Implementation of a Novel Model to Enhance Routine HIV Care and Treatment Capacity in South Africa: Outcomes, Costs, and Cost-effectiveness

by

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Abstract

Introduction: This research evaluated the implementation of a novel public-private partnership (PPP) between the provincial department of health, an NGO, and a local private sector general practitioner (GP) network, which provides routine HIV care and treatment to public sector patients in order to alleviate the patient burden at public sector primary care clinics.

Methods: This was a retrospective cohort study that compared the PPP model to the *status quo* public primary healthcare clinic (PHC) model in terms of patient outcomes, costs and cost-effectiveness. Outcomes data (viral suppression, patient retention and other clinical outcomes) were collected from clinic records and patient files. Cost data included HIV and TB treatment, laboratory tests, down-referral care, and hospital-based outpatient and inpatient care. In addition, a new program performance metric proposed a cost associated with premature treatment attrition. Total and average costs for each model were based on resource utilization. Average cost and incremental cost per patient retained, cost per suppressed patient, and cost per suppressed patient remaining in down-referral care were calculated. Finally, a survey was conducted with a sub-set of study patients in order to incorporate patient experience and perceptions of each care model into the analysis.

Results: The proportion of patients who remained in care at the down-referral site with suppressed viral loads was 83 and 55 percent in the PPP and PHC cohorts respectively. Eighty-eight percent of PPP patients had suppressed viral loads compared to 67 percent of PHC patients. Retention on treatment was 94 percent among PPP subjects and 75 percent among PHC subjects. Total model cost was higher in the PPP model (R2,153,233) compared to the PHC model (R1,556,591) during the study period. The average cost per suppressed patient in down-referral care was R646.41 per month in the PPP model and R724.00 per month in the PHC model, and the cost per patient retained was R570.85 in the PPP model and R516.45 in the PHC model. The incremental cost-effectiveness ratio (ICER) was R724.00 for the PHC model and R505.20 for the PPP model compared to a “do nothing” alternative. The PHC model was dominated (extended dominance), and the ICER for the PPP model compared to a “do nothing” alternative was R638.97.

Discussion: Despite recent progress in scaling-up HIV services in South Africa, an intensified effort will be required to meet the rapidly growing demand for treatment over

the next decade. A lack of human resources has been identified by experts as one of the biggest constraints to achieving further scale-up of ART. The PPP model evaluated here was designed to help alleviate some of the pressure on the public health system by utilizing local private sector GPs to provide routine care for treatment experienced patients in Matlosana, North West Province. Clinical outcomes in the PPP model were significantly better than in the PHC model, it was more cost-effective at producing virally suppressed patients in down-referral care, and PPP patients were equally as happy as PHC patients with the quality of care and the level of convenience that the model offered. Innovative partnerships like the one evaluated here may offer a strategy for boosting public health sector capacity by leveraging existing private sector health resources.

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List of Acronyms

AAI	Accelerating access initiative
AE	Adverse event
AfA	Aid for AIDS
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ARVs	Antiretrovirals
ASRU	AIDS and Society Research Unit
BRHC	BroadReach Healthcare
CBA	Cost-benefit analysis
CEA	Cost-effectiveness analysis
CER	Cost-effectiveness ratio
CUA	Cost-utility analysis
DAI	Drug access initiative
DALY	Disability-adjusted life-year
DLG	Department of Local Government
DOH	Department of Health
DOT	Directly observed therapy
GDP	Gross domestic product
GFATM	Global Fund for AIDS, Tuberculosis and Malaria
GP	General practitioner
HAART	Highly-active antiretroviral therapy
HIPC	Highly-indebted poor country initiative
HIV	Human Immunodeficiency Virus
HST	Health Systems Trust
ICER	Incremental cost-effectiveness ratio
IMF	International Monetary Fund
LOI	Loss on investment
LTF	Lost to follow-up
LYG	Life-year gained
LYS	Life-year saved

MAP	Multi-country AIDS Program
MER	Monitoring, evaluation and reporting
MO	Medical officer
NGO	Non-governmental organization
NHLS	National Health Laboratory Service
NIC	No longer in care
NSP	National Strategic Plan
PDE	Patient-day equivalent
PEPFAR	President's Emergency Plan for AIDS Relief
PHC	Primary healthcare clinic
PLWHA	People living with HIV/AIDS
PMO	Principal medical officer
PMTCT	Prevention of mother-to-child transmission
PN	Professional nurse
PPP	Public-private partnership
QALY	Quality-adjusted life-year
RCT	Randomized controlled trial
SANAC	South African National AIDS Council
SES	Socio-economic status
SUPP	Suppressed
TAC	Treatment Action Campaign
TB	Tuberculosis
TRIPS	Trade-related aspects of intellectual property rights
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
VAS	Visual analog scale
VL	Viral load
WHO	World Health Organization

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Chapter 1

Introduction and Study Rationale

1.1 Introduction

This study compares the cost-effectiveness of public-sector clinic-based management of HIV treatment with that of a novel public-private partnership involving the use of general practitioners (GPs) in South Africa. It demonstrates that private sector health care resources can be mobilized cost-effectively to assist the government reach greater numbers of people in need of chronic care. Although South Africa has the largest antiretroviral treatment rollout in the world, the country also has the highest level of need. The shortage of health care professionals is the key obstacle facing the rollout. Involving GPs can help address this problem, provide people on treatment with choice about their health-care management, and help retain more patients in care.

In mid-2007 the South African National AIDS Council (SANAC) published the HIV & AIDS and STI Strategic Plan for South Africa 2007-2011 (NSP) (Department of Health, 2007) to guide national HIV prevention, care and treatment efforts and establish clear program targets. One of the most important and noteworthy targets laid out by SANAC in the NSP was to meet, by 2011, 80 percent of the need for antiretroviral therapy (ART) among those who qualify for treatment by scaling-up ART care and treatment services and removing barriers to access (Goal 6.5, p.88). According to the most recent data available from the World Health Organization (WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS), and the United Nations Children's Fund (UNICEF) (2008), 5.7 million South Africans were living with HIV at the end of 2007, approximately 460,000 had ever received ART (28 percent coverage), and 1.7 million were in need of HIV treatment (including those already on ART). Based on the WHO data, more than one million South Africans lacked access to treatment at the end of 2007. The amount of unmet need for ART in South Africa will likely soon grow in the wake of recently published research indicating that the risk of progression to AIDS and/or death was significantly greater in patients who waited to start ART until their CD4 counts fell below 350 cells/mm^3 (Kitahata et al., 2009; When to Start Consortium, 2009), and SANAC's subsequent recommendation to the National Health Council that the ART initiation threshold be increased to 350 cells/mm^3 from 200 cells/mm^3 (IRIN, 2009). Recent statements by the deputy director-general of strategic health services expounded on the government's national AIDS ambitions, including treatment for all HIV-infected infants and all patients with HIV and tuberculosis co-infection (Smetherham, 2009) in addition to earlier initiation of treatment. Such changes in the national HIV/AIDS policy could render more than half of South Africa's 5.7 million people living with HIV/AIDS eligible for HIV treatment immediately.

This level of leadership and ambition for addressing the South African AIDS crisis is a striking departure from the failed policies, obfuscation, and disregard for empirical evidence that characterized the past decade of South African HIV/AIDS governance (Deane, 2008; Fourie, 2006; Nattrass, 2007). However, while expanded access to HIV treatment is laudable and important, it is less clear how these treatment aspirations will be achieved given the current level of public sector resources and resourcing. In fact, the Minister of Health, Dr. Aaron Motsoaledi recently announced that South Africa was unlikely to meet the 80 percent ART coverage target laid out in the NSP due to lack of funds and human resources. The lack of capacity in the South African public health system, and particularly the shortage of health professionals in the public sector, has been identified as one of – if not the - major obstacle to scaling up HIV treatment access in South Africa (Wood, 2000, Kober, 2004, Mukherjee, 2003, Nattrass, 2006a, Wilson & Fairall, 2008; Govender, 2009). In 2008, 34,687 doctors were registered with the Health Professional Council of South Africa, but just 10,653 were employed in the public sector (Health Systems Trust, 2008). According to 2008 national health professional staffing data reported by the Health Systems Trust (2008), more than 40 percent of professional nurse posts and 35 percent of doctor posts were vacant in the public sector. As Kober (2004) pointed out, still more worrisome is the absence of a plan to address the critical human resource shortage. Recent health expenditure and staffing data also suggest that the public health system in South Africa is worryingly under-financed. Wilson and Fairall (2008) noted that in 1999, 56 percent of healthcare funds were spent in the private sector to service just 20 percent of the population, while the remaining 80 percent of the population relied on the public health system financed by the remaining 44 percent. Health expenditure data published by the WHO (2008a) indicated that this imbalance has worsened since 1999: only 42 percent of total health spending took place in the public sector in 2005. Further complicating the financial challenges of ART expansion is the global economic recession, the largest economic contraction in South Africa since 1992 (BBC, 2009), a R1 billion HIV budget shortfall (Govender, 2009), as well as the likelihood of reduced donor spending by the President's Emergency Plan for AIDS Relief (PEPFAR), (Dybul, 2009), and The Global Fund for AIDS, Tuberculosis and Malaria (GFATM) which is facing its own multi-billion dollar budget shortfall.

In light of the ambitious scale-up plans articulated in the NSP and more recently by government health officials, and the existing human and financial resource constraints, a better understanding of different HIV care delivery models and their performance is essential in order to minimize system inputs and maximize outputs and longer term outcomes. Little is known about how different combinations of services such as staffing

composition and ratios, data management, the use of technology, incentives or mix of support services impact patient outcomes, and still less about the relationship between the mix of services, model costs and outcomes. In their paper on HIV treatment model costs, Harling and colleagues (2007) highlighted the necessity to identify and implement the most efficient models of ART provision, given the unmet treatment need, the scale of the epidemic, and the limited resources available in the South African public sector.

Unfortunately, there is a paucity of data indicating which models of HIV care and treatment are most efficient. Public-private partnerships (PPP) for health service delivery have been widely discussed in global public health as a potentially important strategy for public health systems in resource constrained settings because costs and other resources are shared. But there is a lack of evidence and a fair amount of skepticism among public sector health professionals regarding their effectiveness (Gray, 2008). The discipline of implementation research attempts to bridge this divide between theory and practice by evaluating outcomes, costs, structures and policies of programs and interventions in local settings, and their potential for replication (Hirschhorn, Ojikutu & Rodriguez, 2007). Hirschhorn and colleagues (2007) suggested that identification of efficient and effective HIV/AIDS care delivery models is key to ensuring a high quality, efficient and durable treatment response. More specifically, they called for greater efforts to define site and provider characteristics that are associated with differences in costs, quality and effectiveness.

Cost-effectiveness analysis (CEA) is routinely used to evaluate and compare novel health interventions in order to inform policy decisions, and has been used extensively in assessing different HIV/AIDS interventions. Initially, CEA was used to advocate for implementing prevention-focused strategies instead of treatment programs in resource-constrained settings (Marseille, Hoffman & Kahn, 2002). Subsequently, CEA was used to demonstrate the cost-effectiveness of certain antiretroviral drugs to prevent mother-to-child-transmission (PMTCT) of HIV (Stringer, 2000; Skordis & Nattrass, 2002; Mofenson, 1999; Navario, 2003), of different combinations of ART in a variety of settings (see Chapter 2, Literature Review), and of different adherence interventions (Freedberg et al., 2006; Goldie et al., 2003). However, there is virtually no published research on the cost-effectiveness of different models of HIV care and treatment service delivery.

This study compares the outcomes, costs and cost-effectiveness of a novel PPP for HIV care and treatment with those of traditional public sector primary healthcare clinics

(PHC) in Matlosana sub-District (Dr. Kenneth Kaunda District) in North West Province. As importantly, it provides a real world example of PPP implementation and scale-up over time to increase HIV care and treatment capacity, and links unique model features (e.g. sites, providers and services) with differences in costs and quality. The PPP examined here was created in 2004 as a partnership between the North West Province Department of Health, a local general practitioner (GP) doctor's network called KOSHMED, and a PEPFAR-funded non-governmental organization (NGO) called BroadReach Healthcare (BRHC), in order to increase HIV care and treatment capacity in the sub-District. Traditionally, all patients in the sub-District start on ART at Tshepong Hospital in Klerksdorp, and once clinically stable with a suppressed viral load, are down-referred[1] to their local PHC for routine HIV care. Down-referring stable patients to local PHCs prevents bottlenecks at the hospital-based outpatient clinic where ART initiation and management of complicated cases takes place, moves routine care closer to the patient's home, shifts the responsibility for patient maintenance to nurses, and places HIV management in the primary care setting where multiple services can be simultaneously accessed. The PPP model was created in order to alleviate some of the overcrowding at the PHCs in the sub-District, and to prevent bottlenecks from occurring at the hospital HIV clinic due to a backlog of patients ready to be down-referred. Under the terms of the partnership, the government supplies and finances the drugs and the laboratory investigations, the GPs provide monthly HIV care, and the NGO pays the negotiated visit fee, manages model operations, and provides data monitoring and evaluation services. The PPP model is for HIV care and treatment only, and adheres to all Department of Health treatment and clinical monitoring guidelines. The essential elements of care (drugs, laboratory tests and visit frequency) are identical in both models. Upon satisfying the criteria for down-referral, patients choose whether they would like to attend their local PHC or select one of the 18 participating GPs in the area for their ongoing HIV care. Chapter 3 contains detailed descriptions of model designs and operations.

The remainder of this chapter places this research in context by reviewing the history of HIV treatment in low and middle-income countries, South African national and regional epidemiology, a brief political history of HIV/AIDS in South Africa, and concludes with the study rationale.

[1] 'Down-referral' is a term used to describe the process of transferring the responsibility for routine HIV care and treatment from a higher-level health care facility to a lower-level facility. Usually this involves a patient transfer from a hospital (secondary or tertiary care facility) outpatient HIV/AIDS clinic to a PHC.

1.2 Access to ART in low and middle-income countries

The era of highly-active antiretroviral therapy (HAART) began in 1996 when research on the life-prolonging effects of triple drug therapy was presented at the 11th International AIDS Conference in Vancouver, Canada. But while high-income countries benefitted from significantly reduced HIV-associated morbidity and mortality following the introduction of a three-drug ART regimen called HAART (Palella, F.J. et al., 1998; Mocroft, A. et al., 2003), high drug costs and skepticism about the feasibility of treatment programs in resource-limited settings meant virtually no access to treatment in hyper-endemic countries (Katzenstein, Laga, & Moatti, 2003). In 1997, the World Bank warned developing countries of the dangers of funding "expensive treatments with uncertain benefits," and urged them instead to focus on prevention citing high costs, drug monitoring difficulties, and patient compliance as obstacles associated with HAART (World Bank 1997). Andrew Natsios, then director of the U.S. Agency for International Development (USAID), captured the prevailing skepticism among some development experts when he told the Boston Globe that Africans couldn't take HIV medicine as prescribed because they lacked a Western concept of time (Rosenberg, 2005). Natsios and other skeptics were eventually proved wrong as empirical evidence mounted from various pilot programs across the African continent that demonstrated efficacy of HAART in developing countries, as well as high levels of patient adherence (see section 1.2.1 below and section 2.4.2 in Chapter 2, Literature Review).

1.2.1 Building an evidence base: ART pilot programs

Despite the warnings and skepticism, developing country governments, multinational institutions, and civil society organizations launched programs to test the efficacy and feasibility of triple-therapy in resource-poor settings. In November 1997, the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the Drug Access Initiative (DAI) with the goal of establishing small pilot programs in Chile, Vietnam, Cote d'Ivoire and Uganda. Published results from the pilot programs in Uganda, Cote d'Ivoire and Senegal (an additional pilot project that was not part of the DAI) showed similar benefits in terms of survival, virologic and immunologic outcomes, and adverse events to those observed in patients in high-income countries (Katzenstein, Laga, & Moatti, 2003; Weidle et al., 2002; Laurent et al., 2002).

Convinced by the evidence presented in Vancouver and recognizing the immediacy of the need, Brazil became the first developing country to launch a national ART program

in 1996, and quickly achieved significant decreases in HIV-associated morbidity and mortality, and reduced demand for inpatient hospital services (Teixeira, Vitoria & Barcarolo, 2004). In Thailand, large-scale clinical trials improved access to ARVs beginning in 1997, and a national rollout followed in 2003, jointly funded by the Thai government and the Global Fund for AIDS, Tuberculosis and Malaria (GFATM). A subsequent analysis of the Thai program showed that for every dollar invested in treatment, the government saved US$43[2] in subsequent healthcare expenses (Revenga et al., 2006).

Buoyed by promising results from the West African pilot studies and a deeply concerning national ART needs assessment, Botswana launched the first ART rollout on the African continent in 2002 after declaring a state of emergency following reports of antenatal HIV prevalence that approached 40 percent nationally, and 50 percent in some areas (Miles et al., 2007). In spite of a slow start and serious operational and management obstacles (Cohen, 2008), the Botswana national ART program proved to be a success: the number of new pediatric infections declined by approximately 80 percent between 2002 and 2007 thanks to near universal access to mother-to-child prevention services. By the end of 2008 over 80 percent of the estimated need for ART treatment had been met (Stover et al., 2008).

The example of the Botswana rollout and West African pilot programs and an influx of funds from the GFATM and PEPFAR galvanized countries across the continent to launch national HIV prevention and treatment campaigns. In South Africa, the government began providing HAART belatedly in April 2004 - two years after the start of the program in Botswana - despite having the highest number of HIV-infected people in the world. Results from ART programs launched in South Africa with donor funds prior to the public sector rollouts showed similar reductions in HIV-associated morbidity and mortality as those observed in high-income countries (Coetzee et al., 2004; Badri, et al., 2004). A brief summary of the history and politics of the South African rollout is provided in section 1.3.1 of this chapter.

1.2.2 Falling drug prices

In the late 1990's HAART was prohibitively expensive for developing country health systems and most individuals, leaving millions who needed life-saving treatment to fall ill

[2] The dollar ($) symbol in this paper refers to the United States dollar unless otherwise specified.

and die. Unable to afford branded HAART for its own citizens and unsuccessful at negotiating reduced prices directly with the drug manufacturers, Brazil broke patents and began manufacturing the drugs in government-owned factories in 1997, and by 1999 almost half of the antiretrovirals in Brazil were manufactured domestically; by 2001 that figure rose to 63 percent (Galvao, 2002). Threats of compulsory licensing and parallel importing of ART to other countries, and significant pressure from treatment activists and the global health community eventually led the HIV drug-makers to slash prices and offer voluntary licenses to a variety of generics makers in India, Thailand, South Africa, and Brazil. In 2003, the Clinton Foundation negotiated a significant reduction in the price of ART to as low as $140 per person per year by guaranteeing bulk purchasing volumes for 16 of the poorest, most-affected countries. A year later, Clinton, UNICEF, the World Bank and the GFATM extended the same preferential pricing using generic manufacturers to over 100 countries, and also negotiated a reduction in the cost of essential diagnostic testing with several medical technology companies (Kaiser Family Foundation, 2009).

The cumulative effect of these efforts (combined with a massive increase in development assistance for HIV treatment (see section 1.2.3)) was greatly expanded access to HIV treatment in developing country public health systems. A recent study of government spending on ART in Brazil showed that between local ART production and the global decline in drug prices, the government saved approximately US$1.2 billion between 2001 and 2005 (Nunn et al., 2007). In South Africa, the price of ARVs dropped 95 percent between 2001 and 2006 (Gedye, 2006).

1.2.3 Resource mobilization and allocation for HIV/AIDS

Between 2000 and 2004 several notable initiatives were launched to mobilize resources to address the shortfall in ARV program financing in low and middle-income countries. In May 2000 UNAIDS launched the Accelerating Access Initiative (AAI), in partnership with five pharmaceutical companies in order to provide ARV medications to developing countries at reduced prices. In 2000, the World Bank had a change of heart regarding the wisdom of rolling out treatment programs in developing countries, and launched the Multi-country HIV/AIDS Program (MAP) in selected countries in Africa with an initial grant of $500 million to support the development of national HIV/AIDS strategies, governance, and monitoring and evaluation systems. As of June 2009, the Bank had committed $1.8 billion in grants in 35 countries through the MAP program (World Bank, 2009a).

Table 1.1 HIV funding sources and commitments: totals as of December 2008

Funding Source	Commitments (US$ Billions)	Disbursed (US$ Billions)
PEPFAR (2004-2008)	$15	$18.8
GFATM (2002-2008)	$10.3	$7.2
WORLD BANK (2000-2008)	$1.5	$1.5
TOTAL	**$26.8**	**$27.5**

One of the most significant events in resource mobilization for HIV/AIDS was the creation in 2002 of the GFATM; a novel funding mechanism intended to reverse the spread of HIV/AIDS, TB and Malaria by providing project-specific grants to applicant nations. By the end of 2008, the GFATM had approved over $10 billion and disbursed just over $7 billion for projects in 139 countries (The Global Fund, 2009). Finally, in 2004 the US government launched PEPFAR to provide funds in support of HIV prevention, care and treatment in 15 focus countries, the majority of which are located in sub-Saharan Africa. By the end of the 2008/09 fiscal year (30 September 2009), PEPFAR had disbursed more than $18 billion, and the U.S. Congress had authorized an additional $39 billion for HIV spending between 2009 and 2013 (PEPFAR, 2009). In 2008 a total of $15.6 billion (from all sources including multilateral institutions, bilateral initiatives, and private sector donations) were available for HIV/AIDS spending in low and middle-income countries (Kates, 2009).

1.2.4 Evolved domestic and international HIV/AIDS policy

Evidence of treatment efficacy, falling drug prices and an order of magnitude increase in donor funds, were complemented by domestic and international health policy developments that further enhanced access to ART in many resource-limited countries. In 2001, most African leaders signed the Abuja Declaration on HIV/AIDS in which they committed to work towards allocating 15 percent of their national budgets to healthcare (Abuja, 2001). At the UN, HIV/AIDS became the first disease to be discussed in the Security Council (Whiteside, 2008), and was the focus of Resolution 1308, raising its profile from global infectious disease threat to a threat to national security the world over (Garrett, 2005). In 2003 the WHO published guidelines on scaling up ART for low and middle-income countries (WHO, 2003a) and announced the "3 by 5 Initiative," which set an ambitious global goal of starting 3 million people on ART by the end of 2005 (WHO, 2003b). Finally, in 1996 the International Monetary Fund (IMF) and the World Bank launched the highly-indebted poor countries initiative (it was modified and updated in

1999), which provided loan forgiveness to 35 developing countries (29 in Africa) totaling $51 billion by the end of 2008. Forgiveness was contingent upon agreement and evidence that funds traditionally spent on servicing debt would be spent on health, education and other essential services (IMF, 2009).

1.2.5 ART programs in developing countries: progress and challenges

Over the past five years significant progress has been made toward increasing access to ART for HIV-infected individuals in developing countries, though the goal of universal access still remains distant. According to the most recent UNAIDS data (2009a) more than 4 million people had started ART in low and middle-income countries by the end of 2008, compared to 3 million at the end of 2007, and just 400,000 at the end of 2003. Several countries met all or most of the domestic need for ART including Brazil, which placed 185,000 on ART (virtually 100 percent of need) by the end of 2008 (Nunn et al., 2009). Namibia met 90 percent of domestic need by the end of 2007 (UNAIDS, 2009a), and Botswana placed nearly 100,000 on ART by March 2008, which equated to 90 percent of estimated domestic need (Cohen, 2008). In addition to achieving the proximal goal of expanded access to ART, there was also some empirical evidence of long-term benefit associated with scaled-up funding for national ART programs. Bendavid and Bhattacharya (2009) showed that between 2003 and 2007 mortality in twelve PEPFAR focus countries[3] in Africa was 10.5 percent lower than mortality in 29 non-PEPFAR control countries.

In spite of these successes, formidable challenges remain. Though the epidemic in many African countries appears to have leveled off, prevention efforts have largely been considered unsuccessful (Cohen, 2008; Piot et al., 2008; Merson et al., 2008) with over 7000 new infections occurring every day (Piot et al., 2008), most of which are happening in southern Africa. UNAIDS (2009b) estimates that in addition to the 4 million currently on ART, an additional 6.7 million require treatment immediately, and this number will grow considerably as countries begin to adopt the new, WHO-recommended ART initiation threshold of CD4 ≤350 copies/mm^3.

Patient attrition has also emerged as a significant challenge in ART programs across Africa. A recent meta-analysis of 32 ART programs in southern Africa (including some South African programs) estimated that patient retention was – on average – 75 percent

[3] The majority of PEPFAR funds are directed to support prevention, care and treatment initiatives in fifteen developing countries, twelve of which are in sub-Saharan Africa.

after one year and just over 60 percent after two years (Rosen, 2007). UNAIDS (2007) reported that only 53 percent of patients in South Africa were still on treatment after just 12 months. It remains unclear how many of the four million people who started ART are still in care, and overemphasis on new initiations at the expense of support to those already on treatment may imperil hard won treatment gains (Navario, 2009).

Following several years of financial expansion and largesse, the global economic recession squeezed the budgets of donors and Ministries of Finance alike. And in spite of the $15.6 billion mobilized in 2008, it still fell short of the estimated need by $6.5 billion (Kates, 2009), and the prospects for additional resources in 2009 are dim. The GFATM faces a $4 billion shortfall by 2010 (Kazatchkine, 2009), and while the PEPFAR budget is projected to increase this year to $6.49 billion from $5.98 last year, this is a relatively modest increase compared to previous years (PEPFAR, 2009). Flat donor spending for HIV in 2009 is still more concerning in light of the unmet treatment need, as well as rising ART program costs due to longer survival times and the need for more expensive, second line regimens. According to UNAIDS (2009b), $19.8 billion in donor funding is needed to meet comprehensive HIV program costs in 2009, and $25.1 billion in 2010. Recent research by Scheffler and colleagues (2009) estimated that $2.6 billion is required annually just to eliminate the health workforce shortage in Africa by 2015. Finally, a widely publicized case of embezzlement of $150 million of Global Fund money in Uganda (PlusNews, 2009), and reports of graft in Mozambique with PEPFAR funds (Johnson, 2009) may stoke fears of corruption and waste among donors and could jeopardize future funding.

1.3 HIV/AIDS in South Africa

1.3.1 Political history of HIV/AIDS in South Africa

The political management and leadership around HIV in South Africa since independence in 1994 have been marked by controversy, failed policies, prevarication and hundreds of thousands of preventable deaths (Fourie, 2006; Nattrass 2007; Nattrass 2004; Deane, 2008; Chigwedere, 2008; Nattrass 2008). The early years of the Mandela administration's handling of HIV were characterized by progressive policies, including a comprehensive 'AIDS Plan' in 1993, and a failure of leadership and lack of capacity (at national and provincial levels) to implement the policies effectively (Fourie, 2006; Nattrass, 2007). By the late 1990's the period of progressive policy ended and was replaced by nearly a decade of political missteps, controversies, and

misinformation. In 1996 the government commissioned a play entitled, “Sarafina II” to educate the public about HIV/AIDS, but a botched tender process, the sizeable portion of the national AIDS budget consumed, and questionable content of the play scuttled production and embarrassed the government (Fourie, 2006; Nattrass, 2004). In 1997 senior government officials were involved in promoting the use of a toxic industrial solvent called virodene to treat HIV, despite a lack of evidence regarding the drugs’ efficacy (Deane, 2008). Subsequent controversies included decisions not to use AZT for PMTCT in 1998, refusal to provide nevirapine (another drug used for PMTCT) in 2000 despite the manufacturer’s offer to donate the drug, and ultimately the refusal to provide ART to patients in 2002 and obstruction of the KwaZulu-Natal Province Global Fund application (Deane, 2008; Fourie, 2006). President Mbeki’s questioning of HIV/AIDS science and his health minister’s promotion of garlic, beetroot and lemons rather than ARVs led to public confusion and further political embarrassment (Nattrass, 2004; Nattrass, 2007; Deane, 2008). The human consequences of South Africa’s failed leadership in the late 1990’s and early 2000’s have been emphasized in recent research. Two independent studies, using different methodologies estimated that the failed government leadership on HIV/AIDS during the Mbeki presidency led to more than 330,000 unnecessary AIDS-related deaths, and 35,000 preventable infant infections (Chigwedere, 2008; Nattrass, 2008).

Government prevention and treatment policy became more rational following a lawsuit against the Minister of Health and provincial health ministers, and heightened public protests and political pressure. In 2001, a court ordered the health minister to begin providing ART for PMTCT following legal action taken by the AIDS activist group Treatment Action Campaign (TAC), and in 2003 a cabinet revolt in response to vigorous protests from the medical community and civil society, along with renewed threats of litigation led to the announcement of free access to ART through the public health system (Nattrass, 2004; Nattrass, 2007; Deane, 2008).

On April 1, 2004 the South African ART rollout began, though some have pointed out that progress in expanding access to treatment has been unnecessarily slow (Nattrass, 2006b). Reasons cited for the slow rollout included continued government recalcitrance (Nattrass, 2006b; Nattrass, 2007), and a lack of capacity due to a chronically under-resourced public health system inherited from the apartheid era and inadequate leadership and management since 1994 (Coovadia et al., 2009). In spite of this, the future of political leadership in South Africa on HIV-related issues appears more promising of late. The new health minister has publicly acknowledged the failed

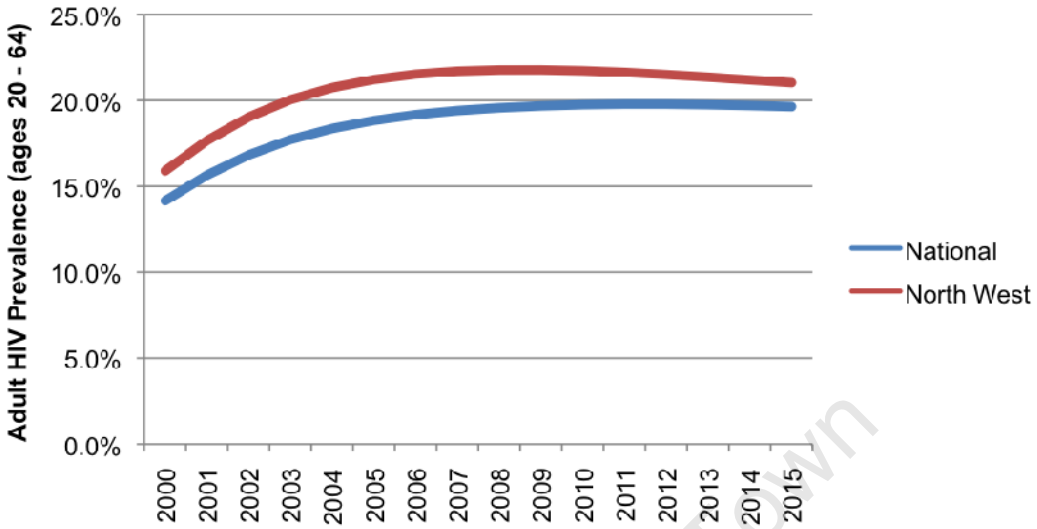
leadership of the recent past (Lancet, 2009), promised health system reform to raise quality and contain costs (Kapp, 2009), and to work toward the goal of 80 percent treatment coverage with an emphasis on reaching infected mothers, infants, and those with HIV and TB co-infection (Smetherham, 2009).

1.3.2 National epidemic data and trends

South Africa has one of the most entrenched HIV epidemics in the world, with an estimated adult prevalence of between 16.9 and18.1 percent (15 – 49 years of age), and between 5.2 and 5.7 million people living with HIV/AIDS (WHO, UNAIDS & UNICEF 2008, Shisana et al., 2009), the largest HIV-infected population of any country in the world. South Africa bears more than 10 percent of the global AIDS burden based on number of people infected. The epidemic in South Africa is predominantly linked to heterosexual sex (Abdool Karim, 2008) and characterized by high rates of infection among young women (one-third of women aged 25-29 are HIV-infected in South Africa) (Harrison, 2008; Gouws & Abdool Karim, 2008; Shisana et al., 2009), intergenerational sex between older men and younger women (Shisana et al., 2009; Harrison, 2008; Abdool Karim, 2008), a migratory workforce (Abdool Karim, 2008; Lurie et al., 2003; Lurie 2008), and concurrent sexual partnerships (Halperin & Epstein, 2004; Mah & Halperin 2008; Shisana et al., 2009).

Shisana and colleagues (2009) from the Human Sciences Research Council in South Africa recently published 2008 epidemic data, which showed that overall the South African epidemic appears to have stabilized. HIV incidence (modeled not observed) dropped in every age group between 15 and 20 years by as much as one percentage point (18 year olds). The report did find that national prevalence increased by 0.7 percent since 2005, but much of this increase could be attributed to a reduction in the number of HIV-associated deaths, and people living longer on treatment. There was considerable provincial variation in HIV prevalence: the eastern-most province of KwaZulu-Natal had the highest adult prevalence of any province at 26 percent, compared to 5.3 percent in the Western Cape Province in 2008. Prevalence in North West Province was slightly higher than the national average at 17.7 percent (Shisana et al., 2009).

Figure 1.1 HIV prevalence: national and North West Province



Modeling done by the Actuarial Society of South Africa (2003) corroborates the recent findings reported by the Human Sciences Research Council, suggesting that the epidemic has now stabilized (Figure 1.1), and that incident infections are waning somewhat (Figure 1.2). Nonetheless, more than 500,000 individuals are projected to be newly infected in 2009, and more than three million cumulative new infections are anticipated between 2009 and 2015 (Figure 1.3).

Figure 1.2 Incidence as a percentage of the population

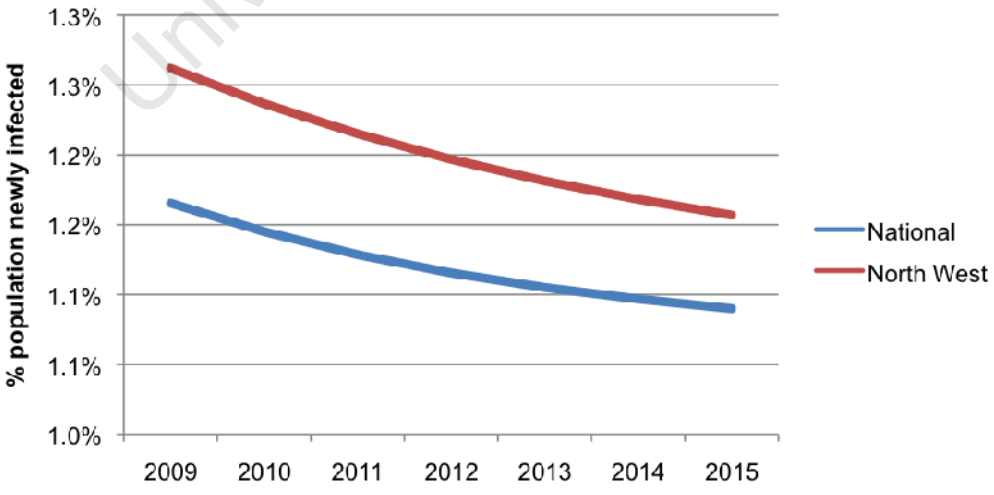
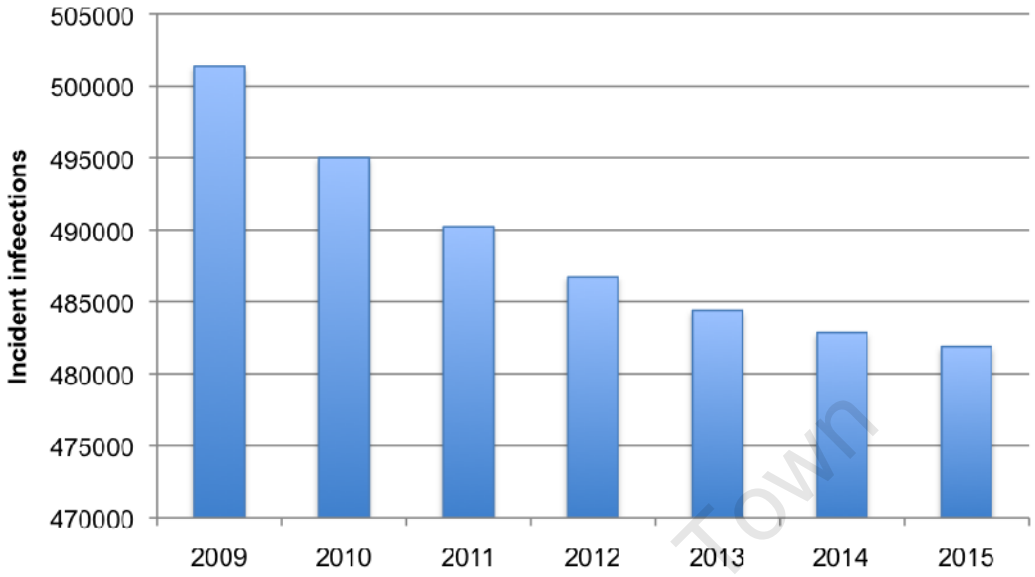


Figure 1.3 Projected HIV incidence in South Africa between 2009 and 2015



Finally, Figures 1.4 and 1.5 show the number of "AIDS sick" individuals who will qualify for treatment on an annual basis nationwide. The demand for HIV care and treatment services will be considerable for years barring the discovery of a therapeutic or curative vaccine.

Figure 1.4 Projected AIDS sick: South Africa

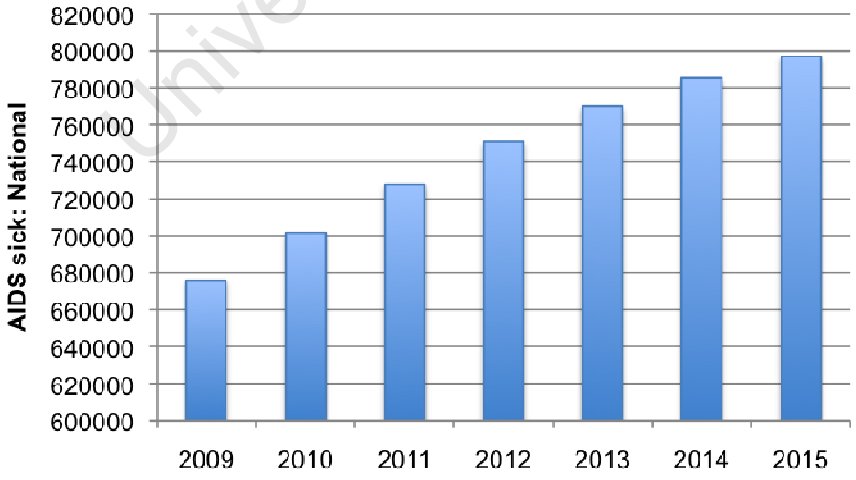


Figure 1.5 Projected AIDS sick: North West Province

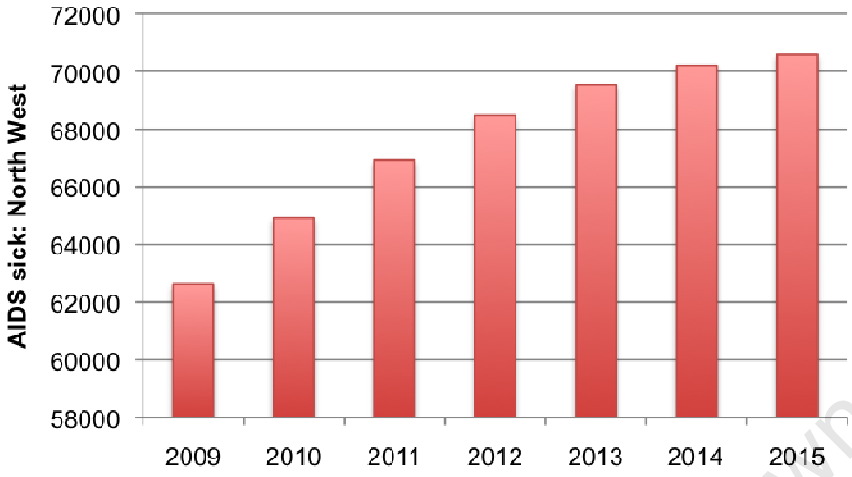


Table 1.2 Key national demographic and HIV/AIDS indicators

Indicator	Data
Population	49,052,489 (CIA, 2009)
HIV prevalence 2008 (adults aged 15-49)	16.9 - 18.1%
Estimated number living with HIV/AIDS 2008	5.2 - 5.7 million
% GDP spent on health	8.5% (5.0% private, 3.5% public) (Health Systems Trust, 2007a)
Per capita expenditure on health: public / private (Rand)	R1,440 / R7,680 (Health Systems Trust, 2007b)
HIV incidence (20 year olds)	1.7% (Shisana et al., 2009)
Pregnant HIV+ women receiving ARVs for PMTCT	57% (WHO, 2008b)
PLWHA receiving ARV therapy (as a % of need)	28% (WHO, UNAIDS & UNICEF 2008)

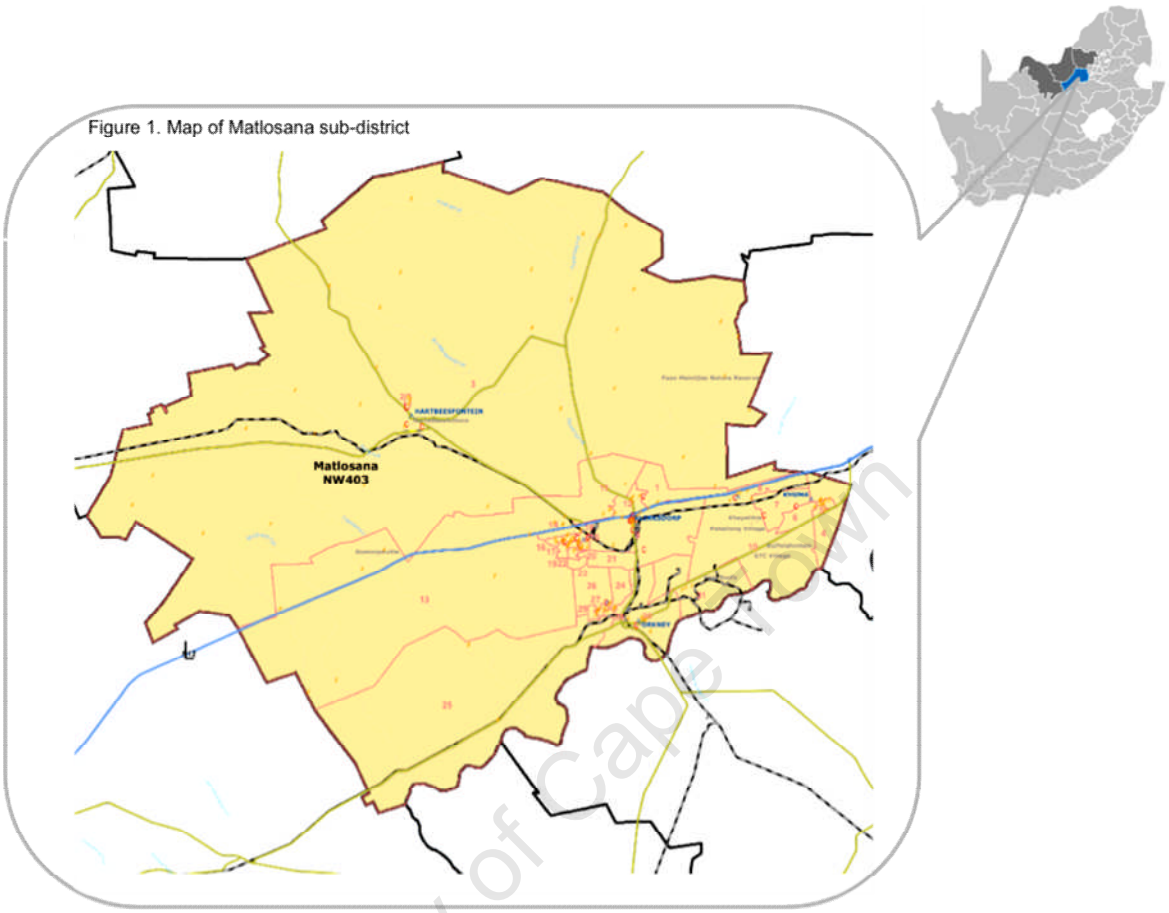
As Table 1.2 shows, the majority of the resources for health are spent in the private sector despite the fact that the majority of the population accesses care through the public sector. In 2007, the South African government spent just over 14 percent of the national budget on healthcare (Health Systems Trust, 2007b). In 2004 the South African government began a national rollout of ARVs in the public sector, and as of January 2009 the number of HIV-infected individuals ever treated with HAART exceeded 500,000 (UNAIDS, 2009a; PEPFAR 2009).

1.3.3 HIV/AIDS in Matlosana sub-District

Tshepong Hospital and the KOSHMED GP Network are located in the Matlosana sub-district in the Southern Region of North West Province. Figure 1.6 provides a map of the sub-district and its location within South Africa, with PHCs identified with a "C." HIV prevalence in North West Province closely approximates the national average: 29 percent[4] according to the most recent HIV ANC prevalence data from the 2007 antenatal clinic survey (Department of Health, 2008) and 30.7 percent according to University of Cape Town statisticians (Dorrington & Bourne, 2008). According to both estimates, this represents a one percent increase over the previous year. The same Department of Health (DOH) report estimated HIV prevalence in the Southern Region of North West Province at 32.5 percent, also a one percent increase over 2006. Without good incidence data, it is difficult to determine whether the increased prevalence is due to greater numbers of individuals receiving ART and longer mean survival times, or to an increase in incident infections relative to the number of deaths (unfortunately the 2009 national HIV survey conducted by Shisana and colleagues at the Human Sciences Research Council included national incidence estimates only). These data contrast somewhat with the national data that indicated a trend toward a stabilized epidemic, but this may be attributed to differences in localized epidemics, data that is one year older, and the representativeness of the antenatal clinic sample used in the provincial estimates as antenatal clinic data are not necessarily indicative of broader population trends. However, the 2008 data cited earlier (Shisana et al., 2009) also indicated that prevalence among women aged 25-29 was stable from 2005 to 2008 across the country. Regardless of any slight variations among epidemic trend data, the burden of HIV disease remains very high in the province and region.

[4] This data reflects antenatal HIV prevalence among pregnant women attending antenatal clinics, and not the general population. Antenatal HIV prevalence is typically higher than in the general population.

Figure 1.6 Location of Matlosana sub-district, North West Province



Geography and a highly mobile population have been cited as potential reasons for the high prevalence in North West Province (Variava, 2006). North West is sandwiched between high prevalence neighbors including Gauteng (10.3 percent in 2008) to the east, Free State Province (12.6 percent in 2008) to the south, and Botswana (23.9 percent) (UNAIDS, 2008) to the north. A major transport route that connects Johannesburg with all points south and west dissects Matlosana, which contains a major local trading post (Klerksdorp, which is identified on the map in Figure 1.1 by a red dot) and is home to a large number of migrant workers who are employed at the nearby mines. HIV tends to follow trade routes and migrant workers have been identified as important vectors for HIV disease (Lurie, 2008).

ART became available in North West in April 2004 and according to a recent report from the Department of Health (2008), nearly 35,000 patients had started HIV treatment by November 2007. In Matlosana, the ART program was launched at Tshepong Hospital in Klerksdorp on April 11, 2004, and the outpatient ART clinic at Tshepong

remains the only place in the sub-District where a patient can initiate ART therapy (although this will soon change as some of the larger clinics in the area will begin initiating patients in the second half of 2009 (Abrams, 2009)). By the end of March 2009, 12,413 patients had been started on ART at Tshepong Hospital (Mlambo, 2009).

1.4 Study rationale

Economist and HIV/AIDS expert Alan Whiteside recently called for a new paradigm for approaching HIV/AIDS within the economics community, lamenting the lack of relevance of recent research:

> Most economic analyses provide little information that will help inform responses to the epidemic…the reality is that most economists have instead focused on the size of the impact, rather than the effectiveness of the responses. This may have been important at the early stages of the epidemic…but it is now critical to move further towards finding the most appropriate way to mitigate impact (Whiteside, 2008, p.417).

This study uses economic analysis to elucidate the impact, costs, quality and feasibility of the expansion of an innovative ART care and treatment model in South Africa. It also compares it with the status quo public sector PHC model and highlights its potential for replication in other settings. As such, the study makes an original contribution to the health economics and HIV/AIDS literature, and has direct relevance for South African AIDS policy with regard to optimal resource allocation and expanding capacity to meet the demand for antiretroviral treatment.

1.4.1 A unique contribution to the literature

This study addresses the high priority need for the evaluation of service delivery strategies in terms of cost and quality identified by the WHO and its partners (2008) in a consensus statement on knowledge gaps in ART provision. Rosen and colleagues (2008) published the only other study known by the author to have analyzed the costs and outcomes of different models of HIV care and treatment. Unfortunately, the results reported in that paper were obscured by two important methodological errors. The first was the authors' failure to control for drug costs between models. Because drug costs accounted for approximately half of total costs across models and were heavily influential in the analysis, the published cost per patient was biased towards models

with access to preferential drug pricing, rather than the cost per effect for each model. Second, the paper examined four different models of care in four different locations and did not control for sampling bias. Due to the influence of drug costs and sampling bias, very little could be determined about the relative performance of each of the models examined.

Like the Rosen paper, this research aims to estimate the cost-effectiveness of two different models of HIV care, but with several distinct advantages. First, the cost of drugs and labs were identical across both models, allowing the unique mix of model services and costs to drive the analysis. Second, patients in both models were matched on key demographic and clinical variables to minimize the risk of sampling bias in the results. Moreover, this study included the costs associated with inpatient care, which is considerably more expensive than outpatient care and a potentially important contributor to model costs, as well as being indicative of quality of care (i.e. better outpatient care should ideally lead to fewer inpatient admissions). Finally, this study enrolled more patients per model (234 compared to 100) over a longer period of time (an average of 18 months compared to 12) for a more robust analysis of model performance and costs. A full review of the paper by Rosen et al. (2008) can be found in Chapter 2, Literature Review.

In addition to filling a knowledge gap in the implementation, cost-effectiveness and general HIV/AIDS literatures, this study proposes a new cost indicator that integrates cost and program quality. The goal of ART is to avert premature death due to HIV infection and extend the number of healthy life years lived, and considerable investment of scare resources (particularly in low and middle income countries) are required to initiate and stabilize patients on ART. The proposed loss on investment metric (LOI) assigns a time-weighted cost to the patient-months associated with any shortfall between years lived on ART and life expectancy on ART. In other words, any patient who stopped treatment (due to death, lost to follow-up, or patient choice) before achieving the estimated life expectancy for their age group represents a cost equal to the cost of stabilizing a patient on ART multiplied by weight that correlates to the amount of time spent on ART (i.e. stopping treatment within the first year post-stabilization incurred a penalty equal to 100 percent of the stabilization cost compared to a penalty of 50 percent for someone who stopped after five years on treatment). The LOI for each patient who stopped treatment prematurely was summed and added to the total model cost in this analysis. ART care models with high rates of attrition prior to the achievement of life expectancy targets incur a higher LOI. Once a patient achieves the

estimated life expectancy on ART, the original investment has been realized the LOI equals zero. As such, LOI provides a method for gauging how effectively a care model's maintains patient health by keeping them on ART – thereby protecting the original investment required to stabilize patients. A detailed discussion of calculating and interpreting LOI can be found in Chapter 4: Methodology.

1.4.2 Retrospective analysis of an innovative chronic HIV care model

This is a retrospective observational study that compares the status quo primary care clinic model of long-term HIV care with an innovative model of HIV care and treatment. Unlike most of the cost-effectiveness analyses in the HIV and AIDS literature that rely on modeling, this analysis reflects actual patient outcomes and experiences. Moreover, whereas the vast majority of CEAs evaluate a single intervention (i.e. a particular antiretroviral regimen), this study assesses how effectively two different models of care – which include different mixes of services, personnel, management and operations -- maintain patients on ART. The comparator model is innovative in terms of its structure (a PPP between the government, a private sector doctors' network and an NGO), and because of its objective to provide additional public sector capacity for routine chronic HIV care and treatment to patients who have been stabilized on ART. The private sector has been called on at various levels – domestically in the NSP (2007) and internationally by various United Nations agencies (WHO, 2008c; UNAIDS, 2007) and the GFATM (The Global Fund, 2008) to support HIV prevention, care, and treatment efforts. South African clinicians and researchers have also highlighted the resource disparities and lack of integration between the public and private health sectors (Wilson & Fairall, 2008), and called for a more collaborative approach to HIV care and treatment:

> A system fractured into a well-resourced private sector for the affluent and an under-resourced public sector for an impoverished majority must find new common ground, a common approach to quality and delivery, and an equitable distribution of resources, skills and capacity. Experience and skill built up in the for-profit environment must be harnessed for the common good, but in ways that are commercially viable (Gray, 2008, p.536).

This call for a multi-sectoral response was echoed by Q.A. Abdool Karim and S.S. Abdool Karim (2008): "If the targets set out in the national AIDS treatment plan are to be

met, South Africa will have to create one of the largest AIDS treatment programs in the world – a feat that will need a concerted approach with assistance from all sectors of South African society as well as international support to achieve success (p.569)."

This study evaluates an innovative attempt to answer this call for a multi-sectoral and timely response to the demand for HIV treatment. The PPP model was designed to provide a short- to medium-term boost to public sector capacity to manage HIV-infected individuals by leveraging private sector resources, and provide an immediate solution to improving ART access while maintaining quality of care.

1.4.3 Policy relevance

Finally, this research aims to obtain and present information that is both relevant to the HIV treatment challenges in South Africa today, and is easily understood by policy makers. This study reports clinical and virologic outcomes for both models, as well as the average cost and incremental cost per outcome by treatment model, rather than presenting the results in traditional (and somewhat esoteric for many policy makers) CEA terms, such as cost per disability-adjusted life-year (DALY) or cost per quality-adjusted life-year (QALY). In addition, this research compares two HIV treatment models that are currently being implemented, which lends a tangible dimension to the results that cannot be replicated by a computer simulation. Finally, a qualitative patient survey conducted among a subset of study patients was included in order to complement the quantitative data, and provide insight into patient perceptions of model performance.

1.5 Study Goal and Objectives

The study has two primary goals:

Goal 1: Inform South African National, Provincial and District-level HIV/AIDS policy regarding the potential value of a unique public-private partnership that leverages existing private sector capacity to provide chronic HIV/AIDS care and treatment in support of the public sector rollout in South Africa.

Goal 2: Make a unique and practically valuable contribution to the global implementation, cost-effectiveness, and HIV/AIDS care and treatment literatures.

In order to achieve the study goals, the following objectives were established:

Objective 1: Utilize cost-effectiveness analysis to compare the cost and outcomes of a novel PPP with the status quo public sector clinic model from the payer's perspective

Objective 2: Describe and compare clinical, immunologic and virologic outcomes between an innovative HIV care model and the status quo model

Objective 3: Describe and compare patient perceptions of quality of care and service between the two treatment models

Objective 4: Provide cogent analysis regarding strengths and weaknesses of both models, as well as the PPP model's potential for replication to help meet public demand for HIV care and treatment services in South Africa and other resource constrained settings.

Chapter 2

Review of the Literature

2.1 Introduction

This study links model operations to clinical outcomes and cost per patient outcome, and therefore draws from two distinct literatures including the research around the cost and cost-effectiveness of HIV interventions, and the literature on HIV care and treatment scale-up initiatives in developing countries. This chapter presents a review of both literatures, beginning with an overview of economic evaluation and commonly used metrics in health economics. This is followed by the CEA and HIV program literature reviews, each of which contains a summary of methodologies, key findings and a brief discussion. The chapter concludes with a discussion that incorporates the trends, gaps and implications of this research for both literatures.

2.2 Overview of economic evaluation in healthcare decision-making

2.2.1 Principal approaches to economic evaluation

In the health decision-making context where multiple interventions with variable costs and outputs are possible, economic evaluation is an important tool for health economists and health policy-makers to clarify costs and outcome tradeoffs. Ultimately the goal of economic analysis in the health policy context is to maximize the impact of health interventions with limited resources (Drummond et al., 2005; Tan-Torres Edejer et al., 2003; Gold et al., 1996; Fox-Rushby & Cairns, 2005; Evans et al., 2005). Drummond and colleagues (2005) have suggested that the two fundamental questions that economic evaluation of healthcare interventions seeks to answer are:

1. *Is a given health intervention worth doing compared with another intervention for the same amount of resources?*

2. *Is this intervention the optimal way to spend resources rather than some other way (opportunity cost)?*

There are four key concepts in evaluating economic costs. These are summarized below. The analysis then turns to measures of outputs, and finally, to a review of the relevant literature.

