	--	--	--	--	3	12	15
-ARV Mean Years (range)	--	--	--	--	--	--	--	10(10-11)	3(0-9)	5(0-11)
High Estimate (N)	0	0	8	47	103	139	73	37	12	419

[1] Estimates based on high-age range.

2.6.1.2. Men

Using the low age-group estimates (Table 3), there was one man born with HIV and two men diagnosed during infancy. There were men diagnosed with HIV across the life-course, including the life stages of childhood (n=19), young adult (n=35), adult (n=56), mid-early adult (n=78), mid-late adult (n=30) and older adulthood (n=18). Using the high age-group estimates (Table 4) men age of HIV diagnosis shifted to slightly higher age groups as expected with the same man diagnosed at birth, fewer diagnosed in childhood (n=7), young adult (n=12), adult (n=27), mid-early adult (n=70), mid-late adult (n=77), older adult (n=32) and oldest adult (n=13). The majority of men diagnosed as mid-early adults (31-39 years) and mid-late adults (40-49 years) are currently in these same age groups, thereby receiving ARV treatment early in Stage 2. There are also 21 men diagnosed during their mid-early adult years, who are now 40-49 years who initiated ARVs a mean of 10 years post-diagnosis (range, 3-15 years). Likewise, 11 men were diagnosed during their mid-late adult years, who are now 50-59 years who initiated ARVs a mean of 9 years post-diagnosis (range, 0-14 years). Finally, there are 6 men who were diagnosed during the older adult years 50-59 years, who are now in their 60+ years who initiated ARV treatment a mean of 9 years post-diagnosis (range, 4-11 years). In general, men were diagnosed with HIV later in their life-course compared to women who were diagnosed at younger ages. More older men also initiated ARV treatment later in Stage 2 and Stage 3 of their HIV disease, compared to women diagnosed at these same ages with a few outlying women initiating ARV treatment in Stage 3.

Table 3. HIV Diagnoses Across the Life Course by Current Age and Low Estimate[1] of Years ARV Initiated Post-HIV Diagnosis—Sample of Men (n=239) Living with HIV in Greater Gaborone, Botswana, 2016.

	HIV Diagnoses Across Life Course									
				Young		Mid-Early	Mid-Late	Older	Oldest	
Life Stage	Birth	Infant	Childhood	Adult	Adult	Adult	Adult	Adult	Adult	Total
Men	< 1 Year	1 Year	1-5 Years	18-24 Years	25-30 Years	31-39 Years	40-49 Years	50-59 Years	60+ Years	Years
Age in 2016 (n)										
18-24 Years	1	1	10	--	--	--	--	--	--	12
-ARV Mean Years (range)	13(13-13)	14(14)	7(3-14)	--	--	--	--	--	--	8(3-14)
25-30 Years	--	1	2	14	1	--	--	--	--	18
-ARV Mean Years (range)	--	11(11-11)	8(7-8)	2(0-6)	0(0)	--	--	--	--	3(0-11)
31-39 Years	--	--	5	15	36	4	--	--	--	60
-ARV Mean Years (range)	--	--	10(1-21)	6(0-11)	3(0-6)	0(0)	--	--	--	4(0-21)
40-49 Years	--	--	2	4	18	65	1	--	--	90
-ARV Mean Years (range)	--	--	7(2-12)	9(8-9)	11(3-15)	4(0-9)	0(0)	--	--	5(0-15)
50-59 Years	--	--	--	2	1	9	25	3	--	40
-ARV Mean Years (range)	--	--	--	30(27-33)	22(22-22)	9(0-14)	4(0-10)	0(0)	--	7(0-33)
60+ Years	--	--	--		--	--	4	15	--	19
-ARV Mean Years (range)	--	--	--	--	--	--	9(4-11)	3(0-10)	--	5(0-11)
Low Estimate (N)	1	2	19	35	56	78	30	18	0	239

[1] Estimates based on low-age range.

Table 4. HIV Diagnoses Across the Life Course by Current Age and High Estimate[1] of Years ARV Initiated Post-HIV Diagnosis—Sample of Men (n=239) Living with HIV in Greater Gaborone, Botswana, 2016.

	HIV Diagnoses Across Life Course									
				Young		Mid-Early	Mid-Late	Older	Oldest	
Life Stage	Birth	Infant	Childhood	Adult	Adult	Adult	Adult	Adult	Adult	Total
Men	< 1 Year	1 Year	1-5 Years	18-24 Years	25-30 Years	31-39 Years	40-49 Years	50-59 Years	60+ Years	Years
Age in 2016 (n)										
18-24 Years	1	--	5	6	--	--	--	--	--	12
-ARV Mean Years (range)	13(13-13)	--	12(10-14)	4(3-5)	--	--	--	--	--	8(3-14)
25-30 Years	--	--	1	4	13	--	--	--	--	18
-ARV Mean Years (range)	--	--	11(11)	6(4-8)	2(0-5)	--	--	--	--	3(0-11)
31-39 Years	--	--	1	2	11	46	--	--	--	60
-ARV Mean Years (range)	--	--	21(21)	3(1-5)	7(2-14)	3(0-8)	--	--	--	4(0-21)
40-49 Years	--	--	--	--	3	21	66	--	--	90
-ARV Mean Years (range)	--	--	--	--	8(2-12)	10(3-15)	4(0-9)	--	--	5(0-15)
50-59 Years	--	--	--	--	--	3	11	26	--	40
-ARV Mean Years (range)	--	--	--	--	--	27(22-33)	9(0-14)	4(0-9)	--	7(0-33)
60+ Years	--	--	--		--	--	--	6	13	19
-ARV Mean Years (range)	--	--	--	--	--	--	--	9(4-11)	3(0-9)	5(0-11)
High Estimate (n)	1	0	7	12	27	70	77	32	13	239

[1] Estimates based on high-age range.

When the number of years ARV is initiated post-HIV diagnosis for women and men in their current age group is plotted against their current CD4 count (Figures 2-5) there are striking differences. Figure 2 shows young adult women and men (ages 20-29 years) with a linear upward trend in CD4 count with increasing length of time between HIV diagnosis and ARV initiation (range, 0 to 12.5 years). All but two women and one man initiated ARV treatment immediately following diagnosis through Stage 2. Women consistently have a higher CD4 count (trend > 500 cells/ml) compared to men (trend < 500 cells/ml).

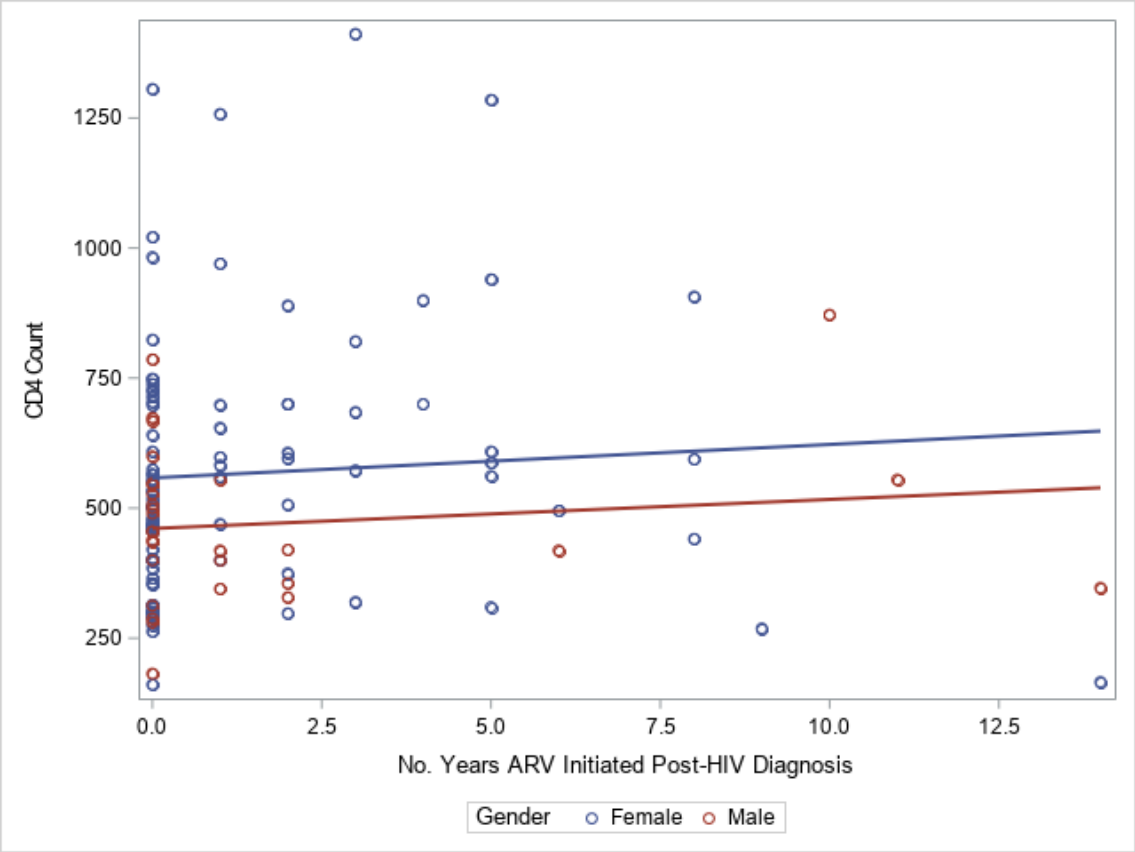


Figure 2: Women and Men Ages 20-29 Years.

Figure 3 shows women and men in their mid-early adult years (30-39 years) with a cross-over effect of ARV initiation around 7.5 years post-HIV diagnosis (range, 0 to 15.0 years). Women at HIV diagnosis show CD4 counts > 500 cells/ml compared to men (CD4 count < 500 cells/ml); however, with increased delay in treatment during Stage 2 of the disease, men's CD4 count improves, while women's CD4 count declines.

At this age-group, there are more women receiving delayed ARV treatment compared to men, which may influence these results. A substantial number of women and men are diagnosed late in the disease as evidenced by a CD4 count < 200 cells/ml.

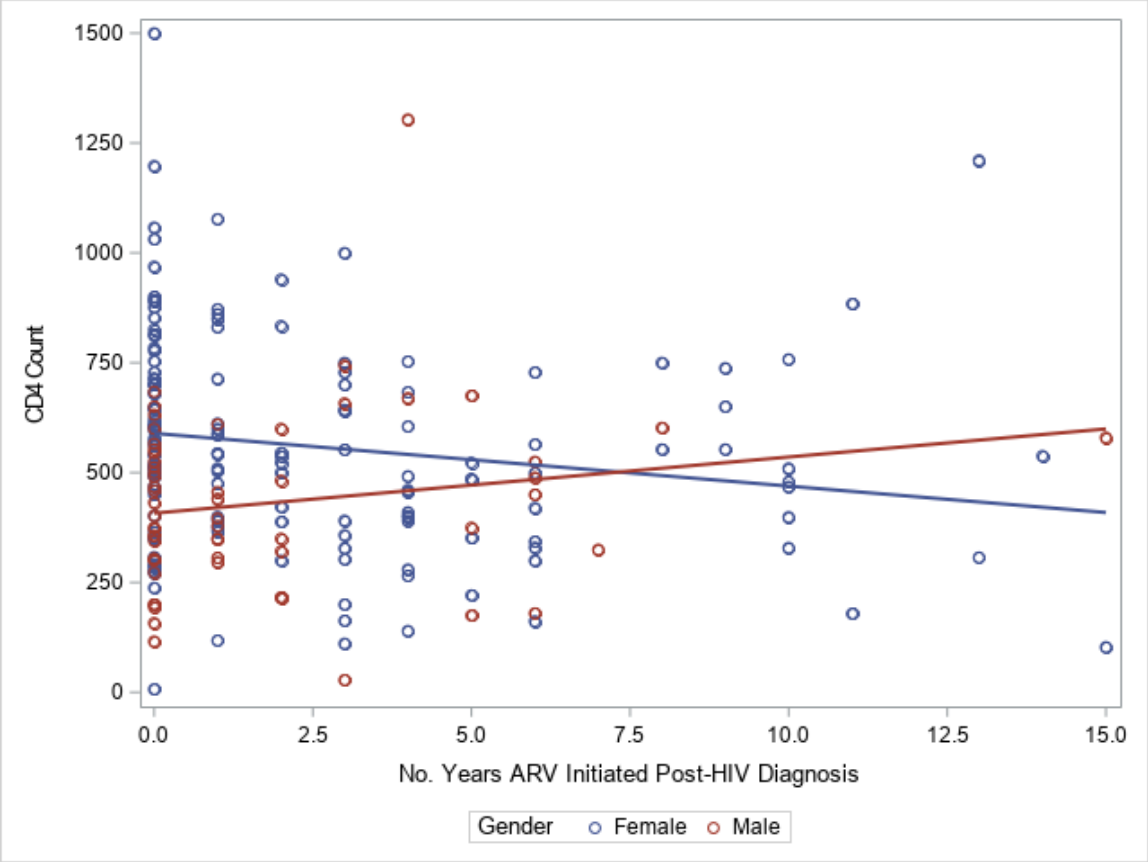


Figure 3: Women and Men Ages 30-39 Years.

Figure 4 shows women and men in their mid-late adult years (40-49 years) running relatively parallel around CD4 count 500 cells/ml with women across the delay in ARV initation having a slightly higher CD4 count compared to men. The range in the number of years ARV initiated post-HIV diagnosis is greatest in this age group (range, 0 to 20+ years).

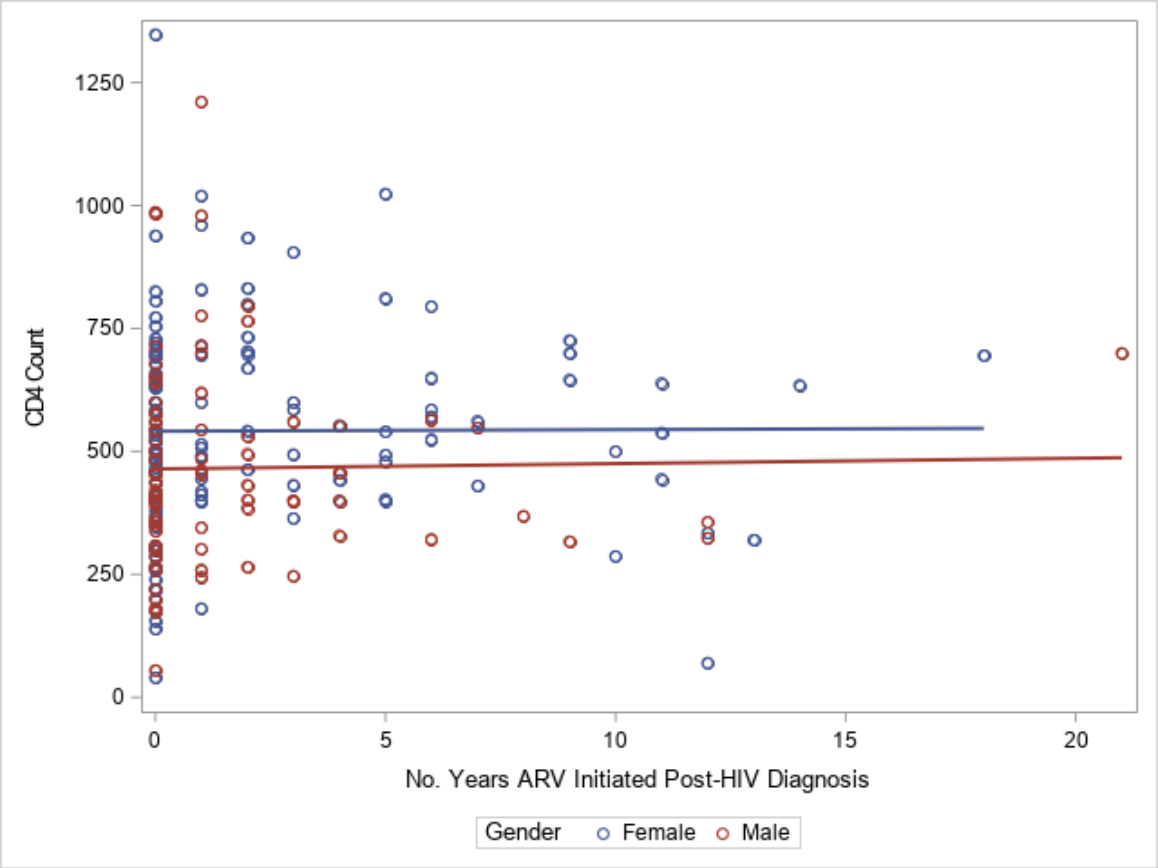


Figure 4: Women and Men Ages 40-49 Years.

Finally, Figure 5 shows women and men of the older and oldest-adult age groups (50+ years) with women and men experiencing a negative linear trend in CD4 count across the delay in ARV treatment (range, 0 to 12.5 years). In general, older men have lower CD4 counts compared to older women with the gap widening with delay in ARV treatment beyond 7.5 years.

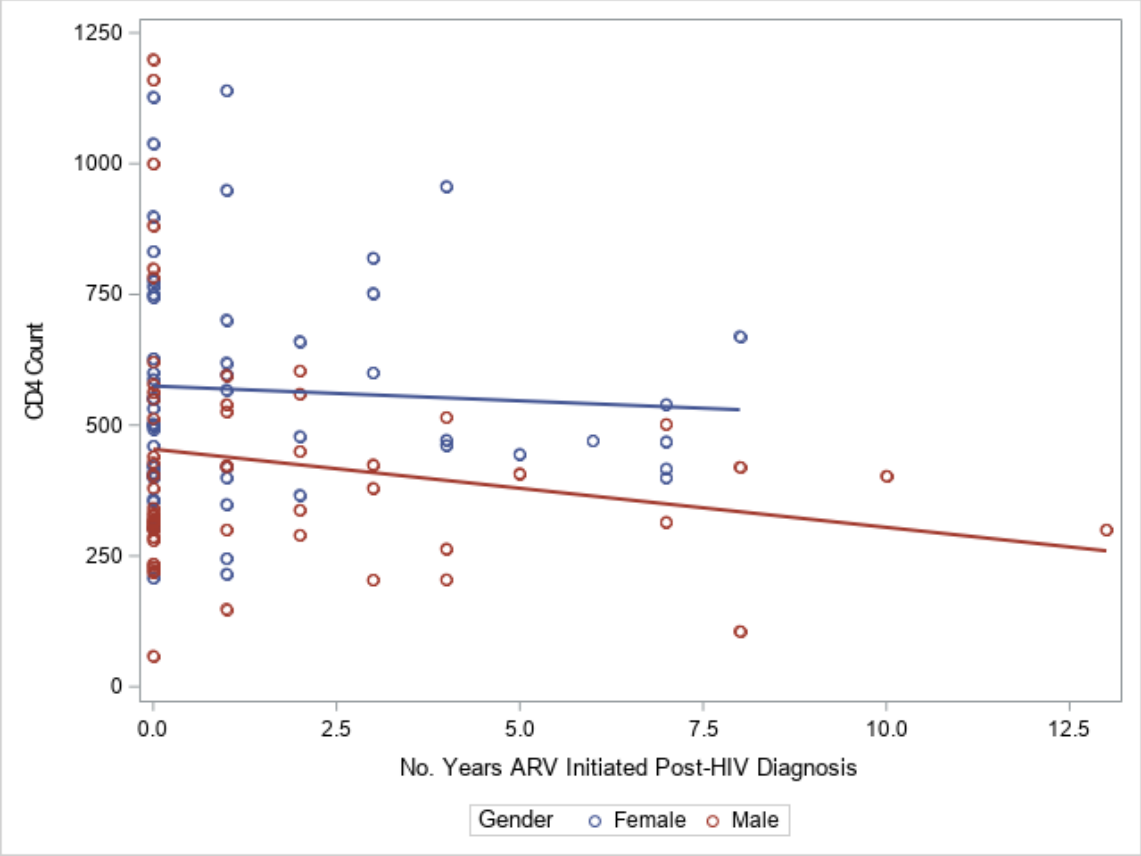


Figure 5: Women and Men Ages 50+ Years.

In summary, these graphs show that in general, women experience higher CD4 counts compared to men at all life-course stages, except those women in their mid-early adult years (30-39 years) with extreme delays in ARV treatment. Women and men in their young adult and adult years of life generally respond to ARV treatment when initiated as evidence by a rising CD4 count. In contrast, women and men in their older and oldest stages of life respond less well to ARV treatment with increasing delays as also evident by a lower of CD4 counts. These population-based graphs are informative because they show general trends in potential ARV treatment success following differing periods of ARV initiation post-HIV diagnosis. With this background understanding of gender differences in year of HIV diagnosis, number of years ARVs initiated post-HIV diagnosis and current age-groups referenced CD4 counts, the population surveyed is further investigated for levels of ARV adherence and non-adherence.

2.6.2. Non-Adherence Levels

Non ART adherence in Greater Gaborone was 29.1% for women and 46.0% for men (Table 5). Across age groups, non-adherence was different among women and men. For young adults and adults (18-29 years) non-adherence was double that for women (21.7%) compared to men (12.6%). This trend cross-over for the older and oldest-adult age groups (50+) where women were substantially less non-adherent (2.9%) compared to men (12.9%). By marital status, both women and men were mostly either single or cohabiting. Single men tended to be more non-adherent (21.3%) than single women (15.9%). There were fewer women 5.5% (1.2% non-adherent) who did not have education compared to 15.9% (7.9% non-adherent) men. There were also high number of women with university education (10.02%) compared to 5.4% of the men with both having about the same non-adherence levels (about 3% each). A majority of women were unemployed (41.1%) compared to men (19.7%) with unemployed women more non-adherent (10.7%) compared to men (8.8%). For religion, women were more of the Christian denomination (87.4%) while the men were having different beliefs. Only 2.6% of the women practiced African beliefs of which 1.0% were non-adherent, compared to 11.3% men of which 5.4% were non-adherent (Table 5).

Table 5. Demographic Characteristics of Sampled Women (n=419) and Men (n=239) Living with HIV in Greater Gaborone, Botswana 2016.

Demographic Characteristics	Women		Non-Adherence	Men		Non-Adherence
	No.	(%)	(%)	No.	(%)	(%)
Age (Years)						
18-29	91	21.7	**6.2**	30	12.6	**4.6**
30-39	148	35.3	11.5	60	25.1	11.7
40-49	124	29.6	**8.6**	90	37.7	**16.7**
50+	56	13.4	**2.9**	59	24.7	**12.9**
Marital Status						
Married	60	14.3	4.3	39	16.3	7.5
Single	223	**53.2**	**15.9**	105	**43.9**	**21.3**
Cohabit	118	**28.2**	**7.9**	88	**36.8**	**15.5**
Widowed	17	4.1	0.9	7	2.9	1.7
Divorced	1	0.2	0.0	0	0.0	0.0
Education						
No. Formal	23	**5.5**	**1.2**	38	**15.9**	**7.9**
Primary	89	21.2	6.2	73	30.5	14.6
Secondary	249	59.4	17.4	100	41.8	19.7
Vocational	16	3.8	1.2	15	6.3	0.8
University	42	**10.0**	**3.1**	13	**5.4**	**2.9**
Occupation						
Unemployed	172	**41.1**	**10.7**	47	**19.7**	**8.8**
Self-Employed	70	**16.7**	**4.3**	57	**23.9**	**11.3**
Farmer	14	3.3	1.9	14	5.9	2.9
Private	99	23.6	8.6	82	34.3	15.5
Government	64	15.3	3.6	39	16.3	7.5
Religion						
Christianity	366	87.4	25.1	156	65.3	30.9
African Beliefs	11	**2.6**	0.9	27	**11.3**	5.4
Other	42	**10.0**	3.1	56	**23.4**	9.6
Total	419	100.0	**29.1**	239	100.0	**46.0**

Of the behavioral characteristics (Table 6), sexual behaviors showed that only 5.5% of the women had more than 2 partners within the past year and of these, 2.4% were non-adherent compared to 18.5% of the men who had more than 2 partners, of which 10.5% were non-adherent. A majority of both women and men (72.5%) did not use a condom each time with a sexual partner and of those who did not use a condom, 21.7% of women were non-adherent compared to 34.7% of men. A majority of the women

(72.6%) and men (74.5%) obtained condoms free from health facilities; however, of these about 20.3% of women, were non-adherent compared to 33.9% of men.

Table 6. Behavioral Characteristics of Sampled Women (n=419) and Men (n=239) Living with HIV in Greater Gaborone, Botswana, 2016.

Behavioral Characteristics	**Women**		**Non-Adherence**	**Men**		**Non-Adherence**
	No.	**(%)**	**(%)**	**No.**	**(%)**	**(%)**
No. Sex Partners						
0	54	12.9	5.0	27	11.3	5.9
1	342	81.6	21.7	167	70.2	29.8
2+	23	**5.5**	**2.4**	45	**18.5**	**10.5**
Condom Use						
Yes	115	27.5	7.4	65	27.2	11.3
No	304	**72.5**	**21.7**	174	**72.8**	**34.7**
Obtain Condoms						
Workplace	2	0.5	0.2	5	2.1	1.3
Stores	113	26.9	8.6	56	23.4	10.9
Health Facility	304	**72.6**	**20.3**	178	**74.5**	**33.9**
Total	419	100.0	29.1	239	100.0	46.0

Of the health care facility characteristics (Table 7), clinic utilization showed that majority of both women (57%) and men (55.6%) attended rural clinics. Of these, 14.8% of women were non-adherent compared to 24.3% men. Non-adherence was double for men who lived in peri-urban areas (13.8%) compared to 6.4% of women in the same location. A majority of women (44.4%) used public transit to reach the ART clinics compared to 28.1% of men who had about the same non-adherence levels (14.6 and 15.1%). Men who waited more than one-hour for a service at the clinic were more likely to be non-adherent (35.2%) compared to 18.9% of the women.

Table 7. Health Care Facility Characteristics for Sampled Women (n=419) and Men (n=239) Living with HIV in Greater Gaborone, Botswana, 2016.

Health Facility Characteristics	**Women**		**Non-Adherence**	**Men**		**Non-Adherence**
	No.	**(%)**	**(%)**	**No.**	**(%)**	**(%)**
Clinic Location						
Urban	82	19.6	7.9	44	18.4	7.9
Peri-urban	98	23.4	**6.4**	62	25.9	**13.8**
Rural	239	57.0	**14.8**	133	55.6	**24.3**
Transit to Facility						
Walk	211	50.4	13.1	138	57.7	23.4
Drive	22	5.3	**1.4**	34	14.2	**7.5**
Public Transport	186	**44.4**	14.6	67	**28.1**	15.1
Distance						
< 30 minutes	329	78.5	**21.5**	186	77.8	**34.7**
>= 30 minutes	90	21.5	7.6	53	22.2	11.3
Waiting Time						
< 1 Hour	122	29.1	10.3	57	23.9	10.9
>= 1 Hour	297	70.9	**18.9**	182	76.2	**35.2**
Total	419	100	29.1	239	100	46

Across all the demographics and socio-economic characteristics, men consistently showed high trends of non-adherence compared to women (Tables 5-7).

2.6.3. Risk Populations and Risk Factors for Non-Adherence

Men of all ages showed a higher odds of non-adherence compared to women. Older and oldest-aged men aged 50+ versus women of the same age, had the highest odds of being non-adherent [OR 4.06, 1.79-9.12] followed by those mid-late adult men ages 40-49 years [OR 1.88, 1.06-3.56] (Table 8). When controlling for the number of years ART initiated post-HIV diagnosis, men in their mid-early ages (30-39 years), were also at increased odds of non-adherence [OR 2.05, 1.06-3.96] (Table 9).

Table 8. Unadjusted Odds Ratio Estimates of Non-Adherence for Men (n=239) vs. Women[1] (n=352) Living with HIV, Greater Gaborone, Botswana, 2016.

Sex by Age	Odds Ratio	95% LCI	95% UCI
Men vs. Women 18-29 Years	1.30	0.52	3.23
Men vs. Women 30-39 Years	1.89	0.99	3.58
Men vs. Women 40-49 Years	**1.88**	**1.06**	**3.56**
Men vs. Women 50+ Years	**4.06**	**1.79**	**9.12**

[1]Excludes women on PMTCT (n=67).

Table 9. Odds Ratio Estimates of Non-Adherence for Men (n=239) vs. Women[1] (n=352) Living with HIV, controlling for the Number of Years ARV Initiated Post-HIV Diagnosis, Greater Gaborone, Botswana, 2016.

