

https://dspace.org/

Risk management in HIV/AIDS: ethical and economic issues concerning the restriction of HAART access only to adherent patients

Chawana, Richard

2011-02-15
http://hdl.handle.net/10539/9038

Downloaded from a DSpace repository. https://dspace.org/

Risk Management in HIV/AIDS: Ethical and Economic Issues Concerning the Restriction of HAART Access Only to Adherent Patients

Richard Chawana

331986

Research report submitted to Steve Biko Centre for Bioethics, University of the Witwatersrand, in partial fulfilment of the requirement for the award of Master of Science in Medicine (Bioethics and Health Law)

November 2010

DECLARATION - STUDENT

This research is my original work, produced with normal supervisory assistance from my supervisor. All the relevant sources of knowledge that I have used during the course of writing this dissertation have been fully credited and acknowledged. Furthermore, this research report has not been submitted for any academic or examination purpose at any other university.

---------- ----------

Richard Chawana Date

DEDICATION

To the millions of victims of HIV/AIDS dying without access to HAART

To those endeavouring for universal access to HAART

ACKNOWLEDGEMENTS

The success of this study owes much to the unwavering support of the individuals identified below in their own capacity or in the capacity of the institutions of which they are a part.

Prof. D. K. van Bogaert (Supervisor & Academic Director Postgraduate Studies – Steve Biko Centre for Bioethics)

Prof. A. Dhai (Head – Steve Biko Centre for Bioethics)

Ms J. Gardner (Postgraduate Coordinator – Steve Biko Centre for Bioethics)

Dr. S. A. Nzenze (PHD candidate Epidemiology – RMPRU)

Miss. M. Maredza (Research Associate & Junior Health Economist –PRICELESS SA)

Mrs. T. P. Ndoro (Elizabeth Glazer Foundation)

Miss J-L Kruger (University of the Witwatersrand)

Your knowledge and understanding of the subject was phenomenal. I appreciate the virtues of patience, prudence and honesty which were characteristic of you all. May God bless you all and I wish you the best in your present and future endeavours.

In the few years I spent at Steve Biko Centre for Bioethics, many times the mountain seemed too high. So often I did not have the courage or the strength to climb. I was running and could not see the finish line. Through my doubts and despair, hope was always restored to me by a particular phenomenal woman blessed with many talents, full of wisdom, understanding and a woman of virtue. She transformed what seemed to be ordinary thoughts, ideas and writings into extraordinary concepts. To Prof. D. K. van Bogaert, I say *merci beaucoup.*

SUMMARY

South Africa, like many other developing nations, is faced with the challenge of mobilising resources to fight the HIV/AIDS pandemic. There is a huge budget gap between the ideal and actual funding provided to achieve universal access to highly active antiretroviral therapy (HAART), which leads to the inevitable rationing of HAART. Although healthcare spending has been increasing in South Africa, new demands are being placed on the HAART roll out programmes. This is particularly due to the emergence of HIV drug resistance (HIVDR). Because non-adherence to HAART is strongly linked to drug resistance, this is a major threat to any successful HAART programme. In the face of restricted resources, this research report looks at some of the ethical and economic implications of non-adherence to HAART. I suggest that there is merit in considering that HAART be restricted only to adherent patients.

TABLE OF CONTENTS

Content		**Page**
Declaration		ii
Dedication		iii
Acknowledgements		iv
Summary		v
List of tables		x
List of diagrams		xi
Preface		xii
Chapter 1	**Introduction**	**1**
1.1	Background and Rationale of Research	1
1.2	Context of the study	4
1.3	HIV/AIDS Management in South Africa	6
1.4	Problem statement	9
1.5	Rationale and justification for the research	10

1.6 Aims and objectives of the study 11

Chapter 2 Literature Review 12

2.1 Introduction 12

2.2 Distributive Justice 14

2.3 Adherence 16

2.4 Adherence-enhancing interventions 18

2.5 Mandatory Discontinuance of HAART 19

2.6 Markov Modelling 20

2.7 Conceptual framework 21

2.7.1 Non-adherence and treatment outcomes 22

2.7.2 Non-adherence and QALYs 23

2.7.3 Non-adherence and treatment effectiveness 23

2.7.4 Non-adherence and Access to Healthcare 24

Chapter 3 Economic Evaluation – Continued supply of ARVs to non-adherent patients: effect on HAART cost effectiveness 26