Cost analysis

A cost analysis simply examines the costs associated with an intervention and does not take into account any benefit associated with an intervention. This typically involves a detailed costing (also called micro-costing) of various direct and indirect unit costs that underlie a given intervention. The outcome is expressed in monetary units. Cost analysis can be used on its own, and is a foundational element of cost-effectiveness, cost-utility, and cost-benefit analyses, which are described next.

Cost-effectiveness analysis (CEA)

CEA is a method of economic analysis that evaluates the outcomes and costs of a given intervention. The results of CEA convey the cost of achieving a single unit of health-related gain as a result of the intervention (Gold et al., 1996), and are expressed in terms of a cost-effectiveness ratio (CER), or the ratio of cost per unit of benefit (e.g., $10,000 per death averted). In cases where at least two different interventions are being compared an incremental cost-effectiveness ratio (ICER) is calculated. The ICER describes the incremental (or marginal) cost per additional unit of health benefit conferred by an intervention relative to a status quo or alternate intervention. ICER is particularly useful when trying to understand the relative cost and benefit of a more expensive intervention that provides greater benefit relative to the alternative. It answers the question: How much will it cost to purchase the additional benefit compared to the alternative? CEA is a useful tool to help policy makers understand the affordability of different interventions in a resource restricted context, and to compare and prioritize different health interventions. Conducting a CEA entails calculating the cost of the intervention (cost analysis), measuring the outcomes or outputs from the intervention (effect), and computing a CER and ICER. CEA is typically employed to make cost and outcome comparisons in the following scenarios:

1. To compare a new intervention to a status quo intervention (a pre-existing intervention)

2. To compare an intervention to a “do nothing” (no intervention) baseline scenario

3. To compare two different new interventions

4. To illustrate the additional benefit of adding complementary interventions to one another

Comparisons of comparable worth may be considered relative to another intervention, and/or relative to a cost threshold that denotes the decision-maker's willingness to pay for the intervention. CEA enables decision-makers to select the intervention that has the greatest effect with a CER that falls under the predetermined cost threshold. CERs and ICERs are commonly expressed as cost per life-years gained (LYG) or cost per disability-adjusted life-years (DALYs). These and other commonly used outcome measures are discussed later in this section.

Cost-utility analysis (CUA)

CUA is used to calculate the cost per quality-adjusted unit of time conferred by an intervention. While CUA is closely related to CEA, the utility ratio relates costs to a combined measure of additional survival time with the quality of any additional time gained from an intervention. Quality weights are derived from surveys where patients indicate preferences for certain health states (e.g. from living with drug side effects to death). The results of CUA are most often expressed in terms of cost per quality-adjusted life-year (QALY). QALYs are discussed in greater detail in the next section.

Cost-benefit analysis (CBA)

Like CEA, CBA compares the costs of an intervention to the effect, but in a CBA the effect is translated into monetary terms (e.g., if a vaccination program costs $1 million and saves 10 million lives, the "benefit" is said to be the additional life-years multiplied by the average value of a life-year). Because the final ratio is expressed in monetary terms, CBA permits comparison of costs and outcomes between very different types of interventions. This is useful for policy-makers who sometimes must choose between a health program and an environmental initiative. It is worth noting that assigning monetary value to a life or given health state is both ethically controversial and difficult as most methods value the wealthy and younger populations more than the poorer and older.

2.2.2 Common outcome metrics used in cost-effectiveness analysis

CEA has become the dominant form of economic evaluation in healthcare today (Johannesson & Meltzer, 1998). The most common output metrics used in CEA are the life-year gained (LYG), the disability-adjusted life-year (DALY), and the quality-adjusted life-year (QALY).

Life-years gained (LYG)

LYG expresses the number of additional years of life conferred by a given health intervention. LYG is a purely quantitative metric, and is also commonly referred to as life-years saved (LYS) in cases where an intervention prevents or delays death.

Disability-adjusted life-year (DALY)

The DALY is a combined measure of years of life lost due to premature death and years of life lived with disability (Murray & Lopez, 1996). The DALY was developed for the World Health Organization (WHO) as a standardized measure of global disease burden in order to compare and rank the impact of various diseases in terms of morbidity and mortality. Disability weights are calculated by multiplying life-years lost (relative to life-expectancy of Japanese women), by a disability score between 0 and 1 (where 0 equals death and 1 equals perfect health). The weighting considers seven possible health states (created by an expert panel) that take into account the age of the individual (younger years are valued more highly than later years) as well as the aforementioned disability score. DALYs can be expressed on their own (i.e. number of DALYs saved per intervention) or in terms of cost per DALY-saved. Despite its usefulness in permitting comparison across diseases and interventions, the DALY is a somewhat controversial metric because it places a higher value on younger life, and the disability states were determined by expert consensus and not empirical evidence. (Drummond et al., 2005)

Quality-adjusted life-year (QALY)

The QALY is a combined measure of the quantity of additional years of life and the quality of those additional years. In order to calculate a QALY, preferences for potential health states have to be ascertained (various survey tools and scales exist for this purpose). The weight – which is multiplied by the additional life-years to arrive at the number of additional QALYs – is most conveniently expressed on a scale of 0 to 1, where 0 equals death and 1 equals perfect health.

2.2.3 Economic evaluation as an HIV policy tool

Economic evaluation has played an important role in shaping global and national HIV policy and resource mobilization and allocation research to ensure treatment access for HIV-infected populations around the world. Numerous studies have projected the

macroeconomic impact on countries and regions (Whiteside, 2008) to help galvanize policy makers and provided impetus for large-scale resource mobilization programs like PEPFAR, MAP, and the GFATM (Stover et al., 2002; Attaran & Sachs 2001; UNAIDS, 2007). In addition, economic evaluation has been used to estimate the costs of HIV to business and industry (Eholie et al., 2003; Rosen et al., 2004), its impact on households and communities (McIntyre et al., 2006), and to elucidate the economic impact of prevention and treatment interventions (Creese et al., 2002). CEA in particular has played a crucial role in the global response to the HIV pandemic. It has been employed to evaluate prevention of mother-to-child transmission (PMTCT) initiatives, and to demonstrate that HAART is cost-effective in wealthy and resource-poor countries alike.

However, while CEA has proved to be a powerful tool for HIV policy and programming, it has some limitations. CEA, as it has been applied, typically does not take into account important issues such as equity (i.e., demographic, geographic), ethics, relative disease burden or patient preferences. CEA is sometimes used to rank various healthcare interventions based on their ICER (these rankings are called *league tables*) to allocate budgets and prioritize among competing health needs within the context of a budgetary or spending limit (Gold et al., 1996); the most famous example of this is the Oregon Health Services Commission (Klevit, 1991). While efforts such as the one in Oregon in the early 1990's are commendable for employing a systematic and transparent approach to decision-making there are significant limitations to utilizing CEA in this way. First, rather than being used to inform the budget and establish a reasonable health-spending limit, CEA implicitly assumes that the budget is rational. More importantly, methods used to calculate CEA vary widely – including differences in methodology for calculating unit costs, costs selected for inclusion in the analysis, discounting practices, and outcome measures to name a few – rendering meaningful comparisons between interventions difficult at best. Direct comparison of interventions for different services is also perilous because the process of ranking ICERs ignores differences in scale and/or scope of interventions, which impacts the ICER. Finally, some researchers have argued that the traditional impact measures used in CEA (i.e. DALY and QALY) have limited usefulness in the policy-making process because they are not well understood outside the realm of health economists, and have eschewed DALYs and QALYs for more easily understood, policy-friendly outcome measures such as cost per infection averted or cost per HIV-related event averted (Skordis & Nattrass, 2002; Navario, 2003; Lacey et al., 1999a; Lacey et al., 1999b).

2.3 Literature review: cost and cost-effectiveness analysis in HIV care

The literature review was conducted using two online database search engines: Academic Search Premier, Pub Med; as well as the University of Cape Town Libraries' ALEPH journal and book search engine. The literature search employed the following keywords in various combinations: *costs; cost-effectiveness; cost-benefit; cost-savings; antiretroviral therapy; South Africa; Africa; HIV and AIDS; ART; HAART; and HIV treatment*. The search turned up original research papers, as well as meta-analyses, both of which were included in the review. CEA from high-income countries was included in this search because their methodologies were relevant to this research, and because there is significant heterogeneity in the metrics and costing strategies in the CEA literature and it was important to understand the variety of methodologies.

Thirty-five published studies from 13 countries and regions (see Table 1 below) that employed economic analysis for the evaluation of HIV care and treatment programs in both developed and developing countries and regions were reviewed.

Comparisons between different cost studies was complicated by differences in methodologies (i.e. cost inputs, discounting practices and modeling), the time-sensitive nature of costs, differing outcome measures, and varying stages of economic development between regions or countries where the research took place. Comparison between CEAs from developing countries was made still more difficult by the significant drop in the price of ARVs between 2002 and 2004 as a result of international political pressure, availability of generic formulations, and negotiated price reductions for branded drugs. Given that many of the analyses found that drug prices were the principal cost-driver, the precipitous drop in prices means that CERs varied significantly between the pre- and post-price reduction studies.

This section summarizes methodologies and key findings from cost analyses and CEAs of ART undertaken in high, middle and low-income countries. It concludes with a discussion of results, gaps in the literature, and recommended future research. The literature search was conducted using various academic databases and included studies published in academic journals (conference abstracts were not included) on ART rollouts, costs of HIV care delivery and treatment scale-up. A summary table of all reviewed studies can be found in Appendix I at the end of this chapter.

Table 2.1 Countries and regions represented in the literature review
(Bolded countries/regions are low and middle income)*

1	Canada	8	**South Africa**
2	**Caribbean**	9	**South East Asia**
3	**Côte d'Ivoire**	10	**Southern Africa**
4	England/UK	11	**Sub-Saharan Africa**
5	Germany	12	Switzerland
6	**India**	13	**Thailand**
7	Italy	14	United States

*Countries included in the Creese et al., 2002 meta-analysis were not specified and therefore are not included here.

2.3.1 Economic evaluation of ART in high-income countries

This section summarizes eighteen studies that examined the cost-effectiveness of providing ART in high-income countries. They included CEAs of ART in Canada (two studies), Germany (one – also took place in the U.K.), Italy (one), Switzerland (one), the United Kingdom (three) and the United States (ten). In addition, one meta-analysis of CEAs from high-income countries is reviewed, as well as two CEAs of interventions to improve patient adherence. The two adherence analyses are included because they represent a broader application of CEA in an HIV treatment program (CEA has typically been used to evaluate treatment (ART) and prevention of mother to child transmission (PMTCT) interventions).

Methods: study design

In the five pre-HAART-era studies reviewed here, investigators compared dual-therapy to mono-therapy (Chancellor et al., 1997; Lacey et al., 1999a; Lacey et al., 1999b; Lacey et al., 1999c; Mauskopf et al., 1998). Two studies used a *before-and-after* study design comparing the pre-HAART and HAART-eras (Tramarin et al., 2004; Beck, Mandalia & Gaudreault, 2004), two were prospective analyses (Lacey et al., 1999a; Lacey et al., 1999b), and the remainder relied on the use of models (Markov/state-transition models or deterministic models) to simulate future costs and outcomes (Lacey et al., 1999c; Chancellor et al., 1997; Cook et al., 1999; Duggan & Evans, 2008; Freedberg et al., 2001; Mauskopf et al., 1998; Miners et al, 2001; Moore & Bartlett, 1996; Sax et al., 2005; Schackman et al, 2001; Sendi et al, 1999).

The HAART-era analyses (triple therapy) modeled novel HAART combinations (i.e. introduction of a new drug) compared to an accepted standard regimen (Duggan &

Evans, 2008; Sax et al., 2005), treatment initiation at different stages of illness (Sendi et al, 1999; Schackman et al, 2001), HAART compared with no treatment (Freedberg et al., 2001; Tramarin et al., 2004; Beck et al., 2004; Mandalia & Gaudreault, 2004), or HAART compared to a dual-therapy regimen (Cook et al., 1999; Miners et al, 2001; Moore & Bartlett, 1996). Six of the analyses modeled costs and effects over the course of a lifetime. Among the three that did not model lifetime costs, outcomes were forecast from as little as six months (Tramarin et al., 2004), and up to twenty years (Cook et al., 1999; Miners et al, 2001 et al, 2001). Twelve studies were conducted from the payer perspective, and three purported to adopt a societal perspective, (Freedberg et al., 2001; Schackman et al, 2001; Sendi et al, 1999) though each study defined the societal perspective differently.[5] The meta-analysis conducted by Moore (2000) reviewed three CEAs of HAART compared to dual therapy.

Freedberg, Hirschhorn, and colleagues (2006) examined costs and outcomes associated with a multi-pronged adherence intervention (nursing support, patient incentives, tools and training) as part of a randomized controlled trial (RCT). Lifetime costs were modeled and it was conducted from the payer perspective. In the second CEA of an adherence intervention, Goldie and colleagues (2003) used a state-transition model to calculate CEAs for a range of adherence interventions costing between $25.00 and $1500.00 (based on published cost analyses of different adherence intervention). Costs were modeled over the course of a lifetime from the societal perspective.[6]

Methods: data sources

Of the fifteen treatment-focused CEA papers, nine derived their data from randomized clinical trials (RCTs) (Chancellor et al., 1997; Cook et al., 1999; Freedberg et al., 2001; Lacey et al., 1999a; Lacey et al., 1999b; Lacey et al., 1999c; Mauskopf et al., 1998; Sax et al., 2005; Schackman et al, 2001). Among the remaining three, data were derived

[5] Gold and colleagues (1996) defined the *societal perspective* as "comprehensive, counting the health effects and costs experienced by all those who are significantly affected by the intervention…" Drummond et al. (2005) define it as "all costs and consequences to whomsoever they accrue." These definitions suggest that a societal perspective should include direct costs from all potential contributors (individual, health system, community etc.), and potentially indirect costs as well. None of these studies conformed to these definitions. In the paper by Schackman et al. (2001) the societal perspective took into account the number of deaths and opportunistic infections, and calculated treatment costs per person for life. Freedberg and colleagues (2001) defined a societal perspective as "all costs and health effects," though they did not include patient out-of-pocket costs or lost wages. Finally, Sendi et al. (1999) included loss of productivity costs in addition to all normal direct costs, but did not consider patient out-of-pocket expenses.

[6] In this study by Goldie et al., the *societal perspective* meant that out-of-pocket patient costs and all health system costs (health professional time, drugs and labs) were taken into account, but didn't take indirect costs associated with lost productivity or costs averted (i.e. hospitalizations) into account.

from a public insurance scheme in the U.S. (Medicare) (Duggan & Evans, 2008), and from hospital data (Tramarin et al., 2004; Beck et al., 2004; Mandalia & Gaudreault, 2004). Data for the adherence studies were abstracted from multiple sources including RCTs, national databases, and the published literature (Goldie et al, 2003; Freedberg et al., 2006).

Methods: costs

The vast majority of the ART studies considered direct care and treatment costs in their analyses including ARVs, drugs to treat opportunistic infections, laboratory monitoring, and patient visits.[7] In addition to these standard costs, some studies also included costs associated with home-based and long-term care (Cook et al., 1999; Chancellor et al., 1997; Sax et al., 2005), capital and overhead costs (Freedberg et al., 2001), and patient out-of-pocket expenses (Freedberg et al., 2001). Only one study calculated indirect costs associated with lost productivity (Sendi et al, 1999). Cost data were obtained from a variety of sources including hospital records and/or RCTs (Lacey et al., 1999a; Lacey et al., 1999b; Beck et al., 2004; Chancellor et al., 1997; Tramarin et al., 2004), previously published cost research (Cook et al., 1999; Mauskopf et al., 1998; Moore & Bartlett, 1996; Sax et al., 2005; Sendi et al, 1999; Miners et al, 2001), the AIDS Cost and Services Utilization Survey (Freedberg et al., 2001; Schackman et al, 2001), or public payer medical schemes (Duggan & Evans, 2008; Lacey et al., 1999c).

While there is no standard annual discount rate for past and future costs in the CEA literature, the WHO CHOICE program (Tan-Torres Edejer et al., 2003) recommended three percent annually for base-case costs, and Drummond (2005) and co-authors suggested a range of between three and five percent. Five of the treatment-focused CEAs discounted costs at three percent (Cook et al., 1999; Mauskopf et al., 1998; Moore & Bartlett, 1996; Sax et al., 2005; Schackman et al, 2001) and two at six percent per annum (Miners et al., 2001; Chancellor et al., 1997). Eight studies did not discount costs or outcomes (Beck et al., 2004; Mandalia & Gaudreault, 2004; Duggan & Evans, 2008; Freedberg et al., 2001; Lacey et al., 1999a; Lacey et al., 1999b; Lacey et al., 1999c; Sendi et al, 1999). Goldie and colleagues' (2003) adherence analysis discounted at a rate of three percent per annum, and utilized a combination of micro-costing for some interventions and patient time (opportunity cost), as well as other

[7] The methodology for costing patient visits varied somewhat: most studies rolled labs and drugs into one cost and called it a "visit," while others included inpatient and outpatient costs including health professional time (Beck et al., 2004; Cook et al., 1999; Freedberg et al., 2001; Sendi et al., 1999; Tramarin et al., 2004). One study neglected visit costs altogether (Sax et al., 2005).

published costs. In their adherence study, Freedberg and colleagues (2006) also discounted costs at three percent per annum, and performed micro-costing of the intervention, which included health professional labor costs, patient incentives and tools, and training expenses.

Key findings

- HAART is cost-effective compared to dual or no treatment (Beck et al., 2004; Chancellor et al., 1997; Cook et al., 1999; Duggan & Evans, 2008; Freedberg et al., 2001; Miners et al, 2001; Moore & Bartlett, 1996; Sendi et al., 1999)
- Dual therapy is cost-effective relative to mono-therapy (Chancellor et al., 1997; Mauskopf et al., 1998)
- Earlier initiation of HAART (CD4=200 v. CD4=500) is cost-effective resulting in an additional half a QALY and reduced morbidity and mortality (Schackman et al, 2001; Mauskopf et al., 1998)
- Cost savings associated with HAART programs was the result of decreased hospitalizations and fewer opportunistic infections (Chancellor et al., 1997; Lacey et al., 1999a; Lacey et al., 1999b; Lacey et al., 1999c; Moore, 2000)
- Drug costs were very influential in the analyses (Freedberg et al., 2001; Miners et al, 2001; Sax et al., 2005; Tramarin et al., 2004)
- Inclusion of indirect costs in CEA (adopting a societal perspective) would likely increase the cost-effectiveness of treatment interventions (Freedberg et al., 2001; Moore, 2000; Sendi et al., 1999)
- HAART improves quality of life (Tramarin et al., 2004; Miners et al, 2001; Mauskopf et al., 1998; Sax et al., 2005; Schackman et al, 2001; Goldie et al., 2003; Freedberg et al., 2006)
- In the short-term (five years), HAART is cost-saving (Cook et al., 1999)
- Interventions that improve adherence reduce costs by keeping patients on first line treatment longer (Freedberg et al., 2006)
- In patients with advanced disease, interventions that reduce non-adherence by at least 50 percent are cost-effective regardless of intervention cost (Goldie et al., 2003)

Discussion: economic evaluation of ART in high-income countries

In high-income countries, interventions costing less than $150,000 are generally considered *cost-effective* (using the WHO suggested threshold of less than three times per capita GDP), and those that cost less than $50,000 are considered *very cost-effective* (less than or equal to per capita GDP) (WHO, 2002). ART - and HAART in particular - was consistently argued to be cost-effective, and not surprisingly drug costs were the main cost-driver in the HIV treatment scenarios evaluated.

Although several papers included a discussion of the potential impact of indirect costs and costs averted on CERs, only the analysis by Sendi et al. (1999) calculated the value of additional productive years into the CER. In two of the treatment scenarios examined in that study, HAART proved to be cost-saving when future productivity was taken into account. Excepting the study by Sendi and colleagues, it is noteworthy that all of the other studies reviewed failed to consider costs associated with absenteeism from work or school or costs averted as a result of the treatment interventions (i.e. funeral costs, welfare benefits) in their analyses. The true cost of HIV care and treatment extends well beyond drugs, laboratory tests and routine patient visits. Several studies also omitted inpatient care costs, which are critically important given the intensive and costly care required for patients not on treatment. These are potentially very important costs (or costs averted) from both the payer and societal perspectives, and if accounted for would, at a minimum, result in more accurate and favorable CERs, and in some circumstances demonstrate cost-savings relative to doing nothing as shown in the Sendi analysis.

HAART has been the standard of care for over twelve years in high-income countries, and yet there are no published prospective (or retrospective) observational cohort studies that track actual patient outcomes and costs over time. The failure to replicate authentic, “real world” HIV treatment scenarios, rather than relying on theoretical models (albeit sophisticated ones), is one of the biggest methodological shortcomings in this literature. Several of the models derived data from RCTs, which do not necessarily reflect “real world” experience and the challenges of taking ART over the course of one’s lifetime. None of the studies reviewed took into account patient out-of-pocket costs or other indirect costs into account (time away from work for clinic visits). Moreover, with the exception of Freedberg and colleagues’ 2006 study of a package of adherence interventions, all of the studies evaluated a single intervention in isolation, rather than as part of a comprehensive package of care comprising multiple interventions as they would in practice. One study even utilized patient data from one country to calculate an ICER for HAART in another (Lacey et al., 1999c).

Future research should ideally include patient costs when calculating ICERs, examine the costs and outcomes associated with *models* of care and treatment rather than evaluating certain elements of treatment programs in isolation, and follow patients over time in a non-RCT setting. They should also consider critical indirect costs averted such as lost productivity in calculating CERs. These advances would provide data that reflect the realities of care and treatment provision and reassure policy-makers that they are making decisions based on the best available information derived from real-life situations. Moreover, such studies would provide data against which modeling research (which is less resource intensive than multi-year studies) could be compared, and used to refine existing models.

2.3.2 Economic evaluation of ART in low- and middle-income countries

This section summarizes seventeen studies that evaluated the use of ART to treat HIV infection in low and middle-income countries. Included here are twelve cost-effectiveness analyses (CEA), along with three meta-analyses of the cost-effectiveness literature, and two cost-analyses that examined the cost of implementing ART in low- and middle-income countries. All CEAs evaluated the costs and benefits of dual or triple antiretroviral therapy (HAART). All but one of the studies used the WHO Commission on Macroeconomics and Health (2000) cost-effectiveness threshold where interventions were deemed to be "cost-effective" if their cost was equal to or less than three-times the per capita national income, and "very cost-effective" if equal to or less than the per capita national income. One study used the Wessex Institute of Public Health Matrix to determine the cost-effectiveness threshold, which varies based on the size of the ICER and the quality of the data (Miners et al, 2001).

Methods: CEA

Eleven CEAs were conducted from the payer/provider perspective and included direct costs only. Only one study adopted a societal perspective, which meant that out-of-pocket expenditures for patient travel were taken into account (Freedberg, 2007). All studies included direct costs for medicines according to national tariffs (ARVs and other medicines including treatment for opportunistic infections), laboratory investigations according to national tariffs (diagnostic and monitoring), and inpatient and outpatient care (facility costs and care provider time). Only two studies included capital costs and overhead in their analysis (Cleary, McIntyre & Boulle, 2006; Freedberg, 2007). None of the studies included patient time away from work, or indirect benefits such as additional

productivity afforded by HAART and/or costs averted (i.e. decreased reliance on social grants) in their analysis. Two studies considered the cost-effectiveness of treatment with HAART and a prevention program compared to a prevention program only (Nattrass & Geffen, 2005) or to a treatment program only (Over et al., 2007).

Costs for inpatient and outpatient care services were most often calculated using a combination of micro-costing (detailed costing analysis) and macro-costing techniques (i.e. use of average cost estimates such as the patient-day equivalents) (Bachmann, 2006; Badri et al., 2006; Cleary, McIntyre & Boulle, 2006; Freedberg, 2007, Goldie et al., 2006; Hogan et al., 2005; Nattrass & Geffen, 2005; Over et al., 2007). The remaining four studies relied exclusively on macro-costing (Boulle et al., 2002; Over et al., 2004; Wolf et al., 2007; Wood et al., 2000).

One study was conducted as part of an RCT (Badri et al., 2006) and the rest were conducted using modeling techniques - including Markov models, Monte Carlo simulations and deterministic models - to predict future outcomes and costs. Three of the studies utilized regional data from original research (Bachmann, 2006n, 2006; Wolf et al., 2007; Hogan et al., 2005) in their models and estimates. Of the remaining papers, four utilized data from a single clinical setting (Badri et al., 2006; Boulle et al., 2002; Cleary, McIntyre & Boulle, 2006; Goldie et al., 2006), and five employed national cost and outcomes data for modeling outcomes and costs (Freedberg, 2007; Nattrass & Geffen, 2005; Over et al., 2004; Over et al., 2007; Wood et al., 2000).

Most studies expressed ICERs in terms of U.S. dollars ($US) (Bachmann, 2006; Badri et al., 2006; Cleary, McIntyre & Boulle, 2006; Freedberg, 2007; Goldie et al., 2006; Over et al., 2004; Over et al., 2007; Wolf et al., 2007; Wood et al., 2000). Two papers presented costs in South African Rand (ZAR) (Boulle et al., 2002; Nattrass & Geffen, 2005), and one used International Dollars ($Int) (Hogan et al., 2005). Only four studies discounted costs: three studies discounted at three percent annually (Bachmann, 2006; Freedberg, 2007; Wolf et al., 2007), and one discounted at an annual rate of ten percent (Over et al., 2004).

Effectiveness was mostly commonly expressed in terms of “life-years gained/saved” (LYG/LYS) (Bachmann, 2006; Boulle et al., 2002; Cleary, McIntyre & Boulle, 2006; Freedberg et al, 2007; Goldie et al., 2006; Over et al., 2004; Over et al., 2007; Wolf et al., 2007; Wood et al., 2000). Two studies expressed results in terms of both LYG and quality-adjusted life-years (QALY) (Bachmann, 2006; Cleary, McIntyre & Boulle, 2006);

one expressed results in terms of LYG and "cost per patient per year" (Badri et al., 2006); one calculated disability-adjusted life-years (DALY) (Hogan et al., 2005); and another calculated the cost per infection averted (Nattrass & Geffen, 2005).

Key findings: CEA

- Highly-active antiretroviral therapy (HAART) was cost-effective (equal to or less than three times the per capita GDP) (Bachmann, 2006; Badri et al., 2006; Boulle et al., 2002; Cleary, McIntyre & Boulle, 2006; Cook et al., 1999; Creese et al., 2002; Freedberg, 2007; Goldie et al., 2006; Hogan et al., 2005; Nattrass & Geffen, 2005; Over et al., 2007; Wolf et al., 2007)
- HAART was "very" cost-effective (equal to or less than the per capita GDP) (Wolf et al., 2007; Cleary, McIntyre & Boulle, 2006)
- In patients with advanced HIV disease (AIDS) in South Africa, HAART was cost-saving compared to no treatment (Badri et al., 2006)
- HAART improved and extended quality years of life (Tramarin et al., 2004; Bachmann, 2006; Cleary, McIntyre & Boulle, 2006)
- Analyses were sensitive to antiretroviral drug prices (Badri et al., 2006; Boulle et al., 2002; Nattrass & Geffen, 2005; Tramarin et al., 2004; Wood et al., 2000), and particularly second-line drugs, which were not available in generic form (Freedberg, 2007; Wolf et al., 2007)
- Regimens that included prophylaxis in addition to HAART were more cost-effective than HAART alone (Freedberg, 2007; Bachmann, 2006; Goldie et al., 2006; Wolf et al., 2007)
- Several authors noted that health system strength and capacity was a greater constraint than affordability (Boulle, Kenyon & Abdullah, 2003; Creese et al., 2002; Wood et al., 2000; Kumaranyake, 2008)
- Starting patients late in infection with low CD4 counts (<200 cells/mm^3) resulted in lower cost effectiveness and/or higher overall healthy system costs (Freedberg, 2007; Bachmann, 2006; Goldie et al., 2006)
- The use of HAART was associated with decreased costs for treatment of opportunistic infections and inpatient hospitalizations (Badri et al., 2006; Tramarin et al., 2004; Nattrass & Geffen, 2005)

- Introduction of HAART among workers resulted in decreased absenteeism, hospitalizations and death, as well as reduced risk for disease progression. Savings associated with the program were three times greater than the costs associated with treatment (Eholie et al., 2003)
- HAART paired with prevention initiatives was more cost-effective than prevention or treatment programs operating in isolation (Over et al., 2007; Nattrass & Geffen, 2005)
- Two studies estimated total costs to treat HIV-infected South Africans; one estimated a cost of $98 billion (Bachmann, 2006) for 4.7 million infected people on ART and antibiotics; a second estimated costs at between 0.9 percent and 2.6 percent of national GDP between 2002 and 2015 (Nattrass & Geffen, 2005).

Methods: meta-analyses

Three meta-analyses of developing country CEAs were reviewed. Boulle and colleagues (2003) compared four potential treatment scenarios in the context of the national HIV treatment program in South Africa in terms of costs and outcomes. In the second meta-analysis, Creese et al. (2002) reviewed 24 published studies that documented the cost-effectiveness of 31 HIV interventions on the African continent, and calculated costs per infection prevented and cost per DALY in $US (2000). Finally, Kumaranayake (2008) reviewed 34 studies that examined cost-effectiveness and issues of scale in HIV interventions in low- and middle-income countries.

Key findings: meta-analyses

- Models overestimated uptake of HIV testing and access to HIV services (Boulle, Kenyon & Abdullah, 2003)
- Significant investments in service capacity are required (Boulle, Kenyon & Abdullah, 2003; Kumaranyake, 2008)
- Economies of scale will likely be achieved with interventions with low fixed costs (e.g. voluntary counseling and testing), but beyond a certain patient volume, services such as treatment will encounter diseconomies of scale without additional investments in capacity (Kumaranyake, 2008)

- There is a dearth of empirical evidence on cost-effectiveness and costs associated with scaling-up HIV interventions (Creese et al., 2002; Kumaranyake, 2008; Boulle, Kenyon & Abdullah, 2003)
- Treatment is cost-effective (Creese et al., 2002)
- ICERs for various HIV-related interventions ranged from US$1.00 per DALY for blood safety measures to more than $US1000 for HAART (Creese et al., 2002)
- There was no data pertaining to costs associated with health system strengthening (Creese et al., 2002)

Methods: cost-analyses

Two studies examining costs associated with implementing HIV treatment were included in this analysis because of their immediate relevance to this research. In the first paper, Harling and colleagues (2007) conducted a retrospective cost analysis of running a dedicated HIV clinic in South Africa. Cost data collected included staff, capital costs, and supplies over a two-year period (2004 – 2006) in order to calculate a per patient per month cost. All costs were converted from South African Rand into US$ (2004). Medicine (including ART) laboratory tests, and patient out of pocket costs were excluded. In the second cost analysis, Eholie and colleagues (2003) examined a workplace HIV treatment program in Côte d'Ivoire using a before and after study design (patients were their own controls) from a payer perspective (employer and employee contributed in this case). The study lasted three years: one year prior to introducing ART, and two years after. Study costs included drugs, labs, and doctor visits, as well as costs to the company including absenteeism, invalid benefits and funeral costs.

Key findings: cost-analyses

- Cost per HIV patient was $54.79 in 2004/05 and $41.62 in 2005/06 (Harling et al., 2007)
- As the number of patients increase, economies of scale are achieved (Harling et al., 2007)
- Costs of running an HIV clinic were largely driven by staff salaries (Harling et al., 2007)

- Introduction of HAART at a total cost of $217,000 resulted in savings of $775,000 over two years due to reduced absenteeism, health costs, and death/funeral benefits (Eholie et al., 2003)

Discussion: economic evaluation of ART low- and middle-income countries

Due to the methodological, geographic, and chronological differences between the cost-effectiveness studies reviewed it is difficult to compare the costs and outcomes modeled. However, it is possible to make some broad comparisons of studies undertaken in South Africa. The first analysis undertaken in South Africa in 2000 estimated the cost per LYG at US$15,000 (Wood et al., 2000). A study from just two years later estimated the cost per LYG to be approximately R9000 (or about US$9000 in 2002) thanks to a significant drop in drug prices. Subsequent drug price reductions were evident in the two studies published in 2006 which estimated the cost per LYG between US$675 - $1622 (Badri et al., 2006) and US$984 (Cleary, McIntyre & Boulle, 2006), a reduction of more than 90 percent in cost per LYG over 2000 prices for the same ART regimen.

Only one of the low and middle-income country studies reviewed took into consideration indirect costs (Eholie et al., 2003) and as discussed in section 2.3.1 (high-income country studies) these averted costs (absenteeism from work, welfare grants, end of life care, etc.) are likely significant for the payer and society, and would improve observed CERs. In their study of HAART plus prevention programming, Nattrass and Geffen (2005) highlighted the inpatient hospitalization costs averted (several of the studies reviewed here considered hospitalization a direct cost) by providing universal treatment access on a large scale, and reported their results in terms of cost per infection averted. This methodology is useful and practical because it spotlights one of the critical benefits of HAART – lower morbidity and mortality and fewer hospitalizations – and because these are terms easily comprehended by policy-makers. In similar fashion, Badri and colleagues (2006) framed their results in terms of cost per patient per year, which is also accessible to non-economist decision-makers.

Some common themes emerged from the three meta-analyses reviewed. All three studies showed that issues of infrastructure, scale and capacity had been neglected in favor of direct program costs when considering feasibility and cost-effectiveness of implementing HIV antiretroviral treatment programs. These studies underscore a potential pitfall in over-emphasizing the role of CEA in health policy decision-making:

while an intervention might be cost-effective, it may not be feasible for a variety of reasons including human resource shortages, lack of physical space, poorly functioning supply chains, or inadequately trained staff. All of these factors - while peripheral to treatment - are increasingly limiting efforts to achieve scale with prevention and treatment interventions in countries with weak health systems.

The Harling (2007) study added valuable clinic cost data to the literature where none previously existed and demonstrated that economies of scale can be achieved in a treatment program. Interestingly, it also demonstrated that even in the absence of drug costs, capital and overhead expenses were not a significant cost driver. It did not however explore the point at which diseconomies of scale begin to occur due to insufficient human resources, laboratory and pharmacy capacity or lack of physical space.

2.4 Literature review: ART rollouts and scale-up

The literature review was conducted using two online database search engines: Academic Search Premier and Pub Med; as well as the University of Cape Town Libraries' ALEPH journal and book search engine. The literature search employed the following keywords in various combinations: *antiretroviral therapy roll out; ART scale-up; ART treatment models; resource-constrained settings; developing countries; South Africa; Africa; HIV and AIDS; ART; HAART; and HIV treatment*. The search turned up original research papers, as well as meta-analyses, both of which were included in the review.

This section reviews 36 published studies in 18 countries (see Table 2.2) that describe the first ARV programs implemented in developing countries, as well as attempts to scale-up HIV care and treatment to meet demand. Appendix II contains a summary table of all 35 studies that were reviewed. This section summarizes study methodologies, key findings, and concludes with a discussion of the scale-up literature.

A literature search was conducted using academic databases and only included studies published in academic journals on ART rollouts and scale-up (conference abstracts were excluded). However, one meta-analysis reviewed here included conference abstracts in its summary (Akileswaran et al., 2005et al., 2005). This literature review is geographically focused on Africa, though it also includes a review of important findings from other parts of the world (Thailand, Brazil and Haiti) that are relevant to the African

literature. The studies reviewed were published between 2001 and 2008, and include outcomes for patients who were enrolled into treatment programs as early as 1996 (Orrell et al., 2003).

Table 2.2 Countries represented in the rollout/scale-up literature review

1	Botswana	10	Morocco
2	Brazil	11	Mozambique
3	Cameroon	12	Nigeria
4	Congo	13	Senegal
5	Cote d'Ivoire	14	South Africa
6	Ghana	15	Swaziland
7	Haiti	16	Thailand
8	Kenya	17	Uganda
9	Malawi	18	Zambia

2.4.1 Summary of study aims

As discussed in Chapter 1, there was considerable doubt in the late 1990's about the feasibility of providing complex and expensive ARV regimens in developing countries. The aim of many of the earliest studies was to provide "proof of concept" regarding the feasibility and efficacy of HAART in resource-poor settings. Subsequent papers detailed lessons learned from initial treatment programs and focused on methods for scaling-up treatment, while some employed modeling techniques to estimate future costs and outcomes of ART rollouts in developing countries. Most recently, several meta-analyses examined efficacy, adherence and patient retention in selected treatment programs. This section describes the methods and key findings of the ART program literature, divided into the four study types: proof of concept, scale-up, modeling studies and meta-analyses.

2.4.2 Proof of concept

Methods

Twenty "proof of concept" studies were reviewed. Ten of these were prospective cohort studies that included between 62 and 1,139 patients (Bekker et al., 2003; Bekker et al., 2006; Coetzee et al., 2004; Landman et al., 2003; Laniece; et al., 2003; Laurent et al., 2002; Laurent et al., 2004; Orrell et al., 2003; Stringer et al., 2006; Severe et al., 2005). Eight studies were retrospective evaluations of cohorts that included between 60 and

788 patients (Laurent et al., 2005; Lively & Chester, 2003; Farmer et al., 2001; Desclaux et al., 2003; Jack et al., 2004; Macharia et al., 2003; Tassie et al., 2003; Weidle et al., 2002), and another described the process and lessons learned from establishing a new treatment program (Mukherjee et al., 2003). Study outcomes included virologic (viral load) and immunologic (CD4) responses to HAART, and some included measures of patient adherence. A few of the studies also looked at the development of resistance to ART and tracked regimen switches in study populations. Studies started enrolling patients as early as 1996 (Orrell et al., 2003) and 1998 (Desclaux et al., 2003; Laurent et al., 2002; Weidle et al., 2002). Studies that pre-dated the HAART-era evaluated the impact and feasibility of mono and dual-therapy (Macharia et al., 2003; Weidle et al., 2002; Orrell et al., 2003; Lively & Chester, 2003; Laurent et al., 2005).

Key findings: feasibility of HAART

- HAART can be provided through primary care clinics (Bekker et al., 2003; Bekker et al., 2006)
- ART can be successfully rolled out in Africa/resource-poor settings (Coetzee et al., 2004; Desclaux et al., 2003; Macharia et al., 2003; Orrell et al., 2003; Stringer et al., 2006; Tassie et al., 2003; Weidle et al., 2002)
- Directly observed therapy (DOT) was a viable model for HAART provision in Africa/resource-poor settings for smaller scale programs (Farmer et al., 2001; Jack et al., 2004; Mukherjee et al., 2003; Mukherjee et al., 2006)
- TB and HIV care and treatment services can be effectively integrated (Farmer et al., 2001; Mukherjee et al., 2003; Mukherjee et al., 2006; Jack et al., 2004; Severe et al., 2005)
- Physical space was an important program limitation (Bekker et al., 2006)
- Poor results were seen when ART was rolled out with inadequate support for providers and patients (Lively & Chester, 2003)
- Inconsistent dispensing and stock outs were observed (Laurent et al., 2005; Severe et al., 2005)
- Drug costs were too high for individuals and health systems (Laniece et al., 2003; Laurent et al., 2005; Macharia et al., 2003; Mukherjee et al., 2003; Mukherjee et al., 2006)

- HAART can be effectively rolled-out in the private sector (Macharia et al., 2003)
- Generic, fixed-dose HAART was as efficacious as branded drugs and had the added advantage of being less expensive and fixed-dose combination pills resulted in a lower pill burden (Laurent, et al., 2004)
- HAART was effective in children (Severe et al., 2005)

Key findings: adherence and retention

- Adherence was comparable to results observed in developed countries (Farmer et al., 2001; Jack et al., 2004; Laniece et al., 2003; Landman et al., 2003; Laurent et al., 2004; Orrell et al., 2003)
- 95 percent or greater self-reported adherence at 12 months (Landman et al., 2003; Laurent et al., 2004;)
- Self-reported adherence ranged between 88 and 95 percent in study cohorts after 12 months (Orrell et al., 2003) or mean adherence during the study period (Weidle et al., 2002; Laniece et al., 2003)
- A wide range of program retention figures was reported. Table 2.3 summarizes retention findings

Table 2.3 Patient retention research: summary of findings

Author(s), Year	Length of study period (months)	Retention % (N)
Orrell et al., 2003	12	84% (242)
Laurent et al., 2005	13	68% (536)
Coetzee et al., 2004	13.9	90% (259)
Severe et al., 2005	14	80% (800)
Stringer et al., 2006	19	72% (11,663)
Weidle et al., 2002	23	52% (248)
Macharia et al., 2003	24	55% (119)
Bekker et al., 2006	36	90% (1025)

- The majority of patient deaths occurred in the first 3 months of treatment (Tassie et al., 2003; Coetzee et al., 2004; Bekker et al., 2006; Laurent et al., 2004; Stringer et al., 2006; Weidle et al., 2002), and 79% of observed deaths took place within 6 months of starting treatment (Severe et al., 2005)

- Reported obstacles to retention and adherence included ART drug costs (Orrell et al., 2003; Laurent et al., 2005; Landman et al., 2003; Tassie et al., 2003; Weidle et al., 2002), a lack of clinic space (Bekker et al., 2006), inadequate human resources (Stringer et al., 2006; Laurent et al., 2005; Livesley & Chester, 2003), drug-associated side-effects (Laurent et al., 2004; Macharia et al., 2003; Severe et al., 2005), regimen type (Laniece et al., 2003; Jack et al., 2004; Laurent et al., 2004), and premature death (see previous bullet).
- Drug stock-outs were reported in a minority of studies, which adversely affected adherence (Laurent et al., 2005; Severe et al., 2005).

Key findings: virologic and immunologic response

- Generally, despite different viral sub-types compared to those in Europe and the United States, virologic and immunologic responses to HAART were strong.
- Not all studies reported viral load (VL) due to cost or access (Stringer et al., 2006; Livesley & Chester, 2003; Laniece et al., 2003). Several studies that reported VL results did so only for a subset of patients (Bekker et al., 2003; Tassie et al., 2003; Severe et al., 2005; Weidle et al., 2002).
- The definition of VL suppression varied. Most studies defined suppression as <400 copies/µl, but a few defined suppression as VL<50 copies/µl (Bekker et al., 2006; Jack et al., 2004; Landman et al., 2003; Laurent et al., 2005).
- The lowest reported VL suppression figures and CD4 increases were among studies that included patients on mono and dual-therapy (Livesley & Chester, 2003; Macharia et al., 2003; Weidle et al., 2002).
- Among studies of patients on triple-therapy (HAART), the percent of patients demonstrating VL suppression (<400 copies/µl and <50 copies/µl) at six months was between 80 percent (Laurent et al., 2004) and 95 percent (Landman et al., 2003); the range at 12 months was between 71 percent (Orrell et al., 2003) and 84 percent (Coetzee et al., 2004); and the range at 24 months was between 58 percent (Laurent et al., 2005) and 70 percent (Coetzee et al., 2004).
- Observed increases in the median CD4 count at six months ranged from 83 cells/mm^3 (Laurent et al., 2004) to 104 cells/mm^3 (Tassie et al., 2003);

between 113 cells/mm^3 (Laurent et al., 2005) and 175 cells/mm^3 (Stringer et al., 2006) at 12 months; and between 143 cells/mm^3 (Laurent et al., 2005) and 288 cells/mm^3 (Coetzee et al., 2004) at 24 months.

- Only two studies reported findings on treatment resistance. One study reported resistance to at least one drug in 65% (n=61) of patients (Weidle et al., 2002), but this included patients on mono and dual-therapy who were known to be at high risk for developing drug resistance. One other study found that out of a cohort of 58, two developed resistance to one of the drugs (Laurent et al., 2002).

2.4.3 Treatment scale-up

Methods

Ten papers other papers reviewed evaluated efforts to scale-up access to HIV treatment in developing countries. They consisted largely of expert policy analysis, and several were devoted to lessons learned from past scale-up efforts. One paper summarized interviews with health policy leaders (Kober & Van Damme, 2004).

Key findings: lessons learned

- Local manufacturing of generic ARVs and the invocation of public health emergency provisions within the Trade-related aspects of intellectual property rights (TRIPS) permitted rapid rollout and free access to ART in Brazil (Galvao, 2002; Phanuphak, 2004; Texeira, 2004)
- HIV and TB treatment services should be integrated (Harries et al., 2001; Mukherjee et al., 2003)
- An over-emphasis on diagnostic and monitoring technology (CD4 and VL) could endanger rollouts in resource-poor settings by overtaxing health systems and cannibalizing limited resources (Harries, Schouten & Libamba, 2006)
- HIV prevention and treatment initiatives were complementary and necessary (Mukherjee et al., 2003)
- The health professional human resource crisis must be addressed as a priority (Nattrass & Geffen, 2005; Nattrass, 2006; Ooms, Van Damme & Temmerman, 2007; Mukherjee et al., 2003; Kober & Van Damme, 2004) and

donor funds should be used to address human resource needs (Kober & Van Damme, 2004; Ooms, Van Damme & Temmerman, 2007)

- National leadership was critical to successful rollouts (Nattrass & Geffen, 2005; Phanuphak, 2004; Galvao, 2002; Texeira, 2004)
- Given the price of ART, the provision of first line drugs only should be policy in order to ensure that as many people as possible have access to treatment (Harries, Schouten & Libamba, 2006; Kenyon et al., 2003)

2.4.4 Modeling

Methods

Three studies used statistical modeling to predict the impact of scaling-up ART access in South Africa. The first study used a compartmentalized deterministic model to assess the impact of ART on HIV transmission (Baggaley, Garnett & Ferguson, 2006). A second study modeled rates of scale-up in order to predict prevalence and incidence outcomes in the future (Walensky et al., 2008), and the third study used a mathematical model to demonstrate the potential impact of assuring equitable access to ART in KwaZulu-Natal Province, South Africa (Wilson & Blower, 2005).

Key findings:

- Universal ART coverage was not an effective prevention strategy in sub-Saharan epidemics (Baggaley, Garnett & Ferguson, 2006)
- A rapid or moderate scale-up could avert as many as 1.2 million deaths by 2012 (Walensky et al., 2008)
- Healthcare facility catchment areas should be increased and ART should be made available at 54 facilities throughout the province (Wilson & Blower, 2005)

2.4.5 Meta-analyses

Methods

Four meta-analyses extracted data from published studies from African ART program literature and evaluated them for statistically significant findings and trends. Three of the studies looked at ART program performance (Akileswaran et al., 2005; Ivers, Kendrick & Doucette, 2005; Katzenstein, Laga & Moatti, (2003) and the fourth looked at ART program retention (Rosen, Fox & Gill, 2007).

Key findings:

- HAART can feasibly be implemented in resource-limited settings (Ivers, Kendrick & Doucette, 2005; Akileswaran et al., 2005; Katzenstein, Laga & Moatti, 2003)
- Adherence was comparable to industrialized settings (Akileswaran et al., 2005; Katzenstein, Laga & Moatti, (2003)
- Providing free ART was associated with significantly higher adherence to ART (Ivers, Kendrick & Doucette, 2005)
- ART programs retained approximately 60 percent of patients after 24 months on treatment (Rosen, Fox & Gill, 2007)
- Earlier initiation and effective patient follow-up will reduce patient attrition (Rosen, Fox & Gill, 2007)
- Katzenstein, Laga & Moatti, (2003) observed that in three of the HAART trials the likelihood of developing resistance was similar to, or less likely than, cohorts studied in the West.

Discussion: ART scale-up in low- and middle-income countries

This body of research provided the first evidence of the efficacy and feasibility of ART treatment in developing countries. Today, ART is available (though not universally) across the African continent. However, massive challenges remain to scaling-up to universal access. The ART program literature highlighted the need for greater investment in infrastructure, supply chains and human resources in particular. Further reductions in drug prices were also identified as important to long-term sustainability of programs. Integration of services – notably HIV and TB treatment along with primary

healthcare services - was recommended for comprehensive patient care (due to high rates of co-infection), and to maximize health system efficiency by avoiding service fragmentation.

Questions about the ability of Africans to take medicines as prescribed were dismissed when observed adherence rates were shown to be analogous to those seen in high-income countries. Viral suppression and immune system recovery (as measured by CD4) were comparable to treatment results in wealthy countries despite the fact that the virus in southern and eastern Africa is a more virulent viral sub-type. More concerning was the retention data among newly established treatment programs. While a few programs were very successful at maintaining patients on ART, many fared poorly, retaining on average just over half of those started on treatment after two years. Poor patient retention in these programs may be the result treatment program emphasis on initiating treatment, and a lack of tools and proven methods for supporting and tracking patients over time. Even if the adherence and retention data are similar to those in the West, the stakes are much higher in sub-Saharan Africa given the lack of resources and treatment options, and where keeping people on treatment means keeping large swathes of the young adult population alive, and households and communities intact. The consequences associated with patient non-adherence are dire, ranging from increased morbidity and mortality to epidemics of drug-resistant virus. The costs to individuals and enfeebled health systems alike could be catastrophic.

Programs would do well to re-orient their focus from ART initiation to a holistic approach to treatment that emphasizes long-term support and patient tracking. Empirically sourced data that demonstrate effective adherence and support interventions would facilitate this programmatic shift in focus. In addition, efforts to bring newer, more tolerable drugs within reach of developing country health budgets are required. Moreover, successful ART programs should aspire to treat children as well as adults and none of the studies reviewed included children. This reflects an unfortunate reality: children are largely overlooked and undertreated in this pandemic. Training for doctors and nurses in pediatric care and treatment is needed, as are more palatable and lower cost pediatric drug formulations. Finally, the role of improved operations and strong management was overlooked in this literature. Improved patient flow, appropriate task shifting and the use of data to inform clinic management and assess clinical performance and program operations would undoubtedly yield much needed efficiencies and merits examination.

2.5 Review and comment: outcomes and associated costs of different HIV care and treatment models in South Africa by Rosen, Long & Sanne, 2008.

This section reviews the only published study that bridges the cost-effectiveness and ART scale-up outcomes literature. This paper, "The outcomes and outpatient costs of different models of antiretroviral treatment delivery in South Africa," by Rosen, Fox & Gill and colleagues (2008) is a CEA of four different models of HIV care and treatment in South Africa.

Methods

This was a retrospective analysis of outcomes and costs of four different ART treatment models: a public referral hospital, private sector GP practices (two), an NGO-run dedicated HIV clinic, and an NGO-run primary care clinic. Outcomes data were collected one year after ART initiation for the first 100 patients at each of the four clinics starting in January 2005, and average model costs were calculated for the year. Clinical outcomes were collected from patient files and used to determine patient status after twelve months on ART. Mutually exclusive outcome statuses included *No longer in care* (NIC), *in care but not responding* (NR) and *in care and responding* (IC). Patients categorized as IC were still on ART at study end and had a viral load result that was <400 copies/µl between 10 and 14 months following ART initiation. Costs for some or all sites included drugs (ARVs and non-ARVs), laboratory tests, outpatient visits, infrastructure, equipment and furnishings, data capture and program management. Costs were not standardized across the four sites. Monthly costs for each model were summed and divided by the total number of active patients in the study period to calculate an average monthly cost per patient. The average cost to produce a patient 'in care' and responding to treatment (IC) was calculated by dividing the total model cost by the number of patients with status equals IC at study end.

Results

Average monthly patient cost ranged from $756 (referral hospital) to $1,126 (primary care clinic). Drug unit costs ranged from $370-$500 per patient year as each model accessed drugs differently and at different prices. Drug costs comprised approximately half of total costs across all care models. Though laboratory unit costs were the same across all models (all had access to the National Health Laboratory Service), average laboratory tests ranged from $74-$300 per person year, and outpatient visits ranged

from $80-$200 per person year. The number of patients still in care after 12 months ranged from a high of 76 percent (primary care clinic) down to 52 percent (private GPs). The average cost to produce a patient in care and responding to ART (status equals IC) ranged from $1128 (public referral hospital) up to $1723 (private GPs).

Discussion

The Rosen, Long & Sanne (2008) study evaluated the costs and outcomes associated with different types of service delivery models for HIV/AIDS care and treatment in South Africa. It remains one of few in the literature that describe the costs associated with providing ART, and the only one to date that systematically related model costs to treatment outcomes. Moreover, this was the first study to calculate the cost of producing a successful ART patient.

However, despite the promising study design, there were several significant shortcomings in the research methodology. First, no attempt was made to control for sampling bias between patient populations, leaving it unclear whether any observed differences were due differences between the care models or due to differences between patient populations at the four study sites. The authors cited geographic diversity as one study strength, but failed to note that it was also a potentially important source of bias.

The second important methodological error was the failure to control for drug costs between models of care. Each of the four sites in the study had access to different drug prices. The public sector hospital had access to preferential drug pricing and therefore benefitted from the lowest unit cost per regimen and a significant unit cost advantage over the other sites that did not have access to public sector drug prices. This advantage was significant, as most cost analyses of HIV treatment programs have shown that HAART comprised approximately 50 percent of total treatment costs. In the end, the final cost-effectiveness ratios were heavily influenced by access to preferential unit drug costs, and obscured any role that unique features of each model might have played in determining patient outcomes. The paper does recognize that following the analysis no conclusions can be drawn between model inputs and patient outcomes. In the end, this study described costs and outcomes in four models of HIV care but failed to isolate and compare the contribution of each model's characteristics in patient outcomes, which according to the manuscript was the study objective.

Two smaller methodological errors also merit mention. First, the study did not take into account HIV-related inpatient hospitalization and costs, despite the expensive nature of inpatient care and its potential impact on total model costs and CERs. Second, the paper did not report ICERs despite the fact that the most expensive model also yielded the best outcomes, leaving the reader wondering about the marginal cost of the model.

2.6 Discussion: CEA and ART scale-up in low- and middle-income countries

Methodological Observations

Several methodological questions remain unanswered following this review of the CEA literature. First, the role of indirect costs, and specifically costs averted, in CEA of HIV interventions remains largely unexplored, and would no doubt strengthen the CERs reported in the literature, and render the argument for treatment more compelling for policy-makers. The lack of research on costs and savings associated with positive and negative externalities associated with treatment is a notable gap in the research literature. In addition, the practice of excluding capital and overhead costs in CEA of HIV treatment appears to be common – the majority of the studies in wealthy and developing countries omitted them. This may be due to the fact that they constitute such a small fraction of the HIV treatment program costs that many investigators considered them to be negligible and ignored them. This may also reflect difficulties in estimating capital costs. In all of the studies reviewed, drug costs and health professional salaries were identified as the two primary cost-drivers, and none mentioned overhead costs (cost analyses included) as playing a noticeable role. Exploration of the importance of capital and overhead costs in CEA for HIV treatment delivered in a public health system is of growing importance, particularly as infrastructure investments are made to accommodate HIV care and treatment demands. Finally, as previously discussed the *societal perspective* was inconsistently defined, possibly due to vague definitions in the published CEA guidelines, as well as difficulties associated with collecting and calculating the real costs and benefits to society of different health interventions, and suggests the need for a more pragmatic definition that reflects data collection constraints.

Conclusion

In general, the literature reviewed in this chapter sought to answer two fundamental questions about ART treatment:

1. *Is ART (and specifically HAART) cost-effective in a range of settings?*

2. *Are ART programs effective and feasible in low and middle-income countries?*

The research showed ART to be cost-effective across a range of socio-economic settings, and ART treatment programs to be effective and feasible in developing countries. In addition, some studies reported on the cost-effectiveness of specific adherence interventions. While the current body of research on the cost-effectiveness of HIV care and treatment interventions is considerable, it reflects a somewhat limited application of CEA in the evaluation of HIV programs.

This study represents a practical and important next step in applying CEA principles to evaluate models of care *holistically*, rather than a single element within a package of services. Important questions remain unanswered regarding the optimal mix and intensity of care and treatment services, and how well they potentiate or detract from one another in the context of patient care. CEA has an important role to play in highlighting cost-effective models of care, identifying cost-saving/minimizing innovations, ensuring that quality of care is considered of the resource allocation process, and demonstrating to donors and Ministries of Health that limited resources are being put to their best possible use. One can imagine evaluating various scenarios intended to establish the optimal mix of:

- Nurses, doctors and other health professionals
- Outpatient visits and home-based care visits
- Adherence and patient tracking interventions
- Laboratory monitoring schedules

This research study builds on the existing CEA literature by attempting to answer one of the next important questions regarding scaling-up HIV care and treatment services in developing countries:

What is the cost per unit of effect for different models of ART care and treatment ?