Sex by Age	Odds Ratio	95% LCI	95% UCI
Men vs. Women 18-29 Years	1.24	0.50	3.11
Men vs. Women 30-39 Years	**2.05**	**1.06**	**3.96**
Men vs. Women 40-49 Years	**1.91**	**1.06**	**3.45**
Men vs. Women 50+ Years	**3.95**	**1.73**	**8.97**

[1]Excludes women on PMTCT (n=67).

Unadjusted odds of non-adherence showed that old and older men have the highest odds of being non-adherent compared to women of all ages. oldest-aged men aged 50+ versus women of the same age, had the highest odds of being non-adherent [OR 4.06, 1.79-9.19] followed by those mid-adult men ages 30-39 years [OR 3.21, 1.42-7.25] (Table 10) and those in their mid-late adulthood [OR 2.93, 1.37-6.28]. When adjusted, highest odds were still evident for oldest men aged 50+ compared to the women of the same age [OR 3.95, 1.74-8.97] followed by those aged 30-39 versus oldest women [OR 3.09, 1.36-7.03] and mid-late adult men [OR 2.86, 1.32-6.16] compared to women aged 50+ (Table 11).

Table 10. Unadjusted Odds Ratio Estimates of Non-Adherence for Men (n=239) vs. Women (n=352) by Age Group.

Gender	Age	N	Gender	Age	N	Estimate	SE	p- value	Odds Ratio	95% LCI	95% UCI
Men	18-29	30	Men	30-39	60	-0.413	0.458	0.368	0.66	0.26	1.62
Men	18-29	30	Men	40-49	90	-0.323	0.434	0.456	0.72	0.30	1.69
Men	18-29	30	Men	50+	59	-0.648	0.459	0.157	0.52	0.21	1.28
Men	18-29	30	Women	18-29	91	0.264	0.464	0.569	1.30	0.52	3.23
Men	18-29	30	Women	30-39	148	0.224	0.427	0.599	1.25	0.54	2.89
Men	18-29	30	Women	40-49	124	0.309	0.431	0.473	1.36	0.59	3.17
Men	18-29	30	Women	50+	56	0.752	0.499	0.132	2.12	0.79	5.65
Men	30-39	60	Men	40-49	90	0.089	0.334	0.788	1.09	0.57	2.11
Men	30-39	60	Men	50+	59	-0.235	0.367	0.521	0.79	0.39	1.62
Men	30-39	60	Women	18-29	91	0.677	0.373	0.069	1.97	0.95	4.09
Men	30-39	60	Women	30-39	148	0.637	0.326	0.051	1.89	0.99	3.57
Men[7]	30-39	60	Women	40-49	124	0.722	0.330	0.029	2.06	1.08	3.93
Men[2]	30-39	60	Women	50+	56	1.165	0.416	0.005	3.21	1.42	7.25
Men	40-49	90	Men	50+	59	-0.324	0.336	0.333	0.72	0.37	1.39
Men[9]	40-49	90	Women	18-29	91	0.587	0.342	0.086	1.80	0.92	3.52
Men	40-49	90	Women	30-39	148	0.548	0.291	0.059	1.73	0.98	2.06
Men[8]	40-49	90	Women	40-49	124	0.632	0.295	0.032	1.88	1.06	3.45
Men[3]	40-49	90	Women	50+	56	1.076	0.389	0.005	2.93	1.37	6.28
Men[5]	50+	59	Women	18-29	91	0.912	0.374	0.015	2.49	1.20	5.19
Men[6]	50+	59	Women	30-39	148	0.872	0.328	0.008	2.39	1.26	4.55
Men[4]	50+	59	Women	40-49	124	0.957	0.332	0.004	2.61	1.36	4.99
Men[1]	50+	59	Women	50+	56	1.401	0.417	0.001	4.06	1.79	9.19
Women	18-29	91	Women	30-39	148	-0.039	0.334	0.905	0.96	0.50	1.85
Women	18-29	91	Women	40-49	124	-0.044	0.337	0.895	1.04	0.54	2.03
Women	18-29	91	Women	50+	56	0.488	0.422	0.247	1.63	0.71	3.73
Women	30-39	148	Women	40-49	124	0.084	0.285	0.767	1.08	0.62	1.90
Women	30-39	148	Women	50+	56	0.528	0.382	0.166	1.69	0.80	3.58
Women	40-49	124	Women	50+	56	0.444	0.385	0.249	1.58	0.73	3.31

Table 11. Adjusted Odds Ratio Estimates of Non-Adherence for Men (n=239) vs. Women (n=352) by Age Group.

Gender	Age	N	Gender	Age	N	Estimate	SE	p- value	Odds Ratio	95% LCI	95% UCI
Men	18-29	30	Women	18-29	91	0.215	0.469	0.647	1.24	0.50	3.11
Men	18-29	30	Women	30-39	148	0.288	0.437	0.511	1.33	0.57	3.14
Men	18-29	30	Women	40-49	124	0.296	0.436	0.497	1.35	0.57	3.16
Men	18-29	30	Women	50+	56	0.697	0.506	0.168	2.01	0.75	5.41
Men	30-39	60	Women	18-29	91	0.647	0.377	0.086	1.91	0.91	3.99
Men[8]	30-39	60	Women	30-39	148	0.712	0.335	0.032	2.05	1.06	3.96
Men[7]	30-39	60	Women	40-49	124	0.728	0.336	0.030	2.07	1.07	3.99
Men[2]	30-39	60	Women	50+	56	1.129	0.419	0.007	3.09	1.36	7.03
Men	40-49	90	Women	18-29	91	0.567	0.346	0.101	1.76	0.89	3.47
Men[10]	40-49	90	Women	30-39	148	0.639	0.300	0.033	1.89	1.05	3.41
Men[9]	40-49	90	Women	40-49	124	0.648	0.301	0.031	1.91	1.06	3.45
Men[3]	40-49	90	Women	50+	56	1.049	0.392	0.007	2.86	1.32	6.16
Men[6]	50+	59	Women	18-29	91	0.890	0.376	0.017	2.44	1.17	5.09
Men[5]	50+	59	Women	30-39	148	0.963	0.335	0.004	2.62	1.36	5.05
Men[4]	50+	59	Women	40-49	124	0.971	0.335	0.004	2.64	1.37	5.10
Men[1]	50+	59	Women	50+	56	1.373	0.419	0.001	3.95	1.74	8.97

[1]Controlling for men vs. men and women vs. women by age group and the number of years ARV initiated post-HIV diagnosis.

[2]Excludes women on PMTCT (n=67).

2.6.4. CD4 Count as a Proxy of Non-Adherence

In the following analysis, only CD4 count was assessed. The decision to do so was based on the fact that after evaluating gender differences on non-adherence levels, low CD4 count accounted for the majority of the non-adherence levels. A continuous variable CD4 count showed that the range of 50-1,450 copies/ml (Figure 6). Women showed high levels of CD4 counts compared to men across the board. The mean CD4 count for women was 548.93 copies/ml (Figure 6) compared to 447.23 of the men (Figure 6). The range CD4 count for men was 50-1,350 copies/ml, slightly lower than the maximum for the women (Figure 7).

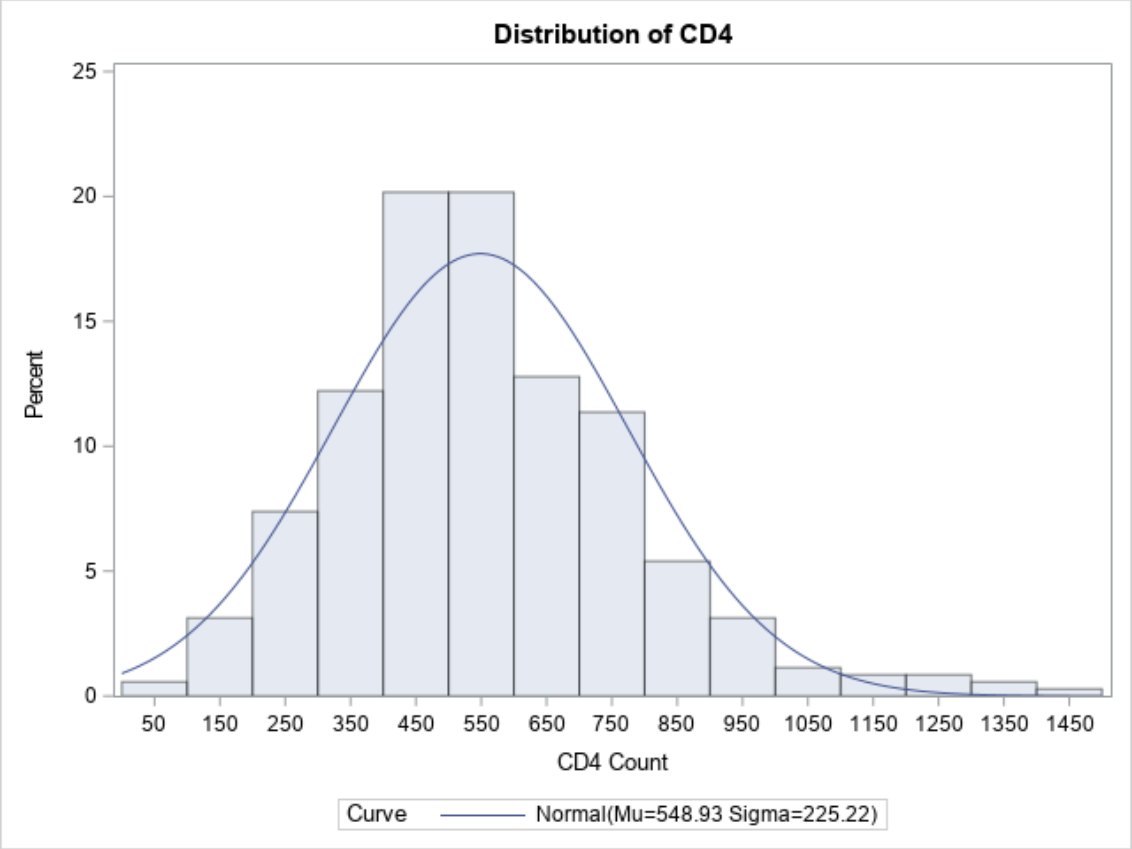


Figure 6: Histogram of CD4 Count for a Sample of Women (n=352) Living with HIV in Greater Gaborone, 2016.

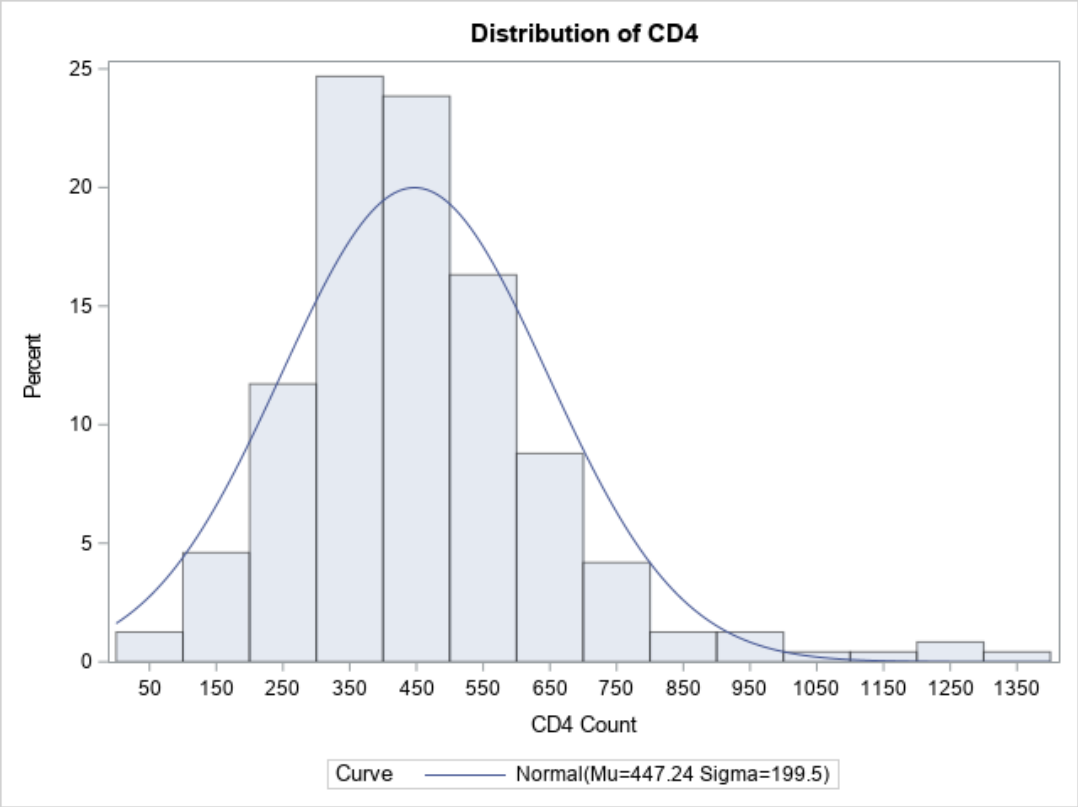


Figure 7: Histogram of CD4 Count for a Sample of Men (n=239) Living with HIV in Greater Gaborone, 2016.

By age, older women had the highest mean CD4 count (566.27 copies/ml) followed by younger women (18-29) with 555.09 copies/ml. The women mode (reoccurring CD4 count was 400 copies/ml across all ages except for those aged 30-39 years. For men, the age group 30-39 had the lowest mean CD4 count 428.68 followed by those aged 50+ at 429.81 copies/ml (Table 12). Unlike the women, men had the lowest mode of 200 copies/ml which was followed by 300 copies/ml, still lower than the women's lowest. Younger males (20-29) had the highest mean CD4 count and mode compared to males of all ages (Table 12).

Table 12. Descriptive Statistics of CD4 Count for Sample of Women[1] (n=352) and Men (n=239), Greater Gaborone, Botswana, 2016.

Sex by Age	N	Mean	Median	Mode	Range	Standard Deviation
Women	352	548.93	522.00	400.00	1405	225.21
Ages 18-29	65	555.09	532.00	400.00	1251	249.72
Ages 30-39	117	542.59	523.00	391.00	1204	232.72
Ages 40-49	114	543.40	523.00	400.00	1278	208.62
Ages 50+	56	566.27	501.50	400.00	9325	216.78
Men	239	447.23	415.00	400.00	1276	199.49
Ages 20-29	30	470.33	447.00	400.00	690	149.88
Ages 30-39	**60**	**428.68**	**399.00**	**200.00**	**1276**	**198.75**
Ages 40-49	90	463.33	418.00	400.00	1156	195.51
Ages 50+	**59**	**429.81**	**380.00**	**300.00**	**1141**	**227.82**

[1]Excludes women on PMTCT (n=67).

Men aged 30-39 (n=60) had low CD4 count due to being sick in the last 2 months (b-99.39 p 0.0092) and taking other drugs (b-98.74 p 0.04). Their CD4 count increased only when they had a healthy BMI and being initiated on ART before 2012 (Table 13).

Table 13. Linear Regression Adjusted Estimates of CD4 Count for a Sample of Men 30-39 Years (n=60) Living with HIV, Greater Gaborone, Botswana, 2016.

CD4 Count	**Estimate**	**Standard Error**	**t-value**	**Pr > [t]**
Intercept	584.19	35.35	16.52	<0.0001
Taking Other Drugs	-98.74	47.74	-2.07	0.0404
Sick in Last 2 Months	-99.39	37.65	-2.64	0.0092
Mean BMI	9.28	2.76	3.35	0.0010
ARVs Initiated < 2012	89.33	36.24	2.46	0.0149
Viral Load	-0.03	0.04	-0.73	0.4639

Model: df (5), F value=7.35, Pr>F <0.001

R-Square = 0.205, Coefficient Variation = 39.21, Root MSE = 219.10 (CD4 Mean=558.83).

Table 14. Health Profile of Men 30-39 Years (n=60).

Illness	Taking Medications		Recent Sick
	Yes	No	Yes
Hypertension	8	3	0
Tuberculosis	3	0	3
Anemia	4	3	1
Body Pains	1	9	1
Other	12	13	5
Total	28	28	10

For males aged 40-49 (n=124), their low CD4 count was due to high viral load (b-0.11 p 0.0032) (Table 15).

Finally, for males aged 50+ (n=56) was mainly to their single status (Table 16; Figure 8).

Table 15. Linear Regression Adjusted Estimates of CD4 Count for a Sample of Men 40-49 Years (n=124) Living with HIV in Greater Gaborone, Botswana, 2016.

CD4 Count	Estimate	Standard Error	t-value	Pr>[t]
Intercept	547.14	35.51	15.41	< 0.0001
Mean BMI	4.71	2.57	1.83	0.0698
ARVs Initiated < 2012	85.53	37.51	2.28	0.0244
Viral Load	-0.11	0.04	-3.00	0.0032

Model: df (3), F value=6.62, Pr>F <0.0004

R-Square = 0.141, Coefficient Variation = 37.03, Root MSE = 203.29 (CD4 Mean=548.91).

Table 16. Linear Regression Adjusted Estimates of CD4 Count for a Sample of Men 50+ Years (n=56) Living with HIV in Greater Gaborone, Botswana, 2016.

CD4 Count	Estimate	Standard Error	t-value	Pr>[t]
Intercept	833.71	76.39	10.91	< 0.0001
Single vs. Cohabiting	-303.21	84.34	-3.60	0.0009

Model: df (1), F value=19.92, Pr>F 0.0009

R-Square = 0.259, Coefficient Variation = 34.55, Root MSE = 202.14 (CD4 Mean=584.92).

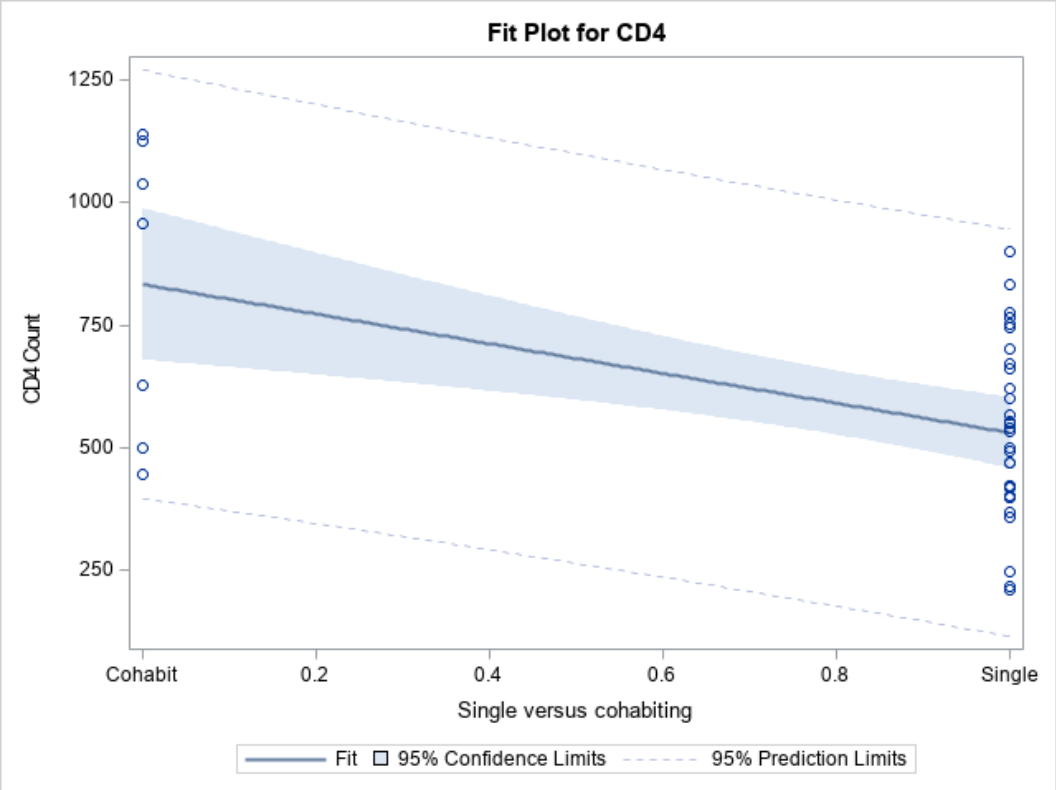


Figure 8: Fitted Plot of CD4 Counts for a Sample of Men 50+ Years (n=56) Marital Status Single vs. Cohabiting, Greater Gaborone, Botswana, 2016.

2.7. DISCUSSION

By life course of how many years a patient can survive without ART post HIV diagnosis, results showed that men turned to survive a longer time than women. For both the women and men, majority were diagnosed with HIV during their reproductive years. There were no women who were born with HIV or diagnosed as infants. Using CD4 count to assess the disease progression, women experience higher CD4 counts compared to men at all life-course stages, except those women aged (30-39 years) with delayed ART initiation. Women and men in their young adult and adult years of life generally respond to ARV treatment when initiated as evidence by a rising CD4 count. In contrast, women and men in their older and oldest stages of life respond less well to ARV treatment with increasing delays as also evident by a lower of CD4 counts. This implies that women are at more risk of acquiring HIV later in their life.

This study also uncovered that non ART adherence was (34%) among adult women (n=122) and men (n=110; 99 being men aged 30 and above) in Greater Gaborone. Men were further found out to have higher non- adherence rates (46%) compared to women (29.1%). In other studies, female gender has been shown to be associated with lower rates of ART adherence across several sub-groups (Tapp et al,2011; Berg et al., 2004; Krawczy et al., 2006; Anderson and Mitchell, 2000). Age was found to be an inhibiting factor when it came to adherence. Men aged 30+ showed to have the highest risk of non-adherence to ART when compared to women of all ages. Men aged 50+ had the highest odds of being non-adherent. Women across all ages were at a low risk of being non-adherent particularly women aged 50+. In Botswana, the age group 30-39, is the one with the highest HIV prevalence (BAIS IV, 2013). The same was observed in this study, and they were the same cohort that had low adherence levels. This age cohort is the working labor as well as the reproductive group, so if they are too sick and cannot work and care for their family, it is detrimental to the economy of Botswana. They are also at high risk of infecting their new babies (women) if they do not take the medications as instructed. Sexual behaviors showed that there were still both women and men who had more than two sexual partners in a year and condom use was minimal even though they obtained the condoms free from public health facilities (Table 6). This shows that a lot must be done particularly with the men who usually tend to seek treatment late as they view health issues as women issues. Self-testing and assisted partner notification remain important but under-utilized methods to increase HIV diagnoses among men (UNAIDS, 2018).

Women and men who lived in rural areas and peri-urban had high levels of non-adherence compared to their urban counterparts (Table 7). Locational and other demographics and socio-economic factors were associated with non-adherence in this study. Majority of the women were unemployed (41.1%) and about a quarter was non-adherent. Female unemployment rate in Botswana is higher (19.1%) than that of their male counterparts (16.3%) (Statistics Botswana, 2016). The Botswana Multi Topic Household Survey of 2015/16 survey estimated youth aged between 15 and 35 years' unemployment at 25.2%, with female

unemployment higher at 26.9% compared to 23.6% for males (Botswana Multi Topic Household Survey, 2016). Unemployment can drive young women to risky behaviors of transactional sex. Other factors such as being single (marital status) showed to be a constraining factor for older men aged 40-49. The lack of social support could be contributing to non-adherence. These findings were corroborated by other studies where social structural factors included low levels of social support (Yang et al., 2018), high-unemployment (Charurat et al., 2010) and poverty. In Bezabhe and colleagues study (2014), patients cited unemployment, food insecurity, religious rituals such as fasting as their main concerns related to non-adherence (Bezabhe et al., 2014).

This study also found that biological factors played an important role in ART adherence. When a patient was healthy (normal weight BMI) and had low viral load, ART initiated before 2012, high levels of adherence were observed. As previously mentioned, at the time of this study, (2016), CD4 count of below 350 copies/ml was used. To achieve viral suppression then becomes a difficulty because at this vulnerable stage, the patient is prone to opportunistic infections such as Tuberculosis (TB). Males aged 30-39 in this study showed that being sick of different illnesses and taking other drugs decreased CD4 count significantly. Having a high viral load was a risk factor for males aged 40-49. Several authors corroborated this study finding that taking medication every day is a challenge for anyone with any additional chronic illness such as diabetes and hypertension as they took their ARVs only about 70% of the time (Hashmi, 2007; Martin, 2005; Brown, 2011; Charurat et al., 2010).

2.7.1. Limitations

The participants were geographically located in the southern part of Botswana, which contains urban, peri-urban and rural areas; however, since Gaborone is the capital city and circular migration happens from Gaborone, the study area may not be representative of Botswana as a whole. Nevertheless, this study utilized an adherence measure to evaluate the levels of non-adherence among adult men and

women that was sensitive in capturing non-adherence behavior and biological confirmation. In terms of survey responses, response bias could be a potential limitation because the participants could have provided answers they thought the principal researcher would like to hear. There could also be issues of recall bias because patients were asked to self-report how they took their medication. Another potential limitation is that the study interviewed only patients on ART and did not include patients lost to follow up/discontinued ART. It is possible that those patients were non-adherent and not attending their monthly appointments. This limitation would underestimate non-adherence levels in the study area.

2.8. CONCLUSIONS AND RECOMMENDATIONS

The current study demonstrated that male gender presents an additional barrier for adherence to ART among patients in Greater Gaborone, independent of other socio-behavioral, structural and clinical characteristics. This is evidence that even within a context where medical care and ART are provided free to HIV-positive individuals, there remain important healthcare access differences between male and female. Other socio-structural factors are also critically important in affecting adherence, and men often face barriers derived from their comorbidities and lack of social support. In order to improve adherence to ART among men and women, gender-specific interventions should be developed which recognize these unique barriers. Low adherence rates were mainly due to CD4 count particularly among the men. CD4 count is an important factor in monitoring the healthy immune system of an HIV patient and if its low it can be an indicator that the medication is not working well. There is a need to educate men about the importance of taking their medications as prescribed because it will improve their viral suppression which in turn will minimize the new infections. Life course in HIV diagnosis and the length of time survival with ART showed that men in the study area tended to survive longer compared to the women. Furthermore, both genders were diagnosed with HIV in their reproductive ages implying the increase in new HIV infections in Botswana. The government of Botswana has made good progress in providing ART, condoms and safe male circumcision free of charge to people living with HIV. All these efforts are commendable

but without high levels of ART adherence, HIV/AIDS will never be kept in check because viral suppression will not be reached. The consequences of this effect are that new infections will grow rapidly as the treatment as prevention strategy will be failing. Education (following medication instructions and awareness) is the most important aspect in the HIV/AIDS /ART matrix because if people hear and understand particularly older men, change can be guaranteed, and the 90-90-90 goals will be successfully reached in Botswana by 2020 as the UNAIDS stipulates.

Future directions will be to understand the matrix of gender and age in non-adherence to ART. Results showed that older males had highest rates of non- adherence when compared to females of all ages. This shows that more needs to be done to reduce the non-adherence rates because in the era where treatment is used as prevention, viral suppression should be reached. The older males have the potential to pass the virus to the females in the intergenerational sexual relations. When females of reproductive ages are infected, an extra burden is incurred because they risk passing the disease in cases of pregnancy and breastfeeding. This further emphasize the need to study the HIV life course to understand the disease progression. There is a need to study the adherence levels of PMTCT to eliminate new infections in children.