3.1 Introduction 26

3.2 Methods 29

3.2.1 Economic Evaluation Assumptions 29

3.2.2 Study Design 29

3.2.3 Outcomes 30

3.2.4 Markov Description 31

3.2.5 Markov Tree 32

3.2.6 Detailed Baseline input for modelling 33
3.2.7 Markov Modelling Assumptions 34
3.2.8 Discounting 35
3.2.9 Sensitivity Analysis 35
3.3 Results 36
3.4 Discussion 39
3.5 Conclusions 42

Chapter 4 Ethical Analysis - To Treat or Not To Treat: HAART, Non-adherence and Justice 43

4.1 Introduction 43
4.2 Distributive Justice 45
4.3 HIV, Health & Human Function 48
4.4 HAART & Rawls' First Principle 51
4.5 HAART & Rawls' Second Principle 53
4.6 Autonomy & Tyranny of Majority 57
4.7 Restricting access to non-adherent HAART patients: Let them die? 61
4.8 Risk, Precaution & Prevention 65
4.9 Conclusion 70

Chapter 5 Concluding Remarks 73

5.1 Introduction 73
5.2 Major Findings 74
5.3 Policy Recommendations 75

5.4 Study Limitations 76

5.5 Areas For Further Research 77

References **78**

Appendices **98**

Appendix A: Antonyms 98

Appendix B: Ethics Clearance 99

Appendix C: WHO treatment guidelines 100

LIST OF TABLES

Table 1: Domestic and International AIDS Spending by service categories and financing sources for South Africa…… p27

Table 2: Baseline input data for modelling…….. p33

Table 3: Undiscounted Cost-effectiveness of HAART for the Adherent and Non-adherent…… p36

Table 4: Discounted Cost-effectiveness of HAART for the Adherent and Non-adherent…… p37

Table 5: Sensitivity analysis on cost of 1st line HAART Drugs…… p37

Table 6: Sensitivity analysis on cost of 2nd line HAART Drugs…… p38

Table 7: Sensitivity analysis in patient care for non-adherent…….. p38

Table 8: Antiretroviral therapy for HIV infection in adults and adolescents.. p100

LIST OF DIAGRAMS

Figure 1: Diagram showing the effects of adherence or non-adherence on treatment outcomes, effectiveness of HAART, effect of patients and the general effect on the ability to provide HAART…… 25

Figure 2: A flowchart showing probabilities in the adherent and non-adherent proportion Markov states during the first year of ART…. 31

Figure 3: A Markov tree showing transitions between Markov Health States…… 33

Preface

This research report was written with a purpose to illustrate the economic and ethical problems associated with non-adherence to highly active antiretroviral therapy (HAART). This followed a realization that non-adherence could be a matter of *choice*, rather than *circumstance*. The title was chosen in order to highlight features of HAART that are pertinent to developing countries like South Africa. It therefore outlines the economic impact of non-adherence and suggests the restriction of HAART access only to adherent patients in order to mitigate the negative impacts associated with non-adherence.

In constructing moral arguments indicating the merit of the suggestion above, this research report began the first three chapters by looking at the burden of HIV/AIDS in South Africa, the progress and current challenges in managing HIV/AIDS and economic implications of non-adherence to HAART. In investigating the economic implications, Markov model was used as a tool of choice for assessing the cost-effectiveness of the current HAART programmes in South Africa, where HAART access is not restricted according to adherence to therapy. This served a purpose of highlighting the moral issues concerning treatment of non-adherent patients. The discussion that followed in the next chapter reflected on moral issues embodied in the suggestion of restricting HAART access to adherent patients. Rawls' theory of justice was used to explore the merit in the suggestion. The use of Rawls' theory was premised on the findings that the theory has been used in the construction of some economic policies and healthcare policies.

The final chapter concludes that as much as restricting HAART access only to adherent patients has economic and ethical merit, it could be politically unpopular. Bearing this in mind, it is recommended that policy reviews take into account the potential implications of non-adherence and give greater consideration to improving adherence to HAART.

Chapter 1: Introduction

1.1 Background and Rationale

The problem of HIV/AIDS has posed numerous economical, social and humanitarian challenges in many developing countries (Katzestein et al. 2003: S1-S4), further compounding these countries' perennial problems of hunger, poverty and social underdevelopment. Sub-Saharan Africa has been the worst affected globally with the highest prevalence rates: Swaziland 26.1%, Lesotho (23.2%), Botswana (23.1%) and South Africa (18.1%) (UNAIDS 2008: 215). Without effective prevention and treatment, 4 – 7 million cumulative AIDS deaths are anticipated by 2010 in South Africa (Badri et al. 2006). The epidemic could cost South Africa as much as 1.0-1.5% in GDP growth per annum through the deaths of mainly young adults resulting in shrinkage of the tax base[1] (Bell et al. 2003:1-118).