Building on the research reviewed in this chapter, this study represents an important progression in the literature by applying the techniques of CEA to evaluate two different

models of HIV care and treatment. In addition, it seeks to provide relevant, policy-friendly results and analysis that can be used to inform efforts to implement and scale-up treatment in South Africa, and make an important contribution to the implementation, cost-effectiveness, and ART scale-up literatures.

Appendix I: Summary Table of Cost and Cost-effectiveness Analysis Literature

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Bachmann, 2006	Southern Africa	Effectiveness and CEA of ART with antibiotics v. no antibiotics; and early v. late initiation; Markov state transition model; public provider perspective	Results modeled over 10 years	-ARVs; antibiotics, labs, labor costs -2 Discounting scenarios: 1. No discount 2. Costs and outcomes discounted 3% annually	-$2784 per LYG (early ART + antibiotics) -$2454 per LYG (late ART + antibiotics) -$3057 per QALY (early ART + antibiotics) -$4937 per QALY (late ART + antibiotics)	-ART was more effective but less cost-effective than antibiotics alone -ART plus antibiotics was more effective and more cost-effective than ART alone -Taking into account QOL, earlier ART initiation is more cost-effective -Early ART + antibiotics to 4.7 million people for life would cost $98 billion; for 500,000 people it would cost approx $7 billion
Badri et al., 2006	South Africa	CEA of HAART in HIV-infected patients with and without AIDS enrolled in a RCT; provider perspective	January 1995 – December 2000	-Direct, public sector program costs: in/outpatient visits, drugs (high and low estimates), labs	Median (50%) survival: -No AIDS: $1622 (high) v. $675 (low) per LYG -AIDS: cost saving regardless of drug cost	-The HAART group used fewer inpatient services than the non-ART group -HAART is clearly cost-effective, though the ICER is highly sensitive to drug prices
Beck et al., 2004	Canada	CEA of HAART; before and after study design in 2 hospitals; 2 cohorts: AIDS v. non-AIDS	Before HAART: 1991-1995 and After HAART: 1997-2001; 10 years total	-Costs calculated in $CAN 2002 and converted to $US 2002 --Direct costs included: visits (inpt/outpt), ART and "other" drugs, labs	-For non-AIDS: $14,587 per LYG -For AIDS: $12,813 per LYG	-HAART was a cost-effective intervention in Canada -Median progression time increased from 6.3 yrs (pre-HAART) to 12.5 yrs (HAART) among non-AIDS patients -Median progression time increased from 3.8 yrs (pre-HAART) to 13.3 yrs (HAART)
Boulle et al., 2002	South Africa	Modeling costs and CEA; 8 different scenarios; provider perspective	Results modeled over 5 years (2002-2007)	Direct, public sector program costs: ARVs, Labs, visits (in/outpatient), TB Rx; no discounting of costs or results	-R5923 per LYG for one line and basic care (generics) v. R9089 (patented) -R8775 per LYG for expanded care, 75% access to 2nd line (generics)	-Drug prices drive costs: use of generic v. patented drugs is the most important factor -Consider rolling out only one line of ART to larger numbers of people rather than two lines to fewer – rationing is inevitable

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Boulle, Kenyon & Abdullah, 2003	South Africa	Meta-analysis of ARV Costing Models; provider perspective	N/A	N/A	N/A	-Models reviewed over-estimated ART uptake and coverage -VL added between 19 and 45% to direct costs -Health system capacity is a greater constraint than affordability
Chancellor et al., 1997	U.K.	CEA of dual ART v. monotherapy; Markov transition model; payer perspective (UK gov't); linked to RCT	Lifetime	-Costs discounted 6% -Direct care costs: drugs, labs, visits, community service costs	-£6276 per LYG	-Dual ART is cost-effective when compared with monotherapy d/t decreased costs associated with hospitalizations and opportunistic infections
Cleary, McIntyre & Boulle, 2006	South Africa	CEA of HAART v. No ART; Markov models used to calculate lifetime costs; provider perspective	Median No ART follow-up = .63 yrs; Median HAART follow-up = 1.03 yrs	-Direct program costs: in/outpatient visits, drugs, labs, TB Rx, capital costs, overhead, *plus* NGO costs	-$1102 per QALY -$984 per LYG -Discounted lifetime costs for No ART = $2743 and HAART = $9435	-HAART is cost-effective in South Africa and well below the level of per capita GDP -While treatment is cost effective, patient costs (travel and time off work) may be barriers to ART uptake and success
Cook et al., 1999	USA	CEA of HAART v. dual ART; Markov model; part of RCT	5 years and 20 years	Direct Costs: in/outpatient visits, drugs (ARVs and non-ART), labs, home-based care and long-term care (derived from Hellinger 1993) and adjusted to 1996$US; payer perspective; costs discounted 3%	5 yrs: HAART was cost-saving v. dual therapy = $5,054 20 yrs: ICER = $13,229 per LYG	-HAART is cost-effective - $13,229 is well within the range of cost-effective therapies ($9,113 to $14,975)
Creese et al., 2002	Unspecified African nations	Meta-analysis of CEA of 31 HIV/AIDS interventions	Studies spanned 13 years: 1988 – 2000	N/A	-Cost per DALY ranged from $1 for STD treatment and condom promotion to over $1000 for HAART.	-Effectiveness of HAART may have been underestimated d/t lack of data on efficacy and costs -No data for the costs to strengthen health systems for ART provision
Duggan& Evans, 2008	USA	CEA of novel HAART combination; simulated model; provider perspective	Lifetime	-Drug, care and lab costs	-$19,000 per LYS	-$19,000 well below the U.S> cost-effectiveness threshold of $50,000, therefore this HAART combination is cost-effective

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Eholie et al., 2003	Côte d'Ivoire	Cost-savings analysis of HAART; before and after study design; payer perspective which in this case includes employer and employees	36 months: 12 months before and 24 months after introduction of ART	-Drugs, visits, labs, absenteeism, funeral costs, invalid benefits -No discounting of costs d/t short period of study	-An investment of $217,000 yielded total savings of $775,000 in reduced absenteeism, health costs and funeral costs/death benefits	-Introduction of HAART resulted in 94% decrease in absenteeism; 81% decrease in HIV hospitalizations; 78% decrease in new AIDS cases and 58% decrease in AIDS-related mortality.
Freedberg et al., 2001	USA	CEA of HAART using a deterministic model and data from three different clinical trials; societal perspective	Lifetime	-Direct program costs: in/outpatient visits, drugs, labs, TB Rx, capital costs, overhead *plus* patient costs excluding time away from work.	-Cost per QALY ranged from $13,000 to $23,000 depending on the cohort	-HAART is cost-effective -CD4 count and drug costs were most influential in costs, clinical outcomes and cost-effectiveness
Freedberg et al., 2006	USA	CEA of an ART adherence intervention in a RCT	Lifetime	-Direct cost of nursing intervention: labor, participant incentives, adherence tools and training time -Costs were discounted at 3% per year	-$14,100 per QALY	-Cost of the intervention was not a cost driver -Adherence intervention enables patients to stay on their first line regimen longer, which is cheaper
Freedberg et al., 2007	India	Clinical outcome analysis and CEA of ART using HIV disease simulation model	Lifetime	-Costs were discounted at 3% per year -Direct program costs: in/outpatient visits, drugs, labs, TB Rx, capital costs, overhead *plus* patient costs	Single line: -$430 per LYG (CD4=250) -$550 per LYG (CD4=350) Double line: -$1880 per LYG (relative to single line)	-Mean survival was 64.7 mos for one line of ART and 88.9 mos for two lines (initiation CD4=350). -Lifetime ART costs were $5430 (two regimens) per person -Cotrimoxazole yielded benefit at little additional cost -HAART is cost-effective: $1880 is approximately 3x the per capita GDP in India (2005)

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Goldie et al., 2003	USA	Modeling CEA of adherence interventions for HIV treatment; societal perspective (patient and health system costs)	Lifetime	-Costs were discounted at 3% per year -Costs included drugs, labs, adherence interventions, monthly costs and equipment for patients	-$100/month intervention, cost/QALY ranged from $22,400 - $40,900 -$500/month intervention: cost/QALY ranged from $33,100 – $131,900 -$1000/month intervention cost/QALY ranged from $45,700 - $242,100	-In all 3 groups adding an adherence intervention to ART was associated with QALY gains -In patients with advanced disease even expensive interventions were cost effective as long as they achieved a 50% reduction in failure
Goldie et al., 2006	Cote d'Ivoire	CEA of HAART: Monte Carlo simulation of do nothing v. prophylaxis v. ART v. ART + prophylaxis	Lifetime	-Costs included in/outpatient care, ARVs and OI drugs, labs -Costs converted to 2002 prices in $US.	-$240 per LYG for prophylaxis -$1,180 per LYG for ART+ prophylaxis (incl. CD4 testing)	-ART + prophylaxis is cost-effective in resource-poor settings -"Very cost-effective" in Cote d'Ivoire = <$708, "cost-effective" = $2,124.
Harling, Bekker & Wood, 2007	South Africa	Retrospective cost analysis; program perspective	2004/5 – 2005/6 (2 years)	-Costs included staff, capital costs, supplies	-Cost per patient visit = $54.79 in 04/05 and $41.62 in 05/06	-Staff salaries comprised over 60% of costs -Decrease in average costs over the two year period demonstrated economies of scale
Hogan et al., 2005	Sub-Saharan Africa and South East Asia	Modeling CEA for HIV prevention and treatment interventions based on regional research data	Lifetime	-Costs = input resources plus unit costs derived from regional studies	-Cost per DALY averted for HAART in SSA ranged from $Int556 (single line) - $Int2010 (2 lines) -Cost per DALY averted for HAART in SEA ranged from $Int542 (single line) - $Int1319 (2 lines)	-HAART is cost-effective in both regions when offered as a single line or two lines (coverage was = ANC coverage) -HAART confers many other benefits not captured in a CEA

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Kumaranyake, 2008	N/A	Meta-analysis of 34 costing studies and methodologies related to scaling-up; literature review	N/A	N/A	N/A	-Scale and volume are drivers in determining costs -Interventions with low fixed cost (VCT) are likely to show consistent economies of scale as volume grows -Interventions linked to health facilities are likely to face diseconomies of scale beyond a certain volume -There is a lack of data on scaling-up
Lacey et al., 1999a	Canada	Prospective CEA of ART, part of a dual-therapy RCT, 3rd party payer perspective, n=1840	1 year	-Direct medical care costs: drugs and visits (no lab costs and no outpatient visit costs)	-Reduction in care costs = $Can1,123 -$Can14,225 per disease progression/death avoided -$Can5,631 per HIV-related illness avoided	-Treatment that slows the progression of HIV can reduce monthly care costs for HIV patients and offset drug costs -It is possible to undertake economic evaluations as part of clinical trials
Lacey et al., 1999b	Germany, U.K.	Prospective CEA, part of a dual-therapy RCT, 3rd party payer perspective, n=1840	1 year	-Direct medical care costs: drugs and visits (no lab costs)	-DM22,405 per disease progression avoided and DM8,869 per HIV-related event avoided (Ger) in 1 yr -£12,030 per disease progression avoided and £4,762 per HIV-related event avoided (UK) in 1 yr	-Hospitalization costs decreased with the addition of the 2nd drug -Treatment that slows the progression of HIV can reduce monthly care costs for HIV patients and offset drug costs -It is possible to undertake economic evaluations as part of clinical trials
Lacey et al., 1999c	USA	Model RCT results from other countries using US healthcare cost data	1 year	-Direct medical care costs: drugs and visits (no lab costs and no outpatient visit costs)	-Decrease in care costs ranged from $1922 to $2645; yielding a savings (minus cost of additional drug) of between $371 and $353 in 1 yr	-Treatment that slows the progression of HIV can reduce monthly care costs for HIV patients and offset drug costs -It is possible to undertake economic evaluations as part of clinical trials

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Mauskopf et al., 1998	USA	CEA of dual ART v. monotherapy in a RCT; Markov transition model; payer perspective	Lifetime	-Costs were discounted 3% -Hellinger costs adjusted to 1995	-$12,603 per LYG -$18,006 per QALY -If ART initiated at >500: $10,063 per LYG and $13,821 per QALY	-Dual ART is cost-effective both in terms of quantitative and qualitative measurements -Quality of life should be included when considering the benefits of ART -ART is more cost-effective when started earlier
Miners et al., 2001	England	CEA of HAART v. dual ART using Markov model; public payer perspective; n=1000 (hypothetical)	20 yrs (hypothetical)	-Cost of dual therapy + community care costs + additional drug -Costs were discounted at 6% per year	-£14,602 per LYG -£17,698 per QALY saved	-Results were sensitive to the cost of drugs – lower cost drugs would improve the CER -HAART is moderately cost-effective compared with dual therapy
Moore & Bartlett, 1996	USA	CEA of HAART v. dual ART; Markov transition model; payer perspective	6 years	--Costs discounted 3% -Hellinger costs adjusted to 1996	-$10,000 per LYG	-HAART is cost-effective compared to dual therapy
Moore, 2000	High-income countries	Survey of CEA studies	N/A	N/A	-HAART studies reviewed demonstrated incremental costs of between $10,000 and $13,000 per LYG over dual therapy	-Further analyses examining indirect costs are needed -ART reduces costs associated with hospitalization and opportunistic infections
Nattrass & Geffen, 2005	South Africa	Revised CEA of HAART and HAART + prevention; public sector payer; ASSA2000 demographic model for population estimates	N/A	-Prevention costs: PMTCT, education, condoms, STD Rx and infrastructure -Treatment costs: ARV drugs and hospitalizations -Assumes 90% coverage	-Ave cost per infection averted dropped from R47,550 to R16,138 with lower drug prices -Ave total cost (direct + hosp) per infection averted in prev. only scenario = R165,495 and R101,280 for prevention + HAART	-Lower cost per infection averted in the new treatment plus prevention scenario argues for a comprehensive approach -ART prices constitute 90% of direct costs -Based on these assumptions a full-scale rollout would require between 0.9% and 2.6% of GDP

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Over et al., 2004	India	Model cost of 3 different approaches to treatment and prevention: VCT v. PMTCT+ v. HAART	Lifetime	-VCT: $100 per person including testing, education and condoms -PMTCT+: $500 per person for all infected pregnant women -HAART: $500 for all below poverty line -10% discount	-VCT: $146 per LYG -PMTCT+: $199 per LYG -HAART: $280 per LYG -HAART *plus* 70% condom usage: $51 per LYG	-HAART plus prevention can be cost effective -Did not take into account the costs associated with hospitalizations or additional outpatient visits
Over et al., 2007	Thailand	CEA of HAART; deterministic difference-equation model (economic and epidemiologic); public payer	20 years: 2006 – 2025	-Uses 2005 prices for visit costs (in/outpatient), drugs, labs, other consumables and health professional training	-$736 per LYG (1st line) -$2145 per LYG (1st and 2nd lines) -$940 per LYG (1st and 90% reduction in 2nd line cost)	-1st and 2nd line HAART would constitute 23% of the total Thai health budget by 2014 -Two-line therapy is affordable given Thailand's strong economic growth
Sax et al., 2005	USA	CEA of salvage HAART; state-transition model based on the short-term results of a RCT; payer perspective	Lifetime	-Direct costs only: Drugs (ARVs and OI Rx), labs, palliative care; no visit costs included -Costs and outcomes were discounted at 3% annually -Prices adjusted to 2001 dollars	-ICER = $69,500 per QALY	-Total lifetime cost of ENF+HAART = $205,900 v. $151,000 for salvage HAART alone -ENF+HAART added 11.1 months of life -CEA was sensitive to drug cost -Despite high cost, this may be worthwhile for patients with no other treatment options
Schackman et al., 2001	USA	CEA of earlier initiation of HAART (CD4=200 v. CD4=500); data derived from RCT; state-transition model; societal perspective(?)	5 years	-Costs and benefits discounted at 3% and costs were adjusted to 1998 USD$ -Direct costs: drugs (ART&OI Rx), labs	-$17,300 per QALY gained compared to no HAART -$16,500 per LYS	-Initiation at CD4=200 yielded 7.64 QALYs v. 8.21 QALYs at CD4=500 -Earlier initiation resulted in 51 fewer deaths per 1000 and 72 fewer opportunistic infections per 1000

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Sendi et al., 1999	Switzerland	CEA of HAART in 3 scenarios of disease history; societal and payer perspectives	Lifetime	-Costs expressed in 1997 CHF -Direct costs: drugs, interventions, visits (in/ outpatient); productivity (healthcare costs minus savings from reduced morbidity and mortality)	Payer: -CHF33,000 per LYG (base) -CHF14,000 per LYG (optimistic) -CHF45,000 per LYG (pessimistic) Societal (productivity): -Base and optimistic cases were cost saving; pessimistic case had a CER of CHF11,000.	-HAART increased patient survival and healthcare costs -When productivity gains are taken into account society will probably save money or pay a small premium
Tramarin et al., 2004	Italy	Cost analysis of HAART; prospective, observational case-control study of 2 cohorts pre-HAART (1994) and post-HAART (1998); pts matched according to CD4 count, clinical stage and age, payer perspective.	6 months after initiation of care	Costs included medicines, labs and diagnostics, in/outpatient care; costs initially expressed in Lira and then converted to Euros (1998)	Average annual direct medical cost: €15,390 pre-HAART and €11,465 post-HAART	-The advent of HAART means that the cost burden shifts from in/outpatient care costs to ARVs. -HAART improved patient QOL and survival, and resulted in fewer deaths, opportunistic infections and total disability days
Wolf et al., 2007	Organization of Eastern Caribbean States (9 countries), Barbados and Jamaica	CEA of HAART; state-transition model using regional data; 1st v. 1st and 2nd line regimens; -Public payer perspective	Lifetime	-Costs and outcomes were discounted by 3% annually -Costs converted to $US (2006) -Direct costs: drugs, labs, visits (in/outpatient)	-$690 per LYS (1st line only) -$10,960 per LYS (2 lines)	-1st line + cotrimoxazole added 8.16 years of life over 'do nothing' scenario and a lifetime cost of $5620 – considered *very* cost-effective -Mean survival increased to 9.20 years when a 2nd line was available Lifetime costs for 1st and 2nd line regimens - $17,020, deemed 'cost effective' -Cost and CEA was driven by expensive 2nd line

Author(s), year	Country/ies	Methods	Study Period	Costs included in the analysis	Cost per unit of effect / ICER	Other Findings
Wood et al., 2000	South Africa	Cost, CEA and impact analysis: demographic and epidemiologic modeling (Monte Carlo simulations); public payer perspective; 4 scenarios (varying levels of prophylaxis and HAART for 25% of infected pop)	5 years	-Costs converted to $US (2000) -Direct costs: drugs and health care expenditure (per person cost of ART / per person health expenditure)	-$15,000 per LYG for ART	-Limited use of ART could have an immediate positive impact on the South African epidemic -ART scenario constituted 12% of health care expenditure compared with <.001% for prophylaxis -ART added 3.1 years to life-expectancy and prevented 430,000 incident HIV cases during the 5 year period -Barriers to ART include insufficient health infrastructure and drug costs

Appendix II: Summary Table of ART program outcomes in low- and middle-income country literature

Author, year	Country	Methods	Study Period	Virologic / Immunologic Outcomes	Adherence & Retention Outcomes	Other Findings
Akileswaran et al., 2005	14 African Countries	Meta-analysis of HAART programs in 14 different African countries	N/A	-All studies reported an increase in mean and median CD4 -Median of 73% of patients VL<400 by study end. -5 studies measured resistance: weighted mean =10.1% of naïve pts	- High levels of treatment adherence -6 studies reported 68-99% of patients were drug adherent >95% of the time	-HAART can feasibly be implemented in resource-limited settings -Adherence comparable to industrialized countries -WHO scale-up guidelines are an appropriate framework for ART treatment
Baggaley et al., 2006	N/A	Compartmentalized deterministic model to assess impact of ART on HIV transmission in resource-poor settings	N/A	N/A	N/A	-ART is not an effective prevention intervention alone; behavior change is critical -Epidemics in sub-Saharan Africa are not amenable to control via treatment regardless of the extent of the rollout
Bekker et al., 2003	South Africa	Prospective analysis of patient performance on HAART; n=62	First 6 months on ART	-VL<400 = 100% (initial 16 patients) after 4 months of treatment	N/A	-A PHC can service approximately 250-300 stable ART patients with dedicated staff running a daily clinic for 4 hrs. -Initial patient results were very encouraging -Drugs and salaries drove program costs -The amount of time required for patient visits during the initiation phase was 6x higher than in the maintenance phase;
Bekker et al., 2006	South Africa	Prospective cohort study; n=1,139	October 2002 – September 2005 (36 months)	-Median VL<400 = 95%; median VL<50 = 82% -VL suppression sustained over 3 yr period; comparable to developed country results	-Retention: 90% (n = 1025)	-Single community-based clinic can provide ART care to >1000 patients - 63% of deaths occurred in first 3 mos (patients started ART late) -Challenge: physical space

Author, year	Country	Methods	Study Period	Virologic / Immunologic Outcomes	Adherence & Retention Outcomes	Other Findings
Coetzee et al., 2004	South Africa	Prospective cohort study; n=287	24 months	-84% VL<400 at 12 mos; 70% at 24 mos; -Median CD4 increase of 288	-Retention: 90% (n= 259)	-15% changed regimens by 24 mos -HAART feasible in resource-poor settings -Previous work by the authors in CPT suggested that median survival for patients w/CD4<50 would be <12 mos
Desclaux et al., 2003	Senegal	Observational study of access to ART in Senegal; n=400	N/A	N/A	N/A	-ART can be successfully rolled out in Africa -Heavily subsidized or free ART ensured access to ART
Farmer et al., 2001	Haiti	Observational study of a community-based provision of DOT-HAART; n=60	Not specified	N/A	N/A	-DOT-HAART is a viable option for ART provision in resource-poor settings
Galvao, 2002	Brazil	Policy analysis: review of Brazilian ART experience	N/A	N/A	N/A	-Local manufacturing and implementation of TRIPS enabled Brazil to provide free access to ART
Harries et al., 2001	Malawi	Policy position paper on ART provision in sub-Saharan Africa	N/A	N/A	N/A	-Integration of TB and HIV treatment services will serve the people better and prevent domination of ART services at the expense of other care and treatment.
Harries, Schouten & Libamba, 2006	Malawi	Policy analysis: report on ART provision in Malawi	Jan 2004 – Sept 2005 (21 months)	N/A	-Retention: 77% (n= ~23,000)	-Additional technology (VL; CD4) will prove problematic and strain capacity
Ivers, Kendrick & Doucette, 2005	N/A	Meta-analysis of 25 ART programs in resource-poor settings	N/A	-Proportion of patients w/suppressed VL at 6 mos = 70%; 12 mos = 57% -Median CD4 increase ranged from 74-288	N/A	-ART efficacy in resource-poor settings similar to those in developed countries -Free ART was associated with significantly higher probability of suppressed VL over those required to pay some/all of ART costs

Author, year	Country	Methods	Study Period	Virologic / Immunologic Outcomes	Adherence & Retention Outcomes	Other Findings
Jack et al., 2004	South Africa	Prospective pilot to integrate ART into urban TB(DOT) clinic program; 20 HIV-infected and TB+ patients	6 months	-80%(16) had VL<50 at 6 mos.	-Good adherence -2 patients developed resistance to ddI+3TC+EFV	-Feasible to integrate HIV treatment into a TB clinic setting with good results
Katzenstein, Laga & Moatti, 2003	Cote d'Ivoire; Senegal; Uganda	Overview of ART in resource-poor settings (drug access initiatives)	N/A	-Resistance found to be similar or lower than those found in the West	N/A	-ART is effective and can be delivered responsibly in African countries -Drug prices remain out of reach for most health systems
Kenyon et al., 2003	South Africa	Comment/opinion: rationing ART care and treatment	N/A	N/A	N/A	-Given high price of ART, rationing is inevitable if some are to have access to treatment -Ration according to: candidate characteristics (stage, disclosure, social circumstances; 1st line only; budgetary restraints
Kober & Van Damme, 2004	South Africa, Swaziland, Mozambique, Malawi	Policy analysis: interviews with policy leaders re: challenges associated with scaling up ART	N/A	N/A	N/A	-Biggest challenge is not money, but human resources in all four countries -None of the countries have a human resource plan to address this critical need -Donors need to focus attention and resources on human resource challenges
Landman et al., 2003	Senegal	Prospective open-label one-arm trial in 40 ART naïve patients	15 months	-95% VL<500 at 6 mos; 77% VL<50 at 12 mos, and 69% VL<50 at 15 mos.	-95% self-reported adherence (in prior 3 days)	-Results are at least as good as those from HAART studies in industrialized countries

Author, year	Country	Methods	Study Period	Virologic / Immunologic Outcomes	Adherence & Retention Outcomes	Other Findings
Laniece et al., 2003	Senegal	Prospective observational study of patient adherence in an ART pilot program; n=158	Nov 1999 – Oct 2001 (24 months)	N/A	-Self reported adherence = 91% in study period -100% adherence for 2/3 study -Adherence better in patients who contributed little/nothing to treatment costs; comparable adherence to developed countries	-Two factors influenced adherence: costs and regimen
Laurent et al., 2002	Senegal	Prospective observational cohort study; ART feasibility study; n=58	Mean follow-up was 19.5 months	-59% of patients had suppressed VL at 18 mos. -Median CD4 increase=180 after 18 mos -2 patients developed resistance	-88% were adherent >80% of the time -Adherence waned over time	-Comparable to results seen in the West despite different viral subtype and advanced patient disease -High mortality rate: 12%
Laurent et al., 2004	Cameroon	Prospective open-label, one-arm multicentre trial of generic fixed-dose combination ART; 60 patients	6 months	-80% VL<400 at 6 mos; -Median CD4 increase = 83 at 6 mos.	-99% self-reported adherence	-Fixed-dose generic regimen has a clear advantage: cheaper ($20/mo. *v*. $35) and fewer pills per day (2 *v*. 6)
Laurent et al., 2005	Cameroon	Retrospective chart review of 19 public and private ART program; n=788	October 2000 – October 2003; (median observation13 months)	-59% VL<50 and 73%VL<400 at ~12 mos; 47% VL<50 and 58%VL<400 at ~24 mos -Median CD4 increase =113 (12 mos) and 143 (24 mos)	-Retention: 68% (n= 536)	-Inconsistent dispensing and stock outs, lack of patient support and social workers and the expense of self-financed treatment resulted in poor retention -6.6% mortality and 25.1% lost-to-follow-up
Livesley & Chester, 2003	South Africa	Retrospective chart review of patients at a private primary care clinic in a rural area; n=72	March 1999 – January 2002 (34 months)	-32% achieved viral suppression	-Poor adherence: 58% of patients were <70% adherent according to drug pick-up date	-45% of patients were on mono or dual therapy -Follow-up data available for about half the sample -Poor results when ART is rolled out with inadequate support for providers and patients

Author, year	Country	Methods	Study Period	Virologic / Immunologic Outcomes	Adherence & Retention Outcomes	Other Findings
Macharia et al., 2003	Kenya	Chart review of 217 patients on HAART	Oct 1996 – June 2001 (44 months)	-59% VL<400 at 6 mos; 47% VL<400 at 12 mos; 32% VL<400 at 24 mos.	-Retention: 53% (n= 119)	-HAART can be effectively prescribed in the private sector in Kenya with similar results to those found in North America
Mukherjee et al., 2003	N/A	Comment/opinion: developing country needs for a sustained response	N/A	N/A	N/A	-Prevention and treatment necessary -integrate TB -Significant infrastructure and health system development required for sustained response -Sustained international funding
Mukherjee et al., 2006	Haiti	Observational study of an ART program in resource-poor setting	N/A	N/A	- Found low rates of death and treatment failure	-Fees waived for HIV, TB and antenatal care services -DOTs -Nutritional support -Psychosocial support by home-based care providers -First line regimen cost =$150pp/yr + care costs = $186pp/yr
Nattrass, 2006	South Africa	Policy analysis: assessment of rollout in South Africa	N/A	N/A	N/A	-Rollout has been uneven across the 9 provinces and slow relative to targets set by the National Strategic HIV Plan -Significant funds from PEPFAR and GFATM -DOH has failed to invest in human resources, particularly nurses
Ooms, Van Damme & Temmeran, 2007	N/A	Policy analysis: human resource needs in sub-Saharan African countries	N/A	N/A	N/A	-The Global Fund should use some of its money to support human resources as this will be the rate-limiting factor in scale-ups across the continent.

Author, year	Country	Methods	Study Period	Virologic / Immunologic Outcomes	Adherence & Retention Outcomes	Other Findings
Orrell et al., 2003	South Africa	Prospective adherence monitoring among patients in Phase III clinical trial; n=289	48 weeks	-71% VL<400 at 12 months	-Retention: 84% (n= 242) -Median/mean adherence = 93.5% at study end	-English-speaking, complex regimens (3x daily) and age were associated with incomplete adherence -Socio-economic status did not predict adherence -Adherence levels comparable to developed countries
Phanuphak, 2004	Thailand	Policy analysis: lessons learned from Thailand	N/A	N/A	N/A	-Activist and academic communities don't always have to wait for governments to start treatment programs -Political commitment is important to a sustained public sector response -Combination of generic drug production and negotiated pricing lowered drug prices
Rosen, Fox & Gill, 2007	Sub-Saharan Africa	Meta-analysis of ART programs in SSA; 33 cohorts included 74,192 patients in 13 countries.	N/A	N/A	-ART programs retained ~60% of patients after 24 mos; ~75% after 12 mos -Retention varied widely between cohorts	-Better training, tracing lost patients and earlier initiation of ART will improve retention
Severe et al., 2005	Haiti	Prospective cohort study, n= 1004	March 2003 – April 2004 (14 months)	-76% VL<400 at 12 months (subset n= 100) -Median CD4 increase = 163 at 12 mos	-Retention: 80% (n= 800)	-12% of study adult study patients also received concurrent TB treatment -87% one year survival among adults and 98% in children -Inconsistent drug supply resulted in regimen change for 7% of study patients
Stringer et al., 2006	Zambia	Open, prospective cohort study of urban ART rollout in 18 primary healthcare facilities; n=16,198	April 2004 – November 2005 (19 months)	-Mean CD4 increase = 175 at 12 mos (n= 1361)	-Retention: 72% (n= 11,663) -Adherence = 100% in 32% (n= 5215) of patients	-Rapid, large scale-up of ART w/good clinical outcomes is feasible in sub-Saharan Africa -Comparable clinical outcomes to developed country programs

Author, year	Country	Methods	Study Period	Virologic / Immunologic Outcomes	Adherence & Retention Outcomes	Other Findings
Tassie et al., 2003	South Africa	Observational study of ART provision in resource-poor setting; n=743	6 months	-VL<400 = 89.8% suppressed at 6 mos (n=118) -Mean CD4 increase of 104 at 6 mos (n=118)	N/A	-Mean time on ART = 4 mos -Survival probability at 6 mos = 89.5% -HAART is successful in resource-poor settings
Teixeira, Vitoria & Barcarolo, 2004	Brazil	Policy analysis: review of Brazilian ART program	N/A	N/A	N/A	-Government commitment to provide free ART resulted in dramatic decreases in patient morbidity and mortality -Treatment is cost-effective
Walensky et al., 2008	South Africa	Modeling of rates of scale-up (zero v. constant v moderate v rapid v full capacity) and predicted outcomes	N/A	N/A	N/A	-More rapid scale up is important to avert 1.2 million deaths by 2012 -Zero or constant scale up met only 28% and 52% of need respectively -Rapid and moderate scale up met 100% and 97% of need respectively
Weidle et al., 2002	Uganda	Retrospective assessment of ART pilot program; chart and lab data reviews; n=476	August 1998 – July 2000 (23 months)	-Mean CD4 increase = approximately 75 at 1 year (subset HAART patients n=67) -40% VL<400 at 1 year (subset HAART patients n=67) -Resistance to at least 1 drug in 65% (n=61) of patients	-88% adherence among patient subset (221) -52%(248) still on ART at study end	-Virologic/immunologic responses comparable to results from developed countries -Challenges: dual therapy; late start on treatment -ART can be effective in African setting
Wilson & Blower, 2005	South Africa	Mathematical model for equitable allocation of ARVs in KwaZulu-Natal	N/A	N/A	N/A	-Increase health care facility catchment areas -Optimize equity by rolling out to 54 facilities

Chapter 3

Background: Care and Treatment Models

3.1 Introduction

This chapter provides an overview of the two treatment models examined in this study. Because this research examines the costs and outcomes associated with two different models of care for down-referred patients, a complete understanding of down-referral and model operations is critical to understanding the study design, methods and results. This chapter opens with a summary of the South African National ART Program guidelines and the role of down-referral in the ART program. It then describes the design and operations of the public-private partnership (PPP) model and concludes with an overview of the public sector HIV patient management model at the primary healthcare clinics (PHCs).

The information in this chapter is derived from key program documents and interviews with individuals who play key roles within each of the stakeholders. Appendix I at the end of the chapter lists key documents and interview sources.

3.2 Overview: South African National ART Program

The South African National Antiretroviral Treatment Guidelines (National Department of Health, 2004) were first published to coincide with the launch of the public sector ART program in April, 2004. The guidelines cover HIV diagnosis, eligibility criteria, treatment regimens, dosing, laboratory monitoring, and management of adverse drug events, adherence and post-exposure prophylaxis. Both models adhere to the national care, treatment and laboratory testing guidelines.

In the public health sector, ART initiation sites (initially just hospitals) were selected and accredited by the Department of Health. Accredited hospitals are charged with initiating and stabilizing patients on ART, and once patients achieve viral suppression and are clinically well, the responsibility for routine care is transferred (henceforth referred to as "down-referral") to the local PHC or next lower level of care. In this study, all patients were started on treatment at Tshepong Hospital in Klerksdorp, which was the only accredited ART initiation site in Matlosana sub-District at the time of writing. Pre-ART and ART outpatient visits take place at the outpatient HIV clinic (Wellness Clinic). ART visits are scheduled at the Wellness Clinic until the patient is down-referred to their local PHC or to the PPP.

3.2.1 Down-referral

The practice of down-referral in the public sector HIV care and treatment program serves mutually reinforcing clinical and operational aims. From the patient perspective, down-referral ensures that routine HIV care is (typically) closer to the patient's place of residence, and integrated with all other primary care services, making it cheaper (lower out-of-pocket travel costs) and more convenient. From a health system perspective, down-referral constitutes a form of task-shifting, where the responsibility for routine care and support for (virally) suppressed and clinically well patients is delegated to nurses from doctors who are a more scarce resource. This saves money (nurses are paid less than doctors) and permits doctors to focus on ART initiation for new patients and management of complicated cases, and minimizes congestion at the hospital-based outpatient clinic. The operational and clinical goals of down-referral are to maintain patient health (viral suppression, immune functioning, and an absence of opportunistic infections), and to maintain patient care at the down-referral site.

Table 3.1 Down-referral eligibility criteria

- Suppressed viral load (<400 copies/µl)
- Absence of clinical signs and symptoms of disease
- On ART > 6 months
- Psychosocial assessment completed

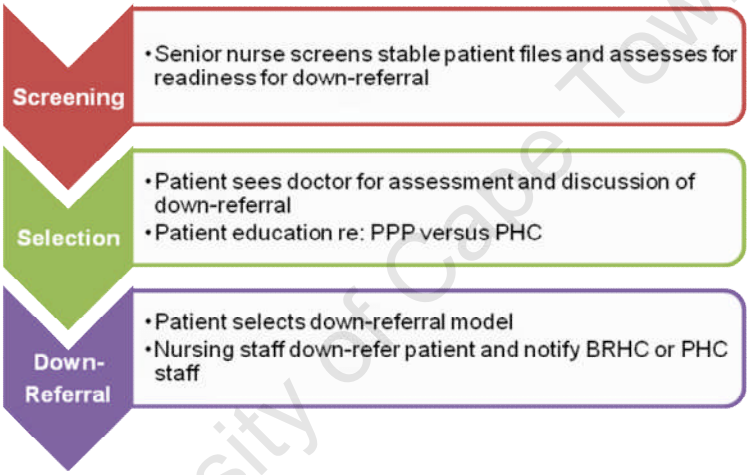
Table 3.1 summarizes the down-referral criteria used at the Wellness Clinic. Patients are considered for down-referral after spending a minimum of six months on ART, show no clinical signs or symptoms of opportunistic infections, and have achieved viral suppression (<400 copies/µl). Patients are also subject to a psychosocial assessment in order to ensure that the change in care will not endanger ART adherence and patient health.

At Wellness, the down-referral process begins with routine screening of patient files by a senior nurse to identify eligible patients (Figure 3.1). At the next visit, screened patients attend a pre-down-referral education session. A Wellness Clinic nurse and the BRHC Regional Coordinator conduct education sessions either individually or in small groups on a daily basis[8]. Following the education session, patients see the down-referral doctor (certain doctors are specifically tasked with down-referral at Wellness)

[8] The BRHC Regional Coordinator manages the day-to-day of the PPP, and is located at the Wellness Clinic. The role of the regional coordinator is discussed in greater detail in section 3.3.5.

who – following a clinical exam - confirms eligibility and discusses the patient's choice of down-referral care model. The patient and his/her file are then passed on to a clinic nurse to start the down-referral process. If the patient selects the PHC, the nurse completes a transfer form and schedules the first appointment at the PHC closest to the patient's residence for approximately one month later. If the patient selects the PPP, the patient meets one-on-one with the BRHC Regional Coordinator. During this meeting, the patient goes through the process of giving consent for participation, selects their GP (subject to availability) and the Regional Coordinator schedules the first appointment for the following month.

Figure 3.1 The down-referral process



3.2.2 Up-referral

"Up-referral" is the process of sending a patient back to the initiating site (in this case it is the Wellness Clinic) for care and treatment services that are not offered at the down-referral site. Common reasons for up-referral include HIV-disease complications, adverse drug events and non-adherence. For HIV-related complications, patients may be up-referred to the outpatient HIV clinic or to Tshepong Hospital for problems requiring inpatient care. The objective of up-referral is to stabilize the patient as quickly as possible and then return him/her to their down-referral care site for continued care. It is important to note that patients can be up-referred and down-referred multiple times. The criteria for up-referral of patients with HIV-related complications are the same for both the PPP and PHC models.

3.3 Public-private partnership model

3.3.1 Program goal

The goal of the PPP is to provide immediate additional capacity in Matlosana for routine HIV care and treatment in the short to medium term by leveraging existing private sector capacity (i.e., GPs).

3.3.2 Concept and implementation

In mid-2005, the Deputy Director General (DDG) of the North West Department of Health, the Tshepong Hospital Complex CEO, and the Principal Specialist and Head of Internal Medicine began discussions with a local general practitioners (GPs) network and BRHC (an HIV/AIDS NGO funded by PEPFAR) in order to increase HIV treatment capacity in the primary care clinics. On November 21, 2005 the memorandum of agreement was signed between the three partners, and one week later on November 28 the first patient was enrolled in the PPP model.

Originally the PPP was designed to provide comprehensive care services (in addition to HIV care), but it was later decided that it would focus on HIV/AIDS care at the outset, leaving the option open regarding model expansion to include comprehensive patient care. At the time of writing, the program remained focused uniquely on HIV care and treatment and no discussions about expanding the scope of care had taken place. Moreover, there has been no discussion about how or when the partnership might end or managing patient reintegration into the public health system.

3.3.3 PPP model rationale and overview

Approximately 50 percent of the health care capacity in South Africa exists in the private sector (and some estimates indicate that 75 percent of all doctors in South Africa are in the private sector), though it provides care to less than 20% of the population. Meanwhile the public sector serves more than 80% of the population with approximately the same amount of resources (Wilson & Fairall, 2008). And the health professional imbalance seems to be worsening: between 1989 and 2007 the percentage of nurses in the public sector decreased from 79 percent to 42 percent, and the percentage of doctors in the public sector decreased from 38 percent to 30 percent (Kapp, 2009). As an emergency intervention to assist the public sector in coping with the overwhelming

demand, the PPP utilizes private sector GPs as down-referral sites (in addition to the public sector primary healthcare clinics) to provide ongoing HIV care and support to public sector patients. The model was designed to provide HIV care and treatment services in Matlosana until the public sector builds sufficient capacity to meet the demand for treatment and re-absorb all of the PPP patients, or until PEPFAR funding expires in 2013. The program operates in accordance with all South African Government (SAG) Department of Health rules and guidelines for managing patients on ART. There is no difference in the essential ART program services (i.e. visits, drugs, laboratory tests) between in the PPP and PHC models.

3.3.4 PPP Stakeholders

The principal stakeholders in the PPP down-referral model include the Department of Health, North West Province / Tshepong Hospital Complex, BRHC, and the KOSHMED Doctors Network. BRHC was charged with overall program coordination, paying the salaries of the GPs, program monitoring and evaluation (including GP performance and patient progress), GP and patient training; and reporting to the Department of Health, the hospital, and to PEPFAR. The 19 KOSHMED doctors provide monthly HIV care and clinical monitoring of patients, monthly prescriptions, refer patients to the hospital for any complications, complete clinical forms, and supply ARVs to their patients. Tshepong Hospital initiates patients on ART and down-refers them once they are stable to the GPs. Tshepong also provides care for patients referred for any complications, opportunistic infections, antenatal care and regimen changes. Finally, Tshepong pharmacy procures and distributes all patient medications to the GP offices for patient collection, and the National Health and Laboratory Services provides laboratory services. Table 3.2 provides a summary of services by stakeholder.

Table 3.2 Summary of stakeholders and roles

Stakeholder	Role in the Public-private partnership (PPP)
North West Province Department of Health	▪ Model oversight
Tshepong Hospital/Wellness Centre (Department of Health)	▪ ART Initiation ▪ Management of complications and severe OIs ▪ Provide all drugs and labs
KOSHMED Network	▪ Routine patient management (monthly) ▪ Referrals to Tshepong/Wellness
BroadReach Healthcare	▪ Finance patient visits to GPs ▪ Monitoring, Evaluation and Reporting ▪ GP Training and Support ▪ Data Management

Department of Health, North West Province

The Department of Health (DOH) in North West Province is the provincial steward of the national ART program. In November 2005, the DOH signed a "Memorandum of Agreement" with BRHC to create a PPP with the goal of providing additional capacity in Matlosana sub-district to maintain patients on ART.

Tshepong Hospital, Klerksdorp, North West Province

The Klerksdorp/Tshepong Hospital Wellness ART Clinic was one of the first accredited ARV treatment sites in North West Province, and at the time of writing remained the only accredited site in the Matlosana Sub-district. The Wellness Clinic is an outpatient HIV clinic on the grounds of Tshepong Hospital where all patients are initiated or stabilized (if they relocate to Matlosana already on ART) on ART prior to being down-referred for ongoing care and treatment. HIV-infected patients who are not yet on ART also attend the clinic. The Wellness Clinic began initiating HIV-infected patients on ART on April 1, 2004. The first patient was down-referred to the PPP on November 28, 2005.

KOSHMED General Practitioner Network, North West Province

The KOSHMED Network was founded in 1995 and consists of 24 private sector GPs who have offices/surgeries in the Klerksdorp, Orkney, Stilfontein and Haartebeesfontein (KOSH) areas in Matlosana. The Network was formed in order to negotiate collectively with the government on issues that concern private practitioners (Khunou, 2008), and is governed by a Board elected from its membership. KOSHMED entered into a contract directly with BroadReach Healthcare, and is not a signatory of the provincial memorandum of agreement. Participation in the PPP is optional for KOSHMED members, and by March 31, 2008, 19 KOSHMED GPs were actively participating in the PPP down-referral model. Table 3 details the distribution and locations of GPs participating in the PPP.

BroadReach Healthcare, Cape Town, Western Cape Province

Founded in 2003, BroadReach Healthcare LLC is a healthcare solutions company that works to expand access to high quality healthcare services across the globe (BroadReach, 2009). The Company focuses on developing new, healthcare financing and delivery systems at scale, with a view to creating new sustainable healthcare markets for its clients and stakeholders.

BRHC is headquartered in Washington, D.C., with additional offices in Johannesburg and Cape Town, South Africa. The non-profit South Africa program started operations in October 2004, employs approximately 100 staff across two principal initiatives: public sector HIV care and treatment capacity building, and direct treatment programs that leverage existing capacity within the private sector to treat traditionally public sector patients (including the PPP model). BRHC HIV/AIDS initiatives in South Africa are funded through a renewable five-year grant from PEPFAR.

Aid for AIDS (AfA), Cape Town, Western Cape Province

AfA is an HIV disease management company based in Cape Town. BRHC contracted AfA to provide data management services for the PPP, as well as its other direct treatment programs. AfA services include data capture and reporting, and maintenance of an electronic medical record for all patients. At the time of writing the system managed over 30,000 HIV-positive patients, with over 16,000 on ART.

PEPFAR

The United States' President's Emergency Plan for AIDS Relief (PEPFAR) was launched in October 2004 in order to provide funding for HIV prevention, care and treatment in 15 heavily affected countries with the goal of preventing 7 million infections, treating 2 million people and providing care to 10 million HIV-infected individuals (PEPFAR, 2009a). Table 3.4 lists the 15 PEPFAR focus countries. Originally conceived as a five-year, $15 billion program, PEPFAR had dispensed a total of $18.8 billion by the end of the 2007/08 fiscal year. In July 2008 President Bush signed into law the PEPFAR reauthorization act (H.R. 5501), extending PEPFAR through 2013 and allocating up to $48 billion to the program. PEPFAR is managed by the Office of the Global AIDS Coordinator who reports directly to the Secretary of State of the United States. PEPFAR funds are disbursed via three principal U.S. government agencies: the United States Agency for International Development (USAID), the Centers for Disease Control and Prevention and the Department of Defense. PEPFAR funds for the PPP are administered by USAID.

Table 3.4 15 PEPFAR Focus Countries

Botswana	Nigeria
Côte d'Ivoire	Rwanda
Ethiopia	**South Africa**
Ghana	Tanzania
Haiti	Uganda
Malawi	Vietnam
Mozambique	Zambia
Namibia	

Between 2004 and 2008 South Africa received nearly $1.5 billion from PEPFAR and was the largest beneficiary among the focus countries (PEPFAR, 2009). Within South Africa, BRHC is one of the five largest PEPFAR treatment partners, with a total annual budget of approximately $20 million for all of its HIV-related activities in South Africa.

3.3.5 PPP: management and operations

At Tshepong Hospital, the Principal Specialist and Head of Internal Medicine of the hospital is responsible for the overall program and is the key hospital point person in the PPP, although he is not involved in the day-to-day. Limited oversight is provided by the hospital CEO, and the provincial Department of Health. Within BRHC, the Regional Coordinator is responsible for the day-to-day program operations, and manages everything from patient down-referral from the Wellness Clinic, to ongoing monitoring of patients and the GPs. The Regional Coordinator's office is located in the Wellness Clinic. The Regional Coordinator reports to the Operations Manager who oversees all BRHC treatment initiatives. BRHC also has a monitoring, evaluation and reporting team that collects data, highlights gaps in data collection and issues reports to GPs, hospital management and BRHC management located in Cape Town. Finally, BRHC provides clinical monitoring and support to GPs through its clinical manager. The clinical manager reviews clinical data, supports GP decision making if necessary (second opinion), and makes recommendations for clinical program improvement.

There is no overall governance mechanism or coordinator for the PPP. Meetings are held with leadership from each of the three partners on an ad hoc basis. It is also notable that while the PPP was designed as an interim solution to provide additional capacity, to date there have been no discussions within the partnership about plans for reintegrating patients into the public sector, or when this might occur. For now, financing

for the PPP appears to be secure through 2013 when the current PEPFAR law is set to expire.

3.3.6 Program Operations and Patient Flow

GP Preparation and Management

KOSHMED GPs enrolled in the PPP were required to complete a credentials check, attend HIV/AIDS clinical training, and training on South African ART guidelines. The BRHC Regional Coordinator tracks GP capacity in order to manage patient load. The BRHC Clinical Manager is responsible for providing oversight and support to participating GPs. All GPs are paid on a per patient visit basis based on a negotiated rate agreed to by the Provincial Department of Health, BRHC and KOSHMED. Because GPs are responsible only for ART management, the negotiated fee is below the standard private sector GP fee. At the time of writing, the GPs received R90 per patient visit, and the average visit lasted between 8 – 10 minutes.

Enrolling Patients

Once patients elect to receive care through the PPP and complete patient education, a referral document (down-referral form) is completed by the doctor that contains relevant information about the patient, their ART regimen and recent laboratory results. The patient is then instructed to take the form and visit the BRHC Regional Coordinator who is located at Tshepong Hospital for a detailed orientation to the program, selection of the GP and scheduling of the first appointment.

Drug and Laboratory Logistics

Once a patient has been down referred to a GP for care, the Regional Coordinator informs the hospital pharmacy of the new GP. The hospital pharmacy then arranges for a courier service to deliver the medicines; a30-day supply of drugs is dispensed on a 28-day cycle. On a weekly basis, a courier service drops off medicines for patients who are due for appointments the following week, picks up new prescriptions, and retrieves any uncollected medications for return to the pharmacy.

South African treatment guidelines require that all patients receive six monthly laboratory monitoring, including a CD4 and Viral load test and any other regimen-specific investigations. Patients in the PPP model are reminded in the month prior to

scheduled laboratory tests that they need to visit the Wellness Centre at Tshepong for their blood draw by their doctor, and they receive a red reminder notice in their packet of medicine. This visit is exclusively for a blood draw, and the patient does not see a nurse or doctor. Laboratory results for BRHC patients are filed by a laboratory technician for pick up by the Regional Coordinator. The Regional Coordinator picks up results every Friday, and faxes copies to the data managers for inclusion in the database, as well as to the patients' GP. The laboratory results should be available by the time of the patient visit in month seven (the month following the blood draw). The Regional Coordinator, GP and/or the BRHC Clinical Manager flag all abnormal or missing results for intervention.

Missed Drug Pick-Up

A patient that misses his/her scheduled drug pick-up day has a one-week grace period. A missed drug pick-up is often called "defaulting." If a week elapses beyond the scheduled drug pick-up, then the doctor completes a new prescription for the patient indicating they have uncollected medication. This information is sent to the database (via fax) and to the pharmacy, resulting in suspension of drug dispensing, and a status change for the patient to "suspended" (see next section on Monitoring and Evaluation). The patient is then tracked by the Regional Coordinator, and, pending the outcome of the investigation, may engage the Wellness Centre program manager, the GP, and/or the BRHC Clinical Manager.

Monitoring, Evaluation and Reporting

BRHC has a department dedicated to monitoring and evaluation for all of its treatment models and capacity building initiatives, including the PPP down-referral model. Data are collected from Tshepong Hospital, the National Health Laboratory Service and the GPs in order to monitor individual patients as well as overall program performance. Table 5 lists the key indicators/data that are collected. Data are collected from various sources including the patient enrollment, monthly prescription and clinical forms, and laboratory reports; which are then collated in the AfA database in Cape Town. Data are reported in a series of program management reports used by the GP, BRHC and Tshepong/Wellness Clinic to monitor patient and program progress. Program Management reports are produced monthly, while PEPFAR, GP and Tshepong/Wellness Clinic reports are disseminated quarterly.

Table 3.5 List of PPP Down-Referral Program Primary Data

CD4 (all values since enrollment)
VL (all values since enrollment)
Date of patient appointment and drug pick up
Date of ART initiation
ART regimen (including regimen history)
Date of death or other end date

Up-referrals

Because the PPP down-referral program does not provide comprehensive patient care, patients are referred back to Tshepong/Wellness for all non-HIV care and HIV-related complications and regimen switches. GPs are only paid to perform routine monitoring and clinical evaluations in this program and all other problems are dealt with by the Wellness Clinic or hospital. Women who become pregnant while on the program are referred back to the hospital for antenatal care and delivery. Once the baby is born, the mother has the option to return to the GP or stay in the public sector and attend their local PHC.

Patients with serious adverse events or opportunistic infections are referred back to the hospital for emergency care. In addition, patients known to be failing a regimen (persistent unsuppressed viral load) and/or requiring a regimen switch are also transferred back to Tshepong/Wellness Clinic. Finally, a patient who is dissatisfied with the program can request to be transferred back to public sector care. In all of the above cases, ART care is transferred back to Tshepong/Wellness Clinic. Once problems are resolved, patients have the option of returning to their GP, or to leave the PPP for their local PHC.

Patients may also be temporarily transferred back to Tshepong/Wellness Clinic for a minor, non-HIV related health issue or problem. Patients who have been temporarily transferred would continue to pick up their medications and attend their monthly GP visit as part of the PPP down-referral program.

3.4 Design and Operations of the Primary Healthcare Clinic down-referral model

Responsibility for public sector healthcare operations in South Africa is divided between the Department of Health (DOH), which is responsible for the hospitals, and the

Department of Local Government (DLG), which is responsible for all community and primary healthcare clinics.

3.4.1 Key Staff

The Principal Specialist and Head of Internal Medicine at Tshepong Hospital and the ART Programme Manager at the Wellness Clinic provide oversight and coordination of the ART program in Matlosana. The DOH leadership at the hospital and Wellness Clinic liaise with their colleagues in the Health Office within the DLG. There are no ART program-specific managers at any of the clinics in Matlosana; the counselors, doctors, nurses and other staff, implement all program operations.

3.4.2 Program Operations and Patient Flow

ARV Treatment in Matlosana is carried out at Tshepong Hospital, the Wellness Clinic (at Tshepong), Klerksdorp Hospital (maternity and pediatrics) and 13 clinics (three of the clinics do not take ART patients). In total, the hospital and its clinics serve a catchment population of approximately 313,409 people. Nine of the sixteen sub-district clinics were included in this study, and are bolded in Table 3.6.

Table 3.6 Matlosana sub-District clinics, catchment population and staffing

Area / Facility	Catchment Pop.	Staff	% fully staffed
Klerksdorp:			
Park Street Clinic	22,387	7	77.8%
Alabama Clinic	16,977	6	66.7%
NM Pretorius Gateway Clinic	12,218	5	100.0%
Empilisweni Clinic	24,342	5	62.5%
Tsholofelo Clinic	11,128	5	83.3%
Jouberton Clinic	29,779	16	80.0%
Orkney:			
Orkney Clinic	11,068	4	66.7%
Kanana Clinic	13,473	5	83.3%
Majara Sephaphu Clinic	0	4	100.0%
Grace Mokgomo Clinic	41,663	14	77.8%
Stilfontein:			
Stilfontein Clinic	15,307	5	83.3%
Marcus Zenzile Clinic	17,200	4	66.7%
Khuma Clinic	27,346	5	100.0%
Botshabelo Clinic	30,215	13	86.7%
Hartbeesfontein:			
Tigane Clinic	14,539	13	108.3%
Delekile Khoza Clinic	11,087	4	100.0%
Mobile Clinics	14,680	5	100.0%
TOTALS	**313,409**	**120**	**83.3%**

As previously discussed, the site functions using a "hub and spoke" model where the Wellness Clinic acts as the hub, initiating patients and managing complex cases up-referred from the clinics. Patients typically attend the clinic that is nearest to their home, though they are permitted to attend other clinics in the sub-district if they choose[9]. Once a patient elects to receive care at their local PHC and completes patient education, a referral document (down-referral form) is completed by the nurse that contains relevant information about the patient, their ART regimen and recent laboratory results. The nurse then calls the PHC and schedules a patient visit for the next month. Upon arrival at the PHC, a new patient file is opened (down-referred patients therefore have files at the hospital outpatient clinic as well as at the PHC).

[9] This information was provided by Dr. Sarmiento, head of down-referral at the Tshepong Hospital Wellness Clinic, during an interview about down-referral operations in Matlosana with the author on March 6, 2008.

Drug and Laboratory test Logistics

South African treatment guidelines require that all patients receive six monthly laboratory monitoring, including a CD4 and viral load test and any other regimen-specific investigations. Patients have their blood drawn at the hospital outpatient clinic in month five, and then receive their results when they see the doctor for their six-month visit. Doctors rotate through the clinics and most clinics have a doctor one or two days per week.

Once a patient has been down referred to a PHC for care, the nurse informs the hospital pharmacy of the patient's PHC. ARVs, along with all other medicines are delivered weekly to all clinics; a 30-day supply of drugs is dispensed on a 28-day cycle.