CHAPTER 3: Prevention of Mother-to-Child Transmission (PMTCT) Adherence and HIV status disclosure in Pregnant Women and New Mothers in Greater Gaborone

3.0. INTRODUCTION

Comprehensive programmes for prevention of mother-to-child transmission of HIV (PMTCT) including ARV therapy and prophylaxis are current measures used to significantly reduce the number of infants who are living with HIV and promote better health for their mothers and families (Government of Botswana, 2015). PMTCT remains central to global HIV initiatives because international organizations such as the World Health Organization [WHO] and Center for Disease Control [CDC] as well as national governments are working together to build PMTCT capacities and achieve the global goal of reducing the HIV incidence rates among infants. National PMTCT programmes provide an important foundation for HIV prevention and treatment programmes. The Ministry of Health in Botswana has found out that the main reason for low rates of infant HIV testing is that early infant diagnosis is too centralized, with the only center in Gaborone (National AIDS Coordinating Agency [NACA], 2015). As of 2015, there were plans of opening a second testing center in Francistown (second city of Botswana) and to roll out to four additional sites. A Sexual Reproductive Health (SRH)-HIV linkage project that was piloted in three districts and will be rolled out to all facilities nationwide to improve family planning for women, within the context of HIV in the near future (NACA, 2015). Benefits of this strategy is that it will increase the capacity of health facilities to cater for the SRH rights of HIV positive women and also specifically targets males to become more involved in SRH issues including partner testing and antenatal care. In addition, the Ministry of Health and Wellness is currently pursuing the treatment of all HIV+ pregnant women with triple antiretroviral therapy (ART), regardless of cluster of differentiation [CD4] count, hence adoption of Option B+ (Ministry of Health and Wellness, Botswana [MoHW], 2015). According to WHO (2010) “Option B+ is a prevention of vertical transmission approach for expectant mothers living with HIV in which women are immediately offered treatment for life regardless of their CD4 count (WHO, 2010)”. Even though, Option B+ is a great step towards eliminating vertical transmissions, Ebuy and Colleagues (2015) caution that with Option B+

PMTCT, as the current alternative, due to prolonged exposure to ART, high levels of non-adherence may arise for HIV -infected pregnant women (Ebuy, Yebyo and Alemayehu, 2015).

3.1. PURPOSE OF STUDY

To investigate barriers to PMTCT adherence and their potential impact(s) on immunodeficiency (as a reflection on HIV transmission) for pregnant women and new mothers in Greater Gaborone, Botswana. The participants in this study included a sample of (n=67 pregnant and new mothers enrolled on PMTCT) and 84 health workers at 21 government clinics, in urban, peri-urban and rural areas of Greater Gaborone. To compare non-adherence levels among mothers and non-mothers, a sample of all women (n=419) was also used. This women sample is explained in detail how it was derived elsewhere (Chapter 2). The findings from this study are used to create awareness of the WHO guidelines that recommend couple HIV counseling and testing which provides an opportunity for partners to test together thus enabling provider-facilitated disclosure and linkage to care if either partner is HIV-infected.

3.2. BACKGROUND

3.2.1. Maternal and Child Mortality in Botswana

In 2017, there were 52,358 live births, of which 52,242 were hospital births, representing 99.8 % of all births in Botswana. Maternal mortality ratio has declined from 156.6 deaths per 100,000 live births in 2016 to 143.2 deaths per 100,000 live births in 2017. There were 75 maternal deaths in 2017 in Botswana classified into direct and indirect causes (Botswana- Maternal Mortality Ratio, 2017). Overall, 76.0 % of all maternal deaths were due to direct causes, while the remainder were due to indirect causes. The leading direct cause of maternal mortality was genital tract and pelvic infection following abortion and ectopic and molar pregnancy which accounted for 20.0% of all maternal deaths, followed by diseases of the circulatory system complicating pregnancy, childbirth and the puerperium at 10.7%, severe pre-eclampsia with 8.0% and rapture of uterus during labor at 8.0% (Botswana- Maternal Mortality Ratio, 2017). On the other hand, diseases of the circulatory system complicating pregnancy, childbirth and the puerperium

were the leading indirect cause of maternal deaths (Botswana- Maternal Mortality Ratio, 2017). The highest maternal deaths were 24 (32.0%) reported among age groups 35-39, followed by ages 30-34 (20.0%), 20-24 with 16%, 25-29 with 14.7% and lastly age-groups 15-19 and 40-44 with 8.0 % respectively (Botswana- Maternal Mortality Ratio, 2017). No case of maternal death was reported for ages 45 and over in both direct and indirect causes. Diarrhea, pneumonia, septicaemia, and severe protein-energy malnutrition are the major causes of deaths among infants in Botswana. Latest statistics of 2016 show that under-5 mortality in Botswana was 28.1, child mortality rate at 11 and infant mortality per 1000 live births was 27 (Statistics Botswana- Selected Statistical Indicators 1966-2016).

3.2.2. ART and PMTCT Programme in Botswana

"The client undergoes an HIV test after counselling, if she is HIV positive blood will be drawn to check her CD4 count. If her CD4 is less than 350 she will be initiated on ART for her own health benefit. But if the CD4 is above 350 she will be taking HAART for prophylaxis reason to transmission risks to the infant. Her partner will also receive HIV counselling concerning their HIV status, available medical care for themselves and their families. HIV exposed babies will be given prophylactic treatment to reduce the transmission rate. And their mothers will be counselled on two breastfeeding methods, including exclusive breastfeeding and exclusive formula feeding. If she chooses exclusive formula feeding she will be provided with free infant formula until the baby is a year old. The baby will be tested for HIV at six weeks using dry blood spots (DBS) for Polymacros Chain Reagent (PCR). The baby will also be given crotrimazole preventive therapy until 12 months or when tested negative for HIV. Confirmatory test will be done immediately when the child is positive. If negative, repeat testing will be done at 18 months using rapid test. All HIV positive infants whether symptomatic or not will be referred to the ARV programme for ART services provided in the programme" (MoHW, 2011).

Prompt and accurate HIV diagnosis in pregnant women is essential for referral for Triple ARV Prophylaxis (TAP), as well as for the mother's health. All pregnant women must be tested for HIV as matter of priority

(MoHW, 2012). All pregnant women in Botswana who test HIV positive must immediately have blood collected for CD4 count to determine ART eligibility status. Regardless of CD4 count, all pregnant HIV-infected women qualify for Triple ART Prophylaxis during their pregnancy, therefore, all women found to be HIV-infected should be immediately referred to local PMTCT services (MoHW, 2012). According to the Ministry of Health and Wellness in Botswana, the absolute number of women who newly tested HIV positive has declined from 14,058 in 2011 to 11, 845 in 2014 (MoHW, 2015). Re-testing at the third trimester of the pregnancy (36 weeks) among pregnant women remained below 2% in the reporting year of 2014 (MoHW, 2015). There was a repeated decrease in the number of pregnant women who received ARVs in 2014 at 90.8% (11,845) of HIV-positive pregnant women received ARV medicine to reduce the risk of mother-to-child transmission compared to 95.9% in 2013 (MoHW, 2015). In the years of 2015 to 2017, the uptake remained unchanged at 95%.

3.2.3. Challenges to PMTCT in Sub Saharan Africa and Botswana

Studies that investigate PMTCT adherence levels and challenges generally fall into three areas: patient-centered barriers, social-structural barriers, and service-centered barriers.

Patient-Centered Barriers include Ochigbo (2013) who conducted a prospective cross sectional study using semi-structured questionnaire to determine the level of adherence among HIV infected pregnant women on PMTCT antiretroviral therapy in Area W Clinic, Francistown Botswana (Ochigbo, 2013). A total of 61 pregnant women participated in the study and were all within three to nine months' gestation, and had been enrolled in the PMTCT program at least more than one month previously. Assessing their demographics, a majority (75%) of the sample were between 26 and 42 years, 90% were single, 81% had attained secondary school education, and 60% were unemployed. Adherence levels were considered optimum if greater than or equal to 95%. Ochigbo (2013) found that the reported optimum adherence levels were 84% by virtual analogue assessment, 82% by pill count and 98% indicated that they did not miss any dose during the last three days before the interview (Ochigbo, 2013). The factors influencing

non-adherence from the study were pregnancy-related illnesses, medication side effects, and month of pregnancy of the patient as participants tended to adhere less as they got closer to delivery (Ochigbo, 2013). The author recommended care-givers should carefully monitor patients for these factors, and to carry out continuous adherence counselling with special attention given to those approaching delivery in order to improve overall adherence to PMTCT therapy. He further stated that even though adherence levels to PMTCT therapy among the population sampled were high, more could be with interventions designed to cover and improve the highlighted areas in the implementation of the preventive therapy (Ochigbo, 2013).

It is evident that there are a number of individual and structural barriers to PMTCT adherence in Botswana. HIV testing is only offered on week days, and this means that there are high chances of missed opportunities to test pregnant women especially in labor and delivery over the weekend because health care auxiliary personnel is off-duty in the evenings and during weekends (MoHW, 2017). Due to the disintegration of SRH and ART services, almost 99% of health facilities still initiate ART at infectious disease care clinics (IDCC) and not at the sexual and reproductive health (SRH) or antenatal (ANC) sections, contributing to delays to treatment (MoHW, 2017). Offering PMTCT late to pregnant women is detrimental because it exposes the unborn baby to HIV infection. The other concern is that there are some hospitals that do not keep ARVs in labor and delivery sections, hence late or non-bookers receive. There are inadequate skills on pediatric treatment initiation by medical officers in Botswana due to the complex systems/services involved in PMTCT therapy. There is still high stigma attached to infant formula feeding where by women still breastfeed their infants even when they are not on treatment to “fit” in the society (Botswana Stigma Index Survey, 2013). There is evidence of low rates of testing among partners of pregnant women enrolled in PMTCT at 19% in 2015, 18% in 2016 and further decline to 16% in 2017 and inadequate involvement of communities and civil society organizations is a challenge. This is mainly in part due to lack of HIV status disclosure of HIV pregnant woman and new mothers to their sexual partners

and family members. Disclosure of HIV status by women living with HIV to their sexual partners is important for the success of PMTCT as a comprehensive program (Rujumba et al., 2012).

Social Structural Barriers for women living with HIV in Sub-Saharan Africa face significant challenges including stigma and disclosure, hunger, cultural factors, lack of accurate health information, lack of social support, medication side effects and overcrowded health systems when seeking HIV care and adhering to antiretroviral therapy (Mepham et al., 2011). Although there is evidence of these noted challenges, studies on challenges facing pregnant women when taking ART for prophylactic purposes in Sub - Saharan Africa is limited. Maintaining adherence to ART over time is a challenge in many settings also in Sub-Saharan Africa where the average 24-month retention rate in ART programs 2007–2009 was found out to be 70% (Fox and Rosen, 2013). Some studies in the region have identified social, cultural and economic barriers to antenatal and postnatal adherence to ART over time (Kirsten et al., 2011; Nachega et al., 2012; Mepham et al., 2001; Nassali et al., 2009; Duff et al., 2010). Low levels of adherence have both individual and structural disadvantages because poor adherence to ART leads to virologic failure, increased risk of MTCT and a high risk of drug resistance that may require a change to more expensive treatment regimens (El-Khatib et al., 2011; Ramadhani et al.,2007; Bennett et al., 2012; Hamers et al., 2013).

A sample of 501 pregnant HIV-1-infected women in Dar es Salaam, Tanzania participated in a study called Mitra Plus (Ngarina et al., 2013). It was an open-label, non-randomized, prospective PMTCT study where participants were initiated on triple ARV drugs from 34 weeks of pregnancy until six months post-delivery (the breastfeeding period). Women enrolled with CD4 cells < 200/ml were put on ART for life and received significant adherence counseling and support in addition to transport incentives, free medical services including management of opportunistic infections, as well as formula or food supplements for their children after stopping breastfeeding if needed (Ngarina et al., 2013). At the end of the study in 2009, viral load testing showed that, in contrast to women's self-reported adherence, a high proportion of the women enrolled on ART for life had high viral loads at one and two years after delivery (Ngarina et al.,

2013). A semi-structured open-ended interviews to explore women own perceived barriers to adherence to ART post-delivery and after the cessation of breastfeeding was conducted to investigate factors associated with better drug adherence among women in need of ART. Results showed that lack of motivation to continue ART after weaning the child, poverty and stigma were factors inhibiting uptake (Ngarina et al., 2013). The authors recommended that projects that simultaneously address stigma, poverty and women's lack of empowerment may be integrated with PMTCT and ART services to reach their full potential (Ngarina et al., 2013).

Elwell (2016) conducted a qualitative study using interviews and focus groups to explore factors influencing women's adherence within PMTCT programs in southern Malawi (Elwell, 2016). Participants included current PMTCT patients, healthcare providers, community leaders, and patients who had dropped out of the program ("defaulters"). Data were analyzed using content analysis and results showed that barriers to PMTCT uptake included fears of HIV disclosure to husbands, community-based HIV/AIDS stigma, and poor interactions with some health workers (Elwell, 2016). Facilitators of PMTCT adherence included the improved survival of PMTCT patients in recent years and the desire to remain healthy to care for one's children (Elwell, 2016). The author recommended that to improve access to medical care for PMTCT patients, there should be integrated services to increase attention to confidentiality and minimize stigma, shared HIV testing and counseling for couples, and peer-led support groups to provide social support from other women with the shared experience of an HIV-positive sero-status (Elwell, 2016).

The "Kesho Bora Study" is a multicenter PMTCT trial in Sub-Saharan Africa evaluating the PMTCT efficacy of triple therapy until cessation of breast feeding compared to short course zidovudine monotherapy in a predominantly breast feeding population (Mepham et al., 2011). To further explain variations during objective adherence assessments, a sub-study was conducted at one site (Kwa Zulu Natal, South Africa) to examine the underlying adherence issues in 100 enrolled Zulu women. Information was supplemented

by unstructured, free-ranging interviews conducted by trained adherence counsellors on 43 consecutive women attending the trial clinic over a two-week period (Mepham et al., 2011). Authors defined adherence as good at (>95% adherence), or poor (<95% adherence). Participants indicated that their poor adherence was due to therapy misconceptions/misunderstandings, ARV use by relatives, domestic violence, poverty and issues relating to disclosure and stigma (Mepham et al., 2011). About 61.0% (57/94) of antenatal women had good adherence with their PMTCT prophylaxis, with no significant difference shown between those taking the long and short course (Mepham et al., 2011).

Simoni et al. (1995) and Kalichman (2003) have shown that women who disclose their HIV status is in part to reduce stress and increase access to social support (personal reasons) and to maintain honesty in relationships as well as protecting others from infection (interpersonal level) (Visser et al., 2008). In a study conducted in Johannesburg, South Africa on HIV pregnant women, the main reason for HIV status disclosure was for the infant well-being such as breastfeeding avoidance (Varga et al., 2006). Other studies done in Africa have shown that lack of HIV status disclosure to partners among women living with HIV inhibited the success of PMTCT program. In southern Malawi, Elwell (2016) conducted a qualitative study using interviews and focus groups to explore factors influencing women's adherence within PMTCT programs (Elwell, 2016). Participants included current PMTCT patients, healthcare providers, community leaders, and patients who had dropped out of the program (“defaulters”). Data were analyzed using content analysis and results showed that barriers to PMTCT uptake included fears of HIV disclosure to husbands, community-based HIV/AIDS stigma, and poor interactions with some health workers (Elwell, 2016). Facilitators of PMTCT adherence included the improved survival of PMTCT patients in recent years and the desire to remain healthy to care for one's children (Elwell, 2016). The author recommended that to improve access to medical care for PMTCT patients, there should be integrated services to increase attention to confidentiality and minimize stigma, shared HIV testing and counseling for couples, and peer-led support groups to provide social support from other women with the shared experience of an HIV-

positive sero-status (Elwell, 2016). Other studies have documented the fear of stigma and abandonment (Mokhoka, 2000; Medley et al., 2004; Awiti et al., 2011; Varga et al., 2006; Visser et al., 2008; Rujumba et al., 2012), loss of economic and emotional dependency (Varga et al., 2006; Maman et al., 2003; Larsson et al., 2011; Visser et al., 2008; Rujumba et al., 2012) and risk loss of control over ones' secret (Varga et al., 2006).

Kebaabetswe (2007) argued that the existing belief that affordability of antiretroviral drugs offered to developing countries, does not translate to utilization for the Prevention of Mother-to-Child Transmission of HIV Program in Botswana (Kebaabetswe, 2007). Botswana government offers free counseling, testing, antiretroviral drugs and infant formula for babies born to infected mothers and yet there are some women who not utilizing the program to protect their infants. She conducted a qualitative study on factors that facilitated and prohibited pregnant women from participating in the PMTCT program in Gaborone, Botswana. Forty subjects (ten HIV-positive pregnant women who accepted the program, eleven who rejected the program, nine PMTCT health workers and ten key informants) participated in in-depth interviews (Kebaabetswe, 2007). Using thematic content analysis found uptake barriers to the uptake included the fear of knowing one's own HIV status, infant feeding distribution stigma, lack of male partners' support and negative attitudes of health workers. Reinforcing factors included availability of free antiretroviral drugs and free infant formula (Kebaabetswe, 2007).

Clinical Services-Related Barriers include non-adherence to guidelines and recommendations made by PMTCT programs is a problem faced by both healthcare providers and HIV-infected women (Mofenson, 2010; du Plessis et al., 2014; Gamell et al., 2013; Spangler et al., 2014). Other problems were late presentation for health care delivery service during pregnancy, inadequate ante-natal visits, poor opportunistic infection screening, non-disclosure of HIV-positive status to partners, and inadequate family planning counseling (du Plessis et al., 2014; Bucagu et al.,2013; Mnyani et al., 2014). Low HIV testing rates during pregnancy, suboptimal healthcare coverage, and poor patient retention are among the issues

experienced by a lot of health institutions in Sub Saharan Africa (Prendergast et al., 2015; Adetokunboh and Oluwasanu, 2016). The accessibility to continuous care for HIV-infected mothers during the post-natal period and Early Infant Diagnosis (EID) for HIV-exposed infants are both low (Mugasha et al., 2014; Adetokunboh and Oluwasanu, 2016). Due to this loss of continuity in health care, there are high cases of delayed testing of HIV-exposed infants, which delays initiation of ART, and results in missed perinatal care opportunities (Lilian et al., 2013; Adetokunboh and Oluwasanu, 2016). Cultural practices were associated with a risk of mixed infant feeding as a result of feeding preferences and poor maternal adherence to recommended infant feeding guidelines (Lawani et al., 2014; Adetokunboh and Oluwasanu, 2016). In a South African hospital, Feucht and colleagues (2014) found that access to HIV services prior to conception, family planning, tuberculosis screening, HIV disclosure, psychosocial support, and post-natal care were not integrated within the PMTCT services and there has been an overall deterioration in consistent infant feeding messages conveyed to HIV-positive women (Feucht et al., 2014). Plans to involve men in PMTCT services were limited to mostly HIV testing and counseling with minimal provision for men treatment, care and support and all these tended to alienate them rather than sustaining their involvement (Sherr and Croome, 2012; Adetokunboh and Oluwasanu, 2016).

3.2.4. Reoccurring Barrier to PMTCT: HIV Status Disclosure

3.2.4.1. HIV Status Disclosure

Varga and colleagues (2006) identified four disclosure forms. “The first two ‘voluntary’ and ‘involuntary’ disclosure speak to motivation: ‘Voluntary’ disclosure is the act of divulging one’s HIV-status through a decision made and undertaken without coercion. The individual is in control of when, how and to whom disclosure takes place. ‘Involuntary’ disclosure typically occurs when HIV-status is revealed without the individual’s permission or intent. The second two ‘direct’ and ‘proxy’ disclosure address mode: an individual who discloses in a straightforward manner illustrates ‘direct’ disclosure. Similar to the clue giving phenomenon described above, ‘proxy’ disclosure occurs when an action or association indirectly

suggests one's HIV status without it being openly articulated" (Varga et al., 2006 pg. 952-953). In their study, Visser and colleagues (2008), explained that disclosure of HIV status involves a series of steps of decision making. These include (1) coming to terms with the HIV diagnosis, decision on the appropriateness of disclosing to a particular person, weighing the anticipated impacts and then choosing the appropriate situation for disclosure (Visser et al., 2008).

3.2.5. Constraints and Promoters of HIV Status Disclosure of Women

HIV status disclosure serves as an important prevention strategy in prevention of mother to child transmission (PMTCT) and enhances adherence to key PMTCT interventions (Madiba and Letsoalo, 2013). Disclosure also leads to increased utilization of preventive strategies and allows an individual to get partner or family support for preventive actions they may decide to undertake (Mucheto et al., 2011; Stirratt et al., 2006). It has been documented that women are more likely to adhere to PMTCT interventions when they have the support of their sexual partners (Medley et al., 2004). However, in order to receive support, the women must disclose their HIV-positive status (Stirratt et al., 2006; Madiba and Alaetsoalo, 2013). Women who hide their HIV status are less likely to adhere to PMTCT interventions and might put their children at risk because they may be unable to take antiretroviral therapy (ART) until delivery (Madiba and Letsoalo, 2013), fail to give nevirapine syrup to the infant for recommended duration, and fail to adhere to the exclusive infant feeding option they selected (Kebaabetswe, 2007; Olagbuji et al., 2011; Rujumba et al., 2012). The importance of disclosure in the prevention of vertical transmission of HIV makes it a fundamental topic for inclusion in counseling HIV pregnant women in the PMTCT program (Baek et al., 2009).

Partner disclosure is a central concept in PMTCT programs (Njunga and Blystad, 2010) and the success of PMTCT interventions requires the support of the woman's partner and other members of her family (Igwegbe and Ugboaja, 2010). However, in Southern African countries such as Botswana and South Africa, the HIV positive pregnant woman is often considered to be the primary target of PMTCT interventions

(Madiba and Letsoalo, 2013). For PMTCT to be fruitful, it is necessary to provide adequate information on PMTCT therapy to the general population, the family, the in-laws, and male partners of HIV-positive pregnant women (Madiba and Letsoalo, 2013). There is a need for transparency about HIV positive status within households to shape community norms on medication adherence, infant feeding, and couple testing.

In their qualitative study, Madiba and Letsoalo (2013) interviewed 25 HIV positive women enrolled in a prevention of mother to child transmission (PMTCT) program in Tshwane, South Africa. Four focus group interviews were used with each having at least seven participants. The women were included in the study if they were HIV positive and enrolled on PMTCT and their babies aged between 6 weeks and 6 months (Madiba and Letsoalo, 2013). Data was analyzed using thematic analysis through Nvivo8. Findings showed that 18 women were single and 7 married. Out of the 25, 10 women have disclosed HIV status to partners only, 8 to partners and close family members, 2 to close members and 5 have not disclosed to their family members (Madiba and Letsoalo, 2013). In addition, 19 women did not know their partners' HIV status (Madiba and Letsoalo, 2013). Women cited their reasons for disclosure as a way to gain support from family members to adhere to PMTCT. Moreover, women also disclosed to family members and friends they trusted. Women who have disclosed experienced various reactions from their partners. Findings showed that women received no support and others were abandoned by their partners (Madiba and Letsoalo, 2013). Other common reasons for non-disclosure were stigma, fear of rejection, protecting feelings of others and protecting then HIV status. For those women who disclosed to partner, they reported that adherence top PMTCT was easy. In conclusion, authors emphasized the need to develop interventions that address social and cultural contexts of HIV positive mothers to encourage HIV status disclosure in PMTCT programs (Madiba and Letsoalo, 2013).

In the longitudinal study conducted among pregnant women (n=390) attending rural antenatal clinics in Kenya, the aim was to explore the influence of HIV positive status (n=145) disclosure on women's use of

PMTCT and maternal health services (Spangler et al., 2014). Baseline questionnaires were administered in the woman's preferred language before the initial antenatal visit. Afterwards offered voluntary HIV counselling and rapid testing followed by post counselling and PMTCT services for those who tested positive. HIV positive status disclosure was defined as having disclosed to anyone; a male sexual partner; immediate family member and to other persons including friends, distant relatives and the community (Spangler et al., 2014). Chi-square test was performed to examine differences between women who reported using the services and those who did not. Bivariate logistic regression using STATA12 statistical software package) then followed to investigate associations of different HIV positive status disclosure categories with the use of antiretroviral drugs for PMTCT and birth in a health facility. Results showed that giving birth at a health facility was the highest among HIV positive women who had disclosed to anyone (49.0%). Those who have not disclosed had a lower rate at 21% ($p<0.001$). For the use of ARVs for PMTCT, HIV positive women (88.0%) who disclosed reported utilizing the service compared to 56.0% of those who had not disclosed. With regard to HIV status disclosure, n=72 (45.0%) of women disclosed to anyone, 44 (28.0%) nonexclusively to a male partner, 32 (20.0%) to a family member and 19 (12.0%) to another person (Spangler et al., 2014). When comparing women who had disclosed to anyone versus those who did not, they were 5 times more likely to use ARVs during pregnancy and 4 times likely to give birth in a health facility. Nonexclusive disclosure to a male partner was significantly associated with ARV use and birth in a health facility. In conclusion, authors highlighted that disclosure of HIV positive status may become critical for adherence to PMTCT programs and disclosure assistance should take into consideration women's social, economic and medical needs (Spangler et al., 2014).

In another Kenyan study, a case-control design was used among 180 mother-baby pairs with HIV-exposed infants. Thirty-six pairs with HIV positive babies (cases) were compared to 144 pairs with HIV negative babies (controls) to investigate whether the failure to disclosure an HIV positive status to a male partner was associated with increased risk of infant HIV acquisition and whether part of the association was

explained by the exclusion of male partner in PMTCT programs (Nyandat and Van Rensburg, 2017). Non-disclosure of HIV status to partner was defined as failure by HIV positive mother to tell her partner prior to learning the infant 's HIV status (it takes 6 weeks after birth for the baby to test accurately to HIV test). Student t-test and chi-square were used for data analysis as well as conditional logistic regression in SPSS, STATA and MPLUS statistical software. Results indicated that 17.0% (n=30) of the mothers in the mother-baby pairs had not disclosed their HIV positive status to their partners (Nyandat and Van Rensburg, 2017). A higher proportion of the cases had not disclosed their HIV status (52.8% vs 7.6%). Another finding was that low male partner involvement (18.3%) was partly responsible for the association between non-disclosure of HIV status on mother to child transmission. In conclusion the authors suggested that stakeholders need to re-examine the policies on disclosure and male partner involvement in an attempt to address the two behavioral contributors to mother to child transmission of HIV (Nyandat and Van Rensburg, 2017).

3.3. GOAL OF THE STUDY

The aim of this paper is to understand the constraining factors associated with PMTCT adherence among pregnant women and new mothers in Greater Gaborone, Botswana. The investigation is assessed through exploring CD4 count as a potential reflection on HIV transmission. Immunology (CD4 count) plays a role in understanding the adherence levels of the mother. For instance, if a pregnant woman/new mother shows decrease in CD4 count over time, it could be indicative of poor adherence. Non-HIV status disclosure among sexual partners can be a potential barrier to PMTCT adherence, hence the need to explore how marital status vary among those who do not disclose and also understand the reasons for non-disclosure among pregnant and post-partum mothers. To get a different perspective on HIV status disclosure, health care workers (n=84) from these study areas were interviewed. The use of mixed methods approach allowed for multiple perspectives and validation of findings (Varga et, 2006). Lack of HIV status disclosure,

do not significantly increase the risk of HIV transmission, however, declining trends in CD4 counts are suggestive of poor adherence levels to PMTCT for both partners.

3.4. THEORETICAL AND CONCEPTUAL FRAMEWORK

3.4.1. Health Belief Model

In this paper, the health belief model is undertaken as a theoretical framework to draw upon [lack of] HIV status disclosure of pregnant and mothers living with HIV and enrolled on PMTCT. The Health Belief Model (HBM) is a psychological model that attempts to explain and predict individual health behaviors by focusing on the attitudes and beliefs (Prochaska et al., 2002). The HBM was first developed in the 1950s by social psychologists Hochbaum, Rosenstock and Kegels working in the U.S. Public Health Services (Prochaska et al., 2002). The model was developed in response to the failure of a free tuberculosis (TB) health screening program (Prochaska et al., 2002) and from that time, HBM has been used to investigate a variety of long- and short-term health behaviors, including sexual risk behaviors and the transmission of HIV/AIDS (Cox, 2009; Lindsay, 2009; Odu and Akante, 2009; Tenkarang et al., 2009; Henderson, 2015). The HBM is based on the understanding that a person will take a health-related action (for instance, adhere to PMTCT therapy) if that individual feels that a negative health condition (disclose HIV status to partner in order to prevent infection to both unborn baby and partner) can be avoided, has a positive expectation that by taking a recommended action, she will avoid a negative health condition (that is, disclosing HIV status will lead to the partner being supportive), and believes that she can successfully take a recommended health action (disclose status so that she attends couple testing, takes the pills as recommended by doctor and attend clinic appointments). The HBM has four main constructs representing the perceived threat and net benefits being perceived susceptibility, perceived severity, perceived benefits, and perceived barriers (Prochaska et al., 2002). These concepts were proposed so as to account for people's readiness to act and a recent added concept, of self-efficacy, usually termed as one's confidence in the ability to successfully perform an action. It was added by Rosenstock and colleagues in

1988 to help the HBM better fit the challenges of changing habitual unhealthy behaviors, such as being sedentary, smoking, or overeating (Rosenstock et al., 1988). These concepts/constructs can then be linked back to knowledge that is accessible to those who design preventive strategies (Henderson, 2015).