Widespread treatment of HIV/AIDS is one of the two key modalities employed in resource-rich countries to reduce the growth of the epidemic as well as mortality, morbidity and healthcare costs (Katzestein et al. 2003: S1-S4). The global effort to provide treatment access to antiretroviral therapy (ART) was initiated by WHO's '3 by 5' initiative, which was targeted at covering three million people by the year 2005 (WHO 2008a). As a result, many African countries initiated ART to HIV infected people with the goal of reducing mortality and improving the quality of life of those infected. Resulting from this initiative, the percentage of people receiving treatment, against people estimated to be in need of treatment, in low and middle-income countries, rose from less than 8% in 2002 (WHO 2003a) to 31% in 2007 (WHO 2008a). Despite such achievements, a scenario maintaining the current treatment capacity (zero growth) would result in estimated 1.2 million more

[1] Kemp (2002) cited in Oberholzer (2007) reported that appproximately 26.6% of the population are economically active and only 15.1% being registerd tax payers.

deaths in South Africa alone (where the coverage is 28%) by 2012 when compared to universal access to ART by 2011 (rapid growth) (Walensky et al. 2008).

Given such a case, in order to maximize the overall benefits of HAART provision, many governments in Sub-Saharan Africa are scaling up ART coverage. However, this scale-up is being slowed down by lack of adequate financial and human resources which are competing with other public priorities. Consequently, difficult choices have to be made on who benefits from the available resources.

To assist in decision-making, biomedical criteria recommended by WHO are being widely used in Sub-Saharan Africa to determine eligibility for treatment. Biomedical criterion uses the patient's immunological (CD4+ <200 cells/dL) and clinical pictures (WHO stages III and IV) as markers for eligibility. However, biomedical criteria alone may not be sufficient to determine eligibility as there may be more people eligible than treatment available. Economic and social criteria, in addition to biomedical criteria, may be required to determine eligibility (Attawell and Mundy 2003: 7)

The emergence of HIV drug resistant strains (HIVDR) exerts additional strain on the limited available resources as more expensive complex treatment regimens are required to contain the virus and prevent catastrophic public health outcomes, such as rapid disease progression and death (Foster et al. 2006: 1330). Biological, virological and behavioural factors have been associated with the emergence of HIVDR strains. Biological and virological factors promoting the emergence of drug resistant variants include intolerance to the drug and a high mutation rate of the virus (10^4 – 10^5) respectively (Menendez-Arias 2010: 211). As for behavioural factors, non-adherence to treatment has been widely associated with the emergence of HIVDR variants. Adherence to treatment ensures that the main goals of HAART are achieved. These goals include durable suppression of viral replication of HIV, as well as the restoration and preservation of

immunological functions and improvement of a patient's quality of life (Lucas 2005: 423). Minimal treatment interruption of a few days can lead to sub-optimal antiretroviral (ARV) blood concentrations with subsequent treatment failure and drug resistance (Bennett et al. 2008: 2). Non-adherence would therefore undermine the effort and idea of ART. It is thus critical that the monitoring[2] of people on ARV treatment becomes a major public health priority so as to preserve virological effectiveness and efficacy of the first line treatment, given the limited available alternatives. This could in turn contribute to the reduction of emerging drug resistant viruses (Bisson et al 2008).

Drug resistance may be containable through appropriate policy implementation (Selgelid 2007: 221). WHO developed a global strategy in 2008 for HIVDR prevention and assessment in countries scaling up ART so as to minimise the economic and clinical consequences of HIVDR. The strategy involves the establishment of HIVDR working groups that are mandated to develop a country-specific HIVDR prevention surveillance and monitoring plan, and make evidence-based recommendations for HIVDR prevention (Bennett et al 2008: 5). Amongst other activities, the HIVDR working group monitors for 'early warning indicators' (EWI) which include both structural and individual factors of non-adherence. It then recommends ways of preventing HIVDR which might include an increase in training and resources for adherence interventions. Nonetheless, the emergence and spread of drug resistant bacteria or viruses in human populations is a social, political, economic and ethical phenomenon (Selgelid 2007: 222). It is in this light that this study seeks to contribute by critically analyzing the economic and ethical consequences of non-adherence

[2] Treatment monitoring of the patients' scheduled 6 monthly visits include the monitoring of adverse drug reactions, laboratory monitoring of CD4+ and viral load and pill return count for missed doses (DoH 2004: 18).

in resource-constrained nations and suggests the use adherence[3] as a viable additional criterion for determining eligibility for initiation and continuance of ART.