Missed Drug Pick-Up

There is no standard protocol for dealing with patients who miss drug pick-ups across clinics. In some clinics staff call patients to remind them to pick-up their drugs. Some clinics have partnered with local non-governmental organizations (NGOs) that provide home-based care and can follow-up with patients where they live. The NGO then feeds back information to the nurses at the clinic. Recently (post-study period) a partner NGO provided a full-time defaulter tracer to assist PHCs.

Monitoring, Evaluation and Reporting

The number of ART patients in care and the number of deaths are reported to the DOH (via Wellness) by each clinic on a monthly basis. The Wellness Clinic has data clerks who collect and collate patient data from the clinics, and report to DOH. Clinics receive a list of patients down-referred from Wellness every month. No summary or operational data are provided by DOH, and operational data are not systematically used to manage the patients or the program.

Up-referrals

Patients with adverse events or opportunistic infections are referred back to the hospital or Wellness Clinic for care. In addition, patients known to be failing a regimen (persistent unsuppressed viral load) and/or requiring a regimen switch are also transferred back to Tshepong/Wellness Clinic. Women who become pregnant while on the program are referred back to the hospital for antenatal care and delivery. Once the

baby is born, the mother has the option to return to the PHC or may switch to the PPP model and see a GP. Once problems are resolved or the pregnancy is over, patients have the option of returning to their PHC or may switch to the PPP model and see a GP.

Patients may also be temporarily transferred back to Tshepong/Wellness Clinic for a minor health issue or problem. Patients who have been temporarily transferred would continue to pick up their medications and attend their monthly clinic visit. Reasons for HIV-related up-referral (as well as pregnancy) are extremely similar across both models of care.

3.4.3 Summary and conclusion

The PHC down-referral model is the status quo model of care in this comparison. Both the PHC and the PPP models access ARVs and laboratory testing through the government, and patients are required to visit the clinic or GP every month for a check-up and to pick-up medicine. All patients have laboratory monitoring every six months at the Wellness Clinic, and the management of complications and regimen switches require up-referral to Wellness Clinic in both PPP and PHC cohorts.

There are several noteworthy operational differences between the two models. First, the PHC model relies primarily on nurse-centered care for down-referred patients, while routine care in the PPP model is provided by GPs. Second, there is systematic use of patient and operational data in the PPP model in order to improve program operations and address problems. Data usage is facilitated by a sophisticated data management system and routine reports produced by BRHC that detail patient outcomes, GP performance (e.g. percentage of patients retained on ART), and operational problems (e.g. GPs who have failed to put women of child-bearing age on regimen 1b). Reports are circulated to upper and mid-level managers, as well as GPs on a routine basis for analysis. The PPP data management system also undergoes regular data quality audits to ensure sensitivity, specificity, integrity, reliability, and timeliness.

In contrast, the PHC model does not have the benefit of an advanced data management system, and there was no data management plan at the time of data collection for this study. While data are routinely used for individual patient management, they are not routinely or systematically collected and used for the purpose of program improvement by clinic managers. PHCs routinely submit reports to

the district that contain the number of patients in care at the site, but they do not receive any reports back regarding their performance or trends in the sub-District. In fact, they don't always receive notification of which patients are being down-referred so they can anticipate their arrival. All PHCs employ paper-based data management systems; only one clinic enters data into a computer that is owned by the head nurse.

The ability to track patients who have failed to pick-up their medicines on time is closely linked to data management and the PPP model employs a formal system for tracking of defaulters that includes operational protocols for patient follow-up in cases of a missed drug pick-up and reporting of patient outcomes, and has staff whose responsibility it is to track patients. In the PHC model, patient tracking is not systematized or consistent; all clinics are expected to track patients but the methods for doing so varies by clinic as previously described. The inability to make direct calls from the clinics and outdated patient contact information hindered tracking efforts in the PHCs. A lack of staff for which patient tracking was an official responsibility likely influenced the effectiveness of patient tracking in the PHC model.

Finally, from a systems and operational perspective it is worth noting that HIV care and treatment in the PHC model is nested in the clinics alongside the other primary care services that a patient might need. In contrast, the PPP model provides only HIV care and treatment; patients with non-HIV health problems either have to pay out-of-pocket at the GP or attend their local PHC. This analysis attempts to reveal some of the ways in which these operational differences play out in terms of patient outcomes in each cohort.

Appendix I: Document and interview sources

The following documents were collected and used as source information by the author in understanding model operations and drafting this chapter:

- *The South African National Antiretroviral Treatment Guidelines, 2004*
- *The BRHC Operations Process Flow for the GP Down-Referral HIV Treatment Model*
- *The Klerksdorp/Tshepong Hospital Comprehensive HIV and AIDS Care, Management and Treatment Down- Referral Plan (dated 20 October 2007)*
- *The BRHC Monitoring and Evaluation Plan*
- *Department of Health, North West Province and BRHC Memorandum of Understanding*

Interviews covering the history of the models, model operations, and program data used in the analysis described in Chapter 4, Methods, as well as thoughts and opinions about the two models were conducted with the following individuals:

BRHC:

- Dr. John Sargent, President, BRHC
- Ms. Wendy Townsend, Deputy Country Director, BRHC
- Mr. Jaco van Tonder, Finance Manager, BRHC
- Ms. Madeleine Feinberg, Monitoring and Evaluation Manager, BRHC
- Dr. Joyce Malaka, Clinical Manager, BRHC
- Mr. Holiness Thebyane, Regional Coordinator, BRHC

North West Department of Health/Local Government:

- Dr. Ebrahim Variava, Principal Specialist and Head of Internal Medicine, Tshepong Hospital
- Ms. Kathy Randeree, CEO, Klerksdorp/Tshepong Hospital Complex
- Mr. Johan Drotskie, CFO, Klerksdorp/Tshepong Hospital Complex

- Ms Erna du Plessis, Laboratory Manager, Klerksdorp/Tshepong Hospital Complex
- Ms. Keitumetse Mlambo, Program Manager, Wellness Clinic
- Dr. Sarmiento, Principal Medical Officer, Wellness Clinic
- Dr. Gomez, Medical Officer, Wellness Clinic
- Sister Lebeko, Nurse Manager, Wellness Clinic
- Ms. Meriam Machwisa, Data Clerk, Wellness Clinic
- Ms. Eunice Abrams, Health Director, Department of Local Government
- Sister Seetha, Professional Nurse, Tigane Clinic
- Sister Kgwete, Senior Professional Nurse, Jouberton Clinic
- Sister Jas, Senior Professional Nurse, Khuma Clinic
- Sister Mokhele, Professional Nurse, Grace Mokgomo Clinic
- Sister Kgaje, Senior Professional Nurse, Gateway Clinic
- Sister Appels, Senior Professional Nurse, Alabama Clinic
- Sister Viljoen, Senior Professional Nurse, Park Street Clinic
- Sister Lebone, Senior Professional Nurse, Tsholofelo Clinic
- Sister Mohonono, Professional Nurse, Empilisweni Clinic

KOSHMED:

- Dr. Khunou, President, KOSHMED Network
- Dr. Leburu, Member, KOSHMED Network

Chapter 4

Methodology

4.1 Study design

This study is a retrospective cost-effectiveness analysis (CEA) comparing a novel PPP for HIV care and treatment maintenance with the status quo PHC model in South Africa from the payer/government perspective. Two samples of patients, one from the list of eligible PHC patients and the other from the list of PPP patients, were drawn in line with a matching algorithm to ensure that the two samples were similar in terms of age, gender, time on ART and time since down-referral. The process resulted in a study population comprising 229 patients from the PHC model and 228 patients from the PPP model. Model performance comparisons were based on costs, patient outcomes, and cost-effectiveness ratios. The counterfactual (how would patients have fared in the absence of the PPP model) is also explored.

4.1.1 Ethics Approval

Ethical approvals were obtained from the Ethics Committee of the Centre for Social Science Research at the University of Cape Town, and the Ethics Board of Klerksdorp/Tshepong Hospital Complex. In addition, BroadReach Healthcare, and the CEO of the Klerksdorp/Tshepong Hospital Complex provided letters of agreement and approval. All documentation is available from the author.

4.2 Study population

The 457 participants enrolled in this study are HIV-infected individuals (>14 years of age) receiving ART in the Matlosana sub-district in North West Province, South Africa. Model performance is determined by patient-specific clinical events during the study period, patient treatment status at the end of the study period, the average cost-effectiveness ratio (CER), and the incremental cost-effectiveness ratio (ICER). Models were also evaluated in terms of LOI, a new metric for model performance proposed in this study.

All study participants were initiated and/or stabilized on ART at the Wellness Clinic at Tshepong Hospital in Klerksdorp[10]. Once selected for down-referral, patients chose either to attend their local PHC or to receive care and treatment through the PPP and see a local general practitioner (GP). All 457 participants were down-referred for routine

[10] Tshepong Hospital is the only government accredited ART initiation site in Matlosana. All patients on ART who relocate to Matlosana are initially seen at Tshepong Hospital, and once stabilized are down-referred for routine care.

care (PHC or PPP) for the first time between 28 November 2005 and 30 June 2007, and the time between the original down-referral date and the end of the study was between 9 (minimum) and 29 (maximum) months.

This study assesses the costs and outcomes associated with each model of care by comparing the matched sample of patients from each:

Cohort 1: 229 patients receiving care and treatment at their local public sector PHC; this cohort will also be referred to as the "**PHC cohort**."

Cohort 2: 228 patients receiving care and treatment at a private sector general practitioner (GP) via the public-private partnership (PPP); this cohort will also be referred to as the "**PPP cohort**."

4.3 Study eligibility

Patients deemed eligible for selection into the study met the following criteria:

1. On ART at the time of down-referral

2. >14 years of age at the time of down-referral

3. Documented record at the Wellness Clinic (doctors note in patient file or nurses note in the Clinic ART Register) that the patient was down-referred including the date of down-referral and the intended down-referral site (name of GP or of PHC)

4. An initial down-referral date between 28 November 2005 and 30 June 2007

5. Wellness Clinic record containing the following data verifiable by a source document:
   - Date of birth
   - Gender
   - Community of residence (Address)
   - Date of ART initiation
   - Date of down-referral

4.4 Data collection and statistical analysis

This section begins with a brief summary of methods used to ensure data quality in this study. The remainder of the chapter details the methods used for the three stages of data collection and statistical analysis:

1. *Matching* data collection and analysis

2. *Outcomes* data collection and analysis

3. *Cost* data collection and CEA

4.4.1 Data quality

Retrospective data collection in clinical settings presents a unique set of challenges. The process of data collection for this study began with a comprehensive audit of the Wellness Clinic and PHC patient data and record keeping. The results of the audit were presented to the ART Program Manager at the Wellness Clinic and documented several threats to data quality. One of the most significant data management problems was the lack of a unique patient identifier or patient identification (ID) number. In fact, most patients had two ID numbers on their files, and different numbers were used in difference electronic databases. There were also problems with the way in which each ID number was assigned. One of the numbers was derived directly from a patient's birth date, so it was possible for more than one patient to have the same ID number. The other ID number was assigned to a patient serially as they started treatment. However, because multiple people were assigning ID numbers at the same time and record keeping was incomplete, which also resulted in duplicate ID numbers (although fewer than using the birth date-derived number). In addition, during the initial search for files of eligible patients (for use in the matching regression) ten percent of the files could not be located. This may have been in part due to the fact that patient files were stored in at least four different places: the main file room; the down-referred patient file room; the hospital file storage room (for patients no longer on treatment); and the defaulter tracer's office. All four locations were checked but filing protocols, or the lack thereof, also made locating files difficult. In most places, files were organized by one of the two ID numbers. In the main file room, files were organized by the serially assigned ID number; in the down-referral file room and the defaulter tracer's room they were filed by PHC and then the birth date-derived ID number; and in the hospital file storage facility,

files were filed by ID number or were left un-filed in boxes on the floor.

There was also the problem of two different pharmacy databases. A dedicated pharmacy database that facilitates dispensing and label printing was in use in the Wellness pharmacy at the time of data collection, and was up-to-date and reliable, but only for patients who had started treatment since the database had been implemented (approximately one year prior to the beginning of this study). The older pharmacy database was less reliable and therefore older regimen data were pulled directly from patient files for this study. We also found that the ART database that was maintained by the data clerks was incomplete. This was because the data for the database was derived from the ART initiation register, which was periodically incomplete because there is only one register, and multiple doctors initiated patients simultaneously and sometimes failed to update the register[11].

There were also some problems with the laboratory data provided by the NHLS. The NHLS database used the patient ID number derived from the patient birth date to identify patients as well as the patient name, which meant that ensuring that laboratory results were assigned to the correct patient required triangulating using both the name and ID number. However, there were also a significant number of patients in the NHLS database who had no ID number listed, and so the only way to identify a patient was by name. There were also a significant number of tests with no results linked to a given test date. Matching laboratory results to patients electronically was further complicated by misspellings or typos in the database.

One final concern was the poor communication of patient data between Wellness and the PHCs. According to several of the nurses interviewed at the PHCs, they rarely received lists of patients who were being down-referred to their clinics in advance of patient arrival (despite the fact that there is one month between the last visit at the Wellness Clinic and the first visit at the PHC following down-referral). This made identifying and tracing patients who never presented at the PHC after down-referral impossible. None of the data or data management practices was audited, and there were no data quality checks routinely performed either at the PHCs or at the Wellness Clinic.

[11] This information was made available to the author through interviews with Wellness Clinic staff about data collection, collation and reporting procedures.

4.4.2 Data validation

PHC cohort data collection began at Wellness outpatient clinic in order to gather eligibility data. Data were collected from a combination of clinic databases, registers, and patient files. All data were double verified manually, and verification included at least one source document (register or patient file). In cases of a missing patient ID, patient records were reconciled manually using birth date, name and address in order to ensure the data belonged to the intended patient. This was time-consuming, but essential. Patients with missing files were only eligible if their data could be validated by at least two sources, one of which had to be a primary source document. If data conflicted and could not be validated against a source document, the patient was excluded from the study. Pharmacy data (i.e. regimens) were manually extracted from the drug prescription card in patient files, and did not rely on the pharmacy databases, which varied in completeness. Laboratory data provided by the National Laboratory Service was electronically merged with the study sample database using the patient name (there were no patients in this study with the same name) and date of birth as identifiers. Laboratory data that did not merge electronically (i.e. exact matches) were manually merged. Missing laboratory data were extracted from patient files manually if documented. Finally, patient clinical histories (i.e. visits, clinical outcomes, referrals and laboratory data) were manually reconstructed by reconciling Wellness files and registers with PHC files and registers.

Data for the PPP model patients were collected from BRHC and AfA, who employ a sophisticated data management system with an electronic medical record for each patient. The PPP data were complete with the exception of some laboratory results around the time of down-referral. All missing data were manually pulled from patient files. The PPP data management system undergoes an annual systems audit by an external contractor, and regular data quality audits by BRHC data management and operations staff. In addition, because BRHC is a PEFPAR recipient, USAID conducts periodic data quality assessments. The most recent assessment was conducted in late 2007, and the report delivered in early 2008 showed no significant threats to data quality in the BRHC data management system. Chapter 3 contains detailed descriptions of data management practices in each of the models.

4.4.3 Matching exercise: data collection and analysis

As costs and outcomes will vary according to patient-specific factors, and because

patients have a choice in selecting a down-referral model, particular effort was made to ensure that the final sample of study subjects was as similar as possible in each cohort. This was accomplished by using logistic regression to 'match' the eligible PPP cohort patients to the sample of eligible patients drawn from the larger PHC cohort.

Preliminary study eligibility in both cohorts was determined by the date of down-referral. Down-referral date data for PHC patients were collected at the Wellness Clinic by cross-referencing the Clinic ART Register (manual record of the ART initiation date), the clinic ART down-referral database, and patient files in order to determine the initial down-referral date[12]. Patients whose down-referral date could not be verified were excluded from the matching sample. Once a list of date-eligible participants was established for both cohorts, the remaining eligibility data were collected using similar methods for data validation. Table 4.1 details the list of matching indicators and sources in the PHC cohort. All patients missing one or more indicators were excluded from the matching sample. All matching data for the 875 eligible patients in the PHC were collated in an electronic spreadsheet.

Table 4.1 PHC cohort data used for matching and data source

Indicator	Data Source
Gender	Patient file; ART initiation database
Age (years)	ART initiation database; patient file; ART initiation register
Time on ART (months)	ART initiation database; ART initiation register
Time since down-referral (months)	Down-referral database; patient file

PPP cohort matching data were obtained in the form of an electronic spreadsheet report from the BRHC/AfA data management system. The report included data for all 594 patients down-referred within the eligibility window. Ten percent of the down-referral dates from the data management system report were validated against the Wellness Clinic patient files. One-hundred percent of all checked files were accurate.

All matching indicators from eligible patients in both cohorts were collated in an Excel spreadsheet, and imported into STATA in order to conduct a logistical regression using the pooled sample. Eight hundred seventy-five and 594 eligible patients from Cohorts 1 and 2 respectively were included in the propensity score matching exercise

[12] Patients may be down-referred more than once. Please see Chapter 3 for greater detail on model operations.

(Rosenbaum & Rubin, 1983). The exercise entailed creating a dummy variable taking the value of 1 for the PPP patients and 0 for the PHC patients. The dummy variable was then regressed on the four matching indicators (see Table 4.1) to generate a model that produced predicted probabilities (*p*) (of being in the PPP sample) for all patients. By matching PHC patients to PPP patients using the "nearest neighbor algorithm" (i.e. by selecting pairs of patients with the same *p*-value), it was possible to generate a study sample of 234 patients from both cohorts 'matched' according to an algorithm taking into account gender, age, time on antiretroviral treatment and time since down-referral. Table 4.2 lists the number of eligible patients and the number that matched in the regression by cohort. 95 percent of the overall sample (n=223) matched with a *p* differential ≤ 0.004. Patients with p differentials of >0.008 were not included in order to ensure a very high degree of comparability in each cohort. Frequencies and *p* differentials from the regression exercise are summarized in Table 4.3.

Table 4.2 Study sample: eligible v. matched

	Eligible	**Matched**
PHC Cohort	875	234
PPP Cohort	594	234

Table 4.3 Logistic regression results

***p* differential**	**Match frequency *n* (%)**	**Cum freq *n* (%)**
0.000	115 (49%)	115 (49%)
0.001	70 (30%)	185 (79%)
0.002	27 (12%)	212 (91%)
0.003	8 (3%)	220 (94%)
0.004	3 (1%)	223 (95%)
0.005-0.008	11 (5%)	234 (100%)

In order to validate the robustness of the match, means, medians and gender ratios were calculated by cohort. As can be seen in Tables 4.4 and 4.5, the matching strategy worked very well in that the two cohorts were virtually identical on all four matching variables.

Table 4.4 Means and medians for quantitative matching variables

MEDIANS	Time on ART (Months)	Time since DR (Months)	Age (Years)
PPP (n=234)	30	19	38
PHC (n=234)	30	19	40
MEANS	**Time on ART (Months)**	**Time since DR (Months)**	**Age (Years)**
PPP (n=234)	30	18	40
PHC (n=234)	30	19	40

Table 4.5 Gender ratios by cohort

	Male	Female
PPP	75 (32%)	159 (68%)
PHC	73 (31%)	161 (69%)

Subsequent to the matching exercise, one or more data elements used in the matching exercise were discovered to be either incorrect or uncertain for eleven patients (five in the PHC cohort and six in the PPP cohort). For this reason these patients were excluded from the study analysis, leaving 229 patients in the PHC cohort and 228 in the PPP cohort.

Matching results: cohort comparability

In terms of gender ratios, both cohorts were remarkably similar; the PHC cohort had two fewer males and two more females than the PPP cohort. The cohorts were also extremely similar in terms of age, time on ART (the amount of time between ART initiation and the study end date) and time since first down-referral (the amount of time between down-referral and the study end date). Patients from both cohorts had spent two and one-half years on ART, and one and one-half years in down-referral care. The average patient age in both cohort was 40 years.

Because viral suppression is one of the pre-conditions for down-referral, all patients were assumed to be virologically suppressed at the time of down-referral, and viral loads were not used as a matching variable in the regression. Clinical staging was also not used in the regression because it was inconsistently noted in patient files and could not reliably be extracted for analysis. Although clinical staging is an indication of past, as well as current clinical status, an absence of clinical signs and symptoms, opportunistic infections and adverse events (drug-related) is also a prerequisite for down-referral, and patients were all assumed (in line with stated policy on patient management) to be clinically well (and therefore comparable) at the time of down-referral.

While CD4 is not necessarily taken into account when down-referring a patient, one of the established predictors of patient success on ART is the CD4 count at baseline (Egger et al. 2002). Because CD4 and viral load are inversely correlated, one assumes that an absence of clinical signs and symptoms and a suppressed viral load indicate a strengthened immune system. Nonetheless, CD4 is not a perfect mirror of viral load, and should ideally be ruled out as a potential confounder. Unfortunately, it was not possible to identify accurate baseline CD4 results from the National Health Laboratory Service data set, and so CD4 was not used in the matching exercise. Instead, a post-regression analysis compared the CD4 counts of matched patients at the time of down-referral, in order to check for immunologic comparability between the two cohorts at the time of down-referral. The CD4 test date that was closest to, and preceding the date of down-referral was manually extracted from the National Health Laboratory Service data set for both cohorts. In the PPP cohort, the CD4 date associated with down-referral was labeled as "baseline" in the data management system database, and was used to confirm the data extracted from the National Health Laboratory Service dataset. For the PHC cohort, there was no such database or record of the CD4 result used for down-referral, so it was assumed that the most recent result prior to down-referral was correct. As Table 4.6 shows, the two matched samples were immunologically indistinguishable at the time of down-referral, although results were missing for fourteen of the PHC patients. Overall, down-referral CD4 results were 100 percent complete for the PPP cohort, and 94 percent complete among PHC patients.

Table 4.6 Mean and median CD4 at the time of down-referral

	Mean CD4	Median CD4
PPP (n=234)	315	283
PHC (n=220)	322	285

Table 4.7 shows the geographic distribution of patients by cohort across communities in Matlosana. Community of residence was not used in the matching exercise on the grounds that it was a poor marker of socio-economic status and because the distribution of patients across them was uneven.

Table 4.7 Post-match patient distribution by community and cohort

Community	Frequency (PPP)	Percent of Total (PPP)	Frequency (PHC)	Percent of Total (PHC)
Jouberton	133	57%	109	47%
Kanana	47	20%	64	27%
Khuma	36	15%	38	16%
Haartebeesfontein	2	1%	9	4.0%
Orkney	5	2%	1	<1%
Alabama	2	1%	2	1%
Stilfontein	5	2%	3	1.0%
Klerksdorp	3	1%	2	1%
Other	1	<1%	6	3%
TOTAL	**234**	**100%**	**234**	**100%**

Table 4.7 suggests that both cohorts are very similar in terms of neighborhood/ community representation. The largest percentage of patients in both groups lived in Jouberton, the largest township in the area located on the outskirts of the city of Klerksdorp. Seven patients in the study sample came from several smaller communities and were grouped together under "other" for this analysis.

Ideally patients would also have been matched according to some measure of socio-economic status (SES). Unfortunately, SES data is not collected by the clinics, and due to the large sample size (and study design) it was not possible to collect this data for each patient.

4.4.4 Outcomes data collection and analysis

Following the patient matching exercise, 15 indicators were collected for the 457 matched study patients in order to evaluate how patients in both cohorts fared in terms of clinical and operational outcomes during the study period. Table 4.8 lists outcome indicators and their definitions.

PPP cohort outcomes data were sourced from the data management system database. "Read only" access to study patient files in the data management system was granted to the author by AfA and BroadReach for a limited period of time during the data collection phase of the research. All patients in the PPP cohort had complete electronic files. For PPP patients who were up-referred to Wellness during the study period and remained there through the end of the study, data were extracted from Wellness files

and from the pharmacy database to complement the data from the BRHC/AfA database.

PHC cohort data were manually extracted from patient files at the Wellness Clinic, the PHC ART Register, and from PHC files onto paper data extraction forms designed to standardize data collection. Patient histories were reconstructed by cross-referencing information collected from the PHC and Wellness files so that complete and accurate outcomes data could be analyzed and reported. The NHLS Laboratory at Tshepong Hospital provided laboratory data (CD4 and VL) for both cohorts. Data were then transcribed from the paper data collection forms into an electronic database for analysis.

Table 4.8 Study outcomes indicators defined

Outcome Indicator	Definition
CD4 count at down-referral	CD4 count that is closest to, and precedes the date of down-referral
CD4 date at down-referral	Date associated with the CD4 count at down-referral
CD4 count (latest)	Most recent CD4 value that is closest to the end of the study period (31 March 2008)
CD4 date (latest)	Date corresponding to the most recent CD4 count result
VL (latest)	Most recent VL result that is closest to the end of the study period (31 March 2008)
VL date (latest)	Date corresponding to the most recent VL result
ART initiation date	Date a patient initiated ART for the first time
Date of down-referral	Date a patient was recorded as having been "down referred" for the first time to the GP / PHC from the Wellness Clinic
ART regimen	Three drug combination of antiretroviral therapy drugs taken by a patient at the end of the study period; classified as Regimen 1a, 1a modified,1b, or 2
Regimen switch	"Yes" or "No" indicator; indicates whether or not the patient changed their regimen after being down referred. A 'switch' refers to either a drug substitution (i.e. NVP for EFV) or a complete regimen change (Regimen 1a to Regimen 2)
Number of Wellness visits	The number of patient visits at the Wellness Clinic resulting from a patient "up-referral" from the PHC / GP to Wellness
Number of days spent in hospital wards	The number of days of inpatient care at either of the public sector hospitals (Tshepong or Klerksdorp Hospital)
Tuberculosis treatment	"Yes" or "No" indicator; indicates whether or not a patient received TB treatment in the study period
TB treatment date	Date a patient started TB treatment

Patient status	▪ **In Care at down-referral site**: a patient is alive, on ART and has picked up their medicine in the month preceding the end of study date. ▪ **In Care at hospital outpatient clinic**: the patient is alive, on ART, and has picked up their medicine in the month preceding the end of study date but has been up-referred from the PHC/GP and is receiving care and treatment at the hospital outpatient HIV clinic. ▪ **No longer in care (NIC):** a patient who is no longer enrolled in the ART program. NIC includes all patients who died, stopped ART or were lost to follow-up by study end
Patient outcome	At the end of the study (31 March 2008), all participants were assigned to one of the following mutually exclusive "outcomes" categories: ▪ **Suppressed**: a patient whose latest VL is ≤400 copies/µl ▪ **Unsuppressed**: a patient whose latest VL is >400 copies/µl ▪ **Deceased**: patient died; date of death is documented and falls between the date of down-referral and the end of study. ▪ **Transferred out:** patient's care and treatment was transferred to a non-participating study site, either outside the sub-district or to a private sector provider. These patients were excluded from analysis. ▪ **Lost to follow-up:** a patient who is no longer receiving ART, has had no contact with the treatment site for a period of time (> 2 months), and was not found after attempts to locate the patient by the treatment site. ▪ **Stopped ART:** patient's that are no longer on ART either because they elected to stop taking treatment or because their doctor decided it was in their best interest to stop treatment.

Clinical, immunologic and virologic events were recorded and analyzed to assess cost-independent model performance, in addition to the CEA (see Section 4.4.6). Model performance in terms of clinical outcomes was determined using the following data:

- Mean / median of latest CD4 and VL result
- Retention: ratio of patients current on ART at study end to the number of patients current on ART at study start
- Number of patients by patient status at study end: suppressed, unsuppressed and no longer in care (NIC)
- Number of patients by outcome: current on ART at GP/PHC, current on ART at Wellness, deceased, lost-to-follow-up, or stopped ART
- Number of inpatient days and outpatient visits (total, mean and median)
- Number of TB treatment-months

Figure 4.1 shows the patient status and outcome decision tree. Outcomes were analyzed by cohort, and then stratified by time on treatment and time since down-referral for comparison within strata. Tables 4.9 and 4.10 define each stratum.

Figure 4.1 Patient outcome and status decision tree

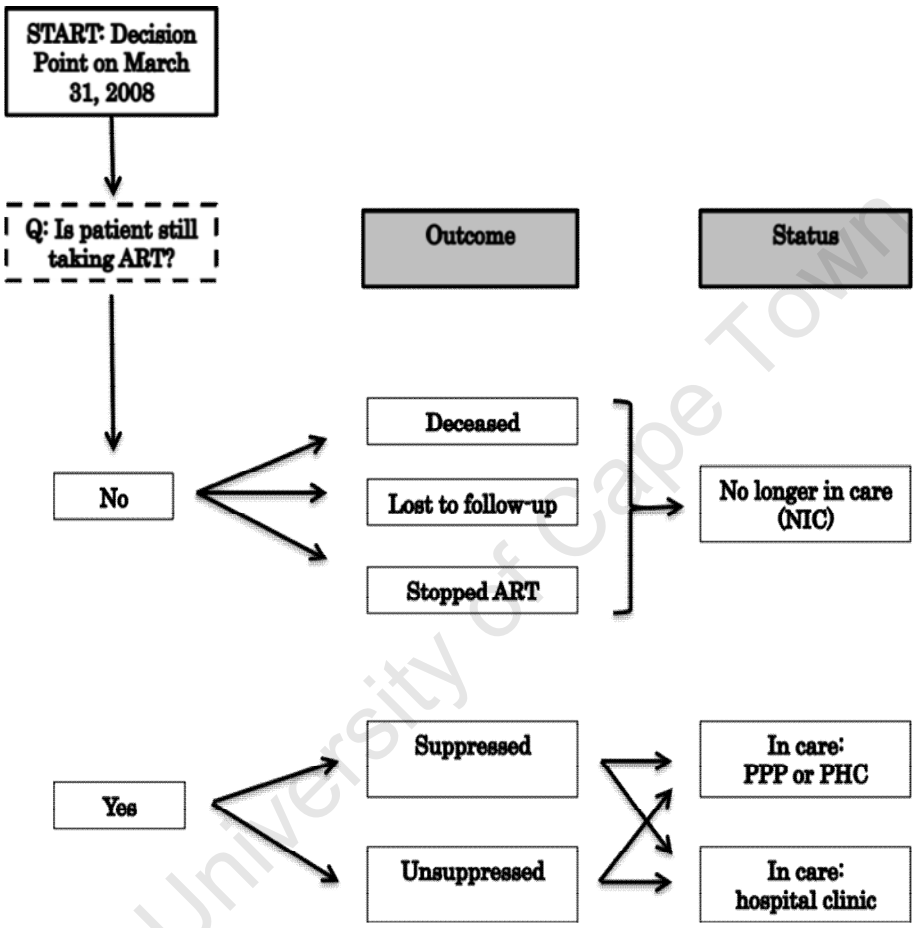


Table 4.9 Stratification by months since down-referral

Strata	Definition
12 month	Patients that have been followed up at the down-referral site for between 9 and 14 months (inclusive) as of 31 March 2008.
18 month	Patients that have been followed up at the down-referral site for between 15 and 21 months (inclusive) as of 31 March 2008.
24 month	Patients that have been followed up at the down-referral site for between 22 and 29 months (inclusive) as of 31 March 2008.

Table 4.10 Stratification by months on ART

Strata	Definition
24 month (n=49)	Patients that received ART for ≤ 26 months as of 31 March 2008.
30 month (n=142)	Patients that received ART for between 27 - 32 months as of 31 March 2008.
36 month (n=216)	Patients that received ART for between 33 – 38 months as of 31 March 2008.
42 month (n=177)	Patients that received ART for between 39 – 44 months as of 31 March 2008.
48 month (n=76)	Patients that received ART for > 45 months as of 31 March 2008.

Analyses were performed using STATA software (version 10.0; Stata Corp., College Station, Texas, USA).

4.4.5 Cost data collection and cost analysis

This study adopted the perspective of a government/public payer and all costs used in the analysis were direct program costs. PPP model-specific (down-referral care) costs were provided by BRHC, and PHC care costs were obtained from the Department of Local government. In addition to model-specific care costs, the costs of ARVs, anti-tuberculosis medicines, laboratory investigations, inpatient care, outpatient care, and a proposed new cost metric called loss on investment (LOI) were calculated. All costs were from the 2007/2008 fiscal year (April 1, 2007 through March 31, 2008). Due to the relatively short-term nature of the study (the mean difference between down-referral and study end was 18 months in both groups) no discounting of costs or outcomes was conducted. Patient out-of-pocket expenses were not considered in the cost-effectiveness analysis, but were explored separately in the context of patient interviews (Chapter 6).

Public sector infrastructure and maintenance costs for clinics and the hospital outpatient

clinic were not available and it proved impossible to isolate them from other operational costs. A decision was thus made to exclude all infrastructure, maintenance, rent and other related costs both from the PHC and PPP costs. Building maintenance costs *were* included in the inpatient patient-day equivalent figure provided by Tshepong Hospital, but because both models utilized Tshepong Hospital for in-patient and out patients care, this was not a problem for our research methodology as the unit cost of inpatient care was identical for both. Similarly, the costs of laboratory tests and ARVs were the same for both models (and the methodology for calculating these costs – see below – was identical in both models). The methodology for calculating these costs is described first in the following section, followed by the methodology for calculating routine down-referral care costs that are unique to each model. Cost categories and cost data included in the analysis in each care model are summarized in Tables 4.11 – 4.14.

Estimating the cost of ARVs and TB treatment

Monthly ARV and tuberculosis drug costs were obtained from the Klerksdorp Hospital pharmacy. Average monthly costs for each of the four ARV regimens (1a, 1a modified, 1b and 2) were calculated based on average monthly cost per drug. Each individual drug was typically available in more than one version (at least one generic and a branded version), and different versions were used interchangeably according to availability. The costs of all available versions of a particular drug were averaged and summed to calculate the average cost per regimen per month. The average drug and regimen cost calculation can be found in Appendix II. Monthly regimen costs were multiplied by the total number of months during the study period patients took each regimen, to calculate the total cost per regimen. Total regimen costs were then summed for the total cost for ARVs. Total ART regimen costs were equal to:

$$\left(\begin{matrix}\text{Reg 1a}\\ \text{cost}\end{matrix} \times \begin{matrix}\text{patient-}\\ \text{months}\end{matrix}\right) + \left(\begin{matrix}\text{Reg 1a}\\ \text{modified}\\ \text{cost}\end{matrix} \times \begin{matrix}\text{patient-}\\ \text{months}\end{matrix}\right) + \left(\begin{matrix}\text{Reg 1b}\\ \text{cost}\end{matrix} \times \begin{matrix}\text{patient-}\\ \text{months}\end{matrix}\right) + \left(\begin{matrix}\text{Reg 2}\\ \text{cost}\end{matrix} \times \begin{matrix}\text{patient-}\\ \text{months}\end{matrix}\right)$$

Tuberculosis treatment consisted of a two-drug regimen over a period of six months. The first drug was taken for the first two months of treatment and the second drug for the next four months. Patient time on TB treatment was recorded and the total number of months spent on the first regimen was multiplied by the cost of the first regimen, and the total number of patient-months spent on the second regimen was multiplied by the cost of the second regimen. The total ART drug cost was added to the total TB drug cost to calculate the total drug cost per cohort.

Laboratory investigation cost

The laboratory at Tshepong Hospital provided CD4 and viral load test costs. South African National ART guidelines recommend CD4 and viral load laboratory investigations for patients receiving ART every six months. However, in practice patients rarely have their CD4 and viral load tested every six months, so in order to estimate the number of laboratory tests conducted in the study period, ranges were created around each six-month laboratory test date. The number of laboratory tests were estimated based on the number of months that patients were active on ART according to the following algorithm: if the total number of patient-months was <4 then 0 laboratory tests were assumed; 5-10 = 1 laboratory test; 11-16 = 2 laboratory tests; 17-22 = 3 laboratory tests; 23-28 = 4 laboratory tests; >29 = 5 laboratory tests. The number of laboratory tests were estimated for all patients in each cohort and multiplied by the cost per test to calculate the total laboratory costs per cohort. The laboratory test cost calculation can be found in Chapter 5, Appendix III.

Outpatient care costs

Patients in both cohorts were up-referred for outpatient care to the Wellness Clinic at Tshepong Hospital. Outpatient visits involved greater time and cost than routine visits because patients saw a doctor, a nurse and sometimes a counselor or social worker. The outpatient visit cost included all clinic staff salaries (nurses, pharmacist, data clerks, etc.), clinic equipment and supplies, and doctor salaries. Annual staff salary data (excluding doctor salaries), equipment and supplies data were obtained from the Wellness Clinic Manager. The sum of these costs was divided by the total number of patient visits in the 2007/2008 year to calculate an average cost per visit per month. Doctor's salary data were provided by the Tshepong Hospital Human Resources Department (doctors are funded from a separate budget). Six doctors were employed at the outpatient clinic (three principal medical officers, two medical officers, and one intern) and because it is not possible to know which doctor patients saw, all doctor salaries were averaged, and then pro-rated to the equivalent of one visit per day based on an estimated average patient load per doctor of 30 visits per day[13] (one visit was assumed to be the monthly cost per patient because patients typically have one appointment per month). Average doctor salary per visit was then added to the average staff, equipment and supplies cost per visit per month to calculate the total outpatient visit cost. Doctor costs were not added to the staff, equipment and supplies cost and

[13] Wellness doctors were interviewed and reported seeing an average of 30 patients per day.

divided by the total number of patient visits because not all patient visits at the Wellness Clinic require a doctor – some come for blood draws, drug pick-ups, or routine visits for pre-ART patients. Pro-rating the doctor salaries (which were one-third of outpatient visit costs) ensured their time was accurately reflected in the average outpatient visit cost.

The estimated average cost per outpatient visit per month was calculated as follows (the detailed outpatient visit costing calculation can be found at the end of Chapter 5, Appendix IV, Costing Table 3c):

$$\frac{\left(\text{Staff salaries} + \text{Equipment costs} + \text{Supplies costs}\right)}{\text{Total patient visits in 07/08}} + \frac{\text{Average doctor salary per day}}{\text{30 visits}}$$

Total cost for the study period was calculated by multiplying the average cost per outpatient visit per month by the total number of months patients spent in outpatient care in each cohort.

Inpatient care costs

All patients suffering from severe HIV-related infections or complications requiring inpatient care were transferred to one of two tertiary care facilities in Matlosana: Klerksdorp Hospital or Tshepong Hospital which operate under a single administrative umbrella. Costing of inpatient hospitalizations in this study was based on the hospitals' patient-day-equivalent (PDE). The PDE for fiscal year 2007/2008 was provided by the office of the CEO of the Klerskdorp/Tshepong Hospital Complex for this study. The PDE calculation includes the following expenses:

- Staff Salaries
- Administration
- Goods/Services
- Inventory (including drugs)
- Specialist Services
- Equipment
- Other expenses

While a PDE is less precise than a micro-costing of HIV-specific hospitalizations, an approximation of inpatient costs was sufficient for the purposes of this study.

Inpatient hospitalization costs were calculated for each cohort by multiplying the total number of days spent on hospital wards for HIV-related infections by the PDE. Hospitalizations for non-HIV associated infections, injuries, chronic diseases and pregnancy were excluded from this analysis as they were not the responsibility of the models of HIV care being assessed here, and were deemed inappropriate items for assessing model performance.

Routine care costs: PPP model costing

This section details the costs that were unique to routine down-referral care offered through the PPP model. PPP patient costs are shared between BRHC and the North West Province Department of Health. BRHC is responsible for covering the cost of monthly GP visits, as well as program support staff who provide data management, monitoring and evaluation, patient enrollment and follow-up, and GP management and clinical support. PPP model routine down-referral care costs were collected from the BRHC Finance Department.

Table 4.11 PPP cost categories

Cost Category	Cost data
Patient care	▪ GP (routine) ▪ Hospital outpatient ▪ Hospital inpatient
Drugs	▪ Antiretroviral drugs ▪ TB drugs
Laboratory investigations	▪ CD4 ▪ VL
Loss on investment[14]	▪ Time-adjusted cost penalty for patients falling off treatment program prematurely
Total PPP cost	**Patient care + Drugs + Labs + (LOI)**

[14] The analysis was conducted with and without LOI. See section 4.4.5 for detailed discussion of LOI.

Table 4.12 PPP patient care services delineated

Cost Category	Cost data
Routine Visit (GP)	▪ GP fee ▪ Data management fee ▪ Support staff salaries (manager, regional coordinators (2), MER officer) ▪ Support staff equipment costs (phones, computers, internet)
Outpatient Visit (Wellness)	▪ Staff costs (salaries) ▪ Supplies and equipment
Inpatient Visit (TSH/KDH)	▪ Patient-day equivalent (PDE): average cost per patient-day includes staff salaries, administrative costs, miscellaneous goods and services, maintenance, drugs and other consumables, specialist services, equipment.

In accordance with national guidelines, each active patient was assumed to have had one GP visit per month, so the cost of a patient visit was the equivalent of the cost per patient per month, (subsequently called a "patient-month"). All costs were calculated in patient-months. As described in Table 4.12, the PPP cost routine care cost per patient-month included the monthly GP fee (per patient per month), the data management fee (per patient per month), and monthly salary and equipment costs derived from the 2007/2008 BRHC budget. Monthly salary costs were determined by weighting BRHC staff salaries according to the average percentage of time spent working on the PPP model. For example, 100 percent of the Regional Coordinators' monthly salaries was included in the calculation because both work full-time on the model, whereas only 10 percent of the clinical manager's monthly salary was included in line with the average amount of time allocated to the PPP model. Monthly costs associated with all model-related travel (flights, rental car and per diem) were calculated by averaging travel receipts from 2007/2008. The life of a laptop was assumed to be two years, and the total cost was divided by 24 (to calculate the cost per month) and weighted based on the amount of time an employee spent working on the model (e.g. 10 percent of the monthly cost of the clinical manager's laptop was included). Monthly cell phone and 3G (wireless mobile internet) fees were also counted and weighted. All of the salary, equipment and travel costs were totaled and then divided by the total number of patients enrolled in the PPP model as of 31 March 2008 in order to calculate the cost per patient-month. Then the monthly GP and data management fees were added to the cost per patient-month of salaries, equipment and travel to arrive at a total PPP cost per patient-month. The routine care cost per patient per month in the PPP model was calculated as follows:

$$\text{Routine Visit Cost}_{PPP} = \left(\frac{\text{Monthly Salaries} + \text{Monthly equipment cost} + \text{Average monthly travel expenses}}{\text{Total PPP Patients}} \right) + \text{GP Fee (per patient per month)} + \text{Data Management Fee (per patient per month)}$$

Total PPP model down-referral care costs for the study period were calculated by multiplying the total number of active patient-months by the average monthly care cost. Total routine down-referral care costs in the study period were added to the PPP drug, laboratory, outpatient and inpatient costs to calculate the total cost of the model in the study period (Table 4.11). A second (alternative) total model cost was calculated which included the LOI. A detailed PPP visit costing calculation can be found at the end of Chapter 5 in Appendix IV, Costing Table 3b.

Routine care costs: PHC model costing

This section details the costs that were unique to routine down-referral care offered through the PHC model. Public sector down-referral ART care is integrated with all other primary care services offered through the PHCs, and falls under the purview of the Department of Local Government Health Office. All costs for this model were obtained from the North West Province Department of Local Government (DLG), or the provincial Department of Health.

Table 4.13 PHC cost categories

Cost Category	Cost data
Patient care	▪ Clinic (routine) ▪ Hospital outpatient ▪ Hospital inpatient
Drugs	▪ Antiretroviral drugs ▪ TB drugs
Laboratory investigations	▪ CD4 ▪ VL
Loss on investment[4]	▪ Time-adjusted cost penalty for patients falling off treatment program prematurely
Total PHC cost	**Patient care + Drugs + Labs + (LOI)**

Table 4.14 PHC patient care services delineated

Cost Category	Cost data
Routine Visit (PHC)	▪ Staff salaries: clinical and support staff
Outpatient Visit (Wellness)	▪ Staff costs (salaries) ▪ Clinic overhead
Inpatient Visit (TSH/KDH)	▪ Patient-day equivalent (PDE): average cost per patient-day includes staff salaries, administrative costs, miscellaneous goods and services, drugs and other consumables, specialist services, equipment.

The routine down-referral care costs at the PHCs were comprised entirely of staff salaries. Only limited and inadequate estimates were available for non-salary costs like equipment, miscellaneous supplies, and drug and laboratory tests. Moreover, these aggregate costs could not be disaggregated or checked. A decision was therefore made to estimate drug and laboratory costs in a separate exercise, and to assume that as no special equipment is required for routine clinic visits, these costs were negligible and thus could reasonably be excluded from the analysis.

Salary and employment data provided by the DLG for the various clinics varied in quality and reliability. Thus, rather than dividing total salaries by total patient visits for each clinic, an average salary cost for a 30-minute visit across all PHCs was calculated. Because patients always see a professional nurse on a routine visit, the cost per professional nurse was used as a proxy for the routine visit cost. Average annual staff costs were divided by the average number of professional nurses in all clinics to arrive at an annual cost per professional nurse. This was then applied to each clinic. In order to calculate the cost per patient per visit per month, total staff salaries for the 2007/2008 fiscal year were pro-rated to 30 minutes, the average time allocated to an ART patient visit[15]. Costs associated with doctor visits were not included because routine visits at PHCs do not typically involve doctors. The detailed PHC visit costing calculation can be found in Chapter 5, Appendix IV, Costing Table 3a):

[15] Interviews were conducted with nursing staff at all clinics, during which nurses were asked to estimate the average length of a routine ART visit.

$$\text{Annual average professional nurse salary} = \text{Average}\left(\frac{\text{clinic A salaries}}{\text{\# prof nurses}} + \frac{\text{clinic B salaries}}{\text{\# prof nurses}} + \frac{\text{clinic C salaries}}{\text{\# prof nurses}} \text{ etc.}\right)$$

$$\text{Daily Visit Cost}_{PHC} = \frac{\text{Annual average nurse salary}}{\text{249 (i.e. \# work days / year)}}$$

$$\text{Routine Visit Cost}_{PHC} = \frac{\text{Daily average nurse salary}}{\text{16 (\# 30 minute segments / day)}}$$

4.4.6 Loss on investment

The amount and rate of patient attrition should be an important indicator of ART program effectiveness (Brinkhof, 2008) but tends to be neglected in conventional cost-effectiveness analysis. Considerable scarce resources are invested in each patient to restore health. If we know the amount of money required to stabilize a patient on ART, and we have reasonable survival estimates for patients on ART, in economic terms we could say that a patient who lives until the average ART survival threshold returned 100 percent of the initial investment (ROI) devoted to restoring a patient's health. Conversely, patients who die or are lost to follow-up before attaining the life expectancy threshold for patients on ART to some degree reflect programmatic failure, and thus make less than a 100 percent ROI. Failure to achieve the life-expectancy threshold thus can be conceptualized as representing a 'loss on the investment' (LOI) in restoring an individual to a healthier state. HIV care and treatment models that keep greater numbers of patients on ART for longer represent a better value to the health system both in terms of patient health and protecting the original financial investment.

Accordingly, my new proposed measure, LOI, assigns a time-adjusted monetary value to premature patient attrition from ART programs due to death or other reasons including lost to follow-up. LOI provides a novel indicator of model performance by quantifying the "waste" or unrealized investment in patient health over time. Unlike total and average program costs that just increase over time and are somewhat counter-intuitive (i.e. more expensive means more effective), LOI assigns an estimated cost associated with failure to achieve life-expectancy targets for patients on ART.

LOI is only incurred when a patient falls off treatment before achieving the mean survival estimate for their age group. No penalty is assessed for patients who remain in care and on ART or for those who surpass the survival threshold while on ART. The

cost penalty is based on the base-case cost of stabilizing a patient on ART, and in this study was equal to twelve months of ART, laboratory tests, and hospital-based outpatient care[16]. In addition to the base-case, stabilization costs were calculated for 8 and 16 months in order to provide a range of estimates. The stabilization cost (the mean cost to stabilize a patient over 12 months at the Wellness Clinic was estimated at R6,680) was multiplied by a time-weighted penalty between 0 and 1 that correlates to the amount of time spent on treatment before stopping it.

Estimates of patient survival on ART were derived from data published by Braithwaite and colleagues (2005)[17] in order to determine the ART life expectancy threshold for the LOI calculation. The threshold adopted for the LOI metric reflected survival rates for patients who started ART late into the illness to correspond with the CD4 $\leq$ 200 cells/mm^3 initiation guidelines in South Africa. Two life expectancy thresholds were used depending on a patient's age. Based on the ART survival data, patients on ART who were 39 years or younger were expected to survive an additional 12 years following ART initiation, while life expectancy for those 40 and older were expected to survive an additional 10 years on ART. A cost penalty per patient was assessed based on the patient end date using a sliding scale, where a 100 percent penalty (the full R6,680) was incurred for patients who were off of treatment within the 12 months following down-referral, down to zero for patients who were either still on ART or had survived 10 or 12 years or longer (depending on the patient's age). The cost penalty was spread evenly over the period between the date of initiation and the estimated life expectancy threshold and discounted (9 percent per year).

The LOI for each model was added to the total drug, laboratory and care costs to calculate an alternative total model cost. LOI was *not* used in the cost-effectiveness calculations in order to avoid double counting. The percentage of LOI in each model that was attributable to loss to follow-up, death and patients who stopped ART was also calculated. Detailed LOI calculation tables can be found in Chapter 5, Appendix VI.

Per Patient LOI = Time-adjusted penalty x average cost to stabilize a patient

[16] Patients in this study spent an average of twelve months being stabilized on ART at the Wellness Clinic before being down-referred.

[17] Data from Braithwaite et al. (2005) were used because there was no published survival estimates for ART patients in sub-Saharan Africa. They estimated survival for individuals aged 30-39 who started ART at a CD4 of 200 or below and had a VL of 1,000,000 at 12.2 years; between 40-49 at 10.9 years; and between 50-59 years at 10.2 years. For this calculation, patients were divided into two groups: 39 and younger and 40 and older with life expectancy of 12 and 10 years on ART respectively.

Total model costs for the study period were calculated with and without LOI as follows:

Total model costs without LOI =

Total care costs + Total drug costs + Total laboratory costs

Total model costs (adjusted to take into account LOI) =

Total care costs + Total drug costs + Total laboratory costs + LOI

4.4.7 Cost-effectiveness analysis

The principal cost-effectiveness ratio (CER) in this study was the cost per suppressed patient still in down-referral care at study end. As previously discussed, this ratio reflects the degree to which each model achieved the clinical and operational goals of down-referral care: to maintain healthy patients with suppressed viral loads at the lowest level of care for as long as possible. Two other CERs were calculated: the cost per suppressed patient per month (regardless of care site), and the cost per active patient per month (still enrolled in the treatment program regardless of suppression status or care site).

Finally, incremental cost-effectiveness ratios (ICER) were calculated, and sensitivity analysis was performed on key cost drivers in each model.

Chapter 5

Results

5.1 Clinical and Operational Outcomes

The operational and clinical objectives of down-referral are to maintain patient health (viral suppression, immune functioning, and an absence of opportunistic infections), and to keep the patient in care at the down-referral site. This study evaluated the degree to which both models of down-referral care achieved these clinical and operational aims. All patients were assigned to one of three, mutually exclusive statuses based on clinical outcomes at study end. All patients who remained in care for the duration of the study period, and whose most recent viral load was VL ≤400 copies/µl were assigned to status *suppressed* (abbreviated SUPP in the tables). All those who remained in care and had a viral load >400 copies/µl at study end were assigned to status *unsuppressed* (abbreviated UN in tables). Finally, all patients who died, elected to stop treatment, or were lost to follow-up (LTF) by the end of the study period were assigned status *no longer in care* (abbreviated NIC in tables).

In addition, specific patient outcomes were calculated based on a combination of patient clinical status and site of care at study end (down-referral site or the hospital-based outpatient clinic). Ratios of patient outcomes to total patients in each cohort, including two retention metrics were used to compare model performance. All patients, whose care was transferred to another site outside the district or between the PHC and PPP models, were excluded from the analysis.

5.1.1 Viral suppression, retention and outcomes

The ratio of patients in care at the down-referral site with a suppressed viral load (VL ≤400 copies/µl) to the total number of subjects enrolled was 83 percent in the PPP cohort, and 55 percent in the PHC cohort (this result is highlighted in boldface type in Table 1, section b). This difference in the ratio of suppressed to the total number of patients in each cohort was statistically significant, substantial, and important given that this is the ideal outcome for any down-referred patient. Of all patients still enrolled in treatment at study end, 94 percent of PPP subjects' most recent viral load was suppressed compared to 90 percent for PHC subjects. Among study participants who remained in care at the down-referral site, viral suppression rates were 89 percent in the PPP cohort and 73 percent in the PHC cohort; this difference was significant. The prevalence of viral suppression was relatively high in both cohorts among patients who remained in care, but there were significantly more PPP patients still in care at study

end overall and at the down-referral site than in the PHC model.

Two different retention statistics were calculated, both of which are reported in Table 5.1. The first was the proportion of study subjects retained in care at the down-referral site relative to the total number of study subjects enrolled. Fifty-eight percent of the PHC cohort remained at the down-referral care site at the end of the study period compared to 89 percent of subjects in the PPP cohort. The second retention figure was the proportion of patients retained on treatment at the end of the study regardless of whether they were still in care at the down-referral site or if they had been up-referred for hospital-based outpatient care. Seventy-five percent of the PHC cohort and 94 percent in the PPP cohort were retained on treatment at study end. Both of these observed differences in patient retention were statistically significant ($p<0.01$).

One-quarter (n=57) of the PHC patients were no longer in care by the end of the study period, and of these, the majority (83 percent) was LTF[18]. Among PPP patients, 14 were no longer in care, and of these five were LTF. A patient was only declared LTF if there was no record of patient contact for more than two months following a thorough investigation that included a review of pharmacy dispensing records, clinic attendance registers, and patient files. For reasons relating to confidentiality (and because no specific consent had been obtained from patients for this), no attempt was made to contact patients or patient's families directly to ascertain the actual reason patients missed their appointments and drug pick-ups. The difference between cohorts in terms of total subjects no longer in care and LTF was statistically significant. There were seven recorded deaths in each cohort, and three PHC patients and two PPP patients elected to stop taking ART during the study period. PPP patients that were no longer in care were more likely to have died as a proportion of the total number no longer in care. Table 5.1 summarizes the number of patients per status and outcome category relative to the total number of study subjects enrolled in each cohort, as well as to the total number that were current in each cohort at study end in order to provide a more complete picture of model performance.

In virtually all of the patient retention, suppression and operational (care site) measures, the PPP model performance was significantly better. By the end of the study period, PPP subjects were more likely to be in enrolled in care, more likely to be in care at the

[18] LTF indicates that there was no record of a patient visit or drug pick-up at either the hospital-based outpatient clinic or the down-referral care site for greater than two months. See Chapter 4: Methods for more information on determining LTF in this study.

down-referral site, and more likely to be suppressed regardless of care site. PHC subjects were significantly more likely to be no longer in care and LTF.

Table 5.1 Status, outcomes and retention ratios

a. Status ratios

	Suppressed / cohort	Suppressed / current	Unsuppressed / cohort	Unsuppressed / current	NIC / Cohort	Deceased / NIC	LTF / NIC	Stopped ART / NIC
PHC	154/229 (67%)	154/172 (90%)	18/229 (8%)	18/172 (10%)	57/229 (25%)	7/57 (12%)	47/57 (83%)	3/57 (5%)
PPP	200/228 (88%)	200/214 (94%)	14/228 (6%)	14/214 (7%)	14/228 (6%)	7/14 (50%)	5/14 (36%)	2/14 (14%)
***p*-Value**[19,20]	0.000***	0.165	0.471	0.165	0.000***	0.001***	0.001***	0.254

b. Outcome ratios

	Current at down-referral site / current	Current at outpatient clinic / cohort	Current at outpatient clinic / current	**Current at down-referral site and suppressed / cohort**	Current at down-referral site and suppressed / current	Current at outpatient clinic and suppressed / cohort	Current at outpatient clinic and suppressed / current	Current at outpatient clinic and suppressed / total outpatient	**Retention at down-referral site**	**Retention on ART Treatment**
PHC	133/172 (77%)	39/229 (17%)	39/172 (23%)	**126/229 (55%)**	126/172 (73%)	28/229 (12%)	28/172 (16%)	28/39 (72%)	**133/229 (58%)**	**172/229 (75%)**
PPP	203/214 (95%)	11/228 (5%)	11/214 (5%)	**190/228 (83%)**	190/214 (89%)	10/228 (4%)	10/214 (5%)	10/11 (91%)	**203/228 (89%)**	**214/228 (94%)**
***p*-Value**	0.000***	0.000***	0.000***	**0.000*** **	0.000***	0.002***	0.000***	0.190	**0.000*** **	**0.000*** **

*** indicates significance at 1%

[19] Significance testing was performed in STATA using Pearson's chi-square test. All chi-square results from Table 1 are located in Appendix I.