Perceived susceptibility stipulate that an individual has his/her own perception of the likelihood of experiencing a condition that could negatively affect one's health and it varies widely in their perception of susceptibility to a disease. Those at low end of the spectrum are usual in denial of the possibility of contracting or even passing an adverse condition to others (HIV knowledge). Individuals in a moderate category admit to a statistical possibility of disease susceptibility. Those individuals at the high extreme of susceptibility feel there is real danger that they will experience a given disease (Prochaska et al., 2002). The second construct being the perceived seriousness analyzes the beliefs a person holds concerning the effects a given disease would have on one's state of affairs. For example, financial burdens, social stigma, and risk loss of control over ones' secret. Perceived benefits of taking action include taking a step toward the prevention of disease or toward dealing with an illness (in this case disclosure of HIV status) is the next step typically expected of individuals after they have accepted the susceptibility of a disease and recognized its severity and it is usually influenced by the beliefs regarding the action (Prochaska et al., 2002).

3.5. STUDY DESIGN

This study utilized an observational, cross-sectional survey (winter, 2016) with retrospective responses. The survey included closed-ended and open-ended questions implemented among pregnant women and mothers (n=67) living with HIV and enrolled on ART for PMTCT in urban, peri-urban and rural areas of Greater Gaborone. Both pregnant women and mothers were recruited because PMTCT continues after delivery thus calling for continuum in health care. The 67 women were taken as the main participants in this study, however, to understand the adherence levels among HIV positive women, all the 419 HIV

positive women attending 21 study HIV clinics and on ART in Greater Gaborone interviewed were included for comparative purposes only. Within these clinics, 84 health care workers were also surveyed for their perspectives in this study. The sampling methodology and mechanisms by which to optimize reliability and validity of the sample is described below.

3.6. DATA AND METHODS

3.6.1. Study Area

This study took place in the Greater Gaborone which is made of the Gaborone city (as its own district) and three surrounding districts, South East, Kgatleng and Kweneng East Gaborone alone has a total population of 231,592, while the larger metropolitan area has about 421,907 people (Botswana Census, 2011). During the country's decennial census of 2011, the HIV prevalence rates were found to be highest in the cities, followed by urban villages and lower in rural area hence the selection of the Greater Gaborone. Gaborone has seen growing trends of HIV prevalence rates because of its strategic location, its proximity to the railway line and Johannesburg, South Africa, its already established administrative offices, its accessibility to most of the major tribes, its non-association with any particular tribe, and most importantly, its closeness to a major water source of Gaborone Dam.

Gaborone and South East were in one district until recently (after the recent population census of 2011) when Gaborone became an independent district on its one (Statistics Botswana, 2015). About 13% of males age 18 months and above were HIV positive, 19.8% were female, which gave the total district HIV prevalence to be 17% (BAIS IV, 2013). About 19% of males age 18 months and above were HIV positive, 14.6% were female, which gave the total district HIV prevalence to be 16.6% (BAIS IV, 2013). There were 33,332 people enrolled on ART in Gaborone district as of February 2017. The patients were distributed across the 22 health facilities in the area (MoHW, 2017). South East district has a fewer ARV patients and clinics as compared to Gaborone with 4,659 people on ARV and six health facilities (MoHW, 2017).

Although the Kweneng East district is close to Gaborone, generally it experienced a modest growth of about three percent per annum between 2001 and 2011 (Statistics Botswana, 2015). A negative growth is usually due to outward migration, which is normally due to lack of employment opportunities in an area (Statistics Botswana, 2015). About 20% of males age 18 months and above were HIV positive, 22.1% were female, which gave the total district HIV prevalence of 21.5% (BAIS IV, 2013). There were 26,587 people enrolled on ART in Kweneng East district as of February 2017. The patients were distributed across the 30 health facilities in the area (MoHW, 2017). About 16% of males age 18 months and above were HIV positive in Kgatleng District, 23.8% were female, which gave the total district HIV prevalence to be 19.9% (BAIS IV, 2013). There were 11,028 people enrolled on ART in Kgatleng district as of February 2017. The patients were distributed across the 26 health facilities in the area (MoHW, 2017). Total fertility rates for the women across the district was 2.88 and the mean age at child bearing was 20 years in 2016 (Statistics Botswana- Selected Statistical Indicators 1966-2016).

3.6.2. Primary Data Collection

The data for this study were generated primarily from a survey administered to adult pregnant women and mothers who are living with HIV and enrolled on ART for PMTCT at public clinics (n=21) (face to face interview) (n=67), as well as a semi-structured interview of key informants who are health personnel working (n=84) at the study areas. The study was a retrospective cross sectional survey which took place in May-August 2016. The questionnaires were administered in Setswana (national) and English (official) languages to the participants. For inclusion criteria, only 18 and above women who were HIV positive and enrolled on ART for PMTCT therapy (WHO Option B+) at a public clinic took part in the study. The women had to also be pregnant or have a child who is at least 6 months and be on PMTCT program. Exclusion criteria, was that women younger than 18 and not on ART for PMTCT therapy be excluded from the study. The women were visited daily at their respective clinics until the maximum number of participants were reached. The questionnaires were administered by the principal researcher and four research assistants.

The principal researcher took a training with the MSU IRB while the research assistants who are all Botswana locals with a bachelor's degree were trained by the principal researcher with materials directly obtained from the MSU IRB. All the assistants are fluent in both the languages.

The self -administered questionnaire to pregnant women and mothers on PMTCT (see **Appendix B**) have 44 variables (with six sections) which ranged from demographics to the water related concerns in the medication. The questions on demographics and maternal characteristics (first three sections) that included annual income, partner HIV status, number of children and education were close ended questions. The remaining portions dealt with knowledge of HIV, treatment seeking behaviors, and water related concerns. These were more open-ended, allowing mothers (new and expectant) to provide detailed information. The sections on access a treatment seeking behaviors included PMTCT adherence questions ("Are you enrolled in PMTCT?" [Q19], "Have you ever missed your pill dosage at home because there was no water [Q33]?", Have you /baby ever missed doctor's appointment? [Q32]. When women came to the clinics, they were required to bring their medical report card and this is where their CD4 count and viral load information was retrieved. Only the latest records were extracted and used in the analysis of the data. The information acquired from the participants was coded and preprocessed and analyzed using descriptives in SAS 9.4 statistical software.

To get a different perspective on non HIV status disclosure and PMTCT adherence, key informants were chosen and a semi structured interview (n=31 variables) used. Their responses were coded and evaluated using thematic analysis method to generate informative themes that augment the survey data compiled from the patients. Their questions were all open-ended except for the demographics (first section) that included their qualifications, nationality and length at the health facility. The seven remaining portions dealt with accommodation (in terms of PMTCT access), adherence, education to the patients and community on PMTCT as well as water related concerns. All these questions were open-ended allowing

health providers to provide detailed Information (see **Appendix C**). Participants' occupation was coded as (doctor 1, nurse 2 and 3 [for the two nurses] and Pharmacist 4) before generation of themes for thematic analysis.

3.6.3. Sampling Methodology

The (n=21) clinics were purposively selected from the three geographies (urban, peri-urban and rural areas) in the four districts (Gaborone, Kgatleng, Kweneng East and South East) of Botswana. These districts were selected because of their high HIV prevalence rates, high number of ART/PMTCT facilities and the proximity to the researcher' residential place. From the urban area of Gaborone (n=5), peri-urban (n=5) and rural clinics (n=11) were selected. From all the clinics, a minimum of two pregnant and mothers who were living with HIV and on ART for PMTCT were purposively selected. The target was to get a total of 42 women (21 clinics * 2 women) from all the 21 clinics and this number was increased to 67 to account for under and over sampling. Every second pregnant and or mother to enter the clinic door or the waiting area, was selected. For the key informants, a total of four from each clinic (doctor, two nurses and a pharmacist [ARV dispenser] were selected. As mentioned earlier, the comparative sample of 419 women, sampling methodology is explained in detail from the previous work (Paper 1). No sampling was done on the key informants as the four mentioned are the ones that have daily and direct contact with mothers attending PMTCT clinics.

3.6.3.1. Reliability and Validity

Two questionnaires were pre-tested with two pregnant women enrolled on PMTCT in the urban clinic of Old Naledi clinic the day before the official start of all the survey data collection. This was done to check how long it took the women to answer questions and how they understood the contents as well as the language they preferred. These two questionnaires were not included in the analysis of the data. All the pregnant females and mothers were visited at their respective clinics at the same time for the duration of the study (from 7:30 am until 2:00pm). In addition to the principal researcher, four experienced research

assistants assisted with the data collection. These assistants were locals who were trained on IRB both from MSU and MOHW requirements and spoke both Setswana and English languages. Descriptive frequencies were run on all variables to inspect if they had enough values to perform statistical tests.

3.6.3.2. Ethical Review

Permission to conduct the study was sought from IRB MSU and Human Research and Development Committee (HRDC) from the Ministry of Health and Wellness in Botswana to ensure that all rights, dignity and safety of study participants were safe guarded. After satisfying the requirements of the MoHW IRB, to get into the different clinics, separate approvals were sought from the District Health Management Teams [DHMTs] in Botswana. MOHW provides primary health care services through DHMTs, which are responsible for running a network of health facilities. Participants were given information about the purpose and objectives of the study. The interviewers also read the consent form to all participants. This form provided information about the freedom to participate or withdraw at any given point during the study without any consequences. A written consent was obtained from all pregnant and mothers living with HIV and on ART for PMTCT who were willing to participate in the study. Confidentiality and privacy of respondents were given numbers as code identifiers (ID), rather than using the participants' names and actual addresses. Anonymity of respondents were assured by the use of codes (number ID) and aggregate analysis (relative addresses).

3.6.4. Descriptive Methods

To answer the posed research questions, 17 variables from the questionnaire were used. These were categorized into four groups being demographics, behavioral, physiological and geographical characteristics. These categories are important because PMTCT adherence is a complex measure that can be better understood by unpacking the individual's personal (biological and behavioral) and physical environment (place of residence) characteristics. From the 17, one behavioral variable (Know status) was a dependent variable. It was derived from question 14 (see **Appendix B**) which asked the women if they

disclosed their HIV status to their sexual partner. It was a dichotomous variable, where (Yes) indicated disclosure and (No) a lack of disclosure of HIV status. As shown earlier by the literature partner disclosure is a central concept in PMTCT programs (Njunga and Blystad, 2010) and the success of PMTCT interventions requires the support of the woman's partner and other members of her family (Igwegbe and Ugboaja, 2010).

3.6.5. Thematic Analysis

In addition, to the women living with HIV and enrolled on PMTCT data, health care workers were also interviewed to argument the findings from the mothers. Thematic analysis is a method for identifying, analyzing, organizing, describing, and reporting themes found within a data set (Braun and Clarke, 2006). To conduct a thematic analysis, six steps recommended by Braun and Clarke (2006) were followed. The first step was to familiarize oneself with the data. This stage involved entering the data from the paper questionnaires into SPSS software (IBM SPSS [2017] Statistics for Windows, Version 25.0. Armonk, NY: IBM Corpas) a database management, and running frequencies in SAS 9.4 Software (SAS Institute Inc., 2002-2012, Cary, NC, USA). Initial codes were generated by the clinics that women attended (rural or urban areas). The third step was to search for themes and tying back to the theory (Health Belief Model). Themes were then reviewed, where initially, four themes emerged based on the questions and the reoccurring terms that the health workers provided but after careful review, only two major themes with four sub themes were used. This reduction was done because even though there were four themes in the beginning, they were interrelated which made them seem repetitive. The fifth step was on understanding the lack of HIV status disclosure to partners and therapy adherence thus the themes revolved around these concepts. The final step produced a summary that tied the information to the theory. Two major themes emerged which were related to the adherence and lack of HIV status disclosure to male sexual partners. Direct quotes were used to emphasize meanings. By conducting all these steps, there was confidence in results generalization because a logical and falsifiable order was followed.

3.7. RESULTS

3.7.1. Non-Adherence Levels

In general, mothers were more likely to be non-adherent compared to non-mothers in the study area. The overall non-adherence was 32.2% for all the women with indications that pregnant women had the highest adherence levels (85.7%) followed by non-mothers (75.0%) and the least for mothers at 60.4% (Table 2). There were 67 mothers living with HIV in Greater Gaborone. By age, there were more women aged 30-39 (41.0% mothers and 36.1% non-mothers. Of these high non-adherence was for mothers. Majority of the women were single (59.7% and 51.9%) respectively and 37.5% of these single mothers were non-adherent compared to 25.5% of non-mothers. About 9.0% mothers had no education and half of them were non-adherent compared to 22.2% of non-mothers. Only two mothers were university educated and were all adhering compared to 9.9% of college educated non-mothers of whom about a third was non-adherent. Majority of the non-mothers were unemployed (40.6%) followed by self-employed (16.7%) while the reverse was true for mothers. Non-adherence was almost double for self-employed mothers (40.0%) compared to non-mothers (22.0%). Majority of the women were Christians (80.6% mothers, 87.7% non-mothers). Christian mothers as well as those with other beliefs have both the highest non-adherence levels (37.0%). The one mother who practiced African beliefs was adherent (Table 17). Non-adherence levels by whether one was a mother or pregnant showed that of the 14 pregnant women, 14% (n=2) were non-adherent compared to mothers (n=53) who had children already of whom, 39.6% were non adherent (Table 18).

Table 17. Demographic Characteristics of Mothers (n=67) vs. Non-Mothers (n=352) Living with HIV in Greater Gaborone, Botswana 2016.

Demographic Characteristics	Mothers		Non-Adherence	Not-Mothers		Non-Adherence
	No.	(%)	(%)	No.	(%)	(%)
Age (Years)						
18-29	10	14.9	50.0	71	20.2	21.1
30-39	28	41.8	32.1	127	36.1	29.1
40-49	29	43.3	31.1	107	30.4	24.3
50+	0	0	0.0	47	13.3	21.3
Marital Status						
Married	5	7.5	20.0	54	15.3	25.9
Single	40	59.7	37.5	183	51.9	24.0
Cohabit	21	31.3	28.6	100	28.4	276.0
Widowed	1	1.5	100.0	14	3.9	28.6
Divorced	0	0.0	0.0	1	<1	0.0
Education						
No. Formal	6	8.9	50.0	18	5.1	22.2
Primary	24	35.8	29.2	75	21.3	28.0
Secondary	32	47.8	40.6	212	60.2	23.6
Vocational	3	4.5	0.0	12	3.1	25.0
University	2	2.9	0.0	35	9.9	28.6
Occupation						
Unemployed	17	25.4	29.4	143	40.6	23.8
Self-Employed	20	29.9	40.0	59	16.8	22.0
Farmer	1	1.5	100.0	13	3.7	53.9
Private	21	31.3	38.1	81	23.1	25.9
Government	8	11.9	12.5	56	15.9	23.2
Religion						
Christianity	54	80.6	37.0	309	87.8	24.3
African Beliefs	1	1.5	0.0	11	3.1	27.3
Other	12	17.9	37.0	32	9.1	31.3
Total	67	100.0	34.3	352	100.0	26.3

Table 18. Maternal Characteristics by Adherence vs. Non-Adherence for a Sample of Women (n=419) in Greater Gaborone, 2016.

Maternal Characteristics	Women		Non-Adherence		Adherence	
	No.	(%)	No.	(%)	No.	(%)
Mother-Pregnant	14	3.2	2	14.3	12	85.7
Mother-Post-Partum	53	12.6	21	39.6	32	60.4
All Other women	352	84.01	88	25.0	264	75.0
Total	419	100.0	111	32.2	308	67.8

Adherence = Mothers vs. All Other Women (Odd Ratio = 1.47, 95% CI 0.84-2.55).

3.7.2. HIV Status Disclosure

All of the women enrolled on PMTCT were diagnosed between 2002-2016. There were more (n=42) mothers who knew their partner's HIV status compared to those who were not sure (n=21) and those who did not know (n=4) (Table 19). Of those who knew their partners' HIV status, 8 were married but none were for both those who did not know (Table 19). Of the 67 mothers, 45 women have told their partners their HIV status while 13 have not and 9 were still finding ways on how to. With regards to duration on PMTCT, 47 have been enrolled for less than 6 months and 20 for more than 6 months. The maximum number of children among the mothers was 6 (Table 20).

Table 19. Partner's HIV Status[1] for Mother's Living with HIV by Partner's Year of HIV Diagnosis and Marital Status, Greater Gaborone, Botswana, 2016.

	Partner's HIV Status		
	Yes	No	Not Sure
Year	N=42	N=4	N=21
2016	$S^1$8M^1,C^1	-	C^1
2015	S^1	-	S^1,C^1
2014	S^1,M^1,C^2	-	S^3
2013	C^1	-	S^2
2012	S^3,C^4	-	C^1
2011	S^3,C^1	S^1C^1	C^2
2010	S^3,M^1,C^1	-	C^2
2009	S^1	-	S^1,C^1
2008	S^1,M^1,C^3	-	C^1
2007	S^1,M^1,C^1	C^1	-
2006	S^1,M^2,C^2	-	-
2005	S^1,M^1,C^1	-	S^1
2004	-	-	C^2
2003	C^1	S^1	S^1
2002	S^1,C^1	-	S^1
Total	S^{16},M^8,C^{18}	S^2,C^2	S^{10},C^{11}

[1]S=Single; M=Married; C=Cohabitate

Table 20. Knowing Partner's HIV Status[1] for Mothers Enrolled in PMTCT by Year of HIV Diagnosis and Number of Children.

HIV Diagnosis Year	Enrolled in PMTCT < 6 Months (n=47)			Enrolled in PMTCT >= 6 Months (n=20)		
	Disclose HIV Status			Disclose HIV Status		
	No	Not Sure	Yes	No	Not Sure	Yes
2016	-	-	1	-	1	2
2015	1	1	1	-	-	-
2014	1	2	2	-	-	2
2013	1	-	-	-	1	1
2012	1	-	2	-	-	4
2011	2	1	2	1	-	-
2010	1	-	6	-	-	-
2009	1	1	1	-	-	-
2008	-	1	4	-	-	1
2007	-	-	3	-	-	1
2006	-	-	3	-	-	2
2005	1	-	3	-	-	-
2004	2	-	-	-	-	-
2003	-	1	2	-	-	-
2002	1	-	2	-	-	-
Total	12	7	32	1	2	13

[1] Mother's disclosure to partner regarding her HIV status
No= No partner does not know, I am still finding out how to tell him (n=13)
Not Sure= Not sure, I do not know how to tell him (n=9)
Yes= Yes, partner knows of my HIV status (n=45)

To further understand the relationships of mothers and their partners, age and marital status was assessed. Young mothers (18-29) who were single did not have older partners and the only one with older partner aged 45-50 was cohabiting. Mothers of middle ages (30-39) were more likely to be in unmarried relationships with men of 35-55 years (15 single and n=10 cohabiting, only 2 married). For the older mothers, their partners were of the same age (45-50) with majority (n=5) of married status (Table 21).

Table 21. Mother's and Partner's Ages by Marital Status, Greater Gaborone, Botswana, 2016.

	Marital Status		
Age Groups (Years)	Single No.	Married No.	Cohabitate No.
Mother 18-29			
Partner 25-34	6	-	11
Partner 35-44	2	1	4
Partner 45-50	-	-	1
Total	8	1	16
Mother 30-39			
Partner 25-34	1	-	1
Partner 35-44	15	2	10
Partner 45-50	1	-	2
Total	17	2	13
Mother 40-49			
Partner 25-34	-	-	-
Partner 35-44	-	-	1
Partner 45-50	3	5	1
Total	3	5	2

To investigate the role of living with family members who are HIV positive and how that affected HIV status disclosure of the mothers, the following analysis was conducted. About 67.0% of the mothers of lived in a household with a member who is HIV positive, have disclosed their status compared to the 33.0% who did not live with HIV positive family members (Table 22).

Table 22. HIV Status Disclosure of Mothers and Family Member Living with HIV.

	Family with HIV		
Disclosure	Yes	No	Total
Yes	30 (66.7%)	15 (33.3%)	45
No	17 (77.3%)	5 (22.7)	22

3.7.3. CD4 Count and Year of HIV diagnosis

Mothers started off with high CD4 count during early years (750 copies/ml in 2002) and gradually decreased with time. Mothers with HIV infected partners and those who did not know (Figure 10) had the declining trends of CD4 count compared to those with HIV negative partners (Figure 10). For mothers who

have disclosed to their partners, they had a high baseline CD4 count compared to those who have not disclosed (Figure 11).

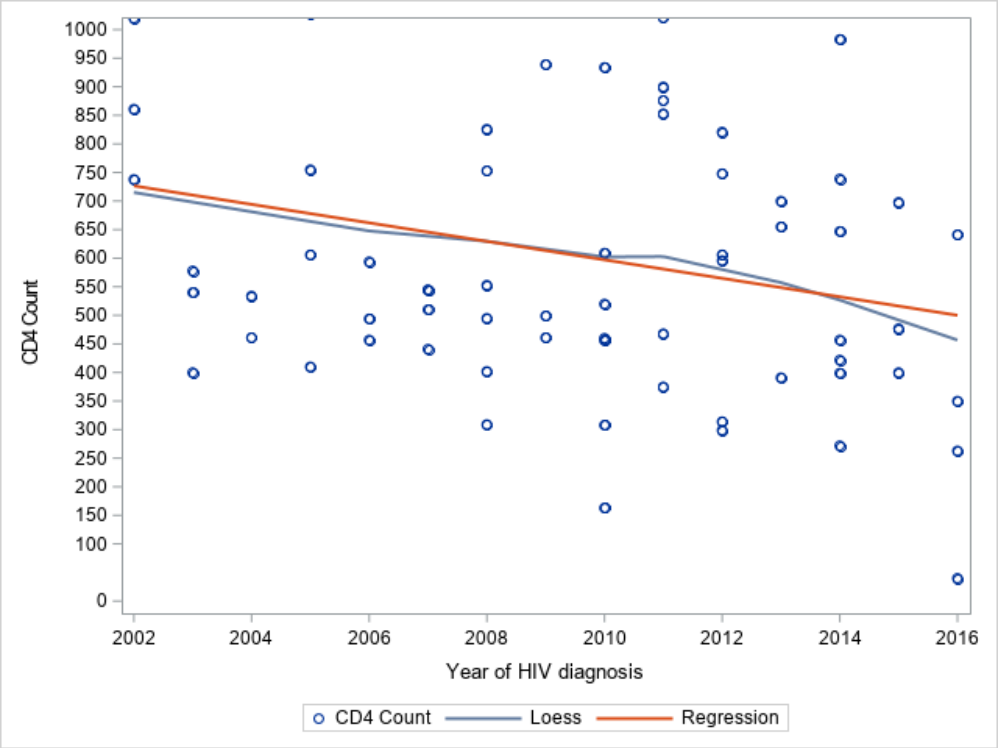


Figure 9: CD4 Count by Year of Diagnosis, Sample of Mothers (n=67) Living with HIV in Greater Gaborone, Botswana, 2016.

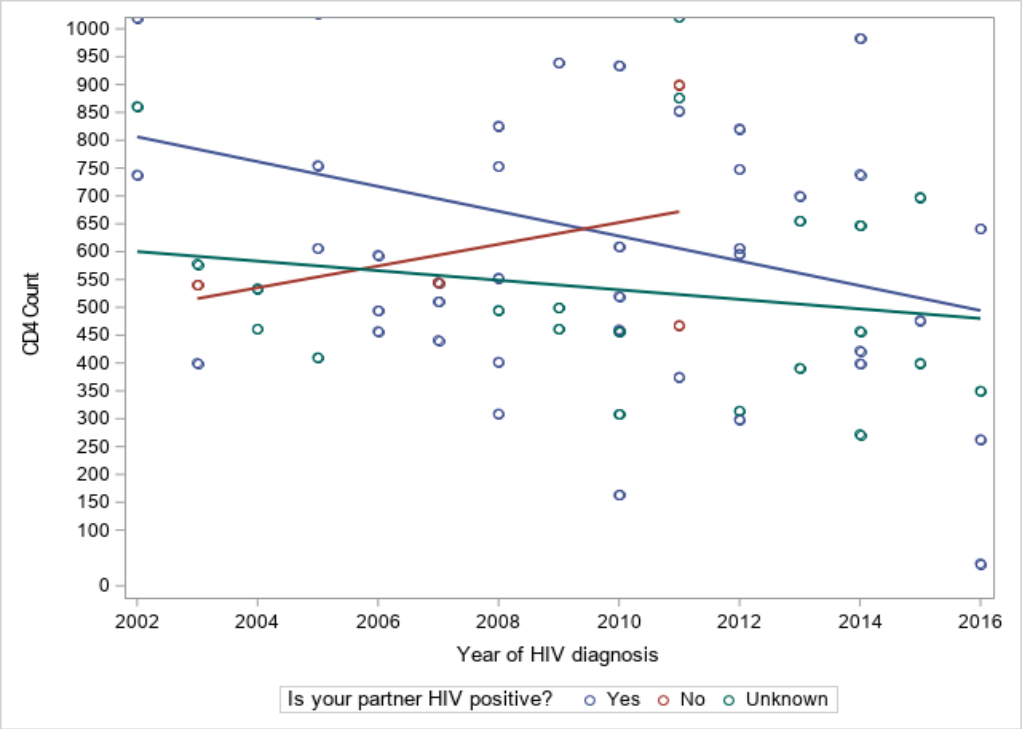


Figure 10: CD4 Count by Year of HIV Diagnosis for a Sample of Mothers (n=67) and Partner's HIV Positive Status, Greater Gaborone, Botswana, 2016.

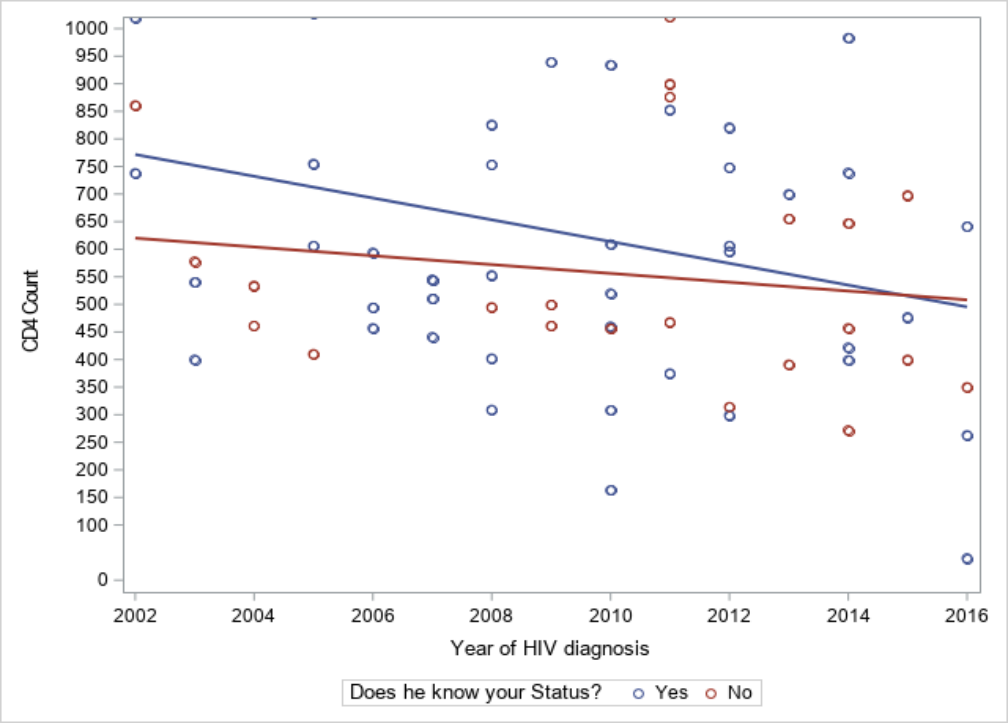


Figure 11: CD4 Count by Year of HIV Diagnosis for a Sample of Mothers (n=67) and HIV Disclosure Status to Partner, Greater Gaborone, 2016.

3.7.4. Thematic Analysis: Qualitative analysis

To answer this research question, semi structured interview conducted with the health workers were used. Four questions surrounding PMTCT guidelines were used and these were on breastfeeding, PMTCT enrolment criteria, social support and compliance. Two major themes emerged which are (i) conflict in autonomous decision making and (ii) adherence and compliance.