1.2 Context of Study

South Africa is a middle income country (World Bank 2009) with a population of 48.8 million people (UNAIDS 2008). The country is typified by a thriving macroeconomy that is characterized by positive GDP growth of 5.1 in 2007 (World Bank 2009), falling poverty levels of 4.55% between 1995 and 2005 (PCAS 2008) and a cash surplus of 1.7% of GDP in 2007 (World Bank 2009). The most important contributors to the economy include mining, manufacturing and agriculture. Despite the positive macroeconomic picture, the society is fragmented and characterized by socio-economic inequalities inherited from the apartheid era. There is a widening inequality gap and huge discrepancies in access to economic opportunities as well as healthcare services, amongst others. Using a narrow definition of unemployment, 25.2 % of the population is unemployed (SSA 2010). In addition, 48% of the population is living below the upper poverty line of R322 (less than US $1.50/day) and 23% below the lower poverty line of R174 (less than US $1/day) (Bhorat and van der Westhuizen 2008).

There exists in South Africa legislation and policies targeted at correcting inequalities and alleviating poverty. Among such policies is the provision of social grants. In 2007, over 12 million people were receiving social grants through the social grant system for poverty alleviation, of which 7.8 million were children (PCAS 2008: 19).

[3] The current Department of Health treatment gudelines mention that adherence should be guaranteed before initiation but is not included as an exclusion criterion. See page 8 of this reseach report for further explanation on this.

Inequalities that existed in healthcare were evidenced mainly by a disproportionate access to healthcare among different economic and racial groups. In order to correct healthcare inequalities, the South African government increased health spending and expanded infrastructure development. The annual health spending per capita compound growth was 2% per annum (PCAS 2008). As a consequence of increased health spending, 95% of South Africans live within a 5-km radius of a health facility (ibid). About 70% had access to in dwelling or on site tap water and 60% had access to flush toilets by 2007 (ibid). Notwithstanding the improvements in healthcare and access to healthcare, it was reported that the mortality rates of adults aged between 25 and 45 years were increasing. The average life expectancy stood at 50 years in 2007 down from 58 in 1997 (World Bank 2009). Infant mortality rates increased from 60 per 1000 live births in 1990 to 69 per 1000 live births in 2006 (Mabandu and Parker 2009). The Health System's Trust of South Africa attributed these poor indices to HIV/AIDS (HST 2009). Any gains in healthcare and economy remain under threat due to HIV/AIDS as there is a strong connection between unemployment, poverty and HIV infection (Nattrass 2004: 13). The surfacing of HIV/AIDS reversed major gains that had been made in medicine.

It is estimated that 5.7 million people in South Africa are living with HIV (UNAIDS 2008). Compounding the problem, South Africa lost at least 3.8 million person-years between 2000 and 2005 by not using ARVs as the government restricted their use and obstructed access to global funding (Chigwedere et al 2008:4). However, the government's policy on HIV/AIDS changed in 2003 and it now has the largest number of people enrolled on HAART in the world (PCAS 2008) though only 22-36% of the people in need of treatment are actually receiving it (UNAIDS 2008). Concerning HIV/AIDS support services, 90% of the government healthcare facilities offer voluntary counselling and testing (VCT) services (Matjila et al. 2008: 92) while there are 1015 accredited public HAART sites for the comprehensive management, treatment and care of HIV and AIDS in the 9 provinces of South Africa (Gov SA 2010). Despite such services, it is not all patients

given ARVs who actually take the medicine thereby increasing the risk of developing HIVDR strains (Bangsberg et al. 2004). There is also anecdotal evidence that certain patients forego their ART so that they can be eligible for the disability grant given to those who are not well enough to work (Nattrass 2007: 186). The number of these individuals was forecasted to rise to hundreds of thousands. Under the conditions of resource scarcity, developments such as non-adherence to therapy by *choice* and not *circumstance* raise some ethical questions concerning distributive justice. In this context, it concerns the methods of enrolling patients and keeping them in the programme. The resultant effects of non-adherence on healthcare expenditure also elicit questions on the affordability and sustainability of the ART roll-out and scale-up programmes.

1.3 HIV/AIDS Management in South Africa

Provision of healthcare is through the private and public utilities in South Africa. The private healthcare sector covers 15% of the population while the public sector covers 85% of the population through a hierarchy of patient referral systems (Hassim et al. 2007: 165). However, it is suggested that 70 - 80% of the population first consults traditional healers and often use traditional remedies (ibid: 204; WHO 2003a).

ART provision trends follow the coverage between these two sectors, that is public and private healthcare sectors. In the context of traditional healers, there has been some effort to "educate" and integrate traditional healers in prevention and support of HIV/AIDS management (Ndhlalambi 2009: 38).