[20] In cases where $n \leq 5$, Fisher's exact chi-square was used.

Retention on treatment provides just a momentary snap-shot of patient outcomes at study end, and does not to take into account differences in the amount of time spent on treatment or in down-referral care. The average time spent on treatment and since down-referral was calculated for patients who remained in care during the study period (regardless of viral suppression status or location of care) and those who were *no longer in care* (Table 5.2). Among those still on treatment at study end, patients from both cohorts spent almost 18 months in care on average following their first down-referral, and approximately 30 months on HIV treatment. There was a difference between the cohorts in terms of the number of months spent in care prior to falling off treatment: in addition to being less likely to be no longer in care, those PPP patients that eventually did stop treatment spent an average of six months longer on ART than PHC patients, and remained in care for approximately two months longer on average following down-referral.

Table 5.2 Time on treatment and time since down-referral by status and cohort

	PHC	PPP
Time on ART		
Mean months for all current patients ***(SUPP+UN)***	29.6	29.5
SD	6.35	6.59
Range	16-44	15-46
Mean months for all patients off ART ***(NIC)***	30.5	36.5
SD	6.25	9.17
Range	18-42	27-63
Time since down-referral		
Mean months for all current patients ***(SUPP+UN)***	17.5	17.7
SD	4.85	5.3
Range	9-28	9-28
Mean months for all patients off ART ***(NIC)***	18.6	20.5
SD	5.29	5.49
Range	9-28	10-28

5.1.2 Laboratory and regimen data

In addition to the status and outcome analysis discussed above, mean and median CD4 and viral load results were analyzed independently. No significant differences were found between cohorts among patients still receiving care at the end of the study in terms of mean CD4 or viral load. Mean and median CD4 was slightly higher among

current PHC patients (461 cells/mm^3 versus 438 cells/mm^3), but the difference was not statistically significant nor was it clinically meaningful. Mean viral load was higher among PPP patients, but further examination revealed a few very high viral load outliers in the PPP cohort that skewed the mean higher. Median viral load was < 25 copies/µl in both groups.

Because patients do not always follow the recommended laboratory examination schedule (South African guidelines recommend a CD4 and viral load test every six months while on ART), the most recent laboratory data used in this analysis varied by patient in relation to the end of study date. For this analysis, the laboratory result that was closest to the study end date (even if the laboratory test was performed after the end of the study), and after the initial down-referral laboratory result was considered the "latest" result. Because of the variance in the date of the latest laboratory test in relation to the study end date, and in order to establish the relevance of latest laboratory results to patient status at study end (viral loads and CD4 counts can change relatively quickly), the median number of months between the end of study date and the date of the most recent laboratory result was calculated. Both groups of patients had similarly recent laboratory results: the median difference between the study end date and the most recent laboratory test result was two months in both groups. Median and average laboratory results, as well as the mean and median differential between laboratory result and study end for patients still in care at the end of the study are presented in Table 5.3.

ART and tuberculosis regimen data were collected and analyzed for costing purposes, as well as to determine any differences between the models regarding prescribing practices and the number of patients that received tuberculosis treatment. Drugs in both models of care were procured through the public sector, and both offer two core lines of triple-therapy in line with the national HIV treatment guidelines. The vast majority of patients in both models of care received the first line ART regimen, called regimen 1a (d4T, 3TC and EFV)[21]. Regimen 1b (d4T, 3TC and NVP)[22] is typically prescribed for women of child bearing age not on contraception or for pregnant women (EFV carries a risk of causing teratogenic effects to a fetus), and was the second most commonly prescribed drug regimen in the PHC cohort.. The modified 1a regimen (ZDV, 3TC and EFV)[23] was the most common alternative to regimen 1a in the PPP cohort, but not prescribed at all for PHC patients. The practice of prescribing regimen 1a modified in

[21] d4T is the commonly used abbreviation for stavudine, 3TC is lamivudine and EFV is efavirenz

[22] NVP is nevirapine

[23] ZDV is zidovudine, and is also known as AZT

the PPP cohort and not the PHC cohort is curious given that a public sector doctor does all regimen switches at the hospital outpatient clinic. This may point to different prescribing preferences among outpatient clinic doctors, and has important cost implications that are discussed later in this analysis. Only four patients in total – three in the PHC and one in the PPP - were on regimen 2. Data on the number of regimen switches was collected in order to understand if switching regimens occurred more frequently in either of the cohorts; reasons for specific regimen changes were not analyzed. There were 13 (6 percent) documented regimen switches that occurred during the study period among participants enrolled in the PHC cohort, and nine (4 percent) in the PPP cohort. Overall, ART prescribing and switching patterns were broadly similar across both study cohorts.

Table 5.3 Laboratory tests, regimen and TB treatment data

	PHC	PPP	*p*-Value	*t*-Statistic
Laboratory Exam Results[24]				
Mean latest CD4 count	502	462	**0.076***	1.78
Median latest CD4 count	461	438	N/A	N/A
Mean latest VL	1098	12,155	**0.079***	-1.764
Median latest VL	<25	<25	N/A	N/A
Median # months between latest laboratory test and study end	2	2	N/A	N/A
Regimen Data (all patients)[25]				
1a	216	210	0.346	N/A
1a modified	0	13	**0.0002****	N/A
1b	10	4	0.106	N/A
2	3	1	0.318	N/A
Total number of regimen switches	13	9	0.389	N/A
Tuberculosis Treatment				
Total number of patients received TB treatment	0	2	N/A	N/A
Total number of patient-months on TB treatment	0	10	N/A	N/A

*** indicates significance at 1%; * indicates significance at 10%

Despite high rates of HIV and tuberculosis co-infection in South Africa, tuberculosis diagnosis and treatment was infrequent in both cohorts. None of the PHC subjects and just two PPP patients were diagnosed and treated for tuberculosis infection during the

[24] Standard *t*-test of means performed in STATA for significance testing.

[25] Significance testing was performed in STATA using Pearson's chi-square test. In cases where $n < 5$, Fisher's exact chi-square was used.

course of the study. This is likely due to the fact that all study participants were treatment experienced and generally doing well on ART when they were enrolled in the study, making TB infection less likely.

5.1.3 Up-referral practices

Patient up-referrals were recorded for costing purposes and to document any differences in up-referral practices between the two models of care. Up-referral is the process of sending a patient from the down-referral care site back to the hospital-based outpatient clinic for a doctor's care, or to the hospital wards for inpatient care for severe complications. Common reasons for up-referral include side-effects from the ARV treatment, change of regimen, poor treatment adherence, failure to respond to treatment, opportunistic infections, antenatal care, and other care and treatment needs that cannot be met at the primary care clinic or GP office.

Table 5.4 Up-referrals and average length of stay by cohort

	PHC	PPP
Outpatient Up-referrals		
Total outpatient up-referrals	84	55
Total outpatient visit-months	621	142
Ave. length of stay (visit-months)	7.4	2.6
Inpatient Up-referrals		
Total inpatient up-referrals	5	6
Total inpatient visit-days	17	20
Ave. length of stay (visit-days)	3.4	3.3

The frequency and duration of up-referrals have clear cost and operational implications as hospital-based outpatient care and inpatient care is more resource intensive than the routine care offered at the down-referral sites. Table 5.4 describes up-referral practices for outpatient and inpatient services by model of care during the study period. Up-referrals for problems known to be unrelated to the patient's HIV disease or for antenatal care for pregnant women were excluded from this analysis (in both cohorts) in order to isolate model performance as it relates to ART care, and also because the PPP model caters uniquely for ART care. Pregnant women were not included in the up-referral analysis because in the PPP model and in most of the clinics, maternity care automatically necessitates an up-referral to the hospital until the pregnancy is over. More importantly for this analysis, up-referrals were used as an indicator of model

performance with operational, cost, and clinical implications related to HIV care; up-referrals for pregnancy do not reflect model performance with regard to HIV care, and including pregnancy in the up-referral numbers would have risked masking up-referrals for HIV-related reasons Over the course of the study, 84 patient up-referrals took place in the PHC model, and once up-referred, PHC patients spent more than seven months on average in the hospital outpatient clinic. By comparison, 55 patients in the PPP model were up-referred during the study period, and the average length of stay at the hospital outpatient clinic was just over two-and-a-half months. In addition, PPP patients enrolled in outpatient care at study end were more likely to be suppressed (91 percent) compared to PHC patients (72 percent), though the difference was not statistically significant. Up-referral for inpatient care was relatively infrequent in both models of care, and the average length of inpatient stay was just over three days in both groups.

5.1.4 Controlling for individual clinic and GP performance within care and treatment models

This study aimed to compare the performance of two difference models of down-referral care, and the preceding analyses were carried out by grouping clinics and GPs in order to ascertain "model" performance. In reality, both care and treatment models were comprised of multiple service outlets, each with distinct features. It is therefore possible that the aggregate results obtained and reported above may be attributable to differences in performance between the service outlets within each cohort. Put differently, it could be the case that the aggregate results could be driven by a few 'outliers' – e.g. one or two seriously underperforming clinics and a few extremely effective GPs. If so, then it would be incorrect to attribute the relative success of the PPP model to the model itself. In order to check to see if the clinics and GPs within each cohort were significantly different from each other, a robust linear regression was conducted on patients "no longer in care" controlling for age, gender, months on ART, months since down-referral, and individual GPs and clinics. Table 5.5 contains the regression results.

Table 5.5 Linear regression for GP and clinic effects

			Number of obs =	451	
			F (29, 421) =	2.9	
			Prob > F =	0	
			R-squared =	0.1286	
			Root MSE =	0.34363	
Not in Care	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]
Age	-0.0025339	0.0019941	-1.27	0.205	-.0064536 .0013858
Female	-0.0176485	0.0392865	-0.45	0.654	-.0948705 .0595736
Months on ART	0.0031234	0.0032241	0.97	0.333	-.0032139 .0094606
Months down-ref	0.0039534	0.004183	0.95	0.345	-.0042688 .0121756
GP 2	0.0233388	0.0299633	0.78	0.436	-.0355574 .082235
GP 3	0.1105874	0.0852453	1.3	0.195	-.056972 .2781468
GP 4	0.0142198	0.0523493	0.27	0.786	-.0886788 .1171184
GP 5	0.0004337	0.0213228	0.02	0.984	-.0414787 .0423461
GP 6	0.0890147	0.0979585	0.91	0.364	-.1035339 .2815634
GP 7	-0.0103732	0.0247275	-0.42	0.675	-.0589778 .0382315
GP 8	0.0450443	0.0604178	0.75	0.456	-.0737139 .1638025
GP 9	0.0197836	0.0457361	0.43	0.666	-.0701159 .1096831
GP 10	0.0432691	0.0559409	0.77	0.44	-.0666892 .1532274
GP 11	0.0192091	0.0390902	0.49	0.623	-.0576272 .0960455
GP 12	-0.0442168	0.0341678	-1.29	0.196	-.1113775 .0229439
GP 13	0.0673017	0.0900906	0.75	0.455	-.1097818 .2443852
GP 14	-0.0129458	0.0234976	-0.55	0.582	-.0591331 .0332415
GP 15	0.0159721	0.0231482	0.69	0.491	-.0295283 .0614724
GP 16	0.0232993	0.0522149	0.45	0.656	-.0793351 .1259336
GP 17	0.2379878	0.2268629	1.05	0.295	-.2079373 .6839129
Clinic 1	0.141812	0.0784748	1.81	0.071	-.0124392 .2960633
Clinic 2	0.1924673	0.1013338	1.9	0.058	-.0067159 .3916506
Clinic 3	0.2364714	0.0713062	3.32	0.001	.0963108 .376632
Clinic 4	0.3178145	0.0694859	4.57	**0.000*** **	.181232 .454397
Clinic 5	0.3342207	0.090802	3.68	**0.000*** **	.155739 .5127024
Clinic 6	0.154883	0.0991218	1.56	0.119	-.0399523 .3497184
Clinic 7	0.0760362	0.0813913	0.93	0.351	-.0839477 .2360201
Clinic 8	0.2642008	0.0987398	2.68	**0.008*** **	.0701164 .4582852
Clinic 9	0.07927	0.1151943	0.69	0.492	-.1471577 .3056976
Constant	-0.0371157	0.0976226	-0.38	0.704	-.2290041 .1547727

*** indicates significance at 1%

First, effects among GPs were examined and F tests run on the parameters to test the notion that there were no differences between the GPs in terms of not retaining patients in care. Note that the individual GP and clinic effects are in relation to the base case of GP number 1. None of the individual GPs was significantly different from GP number 1, and the proposition that all GPs were the same was accepted (Prob > F = 0.7437). Next, the proposition that all clinics were the same (in terms of not retaining patients in care) was tested. All of the clinics had positive parameters (meaning that all had higher rates of patients no longer in care than GP number 1). Although the regression showed

that some clinics (clinics 4, 5 and 8) performed significantly worse than others, because the parameters were imprecisely estimated (note their very large confidence intervals), the hypothesis that the clinics were all the same was accepted (Prob > F = 0.2162). Finally, F-tests were conducted on the joint significance of the parameters to test the hypothesis that GP and clinic effects were the same. Test results indicated that the difference between the clinics and GPs was significant, and the hypothesis that GP and clinic effects were the same was rejected (Prob > F = 0.000).

These results indicated that it was reasonable to group service outlets into models of care and attribute the outcomes reported in this analysis to the models. Based on this initial regression, a more succinct regression was run grouping GPs and Clinics together. The second regression on patients "no longer in care" controlled for age, gender, months on ART, months since down-referral and care model. Table 5.6 shows that the likelihood of being "no longer in care" was 19 percentage points higher if a patient was in the PHC cohort than if they were in the PPP cohort (p = 0.000).

In addition to the regressions, patients were stratified by months on ART and months since first down-referral (patients can be down-referred more than once) in order to compare stratified outcomes and statues. As Table 5.7 shows, patient retention waned over time in both cohorts as expected, but was consistently lower in the PHC cohort, even within the first 12 months following down-referral. Of the 14 PHC patients no longer in care within the first year following down-referral, 12 never made it to the primary care clinic and vanished from care immediately following down-referral. In addition, the number of PPP patients who were current on ART with suppressed viral loads at the end of the study period was greater in all of the down-referral and treatment strata. Among the most experienced patients in the 24-month down-referral stratum, 91 percent of PPP and 68 percent of PHC patients remained in care and treatment. Patient retention (current on ART at study end) was more robust and statistically significant in the PPP model across all strata in which comparison was possible. Based on these findings, no differential effect associated with time on ART or time since down-referral was observed. Strata definitions and frequencies are located at the bottom of Table 5.7.

Table 5.6 Linear regression: no longer in care

					Num of obs =	451
					F (5, 451) =	9.31
					Prob > F =	0.0000
					R-squared =	0.0842
					Root MSE =	0.34896
Not in Care	Coef.	Robust Std. Err.	t	P>|t|	[95% Conf.	Interval]
Age	-0.0012832	0.0019394	0.66	0.509	-0.0050946	0.0025281
Female	-0.0258916	0.0383078	0.68	0.499	-0.1011756	0.0493924
Months on ART	0.0049485	0.003447	1.44	0.152	-0.0018257	0.0117228
Months down-ref	0.0033345	0.0042438	0.79	0.432	-0.0050055	0.0116745
GP	-0.1888313	0.0327953	5.76	**0.000*** **	-0.2532818	-0.1243808
Constant	0.1109928	0.1186135	0.94	0.35	-0.1221109	0.3440965

*** indicates significance at 1%

Table 5.7 Status and retention stratified by time on ART and time since down-referral

	PHC				PPP				
	SUPP	UN	NIC	Retention	SUPP	UN	NIC	Retention	*p*-Value[26]
Down-referral strata									
12 month strata	50	3	14	79%	59	5	1	98%	**0.000*** **
18 month strata	72	9	25	76%	94	6	8	93%	**0.001*** **
24 month strata	32	6	18	68%	47	3	5	91%	**0.003*** **
ART strata									
24 month strata	51	5	11	84%	55	5	0	100%	**0.001*** **
30 month strata	57	8	24	73%	79	5	5	94%	**0.000*** **
36 month strata	29	3	15	68%	47	2	4	92%	**0.002*** **
42 month strata	17	2	7	73%	18	1	4	83%	0.425
48 month strata	0	0	0	N/A	1	1	1	67%	N/A

Number of subjects by strata and definitions	**PHC**	**PPP**
Down-referral strata		
12 month strata (9 - 14 mos since down-referral)	67	65
18 month strata (15 - 21 mos since down-referral)	106	108
24 month strata (> 22 mos since down-referral)	56	55
ART strata		
24 month strata (≤ 26 mos on ART)	67	60
30 month strata (≥ 27 and ≤ 32 mos on ART)	89	89
36 month strata (≥ 33 and ≤ 38 mos on ART)	47	53
42 month strata (≥ 39 and ≤ 44 mos on ART)	26	23
48 month strata (> 45 mos on ART)	0	3

*** indicates significance at 1%

[26] Significance testing of proportion of patients retained by cohort and strata was performed in STATA using Pearson's chi-square test.

5.2 Costs and cost-effectiveness analysis

Total model cost and average cost per patient in each model of care was calculated and compared. Total and average cost calculations included drug costs (ART and tuberculosis regimens), routine laboratory examinations, outpatient care costs, inpatient care costs, and down-referral care costs. Cost-effectiveness ratios (CERs) and incremental cost-effectiveness ratios (ICERs) were calculated for cost per suppressed patient in down-referral care, cost per suppressed patient, and cost per patient in care. Sensitivity analysis was conducted on potentially influential cost indicators. Finally, the loss on investment (LOI) incurred by each model was calculated and added to the drug, care and laboratory costs to compute an alternative total model cost. The costing tables presented in each cost category provide a side-by-side comparison of costs by model, and are followed by notes that provide further explanation of each table's contents. Additional tables containing the cost computations that underpin the costing tables in this chapter can be found in Appendices II - V.

5.2.1 Drug and regimen costs

Unit drug costs were identical in both models because the government supplies all drugs for both. Drug costs were derived from the State Drug Cost table for the 2007/2008 fiscal year. In most cases, the government has approved multiple versions of the same drug from both branded and generic manufacturers, although prices varied and drugs were procured depending on availability. Because of the variability in drug cost, an average cost per drug was used in this analysis, based on the typical adult dose for all drugs in each of the four regimens. The average cost per drug was summed to calculate an average monthly cost per regimen. Tuberculosis treatment consisted of two regimens: one for the first two months of treatment and a second for the third through sixth month. Only one version of each tuberculosis drug was used and prices were provided by the pharmacist at Tshepong Hospital. Table 1a in Appendix II contains the detailed drug costing exercise.

Total cost per drug regimen for the study period was calculated by multiplying the average regimen cost by the total number of months that patients received the regimen. At R264.07 per month regimen 1a was the least expensive, followed by regimen 1b, 1a "modified" and regimen 2. Most patients were on regimen 1a, which comprised 90 percent of total PHC drug costs and 88 percent of PPP drug costs. Only two patients

were on tuberculosis treatment during the study period, both in the PPP cohort. Total drug costs were higher in the PPP cohort because a greater number of patients were on treatment for longer. The average drug cost per patient month was calculated by dividing the total drug costs by the total number of active patient-months in each cohort. The average drug cost per patient per month was slightly higher in the PPP cohort, owing to the number of patients on regimen 1a modified and the two patients on tuberculosis treatment. Costing Table 1 contains the ART and tuberculosis treatment costing algorithms.

Costing Table 1 ART and TB drug costs

	PHC	**PPP**
ART Regimen Costs		
1.1 Total number of months of Regimen 1a	3297	3665
1.2 Monthly cost of Regimen 1a	R 264.07	R 264.07
1.3 Total cost of Regimen 1a (1.1 x 1.2)	R 870,638.79	R 967,816.55
1.4 Total number of months of Regimen 1a Modified	0	212
1.5 Monthly cost of Regimen 1a Modified	R 481.03	R 481.03
1.6 Total cost of Regimen 1a Modified (1.4 x 1.5)	R 0.00	R 101,978.36
1.7 Total number of months of Regimen 1b	187	51
1.8 Monthly cost of Regimen 1b	R 289.10	R 289.10
1.9 Total cost of Regimen 1b (1.7 x 1.8)	R 54,061.70	R 14,744.10
1.10 Total number of months of Regimen 2	58	20
1.11 Monthly cost of Regimen 2	R 790.68	R 790.68
1.12 Total cost of Regimen 2 (1.10 x 1.11)	R 45,859.44	R 15,813.60
1.13 Total cost of ART (1.3+1.6+1.9+1.12)	**R 970,559.93**	**R 1,100,352.61**
TB Regimen Costs		
1.14 Total number of months on TB treatment (months 1-2)	0	4
1.15 Monthly cost of first two months of TB treatment	R 72.46	R 72.46
1.16 Total number of months on TB treatment (months 3-6)	0	6
1.17 Monthly cost of last four months of TB treatment	R 44.69	R 44.69
1.18 Total cost of TB treatment ((1.14 x 1.15) + (1.16 x 1.17))	**R 0.00**	**R 557.98**
1.19 Total Drug Costs (1.13 + 1.18)	**R 970,559.93**	**R 1,100,910.59**
1.20 Total number of patient-months in the study period	**3542**	**3948**
1.21 Average drug cost per patient per month (1.19 / 1.20)	**R 274.01**	**R 278.85**

Costing Table 1 notes:

1.1	Cumulative number of months that patients received regimen 1a (d4T+3TC+EFV) in the study period;
1.2, 1.5, 1.8, 1.11	Monthly cost of all regimens was obtained from the State Drug Cost table provided by the head hospital pharmacist. Because procurement of drug brands varies, and several versions of the same drug are approved, an average cost for each type of drug was calculated and used in costing all regimens. See **Table 1a. Drug regimen costs in Appendix II** for detailed drug and regimen cost calculations.
1.4	Cumulative number of months that patients received regimen 1a modified (ZDV+3TC+EFV) in the study period; number of months patients received regimen 1a modified.
1.7	Cumulative number of months that patients received regimen 1b (d4T+3TC+NVP) in the study period;
1.10	Cumulative number of months that patients received regimen 2 (ZDV+ddI+LPV/r) in the study period;
1.14	Cumulative number of months that patients received first line (months 1-2) TB treatment (AntiTB) in the study period.
1.15	Cost per month of AntiTB (combination isoniazid and rifampicin) which is given during the first two months of TB treatment. TB treatment costs and regimen data were obtained from the Tshepong Hospital pharmacy. TB treatment costs are based on dosing for adult patients >55Kg, and the calculations are presented in **Table 1a. Drug regimen costs** in **Appendix II.**
1.16	Cumulative number of months that patients received second line (months 3-6) TB treatment.
1.17	Cost per month of Epstar 300 which was given during months 3-6 of standard TB treatment.
1.20	Total number of months that patients received ART during the study period.
1.21	Total ART regimen and TB drug costs by cohort divided by the total number of months patients were enrolled in care and treatment.

5.2.2 Laboratory test costs: CD4 and viral load

South African national HIV treatment guidelines recommend CD4 and viral load laboratory examinations every six months for all patients on ART. Because patients do not typically receive a test precisely every six months and the laboratory data provided was incomplete, the number of laboratory tests per patient was estimated using an algorithm that assigned a number of laboratory tests based on the number of months spent on ART (see section 2.1 of Costing Table 2 notes). For example, a patient who spent 20 months on treatment was estimated to have had three laboratory tests (at 6, 12 and 18 months), as the window around the scheduled 18-month test was 17-22 months. The Principal Specialist and Head of Internal Medicine at Tshepong Hospital validated these treatment windows as reasonable[27].

All routine laboratory monitoring was conducted by the South African National Health Laboratory Service, and paid for by the government for the PHC cohort, as well as for the PPP patients under the partnership agreement. CD4 and viral load unit costs therefore did not vary between cohorts, and were obtained from the laboratory at

[27] Personal communication on July 30, 2009 with Dr. Ebrahim Variava of Tshepong Hospital, Klerksdorp.

Klerksdorp Hospital. Total laboratory costs were higher in the PPP cohort because a greater number of patients spent more time on treatment, requiring more laboratory investigations. Average costs were virtually identical. Table 5.9 below contains the laboratory investigation costing calculation.

Costing Table 2 Laboratory costs

	PHC	PPP
2.1 Estimated number of routine laboratory investigations (CD4 and viral load) for active patients during the study period	529	592
2.2 Cost per CD4 test	R 60.00	R 60.00
2.3 Cost per viral load test	R 318.00	R 318.00
2.4 Cost per routine laboratory investigation (2.2+2.3)	R 378.00	R 378.00
2.5 Total cost of laboratory investigations (2.1 x 2.4)	**R 199,962.00**	**R 223,776.00**
2.6 Total number of visits	**3542**	**3949**
2.7 Average laboratory cost per visit-month (2.5 / 2.6)	**R 56.45**	**R 56.67**

Costing Table 2 notes:

2.1	South African National ART guidelines recommend CD4 and viral load laboratory investigations for patients receiving ART every 6 months. The number of laboratory tests were estimated based on the number of months that patients were active on ART as follows: if the total number of visit months was <4 = 0 labs; 5-10 = 1 lab; 11-16 = 2 labs; 17-22 = 3 labs; 23-28 = 4 labs; >29 = 5 labs
2.2, 2.3	Cost per CD4 and viral load investigation was obtained from the 2007/08 National Health Laboratory Service pricing catalogue provided by the laboratory at Klerksdorp Hospital. Laboratory test and associated cost per test is listed in **Table 2a Routine laboratory examination cost.**
2.6	The total number of visits was the same as the total number of patient-months because this study assumes that each patient has one visit per month.
2.7	Total cost of laboratory tests during the period divided by the total number of visits by cohort.

5.2.3 Care costs

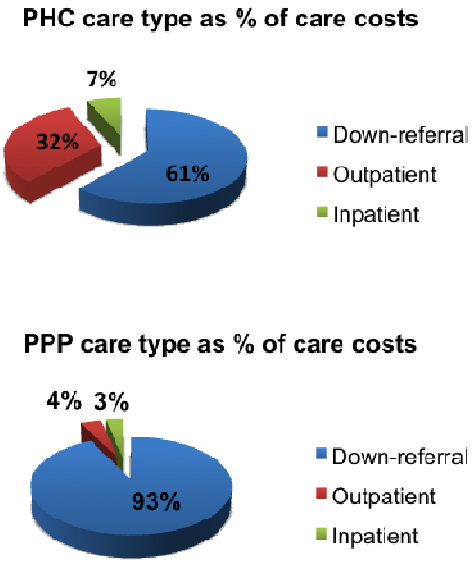
Total care costs comprised three types of care: down-referral care, hospital-based outpatient care, and hospital inpatient care. The number of visits for each type of care was multiplied by the cost per visit, and total care cost was the sum of down-referral (routine), outpatient and inpatient costs. With the exception of inpatient care (the Tshepong Hospital patient-day equivalent was provided by the hospital accounting department), detailed costing algorithms and calculations for a PPP visit, a PHC visit and an outpatient visit are provided in Appendix IV, and discussed in the notes in Costing Table 3.

Total care costs in the PHC cohort were less than half of those observed in the PPP

cohort during the study period, and this difference can be attributed to a couple of factors. First, a routine GP visit in the PPP cohort was nearly 60 percent more expensive than a routine clinic visit in the PHC cohort. This difference can be explained in part because the cost per PHC visit comprised salary costs only, whereas the PPP cost per visit data included non-staff costs including travel, equipment and communications expenses (e.g. cell phones). The inclusion of travel, equipment and communications expenses created a small but necessary degree of incommensurability between the two cost per visit calculations, as the additional costs included in the PPP cost calculation had to do with model-specific inputs that reflected unique features of the PPP model, and the fact that costs were more precisely estimated in the PPP model compared to data available from the PHC. The net result is that the PPP costs are probably over-estimated relative to the PHC. However, this is of little significance to the study because it works against the main finding that, as discussed below, the PPP model had a lower CER than the PHC model on the key performance measure: maintaining virally suppressed patients in down-referral care. In addition, total PPP care costs were higher because more patients remained in care for longer; PPP patients had almost 1000 more down-referral care visits in the study period.

Outpatient care costs were significantly higher in the PHC cohort due to the greater frequency of up-referrals and longer outpatient stays, which resulted in a greater number of total outpatient visits. Outpatient care costs were nearly one-third of the total care costs in the PHC model. Inpatient care costs were slightly higher in the PPP cohort but constituted a small minority of overall care costs in both cohorts.

Figure 5.1 Level of care as percentage of total care costs



The total cost of care in the PHC cohort was R386,069 compared to R803,711 in the PPP cohort. Again, this difference is due to the greater number of PPP patient visits during the period and the higher cost of a down-referral care visit in the PPP model. Average cost per visit per month was R109.00 for PHC patients and R209.87 for PPP patients. Figure 5.1 provides a breakdown of care type as a percentage of overall care costs: 93 percent of PPP care costs took place at the down-referral site, compared to just 72 percent of PHC care costs. Inpatient care did not vary between cohorts because both sets of patients were referred to the Tshepong Hospital - the local secondary care facility – and was a small percentage of total care costs in both cohorts.

Costing Table 3 Down-referral, outpatient and inpatient care costs

	PHC	PPP
3.1 Total number of visits at down-referral site (routine care)	2921	3807
3.2 Estimated cost per down-referral visit	R 81.34	R 202.39
3.3 Total cost of down-referral care (3.1 x 3.2)	R 237,604.96	R 770,498.73
3.4 Total number of visits to hospital-based outpatient clinic	621	142
3.5 Estimated cost per outpatient visit	R 198.13	R 198.13
3.6 Total cost of outpatient specialist care (3.4 x 3.5)	R 123,037.95	R 28,134.28
3.7 Total number of inpatient care days	17	20
3.8 Estimated cost per inpatient day	R 1,495.70	R 1,495.70
3.9 Total cost of inpatient care (3.7 x 3.8)	R 25,426.90	R 29,914.00
3.10 Total cost of care (3.3 + 3.6 + 3.9)	R 386,069.81	R 828,547.19
3.11 Average cost of care per patient per month (3.10 / *1.20*)	R 109.00	R 209.87

Costing Table 3 notes:

3.1 In accordance with South African National ART guidelines this analysis assumes that each active patient has one healthcare visit every month during the study period. This is the number of *visit-months* at the down-referral site (clinic visits for PHC subjects and the GP visits for PPP subjects) for active patients during the study period.

3.2 Routine visit costs for **PHC** patients were calculated using an activity-based costing approach which entailed averaging monthly salary costs (including salaries for nurses, periodic doctor visits, cleaners, clerks, and all other support staff) across all clinics included in this study, and dividing by the number of professional nurses (PN) to arrive at a cost per PN. Because all ART patients see a PN at each monthly visit, the cost / PN was used as a proxy for the total visit cost. The cost / PN was then pro-rated to arrive at a unit cost per visit. The unit cost per clinic visit assumed an average visit length of 30 minutes. This was based on an average of estimates of ART visit length estimates collected in interviews with nurses at participating clinics. The District Manager provided salary data from the Department of Local Government for the 2007/08 fiscal year. The PHC visit calculation can be found in **Appendix IV, Costing Table 3a**. Routine visits for **PPP** patients were based on fixed fee per visit, a fixed data management fee per patient, and costs associated with BRHC support staff (salaries, equipment and travel). BRHC support staff (MER officer, clinical manager, operations manager, and two regional coordinators) estimated the percentage of work time devoted to the PPP model, and their salaries and equipment costs were pro-rated based on estimated time allocated to the model. Only staff that work directly on the program were included (senior management was excluded from the cost calculation). The PPP visit calculation can be found in **Appendix IV, Costing Table 3b.**

3.4 The total number of patient visits that took place at the Wellness Clinic after the *first* time a patient was down-referred. Outpatient visit data were collected from patient files and Wellness Clinic records. The Wellness Clinic operates five days per week and closes at 13h00 on Fridays. It is closed for ART services on weekends and holidays.

3.5 Outpatient visit costs included staff salaries, equipment and supplies for the 2007/08 fiscal year, and the unit cost per visit comprised a combination of fixed and variable costs. Total annual staff salaries (nurses, social worker, pharmacy staff, and all support staff) and annual equipment and supplies costs for the year were divided by the total number of annual visits to arrive at a cost per visit. The cost of doctor time per visit was calculated as a fixed cost using an activity-based costing approach. Salaries of 3 full-time PMOs, 2 full-time MOs and 2 part-time interns were averaged and pro-rated to arrive at a daily salary (annual salary divided by 249, which is the number of work days per year in South Africa). The average daily salary was then divided by the average number of patients seen per day (30 patients per day according to the chief medical officer) to calculate a unit cost of a doctor's time per visit. The total outpatient visit cost was the sum of the unit cost of doctor salaries per visit and staff and equipment cost per visit. Staffing and salary data were provided by the Human Resources Department of the Tshepong Hospital Complex. The total number of outpatient visits per month for 2007/2008 was provided by the Accounting Department of the Tshepong Hospital Complex. Labs and ART costs were removed from the clinic operating costs to avoid double counting. Facility costs and non-ART medicine costs were not included in the calculation. The calculation of the outpatient unit cost per visit can be found in **Appendix IV, Costing Table 3c.**

3.7 The number of days a patient spent in the hospital wards according to patient files. If there was a record of patient admission to the wards, but no discharge summary, then an inpatient stay of two days was assumed (average length of stay on the inpatient wards at Tshepong Hospital). This is likely an underestimate as inpatient admissions are inconsistently noted in patient files at the outpatient clinic, or inpatient referral slips and discharge summaries fall out of files.

3.8 Daily inpatient care cost was based upon Klerksdorp-Tshepong Hospital patient-day equivalent (PDE) cost provided by the Tshepong Hospital Chief Financial Officer. NB: this is the average daily cost per patient and not HIV-specific inpatient costs. The PDE reported by Tshepong is somewhat higher than the North West provincial average of R1,231.00 and the national average of R1,128.00 for 2007/08 as reported in the Health Systems Trust "District Health Barometer" (Day 2009).

3.10 Total cost of care equaled the sum of routine, outpatient and inpatient visit costs.

3.11 Sum of routine, outpatient and inpatient visit costs divided by the total number of patient visit-months in each cohort.

5.2.4 Total cost, average cost and cost per effect

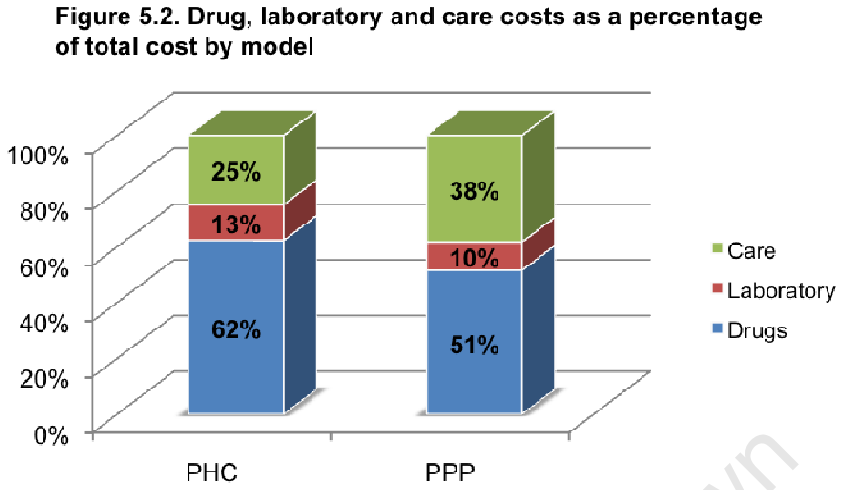
PPP model costs were higher for drugs, laboratory tests and care, and the total model cost for the study period was R2,128,398, compared to a total cost of R1,556,591 for the PHC model. The higher cost of the PPP model is the result of higher down-referral care cost per visit, and the greater number of active patient-months which resulted in more visits, laboratory tests and drug consumption. Due to better patient retention, there were 406 more patient-months on treatment (or approximately 34 patient-years) in the PPP cohort than in the PHC cohort. The average cost per patient per month was approximately R100.00 greater in the PPP model, or R545.38, compared with R439.47 in the PHC model. The total average cost per patient per month was equal to the sum of the average drug, visit and laboratory cost per patient per month.

Costing Table 4 Total and average ART care and treatment costs

	PHC	**PPP**
4.1 Total Drug Costs (1.19)	R 970,559.93	R 1,100,910.59
4.2 Total Laboratory Costs (2.5)	R 199,962.00	R 223,776.00
4.3 Total Care Costs (3.10)	R 386,069.81	R 828,547.19
4.4 Total Care & Treatment Costs (1.19 + 2.5 + 3.10)	**R 1,556,591.74**	**R 2,153,233.78**
4.5 Average Drug Costs (1.21)	R 274.01	R 278.85
4.6 Average Laboratory Costs (2.6)	R 56.45	R 56.67
4.7 Average Care Costs (3.11)	R 109.00	R 209.87
4.8 Average cost per patient per month (1.21 + 2.7 + 3.11)	**R 439.47**	**R 545.38**

Figure 5.2 shows each cost category as a percentage of total cost by model. Drugs constituted the majority of the costs in both models, although they were responsible for a slightly higher percentage of total costs in the PHC cohort. Care costs constituted nearly 40 percent of total cost for the PPP model, compared to just 25 in the PHC model. Laboratory costs comprised the smallest percentage of overall cost in both models.

Figure 5.2 Drug, laboratory and care costs as a percentage of total cost by model



The aim of both HIV treatment models was to maintain virologically suppressed patients in care at the down-referral site, therefore the primary CER calculated in this study was the cost per suppressed patient in care at the down-referral care site at study end. One hundred-ninety patients in the PPP model remained in care with a suppressed viral load at study end compared to 126 in the PHC model, and as a result the PPP model had a more favorable CER, with a total cost per patient of R11,332 compared to R12,353 in the PHC model. In other words, it cost approximately R1000 less to produce a suppressed patient in down-referral care in the PPP model over the course of the study period. The cost per suppressed patient in down-referral care per month was R646.41 in the PPP cohort and R724.00 in the PHC cohort, a difference of R77.58 per month. All CER calculations can be found in Costing Table 5, with additional details on the calculations in the costing table notes that follow. The cost per suppressed patient in down-referral care at the end of study is bolded in Costing Table 5.

CERs were also calculated for the cost per suppressed patient (regardless of care site), and the cost per active patient (still on ART at study end regardless of viral suppression or care site). The total cost per suppressed patient was R10,107.74 for the study period and R579.95 per suppressed patient per month in the PHC cohort, compared to R10,766.17 per suppressed patient and R609.29 per suppressed patient per month in the PPP cohort. Finally, the total cost per active patient was R8,495 for the study period and R10,061 in the PHC and PPP models respectively, and the cost per active patient per month during the study period was R516.45 in the PHC model and R570.85 in the PPP model. In both of the latter scenarios, the PHC model had a lower total and

average monthly CER than the PPP model.

Costing Table 5 Cost-effectiveness ratios

a. Cost per patient in study period	**PHC**	**PPP**
5.1 Number of Suppressed patients at down-referral site at study end	126	190
5.2 Cost per suppressed patient current at d-r site (4.4 / 5.1)	**R 12,353.90**	**R11,332.81.10**
5.3 Number of Suppressed patients at study end	154	200
5.4 Cost per suppressed patient (4.4 / 5.3)	R 10,107.74	R 10,766.17
5.5 Number of active (suppressed & unsuppressed) patients	174	214
5.6 Cost per active patient in study period (4.4 / 5.5)	R 8,945.93	R 10,061.84
b. Cost per patient per month in study period		
5.7 Total number of suppressed and in down-referral care patient-months	2150	3331
5.8 Cost per suppressed patient in down-referral care per month (4.4 / 5.7)	**R 724.00**	**R 646.41**
5.9 Total number of suppressed patient-months	2684	3534
5.10 Cost per suppressed patient per month (4.4 / 5.9)	R 579.95	R 609.29
5.11 Total number of active patient-months	3014	3772
5.12 Cost per active patient per month (4.4 / 5.11)	R 516.45	R 570.85

Costing Table 5.13 notes:

5.1	The number of patients at study end with status “suppressed” and outcome at study end was "current at the down-referral site."
5.2	Ratio of total model cost for the study period to the number of patient in each cohort at study end with status “suppressed” and outcome "current at down-referral site." This describes the optimal case for care in both models both clinically and operationally.
5.3	The number of patients at study end with a status of "suppressed" indicating that they were current on treatment at study end and their most recent viral load result was <400 copies/ml.
5.4	Ratio of total model cost for the study period to the number of patients in each cohort at study end with status “suppressed.”
5.5	The number of patients at study end with status “suppressed” plus those with status “unsuppressed.” Stated differently, this is the total number of patients in each cohort that were still active on ART, regardless of their most recent viral load result.
5.6	Ratio of total model cost for the study period to the number of patients still active on ART at study end (“suppressed” + “unsuppressed”) by cohort.

Incremental cost-effectiveness ratios (ICERs) indicate the “price” of any additional benefit associated with switching from the status quo intervention to a new intervention that may be more expensive but also more effective. ICERs were calculated for each of the three principal outcome scenarios in order to estimate the additional cost and benefit associated with implementing the PPP model versus the PHC model versus a “do nothing” scenario for each of the cost and effect pairings analyzed: cost per suppressed patient in down-referral care, cost per suppressed patient, and cost per active patient (still on ART) at study end. From the ICER calculation for the cost per

patient suppressed and retained in care (Table 5.8), we find that if positioned as competing alternatives, the PHC model would be eliminated from consideration by the principle of *extended dominance,* which occurs when the ICER for a given intervention is higher than the next, more effective one. A rational decision-maker subject to a budget constraint and seeking to maximize the number of suppressed patients in down-referral care would always choose to implement the PPP model with its lower ICER. The PHC model was therefore eliminated from consideration and a final calculation comparing the PPP model to the "do nothing" scenario yielded an ICER of R638.97. If less stringent criteria are applied, the PHC model yielded more favorable ICERs.

The WHO (2005a) suggests that interventions with a CER of less than three-times a country's per capita GDP per DALY are considered *cost-effective*, and interventions with CERs that are less than or equal to per capita GDP per DALY are considered *very cost-effective*. Unfortunately, because the cost per DALY was not calculated in this analysis, we cannot make any assumptions regarding cost-effectiveness based on the WHO threshold. Moreover, we do not know what the South African government's willingness-to-pay threshold is, and therefore cannot make a comparison to a budget threshold or make any specific policy recommendations based on cost parameters. However, as the ICERs reported above indicate, if the outcome of importance is viral suppression and retention in down-referral care, the only economically efficient choices are to do nothing or to implement the PPP model.

Table 5.8 Incremental cost-effectiveness ratios

	Cost (C)	Effect* (E)	ICER
Cost per suppressed patient in down-referral care: Do Nothing v. PHC v. PPP			
Do Nothing	0	0	--
PHC	R 1,556,591.74	2150	R 724.00**
PPP	R 2,128,398.58	3331	R 505.20
Cost per suppressed patient in down-referral care: PPP v. Do Nothing			
Do Nothing	0	0	--
PPP	R 2,128,398.58	3331	R 638.97
Cost per suppressed patient: Do Nothing v. PHC v. PPP			
Do Nothing	0	0	--
PHC	R 1,556,591.74	2684	R 579.95
PPP	R 2,128,398.58	3534	R 672.71
Cost per patient in care: Do Nothing v. PHC v. PPP			
Do Nothing	0	0	--
PHC	R 1,556,591.74	3014	R 516.45
PPP	R 2,128,398.58	3772	R 754.36

*Total patient visit-months

**dominated (extended dominance)

5.2.5 Sensitivity analysis

In this research, obtaining cost data pertaining to ART care services in the public sector and calculating the cost of ART services delivered in a primary care setting was a challenge. Multivariate (two-way) and univariate (one-way) sensitivity analyses were conducted to address uncertainty associated with cost estimates for each care model, as well as to elucidate the influence of potentially important parameters on the ICERs. In the PPP model, sensitivity analysis was conducted on patient enrollment and the cost of the GP fee. Enrollment and the GP fee were co-varied in a two-way sensitivity analysis because of the potentially important effect of increased patient numbers on the variable portion of model costs (support staff salaries, equipment and travel), and in anticipation of future GP fee adjustments. There is precedent for changes in both of these parameters as there has been a significant increase in the number of patients enrolled in the PPP model since data collection for this study ended, and the GP fee has already been adjusted upwards once from R70 per visit to R90 per visit. As shown in Table 5.15, as enrollment increased the ICER dropped relative to the base-case

scenario (based on results from this analysis), and an increase in the GP visit fee increased the ICER. But an increase in enrollment to 1000 patients would result in an overall drop in the ICER even if the visit fee were increased to R100 per visit. The biggest gains would be achieved by scaling up enrollment from between 1000 and 2000 patients (15 percent decrease in the ICER). As of June 30, 2009, the GP fee was R90 and patient enrollment was 1,265[28], which according to this analysis would yield an average cost per patient per month of R518.21 (versus R545.38 observed here), a monthly cost per suppressed patient in down-referral care of R614.22 (versus to R646.42) and an ICER between 10 and 25 percent lower than the base-case ICER reported here.

Table 5.9 Two-way sensitivity analysis: ICERs and percent change relative to the base-case for patient enrolment and GP visit cost in the PPP model

	GP Visit Fee							
Enrolment	**R 70**	**% Δ**	**R 80***	**% Δ**	**R 90**	**% Δ**	**R 100**	**% Δ**
641*	R 472.95	-7%	**R 505.20**	N/A	R 537.43	7%	R 569.66	13.32%
1000	R 383.40	-24%	R 415.63	-17%	R 447.87	-10%	R 480.10	-3.62%
2000	R 303.45	-39%	R 335.68	-32%	R 367.92	-25%	R 400.15	-18.74%
3000	R 276.80	-44%	R 309.03	-37%	R 341.27	-30%	R 373.50	-23.79%

*Base-case

All GPs participating in the PPP were surveyed and asked to estimate the maximum number of PPP patients their practice could accommodate, and the total estimated network capacity was just over 3000 patients. At the current fee of R90 per visit, a scale-up of patient enrolments to two-thirds of PPP model capacity combined with similar patient performance would reduce the ICER by an estimated 25 percent to R367.92 per patient per month. The minimum average cost for this model under these study assumptions was R341.27.

Published estimates of the cost of a PHC visit in South Africa vary considerably, ranging from R45.88 per visit (WHO, 2005b); R120.56 (Cleary, 2005); R131.54 (Day, 2009); and up to R251.56 (Harling, 2007)[29]. Although these visit cost estimates were not all calculated in the same way and are therefore not precisely comparable, they all consistently excluded drug and laboratory costs, and are useful for general comparison, as well as to illustrate the difficulty and variable methodologies used in costing

[28] Personal communication (email) from Mr. Holiness Thebyane, PPP Regional Coordinator with BroadReach Healthcare, on September 2, 2009.

[29] All unit costs listed above were discounted 6 percent annually to approximate 2008 costs for purposes of comparison.

exercises. The PHC visit unit cost used in this study is on the lower end of these published estimates, most likely because it does not include equipment, capital costs or supplies. The WHO estimate appears to be an outlier as it is approximately 60 percent lower than the Cleary (2005) and Day (2009) estimates, and 82 percent lower than the Harling (2007) estimate. PHC visit costs will also vary from site to site, and province to province. Univariate sensitivity analysis was conducted on the PHC visit cost and revealed that if the base-case used in this analysis was indeed an underestimate, then the actual ICER was likely between 10 and 35 percent lower than the base-case ICER (see Table 5.10). The costing model was very sensitive to changes in the PHC visit cost estimates. Further discussion of published unit cost estimates for healthcare visits in South Africa can be found in Chapter 7.

Table 5.10 Univariate sensitivity analysis: PHC visit costs

	Visit cost	ICER	% Δ
Low value	R 60.00	R 557.98	11%
Base-case	**R 81.34**	**R 505.20**	**N/A**
High value	R 100.00	R 459.05	-10%
Higher value	R 150.00	R 335.38	-35%
Highest value	R 200.00	R 211.71	-61%

Finally, one-way sensitivity analysis was conducted on the cost of an outpatient visit to clarify the impact of the significantly larger number of PHC patients receiving care at the hospital-based outpatient clinic at the end of the study period. As shown in Table 5.11 below, the costing model was fairly resilient to changes in outpatient costs: an increase of R50 per visit over the base-case resulted in a drop of only 4 percent in the ICER, and an increase of R100 over the base-case unit cost lowered the ICER just 9 percent.

Table 5.11 Univariate sensitivity analysis: outpatient costs

	Visit Cost	ICER	% Δ
Low value	R 150.00	R 524.72	4%
Base-case	**R 198.13**	**R 505.20**	**N/A**
High value	R 250.00	R 484.16	-4%
Highest value	R 300.00	R 463.88	-9%

In this analysis, average and incremental CERs were strongly influenced by changes in the cost of down-referral care services. This is not surprising given that care costs comprised the second largest portion of total costs in each model, and that the majority

of patients spent their time in down-referral care. Given the likelihood that the PHC visit cost was an underestimate, the actual ICER is probably lower than the base-case estimate found in this study. The ICER was also sensitive to PPP patient enrollment, and greater numbers of patients reduced the monthly incremental cost for PPP care.

Sensitivity analysis was not conducted around ARV drug costs because drug costs were identical in both models, cost data were well documented, there was no indication that first line treatment costs would be reduced further in the near future (generic versions are already available through the government procurement mechanisms), and too few patients were on second line treatment to see any meaningful impact on this analysis. Nonetheless, drug costs comprised more than 50 percent of total model costs in both models and were clearly influential in the ICER calculation. Lower drug costs would significantly lower average and incremental costs per patient per month, and further reductions in second line treatment will be important when greater numbers of patients eventually switch.

5.2.6 Loss on investment

Finally, this research proposed a new cost metric, loss on investment (LOI), for use in the evaluation of HIV treatment programs. LOI assigns a time-adjusted cost to premature program attrition due to HIV-associated mortality, LTF, or stopped treatment. The cost associated with stabilizing a patient on ART over a period of 12 months[30]. Because time from initiation to stabilization varies from patient to patient, a low-end estimate of 8 months and an upper end estimate of 16 months were also calculated to provide a range[31]. The 12-month stabilization cost was R6,680.40, and ranged from R4,453 for eight months to R8,529 for 16 months. The detailed calculation of costs associated with stabilizing a patient on ART at the hospital-based outpatient clinic can be found in Table 5.12a, Appendix V.

Life expectancy data for patients on ART was used to determine the length of the LOI cost penalty period and the annual penalty for stopping treatment prematurely. Because there is no South African or developing country life-expectancy data for people on ART, life-expectancy for the LOI calculation was based on mean survival estimates from the United States for patients with a CD4 nadir of 200 cells/mm^3 and a baseline viral load of

[30] Twelve months was selected as a base-case for the stabilization period because participants in this study were down-referred for the first time after a12 months on average.

[31] Approximately two-thirds of all patients in this study were down-referred between 8 and 16 months.

1,000,000 copies/µl to correspond with national ART initiation guidelines (CD4 must be <200 cells/mm^3). Patients aged 39 or younger had a life expectancy of 12.2 years on ART, compared with 10.9 years for people aged 40 to 49 and 10.2 for people 50 and older (Braithwaite 2005). Because there was no data on risk of falling off ART treatment for reasons other than death, life expectancy was used as a proxy for stopping treatment for any reason in the LOI analysis. Patients in each cohort were split into two groups (≤ 39 years and 40 and older) and the penalty weight spread over 12 years in the younger group, and 10 years in the older. A patient who fell off treatment within the first year following down-referral (i.e. between 12 and 23 months after down-referral), incurred a penalty of R6,680.40 (equal to the 100 percent of stabilization cost), and each subsequent year was weighted so that the penalty decreased toward zero as the patient approached the life expectancy threshold of 12 years in the younger strata, and 10 years in the older one. Stabilization cost and weights were multiplied by the number of patients who fell off in a given year following down-referral and by the weight associated with the year the patient died, was lost, or stopped taking ART. Costing Table 6 contains the aggregate LOI by care model as well as a delineation of LOI by cause. Costing Table 6b (PHC) and 6c (PPP) in Appendix V contains the detailed LOI calculations for each cohort and age group.

In the PHC model, LOI costs associated with premature patient attrition ranged from R226,607 and R433,981 in the low and high-end scenarios respectively, and equaled R339,910 in the base-case scenario. LOI costs in the PPP cohort ranged from R52,422 to R100,396, and equaled R78,634 in the base-case, or more than four times less than PHC LOI (Costing Table 6). LOI costs were higher in the PHC model because fewer patients were retained and patients spent less time on treatment. LOI costs were broken down further by cause. LOI was higher in the PHC model for reason of death, lost to follow-up and stopped ART. LOI due to lost to follow-up constituted more than half of total LOI in the PHC model. Premature death was the largest contributor to LOI in the PPP model. Finally, the total LOI was averaged across all patients who were active at the end of the study in order to get a sense of how much of the average patient cost is driven by premature patient attrition in each model of care. Average LOI per active patient in the PHC model was more than twice the LOI per patient in the PPP model.

Costing Table 6 Loss on Investment (LOI)

	PHC	PPP
6.1 LOI lower estimate (8 months to stabilize)	R 226,607.27	R 52,422.92
6.2 LOI base-case estimate (12 months to stabilize)	**R 339,910.90**	**R 78,634.38**
6.3 LOI upper estimate (16 months to stabilize)	R 433,981.20	R 100,396.44
6.4 LOI due to death (base-case)	R 40,531.81	R 38,934.59
6.5 LOI due to LTF (base-case)	R 282,022.20	R 30,237.92
6.6 LOI due to Stopped ART (base-case)	R 17,356.89	R 9,461.88
6.7 Average LOI per active patient at study end (6.2 / 5.5)	**R 99.75**	**R 44.21**

Costing Table 6 notes:

6.1 The estimated LOI based on costs associated with 8 months required to stabilize a patient on ART

6.2 The estimated LOI based on costs associated with 12 months required to stabilize a patient on ART

6.3 The estimated LOI based on costs associated with 16 months required to stabilize a patient on ART

6.4 The total LOI due to death during the study period. This was calculated using the base-case estimated cost to stabilize a patient.

6.5 The total LOI due to LTF during the study period. This was calculated using the base-case estimated cost to stabilize a patient.

6.6 The total LOI due to patients who elected to stop ART during the study period. This was calculated using the base-case estimated cost to stabilize a patient.

6.7 LOI as a cost per patient on ART at study end.

Finally, total base-case LOI was added to the other principal cost elements to calculate an alternative total cost per model for the study period. With the LOI costs included, the PHC model remained less costly than the PPP model over the course of the study period. However, in comparison to other principal model costs, LOI constituted 18 percent of total PHC model costs, and were nearly equal to the total cost of care (Costing Table 7 below). By comparison, LOI comprised only 4 percent of total PPP model costs.

Costing Table 7. Total and ART care and treatment costs including LOI

	PHC	% of total	PPP	% of total
7.1 Total Drug Costs (1.19)	R 970,559.93	51%	R 1,100,910.59	49%
7.2 Total Laboratory Costs (2.5)	R 199,962.00	11%	R 223,776.00	10%
7.3 Total Care Costs (3.10)	R 386,070.59	20%	R 828,547.19	37%
7.4 Total LOI (6.2)	R 339,910.90	18%	R 78,634.38	4%
7.5 Total Costs with LOI (sum 7.1 - 7.4)	**R 1,896,503.42**	**100%**	**R 2,231,868.16**	**100%**

5.2.7 Counterfactual

In this study the PPP and PHC models were positioned as competing alternatives, but in reality the PPP model was implemented to boost down-referral capacity, not replace the PHC model, and in reality the two continue to coexist. As an exercise in modeling reality, and to explore a scenario where the PPP model never existed, a simulated PHC-only treatment program was compared -- in terms of patient outcomes and costs -- to the reality scenario where both models operate together. No sophisticated modeling was used for this exercise. The "No PPP" scenario assumed all PPP patient outcomes and costs would be identical those observed in the PHC cohort, and PHC outcomes, and costs were simply doubled. In the "PHC + PPP" scenario, outcomes and costs from both models were combined. Costing Table 8 contains scenario outcomes, costs, CER and ICER (cost per patient retained in care). The third column in the table contains the difference in outcomes and costs between the two scenarios.