3.7.4.1. Theme 1: Conflict in Autonomous Decision-Making

This theme was named based on the two questions on breastfeeding and social support. To avoid transmission of virus to the baby, the World Health Organization [WHO] recommends that women breastfeed and PMTCT program offers free formula milk to all mothers living with HIV. The WHO continues to caution that in cases where formula feeding is not a viable option, women living with HIV are recommended to exclusively breastfeed (rather than mixed feeding), providing that they are on ART. This is because, while formula feeding offers the safest option for postnatal HIV prevention, in resource poor settings it is not always easy for families to afford or access things such as clean water which are needed for it use (UNAIDS, 2013). Throughout the years, the government of Botswana has recommended that women living with HIV should exclusively formula feed their infants and provided infant formula free of charge until the infant is 1 year of age to support this recommendation (MoHW 2013; Ndubuka et al., 2013). However, earlier in 2011, MoHW recommended exclusive formula feeding for the first six months of life only for women for whom formula feeding is acceptable, feasible, affordable, sustainable and safe (AFASS) (WHO, 2006; 2007; Ndubuka et al., 2013). On the other hand, the society in Botswana, regards a "true mother "as the one who breastfeed. This task of decision making can be daunting to the new mother who is already battling with the fact that she is HIV positive. A female nurse in a rural clinic said,

> *"It is a tough call with breastfeeding because some women have high viral load, but babies on the other hand need mothers antibodies, but we [Health providers] make sure to give*

them advice on both advantages and disadvantages of infant feeding" (Female Nurse, Rural Clinic).

Another nurse in a rural clinic in Kweneng East district emphasised on the mothers defying the cultural stigmas on bottlefeeding when she said "*We advise mothers to ignore the village talk that looks down on women who bottle feed (Fem Nurse, rural*). A male pharmacist at the same clinic echoed the nurse's concerns when he said,

"We usually bring or try to, the person who takes care of the mother during the confinement period, so that they understand why the woman cannot breastfeed" (Male Pharmacist, Rural Clinic).

Formula milk was provided for free to mothers who choose to, until the baby reaches the first age. According to the Government of Botswana (2011), If a mother chooses exclusive formula feeding she will be provided with free infant formula until the baby is 12 months of age. This aligned with what the doctor in a Gaborone clinic said when asked if mothers living with HIV had a choice of infant feeding. He stated,

"We *provide free formula milk for those who choose to bottle feed"* (Male Physician, Urban Clinic).

It is clear that different clinics and health workers, do have preferences on the type of infant feeding. A doctor in a peri-urban area emphasized that they wanted the mothers to use formula milk but those that choose to breastfeed due to societal pressure, we cautioned to avoid mixed feeding. He said,

"*Those who choose to breastfeed because they want to please their in-laws, particulalry the married ones, we emphasize that they should breastfeed for atleast 6 months exclusively"* (Male Physician, Peri-urban Clinic).

Social support is also important to mothers who are on PMTCT program for the successful execution. PMTCT guideline 2 from Ministry of Health (2011) states that" HIV positive women and their partners receive counselling concerning their HIV status, available medical care for themselves and their families."

This implies that mothers living with HIV should disclose their status to at least their sexual partners, families and health workers particularly when they visit non-PMTCT clinics such as obstetricians. A female nurse in an urban clinic emphasized that most of the mothers living with HIV that they see on daily basis were open to them about their status but the opposite was true when they visited other services (non HIV) health facilities.

> *"We tell the mothers to communicate openly with their gynecologists at other clinics about their HIV status. These women don't say anything to "other" people about their status, they don't realize that it [...non-disclosure] can affect their unborn children. If a gynecologist doesn't know that you are HIV positive, they might keep you on waiting list for important tests like any regular patient because they wouldn't know that you need help urgently"* (Female Nurse in, Gaborone).

As an extension of social support, when health workers were asked if the mothers /pregnant females were required to bring treatment partners –trusted individuals that act as adherence partners particularly their [women's'] sexual partners. There were varied responses among the individuals and clinics. Ten health providers from different clinics responded that women were not required to bring their partners to the clinic appointments. Among those who said no, five were nurses [urban, rural], three pharmacists [urban, peri-urban] and two doctors [in Gaborone]. Majority of the health workers indicated that women were required to bring their sexual partners and if not possible, a close member of the family. A female doctor in a rural clinic added that,

> "*We tell the women that, if their partners refuse to come to the clinic with them usually on treatment counselling days, we require them to tag along their mothers, aunts, as they are the people that are usually responsible to take care of them during their pregnancy and "botnets" (confinement period). It is important to do so, because their caretakers usually force them to breastfeed telling them that bottle feeding is torturing the baby by not providing the required*

nutrients that the breast provides. And I really don't blame them[caretakers] because most of the time, they don't know the mother's HIV status. Would you blame them yourself?" (Female Physician, Rural Clinic).

A female nurse in rural clinic of indicated that even though they asked the mothers to bring their partners to the clinic, they did not deny them the services. She said,

"*yes we ask the women to bring someone with them to the clinic, but it is not enforced really. It is within their rights to be given help regardless of whether they have brought their adherence partners or not"* (Female Nurse, Rural Clinic).

3.7.4.2. Theme 2: Adherence and Compliance

Two questions were posed to the health care workers and they included the criteria that they used to define eligibility for PMTCT and the compliance measures that they used to assess adherence [or lack of] to the program. All the health workers were in agreement that all mothers living with HIV were enrolled in the PMTCT program but it was clear that there were slight differences among clinics. A male nurse in a rural clinic of Siga said that,

"*All HIV positive pregnant women are enrolled at 14 weeks' gestation atleast, not to say that we do not get women who enroll in late stages. Particularly here in rural areas, women don't come to the clinic until they are most of the time in their 7th month of pregnancy. If you think that's worse, there are those that show up during delivery"*(Male Nurse, Rural Clinic).

It is clear that since the adoption of option B+, most clinics were phasing out the CD4 count criteria.

"*In the past, we used the CD4 count criteria like in the ART program, but we are gradually phasing it out. Right now (2016), all the women who come to our health facilities, as long as they are pregnant and HIV positive, we enrol them in the PMTCT program"* (Female, Pharmacist, Peri-urban Clinic).

These sentiments were echoed by 53 other health care providers who stated that they did not use the CD4 count criteria as of the time of the interview (May-August 2016). On compliance with the program, the reoccurring terms among the health care providers were "counselling, education and adherence partners." A doctor in Gaborone expressed concern that mothers living with HIV particularly in the low income areas presented to the clinic in the late stages of pregnancy.

> "*Most of these women sometimes do not understand the importance of early enrolment, and this gives us very limited choices if an unknown HIV positive [..status] mother shows to the delivery room, unregistered , never attended antenatal care classes, HIV testing , .You can imagine the challenge she presents to us as health care providers. So we emphasize the benefits of having a baby born free of HIV. When they hear that their babies can have a different life from theirs, you can see big smailes from their faces"* (Male Physician in, Gaborone).

Among the health care providers who emphasized that non-adherent women were offered counselling sessions, one emphasised the importance of patient-provider relationship.

> "*We encourage them [..women] to treat us as they would a friend, that way it becomes easy for them to confide in us and tell us what they do not understand when it comes to the PMTCT program. And we really understands that the program is intensive and sometimes, culturally foreign to them, but for their sakes and babies, it is important to follow each and every guideline"* (Male Nurse, Rural Clinic).

Health workers added that the use of Setswana language among those women with little formal education was important to make sure the message reaches to everyone. He said,

> "*For the women that we feel do not have the education[..formal training] , we always counsel and give all the instructions in Setswana. We realized that sometimes women*

don't ask questions not because they don't have, but to the fact that they don't understand, so Setswana comes to rescue in cases like those" (Male Nurse, Rural Clinic).

A phamacist in (rural) added that counselling should not be for particular days only as they currently have in their health facility, it should be done on daily basis.

"Ongoing counselling is very important because these women battle HIV on daily basis. And it doesn't have to be provider-patient counselling, it can also be patient-patient, family counselling too" (Male Pharmacist, Rural Clinic).

Adherence partners were shown to be the intergral part of the PMTCT program as they unloaded the burden of the health workers. A female nurse in Gaborone clinic indicated that,

"the adherence partner, usually a family member is required for defaulters. And defaulters I mean the women that , no matter how much we counsel them to follow the program strictly, they will still miss something. It could be mixed feeding, missing clinic appointments for herself and the baby.Those are the ones that we tell them to bring someone for social support because it is very clear that they cant cope on their own. And sometimes we fear that pressurisng them to come with someone deter them from coming at all" (Female Nurse, in Gaborone).

3.8. DISCUSSION

About 67.2% (n=45) of HIV-positive mothers enrolled in the study reported having disclosed HIV positive status to their partner. This finding is comparable to most studies from Sub-Saharan Africa, with disclosure ranges from 16.7% and 86% (Nyandat and Van Rensburg, 2017). Bachanas et al. (2013) reported 80.0% of the 3538 HIV-positive patients in Kenya, Tanzania and Botswana had disclosed their status to their partners. Similarly, 70.0% of 20 HIV-positive pregnant women in Kenya had disclosed their status (Walcott et al., 2013). In their study, Nyandat and Van Rensburg found that 83.3% of the women in their Kenyan study have disclosed their HIV status to their male partners (Nyandat and Van Rensburg, 2017).

In this study findings showed that by age, there were more middle aged women (30-39) (32.1% mothers and 29.1% non-mothers. High non-adherence levels were observed for mothers. Majority of the women were single (59.7% and 51.9%) respectively and 37.5% of these single mothers were non-adherent compared to 24% of non-mothers. About 9% mothers had no education and half of them were non-adherent compared to 22% of non-mothers. Only two mothers were university educated and were all adhering compared to 9.9% of college educated non-mothers of whom about a third was non-adherent. Majority of the non-mothers were unemployed (40.3%) followed by self-employed (16.7%) while the reverse was true for mothers. The single status of the women as well as lack of unemployment showed to be the risk factors of non-adherence. This finding was corroborated by findings from a Kenyan study (Kinuthia et al., 2018) on PMTCT uptake and non-disclosure that shorter duration of relationship and employment status were associated with non-disclosure of HIV-positive status. Being single can compromise of many things not limited to lack of social and financial support. The same can be said about lack of unemployment. It means the woman has to be dependent on a family member or partner when it comes to transport fees for clinic checkups and food for nutrition. This was consistent with other studies (Antelman et al., 2001; Kiula et al., 2013) that women who were unmarried were more likely not to disclose.

All of the women enrolled on PMTCT were diagnosed with HIV in the recent years of 2002-2016. There were more (n=42) mothers who knew their partner's HIV status compared to those who did not know. Of those who knew their partners' HIV status, 8 were married but none were for both those who did not know. It is usually easier for married couples to keep no secrets between themselves hence the reason why a lot of married men knew their partner HIV status. Even though majority of the mothers (n=45) have disclosed their HIV status to their partners, there were still the 22 who have not. This is a real concern because not only the women health is involved, so is the baby's. This also tells a bigger story because PMTCT as a comprehensive program, it involves couple testing. In a case where the mother has not told

the partner her HIV status, it means, she attends the clinic appointments by herself. Other African studies (Kenya-Kinuthia et al., 2018; Kenya –Farquhar et al., 2004) have found that HIV-infected women who had not disclosed their results were less likely to use PMTCT services. Study conducted in Botswana, reported that there was a general concern of low male partner testing (21.0% in 2017) (MoHW, 2017). Visser and colleagues (2008), emphasized that disclosure of HIV status involves a series of steps of decision making. These include (1) coming to terms with the HIV diagnosis, decision on the appropriateness of disclosing to a particular person, weighing the anticipated impacts and then choosing the appropriate situation for disclosure (Visser et al., 2008; Kimberly and Serovish, 1996). Other studies corroborated this study finds why most married mothers disclosed. Simoni et al., 1995; Kalichman, 2003 have shown that women who disclose their HIV status is in part to reduce stress and increase access to social support (personal reasons) and to maintain honesty in relationships as well as protecting others from infection (interpersonal level) (Visser et al., 2008).

Immunology using CD4 count as a potential reflection of PMTCT adherence showed that if a mother's partner was HIV negative, their CD4 count steadily increased compared to those with HIV infected partners (Figure 10). High CD4 count was also associated with mother's HIV status disclosure to their male partner. Low CD4 count can be indicative of poor medication adherence. Other studies have shown that not disclosing HIV results and lack of partner support is associated with poor uptake of antiretroviral medication (Farquhar et al.,2001; Kiarie et al., 2003).

There was evidence that there is a conflict in what's right and wrong among the health officials and the mothers. in 2011, MoHW recommended exclusive formula feeding for the first six months of life only for women for whom formula feeding is acceptable, feasible, affordable, sustainable and safe (AFASS) (WHO, 2006; 2007; Ndubuka et al., 2013). On the other hand, the society in Botswana, regards a "true mother "as the one who breastfeed. Health workers reported that women usually risked their babies' life by

breast feeding when they should not in order to be accepted in the society as strong mothers. Meanwhile a study conducted in Johannesburg, South Africa on HIV pregnant women, showed the opposite that some women will go to uncomfortable measures such as HIV status disclosure to protect their infants and avoid breastfeeding (Varga et al., 2006).

A closer look at the relationships of mothers and their partners, revealed that young mothers (18-29) who were single did not have older partners and the only one with older partner aged 45-50 was cohabiting. Mothers of middle ages (30-39) were more likely to be in unmarried relationships with men of 35-55 years. For the older mothers, their partners were of the same age (45-50) with majority (n=5) of married status (Table 21). Looking back to Paper 1, men who were aged 30-39, were the ones with high risk of non-adherence and comorbidities. Also these mothers earlier (Table 17) showed high non-adherence levels. With these combinations, the risk of further re-transmission is very high making it hard to reach viral suppression. And this could be maybe explained by why mothers who knew their partners' HIV status had the most declining trends of CD4 count over time (Figure 10) and the same trend was observed with the partner knowing mothers' HIV status (Figure 11).

Health workers also reported that women were selective of whom they told /disclosed their HIV status. Women tend to be open with ART health workers but the opposite was true when they visited non-HIV facilities. They did not tell their practitioners because they wanted to be "treated like everyone". Another concern was that most of these women sometimes did not fully understand the importance of early enrolment, as they can only present to the ART facility at the time of delivery but as soon as they are made aware that enrolling in PMTCT early provides an opportuinity with their children being born HIV free, women tend to take better action. Other study confirmed these findings where they reported that PMTCT problems included late presentation for health care delivery service during pregnancy, inadequate ante-natal visits, poor opportunistic infection screening, non-disclosure of HIV-positive status to partners, and

inadequate family planning counseling (du Plessis et al., 2014; Bucagu et al.,2013; Mnyani et al., 2014). Low HIV testing rates during pregnancy, suboptimal healthcare coverage, and poor patient retention were also some of the issues shared by other authors (Prendergast et al., 2015; Adetokunboh and Oluwasanu, 2016).

3.8.1. Limitations

Adherence measure used in this study was not specifically tailored to PMTCT, a general ART measure was used which could have maybe provided specific results. Women were selected based on attendance at the ART study facilities, and thus this sample does not include the population of potentially most at-risk women who do not attend these clinics. Another limitation is that the study relied on self-report for HIV disclosure status, introducing the risk of social desirability bias. Despite all these, the study showed that there is non-adherence among mothers enrolled on PMTCT and there was evidence of lack of disclosure among both female and male partners which is a drawback to the therapy because there is a risk of lack of viral suppression.

3.9. CONCLUSIONS AND RECOMMENDATIONS

This study explored the levels of adherence and HIV status disclosure among pregnant and new mothers living with HIV and enrolled on PMTCT in Greater Gaborone. Study has shown that there are high levels of non-adherence among mothers in Greater Gaborone as well lack of status disclosure. Post-natal women had the highest levels of non-adherence compared to pregnant women. Out of the 67 women, 22 have not disclosed their HIV status to their partners. Majority of the mothers were not married and were involved with males who were aged around 30-45. This is the age cohort where previously we saw that were non-adherent and were sick from other diseases. As potential HIV transmitters, mothers aged 30-39 were at the risk of being receivers. The impact of HIV- related stigma and discrimination was also reported as a barrier of disclosure to family members and medical professionals at non-HIV facilities as mothers preferred to keep their status confidential. Impacts of stigma have several implications in PMTCT

program when it comes to decisions about HIV testing, accepting the HIV+ test results, adherence to medications and recommended child feeding options (Moshi, 2016). There is a need to develop interventions that respond to the social and cultural contexts of HIV positive mothers to improve disclosure decision making in PMTCT programs. Although the counselling sessions in the PMTCT program are focused on the pregnant woman, the raising of a child in the African context is family oriented which has significant implications for the PMTCT program (Madiba and Letsoalo, 2013). It is important that the PMTCT program is geared towards community based interventions that promote awareness and inclusion of male partners, family members and the community leaders about PMTCT adherence. Furthermore, PMTCT interventions in the community should aim at improving the social context of disclosure to reduce stigma and promote HIV disclosure to significant others (Madiba and Letsoalo, 2013). Future directions will be to continue focusing on studying these middle aged women and their partners, as well as addressing issues of status disclosure, breastfeeding, and unemployment. There is a need to learn about other factors that affect the mothers' adherence that are sometimes beyond her control such as water and heat issues that are rampant in Botswana. There is a need for ministries such as Health, Environment and Labour to work together to empower the women and minimize the non-adherence associated risk factors in Botswana.

CHAPTER 4: Impacts of High Ambient Temperatures and Water Rationing on Antiretroviral (ART) and Prevention of Mother-to-Child Transmission (PMTCT) Therapies Adherence in Greater Gaborone, Botswana

4.0. INTRODUCTION

In 2006 the President's Emergency Plan for AIDS Relief (PEPFAR) and integration of safe Water, Sanitation, and Hygiene (WASH) were implemented into HIV programs. The key objective of PEPFAR is to reduce HIV-related morbidity and mortality in affected communities (United States Agency International Development [USAID], (2011). It is important to recognize the significance of safe water, sanitation, and hygiene (WASH) promotion in protecting and caring for people living with HIV and integrate WASH improvement into HIV and AIDS policies and programs. PEPFAR has developed a preventive care package that identifies three key hygiene improvement practices: safe drinking water, washing hands with soap, and safe handling and disposal of feces, and suggests integrating these into all HIV and AIDS programs (USAID, 2011). Many life-threatening opportunistic infections are caused by exposure to unsafe drinking water, inadequate sanitation, and poor hygiene. Diarrhea, a very common symptom affects 90% of people living with HIV, especially in HIV-positive children (United Nations International Children's Emergency Fund [UNICEF], 2008). Diarrheal illness can interfere with the absorption of antiretroviral (ARV) drugs and can contribute to developing HIV strains that are resistant to treatment (USAID, 2011). Good access to safe water and sanitation is important for people living with HIV and for the provision of home based care to AIDS patients. Water is necessary for bathing patients and washing soiled linen. Close latrines are necessary for weak patients who cannot walk long distances. Water also plays a significant role in keeping the house environment and the toilet clean in order to reduce the risk of opportunistic infections such as diarrhea. Water and sanitation provision really plays a significant impact on the dignity of both patients and their caregivers (Haftu et al., 2017). Safe drinking water is needed for absorption of ARVs and to make food easier to swallow for weak patients. Although there are many water needs for HIV patients, access

to WASH may prove difficult for households caring for HIV patients due to declining physical health, stigma and socioeconomic status (USAID, 2007; Haftu et al., 2017).

4.1. PURPOSE OF THE STUDY

To investigate the role of environmental factors (high temperatures and water scarcity and rationing) on ART and PMTCT non-adherence, for adults living with HIV in Greater Gaborone, Botswana. The study sample was comprised of 658 adults living with HIV enrolled on ART (n=419 women, n=239 men) and PMTCT (n=67) and 84 health workers at 21 government clinics, in urban, peri-urban and rural areas of Greater Gaborone. The study sample is explained in detail how it was derived elsewhere (Chapters 2 and 3). Even though ART adherence is important in the assistance of elimination of new infections, physical (built environment and weather variables) that are understudied in the ART adherence literature, can be significant barriers to accessibility and utilization of antiretroviral drugs.

4.2. BACKGROUND

Southern Africa has experienced steadily increased trends in mean, maximum and minimum temperatures with the most significant warming occurring during the recent decades (Zhou et al., 2010; Collins, 2011). In comparison to maximum temperatures, the minimum one have rather increased rapidly over inland Southern Africa (New et al., 2006). Projected temperatures show that mean land surface warming is likely to surpass the global mean land surface temperature increase in all seasons (Sillmann and Roeckner, 2008; Watterson, 2009). It is further projected that towards the end of the 21st century, warming of between 3.4 and 4.2c above the 1981-2000 average under the A2 scenario will exceed natural climate variability (Moise and Hudson, 2008). The semi-arid southwestern parts of the region which cover northwestern South Africa, Botswana and Namibia will experience high warming rates (WGIAR5 Annex 1; Shongwe et al., 2009). Figure 12 shows the steadily increasing temperature trends from 1991-2016 in the whole of Africa. Precipitation is also showing to be fluctuating throughout the period (Figure 12).

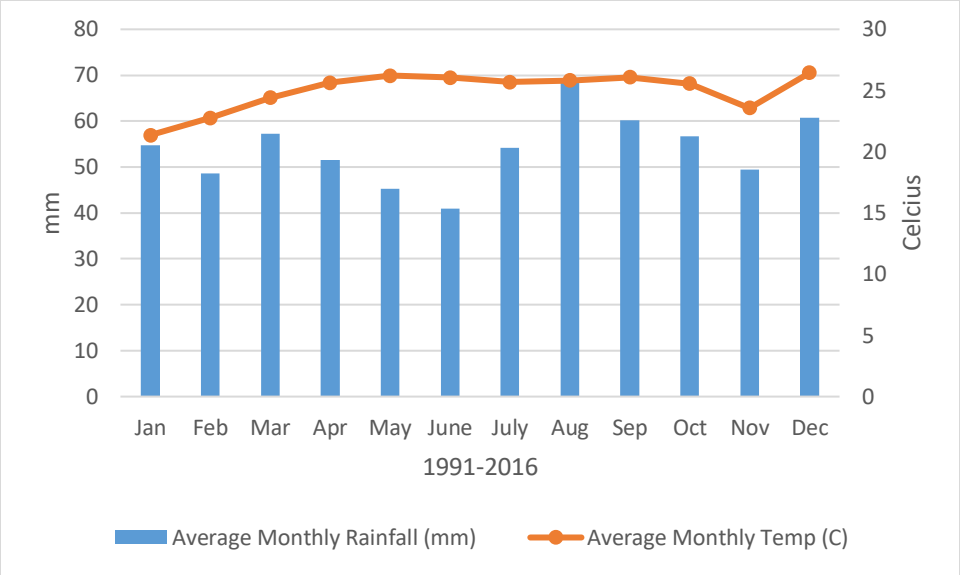


Figure 12: Average Monthly Temperature and Rainfall Trends in Africa from 1991-2016.

All over Southern Africa, there is an observed reduction in late austral summer precipitation extending from Namibia through Angola and towards the Congo (Hoerling et al., 2006; New et al., 2006). This dryness is associated with an upward trend in tropical Indian ocean sea surface temperatures. Modest declining trends in rainfall are found in Botswana, Zimbabwe and western South Africa. Changes have also been observed in the onset, duration, dry spell frequencies and rainfall intensity (Tadross et al., 2005,.2009; Thomaes et al., 2007; Kniveton et al., 2009). The increasing frequency of dry spells is also commonly accompanied by an increasing trend in daily rainfall intensity. This has consequences for run-off characteristics (New et al., 2006).

There are also precipitation projections across the Southern African region. Rainfall projections are more uncertain than temperature projections (Rowell, 2012) because they demonstrate higher spatial and seasonal dependence when coupled to temperature projections (Orlowsky and Seneviratine, 2012). The Coupled Model Intercomparrison Project Phase 3 (CMIP3) projections indicate a drying signal in the annual mean in the dry southwestern extending northeast from the desert areas in Namibia and Botswana (Moise and Hudson, 2008; James and Washington, 2013). Drier winters are projected over a large area in

the region due to the poleward displacement of mid-latitude storm tracks (Shongwe et al., 2009; Seth et al., 2011). There are also projected declines in rainfall during austral spring months implying a delay in the onset of seasonal rains over a large part of the summer rainfall region of Southern Africa (Seth et al., 2011). Besides volumes, rainfall patterns are also expected to change in intensity and frequency, resulting in more extreme events and longer periods between rainfalls. River runoff and water availability are projected to decrease by 10–30.0% in the dry tropics (IPCC, AR5).

4.2.1. Water, Sanitation and Hygiene (WASH) Barriers

Community based cross-sectional quantitative study among 413 participants in Arba Minch town, southern Ethiopia in 2016 assessed water, sanitation and hygiene (WASH) practices and associated factors among people living with HIV (Haftu et al., 2017). A structured questionnaire and observational checklist was used to collect data on households socioeconomic, environmental conditions and behavioral characteristics. Logistic regression in SPSS was used to measure association between WASH practices and other associated factors. Socioeconomic status was derived through running a principal component analysis (PCA) on household asset data. Findings showed that majority (n=403, 97.6%) indicated that water source was tap water and 165 (40.0%) had the drinking water source within their compound (Haftu et al., 2017). By water status, 76.5% (n=316) households had improved water status (piped water into residence, public tap and protected well/spring) compared to 23.5% (n=97) with unimproved water status. Factors associated with WASH practices showed that diarrhea was 10 times likely to affect those with unimproved water status. All other socioeconomic and demographics such as education, sex and age did not have significant association (Haftu et al., 2017). The authors emphasized that special attention should be focused towards people living with HIV as opportunistic illness such as diarrhea can prove to be dire when compared to the general population (Haftu et al., 2017).

Another Ethiopian study conducted by Yallew and colleagues (2012) in Gondar city among 296 people living with HIV assessed WASH practices and other factors. Logistic regression and thematic analysis were

used for data analysis. About 60.0% (n=170) of the HIV patients had a toilet facility like traditional pit and flush latrine and majority 96.0%(n=163) had latrines that did not have hand washing facilities package (Yallew, Terefe, Herchline et al., 2012). Only 59.0% (n=73) washed their hands with soap after using a latrine. When interviewed, one HIV positive female widow reported that her neighbors did not allow her to use their tap as they believed she transmitted diseases so she was forced to travel long distances for water package (Yallew et al., 2012). Another female reported that her landlord prohibited her from using the compound latrine so she had to use a public one a far distance away. In conclusion, almost 50% of the people living with HIV had poor water and sanitation conditions. The authors recommended that WASH should be part of the ART package (Yallew et al., 2012).

A qualitative study was conducted in the north-central of Zimbabwe in 2016 among 8 focus groups and three key informants in 9 study villages (Mbereko et al., 2016). The goal was to assess the relationship between HIV and AIDS and water scarcity (Mbereko et al., 2016). A household (n=20) directly affected by HIV/AIDS was defined as household that 2 months prior to the study has had HIV patient or HIV related death. The indirect affected households (n=20) were the ones where one of their members were involved in assisting a directly affected household. Semi structured interviews were held with households while thematic approach was used with the focus groups. Key informants indicated that at the clinic, 400 liters (20 buckets) of water was needed for caring for HIV bedridden patient while HIV/AIDS affected households used between 2-12 buckets. All the 40 households reported that having an AIDS patient required high quantities of water for washing linen and clothes, cook, bathe and utensils. Directly affected households indicated that average there was a shortage of 103 liters per day while for indirectly affected households was 65 liters. On access to water issues, households in the upland villages, boreholes were privately owned thus often locked and water rationing was frequent. On cultural factors and stigma, communities did not want to mix with HIV patients particularly who were co-infected with TB as they

deemed it contagious. In conclusion, the authors recommended that Zimbabwe and African policy makers should treat HIV/AIDS and water as one issue in rural interventions (Mbereko et al., 2016).

A study in the fishing villages (n=22) of Ngamiland, Botswana assed the effects of HIV/AIDS related stressors at the household level (n=248). Data was collected and analyzed through observational and thematic analysis of interviews (Ngwenya and Mosepele, 2007). Findings showed that the Botswana National Settlement Policy defined a village as a place with minimum of 500 people (Ngwenya and Mosepele, 2007). In Ngamiland, about 50% of the population lived in settlements with less than 500 people therefore could not receive health services directly except through primary centers such as Maun and Gumare. About 53% of the 248 households, reported that they have continuously cared for an HIV patient in the last 5 years (Ngwenya and Mosepele, 2007). Of the households with HIV patients, 29.0% said the illness had a serious impact on fishing activities. In conclusion, the authors recommended that social protection measures should protect households by reducing the vulnerability to HIV infection. The interventions should prevent the poor from becoming more poor by giving them the capacity to grow (Ngwenya and Mosepele, 2007).

4.2.1.1. Physical Infrastructure Barriers

In a qualitative study conducted at Victoria Hospital in Alice, a town in the Eastern Cape, South Africa, 23 isiXhosa-speaking participants (including both men and women) between the ages of 18 and 60 years were interviewed on adherence to antiretroviral drugs (Kheswa, 2017). The study was guided by the social-ecological framework of Bronfenbrenner (1979), which emphasizes that the health-seeking behavior of people living with HIV/AIDS (PLWHA) is influenced by their social, institutional and physical environments. The author found that food insecurity, financial constraints, poor service from health workers, unfair dismissal, fear of the consequences of disclosure, and rejection by church members were the main factors influencing non adherence to medication (Kheswa, 2017). The study suggested the need for supportive community initiatives, and collaborative approach at both local and national level, and

particularly in impoverished communities (Kheswa, 2017). Educating communities and making treatment and counselling facilities more accessible to PLWHA was also recommended (Kheswa, 2017).

In another South African study, using systematic sampling, 735 HIV-positive patients were selected prior to commencing on antiretroviral therapy [ART] from outpatient departments from three hospitals and followed-up at six months and interviewed with a questionnaire (Peltzer et al, 2010). Important factors of ART adherence included urban area of residence and adequate physical environment including transport and access to health services (Peltzer et al., 2010). Living in an urban area was likely to be associated with lower transport costs and fewer disruptions in access to medications (Peltzer et al., 2010). These findings were supported by other studies that found to be a facilitators of adherence [Berg et al., 2004 New York; Kip et al., 2009 Botswana; Sanjobo et al., 2008 Zambia). After adjusting for health-related variables, for both factors, better adherence was associated with low depression and poorer adherence was associated with poor environmental factors (Peltzer et al., 2010).

Tuller and colleagues (2010) conducted semi-structured interviews with 41 patients living with HIV in Mbarara, Uganda (Tuller et al., 2010). The focus of the paper was on transport costs as a barrier to adherence. All participants reported that they used public transit or personal cars. From the findings, one female with 4 children reported that she sometimes missed to refill her ARV prescription because she did not have transport money to the clinic. Another patient (male with 5 children) indicated that since he got HIV, he was weak so could not work in the fields thus did not make any money for transport to the ARV clinic. Other participants said that they borrowed transport money from family, friends and social clubs while the rest having to sometimes sell their assets in order to afford transport costs. In conclusion, the authors showed that patients had a high level of commitment to ART adherence although the high cost of transport for monthly clinic visit was a serious concern. They recommended that there should be creative interventions to address transportation costs barriers (Tuller et al., 2010).

A retrospective cohort study with 537 adults on ART was conducted in two rural districts of Rwanda at 21 health centers (Munyaneza et al., 2018). The primary predictor was the distance between the patient's village of residence and their ART clinic. The cost surface distance which is the distance between location of village and ART clinic weighed by the earth surface was measured using ArcGIS software. Multivariate logistic regression model was used to assess the relationship between the outcome and distance using 2-3 km as a reference. Results showed that median cost surface distance was 5km. cost surface distance to the clinic was significantly associated with missing an appointment (p=0.022) with patients living 0-1km from the clinic having the highest proportion of absence (55.4%). Even though the authors did not assess stigma, they attributed it to those who lived closer by missing because of lack HIV status disclosure. Authors concluded that further studies were needed to better understand why patients living close by missed appointment as these may improve early adherence (Munyaneza et al., 2018).

4.2.1.2. Gender Differences in HIV

Women are more vulnerable to HIV than men because of biological and cultural factors. Biological factors increase a woman's risk of becoming infected. For instance, women can have reproductive tract infections which make them more vulnerable to infection (UNAIDS, 1998). Women are more susceptible to HIV infection than men—male to female transmission of HIV is between two and four times more efficient than female to male (UNFPA, 2002). Socio-cultural factors can increase the risk of HIV infection among women in other societies that promote male dominance. In most Southern African cultures, young women tend to have older, more experienced partners who are more likely to have sexually transmitted diseases from previous sexual activity. Violence against women, particularly coerced sex increases women's vulnerability to HIV/AIDS (Turmen, 2003).

Migration is another social factor that often result in disruption to social and family relationships and increases the likelihood of HIV infection. It is common in Southern Africa for men to leave their wives and families behind to work in mining towns and military camps. This has the potential to increase the

possibility that they will get involved in multiple and concurrent relationships which put both themselves and their families at risk when they return home.

4.2.1.3. Gender and Water

The role of both men and women in the water sector is important. However, there are gender differences and inequalities in the use and management of water resources, which inherently affect women in their efforts to have access to, and manage water resources (Botswana Integrated Water Resources & Water Efficiency Plan, 2013). In households, women are responsible for managing domestic water supplies and these may conflict with productive water needs such as agriculture hence creating tensions for women (Johnson et al., 1997). With regard to access and control over how water resources should be used and allocated, the responsibility often rests with men hence ownership of resources by women is negligible (Johnson et al., 1997). Therefore, women rarely have equal access to water for productive use and are the first to be affected in times of water shortages. Water is interlinked with health impacts and women play a central role in family health and hygiene, especially those of their children. Therefore, if there is increased participation of women in water control, there is likelihood increase in the better handling of environmental health issues associated with water (Botswana Integrated Water Resources & Water Efficiency Plan, 2013).

Asaba and colleagues conducted a cross sectional study in rural Makondo Parish in Uganda investigated the gender differences in water collection. They used a mixed method approach covering 602 households across the 15 villages in the parish (Asaba et al. 2013). In-depth interviews were conducted with key actors and focus groups with 5 women and men respectively and participation observation. Quantitative analysis was done using chi-square test while qualitative were analyzed using content analysis (Asaba et al., 2013). Results showed that majority of water fetching was women responsibility (54.7%) followed by female children (19.4%). Although women had the fetching responsibility, women in household with children tended to be less involved with water collection as they sent the children instead. Stage of relationship

also affected water collection as women who just got married or in the early days of cohabiting were less involved with water collection. Distance travelled to a water source was cited as a barrier. About 20.0% of the household respondents said their homes were located about 2km or more from water sources and 41.5% said they collected water from unimproved sources such as open wells and ponds. Waiting a long period of time queuing at a water source was also reported as a constraint as 26.7% of the respondents indicated (Asaba et al., 2013). During the long dry season (June-August), queuing was reported to be even longer with children spending on average between 2-6 hours. Authors explored water collection in the rural area of Uganda and found that time and distance were crucial in understanding what women and children face during water collection (Asaba et al., 2013).

With regards to gender, water and HIV, women and children bear a disproportionate amount of the time and resource burden of both water/ sanitation management and caring for people living with HIV in Sub Saharan Africa (West et al., 2013). The physical, emotional, and opportunity costs to women are substantial, and while the social arrangements that place women as primary resource managers and caregivers within the home are often treated as ‘‘natural’’, they are part of a broader social order organized around gender that structures both labor and power (Connell, 1987). Women spend long hours daily fetching water and travel long distances, sometimes multiple times per day, to water sources (Buor, 2004; Rathgeber, 1996; Upadhyay, 2005). The physical strain associated with such task may have negative impacts on women’s health (Buor, 2004) as collecting water can be particularly burdensome for elderly women or young girls when water supply points are far away, pump handles are heavy, and if they are living with HIV (Wegelin-Schuringa and Kamminga, 2003; West et al., 2013). Physical strain is further compounded by heat and long queues at water sources (Upadhyay, 2005).

A Botswana study by Ngwenya and Kgathi (2006) in five rural villages of Ngamiland assessed access to portable water in HIV/AIDS households (n=129). Face to face interviews were used as well as participant observations and secondary data. Qualitative data was reduced to themes. The findings showed that

73.0% of the households obtained water from communal standpipes (Ngwenya and Kgathi, 2006). The average time spent on water collection was 21 minutes in a day and 93.0% travelled less than 500 meters. In one village of Shorobe, participants (70.0% compared to 52.0% in other four villages) attributed that access to water was unreliable as humans and animals competed for the same source. They further indicated that water can be unavailable for up to a week. Caregivers of HIV patients had perceptions that provision of ARVs to HIV patients would reduce water demand as ARVs reduces the number of HIV related bed ridden patients (Ngwenya and Kgathi, 2006). About 80.0% of caregivers said they used more water than non-caregivers' household because more water was needed to "eliminate the offensive odor and sanitize for the comfort of the patients and visitors" Caregivers reported that in periods of water stress, they did not bathe the patients but wipe the essential body parts and wounds (Ngwenya and Kgathi, 2006). When asked how regularly they washed their hands after coming into contact with patients' body fluids, 51% reported that they did so regularly. In conclusion the authors stressed that water should not be strictly treated as an economic good (Ngwenya and Kgathi, 2006).

4.2.2. Botswana

Botswana is a semi-arid country that experiences low rainfalls resulting in scarce water resources. The country continues to experience drought years (progressively intensified by climate change) and increased pressure for fresh-water supply due to rapidly increasing urbanization and climate change (Department of Water Affairs - Ministry of Minerals, Energy & Water Resources, 2013). Botswana's water resources are characterized by wide spatial variability, extreme scarcity, and a high dependency on trans-boundary waters (Government of Botswana, 2012). Most of the water is located in the northwest which is remote from the population center in the eastern side of the country. The dependency ratio, reflecting that part of the total renewable water resources originating outside the country, is the highest in southern Africa at 80 % (Government of Botswana, 2012). All of the country's five major drainage basins are shared: (1) The Limpopo River basin, occupying about 14.0% of the country in the east; (2) The Orange-Senqu River

basin, (12.0%) in the south; (3) The Zambezi River basin,(2%) in the north; (4) The Okavango Delta, which is an endorheic basin [stores water and allows no outflow to other external bodies such as rivers] (9.0%) in the northwest; (5) The South Interior, which also is an endorheic basin the remaining area (about 63.0%) including the Kalahari Desert and the Makgadikgadi Pans (Government of Botswana, 2012).

Botswana surface water resources are restricted to ephemeral and perennial rivers and water stored in reservoirs. They are also limited and unevenly distributed over the country. Most sources are in northern Botswana, while most people live in south eastern Botswana in and around Gaborone. The average annual run-off is 1.2mm, ranging from 0 in western and central Botswana to over 50 mm per annum in the north averaging annual run-off of 696Mm^3. Most of the run-off cannot be captured due to the lack of suitable dam sites, high variability of run-off in time and high evaporation. With regard to reservoirs, there about 100 reservoirs in the country most of them small and primarily used for agriculture. The Ministry of Agriculture has listed 92 dams of small to medium size, mostly for livestock use (Department of Water Affairs - Ministry of Minerals, Energy & Water Resources, 2013).

Botswana's total groundwater resources are estimated at around 100 billion m^3 with an average annual recharge at 1 600 Mm^3/annum (Department of Surveys and Mapping, 2001 and SMEC et. al., 1991). Groundwater collects in aquifers, and is abstracted through well fields, mostly for use in villages, mines, power plants, and irrigation; individual boreholes serve the livestock sector as well as small villages. Only a small part of the groundwater resources in Botswana can be economically abstracted due to high abstraction costs, low yields, poor water quality, and remoteness of aquifers in relation to consumer centers (SMEC et. al., 1991, Masedi et. al., 1999). Recharge is virtually zero in western Botswana, rising to 40 mm in the north. Groundwater depth is related to rainfall level (and recharge) at around 20 m in northern Botswana to more than 100 m deep in south western Botswana (Department of Water Affairs - Ministry of Minerals, Energy & Water Resources, 2013).

Water Utilities Corporation (WUC) is responsible for water production in Botswana. There are sixteen management centers throughout the country through which WUC provides portable water. The management centers treat and provide water sourced from both surface and groundwater (Botswana Environment Statistics Water & Climate Digest, 2017). The estimated combined sustainable yield of Botswana's well fields and storage dams is 2 165 Mm3 / annum or 216 L/person/day, based on the 2011 national population census estimate of 2,024,904. This is less than the current water demand of around 200 Mm^3/a or 262L/person/day (Department of Water Affairs - Ministry of Minerals, Energy & Water Resources, 2013). In terms of water consumption by different sectors, agriculture is the largest water user ($63Mm^3$), followed by domestic use/households ($57Mm^3$), mining ($27Mm^3$) and government ($12Mm^3$). Figure 13 shows the historical increase in mean monthly temperatures in Botswana (inland southern Africa), where the highest recorded was in the years 2005 and 2016 (Figure 13). The year 2016 shows the same high maximum monthly temperature in Gaborone, Botswana (Figure 14).

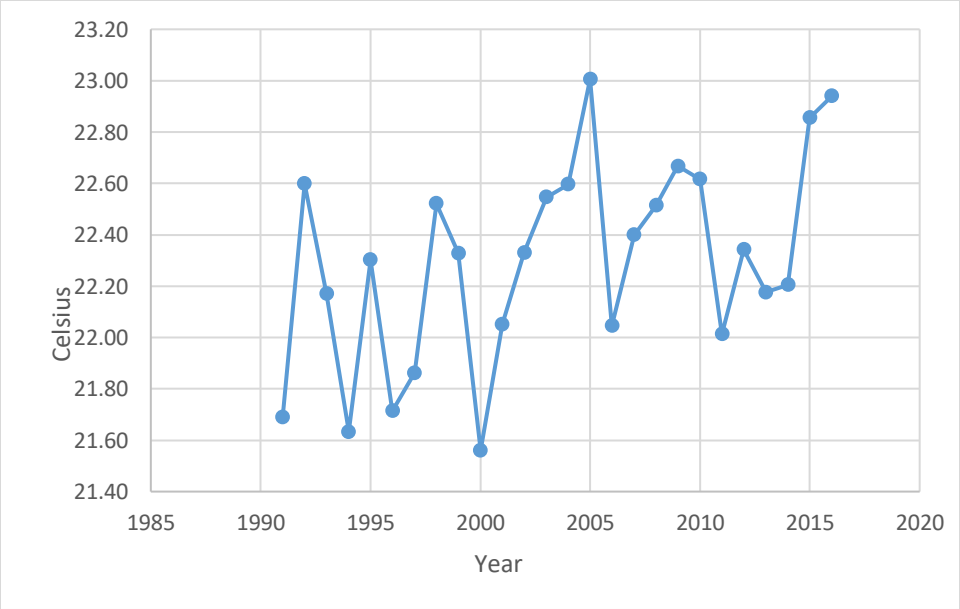


Figure 13: Average Monthly Temperature Trends in Botswana from 1991-2016.

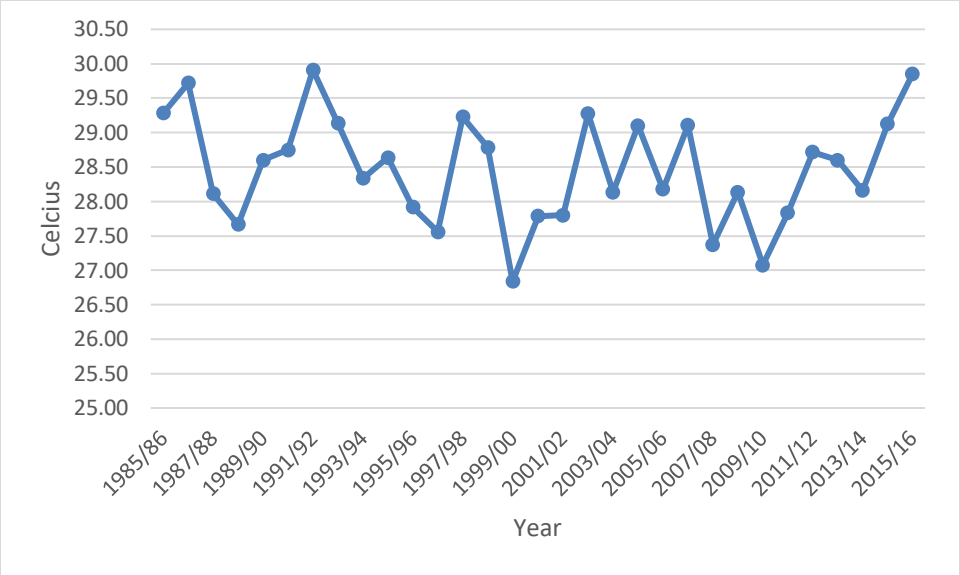


Figure 14: Maximum Monthly Temperature Trends in Gaborone, Botswana from 1985/86-2015/16.

4.2.2.1. Water Rationing

Water rationing is limiting water use due to concerns regarding water supply. Reasons for water rationing can be due to drought and maintenance of infrastructure involved in the water distribution and it can be short or long term. In the beginning of 2015/16, due to climate conditions, the risk of drought remained high all over the country. Despite the good rains towards the end of the year, the exposure to drought remained high as Botswana is generally a water stressed country and rains are erratic (Water Utilities Corporations Botswana ([WUC], 2016]). The rains came late, to dams which had hit rock bottom levels and ground sources whose yields had been greatly reduced. Of WUC's nine dams, Gaborone, Letsibogo, Shashe, Dikgatlhong, Ntimbale, Lotsane, Thune, Nnywane and Bokaa dams only six reached levels over 90.0%. Insignificant inflows were experienced by Gaborone (supplies the Greater Gaborone area) and Thune (Bobonong areas in the Central District) dams which went up to 19.0% and 39.0% respectively. Gaborone and Bokaa (supplies Kgatleng district) Dams failed completely during the 2015/16 due to the worst hydrological drought in decades. The dams replenished in March 2016 resulting in the resuscitation of their operations, which brought significant reappearance to the Greater Gaborone area water supply

situation. The slight recovery of the Gaborone Dam brought relief to the Greater Gaborone area which had been under water rationing for six months. Following these rains, water rationing was suspended and water supply restored to the area. However, some water restrictions were continued in some areas in the Greater Gaborone area and surrounding areas. These restrictions prohibited the use of potable water for many common activities which use a lot of water (WUC, 2016). According to the Ministry of Minerals, Energy and Water Resources (MMWER, Botswana), the Greater Gaborone area's average demand surpasses supply by 32.9 million liters a day (MMWER, 2015). Even with rationing, the demand surpasses supply by 18.2 million liters a day (MMWER, 2015). Due to this, the area continues to experience erratic low pressure to no water supply and should expect unannounced interruptions at any given time. Areas which were supplied by the Gaborone Dam were the most affected because of the layout of the water network which is not efficient in bringing water from the northern part of the city to the southern part for re-distribution (MMWER, 2015).

4.2.2.2. Power Infrastructure and Water Extraction in Botswana

Power plays a significant role in extraction of water from boreholes and dams countrywide. Botswana currently generates the bulk of its power from coal, and sits on large coal reserves of around 200 billion tons. Botswana Power Corporation (BPC) is a public company for electrical power generation, transmission and distribution in Botswana. It is currently the only electricity supplier in the country. Only a portion (450 MW) of installed capacity is available to produce power, and additional demand is met through electricity imports, primarily from South Africa which is also grappling with severe power shortages. Due to Botswana 's growth seen in the recent years, this has increased power demand which leads to frequent and untimely power cuts. They can go from hours in the urban areas and days in rural areas. Unlike the Water Utilities Corporation, BPC hardly announces warnings ahead of time on scheduled power cuts. The overall current power access rate is 60.0%, which is rural: 54.0% and urban: 65.0%. As of

2018, there were 211,000 people in Botswana without power and the target is to reach 100% access by 2030 (USAID Power Africa, 2018).

4.2.3. Gaps in the Literature

In almost all of the literature on climate and HIV medication in the region, the environmental barriers were cited as food insecurity (physical environment) and transportation system to access services (built environment). In addition, the studies were also looking at the relationship between HIV/AIDS and water keeping focus on sanitation and hygiene (Obi et al., 2006; UNICEF, 2006; Nkongo & Chonya, 2009). The assumed benefit of improved sanitation and potable water was mainly to reducing diarrhea morbidity (Obi et al., 2006). Diseases associated with fecal contamination of water usually exacerbates one's progression from being HIV positive to full-blown AIDS due to the rapid weakening of the immune system (Fewtrell et al., 2005; Yates et al., 2015; Nkongo & Chonya, 2009). Most of these studies assumed the cause and effect relationship of the interaction of HIV and AIDS and water scarcity, yet the factors and impacts of the complex interaction of multiple stressors have multiple social realities including high ambient temperatures, low antiretroviral adherence, food insecurity, poverty, and other structural barriers (Mbereko et al., 2016). Multiple social realities are the products of the interaction of multiple stressors and the household's livelihood assets, and these are heterogeneous (Mbereko et al., 2016).

4.3. GOAL OF THE STUDY

The aim of this study is to assess the impacts of environmental factors that include ambient temperatures and water rationing on ART and PMTCT adherence at individual and health care levels for adult men and women, and pregnant women and new mothers. This assessment will be carried out by investigating the adherence levels on both adult men and women who are living with HIV and on ART and PMTCT therapies in relation to water rationing and heat. Clinic attendance will also be assessed to understand if it is impacted by environmental factors. Finally, unpack the specific environmental barriers that affect mothers on PMTCT in particular.

4.4. DATA AND METHODS

4.4.1. Study Area

Botswana is a landlocked country in southern Africa characterized by a semi-arid climate. With an area covering 224,607 square miles, Botswana is sparsely populated with 2.2 million people. The country is mainly flat, dominated by the Kalahari Desert, which covers up to 70% of its land surface (Figure 15). The Okavango Delta, one of the world's largest inland deltas, is in the northwest district (Figure 15). The Makgadikgadi Pan, a large salt pan, lies in the north. The capital city of Gaborone is located in the south east where around 10% of the population reside (Figure 15). It is hot and dry for much of the year but there is a rainy season which runs through the summer months. The summer season begins in November and ends in March. It usually brings very high temperatures. The winter season begins in May and ends in August. This is also the dry season when virtually no rainfall occurs. Winter days are invariably sunny and cool to warm; however, evening and night temperatures can drop below freezing point in some areas, especially in the southwest. Rainfall tends to be erratic, unpredictable and highly regional. Often a heavy downpour may occur in one area while 10 kilometers away there is no rain at all. The mean annual rainfall varies from a maximum of over 650mm in the extreme northeast area of the Chobe District to a minimum of less than 250mm in the extreme southwest part of Kgalagadi District where the Kalahari Desert is located (Botswana Tourism Organization [BTO], 2019). Showers are often followed by strong sunshine which means that a good deal of the rainfall does not penetrate the ground but is lost to evaporation and transpiration. Summer days are hot as temperatures rise to the 38°C (100.4 F) and now more often than not reaching a blistering 44°C (111.2 F). Winters are clear-skied and dry, warm during the daylight hours but, because there is no cloud cover, cold at night and in the early mornings (BTO, 2019).

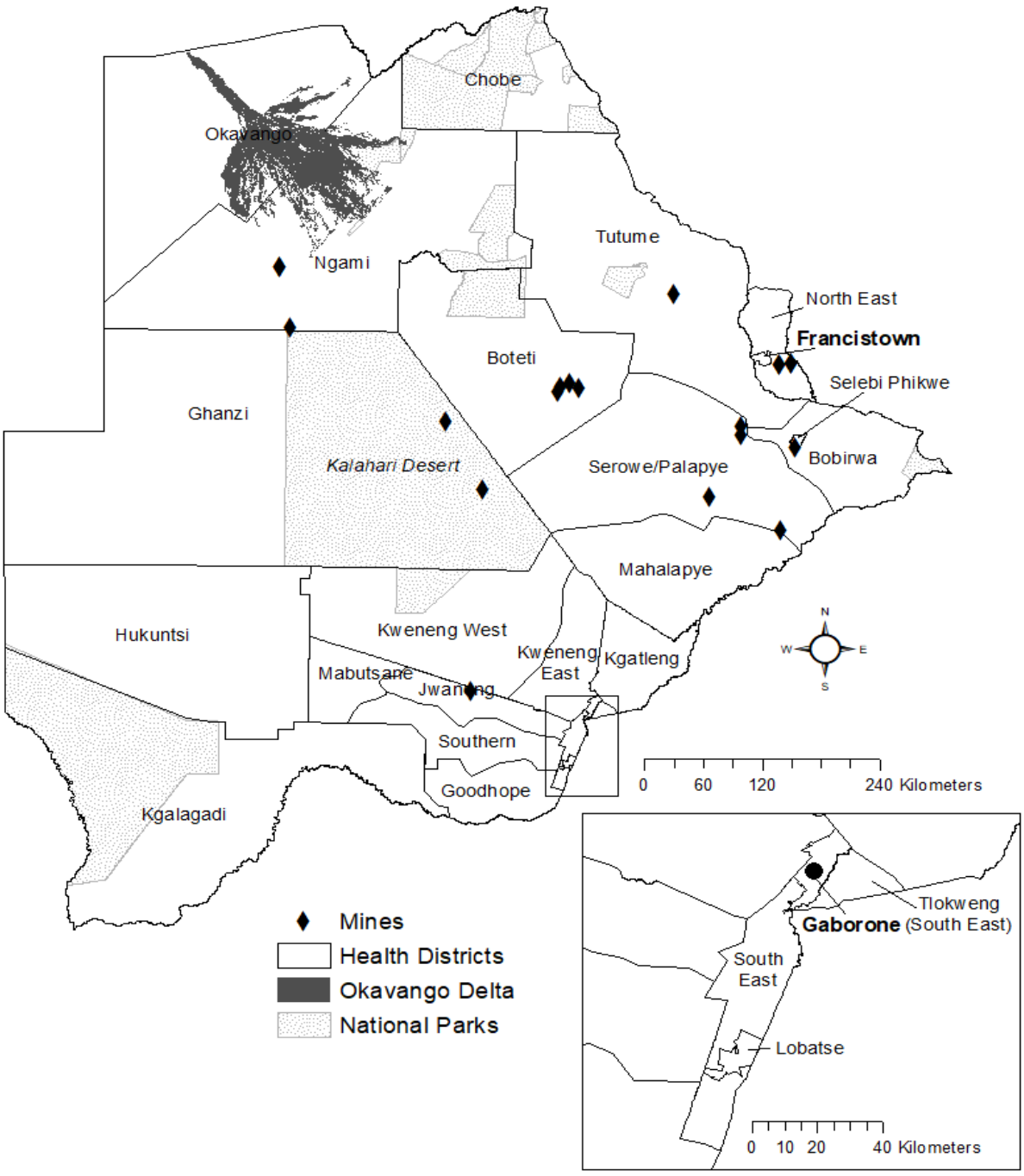


Figure 15: Map of Botswana Showing Wet (Okavango Delta) and Dry (National Parks and Kalahari Desert) Areas and Mining Places.

Source: (Kelepile and Grady, 2019).

4.4.1.1. Greater Gaborone

This study took place in the Greater Gaborone which is made of the Gaborone city (as its own district) and three surrounding districts, South East, Kgatleng and Kweneng East Gaborone alone has a total population of 231,592, while the larger metropolitan area has about 421,907 people (Botswana Census 2011). During the country's decennial census of 2011, the HIV prevalence rates were found to be highest in the cities, followed by urban villages and lower in rural area hence the selection of the Greater Gaborone. Gaborone has seen growing trends of HIV prevalence rates because of its strategic location, its proximity to the railway line and Johannesburg, South Africa, its already established administrative offices, its accessibility to most of the major tribes, its non-association with any particular tribe, and most importantly, its closeness to a major water source of Gaborone Dam.