Costing Table 8. Counterfactual

		Scenario: No PPP	**Scenario: PHC + PPP**	Δ
8.1	ART Retention	344	386	42
8.2	ART Retention at down-referral site	266	336	70
8.3	Suppressed	308	354	46
8.4	Suppressed at down-referral site	252	316	64
8.5	Total patient-months	7084	7490	406
8.6	Total cost	R 3,113,183.48	R 3,709,825.52	R 596,642.04
8.7	CER: Average cost per patient per month (8.6 / 8.5)	R 439.47	R 495.30	R 55.83
8.8	Total patient months suppressed and down-referred	4300	5481	2362
8.9	CER: Average cost per suppressed and down-referred patient (8.6 / 8.8)	R 724.00	R 676.85	R47.15
8.10	ICER (Δ**8.6 / Δ8.8)**	N/A	N/A	R 252.60

The combined performance of the PHC and PPP models compared to the PHC-only scenario resulted in an additional 42 patients retained on ART, an additional 406 patient-months (34 patient years) of treatment, and an additional 2,362 patient-months

of treatment where patients were suppressed and in care at the down-referral site, for a marginally higher cost per patient. In terms of outcomes, patients in Matlosana appear to have benefitted from the presence of the PPP model, and PHCs have had to manage far fewer patients. The additional cost per patient-month for better outcomes as a result of dual-implementation of the models was just R252.60.

Appendix I: Chi square tables for Table 1

Table 1a. Patients suppressed by cohort relative to total cohort

Cohort	supp_all 0	1	Total
0	75 32.75	154 67.25	229 100.00
1	28 12.28	200 87.72	228 100.00
Total	103 22.54	354 77.46	457 100.00

Pearson chi2(1) = 27.4219 Pr = 0.000

Table 1b. Patient suppressed by cohort relative to current patients

Cohort	supp_cohort 0	1	Total
0	18 10.47	154 89.53	172 100.00
1	14 6.54	200 93.46	214 100.00
Total	32 8.29	354 91.71	386 100.00

Pearson chi2(1) = 1.9303 Pr = 0.165

Table 1c. Patients unsuppressed by cohort relative to total cohort

Cohort	unsupp_all 0	1	Total
0	211 92.14	18 7.86	229 100.00
1	214 93.86	14 6.14	228 100.00
Total	425 93.00	32 7.00	457 100.00

Pearson chi2(1) = 0.5190 Pr = 0.471

Table 1d: Patients unsuppressed by cohort relative to current patients

Cohort	unsupp 0	1	Total
0	154 89. 53	18 10. 47	172 100. 00
1	200 93. 46	14 6. 54	214 100. 00
Total	354 91. 71	32 8. 29	386 100. 00

Pearson chi2(1) = 1. 9303 Pr = 0. 165

Table 1e. Patients no longer in care by cohort relative to total cohort

Cohort	nic 0	1	Total
0	172 75. 11	57 24. 89	229 100. 00
1	214 93. 86	14 6. 14	228 100. 00
Total	386 84. 46	71 15. 54	457 100. 00

Pearson chi2(1) = 30. 6102 Pr = 0. 000

Table 1f. Patient deaths relative to the number no longer in care

dead	Cohort 0	1	Total
0	50 87. 72	7 12. 28	57 100. 00
1	7 50. 00	7 50. 00	14 100. 00
Total	57 80. 28	14 19. 72	71 100. 00

Pearson chi2(1) = 10. 1015 Pr = 0. 001

Table 1g. Lost to follow-up relative to the number no longer in care

Cohort	ltf 0	1	Total
0	10	47	57
	17. 54	82. 46	100. 00
1	9	5	14
	64. 29	35. 71	100. 00
Total	19	52	71
	26. 76	73. 24	100. 00

Fisher's exact = 0. 001
1-sided Fisher's exact = 0. 001

Table 1h. Stopped ART relative to the number no longer in care

Cohort	stopped 0	1	Total
0	54	3	57
	94. 74	5. 26	100. 00
1	12	2	14
	85. 71	14. 29	100. 00
Total	66	5	71
	92. 96	7. 04	100. 00

Fisher's exact = 0. 254
1-sided Fisher's exact = 0. 254

Table 1i. Down-referral retention

Cohort	retain_dr 0	1	Total
0	96	133	229
	41. 92	58. 08	100. 00
1	25	203	228
	10. 96	89. 04	100. 00
Total	121	336	457
	26. 48	73. 52	100. 00

Pearson chi2(1) = 56. 2426 Pr = 0. 000

Table 1j. Care and treatment retention

Cohort	retaint_art 0	1	Total
0	57	172	229
	24. 89	75. 11	100. 00
1	14	214	228
	6. 14	93. 86	100. 00
Total	71	386	457
	15. 54	84. 46	100. 00

Pearson chi2(1) = 30. 6102 Pr = 0. 000

Table 1k. Ratio of patients in down-referral care relative to total in care

Cohort	downrefsite 0	1	Total
0	39	133	172
	22. 67	77. 33	100. 00
1	11	203	214
	5. 14	94. 86	100. 00
Total	50	336	386
	12. 95	87. 05	100. 00

Pearson chi2(1) = 26. 0012 Pr = 0. 000

Table 1l. Patients in outpatient care relative to total cohort

Cohort	outpt 0	1	Total
0	190	39	229
	82. 97	17. 03	100. 00
1	217	11	228
	95. 18	4. 82	100. 00
Total	407	50	457
	89. 06	10. 94	100. 00

Pearson chi2(1) = 17. 4691 Pr = 0. 000

Table 1m. Patients in outpatient care relative to all current patients

Cohort	outpt_current 0	1	Total
0	133 77. 33	39 22. 67	172 100. 00
1	203 94. 86	11 5. 14	214 100. 00
Total	336 87. 05	50 12. 95	386 100. 00

Pearson chi2(1) = 26. 0012 Pr = 0. 000

Table 1n. Suppressed patients in care at down-referral site relative to total cohort

Cohort	supp_dr 0	1	Total
0	103 44. 98	126 55. 02	229 100. 00
1	38 16. 67	190 83. 33	228 100. 00
Total	141 30. 85	316 69. 15	457 100. 00

Pearson chi2(1) = 42. 9246 Pr = 0. 000

Table 1o. Suppressed patients in care at down-referral site relative to all current patients

Cohort	supp_dr 0	1	Total
0	46 26. 74	126 73. 26	172 100. 00
1	24 11. 21	190 88. 79	214 100. 00
Total	70 18. 13	316 81. 87	386 100. 00

Pearson chi2(1) = 15. 4897 Pr = 0. 000

Table 1p. Suppressed patients in outpatient care relative to total cohort

Cohort	supp_outpt 0	1	Total
0	201 87. 77	28 12. 23	229 100. 00
1	218 95. 61	10 4. 39	228 100. 00
Total	419 91. 68	38 8. 32	457 100. 00

Pearson chi2(1) = 9. 2139 Pr = 0. 002

Table 1q. Suppressed patients in outpatient care relative to current patients

Cohort	supp_outpt 0	1	Total
0	144 83. 72	28 16. 28	172 100. 00
1	204 95. 33	10 4. 67	214 100. 00
Total	348 90. 16	38 9. 84	386 100. 00

Pearson chi2(1) = 14. 4725 Pr = 0. 000

Table 1r. Suppressed patients in outpatient care relative to total in outpatient care

Cohort	outpt_supp 0	1	Total
0	11 28. 21	28 71. 79	39 100. 00
1	1 9. 09	10 90. 91	11 100. 00
Total	12 24. 00	38 76. 00	50 100. 00

Pearson chi2(1) = 1. 7186 Pr = 0. 190

Appendix II: Drug regimen costs

Costing Table 1a. Drug regimen costs

	Regimen Name	Drug Names and Dose	Average Cost
	Regimen 1a		
1a.1		d4T 40MG	R 42.47
1a.2		3TC 150MG	R 73.25
1a.3		EFV 600MG	R 148.35
1a.4	**Average regimen cost / month (sum 1a.1 - 1a.3)**		**R 264.07**
	Regimen 1a Modified		
1a.5		ZDV 300MG	R 259.42
1a.6		3TC 150MG	R 73.25
1a.7		EFV 600MG	R 148.35
1a.8	**Average regimen cost / month (sum 1a.5 - 1a.7)**		**R 481.02**
	Regimen 1b		
1a.9		d4T 40MG	R 42.47
1a.10		3TC 150MG	R 73.25
1a.11		NVP 200MG	R 173.38
1a.12	**Average regimen cost / month (sum 1a.9 - 1a.11)**		**R 289.10**
	Regimen 2		
1a.13		ZDV 300MG	R 259.42
1a.14		ddI 400MG	R 212.19
1a.15		LPV/r 400/100MG	R 319.07
1a.16	**Average regimen cost / month (sum 1a.13 - 1a.15)**		**R 790.68**
	TB Regimen		
1a.17		First two months: AntiTB	R 72.46
1a.18		Months 3-6: Epstar 300	R 44.69
1a.19	**Cost of 6 month course (sum 1a.17 - 1a.18)**		**R 323.68**

Appendix III: Drug laboratory examination costs: CD4 and viral load

Costing Table 2a. Routine laboratory examination cost

	Test Name	Cost per test
2a.1	EasyQ Viral Load	R 318.00
2a.2	CD4 PLG	R 60.00
2a.3	**Total cost (2a.1 + 2a.2)**	**R 378.00**

Appendix IV: Estimation of down-referral and outpatient care costs

Costing Table 3a. PHC cost per patient-month

	Clinic	Annual Salary 2007/2008	Number of professional nurses (PN)	Salary / PN
3a.1	Alabama	R 918,200	4	R 229,550.00
3a.2	Botshabelo	R 4,132,000	13	R 317,846.15
3a.3	Grace Mokgomo	R 4,132,000	12	R 344,333.33
3a.4	Jouberton	R 4,132,000	17	R 243,058.82
3a.5	Kanana	R 820,000	4	R 205,000.00
3a.6	Khuma	R 918,000	4	R 229,500.00
3a.7	Gateway	R 1,250,000	5	R 250,000.00
3a.8	Orkney	R 1,200,000	3	R 400,000.00
3a.9	Park Street	R 1,600,200	6	R 266,700.00
3a.10	Stilfontein	R 1,408,000	2	R 704,000.00
3a.11	Tigane	R 4,123,000	11	R 374,818.18
3a.12	Average salary / PN (average 3a.1-3a.11)			R 324,073.32
3a.13	Average salary / day (3a.12 / 249[32])			R 1,301.50
3a.14	Average salary / hour (3a.13 / 8[33])			R 162.69
3a.15	**Average salary / visit (3a.14 / 2[34])**			**R 81.34**

Costing Table 3b. PPP cost per patient-month

Role	% Time on PPP	Salaries	Transport -ation	Laptop	Cell	3G	Total
Operations Manager	33%	R 10,740	R 4,480	R 206	R 495	R 165	R 16,086
Regional Coordinator #1	100%	R 13,992	R 1,627	R 625	R 1,500	R 500	R 18,244
Regional Coordinator #2	100%	R 7,000	R 0	R 625	R 1,500	R 500	R 9,625
MER Officer	13%	R 1,470	R 0	R 0	R 0	R 0	R 1,470
Clinical Manager	10%	R 3,917	R 0	R 62.50	R 150	R 50	R 4,179.50
SUM		**R 33,202**	**R 6,107**	**R 1,456**	**R 3,495**	**R 1,165**	**R 49,605**
% of Total		67%	12%	3%	7%	2%	**100%**
Number of active patients on ART on 31 Mar 08							641
Average monthly cost per patient (total monthly cost / number active patients)							R 77.39
Monthly data management fee per patient							R 45.00
GP fee per monthly patient visit							R 80.00
TOTAL monthly PPP visit cost							**R 202.39**

[32] 249 is the total number of working days per year in South Africa

[33] 8 hours of work per day

[34] Based on interviews with nurses at all of the PHCs, visits lasted an average of 30 minutes; the salary per hour is divided by 2 to calculate the cost per 30 minutes.

Costing Table 3c. 2007/2008 Hospital-based outpatient clinic visit cost

Total outpatient visits by month

	Month	Total visits
3c.1	April 2007	4218
3c.2	March 2007	3795
3c.3	June 2007	3692
3c.4	July 2007	4003
3c.5	August 2007	4504
3c.6	September 2007	3683
3c.7	October 2007	4424
3c.8	November 2007	4313
3c.9	December 2007	2482
3c.10	January 2008	4647
3c.11	February 2008	4113
3c.12	March 2008	3972
3c.13	**Sum (3c.1 - 3c.12)**	**47846**

2007/08 fiscal year outpatient clinic expenditures

3c.14	Supplies, equipment and stationery	R 180,319.29
3c.15	Staff Salaries	R 4,084,199.00
3c.16	Total outpatient costs (3b.1 +3b.2)	R 4,264,518.29
3c.17	**Average staff and equipment cost per visit (3b.3 / 3c.13*)***	**R 89.13**

2007/08 fiscal year outpatient doctor salaries

	Doctor Level	Annual Salary	Number employed	Total Salary
3c.18	PMO	R 520,002.00	3	R 1,560,006.00
3c.19	MO	R 357,524.91	2	R 715,049.82
3c.20	Intern	R 223,472.00	0.75	R 167,604.00
3c.21	**Total doctor salaries**			**R 2,442,659.82**

Doctor salary per visit

3c.22	Average doctor salary (3c.21 / 3)	R 814,219.94
3c.23	Average doctor salary /day (3c.22 / 249[35])	R 3,269.96
3c.24	**Average doctor salary / visit (3c.23 / 30[36])**	**R 109.00**

Total cost per outpatient visit for 2007/08 fiscal year

3c.25	**Cost per outpatient visit (3c.17 + 3c.24)**	**R 198.13**

[35] 249 is the total number of working days per year in South Africa

[36] 30 is the average number of patients seen per day by doctors at the Wellness outpatient clinic according to interviews conducted by the author with three of the doctors.

Appendix V: Loss on Investment

Costing Table 6a. Total cost of producing a stable adult patient on ART at the hospital-based outpatient clinic

6a.1 # of months before down-referral (time until stable)	8	12	16
6a.2 Outpatient care costs (6a.1 x 3.5)	R 1,585.04	R 2,377.56	R 3,170.08
6a.3 Regimen 1a costs (6a.1 x 1.2)	R 2,112.56	R 3,168.84	R 4,225.12
6a.4 Laboratory examinations required in the period	2	3	3
6a.5 Laboratory exam costs (6a.4 x 2.4)	R 756.00	R 1,134.00	R 1,134.00
6a.6 Total cost of stabilizing patient on ART	**R 4,453.60**	**R 6,680.40**	**R 8,529.20**

Costing Table 6b. PHC Loss on investment calculation

LOI: Ages ≤39 years (life expectancy = 12.2 yrs)														
Months on ART	**# patients no longer on ART**	**Penalty (% discounted for time on ART)**	**Cost per Stable Patient (Lower estimate)**	**LOI (Lower)**	**Cost per Stable Patient (Mean estimate)**	**LOI (Mean)**	**Cost per Stable Patient (Upper estimate)**	**LOI (Upper)**	**# LTF**	**LOI d/t LTF (mean)**	**# Deaths**	**LOI d/t death (mean)**	**# Stopped**	**LOI d/t stopped (mean)**
12 - 23	5	1	4,453.60	22268	6,680.40	33402	8,529.20	42,646.00	4	26,721.60	1	6,680.40	0	0.00
24 - 35	17	0.91	4,453.60	68,828.36	6,680.40	103,242.55	8,529.20	131,814.91	14	85,023.27	1	6,073.09	2	12,146.18
36 - 47	7	0.82	4,453.60	25,506.98	6,680.40	38,260.47	8,529.20	48,849.05	6	32,794.69	1	5,465.78	0	0.00
48 - 59	0	0.73	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
60 - 71	0	0.64	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
72 - 83	0	0.55	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
84 - 95	0	0.45	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
96 -107	0	0.36	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
108 - 119	0	0.27	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
120 - 131	0	0.18	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
132 - 143	0	0.09	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
≥144	0	0	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
Total ≤39 yrs	29			R 116,603		R 174,905		R 223,310	24	R 144,540	3	R 18,219	2	R 12,146

Costing Table 6b. PHC Loss on investment calculation (continued)													
LOI: Ages >39 years (life expectancy = 10.9 (40-49 yrs) and 10.2 (>50 years))													
Months on ART	**# no longer on ART**	**Penalty (% discounted for time on ART)**	**Cost per Stable Patient (lower)**	**LOI (lower)**	**Cost per Stable Patient (base-case)**	**LOI (base-case)**	**Cost per Stable Patient (upper)**	**LOI (upper)**	**# LTF**	**LOI d/t LTF (base-case)**	**# Deaths**	**LOI d/t death (base-case)**	**# Stopped**	**LOI d/t stopped (base-case)**
12 - 23	4	1	4,453.60	17,814.40	6,680.40	26,721.60	8,529.20	34,116.80	4	26,721.60	0	0.00	0	0.00
24 - 35	18	0.89	4,453.60	71,346.67	6,680.40	107,020.01	8,529.20	136,637.78	16	95,128.90	2	11,891.11	0	0.00
36 - 47	6	0.78	4,453.60	20,842.85	6,680.40	31,264.27	8,529.20	39,916.66	3	15,632.14	2	10,421.42	1	5,210.71
48 - 59	0	0.67	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
60 - 71	0	0.56	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
72 - 83	0	0.45	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
84 - 95	0	0.34	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
96 -107	0	0.23	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
108 - 119	0	0.11	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
≥120	0	0	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
Total >39 yrs				R 110,004		R 165,006		R 210,671	23	R 137,483	4	R 22,313	1	R 5,211
TOTAL PHC LOI				**R 226,607**		**R 339,911**		**R 433,981**	**47**	**R 282,022**	**7**	**R 40,532**	**3**	**R 17,357**

Costing Table 6c. PPP Loss on investment calculation

LOI: Ages ≤39 years (life expectancy = 12.2 yrs)

Months on ART	# no longer on ART	Penalty (% discounted for time on ART)	Cost per Stable Patient (lower)	LOI (lower)	Cost per Stable Patient (base-case)	LOI (base-case)	Cost per Stable Patient (upper)	LOI (upper)	# LTF	LOI d/t LTF (base-case)	# Deaths	LOI d/t death (base-case)	# Stopped	LOI d/t stopped (base-case)
12 - 23	0	1	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
24 - 35	4	0.91	4,453.60	16,194.91	6,680.40	24,292.36	8,529.20	31,015.27	4	24,292.36	0	0.00	0	0.00
36 - 47	1	0.82	4,453.60	3,643.85	6,680.40	5,465.78	8,529.20	6,978.44	0	0.00	1	5,465.78	0	0.00
48 - 59	0	0.73	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
60 - 71	1	0.64	4,453.60	2,834.11	6,680.40	4,251.16	8,529.20	5,427.67	0	0.00	0	0.00	1	4,251.16
72 - 83	0	0.55	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
84 - 95	0	0.45	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
96 -107	0	0.36	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
108 - 119	0	0.27	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
120 - 131	0	0.18	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
132 - 143	0	0.09	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
≥144	0	0	4,453.60	0	6,680.40	0	8,529.20	0.00	0	0.00	0	0.00	0	0.00
Total ≤39 yrs	6			R 22,673		R 34,009		R 43,421	4	R 24,292	1	R 5,466	1	R 4,251

Costing Table 6c. PPP Loss on investment calculation (continued)														
LOI: Ages >39 years (life expectancy = 10.9 (40-49 yrs) and 10.2 (>50 years))														
Months on ART	**# no longer on ART**	**Penalty (% discounted for time on ART)**	**Cost per Stable Patient (lower)**	**LOI (lower)**	**Cost per Stable Patient (base-case)**	**LOI (base-case)**	**Cost per Stable Patient (upper)**	**LOI (upper)**	**# LTF**	**LOI d/t LTF (base-case)**	**# Deaths**	**LOI d/t death (base-case)**	**# Stopped**	**LOI d/t stopped (base-case)**
12 - 23	0	1	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
24 - 35	4	0.89	4,453.60	15,854.82	6,680.40	23,782.22	8,529.20	30,363.95	1	5,945.56	3	17,836.67	0	0.00
36 - 47	4	0.78	4,453.60	13,895.23	6,680.40	20,842.85	8,529.20	26,611.10	0	0.00	3	15,632.14	1	5,210.71
48 - 59	0	0.67	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
60 - 71	0	0.56	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
72 - 83	0	0.45	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
84 - 95	0	0.34	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
96 -107	0	0.23	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
108 - 119	0	0.11	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
≥120	0	0	4,453.60	0.00	6,680.40	0.00	8,529.20	0.00	0	0.00	0	0.00	0	0.00
Total >39 yrs	8			R 29,750		R 44,625		R 56,975	1	R 5,946	6	R 33,469	1	R 5,211
TOTAL PPP LOI				**R 52,423**		**R 78,634**		**R 100,396**	**5.0**	**R 30,238**	**7.0**	**R 38,935**	**2.0**	**R 9,462**

Chapter 6

Qualitative Patient Survey

6.1 Methods

The aim of this qualitative patient survey was three-fold: first and foremost, to provide an important opportunity to ground the interpretation of the quantitatively focused outcomes and cost-effectiveness analyses in this research in real patient experience. Secondly, it was conducted as a means of exploring the reasons why patients selected the PPP or the PHC models. Thirdly, the survey intended to illuminate patient perceptions of their own health and the quality of care they receive, as well as any important differences between the models of care that were not apparent from the quantitative analysis. This chapter presents the survey methods, results, and a discussion of the findings.

6.1.1 Survey Tool

The survey questionnaire was adapted from the Khayelitsha Select Panel Survey (ASRU, 2008) conducted by the AIDS in Society Research Unit at the University of Cape Town amongst people on ART in Khayelitsha. Some questions were modified slightly in order to fit the different care and treatment models in this study. The "health state" measure was adapted from the EuroQoL EQ-5D (Oppe, 2008), which has been validated for use in South Africa. Once finalized, the questionnaire was translated into Setswana, and back translated into English to ensure accurate translation.

Table 6.1 Survey topics

Demographics	Health
Employment	Adherence
Education	Treatment support
Outlook and beliefs	Quality of care and service delivery

The first three sections of the survey covered demographic, education and employment data, as well as patient's general outlook on life. The second part of the survey was designed to capture patient experience relating to the key ART service provision elements including: clinical services and program monitoring (laboratory tests, medicines, clinical visits); patient support services (adherence interventions, training/information, psychosocial support services, patient follow-up in cases of non-adherence or other problems); as well as perceptions about the quality of service provision (timeliness of services, friendliness and helpfulness of staff) and quality of life. Table 6.1 outlines the topics covered in the survey. The English and Setswana versions

of the questionnaire can be found in Appendices I and II, respectively. All of the survey questions were multiple choice with the exception of three in which patients were asked to indicate their feelings using a visual analogue scale (VAS), and several open ended questions pertaining to demographics (education, employment and income), and reasons for their choice of down-referral site.

6.1.2 Eligibility

In order to be eligible for the survey, patients had to be enrolled in this study, current (at the time) on treatment, and receiving care at the down-referral site (GP or PHC). Of those eligible, a total of 50 patients from each cohort (i.e. those opting for down-referral to PHC clinics or GPs respectively) were selected at random to participate in the study. Patients were then contacted by telephone by a research assistant to schedule interviews. In cases where zero patients were selected from certain clinics or GPs, an effort was made to recruit at least one patient from these sites in order to obtain a more inclusive and representative sample.

6.1.3 Interviews

The interviews (including the process of obtaining consent) were conducted in Setswana by native Setswana-speaking research assistants. Neither research assistant was affiliated with or employed by the PPP or the Department of Health at the time. Both research assistants were certified HIV counselors, and were trained in patient recruitment, administering the survey, and post-survey data management by the author. Training was conducted in accordance with the Survey Study Guide (see Appendix III), which was developed by the author specifically for this activity. Interviews were held by appointment either at the Wellness Clinic at Tshepong Hospital or at a local PHC. All interviews were conducted by one of the research assistants in a private room, and they typically lasted 35 minutes. Research assistants completed the questionnaires during the interview, and were asked to conduct quality audits on all forms following the completion of interview. All survey participants were reimbursed for travel costs (to and from the interview site), and were provided with a voucher for R50.00 to a local grocery store as compensation for their time.

6.1.4 Analysis

Thirty-nine patients from the PHC and 35 patients from the PPP cohorts completed

interviews. Of those initially selected for participation in the survey, none refused to participate, and 26 either missed their interview appointment and did not reschedule or could not be contacted. Data from these questionnaires were entered manually into an excel database by two data capturers. Once data entry was completed, the data capturers switched forms and checked ten percent of all entered data for accuracy. All quantitative data were then entered into STATA (version 10.0) to calculate means, medians and frequencies. Significance testing for mean differences was conducted using Pearson's chi-square and *t*-tests.

6.1.5 Ethics approval

Ethics approval was granted by the ethics review committee of the Centre for Social Science Research at the University of Cape Town, and from the Matlosana sub-District ethics review board. In addition, approval letters were obtained directly from the Tshepong Hospital Complex CEO, and from BRHC.

6.2 Results

6.2.1 Demographic indicators

Both groups were similar in terms of gender ratio, age, educational attainment, and employment status (see Table 6.2). Incomes appeared to be slightly higher within the PHC cohort, although not significantly so, as the number of respondents on this question was relatively few.

Table 6.2 Socio-economic and demographic profile

	PHC	PPP
Participants		
Male	10	10
Female	29	25
Total	39	35
Age		
Mean years	39	39
Educational Attainment		
Mean grade completed	8	7
Grade 0-5 complete	19%	29%
Grade 6-11 complete	57%	58%
Grade 12 or > complete	24%	13%
Employment and income		
Employed	8	9
Unemployed	28	25
Household income (mean)	R5,442 (n=9)	R3,151 (n=10)
Household income (median)	R3,000	R1,450

No significant differences in educational attainment were reported between the two patient cohorts, although more of the PHC cohort reported completing grade 12 or beyond. Most patients interviewed were unemployed in both cohorts, although household incomes were higher in the PHC cohort. However, the number of respondents who answered income questions was few in both cohorts. This may have been due to a somewhat confusing format in the questionnaire, which the research associates found confusing, or to reluctance on the part of participants to discuss their finances. The pool of patients interviewed from the PHC cohort were in care at nine of the eleven clinics included in this study; the largest number of participating patients came from Gateway Clinic (10, or 26 percent). At least one patient from all 19 GPs was interviewed; the GP with the largest number of participating patients had 7 patients (or approximately 20 percent).

6.2.2 Outlook, beliefs and HIV knowledge

This section contained four questions intended to explore potential differences between the patient groups in terms of overall happiness and sense of control over the events in their lives, as well as two commonly held traditional beliefs. Both cohorts were similar in terms of overall happiness, but the participants from the PPP cohort were more likely to indicate that they have "total control" or "control most things" in their lives compared to participants from the PHC cohort (*p=0.01*). Next, patients were asked to indicate whether or not they agreed with two statements that corresponded to commonly held beliefs:

Belief 1: "HIV was invented by White people to kill Black people."

Belief 2: "If a young adult dies of illness, their family should suspect witchcraft."

The PHC cohort was significantly more likely to agree with the possibility that the first belief was true or might be true (*p=0.016*), while the PPP cohort was more likely to agree that the second belief was "always" or "sometimes" true (*p=0.049*). Overall, theories regarding the origin of the HIV epidemic and the role of witchcraft in premature death were prevalent in both groups. Linear regressions revealed a relationship between an internal locus of control and belief in the possibility of witchcraft in premature deaths (p=0.003) in the combined patient sample. Within cohorts the relationship was only significant in the PPP cohort (p=0.015). No statistically significant correlation was found between locus of control and acceptance of Belief 1.

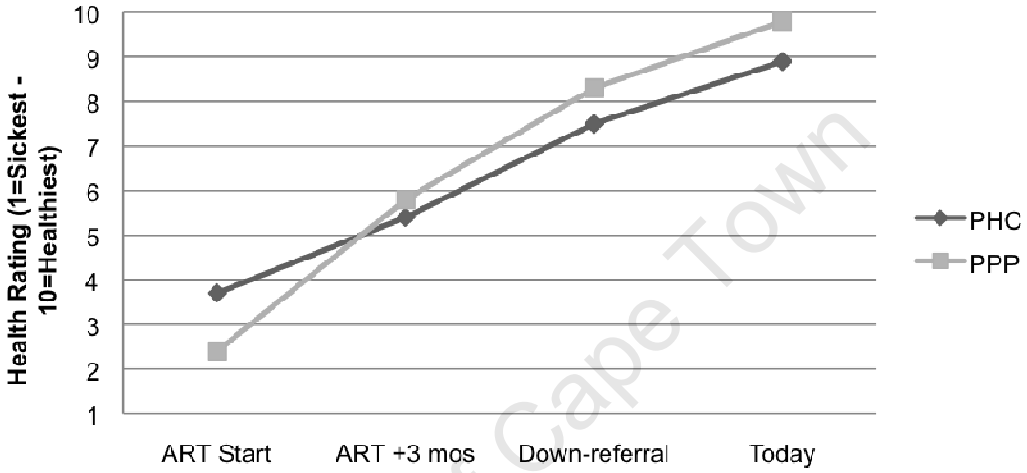
In addition, patients were asked four questions about HIV and ART in order to assess any differences between the groups in terms of HIV knowledge. Levels of basic HIV knowledge were very high in both groups of patients: 97 percent of PHC patients and 100 percent of PPP patients answered the questions correctly. Belief and knowledge results are listed in Table 6.3.

6.2.3 Health

Participants from both cohorts were asked several questions about their health and any adverse events associated HIV treatment. The EuroQoL EQ-5D VAS was used to assess the state (at the time of the interview) of each participant's health. Patients were

presented with the scale that ranged from zero (worst imaginable health state) to one hundred (best imaginable health state), and were asked to place a mark on the scale that corresponded to how healthy they felt at that time (see Appendix I, p.13 for the VAS). On average, PHC participants rated their current state of health as 86/100 and PPP participants somewhat higher at 91/100 (see Table 6.3); this difference was significant (p=0.048).

Figure 6.1 Patient reported health state over time by cohort



In addition to the VAS, patients were asked to recall how they felt at four different moments over the course of their treatment: at ART initiation, three months after ART initiation, at first down-referral, and today. Ratings were marked on a ten-point scale, where one indicated "sickest possible," and ten indicated "healthiest possible." Both cohorts showed consistent improvement in health state over time as shown in Figure 6.1. PPP patients reported feeling less healthy at ART initiation, but significantly healthier at the time of down-referral and today than PHC patients (see bottom of Table 6.3 for mean ratings and *p*-values). The difference in reported health "today" was significant and consistent with the VAS results where PPP participants reported feeling somewhat healthier on average than their PHC peers.

Finally, patients were asked about the incidence of side effects from the ART. More PHC participants reported having experienced adverse events associated with their ARVs in the past three months than PPP participants, but the difference was not statistically significant (Table 6.3).

6.2.4 Adherence and treatment support

Self-reported treatment adherence was measured using a ten-point scale (1=took no pills, 10=took all pills) where patients were asked to recall the number of missed doses during two different periods of time: the past three days, and the past seven days. Both groups reported high levels of adherence in both periods (between 96 and 100 percent). In addition, patients were asked whether or not they had ever missed a dose of ARVs because the medicine was not available when they went to pick it up at the down-referral site. As Table 6.3 shows, missed doses due to lack of drug supply were reported more often among PHC patients, and the difference between the two groups was highly significant (*p=0.0001*).

Finally, patients were presented with a list of adherence and support services available to them and asked to indicate all treatment support services that they utilized or benefitted from at any point since they were down-referred to their local clinic or GP. Services surveyed included treatment buddy or supporter, community health worker (PHC cohort only), Regional Coordinator (PPP only), counseling, HIV support group, social grant, nutritional support, local NGO, and adherence training. Table 6.3 lists support services and reported usage by cohort. While overall treatment support service utilization was low in both cohorts, there was a statistically significant difference in accessing counseling services (*p=0.002*) and adherence training (*p=0.009*), both of which were reported more frequently among PPP patients. In addition, there was a significant difference between the number of patients who accessed the Regional Coordinator in the PPP model and a community health worker in the PHC cohort, but because their roles are not analogous, these findings were not compared here.

Table 6.3 Summary table of patient knowledge, adverse events, beliefs, support, adherence, and health state

	PHC	PPP	*p* Value
Knowledge (% Correct)	%	%	
People on ART can transmit HIV	97	100	0.334
Continue ART after gaining weight	97	100	0.334
ART cures HIV	97	100	0.334
Can stop ART after a couple years	97	100	0.334
Adverse Events	% (n)	% (n)	
At least one AE in the past 3 months	58 (22)	41 (14)	0.157
Beliefs (% Agree or Maybe)	% (n)	% (n)	
Conspiracy	65 (24)	40 (14)	**0.016****
Witchcraft	55 (21)	77 (27)	**0.049***
Happy	95 (37)	100 (35)	0.174
Control	74 (29)	97 (30)	**0.010****
Adherence			
3 day (10 pt scale)	9.6/10	10/10	0.168
7 day (10 pt scale)	9.6/10	10/10	0.185
	% (n)	% (n)	
Missed dose due to dispensing error	36 (14)	3 (1)	**0.000*****
Support services utilized	% (n)	% (n)	
Treatment Buddy	28 (11)	20 (7)	0.0411
Community Health Worker (PHC Only)	18 (7)	**N/A**	**N/A**
Regional Coordinator (PPP Only)	**N/A**	59 (20)	**N/A**
Counseling	8 (3)	66 (23)	**0.002*****
Support Group	8 (3)	9 (3)	0.861
Social Grant	8 (3)	6 (2)	0.713
Nutritional Support	3 (1)	6 (2)	0.489
Local NGO	10 (4)	6 (2)	0.475
Adherence Training	47 (18)	77 (27)	**0.009*****
Health state self-report *(Means)*			
ART Start (10 pt scale)	3.7	2.4	**0.058***
ART Start + 3 months (10 pt scale)	5.4	5.8	0.407
At down-referral (10 pt scale)	7.5	8.3	**0.011*****
Today	8.9	9.7	**0.008*****
VAS Health state rating (100 pt scale)	86/100	91/100	**0.048****

*** indicates significance at 1%; ** indicates significance at 5%; * indicates significance at 10%

6.2.5 Quality of Care

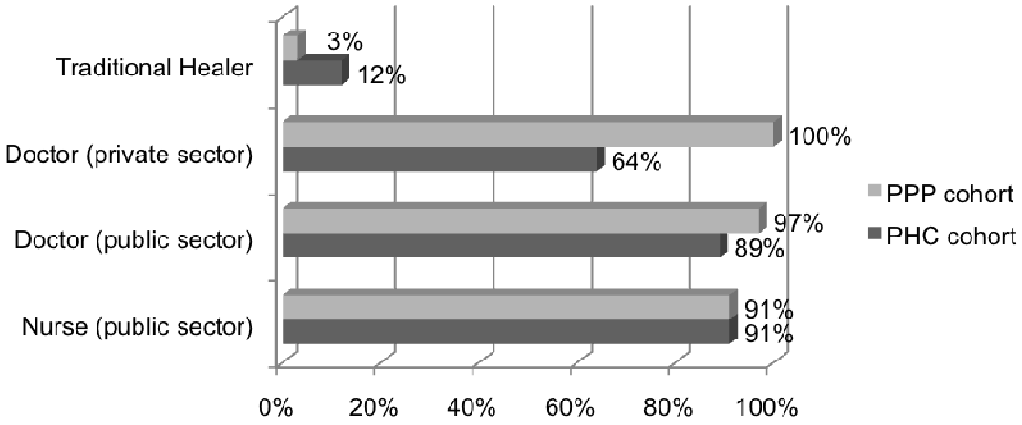
Participants were asked to rate the quality of their care-givers using a 5-point Likert scale, which ranged from 1 = Strongly Agree to 5 = Strongly Disagree, on characteristics including concern for patient health, knowledge, friendliness, willingness to discuss patient problems, perceived ability to be honest with their care-giver, and perceptions of overall quality of care. On average, all survey participants rated their caregivers consistently highly on all of the quality indicators listed above, including overall care quality. Table 6.4 shows the quality of care statements and the percentage of patients who "strongly agreed" or "agreed," by cohort.

Table 6.4 Percent of patients who "strongly agree" or "agree" with the quality of care they received

Quality of care statement	PHC (%)	PPP (%)
The nurse/GP cares about my health.	87	94
The nurse/GP is knowledgeable.	85	94
The nurse/GP is friendly.	97	94
I believe I can talk to the nurses/GP when I have problems with my health.	97	94
I believe I can talk to the nurses/GP when I have social problems that impact my HIV treatment.	100	94
I am able to be honest and tell the nurses/GP when I have missed a dose of my ARVs.	97	94
Overall, I believe that I am receiving good quality HIV care and treatment.	97	94

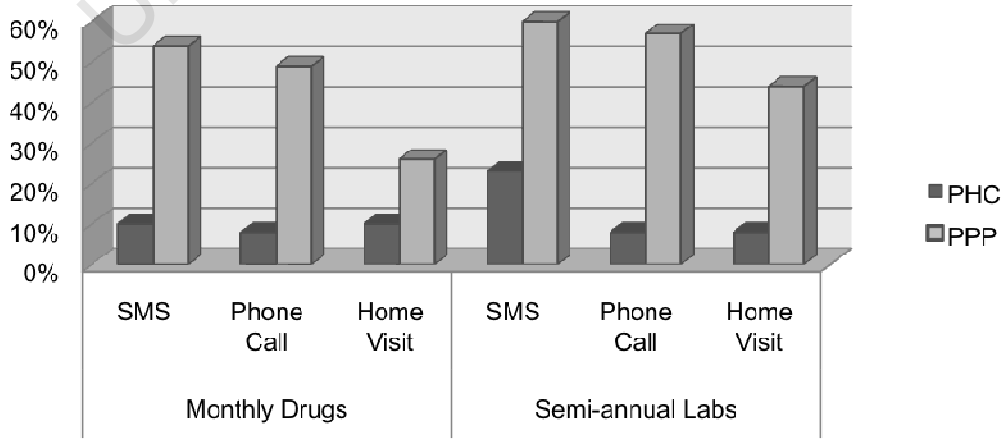
Patients were also asked to indicate the degree to which they trusted different health professionals to care for them and their HIV infection. Level of trust was measured using a five-point scale where 1 = "None can be trusted," and 5 = "Most can be trusted." Figure 6.2 shows the percentage of patients in each group who indicated that "most can be trusted," by service provider type. Trust was consistently high with regard to doctors with the exception of PHC respondent trust in private sector doctors; only 64 percent of public sector patients indicated that "most" private sector doctors could be trusted, whereas 100 percent of the patients who see GPs for their HIV care believed they could be trusted. Traditional healers garnered low levels of trust overall in both groups.

Figure 6.2 Patient trust by health profession



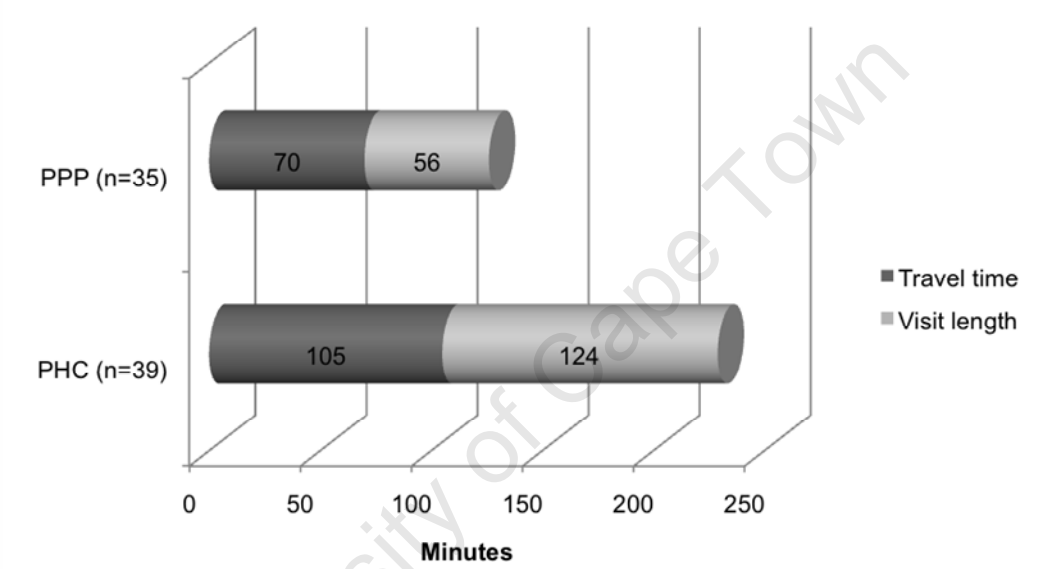
The use of interventions to remind patients about missed monthly drug pick-ups and semi-annual laboratory visits was also surveyed. Using a 5-point Likert scale patients indicated on average how often they received reminders by SMS (text message), phone call, or home visit if they missed a drug pick-up or were late for an appointment to draw blood for laboratory tests. PPP patients more frequently reported receiving all types of reminders, and the difference was statistically significant for the use of SMS reminders (*p=0.0001* and *p=0.021* for monthly and semi-annual visits respectively) and phone calls (*p=0.001* and *p=0.0001* for monthly and semi-annual visits respectively). The reported difference in the frequency of home visits was not statistically significant (see Figure 6.3).

Figure 6.3 Visit reminders by type and cohort



Finally, patients were asked to estimate how long it took them to travel to and from the clinic or GP office for monthly visits, and how long those visits lasted on average. The results are shown stacked in Figure 6.4, and while the difference in travel time was not statistically significant, the difference in visit time was (*p=0.0001*). Patients who attended their local clinic devoted an average of nearly four hours every month for a quick check-up and to retrieve medicine, compared to approximately two hours among patients who saw GPs in the PPP model.

Figure 6.4 Total time devoted to monthly drug pick-up visits



6.2.6 Model choice

Finally, all survey participants were asked open-ended questions about quality of care and why they chose the down-referral model they did. Overall, most participants were satisfied with the model of care they were currently enrolled in, although five from the PHC cohort and two from the PPP cohort indicated that they would like to switch models of care. When asked why they chose the model they did, PHC patients most often cited (reasons were not mutually exclusive):

- Proximity to home or work (n=23, [59 percent])
- Helpful or friendly staff (n=14, [36 percent])
- Short visit/quick service (n=4, [10 percent])

- Good care (n=2, [5 percent])

The most common reasons patients selected the PPP model included:

- Proximity to home (n=22, [63 percent])
- Save money[37] (n=18, [51 percent])
- Quick visit/no queue (n=17, [49 percent])
- Friendly staff (n=13, [37 percent])
- Good care (n=10, [29 percent])

When asked what they liked best about the clinics, PHC patients most commonly noted friendly or caring staff (n=25), while PPP patients cited friendly staff (n=14) and good care (n=11). According to the survey the worst thing about attending a PHC for HIV care was the long wait (n=13) and incorrect or unavailable treatment (n=3), while PPP patients indicated that the worst thing about the GPs was wait times (n=10).

6.3 Discussion

The majority of patients in both cohorts were pleased with their care, reported feeling healthy, and indicated that they were receiving quality care from trustworthy, friendly, knowledgeable and caring staff. Both groups reported high levels of adherence to treatment. There also appeared to be no significant difference between the groups in terms of reasons for selecting their model of care; the most important factor cited by patients in both cohorts was proximity to home or work. This corroborated information provided by the Wellness Clinic staff that suggested the main motivation behind model selection was patient convenience.[38] However, it is noteworthy that people who selected the PPP were also more likely to trust private sector doctors and were less likely to believe in AIDS conspiracy theories than those who selected the PHC site, and this may explain in part why some patients chose to attend their local PHC for down-referral care.

[37] It was not immediately clear from the survey responses what was meant by the term “save money,” which was frequently reported in the PPP cohort and only infrequently reported in the PHC cohort. The author inquired with the research assistants, who explained that patients were indicating that by choosing a GP that was close to home or work they were saving money on travel costs; therefore it was assumed to be a proxy indicator for proximity.

[38] Doctors and nurses involved in the down-referral process at the Wellness Clinic were interviewed regarding their thoughts on the down-referral process and each model. In those interviews, several doctors and nurses indicated that patients selected their model of care based on proximity to home or work.

While both groups of survey patients reported feeling healthy, PPP patients asserted they felt healthier at the time of the survey than their PHC counterparts did on two different health state measures. PHC patients reported more adverse events than PPP patients, which may explain some of the differences in self-reported levels of health. There were no observed differences between the groups in terms of education, employment status, income, and HIV knowledge. This survey did not uncover any obvious systemic socio-economic bias between the two cohorts among patients selected for this study, although due to a lack of data no definitive conclusions could be drawn regarding any differences between the groups in terms of household income. However, this exercise did highlight some differences in model operations and service delivery that could potentially impact patient outcomes over time, as well as some psycho-cultural differences that merit further exploration.

Given the life-long nature of ARV treatment and the myriad complicating factors one confronts daily when living with HIV/AIDS, the infrequent use of treatment support services reported here is concerning. Very few patients reported having treatment buddies or supporters, and still fewer indicated they attended support groups. It was also surprising that so few patients said they received a social grant given the high levels of unemployment and low monthly incomes reported. The most frequently cited support service among PHC participants was “adherence training,” but still only 47 percent indicated that they had been trained. In light of the risks associated with poor adherence, including clinical progression and ultimately death, as well as the development of drug-resistant virus, it is deeply concerning that so few patients received adherence training. Adherence training was more frequently reported among PPP patients (77 percent), which could translate into better outcomes over time. Nonetheless, ideally 100 percent of patients in both models of care should receive regular and ongoing adherence counseling, particularly given that adherence wanes over time. Nonetheless, self-reported adherence in survey patients was very high. According to the survey, counseling services were also more frequently accessed by PPP patients. However, one must be cautious in interpreting this finding as different people may understand the term “counseling” differently, and a specific counseling type was not specified in the questionnaire. It could also be that PPP patients had more concerns or questions and therefore needed the services more than their PHC peers. Nevertheless, PPP patients reported having more frequent contact with various support services overall, which should lead to quicker identification of patient problems, fewer patients lost to follow-up, and better outcomes over time.

PPP patients were more likely to report receiving phone or text message reminders in instances where visits were missed. These reminders are not only important because they help to ensure patients get their drugs and laboratory tests on time, but also because they provide an important opportunity to reach out to patients immediately following a missed appointment and address any potential problems. The sooner a patient is identified as having deviated from the treatment protocol, the more time there is to get the necessary support to the patient.

It is overly simplistic and spurious to reduce the concept of adherence to patients taking drugs as prescribed. In fact, the medicine supply chain, from drug procurement to dispensing at the local service outlet, is indispensable to patient adherence. Failure to supply the right drugs to the right person at the right time constitutes a systemic breach of adherence, and the relatively high incidence of missed doses due to distribution or dispensing failures in the PHC cohort is troubling. More than one-third of this relatively small sample reported having missed doses as a result of failed service delivery, and several others noted in the open-ended comments that they had received drugs belonging to another patient. Not only is this dangerous to patient health and adversely impacts adherence, but it often requires a return visit, increasing patient out-of-pocket costs and wasted time.

Both groups of patients reported devoting long periods of time to monthly patient visits: half a workday in the case of the PHC patients. This is a significant amount of time in every month that entails direct patient costs (i.e. travel, lost wages), as well as important indirect costs such as lost productivity due to absenteeism from work and school. Four hours per clinic visit per month equates to six days per year, and significant opportunity cost. These findings would suggest that patient costs (direct and indirect) are higher in the PHC model due to longer travel time and more time away from work, school or family. Long periods of time spent by patients waiting in public clinics is likely attributable to the well-documented lack of health professionals in the public sector, and suggests that HIV policy and treatment guidelines should be re-examined to make treatment adherence less demanding on patient time and resources, particularly in light of high unemployment, low wages, and low educational attainment among those accessing public healthcare. HIV treatment programs should be designed to maximize clinical outcomes and minimize their adverse impact on employment, educational achievement, out-of-pocket expenses, and patient quality of life; this is going to become imperative as the number of individuals accessing ART continues to grow over the years to come (see projections of HIV incidence and AIDS sick between 2009 and 2015

in Chapter 1, section 1.3.2). There is a need to re-examine the ART guidelines and evaluate the impact of modifying the frequency of clinic visits, drug dosing periods, and laboratory examination schedules in order to reduce patient and health worker burden.

It is interesting to note the high levels of belief in HIV conspiracies and witchcraft within both groups of patients. It is unclear why PHC patients were more likely to accept the conspiracy theory while more PPP patients tended to believe in the role of witchcraft. The fact that fewer PPP patients thought that White people had created HIV to kill Black people could be attributed to the fact that an American NGO with several White staff were known to be supporting their treatment, and therefore, demonstrated an interest in their well-being rather than their demise. Conversely, patients who believed that Whites were trying to kill Blacks might have avoided the PPP entirely knowing that it involved a U.S.-based NGO. Of course this is all conjecture. But these beliefs were surprising particularly in light of the high levels of distrust of traditional healers reported in the survey; these findings appear contradictory for patients who believed that the statement about witchcraft was true given that it is linked to some traditional beliefs. Unfortunately, there were too few participants who indicated a trust in traditional healers to conduct a meaningful analysis of the relationship between traditional healer trust and beliefs in witchcraft and conspiracy theory.

PPP patients reported feeling more in control of their lives than their PHC counterparts. This raises the question of whether or not locus of control is an important psychological factor in long-term treatment success. And yet it is unclear how an internalized locus of control reconciles with a traditional belief in witchcraft, which ostensibly lies outside individual control. The prevalent and conflicting nature of these findings – while beyond the scope of this analysis – suggests a need for further exploration of psycho-cultural issues and their impact on patient understanding of HIV and the importance of adherence, as well as more targeted adherence and support interventions.

This survey had a few methodological weaknesses. Although, it was designed to collect frequencies on a wide-range of HIV-treatment related issues, it did not delve into issues of causality. Nonetheless, every effort was made to eliminate bias and obtain useful, valid data. In the interest of obtaining a representative and inclusive sample, patient selection for this survey was initially random, but in the end an effort was made to recruit patients from under-represented GPs and PHCs. This was successful to some degree, although not all clinics were represented in the final sample. This was also just a sub-set of patients included in the study (15 percent of PPP patients, and 17 percent of PHC

patients), and therefore it is not necessarily representative of the entire study population. There was also some patient self-selection as participation was limited to those who were contactable by phone and able to attend the interview appointment. Some of the questions had very low response rates, and in most cases this was likely due to the complicated table format used for some questions. Examples of this include the employment and salary data (questionnaire section B) and the adverse event data (section D). Others were difficult for patients to recall such as the laboratory data in section E. Social desirability is always a risk when asking patients about their behaviors and beliefs, and although attempts were made to ensure patient anonymity and comfort during the interview process, it cannot be ruled out as a potential influence on the results of this survey.

The ultimate goal of all HIV treatment programs should be to sustain patients on treatment for as long as possible, and the key to this is no less than excellent adherence to ART. Although the majority of patients surveyed reported high levels of adherence, and felt healthy and pleased with the HIV care and treatment they received, this survey identified some potential threats to long-term treatment adherence, particularly in the public sector model. These threats include limited use of treatment support services, inadequate adherence training, and poor tracking of patients who have missed drug pick-ups and laboratory tests appointments. Given that excellent adherence is required for the drugs to be clinically effective, the lack of training on patient adherence is worrying. Equally as concerning are the delays and inaccuracies reported in dispensing practices, as well as the hours of patient waiting time required monthly for an appointment that typically lasts 15 minutes. In the interest of protecting patient and community health, as well as the public sector investment in HIV patients, a deliberate focus on long-term patient care and support is needed, regardless of treatment model or provider type. This survey highlights some of the strengths and shortcomings of the current model of down-referral care employed in South Africa, and argues for a re-examination of current guidelines and model operations in order to maximize patient health and minimize patient and provider burden in HIV care and treatment. In addition, further exploration of the psychological and cultural factors that influence HIV care and treatment are also crucial to improving patient adherence and clinical outcomes.

Appendix I: Questionnaire (English)

A.1 Study ID:	A.2 Date of Interview: __ __ - __ __ - __ __ __ __ (D D - M M - Y Y Y Y)

Patient Perceptions of Quality of HIV Care and Treatment in Matlosana Sub-district, North West Province

INSTRUCTIONS TO INTERVIEWER: Please complete this section before starting the interview. After consenting the patient, please confirm the information on this page prior to beginning the questionnaire. For public sector patients, complete question A.7. For private sector patients, please skip A.7 and complete A.8.

A.3	Gender	Male	1	
		Female	2	
A.4	Community/Suburb (Patient Residence)			
A.5	ART Program	PHC	1	If 1, go to A.7;
		BroadReach	2	If 2, go to A.8

A.6.1	What is your date of birth?	DAY (2-digits: 01-31)	«birthday_day»
A.6.2		MONTH (2-digits: 01-12)	«birthday_month»
A.6.3		YEAR (4-digits: e.g. 1985)	«birthday_year»

A.7	What clinic do you get your ARVs from? *(Public sector patients ONLY)*	Alabama	1	Khuma	7
		Botshabelo	2	Orkney	8
		Gateway	3	Park Street	9
		Grace Mokgomo	4	Stilfontein	10
		Jouberton	5	Tigane	11
		Kanana	6	Tsholofelo	12

A.8	What GP do you get your ARVs from? *(BroadReach ONLY)*	Akuoko	1	Leburu	10
		Baninzi	2	Masudubele	11
		Benjamin	3	Mohammed	12
		Ebrahim	4	Motala	13
		Mangaba	5	Mphatsoe	14
		Hellmann	6	Nassir	15
		Hoosen	7	Rawat	16
		Jaworski	8	Senyatsi	17
		Khunou	9	Selomane	18

INTERVIEWER PRE-QUESTIONNAIRE CHECK-LIST:

I completed and verified all information in Section A above.	N	Y
I explained the nature and purpose of the study to the respondent.	N	Y
I fully consented the patient (read the consent and answered all questions about the study).	N	Y
I provided the participant with a copy of the consent form.	N	Y

Signature of interviewer/fieldworker _____ Date _____

Name of Investigator: Peter Navario, MPH (PhD Candidate)
Institution: University of Cape Town
Advisor: Professor Nicoli Nattrass
Collaborator: Dr. Ebrahim Variava

CONSENT FORM

STUDY TITLE: Patient Perceptions of Quality of HIV Care and Treatment in Matlosana Sub-district, North West Province

What is the purpose of the study?

You are being asked to take part in a research survey. This is a survey about the quality of care provided to patients on ART in Matlosana. The purpose of this study is to learn more about patient care and treatment experiences at the primary healthcare clinic or at a BroadReach General Practitioner (GP), after down referral from the Wellness Centre at Tshepong Hospital.

This survey is being conducted by Peter Navario as part of his PhD thesis research at the University of Cape Town. Before you decide whether or not to take part in this study, we would like to explain the purpose of this study, any risks, and what is expected of you. You should ask the person going over this consent (the study researcher) to explain any parts that are unclear to you and to answer any questions that you have.

What are the possible benefits of participating?

You may not get any direct benefits from being in this study. But, the answers you give will be used to understand the quality of care provided to patients in Matlosana. This information may help us give better medical care and support to help people take their medications.

What are the possible drawbacks or discomforts in participating?

There are no known risks to being in this study.

Do I have to participate?

Participation in this study is voluntary. You can choose not to be in the study, and can refuse to answer any questions or withdraw your consent at any time. The interview should take approximately 30 minutes. All participants in this study were randomly selected from a pool of patients that were down referred to local clinics or BroadReach from Tshepong Hospital.

Costs and Compensation

In order to compensate you for your time and travel costs, you will receive a stipend for your participation in this study.

Will the information be treated confidentially?

This study has been designed to keep information private. The following steps are taken to keep information private:

1) Your name will not appear on any study materials or be connected to your responses.
2) Once you complete the interview, the information you provide will be entered into a computer. The information we enter into the computer will not have your name on it.
3) The interviewers have been trained to keep information private.

Contact details

If you have questions about this interview contact Peter Navario (Tel 072-831-6847 or Email: navario@gmail.com). This study has been reviewed and approved by the Centre for Social Science Research Ethics Committee at the University of Cape Town.