Gaborone and South East were in one district until recently (after the recent population census of 2011) when Gaborone became an independent district on its one (Statistics Botswana, 2015). About 13% of males age 18 months and above were HIV positive, 19.8% were female, which gave the total district HIV prevalence to be 17% (BAIS IV, 2013). About 19% of males age 18 months and above were HIV positive, 14.6% were female, which gave the total district HIV prevalence to be 16.6% (BAIS IV, 2013). There were 33,332 people enrolled on ART in Gaborone district as of February 2017. The patients were distributed across the 22 health facilities in the area (MoHW, 2017). South East district has a fewer ARV patients and clinics as compared to Gaborone with 4,659 people on ART and six health facilities (MoHW, 2017). Although the Kweneng East district is close to Gaborone, generally it experienced a modest growth of about three percent per annum between 2001 and 2011 (Statistics Botswana, 2015). A negative growth is usually due to outward migration, which is normally due to lack of employment opportunities in an area (Statistics Botswana, 2015). About 20% of males age 18 months and above were HIV positive, 22.1% were female, which gave the total district HIV prevalence of 21.5% (BAIS IV, 2013). There were 26,587 people enrolled on ART in Kweneng East district as of February 2017. The patients were distributed across the 30

health facilities in the area (MoHW, 2017). About 16% of males age 18 months and above were HIV positive in Kgatleng district, 23.8% were female, which gave the total district HIV prevalence to be 19.9% (BAIS IV, 2013). There were 11,028 people enrolled on ART in Kgatleng district as of February 2017. The patients were distributed across the 26 health facilities in the area (MoHW, 2017).

Access to sanitation facilities is measured at household level by assessing whether it has access to flush toilet either in-house, communal or shared with a neighbor or had access to a sanitary pit latrine (Statistics Botswana, 2015). Overall, the proportion of households in Gaborone with access to flush toilets was 50%, pit latrine 2.1%. In total, 99.1 per cent of the total population in Gaborone had access to toilet facilities (Statistics Botswana, 2015). With access to portable water in Gaborone, 58.4% of the population had piped water indoors, 31.9% piped outdoors, 7.7% communal tap with a total access of 99.4% (Statistics Botswana, 2015). About 74% of the population in Gaborone used electricity for lighting and heating (Statistics Botswana, 2015).

4.4.1.2. Study clinics (n=21)

The (n=21) clinics were purposively selected from the three geographies (urban, peri-urban and rural villages) in the four districts of Botswana. These districts were selected because of their high HIV prevalence rates, high number of ART/PMTCT facilities and the proximity to the researcher' residential place. The greater Gaborone area is located on the southern part of Botswana whereas mentioned earlier is dry and receives little rainfall so vegetation is minimal in this side of the country. From the urban area of Gaborone, five clinics were selected. Among these urban clinics, three clinics (Broadhurst, Bontleng and Old Naledi) are located in low-income neighborhoods. Old Naledi is mainly a squatter settlement in the outskirts of Gaborone characterized by small businesses and relatively high population density. This neighborhood is also close to Gaborone dam which is the city is major source of water, so minor fishing is evident as well as less dry landscapes. Five peri-urban are located in the peri-urban villages close to Gaborone. Due to the growing population of Gaborone, most people commute and reside in these peri

villages. Due to high densities of people, clinics in these areas, are usually located around residential neighborhoods which means are closer to people's homes. There are also decent tarred roads close to the peri-urban clinics. The eleven rural clinics usually had limited tarred roads and people use dirt roads to reach to these facilities. They are usually not as busy and congested as urban and peri-urban clinics, so tend to be relative small in physical structure. The images were sourced from Google Earth using a radius of 2km. All the images were updated as of November 2018 (summer in Botswana) except for three in the Kgatleng district (Makakatlela, Mochudi1 and Morwa) which were from February 2019 (still the summer season).

4.5. STUDY DESIGN

This study utilized a cross-sectional survey (winter, 2016) with retrospective responses. It is a mixed method study with quantitative data from survey administered face-to face 658 women and men living with HIV attending 21 HIV clinics in Greater Gaborone. Within these clinics, 84 health care workers were also surveyed using qualitative semi-structured questionnaire for their perspectives. The sampling methodology and mechanisms by which to optimize reliability and validity of the sample is described below.

4.5.1. Primary Data Collection

The data for this study was collected during the winter in Botswana. A sample of adults living with HIV, who were enrolled in ART (n=658) and PMTCT (n=67) therapies at government clinics, in urban, peri-urban and rural clinics were interviewed for this study. The data for this study were generated primarily from a survey (quantitative) administered to adult men and women who are living with HIV and enrolled on ARV and pregnant and mothers enrolled on PMTCT at public clinics (face to face interview), as well as a semi-structured interview (qualitative) of key informants who are health personnel working at the study area. The questionnaires were administered in in Setswana (national) and English (official) languages to the participants. All participants were asked to sign an informed consent before they can partake in the study

to ensure confidentiality. The use of Setswana language (local) was useful in this study because patients understood it better than English. For inclusion criteria, only 18 and above participants who are HIV positive and enrolled on ARV therapy at a public clinic took part in the study. The questionnaires were administered by the principal researcher and four research assistants. The principal researcher took a training with the MSU IRB while the research assistants who are all Botswana locals with a bachelor's degree were trained by the principal researcher with materials directly obtained from the MSU IRB. All the assistants are fluent in both the languages.

The self -administered questionnaire to pregnant women and mothers on PMTCT have 44 variables (with six sections) which range from demographics to the water related concerns in the medication. The questions on demographics and maternal characteristics (first three sections) that included annual income, partner HIV status, number of children and education are close ended questions. The remaining portions that dealt with knowledge of HIV, treatment seeking behaviors, and water related concerns. These were more open-ended, allowing mothers (new and expectant) to provide detailed information. The sections on access a treatment seeking behaviors included PMTCT adherence questions ("Are you enrolled in PMTCT?" [Q19], "Have you ever missed your pill dosage at home because there was no water [Q33]?", Have you /baby ever missed doctor's appointment? [Q32]). As already mentioned, these questions are open-ended and important because they allow for gaining in-depth information.

Biological data such as CD4 count (the blood cells in the body that fights the infections which indicate the health of the immune system), viral load (amount of HIV virus in the body which is used to monitor the efficiency of the ART), weight and height were collected from the patients' medical cards. Patients are required to bring their medical file each time they visit their ART facility. Only the latest readings were taken as the patients take new readings at least three times a year. From all the clinics, a total of four from each clinic (doctor, two nurses and a pharmacist [ARV dispenser] key informants were selected. No

sampling was done on the key informants as the four mentioned are the ones that have daily and direct contact with patients attending ARV clinics.

4.5.2. Sampling Methodology

The districts were selected using purposive sampling technique. The research focus was on the adult men and women living with HIV who are also on ART. The selected study area has a high HIV prevalence, high number of HIV positive patients as well as high number of ART clinics. The study covered both urban, peri-urban and rural villages. Gaborone (urban), South East (peri-urban), Kgatleng and Kweneng (both rural) are close to the researcher 's residence and have all the identified characteristics based on geography and HIV prevalence. In total, four districts were selected based on the finding that the prevalence in urban areas is higher (19.2 percent) than rural areas (17.4 percent). Rural areas had consistent prevalence rate over the years, 17.1 percent in 2008 and 17.4 percent in 2013 (BAIS IV, 2013). To calculate the number of clinics needed, first the national prevalence (22%) was used since the study did not consider district as rigid boundaries. There are 84 ARV health facilities in the study area, 22 Gaborone, 6 in South East, 26 in Kgatleng and 30 in Kweneng East. Using the national prevalence (.22*84 clinics), 18 clinics was recommended. To account for over and under sampling other facilities, the number was increased to 21 clinics. Selection of adult men and women in the chosen districts (Equation 1.1) was calculated using the formula below: The formula was adopted from a national stigma associated with HIV/AIDS survey conducted in 2014 (Botswana Stigma Index Survey Report, 2014).

$N= (t^2pq)/ (d^2)$ [Equation 1.1]

Where;

n = minimum sample size required

t = z value of confidence level desired (95% confidence level)

p = estimated prevalence in target population (the national adult prevalence rate of 22%).

d = precision. The higher the precision desired the larger the sample size will be. 0.05 (5%) is the most common d value.

q = 1-p. Assuming 95% confidence and a precision of 0.05

Formula: Equation 1.1

N= (1.96^2)*0.22*(1-0.22))/ (0.05^2) = 263.6. Design effect = 263.6 x 2 = 527.2

= **527** was the minimum sample size required for adult men and women living with HIV and taking ART and the interview continued until the last patient was interview at the close of the day giving the final sample to be 658.

Selection of pregnant women and mothers in the chosen clinics involved purposive sampling, where from each clinic, two women were selected giving a total of 67. In some instances, where there was comparison of mothers and non-mothers, a full sample of all the women (n= 419) was used. This sample is explained in detail in Chapter 2. Following the selection of clinics and participants, a systematic random sampling was employed to select the ART/PMTCT patients at their respective clinics. Within the context of this study, at each clinic, every second ART/PMTC patient/mother to enter the door was selected until the minimum required sample each clinic was reached. Participants were visited daily at their respective ART /PMTCT facilities in the study area.

To complement the information that was gathered from patients on ART key informants were chosen and a semi structured interview (30-60 minutes interviews) used. From all the clinics, a total of four from each clinic (doctor, two nurses and a pharmacist [ART/PMTCT dispenser] health care workers were selected (n=84 for the 21 clinics). The responses collected from the key informants during the semi-structured interview were grouped into categories to find out emerging themes. Direct quotes were used where necessary.

4.5.2.1. Reliability and Validity of Data

A sample of 658 ART patients including 67 mothers on PMTCT is relatively adequate for statistical analysis of factors influencing ARV/PMTCT adherence among adult men and women living with HIV in the urban, peri-urban and rural areas of Botswana. For reliability purposes, all the patients were visited at their respective clinics at the same time (from 7.30 am until 2:00 pm). In addition to the principal investigator, four experienced assistants helped with the data collection. The study was also voluntary and participants signed a consent form before taking part in the survey. The data was coded only by the principal researcher to remove the differences which could be incurred if all the assistants coded the data. To avoid or minimize multi-collinearity when using a multivariate model in this case measuring ART/PMTCT adherence, variables were tested one by one. Variables that turn out to be highly significant, further statistical analysis were performed.

4.5.2.2. Ethics Overview

The survey took place in the urban, peri urban and rural villages of Botswana from May until August 2016. Given the sensitivity of this research, an approval from the IRB was secured from both Michigan State University, and the Ministry of Health in Botswana prior to administering the survey. After satisfying the requirements of the MoHW IRB requirements, to get into the different clinics, separate IRBs were sought from the District Health Management Teams in Botswana.

4.5.3. Non-Adherence Definition

Adherence in this paper is a dichotomous composite variable defined by three questions. Antiretroviral (ARV) drugs should be taken daily for the rest of the patient's life as soon as they are enrolled in the therapy. When a patient had CD4 count of 350 copies/ml and more [CD4_REC], taking the pills as instructed by the doctor (100% dosage) [ARVPrescribe] and having missed one a dosage sometimes [MissDose] (95% or at least missed 1 pill a month). If all of these variables were satisfied, one was considered to be adherent (code 0), but if one or more were not met then a patient was considered non

adherent (code 1). Modelling in this paper, is non adherent (code1). Non-adherence in this study was therefore defined as either having a CD4 count less than 350 copies, not taking antiretroviral (ARV) drugs as prescribed by the doctor and missing ART dosage sometimes. In summary: non adherence means (1) CD4 >= 350 copies/ml AND (2) ARVPrescribe = No AND (3) MissDose = Yes.

In this study, six independent variables were chosen to be included in the models as a way to investigate low ARV adherence levels among adult men and women. Explanatory variables potentially associated with the dependent variable included: Sex (female vs. male). Gender was defined as a dichotomous variable with females being at risk of non-adherence hence the code of 1 for females versus 0 for males. If participants had missed an appointment due to heat [AppHeat], this variable was coded as 1, and 0 for not missing the appointment. The same was done for variable on [AppWater} which asked participants if they have missed an appointment due to lack of water at home. As mentioned earlier, patients are required to attend the clinic every month and this is where they refill their prescription. This means that, missing an appointment can be detrimental because it means not collecting a dosage for a month. To understand the side effects of water rationing on patients' health, the question on how water rationing affected their health [Ration Health], was asked, and if one felt no side effects, the response was coded as a 0. The final variable [ClinicWater], asked patients if they have been turned away from acquiring clinical services because the clinic did not have water. If they answered yes, it was coded a 1 and 0 for those who have not been turned away. The mode of transport [TransportMode] was a variable to assess the type of transit patients used to attend their various clinics. Public transport was coded as 1, walking as 2 and private car as 3. The final variable was the type of clinic patients attended. If the clinic was in an urban area, it was coded as 1, peri-urban as 2 and 3 for rural clinic.

4.5.4. Descriptive Methods

All the continuous variables were assessed to check for distribution and normality through histograms and correlation techniques. The variable 'viral Load'- which is the amount of virus in a patient's body was

skewed with many outliers, so patients with high numbers (<7000 copies/ ml) were removed. Further the variable 'SexPartner'-which the number of partners that one had over the past year, had a couple of extreme values such as 16 partners in 12 months, so two patients were removed, leaving the n=658 in the analysis. To prepare the variables for logistic regression, frequencies and cross tabulations [descriptive statistics] were run for all the dichotomous variables. This was helpful because it was a measure to check if all the assumptions of logistic regression were being meant.

4.5.5. Analytical Methods

Logistic regression and multilevel modeling were used as analytical methods to assess physical environment barriers to ART adherence. The PROC MIXED technique in SAS 9.4 statistical software was used. PROC MIXED is used to estimate (a) two-level organizational models, (b) two-level growth models, and (c) three-level organizational models. Both random intercept and random intercept and slope models were estimated. When building the model, the first thing is to always start with an unconditional model (i.e., a model that has no predictors) as this model is used to calculate the infraclass correlation coefficient (ICC) which estimates how much variation in the outcome exists between level-2 units and gradually adding independent variables while checking for improvement in model fit after each model is estimated (Bell et al., 2013). The full maximum likelihood (ML) was used examining the improvement in model fit using Akaike's Information Criterion (AIC) where smaller values represented better fitting models. For the degrees of freedom, Kenward-Roger DF methods was used as it is well-suited as is intended to be used in models with unbalanced designs and can handle complex covariance structures (Bell et al., 2013).

4.5.6. Thematic Analysis (Qualitative)

The health care workers' questionnaire has more open-ended questions that enables for rich analysis and the emergence of themes that help in answering the posed research questions. To conduct a thematic analysis, steps recommended by Braun and Clarke (2006) were followed. The interest was on understanding levels, and water scarcity and ambient temperatures as barriers of ARV/PMTCT adherence,

so the themes revolved around this concept. By conducting all these steps, there was a confidence in results generalization because they followed a logical and falsifiable order.

4.6. RESULTS

The environmental characteristics in relation to non-adherence among surveyed women and men in Greater Gaborone are presented in Table 23. Of the 21 women who missed an appointment due to heat, 12 were non adherent and for men (n=14), 11 were non-adherent. The relationship between gender and missing appointment was significant for non-adherence. Most women (57.1%) indicated that water rationing affected their health and the same was observed for the men (57.7%) even though the association with non-adherence was not significant (X^2=0.11, p 0.72). Fourteen women compared to 13 men reported that they have been turned away by the clinic because there was no water available (Table 23). This relationship was significant for men but not for women.

Table 23. Environmental Characteristics and ARV Adherence vs. Non-Adherence[1] in a Sample of Women (n=419) and Men (n=239) in Greater Gaborone, Botswana, 2016.

Environmental Characteristics	Women		Non-Adherence	Men		Non-Adherence	Women[1] Chi-Square	Men[1] Chi-Square
	No.	(%)	(%)	No.	(%)	(%)	p-value	p-value
Missed Appointment due to Heat							8.4 (0.003)	6.3 (0.011)
Yes	21	5.0	2.9	14	5.9	4.6		
No	398	94.9	26.2	225	94.1	41.4		
Missed Appointment due to Water Scarcity							4.4 (0.035)	1.9 (0.171)
Yes	8	1.9	1.2	7	2.9	2.1		
No	411	98.1	27.9	232	97.1	43.9		
Missed Appointment due to Water Rationing							0.11 (0.729)	0.02 (0.892)
Yes	239	57.1	16.2	138	57.7	26.4		
No	180	42.9	12.9	101	42.3	19.6		
Turned away from Clinic due to Water Scarcity							3.06 (0.80)	5.28 (0.021)
Yes	14	3.3	1.7	13	5.4	4.2		
No	405	96.7	27.4	226	94.6	41.9		
Total	419	100	29.1	239	100	46.1		

A sample of 658 men and women who were surveyed were asked how the four environmental variables affected their adherence to ART. These were compared by their location (Table 24). Majority of the patients' health (55.7% urban), 61.7% peri and 54.7% rural were affected by water rationing in their homes (Table 24). There were n=126 patients who lived in urban areas and of those 52 were non-adherent. Of the 160 patients who lived in peri-urban areas, n=60 were non-adherent and 120 of rural patients (n=372) were non-adherent. Association was significant for rural areas by missing appointment due to heat and being turned away by the clinic due to lack of water (Table 24).

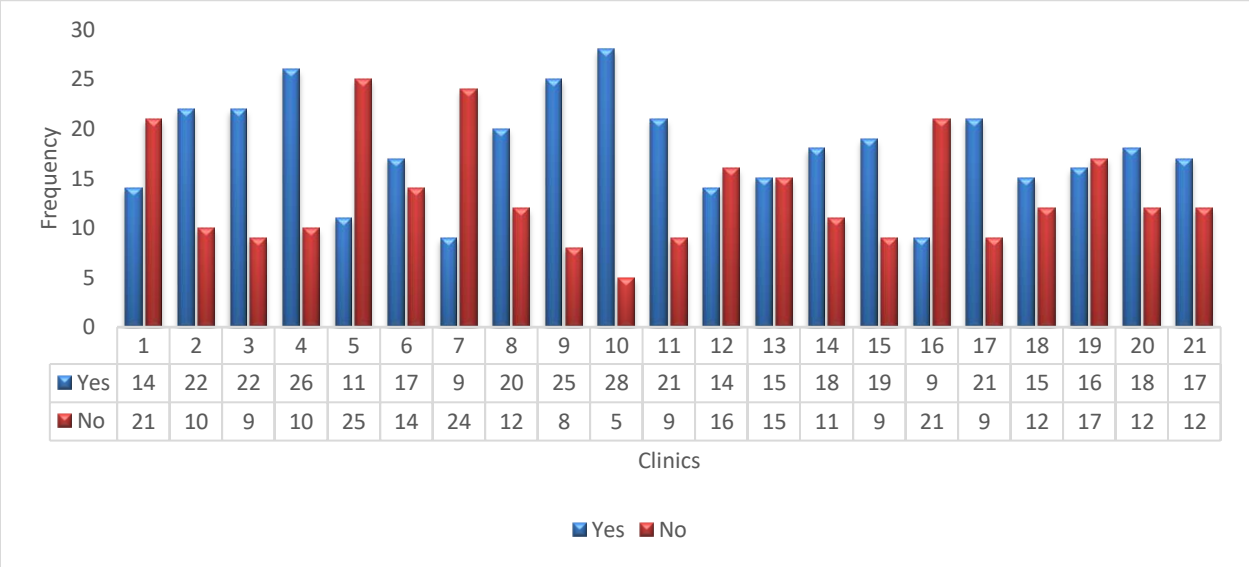
Table 24. Environmental Characteristics and ART Non-Adherence Stratified by Location in Greater Gaborone, Botswana, 2016.

Environmental Factors	**Urban**		**Peri-Urban**		**Rural**	
	Adherence	**Non-Adherence**	**Adherence**	**Non-Adherence**	**Adherence**	**Non-Adherence**
[1]Appointment Missed due to Heat						
Yes	9 (7.1)	3 (5.7)	3 (3.0)	5 (8.3)	3 (0.81)	15 (12.5)
No	68 (91.9)	49 (94.2)	97 (97.0)	55 (91.7)	249 (99.8)	105 (87.5)
[2]Appointment Miss due to Water Rationing						
Yes	1 (0.8)	1 (0.8)	2 (2.0)	6 (10.0)	2 (0.8)	3 (2.5)
No	73 (98.6)	51 (98.1)	98 (98.0)	54 (90.0)	250 (99.2)	117 (97.5)
[3]Water Ration affects Health						
Yes	39 (52.7)	29 (55.7)	57 (57.0)	37 (61.7)	150 (59.5)	65 (54.7)
No	35 (47.3)	23 (44.2)	43 (43.0)	23 (38.3)	102 (40.5)	55 (45.8)
[4]Clinic Turned You away due to Lack of Water						
Yes	2(2.7)	0 (0.0)	3 (3.0)	6 (10.0)	5 (1.9)	11 (9.2)
No	72 (97.3)	52 (100.0)	97 (97.0)	54 (90.0)	247 (98.0)	109 (90.8)
Total	74 (17.4)	52 (22.4)	100 (23.5)	60 (25.9)	252 (59.2)	120 (51.7)

[1] Urban (Chi-square=0.252, p-value=0.616); Peri-urban (Chi-square=2.24, p-value=0.134); Rural (Chi-square=22.6, p-value=<0.0001).
[2] Urban (Chi-square=0.064, p-value=0.800); Peri-urban (Chi-square=5.05, p-value=0.025); Rural (Chi-square=1.78, p-value=0.182.
[3] Urban (Chi-square=0.116, p-value=0.734); Peri-urban (Chi-square=0.337, p-value=0.562); Rural (Chi-square=0.956, p-value=0.328).
[4] Urban (Chi-square=1.428, p-value=0.232); Peri-urban (Chi-square=3.46, p-value=0.063); Rural (Chi-square=10.188, p-value=0.001).

To understand water rationing of women and men at home, patients grouped by clinic they attended were asked how water rationing affected their health (Figure 16). Water rationing affected more patients (n=28) than not (n=5) attending clinic 10 compared to all other clinics (Figure 16). They were followed by

clinic 4 with n=26 affected and n=10 not affected patients. For patients attending clinic 13, there was no difference in how water rationing affected their health (n=15 respectively).



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Yes	14	22	22	26	11	17	9	20	25	28	21	14	15	18	19	9	21	15	16	18	17
No	21	10	9	10	25	14	24	12	8	5	9	16	15	11	9	21	9	12	17	12	12

Figure 16. The Responses of Patient's Attending 21 Clinics in Greater Gaborone on whether Water Rationing Affected their Health at Home.

Built environment such as road infrastructure can impact the patients' abilities to adhere to their ARV regime, so in this study, participants were asked the mode of transport they used to reach their respective clinics controlling for missing appointment due to heat. Patients who used public transport and missed an appointment due to heat compared to those who walked and did not miss had high significant odds ratio of being non- adherence levels [OR 8.48, 2.32-31.06] (Table 25).

Table 25. Unadjusted Estimated Odds of Non-Adherence if Missed an Appointment due to Heat by Travel Model, Greater Gaborone, Botswana, 2016.

Gender	Heat Miss Appt.	N	Gender	Heat Miss Appt.	N	Estimate	SE	p- value	Odds Ratio	LCL	UCL
Drive	No	56	Public	No	239	0.2884	0.302	0.339	1.33	0.74	2.41
Drive	No	56	Public	Yes	14	-1.5869	0.705	0.024	0.21	0.05	0.82
Drive	No	56	Walk	No	328	0.5509	0.296	0.062	1.74	0.97	3.09
Drive	No	56	Walk	Yes	21	-0.575	0.517	0.266	0.56	0.2	1.55
Public	No	239	Public	Yes	14	-0.1875	0.665	0.005	0.15	0.04	0.57
Public	No	239	Walk	No	328	0.2625	0.181	0.146	1.3	0.91	1.85
Public	No	239	Walk	Yes	21	-0.8634	0.461	0.061	0.42	0.17	1.04
Public	Yes	14	Walk	No	328	2.1378	0.662	0.001	8.48	2.32	31.06
Public	Yes	14	Walk	Yes	21	1.0119	0.787	0.198	2.75	0.59	12.85
Walk	No	328	Walk	Yes	21	-1.1259	0.457	0.014	0.32	0.13	0.79

Tables 26 and 27 show the predictor variables that were used in the model adherence by patients nested within clinics. Missing appointment due to heat, water, being turned away by clinic, controlling for male gender and distance all reduced adherence but did not vary by clinic. Only missing due to heat (β-0.22 p 0.008) varied by clinic (Table 26). Previous table (Table 24) showed that rural areas had significant non-adherence levels due to missing due to heat and being sent away by clinic due to lack of water, further investigation of fixed effects by rural location were explored (Table 27). All the variables in Table 26 reduced adherence but variation by clinic was evident through missing appointment due to heat (β-0.41 p 0.004. Residing in the rural without the interaction increased adherence (β 0.10 p 0.02) (Table 27).

Table 26. Multilevel Model Estimating the Effects of Environmental Variables on Adherence among Adults Living with HIV attending Clinics in Greater Gaborone, 2016.

Covariance Parameters		Estimate			
Intercept	Clinic	0.0068			
Intercept	Patient ID(ClinicID)	0.0276			
Residual		0.1819			
Fixed Effects	Estimate	S.E.	DF	t-value	p-value
Intercept	0.7388	0.0467	157	15.80	<.0001
Missed Appointment due to Heat	-0.2224	0.0845	647	-2.63	0.0087
Missed Appointment due to Lack of Water	-0.1927	0.1260	650	-1.53	0.1268
Does Water Rationing Affect your Health	0.4330	0.0375	650	1.15	0.2494
Clinic Turned Away due to Lack of Water	-0.1636	0.0945	637	-1.73	0.0839
Sex (Men=1)	-0.1637	0.0374	641	-4.38	<0.0001
Distance	-0.0013	0.0011	647	-1.11	0.2658

Clinics: N= 21, Patients 36 each clinic total N=658, AIC 887.9.

Table 27. Multilevel Model Estimating the Effects of Environmental Variables on Adherence among Adults Living with HIV attending Rural Clinics in Greater Gaborone, 2016.

Covariance Parameters	Estimate				
Intercept (Clinic)	0.0051				
Intercept (Patient nested within Clinics)	0.0322				
Residual	0.1751				
Fixed Effects	Estimate	S.E.	DF	t-value	p-value
Intercept	0.7167	0.04479	108	16.00	<.0001
Missed Appointment due to Heat*Rural	-0.4161	0.1165	650	-3.57	0.0004
Missed Appointment due to Lack of Water*Rural	-0.2258	0.1217	651	-1.86	0.0640
Clinic Turned Away due to Lack of Water*Rural	-0.2117	0.1217	648	-1.74	0.0824
Sex (Men=1)	-0.1641	0.0371	642	-4.42	<0.0001
Distance	-0.0018	0.0011	585	-1.64	0.1025
Rural	0.1092	0.0458	55.5	2.38	0.0207

Clinics: N= 21, Patients 36 each clinic total N=658, AIC 876.8.

4.6.1. Descriptive statistics

Mothers (n=67) were asked the environmental factors that impacted their adherence. Majority (n=55) indicated that year 2016 was drier and very hot (n=47) than previous years. Three mothers reported that they have experienced water rationing; sent home without service at clinic due to lack of water (n=1), not preparing baby formula because of lack of water (n=1) and miss appointment due to lack of water (n=1). The mothers (n=5) also expressed that they have experienced loss of children due to HIV related illnesses, malnutrition, traditional causes and undisclosed causes (Table 28).

Table 28. Environmental Variables of Concern to Mothers (n=67), Children and Infants, Greater Gaborone, Botswana, 2016.

Environmental Variables	**No.**
Very Hot Compared to Previous Years	47
Drier Compared to Previous Years	55
Sent Home from Clinic due to No Water	1
Missed Appointment due to No Water	1
No Prepared Baby Formula due to Water Scarcity	1
No. Children Die	5
Causes of Death: HIV-related illnesses (1-year, 4 years) Malnutrition (2-years) Traditional Causes (12-years) Other (5-years)	

4.6.2. Health Workers Analysis on Water issues, High Temperatures and Non-adherence: Qualitative Results

4.6.2.1. Clinic Operations and Water Issues

In order to complement the findings related to lack of water and non-adherence, the health practitioners were asked using a semi-structured interview their water rationing opinions. There were three questions that were compiled to come up with the relevant theme of clinic operations and water issues. The first question was whether in their respective clinics, has water been a problem with regards to provision of clinical services. The second one was on whether they had water backup in case of no water supply and finally if they ever denied a patient service because of water scarcity. Responses were categorized by provider (doctor, pharmacist and nurse) as well as by the clinic location (urban, peri-urban and rural villages). Direct quotes were used to emphasize the important points relayed by the health practitioners. Out of the 84 providers, only 17 from 7 different clinics indicated that water was not an issue in service provision. Of all the 7 clinics, 5 were located in the city of Gaborone and 2 in the rural districts of South East and Kgatleng. The providers reported that they did not encounter water issues because they had a water reservoir in their clinic which they relied on rainfall and purchasing of water. They also added that they never turned back a patient without providing service because of lack of water. The rest of the health workers (n=67) lamented that water rationing was a hindrance in their ART facilities. Doctors across the board complained about the poor water supply that can be shutdown at any point without prior notification from Water Utilities Corporation. Pharmacists decried of unreliable water supply that could sometimes go for days with just slow drops from the taps. While the nurses indicated that they longed for a backup water plan such a *Jojo* (water reservoir locally called by its brand name) that are found in urban clinics and hospitals.

When asked how water rationing interrupted their day to day activities at the clinic, a doctor in a rural clinic said,

"*We tend to see weak patients when there is no water because facilities such as toilets are unusable, and this forces patients to use unsanitary toilets that are a breeding places for opportunistic infections"* (Doctor, Rural Clinic).

Other services such as blood screening were halted on water rationing days.

"We *do not screen for blood which is important for their CD4 count and viral load when there is no water, so it really throws us out of schedule"* (Nurse, Rural Clinic).

Even though the health workers complained about slow services due to lack of water, all of them denied ever turning back a patient without a service.

4.6.2.2. Clinic Attendance and the Impact of Heat

This theme was made up of five questions which were surrounding on how high temperatures affected the services received by patients. They included whether clinic attendance decreased due to heat and the type of temperature controls available in the respective clinics. From what the health workers said, high temperatures posed as a constraint in their health facilities. A pharmacist in Gaborone clinic reported that,

"O*ur drugs expire really quickly because of being exposed to high temperatures"* (Pharmacist, in Gaborone).

Meanwhile a doctor in peri-urban clinic of Mopane said

"*on very hot days, blood samples expire even before we have the chance to send them to the technical labs"* (Doctor, Peri-Urban Clinic).

High temperatures also slowed down other departments such as the women section

"*Women section run slow when it's too hot because they [women] are required to provide a lot of fluid samples"* (Nurse, Rural Clinic).

Health workers were asked about clinic attendance on hot days as missing clinic appointments can be one of the factors influencing non-adherence. Only 19 of the health providers indicated that heat did not have

any impact on attendance as the patients visited the clinic on scheduled appointments. However, 65 differed as they reported that heat had a significant impact on clinic attendance.

> "*Yes, they miss appointments because of the heat particularly the elderly and women with small babies*", said a nurse in, Kweneng East. Most of the health providers were particularly concerned about mothers 'attendance during hot days. A nurse in the Kgatleng district rural clinic said "*Mothers also tend to skip their appointment when it's too hot because most of these women walk to this clinic* "(Nurse, Rural Clinic).

In the same district, a nurse from rural clinic reported that

> "*babies seem to be irritated in the summer, as they cry a lot during the appointments with their mothers. This most of the time delays the que"* (Nurse, Rural Clinic).

Finally, on how they controlled the temperatures in their respective clinics, fans and air conditioning were common temperature controls. All the urban clinics had air conditioning but was only limited to the consultation room (nurse/doctor office) not at the patient waiting area. At, a peri-urban facility, there was a fan where the ARV drugs and blood samples were kept. For the rural areas, whenever there was air conditioning or fan, it was reserved for drugs and blood sample storage areas.

4.7. DISCUSSION

These findings confirm that even when patients have a high level of commitment to antiretroviral therapy adherence, environmental factors in particular, the high frequency of water rationing and elevated day temperatures—are significant barriers to achieving the United Nations' s 90-90-90 of eliminating HIV/AIDS by 2030. From the findings, it is evident that environmental factors play a role in ART non-adherence in Greater Gaborone. From Table 23, 21 women missed a clinic appointment due to heat on that particular day and of those 12 were non-adherent. For the 14 men, 11 were non-adherent (Table 23). In summary, missing appointment due to heat was a risk factor for both genders, while missing due to water was associated with non-adherence in women and being turned away by clinic for lack of water was associated

with males. Table 24 showed that more patients lived in rural areas (n=372 and 120 of them non-adherent) than in peri-urban and urban locations. Other factors that were associated with non-adherence in rural areas was missing due to heat and being turned away by clinics due to lack of water. Majority of the patients reported that water rationing negatively affected their health and this was evident that it was a common factor across all locations even though peri-urban residents were mostly affected (61.7%) (Table 24). This agrees with the fact that condition of the physical infrastructure that supports human settlements also influences health risks. This includes power supply, roads, provision of water for drinking and washing, waste management and sanitation (Smith et al., 2014). Patients in the rural areas are usually the ones who carry the most burden of water rationing because sometimes frequency of water cuts is exacerbated by the unreliable power supply to the villages as shown previously that this is common in rural Botswana.

The mode of transport that patients use to reach their respective clinics played a significant role in adherence levels of ART. Those who used public transport and missed appointment due to heat were 8 times likely to be non-adherent compared to those who walked and did not miss an appointment. These findings agree with a South African study where important factors of ART adherence included urban area of residence and adequate physical environment including transport and access to health services (Peltzer et al., 2010). In their study, living in an urban area was likely to be associated with lower transport costs and fewer disruptions in access to medications (Peltzer et al., 2010). In this study, the patients were coming from almost similar places meaning that their locations were more clustered than dispersed, so tend to have similar geographic characteristics. They also attended public clinics that are somewhat regulated the same by district health management teams. This makes it a little difficult to tease out the variations by facilities. However, the multilevel modelling showed that there were variations by missing clinic appointments due to heat when controlling for male gender (Tables 26-27). It showed that patients within clinics that did not miss an appointment due to heat, had a better adherence level. Mothers on the

other hand did not only risk their health due to lack of water, they were re likely to put their children's lives in danger if they do not have water to prepare sanitary formula milk. They can be forced to mix feed (breastfeed and bottle feeding) which is not advisable when a mother has unsuppressed viral load (Table 28). Other studies agreed with this finding of the study that poor adherence which could be due to cultural and other practices were associated with a risk of mixed infant feeding as a result of feeding preferences and poor maternal adherence to recommended infant feeding guidelines (Lawani et al., 2014; Adetokunboh and Oluwasanu, 2016). Mothers from this study also reported that they felt that 2016 was the drier and hotter year compared to other years. This was corroborated by the earlier temperature trends of 2016 in Gaborone and across the country (Figures 13-14).

The health workers are the caretakers of the patients thus their opinions mattered as much as the patients. They complained that water rationing was a hindrance to their day-day running of the health facilities and this impacted the adherence levels of the patients because activities such as blood screening stops. Blood screening is important because it assists in monitoring CD4 and viral load levels. However, all of them contradicted the patients to say that they have never sent back patients without service even no water days. They also mentioned that when there was no water, patients tend to use dirty toilets which are conducive places for opportunistic infections such as diarrhea. These findings are corroborated by those from an Ethiopian study where they found that factors associated with water, sanitation and hygiene (WASH) practices showed that diarrhea was 10 times likely to affect those with unimproved water status (Haftu et al., 2017). The authors emphasized that special attention should be focused towards people living with HIV as opportunistic illness such as diarrhea can prove to be dire when compared to the general population (Haftu et al., 2017).

With regards to the impact of heat on non-adherence, the health practitioners in Greater Gaborone emphasized that heat was a constraint because some patients missed their clinic appointments specifically the elderly and mothers. The clinics also incurred additional expenses and delays because the

ARV drugs expired quickly due to the exposure to the sun. As showed previously on the climate change and impacts on human health (IPCC 5 Smith et al., 2014), the public health capacity and adaptation plays a role on indicating the extent to which the three categories of exposure translate to the actual health burden and moderated by factors such as accessibility of public health and the socioeconomic conditions of the people involved as well as the adaptation measures. With direct exposure to heat, in clinics which did not have adequate resources such as air conditioning, clinic operations tend to be limited because necessities such as drugs expire quickly. Socioeconomic status also increases vulnerability to those with already compromised immune systems such as the elderly, and mothers with young babies who cannot stand long periods of being exposed to the intense heat.

4.7.1. Limitations

The survey was done in health facilities, and may have been unable to capture the experiences of the adult women and men who never utilize the ART facility. The findings may as well not be representative of the general population of adult women and men enrolled on ART and PMTCT. The issue of recall bias cannot be ignored in this study. On the questions related to missing an appointment due to heat, it could prove to be that answers on 2016 being very hot could be attributed to the fact that patients were interviewed during the winter season. This could exaggerate their perspectives. Multilevel modelling to show variations by clinics indicated small variations because patients came from clustered locations that were somewhat similar. They also attended public clinics that had almost same resources. Despite all these, the study showed that water rationing and elevated temperatures increased non-adherence in Greater Gaborone.

4.8. CONCLUSIONS AND RECOMMENDATIONS

It was evident that water rationing affected the patients' health negatively across Greater Gaborone with the rural dwellers receiving the short end of the stick. Elevated temperatures also increased the non-adherence because both men and women who reported missing the clinic appointments due to heat were

non-adherent. It has shown that water rationing affects more women compared to males and this can potentially reduce their adherence on ART/PMTCT. This study also highlighted that even though heat affected both gender's ability to adhere to ART, women were mostly affected. The latter are usually burdened with the responsibility of caring for their babies which means sometimes bringing them to the clinics. The study also highlighted the importance of location where findings showed that patients living in rural villages, were more affected by water rationing as compared to their counterparts. This shows that, geography is important in understanding health because this can explain why rural patients could be defaulting on their clinic appointments. It is adding to the limited literature on environmental factors that affect ART adherence particularly at low scale (clinics and districts within the country). Weather does not only impact human health through direct exposure, human systems such as physical structures (built environment) do play a significant role. The location (whether rural or urban) influences adherence to ART. Future directions call for continuing to study the rural populations as they are likely to they practice unsafe WASH practices which puts them at a higher risk of opportunistic illnesses. The intervention therefore will be for the relevant authorities to warn patients well in advance if there is going to be water cuts. Clinics can have showers at their facilities to provide for basic needs of rural populations. Heat was also a constraining factor at the various clinics because health workers indicated that sometimes drugs expired due to exposure to the heat. This decreases the supply of drugs and can in turn reduce the services of the clinics. On sunny days, patients particularly the elderly and mothers were likely to miss the clinic appointments because patients waiting areas are not equipped with fans or air conditioning. For patients such as mothers and elders, services such as adherence counselling that did not require patients to be present at the clinic can be done at home. Health workers can dedicate at least one day a week to visit patients at home. As long as we keep investigating the constraints of ART adherence, we are definitely on the right path to eliminate new HIV infections and achieve the goal of having a free HIV generation sooner than the target year of 2030.

CHAPTER 5: Discussions and Conclusions

5.0. DISCUSSION

This study sought out to assess three objectives which were to investigate (i) barriers to ART adherence and their potential impact(s) on immunodeficiency (as a reflection of HIV transmission potential) for adult women and men (ii) as well as mothers on PMTCT and (iii) the role of environmental factors (high temperatures and water scarcity and rationing) on ART and PMTCT non-adherence in Greater Gaborone, Botswana. The first objective which was tested using three research questions found that there were main contributions that this study made. The first was learning about the HIV life course which was calculated as the time period to when the patient was first diagnosed with HIV and the length before being first initiated on ART and the age of the patient considered. Men as compared to women tend to survive longer without ART going for as long as 22-30 years. Results further showed that for both the women and men, majority were diagnosed with HIV during their reproductive years. The same men had low adherence rates and CD4 count. All these factors could be due to not used to taking medication for a long time and low CD4 count taking low to pick up because the body has been run down for a long time. Whichever the reason is, this study teased out the need to further investigate HIV disease progression by looking at historic narratives.

The study further showed that men have lower adherence to ART than women; and men 30+years are the primary transmitters. Non- adherence in men 30-40 years was mainly due to having low CD4 count, having other diseases such as Tuberculosis, high blood pressure and anemia. These men were also taking other drugs in addition to ARVs. Several authors corroborated this study finding that men tend to initiate ART at older ages and with more advanced HIV disease than women (Braitstein et al., 2008; Muula et al., 2007; Stringer et al., 2006) and markers of advanced HIV disease at the time of ART initiation strongly predict early mortality on ART.

With increasing age, lower adherence among men 50+ years is largely explained by single marital status and the need to seek other companions for support later in life. By location, patients in rural areas had low adherence (51.7% non-adherence) rates when compared to their counterparts (22.4% urban; 25.9% peri-urban). Peltzer and colleagues in their 2011 study found that generally, adherence was better in urban vs. rural areas (Peltzer et al., 2011).

Among pregnant women and mothers, a majority cohabit with HIV infected men (n=45) and many (n=22) do not know their partner's HIV status. Majority of the mothers were also non-adherent and aged 30-39 years. These age cohort was cohabiting with males of the same age which we previously saw that they were non-adherent and had other comorbidities such as TB and taking other drugs in addition to ARVs. Re-infection is very high in an environment like that as there is a high risk of increased viral loads which in turn can lead to ART failure. In their study, Damian et al (2019) found that HIV status disclosure was higher among women who were married/cohabiting (Damian et al., 2019). Post-partum, many women do not disclose their own HIV status until later in their infant's first year of life, in part because mother's are processing their own HIV status while trust is evolving in the relationship. Majority of these women were not married, so trust issues among partners can be limited. A study conducted in Tanzania corroborated this finding where in their study, found that prevalence of disclosure to a partner started at 22% within 2 months and increased to 40% after nearly 4 years (Antelman et al., 2001). They further explained that women were less likely to disclose to their partners if they were in cohabiting relationships, had low wage employment, had previously disclosed to a female relative, or reported use of contraceptive method (Antelman et al., 2001).

Finally, high ambient temperature is an important barrier to monthly clinic visits for both men and women living in urban, peri-urban and rural areas; and water rationing is a significant risk factor for non-adherence in rural areas. Being turned away by the clinic because of no water availability, is another important barrier for women including, pregnant and post-partum mothers and men living with HIV in Greater Gaborone.

There were clinics in the study area particularly in rural areas which did not have air conditioning and fans and on hot days reduced the clinic capacity because ARV drugs and blood samples for CD4 count monitoring expired. Mothers and elderly patients tend to miss the appointments on these hot days due to the heat discomfort anticipated to be experienced at the clinics. Other factors included the distance and mode of transport used to reach the respective clinics. It was evident that those who used public transport (insinuating that they lived far from clinics) had lower adherence rates compared to those who walked (lived close by).

5.1. CONCLUSION

This study showed that non-adherence was high among men living with HIV in Greater Gaborone particularly the older men (30-50+) with the middle aged men as the highest risk because they had other comorbidities and low CD4 count. The study showed that there were people who survived long periods of time without ART and most were men and as the major transmitters of HIV infection, these men require additional attention in terms of ensuring ARV adherence, to reduce HIV infection. There were also mothers who were still not disclosing their HIV status to their partners and also not knowing their partner's HIV status. Non-adherence in Greater Gaborone was also exacerbated by the climate direct exposures such as heat and indirect human systems such as water rationing both at home and at the clinic. Earlier it was mentioned that Botswana have met its 90-90-90 programmatic goals already (UNAIDS, 2019); however, significant number of new infections and AIDS-related deaths persists (n=8,500 incidence rate, 4.36 new HIV infections). The strength of this study is that it utilized the large population estimates from secondary sources to understand the global scale. It then went further to follow the people on the ground by zooming into the 658 adults on ART and PMTCT in Greater Gaborone to further investigate the potential causes of increased new infections. Without ART adherence, an HIV free generation is nothing but a dream.

5.2. RECOMMENDATIONS

With regards to these findings the 90-90-90 Treat All Program can achieve its maximum potential through the following recommendations:

- Initiate and implement more HIV and ART programs that are geared towards men in order to increase awareness and openness on health issues
- Regular teachings on CD4 count and viral load at counselling sessions within the ART facilities
- Promotion of PMTCT education in a general population, including sexual partners and not only limited to pregnant women at antenatal setting to increase the understanding of the purpose and benefits of PMTCT program
- Mothers counselling is needed to address issues of HIV status disclosure and this should not only be the burden of health workers.
- Communities and social networks where these mothers spend more time such as churches and community meetings should be involved.
- As climate change is something that cannot be eliminated, mitigation and adaptation measures can be taken. These include addressing basic needs such as provision of water in people's home and sending warning water cut messages well in time for people to prepare.
- ART health facilities can also invest in providing showers facilities for patients particularly mothers.

5.3. FUTURE RESEARCH

There is a need to study the people who survived long periods of time without ART to better understand HIV disease progression. The time is now because in the near future, this cohort of people will be gone and all new HIV infected persons will be immediately cared for with ARVs in the current "Treat All Program" (where one does not have a lower CD4 count to be enrolled on ART).

When individual, social structural and environmental barriers are minimized, it is a step in the right direction of the "Treat All Program" goals of identifying sick populations (test), administer ART (treat) to ensure high ART adherence, achieve viral suppression and eliminate new HIV infections by 2030. There is also a need to further research on UNAIDS indicators such as the Incidence Mortality Ratio (IMR) which identifies a point at which HIV related health care costs diminish, with an IMR < 1.0 (in a scenario of low mortality) indicating a decline in the HIV population, thereby, the ability to reduce the costs of ART services. It is common recently for donors to pull HIV funds from affected countries simply because there are reduced number of HIV cases with time. More funds are needed to educate people on prevention and importance of ART so as to not see people die off but to eliminate HIV by not getting it at all.

APPENDICES

APPENDIX A: Adults on ART Survey

Questionnaire for the Patients

My name is Matlhogonolo Bene. My home is Botswana. I am a PhD student in the Geography Department at Michigan State University, in the USA. The title of my dissertation research is "HIV Treatment Seeking Behaviors for Antiretroviral (ARV) and Prevention of Mother-To-Child Transmission (PMTCT) in Botswana." The purpose of my study is to better understand the barriers to using ARV and PMTCT treatments for men and women and mothers with HIV in the urban, peri-villages and rural areas of Botswana. The findings from this study will be used to help people in the future to receive ARV and PMTCT therapy. Your participation in this study will be voluntary. I would really appreciate it if you can take your time to answer the following questions. Thank you!

Date:
ID:
Checkbox [ ]

A. Demographics

1. Sex/Gender: Female [ ] Male [ ]
2. Where do you live? ……
3. How long have you lived in this community?
4. Age: 18- 24 [ ] 25-30[ ] 31- 39 [ ] 40 -49 [ ] 50-59 [ ] 60 and above [ ]
5. Marital Status Single: [ ] Married [ ] Living together/cohabiting [ ] Widowed [ ]
6. Religion: Christianity [ ] Islam [ ] African Traditional Beliefs [ ] Other …….
7. Occupation: Government employee [ ] Private sector [ ] Farmer [ ] Self-employed [ ] Unemployed [ ]
8. What is your monthly? ……..

   If you are not employed, what is your means of support? …….
9. What is the highest education you have completed? Never attended school [ ] Primary school [ ] Secondary [ ] Technical/Vocational [ ] University [ ]

B. Health Status

10. Year of HIV diagnosis …….
11. Other illnesses or conditions? ……
12. How often do you feel sick or unhealthy?
13. Have you been sick or unhealthy in the last two months?
14. How many times have you felt unhealthy this year?

C. HIV/AIDS Knowledge

15. Do you use a condom each time with a sexual partner? Yes [ ] No [ ]
16. Where do you get condoms?
17. How many sexual partners have you had over the last 12 months?
18. Have you ever had sexual intercourse while drunk (intoxicated)?

19. Do you think a person can get HIV/AIDS through witchcraft? Yes [ ] No [ ]
20. Do you think a person can get HIV/AIDS through a mosquito bite? Yes [ ] No [ ]

D. Treatment Seeking Behaviors

21. Where do you go for help or treatment whenever you are feeling sick?
22. When did you start/enrolled in ARV therapy (Year) ……
23. Where do you get ARVs from? Government hospital [ ] Private Doctor [ ] Government clinic [ ] other
24. Are you taking any other drugs apart from ARVs? Yes [ ] No [ ]
    If yes, what are they……, for what? .....

E. Access to ARV Therapy

25. Is this closest ARV facility to you? Yes [ ] No [ ]
    If not, why not go to other closer facility?
26. How far is the ARV facility from your house?
27. How do you get to the ARV facility?
28. How often are you required to go for the treatment?
29. How long do have to wait before you can be attended to at the ARV facility?
30. Which days and times do you generally go to the clinic?

F. Family/Household/Community

31. Does anyone else in your family/household have HIV?
32. Is anyone else in your family/household on ARV treatment?
33. Should children be taught about condoms, HIV/AIDS and ARVs?

G. Adherence to the Medication

34. Do you take the ARV medication as prescribed by the doctor? Yes [ ] No [ ]
    If no, why……
35. Do you miss doses sometimes? Yes [ ] No [ ]
    If yes, why? ……
36. Do you feel better after taking ARVs? Yes [ ] No [ ]

H. Water Related Concerns

37. Have you ever missed a doctor's appointment because it was too hot to go to the clinic?
    Yes: [ ] No: [ ] What was the temperature on that day?
38. Have you ever missed a doctor's appointment because there was no water?
    Yes: [ ] No [ ] Explain: ……
39. Has the clinic ever sent you back home without offering a service because they did not have water?
    Yes: [ ] No [ ] Explain: ……
40. How many days of water rationing have you experienced in a week at home?
41. Does water rationing affect your health?
42. Have you ever missed your pill dosage at home because there was no water?
43. How hot was it this year compared to other years?
44. Since January, how many times it rained this year?

45. Have you ever missed a doctor's appointment because it rained?
46. Did you feel it was drier this year than other years?

I. Anything else you would like to tell me?

Thank you for your time!

CD4 Count	
ARV Initiation Date	
Height	
Weight	

APPENDIX B: PMTCT (Mother's Survey)

Questionnaire for Mothers

My name is Matlhogonolo Bene. My home is Botswana. I am a PhD student in the Geography Department at Michigan State University, in the USA. The title of my dissertation research is "HIV Treatment Seeking Behaviors for Antiretroviral (ARV) and Prevention of Mother-To-Child Transmission (PMTCT) in Botswana." The purpose of my study is to better understand the barriers to ARV and PMTCT treatments for men and women and mothers with HIV in the urban, peri-villages and rural areas of Botswana. The findings from this study will be used to help people in the future to receive ARV [and PMTCT] therapy. Your participation in this study will be voluntary. I would really appreciate it if you can take your time to answer the following questions. Thank you!

Date:

ID:

Checkbox [ ]

A. Demographics

1. Where do you live? ……..

2. How long have you lived in this community? Months [ ] Years [ ]

3. Age 18- 24 [ ] 25-30 [ ] 31- 39 [ ] 40 -49 [ ]

4. Marital Status Single [ ] Married [ ] Living together/cohabiting [ ] Widowed [ ]

5. Religion Christianity [ ] Islam [ ] African Traditional Beliefs [ ] Other ……..

6. Occupation Government employee [ ] Private sector [ ] Farmer [ ] Self-employed [ ] Unemployed [ ]

7. Annual income: How much do you make in a year?

8. What is your monthly income? ……..

If you are not employed, what is your means of support? ……

9. What is the highest education you have completed?

Never attended school [ ] Primary school [ ] Secondary [ ] Technical/Vocational [ ] University [ ]

B. Maternal Characteristics (Mother)

10. Year of HIV diagnosis

11. Do you have any other illness?

12. Is your partner HIV positive?

13. How old is your partner?

14. Does he know your HIV status?

15. Who is the decision maker in your relation for using contraception?

What are the reasons for using contraception?

16. Do you know about female condoms?

C. Maternal Characteristics (Child)

15. Do you have any children?

If no, do you plan on having a family in the future?

16. Do you know about Prevention of Mother –To- Child Transmission (PMTCT) therapy?

If yes,

As part of the antenatal care visit for last birth, were you offered HIV test between time for delivery and before/after baby was born?

If yes, how many do you have?

If yes, how old are the children?

17. Where were the child [ren] born? Government Hospital/Clinic [ ] Private Hospital/Clinic [ ] Home [ ] other?

18. Are any of your child [ren] HIV positive?

D. Treatment Seeking Behaviors

19. Are you enrolled in PMTCT?
20. How long have you been enrolled?
21. Did you know about PMTCT before child birth/pregnancy?
22. Are you taking ARV drugs in addition to the PMTCT therapy?
23. Where do you go for help if your child is sick/not feeling well?
24. Where do you go for help if you are sick/not feeling well?
25. How long does it take you to get to this facility in Q 23and 24?
26. How far is any health facility from where you stay?
27. Did any of the children die?

    If yes, how old was the child when s/he died?

    If yes, what was the cause of child's death?

E. HIV/AIDS Knowledge

28. When was the last time you had sexual intercourse while drunk (alcohol intoxicated)?
29. Do you think a healthy looking person can have HIV?
30. Tell me ways that you know of which HIV can be transmitted from mother to her unborn child.

F. Water Related Concerns

31. Have you ever missed a doctor's appointment because it was too hot to go to the clinic?
    Yes: [ ] No: [ ] What was the temperature on that day?
32. Have you ever missed a doctor's appointment because there was no water?
    Yes: [ ] No [ ] Explain: ……
33. Have your baby ever missed a doctor's appointment because there was no water?
34. Yes: [ ] No [ ] Explain: ……
35. Has the clinic ever sent you or your baby back home without offering a service because of no water?
    Yes: [ ] No [ ] Explain: ……
36. Have you ever missed your pill dosage at home because there was no water?
37. How many days of water rationing have you experienced in a week at home?
38. Does water rationing affect your health?
39. Have you or the baby ever gotten an infection because of water scarcity?
40. Have you ever not prepared baby's formula milk because of water scarcity?
41. How hot was it this year compared to other years?

42. Since January, how many times it rained this year?
43. Have you ever missed a doctor's appointment because it rained?
44. Do you feel it was drier than other years?

G. Do you have anything you would like to share with me?

Thank you for time!

APPENDIX C: Health Workers' Survey

Semi-Structured Interview for Key Informants (Doctors, Nurses and Pharmacists)

My name is Matlhogonolo Bene. My home is Botswana. I am a PhD student in the Geography Department at Michigan State University, in the USA. The title of my dissertation research is "HIV Treatment Seeking Behaviors for Antiretroviral (ARV) and Prevention of Mother-To-Child Transmission (PMTCT) in Botswana." The purpose of my study is to better understand the barriers to using ARV and PMTCT treatments for men and women and mothers with HIV in urban, peri-villages and rural areas of Botswana. The findings from this study will be used to help people in the future to receive ARV and PMTCT therapy. Your participation in this study will be voluntary. I would really appreciate it if you can take your time to answer the following questions. Thank you!

Date:
ID:

A. Demographics

Facility name:

Provider

Gender:

Nationality:

Highest education attainment:

How long have you worked at this facility?

B. Accommodation and Affordability

1. What are the operating hours of this facility?
2. With regards to staffing resources in your facility, can you say that they are adequate? And if not, why?
3. Do patients pay for the services?
4. Are the needs of the patients met? How do you assess that?

C. Distance and Access

5. Which places do your patients usually come from?

6. Are there any steps to helping those patients coming from far places? Explain.

D. Socioeconomic Status of Patients

7. How will you describe those who are mostly enrolled in the therapy?

E. Education on HIV & ARV

8. Do you counsel patients? If yes, explain:
9. Do you provide patients with condoms? If yes, explain:

10. Do you educate the patients about alcohol and HIV?

11. How do you educate both the patients and community about HIV and the ARV therapy?
12. Are there instructions given to the patients on how to take the treatment?
    If yes, in which language (s)?
13. Are the ARV patients required to bring others for consultation and why? If yes, explain:

14. How do you ensure adherence to ARV therapy among patients?

15. How do you deal with issues of loss to-follow up?

F. Education and Adherence on PMTCT

16. Which criteria do you use to enroll pregnant women/mothers on PMTCT?

17. How do you deal with issues of breastfeeding and PMTCT?

18. Are the women on PMTCT required to bring their spouses during consultation?

19. What measures do you use for women who do not comply?

G. Test Results

20. If a patient's CD4 count is below the recommended guidelines for ARV treatment, what information is given to the patient?

21. How long is the patient given before they are told to come back?

22. Do you think there are patients who don't come back?

H. Water Related Concerns

23. Has water been a problem this managing the clinic? Explain:

24. What do you do when there is a lack of water?

25. Have you ever turned a patient away because of lack of water?

26. Has the temperature affected the operations of the clinic?

27. Do you see fewer patients come in on a hot day?

28. How does the heat affect mother's (and babies) attendance at the clinic?

29. How do you control temperature in the clinic?

30. Where do you get water?

31. Do you think it was drier this year?

I. Do you have any other questions for me?

Thank you for your time!

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