I, ... (Name of respondent in BLOCK LETTERS) have read and understood all the information given to me about my participation in this study and I was given the opportunity to discuss it and ask questions. I volunteer to take part in this study. I have received a copy of this consent form.

....
Signature of respondent **Date**

****STUDY COPY: PLEASE RETAIN FOR STUDY RECORDS**

Name of Investigator: Peter Navario, MPH (PhD Candidate)
Institution: University of Cape Town
Advisor: Professor Nicoli Nattrass
Collaborator: Dr. Ebrahim Variava

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....
Signature of respondent **Date**

****PARTICIPANT COPY: PLEASE PROVIDE TO PARTICIPANT**

B. Employment and Education

B.1	Are you currently a student?	Yes	1
		No	2

B.2	What is the highest level of schooling that you passed (e.g., Standard 5) and/or highest degree attained (e.g. Bachelor of Arts)	Grade:
		Degree (if applicable):

B.3	Are you currently working?	Yes	1	**Go to B.4**
		No	2	**Go to C.1**

Job/Work table

Interviewer instruction: For each job or work that the respondent has done, ask the following questions and complete the boxes below. If respondent has more than 3 jobs, just complete the information on the first three, and indicate on the sheet the total number of jobs he/she currently has.

	Work/Job number	JOB/WORK 1 (J1)	JOB/WORK 2 (J2)	JOB/WORK 3 (J3)
B.4	What kind of work do you do? *[Interviewer: please record the person's occupation or job title (e.g. supermarket cashier) using 2 or more words; if a domestic worker in a private household or if self-employed, circle # in box and don't write employer name].*	Domestic worker, private household 2 Self-employed 3	Domestic worker, private household 2 Self-employed 3	Domestic worker, private household 2 Self-employed 3
B.5	Is this work Full Time or Part Time?	Part Time 1 Full Time 2	Part Time 1 Full Time 2	Part Time 1 Full Time 2
B.6	How much money do you earn from each job in a typical month? Please tell us your take-home pay after tax and other deductions. If your work involves making or selling goods, how much money do you take away and spend or save after paying expenses?	Rand per month: Refused 98 Don't know 99	Rand per month: Refused 98 Don't know 99	Rand per month: Refused 98 Don't know 99
B.7	How many people live (most of the year) in your household (total number)?			
B.8	What is the total amount of money the household brings in on average each month? *(Interviewer note: this should include ALL sources of funds: all grants, wages, gifts etc.).*	Rand per month: Refused 98 Don't know 99		

B.9	How often do physical disabilities or poor health interfere with your ability to work?	Never	1
		Occasionally	2
		Fairly often	3
		Most of the time	4
		Always (permanent disability or ill-health)	5
		Don't know	99

B.10	When you have your monthly doctor/clinic appointment to pick up your ARVs and have a check up, how much time do you usually take off from work?	No time off from work.	1
		About 1 hour	2
		Between 1-2 hours	3
		Half a day (about 4 hours)	4
		A full day off work (8 hrs)	5
		Don't know	99

C. Patient Outlook and beliefs

A few questions about your general life outlook and beliefs:

C.1	Taking all things together, are you: very happy, happy, a little happy or not happy?	Very happy	1
		Happy	2
		A little happy	3
		Not happy	4
		Don't know	99
C.2	How much control do you think that you have over what happens in your life? Are you totally in control, do you control most things, do you have little control or do you have no control?	Totally in control	1
		Control most things	2
		Have little control	3
		Have no control	4
		Don't know	99

C.3	HIV was invented by White people to kill Black people.	Agree	1
		Disagree	2
		Maybe	3
		Don't know	99

C.4	If a young adult dies of illness, their family should suspect witchcraft.	Always	1
		Sometimes	2
		Never	3
		Don't know	99

D. Health

I now want to ask you some questions about your health.

D.1	In general, how is your health lately? Would you say it is poor, fair, good, very good or excellent?	Poor	1
		Fair	2
		Good	3
		Very good	4
		Excellent	5
		Don't know	99

D.2	In the last month, how often did physical disabilities or health problems interfere with your ability to work at a job, look for a job, study, or work around the house?	All of the time	1
		Most of the time	2
		Some of the time	3
		A little of the time	4
		None of the time	5

D.3	Have you had any side-effects from your ARVs in the last three months?	Yes	1
		No	2
		Don't know	99

We would now like to ask you some questions about your ARV Treatment.

D.4	If 10 is the **healthiest** you have been in your life, and 1 is the sickest, what score would you give for how you felt:						
D.4.1 When you had to start ARVs	10	**D.4.2** Three months after the start of ARVs	10	**D.4.3** Six months after the start of ARVs **(at down referral)**	10	**D.4.4** How do you feel now?	10
	9		9		9		9
	8		8		8		8
	7		7		7		7
	6		6		6		6
	5		5		5		5
	4		4		4		4
	3		3		3		3
	2		2		2		2
	1		1		1		1

				D.5a	**D.5b**
D.5a	Have you experienced any of the following side-effects from the ARVs in the past three months? *__Interviewer__: Read out the side effects. Mark yes or no for each one.*	D5a/b.1 Nausea/stomach problems	Yes	1	1
			No	2	2
		D5a/b.2 Headaches	Yes	1	1
			No	2	2
		D5a/b.3 Fevers, chills, sweats	Yes	1	1
			No	2	2
		D5a/b.4 Felt sad or depressed	Yes	1	1
			No	2	2
		D5a/b.5 Unwanted loss of weight	Yes	1	1
			No	2	2
		D5a/b.6 Problems with having sex such as loss of interest or lack of satisfaction?	Yes	1	1
			No	2	2
D.5b	Did you tell your doctor or nurse about the side effect? *If they answer **YES** to D.5a, please ask if they told their doctor about the side effect. Circle '1' if they did, '2' if they didn't in column D.5b.*	D5a/b.7 Skin problems	Yes	1	1
			No	2	2
		D5a/b.8 Muscle-aches and joint pain	Yes	1	1
			No	2	2
		D5a/b.9 Pain, numbness or tingling in the hands and feet	Yes	1	1
			No	2	2
		D5a/b.10 Feeling dizzy and light-headed	Yes	1	1
			No	2	2
		D5a/b.11 Feeling very tired/exhausted	Yes	1	1
			No	2	2
		D5a/b.12 Trouble remembering	Yes	1	1
			No	2	2
		D5a/b.13 Other (specify)	Yes	1	1
			No	2	2

E. Adherence/Support

We would now like to ask you some questions about taking your ARVs.

E.1	Have you ever missed a dose because your ARVs were not ready for you on the day you went to fetch them?	Yes	1
		No	2
		Don't know	99

E.2	On a scale from 1 – 10, where 1 means "I take NO pills" and 10 means "I take ALL my pills", how would you rate your own adherence in **the last 3 days**? 1 2 3 4 5 6 7 8 9 10

E.3	On a scale from 1 – 10, where 1 means "I take NO pills" and 10 means "I take ALL my pills", how would you rate your own adherence in **the last 7 days**? 1 2 3 4 5 6 7 8 9 10

We would now like to ask you about your most recent CD4/VL results. Please try to remember the numbers as best you can. If you cannot remember exactly, please make a guess.

	Please tell us the month and year of your MOST RECENT CD4 & VL tests:	**Month** (2-digits: Jan=01)		Don't Know	**Year** (4-digits)		Don't Know
		E.4.1		9999	**E.4.2**		9999

	Please tell us about the MOST RECENT CD4 & VL results that you had:	**CD4 Count** (Write Number)		Don't Know	**VL Result** (Write Number)		Don't Know
		E.5.1		9999	**E.5.2**		9999

[**Interviewer note**: E.6a is only for patients attending a PHC. Please skip to E.6b for BRHC patients]

E.6a	Please indicate which of the following HIV support services you have used/received since being down referred to the PHC in order to help you to stay on your ARVs.. You may indicate more than one service. ***Interviewer**: Read out the list of services. Mark yes or no for each one.*	E.6a.1 Treatment Buddy/Supporter	Yes	1
			No	2
		E.6a.2 Community Health Worker	Yes	1
			No	2
		E.6a.3 Counseling at PHC (Doctor, nurse or counselor)	Yes	1
			No	2
		E.6a.4 HIV Support Group	Yes	1
			No	2
		E.6a.5 Social Grant (Disability, Child Support or Foster Care grants).	Yes	1
			No	2
		E.6a.6 Nutritional Support	Yes	1
			No	2
		E.6a.7 Local NGO	Yes	1
			No	2
		E.6a.8 Adherence Training (from PHC nurse or doctor)	Yes	1
			No	2
		E.6a.9 Other: [Please list:]	Yes	1
			No	2

[**Interviewer note**: Section E.6b below is only for BRHC patients]

E.6b	Please indicate which of the following HIV support services you use or have used since being down referred to the BroadReach in order to help you to stay on your ARVs. You may indicate more than one service. ***Interviewer**: Read out the list of services. Mark yes or no for each one.*	E.6b.1 Treatment Buddy/Supporter	Yes	1
			No	2
		E.6b.2 BroadReach Regional Coordinator (Holiness)	Yes	1
			No	2
		E.6b.3 Aid for AIDS/BroadReach counseling call centre	Yes	1
			No	2
		E.6b.4 HIV Support Group	Yes	1
			No	2
		E.6b.5 Social Grant (Disability, Child Support or Foster Care grants).	Yes	1
			No	2
		E.6b.6 Nutritional Support	Yes	1
			No	2
		E.6b.7 Local NGO	Yes	1
			No	2
		E.6b.8 Adherence Training (from GP or BRHC staff)	Yes	1
			No	2
		E.6b.9 Other: [Please list:]	Yes	1
			No	2

F. Quality of Care

[**Interviewer note**: This part of Section F is **only for BRHC patients**]

Please indicate your level of agreement with the following statements:		Strongly agree	Agree	Neither	Disagree	Strongly disagree	Don't know
F.1a	My GP Cares about my health.	1	2	3	4	5	99
F.2a	My GP is knowledgeable.	1	2	3	4	5	99
F.3a	My GP is friendly.	1	2	3	4	5	99
F.4a	I believe I can talk to my GP when I have problems with my health.	1	2	3	4	5	99
F.5a	I believe I can talk to my GP when I have social problems that may impact my HIV treatment.	1	2	3	4	5	99
F.6a	I am able to be honest and tell my GP when I have missed a dose of my ARVs.	1	2	3	4	5	99
F.7a	Overall, I believe that I am receiving good quality HIV care and treatment.	1	2	3	4	5	99

[**Interviewer note**: This part of Section F is **only for PHC patients**]

Please indicate your level of agreement with the following statements:		Strongly agree	Agree	Neither	Disagree	Strongly disagree	Don't know
F.1b	The Nurses care about my health.	1	2	3	4	5	99
F.2b	The Nurses are knowledgeable.	1	2	3	4	5	99
F.3b	My Nurses are friendly.	1	2	3	4	5	99
F.4b	I believe I can talk to the Nurses when I have problems with my health.	1	2	3	4	5	99
F.5b	I believe I can talk to the Nurses when I have social problems that may impact my HIV treatment.	1	2	3	4	5	99
F.6b	I am able to be honest and tell the Nurses when I have missed a dose of my ARVs.	1	2	3	4	5	99
F.7b	Overall, I believe that I am receiving good quality HIV care and treatment.	1	2	3	4	5	99

Please indicate the level of trust you have in the following people's ability to take care of your HIV:		None/ Almost none of them can be trusted	Very few of them can be trusted	I don't know enough about them to say	Some of them can be trusted	Most of them can be trusted
F.8.1	Nurses in the Public Sector (PHCs)	1	2	3	4	5
F.8.2	Doctors in the Public Sector (PHCs)	1	2	3	4	5
F.8.3	Doctors in the Private Sector (GPs)	1	2	3	4	5
F.8.4	Traditional Healer (Sangoma, Herbalist etc.)	1	2	3	4	5

F.9	Given a choice, who would you prefer to see for your monthly ARV visits?	Public Sector Nurse	1
		Public Sector Doctor	2
		Private Sector Doctor (GP)	3
		No preference	4

F.10	Given a choice, who would you prefer to see when you have a problem (non-routine) with your HIV or ARVs?	Public Sector Nurse	1
		Public Sector Doctor	2
		Private Sector Doctor (GP)	3
		Traditional Healer	4
		No preference	5

If you miss your monthly drug pick appointment, then the following happens (you can have more than one answer):	Always	Most of the time	Sometimes	Rarely	Never	Don't know
F.11.1 You get an SMS to remind you to come in.	1	2	3	4	5	99
F.11.2 You get an phone call to remind you to come in.	1	2	3	4	5	99
F.11.3 You get a home visit from a health professional/NGO.	1	2	3	4	5	99
F.11.4 Other?	1	2	3	4	5	99

If you miss your twice yearly blood draw appointment, then the following happens (you can have more than one answer):	Always	Most of the time	Sometimes	Rarely	Never	Don't know
F.12.1 You get an SMS to remind you to come in.	1	2	3	4	5	99
F.12.2 You get an phone call to remind you to come in.	1	2	3	4	5	99
F.12.3 You get a home visit from a health professional/NGO.	1	2	3	4	5	99
F.12.4 Other?	1	2	3	4	5	99

F.12	On average, how much time does it take for you to travel <u>to and from</u> your monthly visit for your ARVs? (Total travel time).	Hours (2-digits):	
		Minutes: (2-digits):	

F.13	On average, how much does it cost for you to travel to and from a monthly visit for your ARVs? (Total cost of the trip in Rands).	**R**_____ . ____

F.14	On average, how much time does your **monthly ARV pick-up visit last** (from the time you arrive at the clinic/GP surgery until you leave)?	Hours (2-digits):	
		Minutes: (2-digits):	

F.15	On average, how much time does your **twice yearly doctor visit and blood draw** last (from the time you arrive at the clinic/GP surgery until you leave)?	Hours (2-digits):	
		Minutes: (2-digits):	

G. KNOWLEDGE ABOUT HIV/AIDS AND ARV TREATMENT

		True	False
G.1.1	People receiving ARV treatment can still transmit HIV to other people through unprotected sex.	1	2
G.1.2	One should continue to take ARV treatment after gaining weight.	1	2
G.1.3	ARV medication completely removes HIV from my body.	1	2
G.1.4	After a couple of years, one can stop taking ARV medication.	1	2

H. Quality of Life

We are now going to ask you questions about your quality of life. Please choose the best answer that describes how you feel today.

Interviewer note: Please circle the number that corresponds to the participant response. For H.6 please show the participant the scale and read the instructions in the box on the right along with them.

H.1 MOBILITY	
I have no problems in walking about	1
I have some problems in walking about	2
I am confined to bed	3

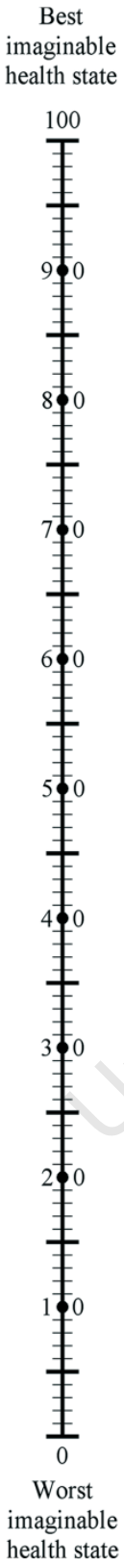
H.2 Self-Care	
I have no problems with self-care	1
I have some problems washing or dressing myself	2
I am unable to wash or dress myself	3

H.3 Usual Activities *(e.g. work, study, housework, family or leisure activities)*	
I have no problems with performing my usual activities	1
I have some problems with performing my usual activities	2
I am unable to perform my usual activities	3

H.4 Pain/Discomfort	
I have no pain or discomfort	1
I have moderate pain or discomfort	2
I am have extreme pain or discomfort	3

H.5 Anxiety/Depression	
I am not anxious or depressed	1
I am moderately anxious or depressed	2
I am extremely anious or depressed	3

H.6 YOUR HEALTH STATE TODAY:



To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line on the scale indicating how good or bad your health state is today.

I. Model Choice

Finally, we would like to ask you why you chose to see a GP and join BroadReach, or why you decided to attend your local primary healthcare clinic when you were down referred from Wellness Clinic.

[**Interviewier**: Please list all reasons for their choice or if they don't know, circle Reason 6 below.
Make sure they know they can give more than one reason for their choice]:

I.1a	The reasons I chose to join **BroadReach** and see a GP include:	Reason 1 **(I.1a.1):**
		Reason 2 **(I.1a.2):**
		Reason 3 **(I.1a.3):**
		Reason 4 **(I.1a.4):**
		Reason 5 **(I.1a.5):**
		Reason 6 **(I.1a.6):** **I don't know why I made the choice I did.**

I.1b	The reasons I chose to go to my local **PHC** include:	Reason 1 **(I.1b.1):**
		Reason 2 **(I.1b.2):**
		Reason 3 **(I.1b.3):**
		Reason 4 **(I.1b.4):**
		Reason 5 **(I.1b.5):**
		Reason 6 **(I.1b.6):** **I don't know why I made the choice I did.**

I.2 Are you happy that you chose the program you did?

I.3 If you were given the opportunity to switch programs, would you like to? Y / N

I.4 Tell me the best thing about going to the GP/Clinic:

I.5 Tell me the worst thing about going to the GP/Clinic:

END OF QUESTIONNAIRE

J. Interview Evaluation – *To be completed by Interviewer <u>after</u> interview*

J.1	How would you describe the respondent's vocabulary (the variety of words the respondent used during the interview to express his/her thoughts)?	Below average	1
		Average	2
		Above average	3
J.2	In general, how did the respondent act towards you during the interview?	Hostile	1
		Neither hostile nor friendly	2
		Friendly	3
J.3	How attentive was the respondent to the questions during the interview?	Not at all attentive	1
		Somewhat attentive	2
		Very attentive	3
J.4	Were other persons within hearing range at any time during the interview?	No other person within hearing range at any time	1
		1+ persons within hearing range for **part** of interview	2
		1+ persons within hearing range for **all** of the interview	3
J.5	I have **quality controlled** this questionnaire according to the Quality Control checklist provided:		
	(Signature of Interviewer)		
Interviewer: Any additional comments about specific questions or data quality should go on inside back of cover page			

Appendix II: Questionnaire (Setswana)

A.1 Study ID:	A.2 Letlha la gobotsolotswa: __ __ - __ __ - __ __ __ __ (D D - M M - Y Y Y Y)

Maikutlo a balwetse ka boleng ba tlhokomelo ya HIV le kalafi mo Matlosana Sub- District,province ya Bokone bophirima

INSTRUCTIONS TO INTERVIEWER: Please complete this section before starting the interview. After consenting the patient, please confirm the information on this page prior to beginning the questionnaire. For public sector patients, complete question A.7. For private sector patients, please skip A.7 and complete A.8.

A.3	Boleng	**Monna**	**1**	
		Mosadi	**2**	
A.4	Lefelo la bodulo			
A.5	Lenaane la ART	**Tliliniki/ Cliniki**	**1**	Ga ele 1, fetela go A.7;
		BroadReach	**2**	Ga ele 2, fetela go A.8

A.6.1	Letlha la matsalo?	**LETSATSI (2-digits: 01-31)**	**«birthday_day»**
A.6.2		**KGWEDI (2-digits: 01-12)**	**«birthday_month»**
A.6.3		**NGWAGA (4-digits: e.g. 1985)**	**«birthday_year»**

A.7	Ke tliliniki efe e o tsayang diARV tsa gago mo go yona? *(Balwetse ba puso fela)*	Alabama	1	Khuma	7
		Botshabelo	2	Orkney	8
		Gateway	3	Park Street	9
		Grace Mokgomo	4	Stilfontein	10
		Jouberton	5	Tigane	11
		Kanana	6	Tsholofelo	12

A.8	Ke ngaka efe e o tsayang diARV tsa gago mo go yona? *(BroadReach fela)*	Akuoko	1	Masudubele	10
		Baninzi	2	Mohammed / Lala	11
		Benjamin	3	Motala	12
		Ebrahim	4	Mosam	13
		Mangaba	5	Mphatsoe / Mangaba	14
		Hellmann	19	Nassir	15
		Hoosen	6	Rawat	16
		Jaworski	7	Senyatsi	17
		Khunou	8	Selomane	18
		Leburu	9		

INTERVIEWER PRE-QUESTIONNAIRE CHECK-LIST:

I completed and verified all information in Section A above.	N	Y
I explained the nature and purpose of the study to the respondent.	N	Y
I fully consented the patient (read the consent and answered all questions about the study).	N	Y
I provided the participant with a copy of the consent form.	N	Y

Signature of interviewer/fieldworker

Date

Name of Investigator: Peter Navario, MPH (PhD Candidate)
Institution: University of Cape Town
Advisor: Professor Nicoli Nattrass
Collaborator: Dr. Ebrahim Variava

CONSENT FORM

STUDY TITLE: Maikutlo a balwetse ka boleng ba tlhokomelo ya HIV le kalafi mo Matlosana Sub- District,province ya North West

Maikaelelo a thuto e ke eng?

O kopiwa go tsaya karolo mo thutong. Ke thuto ka boleng ba tlhokomelo e e fiwang balwetse ba ART mo Matlosana. Maikaelelo a thuto e ke go ithuta thata ka tlhokomelo e e fiwang balwetse le maitemogelo a bona ko ditlininking le dingaka(BroadReach), morago ga go romelwa gotswa mo Wellness ko Tshepong Hospital.

Thuto e e tsamaisiwa ke Peter Navario jaaka karolo ya thuto ya gagwe ya PhD mo University ya Cape Town. Pele o ka tsaya tshwetso ya go tsaya karolo kgotsa go sa tseye karolo mo thutong e, re batla go go tlhalosetsa maikaelelo a thuto e, dikotsi le gore go kopiwa eng mo go wena. O tshwanetse go botsa motsamaisa puisano/ tumellano go go tlhalosetsa dikarolo tse di sa tlhaloganyegeng le go araba ditpotso tsa gago.

Dipoelo tsa go staya karolo e ka nna dife?

O ka nne wa se bone **dikuno/ dipoelo** (**any direct benefits) tse di go lebaganeng** ka go nna mo thutong ena. Mme dikarabo tsa gago di tla dirisiwa go itse boleng ba tlhokomelo e e fiwang balwetse mo Matlosana. Kitso ena e ka re thusa go fa batho tlhokomelo e e botoka le tshegetso gore ba tseye melemo ya bona sentle.

Mathata a a ka nnang teng ka ntlha ya go staya karolo ke afe?

Ga gona mathata/ kotsi ya go tsaya karolo e e itseweng.

A ke pateletsega go tsaya karolo?

Go tsaya karolo mo thutong e, ke ithaopo. O ka nne wa se tseye karolo mo thutong e, o ka nne wa gana go araba dipotso tse dingwe kgotsa wa gana go fa tetla ya puisano kgotsa go gogela tetla ya gago ko morago. Puisano ena e tla tsaya bokana ka metsotso ele 30. Batsayakarolo botlhe ba tlhopilwe fela go sena thulaganyo(randomly).

Ditshenyegelo le dituelo/ ditebogo

Go go leboga ka nako ya gago le ditshenyegelo tsa leeto, o tla fiwa madi ka ntlha ya go tsaya karolo mo thutong e.

A diteng tse di tla tsholwa e le sephiri?

Thuto e e rulagantswe gore e tshole dintlha e le sephiri. Dikgato tse di latelang di diragadiwa go tshola diteng e le sephiri:

1) Leina la gago ga le kitla le tlhagelela mo dikgatisong tsa dithuto kgotsa le golaganngwa le ditshwaelo tsa gago.
2) Fa o feditse puisano, ditshwaelo tsa gago di tla tsenngwa mo computeng. Dintlha tse di tla tsenngwang mo computeng di tla bo di sena leina la gago mo go stona..
3) Batsamaisi ba puisano ba rutilwe go tshola sephiri.

Diteng tsa kgolagano

Fa o na le dipotso ka patlisiso/ puisano ena, ikgolaganye le Peter Navario (Tel 072-831-6847 kgotsa Email: navario@gmail.com). Thuto ena e sekasekilwe le go netefadiwa ke Centre for Social Science Research Ethics Committee ya University ya Cape Town.

Nna, ... (Leina la motsayakarolo ka ditlhaka tse ditona) ke badile le go tlhaloganya diteng tse ke di filweng mabapi le go tsaya karolo ga me mo thutong e ebile ke filwe tlhaloso le tetla ya go botsa dipotso. Ke ithaopa go tsaya karolo mo thutong e. Ke filwe kgatiso ya tumellano e.

....
Signature of respondent **Date**

****STUDY COPY: PLEASE RETAIN FOR STUDY RECORDS**

Name of Investigator: Peter Navario, MPH (PhD Candidate)
Institution: University of Cape Town
Advisor: Professor Nicoli Nattrass
Collaborator: Dr. Ebrahim Variava

CONSENT FORM

STUDY TITLE: Maikutlo a balwetse ka boleng ba tlhokomelo ya HIV le kalafi mo Matlosana Sub- District,province ya North West

Maikaelelo a thuto e ke eng?

O kopiwa go tsaya karolo mo thutong. Ke thuto ka boleng ba tlhokomelo e e fiwang balwetse ba ART mo Matlosana. Maikaelelo a thuto e ke go ithuta thata ka tlhokomelo e e fiwang balwetse le maitemogelo a bona ko ditlininking le dingaka(BroadReach), morago ga go romelwa gotswa mo Wellness ko Tshepong Hospital.

Thuto e e tsamaisiwa ke Peter Navario jaaka karolo ya thuto ya gagwe ya PhD mo University ya Cape Town. Pele o ka tsaya tshwetso ya go tsaya karolo kgotsa go sa tseye karolo mo thutong e, re batla go go tlhalosetsa maikaelelo a thuto e, dikotsi le gore go kopiwa eng mo go wena. O tshwanetse go botsa motsamaisa puisano/ tumellano go go tlhalosetsa dikarolo tse di sa tlhaloganyegeng le go araba ditpotso tsa gago.

Dipoelo tsa go staya karolo e ka nna dife?

O ka nne wa se bone **dikuno/ dipoelo** (**any direct benefits) tse di go lebaganeng** ka go nna mo thutong ena. Mme dikarabo tsa gago di tla dirisiwa go itse boleng ba tlhokomelo e e fiwang balwetse mo Matlosana. Kitso ena e ka re thusa go fa batho tlhokomelo e e botoka le tshegetso gore ba tseye melemo ya bona sentle.

Mathata a a ka nnang teng ka ntlha ya go staya karolo ke afe?

Ga gona mathata/ kotsi ya go tsaya karolo e e itseweng.

A ke pateletsega go tsaya karolo?

Go tsaya karolo mo thutong e, ke ithaopo. O ka nne wa se tseye karolo mo thutong e, o ka nne wa gana go araba dipotso tse dingwe kgotsa wa gana go fa tetla ya puisano kgotsa go gogela tetla ya gago ko morago. Puisano ena e tla tsaya bokana ka metsotso ele 30. Batsayakarolo botlhe ba tlhopilwe fela go sena thulaganyo (randomly) go tswa mo maineng a batho ba ba rometsweng ko ditliniking le dingaka(brhc).

Ditshenyegelo le ditebogo

Go go lebogela nako ya gago le ditshenyegelo tsa leeto, o tla busediwa madi a gago le setlankana (voucher) ka ntlha ya go tsaya karolo mo thutong e.

A diteng tse di tla tsholwa e le sephiri?

Thuto e e rulagantswe gore e tshole dintlha e le sephiri. Dikgato tse di latelang di diragadiwa go tshola diteng e le sephiri:

1) Leina la gago ga le kitla le tlhagelela mo dikgatisong tsa dithuto kgotsa le golaganngwa le ditshwaelo tsa gago.
2) Fa o feditse puisano, ditshwaelo tsa gago di tla tsenngwa mo computeng. Dintlha tse di tla tsenngwang mo computeng di tla bo di sena leina la gago mo go stona..
3) Batsamaisi ba puisano ba rutilwe go tshola sephiri.

Diteng tsa kgolagano

Fa o na le dipotso ka patlisiso/ puisano ena, ikgolaganye le Peter Navario (Tel 072-831-6847 kgotsa Email: navario@gmail.com).Thuto ena e sekasekilwe le go netefadiwa ke Centre for Social Science Research Ethics Committee ya University ya Cape Town.

Nna, ... (Leina la motsayakarolo ka ditlhaka tse ditona) ke badile le go tlhaloganya diteng tse ke di filweng mabapi le go tsaya karolo ga me mo thutong e ebile ke filwe tlhaloso le tetla ya go botsa dipotso. Ke ithaopa go tsaya karolo mo thutong e. Ke filwe kgatiso ya tumellano e.

....
Signature of respondent **Date**

****PARTICIPANT COPY: PLEASE PROVIDE TO PARTICIPANT**

B. Mosebetsi le dithuto

B.1	A o santse o tsena sekolo?	Nnete	1
		Nyaya	2

B.2	O feletse ka mophato ofe mo dithutong tsa gago o o o falotseng (e.g., Standard 5) le / kgotsa grata/ degree e o e boneng (e.g. Bachelor of Arts)	Mophato:
		Degree/ Grata (if applicable):

B.3	A o a bereka?	Nnete	1	**Fetela go B.4**
		Nyaya	2	**Fetela go C.1**

Tiro/ Thulaganyo ya mosebetsi

<u>Interviewer instruction</u>: For each job or work that the respondent has done, ask the following questions and complete the boxes below. If respondent has more than 3 jobs, just complete the information on the first three, and indicate on the sheet the total number of jobs he/she currently has.

	Mosebetsi/ Nomore ya tiro	**Tiro/ Mosebetsi 1 (J1)**	**Tiro/ Mosebetsi 2 (J2)**	**Tiro/ Mosebetsi 3 (J3)**
B.4	K e mosebetsi wa mofuta mang o o o dirang? *[Interviewer: please record the person's occupation or job title (e.g. supermarket cashier) using 2 or more words; if a domestic worker in a private household or if self-employed, circle # in box and don't write employer name].*	Mothusi mo lelapeng 2 Ke a itshebetsa 3	Mothusi mo lelapeng 2 Ke a itshebetsa 3	Mothusi mo lelapeng 2 Ke a itshebetsa 3
B.5	Ke mosebetsi wa leruri kgotsa wa nakwana?	Nakwana 1 Wa leruri 2	Nakwana 1 Wa leruri 2	Nakwana 1 Wa leruri 2
B.6	O amogela bokae mo mosebetsing mo kgweding morago ga lekgetho/ tax le diphokotso tse dingwe. Ga ele gore tiro ya gago ke go dira dilo kgotsa go rekisa dilo, o sala ka bokae morago ga go duela ditshenyegelo.	Rand ka kgwedi O ganne 98 Ga ke itse 99	Rand ka kgwedi O ganne 98 Ga ke itse 99	Rand ka kgwedi O ganne 98 Ga ke itse 99
B.7	Ke batho ba le ba kae ba ba dulang mo lelapeng(nako e ntsi mo ngwageng) la gago. (palo e e feletseng)			
B.8	Ke bokae madi/ chelete ka kakaretso a a tsenang mo lapeng ka gale kgwedi e nngwe le enngwe? *(Interviewer note: this should include ALL sources of funds: all grants, wages, gifts etc.).*	Rand ka kgwedi: O ganne 98 Ga ke itse 99		

B.9	Bolwetse kgotsa bogole ba gago bo ama bokgoni ba gago go dira mosebetsi go le gontsi yang.	Leeseng	1
		Nako e nngwe	2
		Go le gontsinyana	3
		Go le gontsithata	4
		Ka nako tsotlhe (bogole ba leruri kgotsa pholo e e bokowa)	5
		Ga ke itse	99

B.10	O tsaya nako e e kanakang ya gago ya tiro go ya go tsaya diARV ko ngakeng ya BroadReach kgotsa tliniki	Ga ke tseye nako ya me ya tiro	1
		Ura ele nngwe	2
		Magareng ga ura ele nngwe le tse pedi	3
		Halofo ya letsatsi (e ka nna ura tse nne)	4
		Letsatsi lotlhe (ura tse robedi)	5
		Ga ke itse	99

C. Tebego le tumelo/ maikutlo a molwetse

Dipotso di se kae ka botshelo ba gago ka kakaretso le maikutlo a gago:

C.1	Ka kakaretso a o itumetse thata, o itumetse, o itumetsenyana kgotsa ga o a itumela?	Ke itumetse thata	1
		Ke itumetse	2
		Ke itumetsenyana	3
		Ga ke a itumela	4
		Ga ke itse	99
C.2	O nagana gore o na le taolo e e kanakang ka ga seo se diragalang mo botshelong ba gago. A o na le taolo e e feletseng, a o laola dilo tse dintsi, o na le taolo e nnye kgotsa gaona taolo gotlhe gotlhe?	Taolo e e feletseng	1
		O laola dilo tse dintsi	2
		Taolo e nnye	3
		Gaona taolo	4
		Ga ke itse	99

C.3	HIV e tlhodilwe ke makgowa/ morafe o mosweu go bolaya batho ba bantsho	Ke dumela yalo	1
		Ga ke dumele	2
		Gongwe	
		Ga ke itse	99

C.4	Ga mocha a tlhokofala ka ntlha ya bolwetse, ba lelapa ba tshwanetse go belaela boloi.	Ka gale	1
		Nako tse dingwe	2
		Leeseng	3
		Ga ke itse	99

D. Boitekanelo

Ke batla go go botsa dipotso ka boitekanelo ba gago.

D.1	Ka kakaretso boitekanelo ba gago bo ntse yang yaanong? O kare bo bokowa, bo botoka, bo ntse sentle, bo ntse sentle thata kgotsa bo ntse sentle thatathata?	Bo bokowa	1
		Bo botoka	2
		Bo ntse sentle	3
		Bo ntse sentle thata	4
		Bo ntse sentle thatathata	5
		Ga ke itse	99

D.2	Mo kgweding e e fetileng bolwetse kgotsa bogole ba gago bo amile jang bokgoni ba gago go dira mosebetsi, go batla mosebetsi, go tsena sekolo/ ithuta le go bereka mo lapeng	Ka dinako tsotlhe	1
		Ka dinako tse dintsi	2
		Ka dinako tse dingwe	3
		Ka nako e nnye	4
		Ga ise go diragale	5
D.3	A o kile wa itemogela mathata(side-effects) mo diARV tsa gago mo dikgweding tse tharo tse di fetileng	Nnete	1
		Nyaya	2
		Ga ke itse	99

Re batla go gobotsa dipotso ka tlhokomelo ya gago ya ARV

D.4	Ga ele gore 10 e kaya boitekalo bo bontle mo botshelong ba gago, 1 e kaya go lwala thata, o ka fana ka maduo a le makae go supa maikutlo a gago ka nako eo:						
D.4.1 Fa o ne o tshwanetse go simolola diARV	10	**D.4.2** Dikgwedi tse tharo morago ga go simolola diARV	10	**D.4.3** Dikgwedi tse thataro morago ga go simolola diARV **(ka nako ya go romelwa ntle/ down referral)**	10	**D.4.4** O ikutlwa jang yaanong	10
	9		9		9		9
	8		8		8		8
	7		7		7		7
	6		6		6		6
	5		5		5		5
	4		4		4		4
	3		3		3		3
	2		2		2		2
	1		1		1		1

				D.5a	D.5b
D.5a	A o kile wa itemogela nngwe ya mathata a a latelang (side-effects) mo diARV tsa gago mo dikgweding tse tharo tse di fetileng ***Interviewer**: Read out the side effects. Mark yes or no for each one.*	D5a/b.1 Go tlhakatlhakana le mathata a mala	Nnete	1	1
			Nyaya	2	2
		D5a/b.2 Go opiwa ke tlhogo	Nnete	1	1
			Nyaya	2	2
		D5a/b.3 Mocheso, go fufulelwa	Nnete	1	1
			Nyaya	2	2
		D5a/b.4 Go sa itumela kgotsa go imelega	Nnete	1	1
			Nyaya	2	2
		D5a/b.5 Phokotsego ya mmele e ke sa e batlang	Nnete	1	1
			Nyaya	2	2
		D5a/b.6 Mathata a thobalano jaaka go tlhoka keletso kgotsa go sa kgotsofaleng	Nnete	1	1
			Nyaya	2	2
D.5b	A o boleletse ngaka kgotsa mooki wag ago ka mathata a (side-effects) *If they answer **YES** to D.5a, please ask if they told their doctor about the side effect. Circle '1' if they did, '2' if they didn't in column D.5b.*	D5a/b.7 Mathata a letlalo	Nnete	1	1
			Nyaya	2	2
		D5a/b.8 Gobaba ga mesifa le ditokololo tse di botlhoko	Nnete	1	1
			Nyaya	2	2
		D5a/b.9 Go opelwa, goswa bokidi/ bogatsu kgotsa go tsikinyega mo mabogong le maoto	Nnete	1	1
			Nyaya	2	2
		D5a/b.10 Go tsewa ke sedidi le go sa ikutlwe sentle mo tlhogong	Nnete	1	1
			Nyaya	2	2
		D5a/b.11 Letsapa le le ntsi/ mokgatala	Nnete	1	1
			Nyaya	2	2
		D5a/b.12 Go sa kgone go gopola sentle	Nnete	1	1
			Nyaya	2	2
		D5a/b.13 Tse dingwe (tlhalosa)	Nnete	1	1
			Nyaya	2	2

E. Go nwa melemo ka tshwanelo/ kemonokeng

Re batla go go botsa dipotso ka ga go nwa diARV tsa gago.

E.1	A o kile wa fosa gonwa dipilisi ka ntlha ya gore diARV tsa gago di ne di sa romelwa ka letsatsi le o dilatetseng ka lona?	Nnete	1
		Nyaya	2
		Ga ke itse	99

E.2	Mo sekaleng sa 1 – 10, 1 e kaya gore “Ga ke nwe dipilisi” mme 10 e kaya gore “ke nwa dipilisi tsa me tsotlhe”, o tla kala yang gonwa dipilisi ga gago mo **malatsing a mararo a a fetileng?** 1 2 3 4 5 6 7 8 9 10

E.3	Mo sekaleng sa 1 – 10, 1 e kaya gore “Ga ke nwe dipilisi” mme 10 e kaya gore “ke nwa dipilisi tsa me tsotlhe”, o tla kala yang gonwa dipilisi ga gago mo **malatsing a supa a a fetileng?** 1 2 3 4 5 6 7 8 9 10

Re batla go gobotsa ka CD4/VL tsa gago tsa sesheng. Ka kopo leka go gopola dinomoro ka bokgoni bo o ka bo kgonang. Ga osa gopole sentle, ka kopo fopholetsa.

	Re bolelle kgwedi le ngwaga wa diteko tsa CD4/VL tsa gago tsa sesheng:	**Kgwedi** (2-digits: Jan=01)		Ga ke itse	**Ngwaga** (4-digits)		Ga ke itse
		E.4.1	__ __	9999	**E.4.2**	__ __ __ __	9999

	Re bolelle dipholo tsa CD4/VL tsa gago tsa sesheng:	**CD4 Count** (Write Number)		Ga ke itse	**VL Result** (Write Number)		Ga ke itse
		E.5.1		9999	**E.5.2**		9999

E.6a (PHC)	Tlhalosa gore ke mokgwa ofe wa tshegetso ya ARV mo go e e latelang e o e amogetseng/ dirisitseng ga o sale o rometswe ko tliliniking go go thusa go nna o nwa diARV. O ka nne wa tlhalosa go feta bongwe. ***Interviewer**: Read out the list of services. Mark yes or no for each one.*	E.6a.1 Moemanokeng mo kalafong/ motshegetsi	Nnete	1
			Nyaya	2
		E.6a.2 Modiredipuso wa boitekanelo	Nnete	1
			Nyaya	2
		E.6a.3 Kgakololo(Counseling) mo tliliniking (Ngaka, mooki kgotsa mogakolodi/ counsellor)	Nnete	1
			Nyaya	2
		E.6a.4 Mokgatlo wa kemonokeng wa HIV	Nnete	1
			Nyaya	2
		E.6a.5 Matlole a katlatleloloago/ Social Grant (Bogole, tlhokomelo ya bana, kgodiso ya bana).	Nnete	1
			Nyaya	2
		E.6a.6 Thuso ya dijo	Nnete	1
			Nyaya	2
		E.6a.7 Mokgatlo wa selegae o eseng wa puso/ Local NGO	Nnete	1
			Nyaya	2
		E.6a.8 Thuto ka ga gonwa le go tlhokomela melemo (gotswa mo mooking kgotsa ngaka ya tliliniki)	Nnete	1
			Nyaya	2
		E.6a.9 Tse dingwe: [Tlhalosa:]	Nnete	1
			Nyaya	2

E.6b (BRHC)	Tlhalosa gore ke mokgwa ofe wa tshegetso ya ARV mo go e e latelang e o e amogetseng/ dirisitseng ga o sale o rometswe ko BroadReach go go thusa go nna o nwa diARV. O ka nne wa tlhalosa go feta bongwe. ***Interviewer**: Read out the list of services. Mark yes or no for each one.*	E.6b.1 Moemanokeng mo kalafong/ motshegetsi	Nnete	1
			Nyaya	2
		E.6b.2 BroadReach Regional Coordinator (Holiness)	Nnete	1
			Nyaya	2
		E.6b.3 Kgakololo ka ngaka ko sejering	Nnete	1
			Nyaya	2
		E.6b.4 Mokgatlo wa kemonokeng wa HIV	Nnete	1
			Nyaya	2
		E.6b.5 Matlole a katlatleloloago/ Social Grant (Bogole, tlhokomelo ya bana, kgodiso ya bana)	Nnete	1
			Nyaya	2
		E.6b.6 Thuso ya dijo	Nnete	1
			Nyaya	2
		E.6b.7 Mokgatlo wa legae o e seng wa	Nnete	1

		puso	Nyaya	2
		E.6b.8 Thuto ka ga gonwa le go tlhokomela melemo (gotswa mo ngakeng kgotsa modiredi wa BroadReach)	Nnete	1
			Nyaya	2
		E.6b.9 Tse dingwe: [Tlhalosa]:	Nnete	1
			Nyaya	2

F. Boleng ba tlhokomelo

[**Interviewer note**: This part of Section F is **only for BRHC patients**]

Tlhalosa ka mokgwa o o dumalanang ka teng le dintlha tse di latelang:		Ke dumela thata	Ke a dumela	Ga ke dumele ebile ga ke ganetse	Ga ke dumele	Ga ke dumele thata	ga ke itse
F.1a	Ngaka ya me e a kgathala ka boitekanelo ba me.	1	2	3	4	5	99
F.2a	Ngaka ya me e na le kitso	1	2	3	4	5	99
F.3a	Ngaka ya me e botsalano	1	2	3	4	5	99
F.4a	Ke dumela gore nka bua le ngaka ya me fa ke na le mathata ka boitekanelo ba me	1	2	3	4	5	99
F.5a	Ke dumela gore nka bua le ngaka ya me fa kena le mathata a selegae a a ka amang gonwa/ tlhokomelo ya melemo ya me.	1	2	3	4	5	99
F.6a	Ke kgona go bua nnete mo ngakeng ya ka le go mmolella fa ke sa nwa diARV tsa me.	1	2	3	4	5	99
F.7a	Ka kakaretso ke dumela gore ke amogela tlhokomelo ya kalafi ya HIV ya boleng bo bo siameng.	1	2	3	4	5	99

[**Interviewer note**: This part of Section F is **only for PHC patients**]

Tlhalosa ka mokgwa o o dumalanang ka teng le dintlha tse di latelang:		Ke dumela thata	Ke a dumela	Ga ke dumele ebile ga ke ganetse	Ga ke dumele	Ga ke dumele thata	ga ke itse
F.1b	Baoki ba a kgathala ka boitekanelo bame	1	2	3	4	5	99
F.2b	Baoki ba na le kitso.	1	2	3	4	5	99
F.3b	Baoki ba me ba botsalano	1	2	3	4	5	99
F.4b	Ke dumela gore nka bua le baoki fa ke na le mathata ka boitekanelo ba me.	1	2	3	4	5	99
F.5b	Ke dumela gore nka bua le baoki fa kena le mathata a selegae a a ka amang gonwa/ tlhokomelo ya melemo ya me.	1	2	3	4	5	99
F.6b	Ke kgona go bua nnete mo baoking le go ba bolella fa ke sa nwa diARV tsa me.	1	2	3	4	5	99
F.7b	Ka kakaretso ke dumela gore ke amogela tlhokomelo ya kalafi ya HIV ya boleng bo bo siameng.	1	2	3	4	5	99

Tlhalosa ka mokgwa o o tshepang batho ba ba latelang gore ba ka kgona go tlhokomela HIV ya gago:		Ope/ gongwe ope wa bona o a Tshepagala	Ke palo e nnye ya bona e e tshepagala ng	Ga ke itse go le gontsi ka bona gore nka bua	Ba bangwe ba bona ba ka tshepagala	Bontsi ba bona bo ka tshepagala
F.8.1	Baoki mo tliliniking tsa puso (PHCs)	1	2	3	4	5
F.8.2	Dingaka tsa puso (PHCs)	1	2	3	4	5
F.8.3	Dingaka tse eseng tsa puso (GPs)	1	2	3	4	5
F.8.4	Dingaka tsa setso (Sangoma, Herbalist etc.)	1	2	3	4	5

F.9	Ga ona le tlhopo, o ka eletsa go bona mang kgwedi le kgwedi mabapi le di ARV tsa gago?	Mooki wa bosechaba	1
		Ngaka ya bosechaba	2
		Ngaka e e seng ya puso (GP)	3
		Ga ke na tlhopo	4

F.10	Ga o ne o na le tlhopo, o ka eletsa go bona mang fa ona le bothata (side effects) ka HIV kgotsa ARV tsa ga go?	Mooki wa bosechaba	1
		Ngaka ya bosechaba	2
		Ngaka e e seng ya puso (GP)	3
		Ngaka ya setso	4
		Ga ke na tlhopo	5

Ga o tlotswe ke letlha la go tsaya dipilisi tsa kgwedi, dilo tse di latelang di a diragala (o ka nne wa nna le karabo tse dintsi):	Ka gale	Ka dinako tse dintsi	Nako e nngwe	Ga go diragale gantsi	Ga go diragale	Ga ke itse
F.11.1 O romellwa molaetsa ka founu go go gopotsa (SMS).	1	2	3	4	5	99
F.11.2 O a founelwa go go gopotsa go tla.	1	2	3	4	5	99
F.11.3 O etelwa ke modiredi wa boitekanelo ko tlung ya gago.	1	2	3	4	5	99
F.11.4 Tse dingwe?	1	2	3	4	5	99

Ga o tlotswe ke letlha la go tsewa madi, dilo tse di latelang di a diragala (o ka nne wa nna le karabo tse dintsi):	Ka gale	Ka dinako tse dintsi	Nako e nngwe	Ga go diragale gantsi	Ga go diragale	Ga ke itse
F.12.1 O romellwa molaetsa ka founu go go gopotsa (SMS).	1	2	3	4	5	99
F.12.2 O a founelwa go go gopotsa go tla.	1	2	3	4	5	99
F.12.3 O etelwa ke modiredi wa boitekanelo ko tlung ya gago.	1	2	3	4	5	99
F.12.4 Tse dingwe?	1	2	3	4	5	99

F.12	Ka gale o tsamaya nako e e kanakang go ya le go bowa go tsaya diARV tsa kgwedi? (nako ka botlalo).	Diura (2-digits):	___ ___
		Metsotso: (2-digits):	___ ___

F.13	Ka gale o duela bokae go ya le go bowa go tsaya diARV tsa kgwedi? (dituelo tsotlhe tsa tsela).	**R**_____ . ____

F.14	Ka gale o tsaya nako e e kanakang go	Diura (2-digits):	___ ___

	tsa diARV tsa kgwedi. (go tloga ka nako e o gorogang ka yona ko tliliniking/ ngakeng(GP) go fitlha o tswa)?	Metsotso: (2-digits):	___ ___

F.15	Ka gale o tsaya nako e e kanakang go go ya le go tsewa madi (go tloga ka nako e o gorogang ka yona ko tliliniking go fitlha o tswa)?	Diura (2-digits):	___ ___
		Metsotso: (2-digits):	___ ___

G. KITSO KA HIV/AIDS LE MELEMO YA ARV

		Nnete	Ga se nnete
G.1.1	Batho ba ba amogelang melemo ya ARV ba santse ba ka kgona go fetisetsa HIV mo bathong ba bangwe ka thobalano e e sa sirelediwang.	1	2
G.1.2	Motho o tshwanetse go tswella go tsaya melemo ya ARV morago ga go oketsega ga bokete ba mmele.	1	2
G.1.3	Melemo ya ARV e tlosa HIV mo mmeleng wa me.	1	2
G.1.4	Morago ga dingwaga, motho a ka nne a tlogela go tsaya melemo ya ARV	1	2

H. Boleng ba botshelo

Re batla go go botsa dipotso ka boleng ba botshelo ba gago. Tlhopa karabo ya nnete e e tlhalosang maikutlo a gago kajeno.

*[**Interviewer note**: Please circle the number that corresponds to the participant response. For H.6 please show the participant the scale and read the instructions in the box on the right along with them.]*

H.1 Go tsamaya	
Ga ke na bothata ba go tsamaya	1
Ke na le bothata (nako e nngwe) fa ke tsamaya	2
Ke nna fela mo bolaong (ga ke kgone go tsamaya)	3

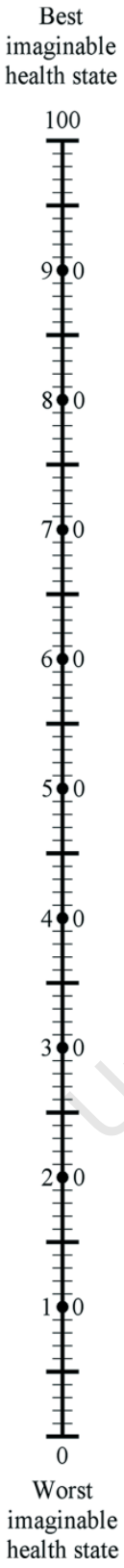
H.2 Go itlhokomela	
Ga ke na bothata go itlhokomela	1
Ke na le bothata go itlhapisa le go ikapesa (nako e nngwe)	2
Ga ke kgone go itlhapisa le go ikapesa	3

H.3 Dilo tsa ka gale *(e.g. go bereka, go ithuta,tiro ya mo lapeng,dilo tsa mo lapeng)*	
Ga ke na bothata go dira dilo tsa me tsa ka gale	1
Ke na le bothata go dira dilo tsa me tsa ka gale (nako e nngwe)	2
Ga ke kgone go dira dilo tsa me tsa ka gale	3

H.4 Ditlhabi/ go sa ikutlwe sentle	
Ga ke na setlhabi(go opelwa) kgotsa go sa ikutlwe sentle	1
Ke na le setlhabi(go opelwa) se se nnye le go sa ikutlwe sentle	2
Ke na le go opelwa go go tseneletseng le go sa ikutlwe sentle go go tseneletseng	3

H.5 Letsapa/ go imelega	
Ga ke na letsapa kgotsa go sa ikutlwe sentle	1
Ke na le letsapa le le nnye kgotsa go imelega go go nnye	2
Ke na le letsapa kgotsa go imelega go go tseneletseng	3

H.6 SEEMO SA BOITEKANELO BA GAGO KAJENO:



Go thusa batho gore ba tlhalose go siama kgotsa go sa siama ga boitekanelo ba bone, re dirile mola mo letshwao la 100 le kayang boitekanelo bo bo ntle mme boitekanelo bo bo sa siamang bo bontshiwa ka letshwao la 0.

Re batla gore o bontshe mo sekaleng se, boemo bo bo siameng kgotsa bo bo sa siamang ba boitekanelo ba gago go ya ka wena. Dira mola go tswa mo lebokosong le le fa tlase go fitlha mo letshwaong le le bontshang go siama kgotsa go sa siama ga boitekanelo ba gago.

I. Tlhopo ya lenaneo la thomelo

Labofelo, re batla go go botsa gore goreng o tlhopile go yak o ngakeng e e seng ya puso (GP) le go kwadisiwa mo BroadReach, kgotsa goreng o tlhopile go ya ko tliliniking fa o ne o romelwa gotswa mo Wellness clinic.

[**Interviewier**: Please list all reasons for their choice or if they don't know, circle Reason 6 below.
Make sure they know they can give more than one reason for their choice]:

I.1a	Mabaka a a dirileng gore ke tlhope go kwadisiwa mo BroadReach le go bona ngaka a akaretsa:	Lebaka 1 **(I.1a.1):**
		Lebaka 2 **(I.1a.2):**
		Lebaka 3 **(I.1a.3):**
		Lebaka 4 **(I.1a.4):**
		Lebaka 5 **(I.1a.5):**
		Lebaka 6 **(I.1a.6):** **Ga ke itse gore goreng ke dirile tlhopo e.**

I.1b	Mabaka a a dirileng gore ke tlhope go ya ko tliliniking a akaretsa:	Lebaka 1 **(I.1b.1):**
		Lebaka 2 **(I.1b.2):**
		Lebaka 3 **(I.1b.3):**
		Lebaka 4 **(I.1b.4):**
		Lebaka 5 **(I.1b.5):**
		Lebaka 6 **(I.1b.6):** **Ga ke itse gore goreng ke dirile tlhopo e.**

I.2 A o itumeletse tlhopo e o e dirileng?

I.3 Ga one o ka fiwa tetla ya go fetola lenaneo la gago, a o ka dira jalo? **Nnete / Nyaya**

I.4 Mpolelle selo se se ntle ka ga go ya ko ngakeng kgotsa ko tliliniking:

I.5 Mpolelle selo se se seng sentle ka ga goya ko ngakeng kgotsa ko tliliniking:

END OF QUESTIONNAIRE

J. Interview Evaluation – *To be completed by Interviewer <u>after</u> interview*

J.1	How would you describe the respondent's vocabulary (the variety of words the respondent used during the interview to express his/her thoughts)?	Below average	1
		Average	2
		Above average	3
J.2	In general, how did the respondent act towards you during the interview?	Hostile	1
		Neither hostile nor friendly	2
		Friendly	3
J.3	How attentive was the respondent to the questions during the interview?	Not at all attentive	1
		Somewhat attentive	2
		Very attentive	3
J.4	Were other persons within hearing range at any time during the interview?	No other person within hearing range at any time	1
		1+ persons within hearing range for **part** of interview	2
		1+ persons within hearing range for **all** of the interview	3
J.5	I have **quality controlled** this questionnaire according to the Quality Control checklist provided:		
	(Signature of Interviewer)		
Interviewer: Any additional comments about specific questions or data quality should go on inside back of cover page			

Appendix III: Patient Perceptions of Quality of HIV Care and Treatment in Matlosana Sub-district, North West Province

Interview Guide

This document supplements the quantitative instruments (questionnaire) and the interviewer training sessions. It begins with a brief overview of the roles and responsibilities of the research assistant (RA), as well as a discussion of quantitative interviewing procedures and the general guidelines for conducting the interviews. It then covers the step-by-step process of enrolling patients, administering informed consent and the questionnaires, data collection and processing, and stipends. Finally, this guide provides a question-by-question (QxQ) set of instructions for the instruments. The overall objective is to help you, the interviewer, be consistent. Consistency is crucial for the data to be meaningful. Quantitative interviews must be conducted in the same way to avoid biasing any of the respondents' responses in any way.

I. Roles and Responsibilities of the Research Assistant

During this project, the RA will play a pivotal role in the day-to-day coordination of activities. The specific duties include the following:

- Recruit out to prospective participants
- Schedule interviews
- Educate participants about the study
- Confirm participant eligibility for the study
- Obtain and document informed consent
- Answer questions from participants about the study
- Assign participant IDs
- Administer participant questionnaires
- Manage and distribute participant stipends
- Ensure that research data is complete
- Maintain a well organized record keeping system – hard copies and electronic
- Maintain security and confidentiality of study records
- Enter data from completed questionnaire into study database
- Bring any problems or questions to the attention of the principal investigator (PI)

II. Study Activities

Eligibility

The RA will receive a list of pre-screened participants for the study from the principal investigator. There will be approximately 40 participants from the BroadReach program and 40 from the public sector primary healthcare clinics. The RA must confirm eligibility when recruiting participants (see Recruitment section below). All patients should meet the eligibility criteria described below. The eligibility and exclusion criteria are the same for both groups of patients.

Eligibility Criteria:

- HIV (+) and on ARVs at the time of the interview;
- First down-referred between 28 November 2005 and 30 June 2007 (inclusive);

- Receiving care either through BroadReach / KOSHMED GP network or the Matlosana public sector ARV program
- >18 years of age
- Able and willing to give informed consent

Exclusion criteria:

- <18 years of age
- Unable or unwilling to give informed consent
- Does not meet eligibility criteria

Recruitment

The RA will receive a list of potential participants from the PI, and will make phone calls to all potential participants (see phone script below), and schedule interviews with those that agree to participate in the study. The RA may receive assistance with recruitment from the BroadReach Regional Coordinator, who has existing relationships with many of the patients, and can facilitate setting up interviews and confirming eligibility.

Telephone Script/Talking Points:

- I am interviewing ART patients who live in Matlosana in order to understand their quality of life on ARVs and the quality of HIV care and treatment;
- The goal of this study is to improve the quality of care in the sub-district;
- Participation in the study is voluntary; and you can decide not to participate at any point without consequences;
- Participant identities will be kept confidential and only known by the RA and the principal investigator;
- If you agree to participate, you will be compensated for your round trip travel costs, and receive a meal voucher worth R50.00.
- The interview will take no more than 30 minutes total;
- If you're interested in participating, I would be happy to schedule a place and time for the interview right now.

Informed consent

Obtaining Informed Consent to Participate

At the beginning of the interview, the RA will provide detailed information about the study to the prospective participants and answer any questions they might have. If the patient agrees to participate, the RA will obtain written informed consent using an IRB-approved document prior to starting the interview. Only the informed consent provided to you by the PI should be used. Ensure that the participant receives a copy of the informed consent, and the study copy is appropriately filed.

General Principles of Obtaining Informed Consent

- Informed consent refers to the voluntary choice of an individual to participate in research based on an accurate and complete understanding of its purposes, procedures, risks, benefits, alternatives, and any other factors that may affect a person's decision to volunteer. Informed consent is based on the ethical principle of "respect for persons" and recognizes that each individual should have autonomy and freedom to make their own decisions.
- A decision to volunteer for research should be made freely and without pressure, coercion or any undue influence.
- Potential participants must understand that their decision about whether to participate or not will have NO effect on their relationship to their providers or the services they receive from the clinic.
- Informed consent is not a single event or just a form to be signed. Rather, it is an ongoing process that takes place between the research team and the participant over the course of a project. The consent form is merely the documentation of informed consent and does not, in and of itself, constitute informed consent.
- A signed copy of the consent form must be offered to all participants who volunteer. If they refuse the copy, keep it in the files and document refusal.
- Information must be conveyed in language that is understandable to the participant. If the participant does not understand certain aspects of the study, review those aspects again until the participant fully understands them. <u>If after all possible efforts are exhausted, the participant is not able to demonstrate a full understanding of the study, do not ask him/her to sign the consent form.</u> The subject must be given sufficient opportunity to consider whether or not to participate.

- If the participant is literate, give him/her a copy of the consent form to read. After the participant has read the written material (or had it read to him/her), verbally review the information provided.
- If the participant is not able to read, read the materials to him/her word for word. The informed consent process for illiterate participants has to be verified by signature of an impartial witness on the signature page of the informed consent document.The Regional Coordinator (RC) can serve as a witness to the consent.
- Also, emphasize to the participant that his/her medical care and any other services received from the recruitment site will not be affected by his/her decision whether or not to take part in the study. Encourage the participant to take as much time as needed before making a decision.
- An environment of privacy and confidentiality is essential for this project so that participants can feel free to answer the surveys honestly. The fact that their Doctor will not see their responses is a critical point to emphasize.
- Security of the data overall, including use of codes rather than names, should also be emphasized.

Steps for Research Analyst in Conducting the Informed Consent Process

- Sit with participant in a quiet and private area (and witness if participant is illiterate).
- Give general description of what the study participants are asked to do
- Review the highlights of the informed consent document.
- Give participant time to read entire consent form.
- Answer any questions and reiterate the voluntary nature of the study.
- Have patient sign and date 2 copies of form; add your signature to form. Offer the participant a copy of the signed informed consent. If they choose not to take it that is fine.
- NB: If the participant is not able to sign, study staff should bring in a third party (RC if available) to witness the delivery of the consent, to verify that to the best of their knowledge the participant understood and agrees with the consent form. For an illiterate participant, the study staff delivering the informed consent may print the participant name on the name line and have the participant “make their mark” (sign

an “x”) on the signature line. The third person then writes and signs name and dates as witness.

Assigning Unique Identification (ID) Numbers:

To maintain patient’s confidentiality, a unique participant identification (ID) number will be assigned by the research analyst to each participant upon enrollment into the study. The RA must maintain a spreadsheet that includes the Study ID and corresponding BRHC ID# or Wellness Clinic file # for quality control purposes. This is the only place the participants and their personal information will be linked, and once the study is complete the file will be destroyed.

The Study ID# consists of 8 digits. The digits are assigned as follows:

Digits 1 – 4: This is a randomly assigned number starting with ‘”1” for all public sector patients, and “5” for all PPP (GP) patients. Therefore the first 4 digits for patient #1 from the public sector would be “1001.” The first 4 digits for patient #35 from the GP program would be “5035.”

Digits 5 and 6: These 2 digits indicate patient gender. “01” equates to a male, and “02” equates to a female.

Digits 7 and 8: These two digits indicate the patients’ service outlet. Tables 1 and 2 below provide the codes for the PHC patients and the GP program respectively:

TABLE 1: Codes for PHC patients

Alabama	01	Khuma	07
Botshabelo	02	Orkney	08
Gateway	03	Park Street	09
Grace Mokgomo	04	Stilfontein	10
Jouberton	05	Tigane	11
Kanana	06	Empilisweni	12

TABLE 2: Codes for BRHC Patients

Akuoko	01	Masudubele	11
Baninzi	02	Mohammed	12
Benjamin	03	Mosame	13
Ebrahim	04	Motala	14
Mangaba	05	Mphatsoe	15
Hellmann	06	Nassir	16
Hoosen	07	Rawat	17
Jaworski	08	Senyatsi	18
Khunou	09	Selomane	19
Leburu	10		

Examples:

The 33rd male patient from the GP model who is seeing Dr. Nassir would have the following Study ID: **50330115**

The 100th female patient from the PHCs who is attending Jouberton Clinic would have the following Study ID: **11000205**

III. General Guidelines for Administering a Questionnaire

Administering the Questionnaire:

You will administer the quantitative questionnaires by reading each item aloud to the respondent, at a relaxed conversational pace. Questions should be read in the order they appear on the questionnaire. Your intonation should go up slightly (a raised voice pitch) at the end of each question, to indicate that it is a question. You should be attentive and respectful during the interview. You will record the responses onto the questionnaire. There are some brief explanations of items that go with certain questions. Avoid adding any extra words between questions, other than mild occasional general encouragement such as, "You're giving this good effort," and "We're making good progress." Inform the respondent that is okay to tell you if the pace is too fast or too slow.

Problem Answers:

Refusal to Answer: Respondents may of course refuse to answer specific questions. However, they should be encouraged by reminding them of the confidential nature of the survey and the importance of the information. In addition, they should be reminded that there is no right or wrong answer. If after reminding them of this they still wish to refuse a question, move on.

"I don't know." Many of the questions give "I don't know" as a possible response. Please DO NOT read this option to the patients. The goal here is to get them to give an answer. If the respondent offers an "I don't know" answer, respond with "Well, let me repeat the question…" If the respondent is vacillating between two responses reply, "Well, in general, how do you feel/what do you think?" Read each question verbatim. If the respondent wants the question repeated, read it again verbatim. If the respondent does not understand ask him to give it his best shot, based on their current interpretation. If the respondent asks "Do you mean _____ " , respond "yes" or "no". You should NOT try to interpret the words or paraphrase the question. If there are questions that many patients seem to struggle with, call the PI and report this.

Completeness and Accuracy:

For most items on the quantitative measures you must obtain answers to the questions in the form of the choices provided, rather than allowing the respondent to answer questions with his/her own response wording. Even when there is an open-ended question in a quantitative interview you are trying to determine how to categorize their responses within set predetermined categories. If you are unsure how to categorize, write in the responses and the team will assist in determining. Please do your best to obtain responses to all of the study questions.

If you need to change or correct an answer you've written on the questionnaire (if for example the participant changes their mind on a certain question), then please cross out the first response and circle the correct response and sign your initials next to the scratched out answer.

Privacy and Contextual Consistency:

The quantitative interview needs to be conducted in private. Otherwise, the respondent may not feel comfortable answering the questions. If respondents ask for others to be present, indicate that "because this is a study which is being done with many people, we need to make this interview the same for everyone, including doing it in private. Bringing other people into the situation would make this interview different, even if they didn't say anything." This type of response can also address other deviations that respondents may request, such as breaking the interview up into smaller sessions or completing it in their own handwriting.

Impartiality:

Please do not agree with, disagree with, or correct statements made by respondents. If they ask questions about the study itself, you may decide to provide a brief and straightforward answer in the interest of the ongoing informed consent process, or you may need to direct them to the PI's phone number on the informed consent form in the case you are uncertain how to answer. It is preferable to politely defer general questions to the end of the interview, at which point you may need to consult a local referral sheet, which should list sources of information. It is important not to offer feedback: no implications or judgments.

Participant Management:

The respondent may bring up concerns that we must address for ethical reasons. You cannot try to solve the respondents' problems yourself in the interview situation via counseling or practical assistance such as money, goods, or transportation. This is inappropriate for your role as interviewer and could compromise the study. This does not mean that you cannot listen to comments that the respondent makes about his/her problems. State that it sounds like he/she has some important concerns, and that you would like to address it at the end of the interview. If he/she is emotionally upset, however, the interview may need to be postponed in light of this distress. If you are in a situation that you are not sure how to handle, call the PI.

Preparation:

Because the time of the interview must be held to a minimum, familiarity and practice with the measures are essential. A professional approach in the interview session will involve being courteous while moving quickly through the procedure. If you are comfortable with the administration and the content then they should be as well. The PI will practice the interview with you to ensure you're comfortable with the process, and there will be several pilot interviews to ensure the questionnaire is understood and so the RA can practice.

Interviewer Safety:

Once in awhile a respondent may make what you judge to be inappropriate or offensive

comments about others or yourself. Isolated comments can usually be ignored and might not be repeated, whereas ongoing harassing behavior can be met with a request not to make those types of comments. If you feel threatened you should terminate an interview and leave the situation. Respondent interviews should be conducted only in locations and situations approved by the PI.

Stipends:

Study subjects will receive a stipend to compensate them for their time and travel, as well as a food voucher. Study participants will receive a R50.00 voucher to Checkers for their participation. Vouchers will be provided to the RA prior to the interview.

Participants should receive their voucher after completing the interview. Research analysts must keep a record of vouchers disbursed to participants (by ID#), and participants must sign to indicate that they have received their stipend. The RA must keep a spreadsheet to track voucher payments.

Data Management:

- All interviews will be reviewed for quality assurance; the PI will check all questionnaires prior to data entry into the study database.
- Each item on the instrument must have a response (if there is no response the interviewer must put a note on the margin next to the relevant item explaining why there was no response so that the data capturer can know that the data is not missing).

IV. Question by Question Instructions (Q x Q):

QUESTION	INSTRUCTIONS TO THE INTERVIEWER
B.2	Be sure to record the last year of study they COMPLETED
B.3	If they answer NO, then skip ahead to C.1.
B.4-B.7	Complete each question for all jobs worked
B.8	Ensure that they report ALL income – not just work (grants, gifts etc).
D.1	If they ask, define lately as w/in the past month or so
D.4	Make sure they understand that 10 = PERFECT Health and 1 = as sick as they can imagine
D.4.3	Ask them to think about when they were down referred from Wellness – how healthy did they feel at that point?
D.5	Ask about each side-effect and if they answer YES ask if they told their doctor or nurse and complete the second column; if they didn't have the side-effect move to the next one; be sure to read ALL 13 listed side-effects.
E.2	Allow the patient to mark on the line – tell them they are allowed to mark ANYWHERE on the line; provide guidance (for example tell them that if they mark on the "5" it means they take their pills half of the time. Same for E.3
E.4/E.5	Write the number they indicate even if it's just a guess/approximation
E.6a	PHC patients only. Make sure that they understand that we want to know about the use of these services AFTER down referral from Wellness; please read the entire list; then ask if they have used any other HIV-support services of any kind.

E.6b	BRHC patients only. Make sure that they understand that we want to know about the use of these services AFTER down referral from Wellness; please read the entire list; then ask if they have used any other HIV-support services of any kind.
F.1a-F.7a	BRHC ONLY
F.1b-F.7b	Public Sector ONLY
F.9	Refers to ROUTINE monthly visits
F.10	Refers to if they get sick; can give example like a severe side-effect
F.11.1-F.11.4	Ask the participant to remember the times they have missed a drug pick-up and to tell you what happened. If they say they have never missed a pick up, then circle "Don't know" for each question.
F.11.1-F.11.4	Ask the participant to remember the times they have missed a 6-monthly blood-draw appointment and to tell you what happened. If they say they have never missed a pick up, then circle "Don't know" for each question.
F.12	Make sure they understand that they give us total travel time to and from the clinic/surgery. If it takes an hour and a half, then enter 01 for Hours and 30 for min. If it's a total of 45 min, then enter 00 for hours and 45 for minutes.
F.13	Round-trip costs to pick-up drugs every month
F.14	This should not include travel time…visit time only from arrival to departure.
F.15	This refers to the 6 monthly visit that includes their blood draw for CD4/VL results.
H.1 – H.5	Please ask them to rate their quality of life today.
H.6	Ask the patient to indicate their health today. They can mark anywhere on the line. Make sure they understand that 100 is perfect health and 0 is worst imaginable health.
I.1a/I.1b	Please write down all specific reasons a person chose to attend BroadReach or the PHC. Give them time to think, and remind them that it's ok to give several reasons. Only select reason 6 if they really cannot think of anything after some time has passed.
I.2	Please note if they are happy with their choice and why.
I.3	Please mark down either YES or NO
I.4/I.5	If they give more than one thing, please note all.
J.	Please complete once the interview is over.

REMINDER: Please do NOT read "I don't know" as a potential answer to participants. Only indicate on the questionnaire if they cannot provide an answer after repeating and clarifying the question. The goal is to get answers to all questions.

V. Interview Talking points and Checklist:

Before Interview:

- Please be sure to pre-fill Section A. All of this information will be made available to you before subjects are recruited.
- Ensure that the Study ID and Date are on every page at the top (header), **EXCEPT** on the Informed Consent. Study ID should NOT be written on the Informed Consent.

Introduction:

"Hi, my name is _____, and I am working on a University of Cape Town research study that is trying to understand patients experiences on ARVs and the quality of care and quality of life they are experiencing. Thank you for taking the time to participate in this interview."

Then:

- Administer Informed Consent:
- Review IC with participant (Literate = allow participant to read and then review; Illiterate = Read word for word and assess understanding).
- RC witness if necessary (Illiterate participants)
- IC signed
- Offer copy of IC to all participants (you must have 2 copies for each participant
- Ask if they have any final questions before starting
- Complete Pre-questionnaire Checklist at the bottom of the first page
- Administer questionnaire (see Manual for QxQ instructions)
- "I'd like to start by asking you a few general questions about yourself. Then we will be talking about HIV and taking HIV medicines, but I will explain more about that when we get there."

After the Interview:

- Give the respondent some praise for completing the task and hanging in there with you, despite the sensitive and personal nature of the questions.
- Provide respondent with stipend and voucher.
- Ensure that all forms are correctly coded and information is filled out as completely as possible: complete **Section J** on last page.
- Organize and file hard copies of all research related documents by participant ID #.
- Do not leave any interview data unattended or open for public viewing – it must be kept secure at all times. The patient log which links patients to the study ID is particularly sensitive.
- Enter the data into the database.
- Report any problems or anomalies encountered during the research to the PI.

Chapter 7

Discussion

7.1 Principal findings

Efficient and effective ART care and treatment models are among the most important, but least researched components of HIV service provision in developing countries. Published economic analyses have focused on the costs and cost-effectiveness of HIV treatment program inputs, on some but not all relevant program outputs and outcomes, and have overlooked the importance of the service delivery mechanism. Little is known about how different models of care with different features such as staffing composition, support interventions, and management and operations compare in terms of costs and patient outcomes. This is an egregious oversight considering the paucity of health professionals in most public health systems, and that human resources are the second most costly component of care after drugs. Several published papers in the HIV program literature have called for an examination of models of care, with an emphasis on implementation, costs, and outcomes (Hirschhorn, Ojikutu & Rodriguez, 2007; Bekker et al., 2006; Rosen, Long & Sanne, 2008; Creese et al., 2002). This study is the first to evaluate different models of down-referral care in South Africa in terms of costs, cost-effectiveness, and outcomes, and patient satisfaction.

This study reports on the implementation and performance of an innovative PPP model for down-referral care for patients who are stable on HIV treatment, and compares it to the status quo public sector clinic-based model. There is no consensus in the ART program or health economics literature on how to measure the success of an HIV treatment intervention or program, and this study reports a range of quantitative and qualitative indicators to assess model performance. For this study's primary outcome measure, the clinical and operational objectives of down-referral care -- to maintain patients at the down-referral site with suppressed viral loads -- were adopted and combined into a single metric of effect. Other performance metrics including total model cost, LOI, cost per patient suppressed and per patient retained, patient retention, and patient perceptions of quality of care helped provide a more complete picture of each model's performance for the analysis.

In the PPP cohort, 83 percent of all study patients were suppressed and in care at the down-referral site, compared to 55 percent in the PHC cohort. Cost-effectiveness analysis showed that given a budget constraint and a mutually exclusive choice, policy makers should always implement the PPP model that had a lower ICER of R505.20 and dominated (extended dominance) the PHC model. The biggest contributor to attrition in

the PHC model was LTF (47 patients) followed by up-referral to the hospital outpatient clinic (39 patients). By comparison, five patients were LTF and 11 in care at the hospital outpatient clinic. In terms of overall patient retention (regardless of viral suppression status or site of care), 94 percent of PPP patients remained in the program at study end compared to 75 percent of the PHC patients. Twenty-five percent of the PHC cohort was no longer in care within 19 months after down-referral (and just over 30 months on ART), and one-third were no longer suppressed. This is particularly concerning because all of the patients had suppressed viral loads and were stable on treatment at the time of down-referral. At the time of writing, there was no comparable published data on ART program retention among previously suppressed patients, but in their meta-analysis of ART program retention, Rosen and colleagues (2007) found that on average, programs in southern Africa retained 75 percent of patients after just twelve months of treatment. Greater emphasis on patient tracking and follow-up could help to catch people before they fall off treatment, and to document patients who simply transfer to other clinics for care. LTF is discussed in greater detail later in this chapter. Total costs for the study period were higher in the PPP model, regardless of whether or not LOI was included in the total cost calculation. The average total cost per patient per month for care, drugs, and laboratory tests was R545.38 in the PPP cohort and R439.47 in the PHC cohort. From a purely economic perspective, the PPP model provided better protection of the original investment required to stabilize patients on ART, incurring an estimated R78,634 LOI compared to R339,910 LOI in the PHC cohort over the course of the study. Patients from both cohorts reported high levels of treatment adherence, felt healthy (although PPP patients reported feeling somewhat healthier), and were satisfied with the care they received. Among the patients interviewed, there were no observed differences in terms of HIV/AIDS knowledge, employment, or level of educational attainment.

7.2 Cost drivers

Like most other published economic analyses of ART programs reviewed in Chapter 2 in this paper, this study adopted a payer perspective on drug, patient care and laboratory examination costs. Also typical of the existing literature, differing levels of precision were employed for estimating the costs of the ART services in this analysis, ranging from a simple macro-costing of hospital per diem (PDE) for inpatient care, to a micro-costing of PPP services. The rule of thumb in economic analysis with regards to costing precision is that the more germane the service cost is to the overall analysis, the more precise the costing method should ideally be, and every effort was made to

adhere to this principle.

7.2.1 Care cost

While a micro-costing of services was feasible for the PPP model, public sector cost data were either too limited or too difficult to isolate from other primary care (non-HIV) service costs. Challenges encountered while collecting public sector cost data for this analysis included insufficient data on infrastructure or overhead costs at the hospital outpatient clinic and the PHCs, a lack of separate accounting for clinic supplies, equipment, antiretrovirals, and all other non-antiretroviral drugs at the PHCs, and inadequacies in the reporting of, and budgeting for, key health-care personnel costs at the out-patient clinic. It is noteworthy that there are no published estimates in the literature of the cost of HIV care delivered in the context of a primary care facility in South Africa or elsewhere. This may be due in part to challenges associated with isolating HIV-specific costs from the non-HIV costs at a PHC. In the end, this analysis relied on clinic health worker salary data to estimate the cost of a routine ART visit at the PHCs. Although this likely resulted in an underestimate of the true cost of a visit, previous research from dedicated ART clinics in South Africa demonstrated that health worker salaries comprise the vast majority of care costs once ARV drugs and laboratory exams were taken into account (Harling, Bekker & Wood, 2007; Bekker et al., 2003). In the cost analysis by Harling, Bekker and Wood (2007), capital costs were just three percent of total visit costs (they increased to nine percent when the clinic moved to a new, larger facility). While facility costs should ideally have been included, they would have likely been negligible on a per visit basis given that these costs would have been spread across all primary care clinic patients and not just the ART patients. Finally, because no special equipment is required for routine ART monitoring visits, and all non-ART drugs were provided by the public sector for both cohorts (PPP doctors cannot prescribe other medications for patients), it was felt that an activity-based estimate (pro-rating of salaries according to the estimated amount of time spent on ART visits) of total health worker salaries per hour would provide a reasonable, albeit it slight under-estimate of the cost of a routine ART visit in the PHCs.

Although there are no published estimates of the cost of ART care delivered in a PHC, the literature does contain published estimates of the cost of the costs of care in dedicated ART clinics and of general primary care costs in South Africa, which provide useful points of reference for the estimates used in this study. Cleary and colleagues (2005) reported that a routine ART visit to a dedicated ART clinic in Khayelitsha in the

Western Cape in the 2002/2003 fiscal year cost R145.15, excluding medicines and laboratory examinations. A more recent study (Harling, 2007) also examined the cost of running a doctor-intensive, dedicated ART clinic in the Western Cape over a two year period and found that the cost per visit was US$41.62 (approximately R267.62) in 2005/2006, again excluding medicines and laboratory examinations. Rosen and colleagues (2008) estimated the unit cost per visit at a hospital-based outpatient ART clinic and a dedicated ART clinic was R170.88 and R267.31 respectively. Finally, the Health Systems Trust (Day, 2009) estimated the 2008 unit cost of a primary care visit (not HIV-specific) for the Dr. Kenneth Kaunda District in North West Province at R131.54 all inclusive, and an inpatient PDE averaged R1,438.00. Table 7.1 summarizes the unit costs per visit published in these studies and compares them to the costs published in this paper. Because each of these estimates were collected in different years, the bottom of Table 7.1 lists adjusted estimates of 2008 costs to facilitate cross-study comparison[39].

Table 7.1 Estimates of unit costs for healthcare visits at different facilities in South Africa

	Cleary 2005^	Harling 2007§	Rosen 2008‡	HST 2009∆	**PHC**	**PPP**
PHC	R145.15	R267.62	R267.31	R131.54	**R81.34**	**R202.39**
Outpatient	N/A	N/A	R170.88	N/A	**R198.13**	**R198.13**
Inpatient	N/A	N/A	N/A	R1,438.00	**R1,495.70**	**R1,495.70**
^ Dedicated ART clinic; costs excluded medicines and laboratory tests; cost data were from 2003						
§ Dedicated ART clinic; costs excluded medicines and laboratory tests; cost data were from 2004						
‡ PHC cost was for a dedicated ART clinic run by an NGO; outpatient clinic at secondary level hospital; all costs excluded medicines and diagnostics; cost data were from 2006						
∆ All costs included personnel, equipment, supplies, medicines, and laboratory tests; cost data from 2008						
Discounted estimated unit cost for a PHC (routine) visit*						
Routine visit	R194.24	R337.86	R300.35	R131.54	**R81.34**	**R202.39**

*All estimates were discounted 6 percent annually to approximate 2008 costs

The average unit cost of a PPP visit (R202.39) in this study is lower than the published cost of a dedicated ART clinic visit in the papers by Harling et al. (2007) and Rosen, Long and Sanne (2008), and only marginally higher than a visit at the ART clinic reported in the study by Cleary et al. (2005). This suggests that in terms of costs the PPP model compares very favorably with dedicated ART clinics in South Africa in terms of cost of routine care. Further research comparing PPP model performance with a

[39] All unit costs per visit were discounted at a rate of six percent annually.

dedicated ART clinic, which in some ways is more comparable in terms of the scope of services and type of healthcare provider (both rely on doctors to provide care), would further clarify its potential for replication. Predictably, PHC visit costs were lower than the published estimates of dedicated ART clinic visits with doctor-centered care, and where overhead costs may comprise a larger percentage of visit costs if patient populations were smaller and economies of scale had not be achieved (Harling, Bekker & Wood, 2007). Overall, the PHC model provides a low-cost service delivery model.

7.2.2 Drug prices

Despite drastic price reductions for first-line therapy, ART was the largest cost component in this analysis, echoing the findings from several of the studies reviewed earlier in this paper (Boulle et al., 2002; Boulle, Kenyon & Abdullah, 2003; Nattrass & Geffen, 2005; Wolf et al., 2007; Wood et al., 2000; Rosen, Long & Sanne, 2008). Drug costs comprised more than 60 percent of PHC and 50 percent of PPP total model costs despite the fact that few patients in either model were on the more expensive second-line regimen. In fact, second-line drugs constituted less than five percent of total ART costs in the PHC model, and less than one percent in the PPP model. Price reductions have been negotiated for only a limited number of antiretroviral medicines (including those used in the first-line regimen in South Africa), and few alternatives exist for patients who experience severe side-effects from these drugs. Furthermore, newer, more tolerable drugs at reduced prices would likely lead to improved adherence, which would, in turn, yield better patient outcomes and prevent or delay the need for second-line treatment. Second-line treatment is typically twice as expensive as the first-line in most countries (including in this study), and as greater numbers of patients switch to second-line therapy, overall program costs will quickly outgrow health budgets. Little progress has been made on reducing the costs of second-line and alternative first-line drugs, and renewed efforts to reduce ARV drug costs through voluntary licensing agreements, patent pools, compulsory licensing, or other creative remuneration models are required.

7.3 Lost to follow-up

As many low and middle-income countries scale-up access to ART, there is mounting empirical evidence that a significant percentage of patients are no longer on treatment within the first 12 months following initiation. Brinkhof and colleagues (2008) reviewed 15 different developing country ART programs and found that within six months of

starting treatment, approximately 23 percent of patients were no longer in care, and 20 percent were LTF (the remaining 3 percent died). Remarkably, four of the programs reviewed had no system in place to trace patients who missed an appointment or drug pick-up. Rosen and colleagues (2007) conducted a meta-analysis of 33 treatment cohorts in low and middle-income countries and reported that after by 10 months on treatment, approximately 23 percent were no longer on ART, over half of whom were LTF. After 24 months approximately 40 percent of patients were off treatment. Although both analyses reported significant heterogeneity in patient retention data from the HIV treatment programs surveyed, their findings suggest that a significant minority of patients enrolled in ART programs in low and middle-income countries are no longer on treatment within two years of ART initiation. A study in Malawi that examined the true outcomes of LTF patients found that 50 percent of LTF patients were actually deceased (Yu et al., 2007). A more recent meta-analysis of true outcomes among LTF patients reported a combined mortality among African adults of 46 percent (Brinkof, Pujades-Rodrigues & Egger, 2009). At the policy and planning level, high rates of LTF are of concern for many reasons, not the least of which is because they mask true patient outcomes, including mortality rates, and could lead to overstating the performance and impact of HIV treatment programs (Losina et al., 2009). High rates of LTF could also contribute to higher medical costs as patients who are still alive seek resource-intensive care for HIV-related complications. These results highlight the importance of measuring and reporting retention data as part of a comprehensive HIV monitoring and evaluation program, and suggest that patient retention may be a better indicator of program quality than mortality due to high rates of LTF and inconsistent documentation of patient deaths.

In contrast to the published ART program retention literature (which has focused on patient retention during the first two years of treatment), this is potentially the first study to report on patient retention and LTF in two cohorts of previously suppressed, treatment-experienced patients. Within 18 months of being down-referred for routine care, 25 percent of the PHC cohort was no longer in care, and 83 percent of those were LTF. PHC study participants spent an average of 31 months on ART, and a maximum of 44 months. Twenty-five percent of LTF patients in the PHC cohort were lost within the first nine months following down-referral. In the PPP cohort, 6 percent were no longer in care after an average of 18 months of down-referral care, and 36 percent of these were LTF after an average of 37 months on ART. The number of recorded deaths was identical in each model (n = 7).

The findings from this research, like those from other published retention studies, (Brinkhof et al., 2008; Rosen, Fox & Gill, 2007; Brinkof, Pujades-Rodrigues & Egger, 2009), suggest that LTF is the biggest cause of patient attrition, followed by death. While it is not surprising that treatment adherence waned over time, the rate at which patients stopped treatment in the PHC cohort was greater than anticipated. These results are concerning in light of the fact that all of the patients enrolled in this study had suppressed viral loads and were clinically stable at the time of down-referral. If the 46 percent mortality rate reported by Brinkof and colleagues (2009) is applied to those LTF in this study, then an estimated 29 (13 percent) PHC patients had died by study end (including the 7 documented deaths). Of course, it is possible that several PHC patients who were LTF moved or transferred their care outside the district without informing anyone, but without an investigation of true patient outcomes the number of deaths and transfers will remain speculative.

While much of the published data suggested that incidence of LTF and death tended to cluster in the first twelve months of treatment due in part to late ART initiation (Brinkof, Pujades-Rodrigues & Egger, 2009; Yu et al., 2007; Boulle et al., 2008), this study shows that reasonably high rates of LTF can occur several years into treatment among previously suppressed patients. It also shows that there can be a high degree of heterogeneity between ART programs in the numbers of patients declared LTF[40]. Similarly, the meta-analysis by Brinkhof and colleagues (2009) reported significant heterogeneity in LTF results ranging from 45 percent to 86 percent. The high rate of attrition, and LTF specifically, observed in the PHC cohort (21 percent of the PHC cohort was LTF by study end), may have been due in part to the lack of systems (including a reliable patient database) devoted to identifying at risk patients, and providing patient follow-up as necessary. The clinics in Matlosana lacked a standardized protocol for identifying, reporting on, and tracing patients who missed an appointment or drug pick-up. The lack of available phone lines at some clinics is a significant obstacle to patient tracing efforts. Some clinics have partnered with local NGOs to conduct home visits, although the partnerships remain informal, and the NGO staff is not always available, and do not get paid for the service. The hospital outpatient clinic hired a single, full-time employee (paid for by a donor partner) to help track LTF patients for the clinics, but the system for identifying and tracing patients was inconsistent, slow, and ad hoc, not to mention overwhelming for just one individual. Lower rates of LTF observed in the PPP model may be attributed to prompt

[40] The difference in LTF between the PHC and PPP models (47 versus 5) was highly significant at the 1 percent level.

identification of patients who miss appointments, systematized communication between the GPs and the NGO staff (including quarterly performance reports), routine data collection, and staff specifically tasked with patient follow-up[41]. The patient survey results reflected some of these operational differences between the treatment models. PPP patients reported more frequent contact with, or use of, support services including counseling, and adherence training, and the majority reported some contact the regional coordinator. PPP patients were also far more likely to report having received an appointment reminder via text or phone call, and reported higher rates of adherence training. PHC patients were more likely to have used a treatment buddy, although the total number was still relatively small (28 percent of the sample interviewed).

Given the limited resources for ART and the overwhelming demand for ART services across sub-Saharan Africa, particularly in the hyper-endemic southern region, it is unfortunate, but not altogether surprising, that patient support services including tracing of missing patients has not been more of a priority. Many of the HIV treatment programs in the region are funded by donors including PEPFAR, the World Bank and the GFATM, who, along with their country partners, focused initially on starting the maximum number of people on treatment as quickly as possible. This is reflected in the ART program monitoring and evaluation metrics implemented by governments and the large HIV donor organizations, which collect and report data on the number of new patient initiations on ART, rather than retention data or other qualitative data that would be indicative of program outcomes over time. In fact, PEPFAR still does not report or publicize program retention data despite claims to the contrary[42]. This initiation-induced myopia, to some degree imposed on ART programs by donor-mandated monitoring and evaluation metrics, has in many instances informed program design, or at a minimum influenced resource allocation decisions which prioritize new initiations at the expense of ongoing support for patients already on treatment (Navario, 2009). Failure to track patients over time and report retention data may also reflect a desire to report bigger numbers (more people have started treatment than are on currently), a lack of staff to track patients, poor data management systems, or a combination of the three.

Millions of people, particularly in sub-Saharan Africa, still lack access to HIV treatment, and new initiations should remain a priority. But the programmatic commitment to new

[41] It is important to note that patient follow-up and tracing is written into the job descriptions of both BRHC support staff, and it is one of their principal responsibilities.

[42] Holmes, Williams-Sherlock & Bouey (2009) recently published a letter in the Lancet correcting this author's assertion that PEPFAR does not publicize retention data (Navario, 2009). The letter stated that PEPFAR does in fact make public the number of patients currently on treatment. However, despite an exhaustive search these data have not been located.

initiations should be matched by an equal commitment to long-term support for patients already enrolled in ART treatment programs. Some might argue that rates of attrition in developing countries are similar to those observed in high-income countries, and are therefore not of sufficient concern to warrant additional attention or resources. Others might suggest that scarce resources should be focused on new initiations and not on patients unable to collect drugs and keep appointments. However, the individual and societal risks of ART attrition are much higher in high prevalence, resource-limited settings; these include higher morbidity and mortality rates, adverse socio-economic consequences due to absenteeism from work and school, the spread of drug-resistant virus, and greater numbers of vulnerable hosts for parallel epidemics like tuberculosis. Moreover, programs that only manage to keep half of their patients on treatment after two years may risk discouraging the donor support on which they rely, if donors decide that their money could achieve greater long-term impact in other ways. Finally, high rates of LTF obscure true patient outcomes, and hence disguise real morbidity and mortality rates. Recent research suggests that interventions to prevent LTF including eliminating patient co-payments and user fees (where these exist), providing meals, and reimbursing transportation can be cost-effective in resource-limited settings and should be considered an essential service in all ART treatment models (Losina et al., 2009).

The high rates of patient attrition observed in this study, as well as those reported by Rosen, Fox & Gill (2007) and Brinkof et al., (2008), highlight the need for greater emphasis on ART patient support services. Programs should make every attempt to minimize potential barriers to adherence such as direct and indirect patient costs (i.e. co-payments and transport costs), drug stock-outs and dosing errors (dispensing the wrong drugs to the wrong patients), replacing toxic drugs with newer ones that are more tolerable, and minimizing the frequency and duration of patient visits. In addition, early intervention at the first sign of non-adherence and systematic patient tracking is essential. At a minimum this requires a simple but effective data monitoring and evaluation system with clearly defined patient tracing systems in place, with specific responsibilities (from collecting patient contact information at every visit to contacting the patients) written into the job descriptions of clerks, pharmacy staff, nurses and the clinic manager. Relationships with community-based organizations and the use of media and technology interventions (i.e. texting) have also been shown to be beneficial (Harries, 2009), and should be considered when devising retention plans.

7.4 Loss on investment

This study has shown that patient attrition can continue at high rates well after the first year of treatment. High rates of premature death and LTF have important health and economic consequences for individuals, families, communities and the health system. In hyper-endemic countries with limited resources and a lack of treatment options, patient retention must be a priority. ART-delivery programs that focus solely on initiating patients and fail to implement long-term patient support and tracking initiatives have higher attrition (Braitstein et al. 2006), and risk preventable morbidity and mortality, transmission of resistant virus, and higher patient costs due to the need for specialized, inpatient care. For this reason, a new metric, LOI, was formulated to focus attention on, and account for, patient retention in cost-effectiveness analysis.

Several factors inspired the creation of the LOI metric. The first was the realization that patient attrition was happening beyond the initial twelve months and more frequently than originally anticipated. In addition, donor and government-funded ART programs appeared to be so concerned with getting people started on treatment that support for existing patients was being neglected. This was made evident by the collection and reporting of initiation data, but not retention data in most programs. Whereas most cost-effectiveness studies of ART programs consider the costs of initiating and stabilizing patients on treatment, this study deliberately concentrated on evaluating how well each down-referral model protected (or failed to protect) the initial investment required to start and stabilize patients on ART. In sum, the lack of emphasis on patient retention, billions spent on ART, and high rates of early patient attrition suggested that donors, governments, communities and individual patients were getting a suboptimal return on their investment.

LOI explicitly relates care and treatment costs to model non-performance (as measured by premature patient attrition from ART programs) in order to focus on patient retention by highlighting the cost of patient attrition in a way that CEA does not. Furthermore, whereas CEA (i.e. cost per DALY) and total and average program cost (higher cost means better model performance) can be confusing and counterintuitive metrics for policy makers and health-care practitioners, LOI provides a simple estimate of the cost of early death, LTF or electing to stop treatment. Moreover, because the LOI calculation takes into account the exact number of patient-months spent in care, it is useful for analyzing and comparing model performance without having to stratify by time spent on treatment. Finally, LOI complements CEA by providing a method for estimating the amount of extra cost in the cost per unit of effect ratio due to model non-performance. In this study, the LOI per active patient was R44.21 in the PPP cohort and R99.75 in the

PHC cohort (see Chapter 5, Costing Table 6, row 6.7), suggesting that nearly R100 of the R516.45 per patient retained in the PHC cohort was unrealized investment, compared to approximately R44 of the R570.85 per patient retained in the PPP cohort (see Chapter 5, Costing Table 5, row 5.10). In total, LOI comprised 18 percent of total PHC model costs and 4 percent of PPP costs. Reduction of premature patient losses in the PHC model in particular would have significant impact on patient outcomes and the cost per patient retained reported in this study. LOI provides an alternative, policy-friendly metric for relating costs to ART care and treatment program performance that encourages program and clinic managers to focus on patient retention by explicitly stating the costs associated with patient attrition.

7.5 Model analysis

7.5.1 PPP model

This analysis demonstrated that private sector GPs can provide a high quality of HIV care, and that there is great potential for the expansion of public-private partnerships to harness private sector GPs to assist government in managing long-term ART patients. The patients who participated in the survey reported high levels health and satisfaction with the quality of care. Data were very accessible thanks to the data management system, and quality was excellent thanks to mature monitoring and evaluation systems, dedicated data management staff, and quality assurance protocols. Perhaps most importantly, data were used to inform program operations (through routine monthly and quarterly reports for BRHC management, the GPs, PEPFAR, and the hospital-based outpatient clinic), and follow-up with patients, the pharmacy and the laboratory in cases of irregularities.

The PPP model had several shortcomings. Some GPs complained that the model was too restrictive by limiting their role to ART and patient monitoring, and suggested that the program needed to expand to include holistic patient care in order for them to maintain their interest. Despite the fact that this was how the model was originally conceived, discussions on about an expanded GP role have not resumed. Both GPs and several members of the public sector leadership lamented a lack of regular communication during interviews with the author (see Chapter 3). Meetings between the Department of Health, BRHC and KOSHMED continue to be held on an ad hoc basis, but the PPP lacks a formalized management committee. In addition to providing a forum to raise issues and problem solve, a PPP management committee or governing body

could add legitimacy to the partnership and coordinate program improvements that would ideally result in even better patient care. Furthermore, the issue of eventual reintegration of PPP patients into the public sector for ART care has not been discussed, nor has there been any discussion of how long the PPP model will be needed.

The results of this analysis suggest that the government should consider replicating the PPP model to boost public sector capacity in areas where existing ART capacity is limited or has been exhausted, where there is an able and willing private sector partner, or possibly where there are not yet any ART-accredited health facilities. It is even more compelling if, as is the case here, that a foreign donor is covering the routine ART care costs. Finally, the PPP model is easily scalable; when new doctors join the partnership they provide additional capacity without contributing any additional fixed costs. Looking ahead over the short to medium-term, additional capacity and greater patient numbers would drive down average costs (at least until additional support staff are required for BRHC). It is, however, important to note that any effort at replication of this model would require significant up-front investment in a database or contracting out data management services as BRHC elected to do.

The PPP model offers a viable interim solution for meeting the demand for treatment while health system capacity is enhanced, particularly in light of government plans to expand ART access to pregnant women, patients co-infected with TB, children, and all infected individuals with a CD4 count of less than 350 cells/mm^3. One option for reducing program costs would be to drop the data management service that costs R45 per patient per month, and instead institute an improved government monitoring and evaluation system.

7.5.2 PHC model

Overall, PHC patients who were still in care at the end of the study were generally doing well, and most patients reported being satisfied with the quality of their care. Unfortunately, 25 percent of the patients were no longer on treatment after an average of 18 months in down-referral care, which may be related to several programmatic shortcomings that were identified in this research. The first is the poor quality of data collection, storage and reporting. The hospital outpatient clinic has multiple computer databases, none of which could be relied up for data collection for this study, and the data clerks did not appear to be working according to a clear data management plan. A

study of ART program data management systems in developing countries found that high quality data management could contribute to higher patient retention (Foster et al., 2008). Common problems encountered while collecting data for this study (at both the hospital outpatient clinic and the PHCs) included missing patient files, multiple files for a single patient, multiple patient identification numbers for each patient, missing clinical forms and laboratory reports inside patient files, multiple file storage locations, and incomplete and out-of-date databases and patient registers. Data quality at the clinics was highly variable; some had very clear, well-organized records, and others had very poor quality record keeping. Patient contact information in many clinics was not well maintained and often out-of-date. There were also several reports of laboratory results being given to the wrong patient[43] and several patients reported receiving another patients' medicine or that their drugs were not ready for pick-up at the scheduled time in the patient surveys. Secondly, communications between the clinics and the hospital outpatient clinic were found to be poor. Nurses at the clinics complained that they rarely received reports from the hospital outpatient clinic with lists of down-referred patients; clinic nurses did not know who or how many patients to expect and therefore did not know if a patient missed an appointment (see Chapter 3). The lack of a systematic patient-tracking plan at the hospital outpatient clinic and the PHCs has already been discussed and is a concern.

PHC patients reported devoting more than four hours on average to their routine monthly clinic visit, two hours of which was spent at the clinic for a 30-minute visit. The direct costs associated with travel, combined with any lost wages and absenteeism from school adversely impacts patients and their families, and over time could have implications for patient adherence and program retention. Just as data management practices varied by clinic, so did patient management. Some of the clinics created expedited queues for ART patients so they could quickly see a nurse and pick up their drugs and leave, others dedicated certain days of the week to ART patients, and still others had no specific ART patient management plan. Although the regression in Chapter 5, section 5.1.4 showed no significant difference in patient outcomes between the clinics, a systematic evaluation of the impact of clinic management and patient flow on patient satisfaction, adherence and visit length would be useful, and could improve patient outcomes over the long-term.

Finally, it was not clear why PHC patients were up-referred to the hospital outpatient clinic more frequently and for longer stays than PPP patients. PHC patients did report

[43] Personal communication from Mr. Holiness Thebyane, BroadReach Regional Coordinator in Matlosana.

feeling somewhat less healthy than PPP patients, although 90 percent of PHC patients still in care at study end had suppressed viral loads. It is possible that the PHC patients had more frequent or severe complications and required longer periods of doctor follow-up at the hospital outpatient clinic. It could also be that overburdened PHC staff up-referred patients with minor issues rather than deal with them themselves, whereas the GPs managed the minor problems. Regardless, high rates of up-referral combined with an increased demand for ART has led to overcrowding at the hospital outpatient clinic[44] and could result in fewer numbers of qualified patients starting treatment.

This appraisal of the PHC ART program is not intended to impugn the efforts of all the dedicated and hard-working employees of the outpatient and primary care clinics in Matlosana. Rather, this section attempts to identify some program areas that require improvement and would undoubtedly further improve patient outcomes and employee satisfaction. Strong management is fundamental to all of the problems identified here, and priorities should include the development and implementation of a new comprehensive data management protocol that includes everything from file storage to data collection and reporting. Although the development of a database requires senior provincial leadership before significant action can be taken, this should not preclude clinic managers from addressing basic data quality issues. Another priority should be consistent, systematized patient tracking across all clinics that is written into the appropriate job descriptions. Tasking one person in the district with tracking all patients who miss appointments is inadequate for such an essential service. Finally, some discussion among clinic managers and the DLG is required to improve communications between the hospital outpatient clinic and the PHCs; the PHCs themselves should agree on a uniform operational protocol for managing routine ART patient visits with the goal of minimizing the amount of time patients wait for vital signs and to retrieve their medicine, as well as improving overall patient flow in the clinics. Over the next several years tens of thousands of new patients will require down-referral care in Matlosana (see Figure 1.5, Chapter 1), and failure to address some of these issues could adversely affect the number of patients that can be managed as well as the quality of care.

7.6 Study weaknesses

This study had four principal shortcomings related to limited availability of cost, laboratory and socio-economic data. As discussed in section 7.2.1, there are numerous

[44] Author's observation from spending several months at the hospital outpatient clinic.

challenges associated with estimating the precise cost of HIV care and treatment services offered in a primary care clinic. Unfortunately, the DLG, which manages the PHCs, was unable to provide average monthly capital costs including clinic infrastructure costs, or the individual costs of supplies and equipment. In addition, the DLG indicated that they did not pay utility bills, and so those data were also not available. Therefore, routine ART visit unit costs consisted uniquely of staff salaries and resulted in an underestimate of actual visit cost. This was deemed acceptable for this analysis for a couple of reasons. First, the exclusion of equipment and supply costs from the PHC cost estimate while including it in the PPP estimate biased the analysis slightly against the PPP model and set a higher performance threshold for the PPP when compared to the PHC model. More importantly, equipment and supply costs were included in the PPP cost estimate because those costs related to unique and fundamental features of the PPP model linked to patient services (i.e. cell phones were used to trace patients, laptop computers were used to manage patient data). Second, previous published research on a dedicated ART clinic showed that capital costs were minor, ranging from three to nine percent (Harling, Bekker & Wood, 2007). Because PHC patients received care in existing primary care clinics, we felt it was reasonable to assume that capital costs attributable to an ART patient visit would be lower than those observed at a dedicated ART clinic. For methodological consistency, capital costs were also excluded from the PPP model. Post hoc analysis was conducted to understand whether this introduced any cost bias in the analysis and found that capital costs amounted to between three and four percent (approximately R7 per patient per visit) of total model costs. Finally, senior management costs were excluded from the analysis, although program and facility manager costs were included for both models. Patient costs were excluded from the calculation consistent with the provider perspective adopted for this analysis.

Propensity score matching is not the only method available to control for selection bias, and it does not completely eliminate the risk of selection bias. One alternative would be to perform multivariate modeling on data from the entire cohorts, and thereby including larger numbers of patients. However, due to resource constraints, it was not feasible to collect an expanded set of data on all 1,469 eligible patients, and so propensity score matching was used for a small subset of key patient data.

Although CD4 nadir is the best predictor of future deaths and the viral load set point has been shown to help predict long-term viral suppression, it was not feasible to collect all viral load and CD4 data for all eligible patients in both models for reasons of poor data

quality and limited resources. Laboratory data report provided by the NHLS for this study was incomplete and much of the CD4 and VL data had to be pulled from patient files, and even then it was found to be missing in several instances. Because the starting point for study eligibility was the outpatient clinic down-referral register and down-referral date, it was possible to find patient laboratory data that correlated with the down-referral date. Without a treatment initiation date for each eligible patient, it was not feasible to search through four years of laboratory data. Post-matching analysis on the CD4 result that preceded down-referral among matched patients with identifiable results showed that the immunological status of each cohort was similar, and by controlling for time on ART and time since down-referral, the patient selection process aimed to include patients with similar immunologic and clinical profiles. Despite these efforts, it is possible that one patient population started treatment sicker on average than the other. However, there was no known systemic bias that would result in initially sicker patients being more likely to choose one cohort versus another.

Socio-economic status (SES) data were not used in the matching process and constitute a potential source of confounding in this analysis. The hospital outpatient clinic does not collect SES data, and it was not feasible to collect employment, education and income data for all eligible patients. Following the matching exercise, a post hoc analysis of community of residence was conducted to see if the communities of residence profiles were similar across both patient populations (see Table 4.7 in Chapter 4) – and they were. In addition, the patient survey included questions about educational attainment, employment and income in order to explore any potential differences between the cohorts in terms of SES. As indicated in Chapter 6, no differences were observed between cohorts on SES variables. There is, however, some risk in generalizing the results of the patient survey for two principal reasons. First, those surveyed were only a subset of the total study population (approximately 15 percent of each cohort), and second, everyone interviewed was still enrolled in the ART programs and may not have been representative of those patients no longer in care.

Caution is advisable when making generalizations regarding the results of this study and their relevance to other settings. Both of these models evaluated a geographically homogeneous study population in a mostly suburban environment. Moreover, although the patient matching was essential to this analysis in order to eliminate selection bias, it may also have resulted in a patient population that was not necessarily representative of the larger patient population in Matlosana. Cost data presented here may not be relevant to other settings in South Africa given the variation in healthcare costs between

provinces. Finally, the data presented do not allow conclusions to be drawn about a causal relationship between specific model features and patient outcomes. However, every attempt was made to isolate model-specific features and associated costs and to control for non-model influences (i.e. individual patient factors, laboratory, drug, outpatient and inpatient costs), in order to reasonably attribute patient outcomes to each model.

Table 7.2 Summary of principal study limitations and methods used to minimize them

Limitation	Method for addressing the limitation	Estimated impact on analysis
Lack of disaggregated cost data at the primary care clinics	Visit unit cost based on health worker salaries using activity-based costing methods	Under-estimated PHC visit unit cost resulted in a slight bias against the PPP model in total costs and CERs.
Lack of clinic capital costs	Excluded capital costs for both models. By excluding capital costs from both model analyses, any bias was minimized.	Capital costs in the PHC model assumed to be minimal, as total costs would have been averaged across all clinic patients. Harling et al. 2007 found that between 3% and 9% were capital costs for a dedicated ART clinic. Capital costs in the PPP model (for the NGO) were estimated at between R6.5-R8 per patient per month, or between 3% and 4% of total PPP care costs.
Could not identify patient's CD4 nadir and therefore could not use it in patient matching	Matched on CD4 result that was closest to the date of down-referral, as well as amount of time on treatment.	It is possible that one cohort was sicker on average when they started treatment, but there is no reason to suspect the bias would have run in one direction.
No available socio-economic status data and therefore could not control for SES in patient matching	Collected SES indicators on the patient survey; income data from the survey was unreliable, but no significant differences were observed in employment status or educational attainment.	Post-hoc analysis of community of residence revealed that residence profiles of both cohorts were very similar. In addition, the doctor in charge of down-referral indicated that he did not note any obvious differences in terms of income, education or employment status between PHC and PPP patients.

7.7 Future research

This study represents one of the first, and most comprehensive evaluations linking costs and outcomes of two different HIV care and treatment models. Given the high demand, high cost nature of HIV treatment in South Africa and elsewhere, identifying models that maximize patient outcomes while minimizing costs is essential, and has unfortunately been a neglected area of research to date. Future studies should challenge some of the status quo policies and guidelines. For example, recent research from Uganda found that the current policy of twice-yearly laboratory testing is not cost-effective (Mugyenyi, 2009). This should also be evaluated in the South African setting, along with an evaluation of the impact on costs and patient outcomes of reducing routine patient visits from monthly to once per quarter. If effective, such changes could boost public sector capacity, and the savings resulting from fewer patient visits and laboratory tests could be used to further expand access. It could also help to boost patient adherence due to fewer clinic visits and lower out-of-pocket travel costs. Other examples of recent research that have begun to challenge the status quo model of HIV treatment in developing countries include evaluations of task-shifting models of care (Morris et al., 2009) and nurse-centered care models (Shumbusho et al., 2009). There are inherent cost and quality trade-offs in task shifting and nurse-centered care, and the cost-effectiveness of these models should be evaluated.

However, research should not just be confined to innovative models designed to meet treatment demand; there is also a considerable need for research to improve management and operations at the PHCs. As the number of patients receiving routine down-referral care at clinics continues to grow, better information is also needed on how best to integrate routine ART care into primary care clinics in order to optimize staffing ratios and composition, patient flow, data management, and ultimately patient outcomes and satisfaction.

7.8 Conclusion

Despite progress in scaling-up HIV services in South Africa and emboldened leadership on HIV from the Zuma Administration, an intensified effort will be required to achieve the ambitious targets laid out in the 2007 – 2011 National Strategic Plan and to meet the growing demand for treatment over the next decade. Significant challenges to mounting such an effort loom. The global economic down-turn will likely result in reduced or stagnant donor support for HIV[45], and internecine disputes in the global health community over the consequences of vertical programming for HIV[46], combined with South Africa's recession means an expanded domestic effort will be difficult to finance. Nonetheless, the need for HIV treatment services continues to grow as prevention programs have thus far failed to gain traction, and hundreds of thousands become newly eligible for ART every year. The South African National AIDS Council (SANAC) and the Ministry of Health recently announced intentions to start patients on treatment earlier, (350 cells/mm^3 instead of 200 cells/mm^3), as well as to treat all infected infants, pregnant women, and everyone co-infected with tuberculosis (Smetherham, 2009). This is laudable and good public health policy, but it also means exponential increases in the number of individuals who will qualify for ART access, in spite of extant health system capacity and financing constraints.

The increase in demand for ART treatment and the financial and capacity constraints requires innovative, cost-effective interventions and models of care that can boost health system capacity immediately. Failure to identify and implement such solutions to the current capacity crisis will mean more unnecessary deaths. Walensky and colleagues (2008) modeled treatment expansion scenarios in South Africa and found that maintaining the current rate of scale-up would result in 1.5 million deaths by 2012, while rapid scale-up would cut the number of deaths by 200,000. Constructing health facilities and training and hiring health workers requires years of lead time and is appropriate as part of a three-to-five year strategy; the more pressing need is for six-to-twelve *month* tactics for rapid scale-up. The PPP model in Matlosana was designed to

[45] The Global Fund for HIV/AIDS, Tuberculosis and Malaria is currently facing a $3 billion deficit (MacInnis, 2009), and PEPFAR funding is expected to remain flat through 2013 (White House, 2009), while the post-2013 PEPFAR commitment remains unclear. Finally, a recent internal investigation of global health programs funded by the World Bank found that eight out of ten AIDS projects showed unsatisfactory outcomes, calling into question the future of the Bank's role in funding HIV programs (Dugger, 2009).

[46] The dispute regarding the impact of well-funded, vertical HIV programs on developing country health systems and financing for other health priorities has been well publicized in global health. Numerous articles have been published that argue that HIV funding has had a deleterious impact on health systems (England, 2007; Garrett, 2007; Shiffman, Berlan & Hafner, 2009), others insist these funds have in fact strengthened health systems (Yu et al., 2008; Piot et al, 2009), and still others who argue that the impact has been mixed and that health system strengthening can be accomplished in the context of vertical programs (Navario, 2009; Chan, 2009; Ooms et al., 2008).

leverage existing private sector capacity for public sector benefit, and this study evaluated just how effectively it performed as an interim solution to boost ART treatment capacity. The model is not without shortcomings as it costs more than PHC care, fragments primary care and HIV care, lacks formal leadership, and does not include plans for eventual patient reintegration into the public sector. Nonetheless, this analysis has shown that the PPP is a compelling model for increasing public sector capacity to meet the immediate demand for ART. Patient outcomes in the PPP model were notably better than in the PHC model, it was more cost-effective, and PPP patients were equally as happy with the quality of the care and the level of convenience that the model offered.

In Matlosana, the care and monitoring costs for the PPP are underwritten by PEPFAR, which means that the superior outcomes demonstrated by the PPP model in this study come at no additional cost to the government. In fact, taking into account the additional benefit of lighter patient loads[47] and lower public sector care costs makes the PPP model still more appealing as a capacity-building strategy. Based on these results, expanding the model to other areas around South Africa where there are private sector doctor networks with spare capacity could yield excellent patient outcomes and relieve some of the pressure on public sector treatment programs (which may in turn yield better public sector outcomes) cost-effectively.

[47] In Matlosana, by March 31, 2008 12,413 patients had started ART, approximately 10 percent of whom were enrolled in the PPP.

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