Using data obtained from the UNAIDS 2008 report, the public healthcare sector is providing ART to 22% of the country's total estimated needs while the private healthcare sector is providing ART to 7%. Various donors and companies in South Africa are contributing to the management of

HIV/AIDS through provision of some form of care, support and treatment to their employees, mostly through the private sector. Employers and donor contracts standing alone or in connection with a network of health facilities, provide health services including ART (Feeley et al. 2007: 195). Seventy-one percent of large companies and 38% of medium-size companies had systems in place for care, support and treatment in 2006 while 40% of large and 17% of medium-sized companies were actually providing ART services (George and Quinlan 2009: 19-29). Multilateral and bilateral partners provide support to specific groups of people in HIV/AIDS programmes in South Africa, through an organized network of private providers like BroadReach and Right to Care's Thusong Program (Feeley et al. 2007: 195). These partners include United Nations (UN) agencies, United States Agency for International Development (UNAID) and The President's Emergency Plan for AIDS Relief (PEPFAR).

In the public sector where there are 0.6 doctors per 1000 people, more than 370 000 people are being provided with ART. The total needs of ART are estimated to be 1 700 000 patients (UNAIDS 2008). The doctor to patient ratio makes it difficult for the public sector to provide a treatment regimen specific to an individual patient. In these circumstances, the Department of Health (DoH) in South Africa followed WHO recommendations on developing treatment guidelines for people with HIV which could be easily administered and followed up by other health personnel, for example, nurses. The guidelines involve roughly four stages which are: (i) screening, (ii) clinical assessment and counselling (iii) treatment initiation and (iv) monitoring (DoH 2010; DoH 2004). The screening stage involves the biomedical investigations for eligibility of the individual for ART. The biomedical inclusion criteria for initiation of ART in an adult and adolescent include the following (DoH 2010: 9):

1. CD4 < 200 cells/ mm^3 and/or symptomatic, irrespective of stage; or
2. CD4 < 350 cells/mm^3 in patients with TB/HIV or pregnant women; or

3. WHO stage IV, irrespective of CD4 count; and
4. MDR-/XDR-TB irrespective of the stage

Other activities carried out in the screening stage include TB and pregnancy screening as well as treatment of opportunistic infections. Treatment counsellors are supposed to visit patients' homes to assess the various support structures available for the patient. The patient's second visit involves clinical assessment for the treated opportunistic infections and cotrimoxazole prophylaxis. It is at this stage that patients are counselled on the importance of adherence to treatment and other psycho-social considerations. However, some psycho-social considerations like alcoholism, which has an effect on adherence, are not an exclusion criterion for these patients (DoH 2010; DoH 2004: 2). Treatment is then initiated where tenofovir, lamivudine and nevirapine or effavirenz are used as first line treatments. Treatment monitoring of the patients' scheduled 6 monthly visits include the monitoring of adverse drug reactions, laboratory monitoring of CD4+ and viral load and pill return count for missed doses. However, ART pill-return counts are dependent upon the clinic patient load and capacity to undertake this activity (ibid: 18). This lack of adherence monitoring poses a shortcoming in the HIV/AIDS public sector management as the risk of virologic failure and subsequent consequences can be identified through this cheaper method of quantifying and monitoring adherence to ART (pill-return counts) (Bisson *et al* 2008).

The private sector is classified as private for profit and private not-for-profit (Wang et al. 2010: 5). In the private for profit sector, though there might be adherence to the available treatment guidelines, HIV/AIDS management is mostly tailored to suit the individual being treated. There is intense monitoring of the patient's response to treatment and changes are made accordingly. Private networks such as Médecins Sans Frontières (MSF) are also playing a role in the management of HIV/AIDS in South Africa as private not for profit. MSF-Khayelitsha HIV management is not extensively different from the one that is being provided by the government of South Africa. The

Khayelitsha project is centred on the provision of first line treatment of stavudine, lamivudine and nevirapine or effavirenz (Fox and Goemaere 2006: 302). It differs from the government ART roll-out in its emphasis on the social and adherence criteria for inclusion in the project – the so called 'patient selection' and in their monitoring for adherence. Furthermore, adherence to ART is a necessary condition in the Khayelitsha project for continued supply of ART as they can withdraw treatment from a patient failing to meet the minimum level of adherence during therapy despite adherence intervention strategies employed (ibid: 307).

The HIV management styles in the public and private sectors mentioned above have both economic and ethical consequences that need to be explored. Economic questions are raised on the sustainability of the programmes in the face of activities like non-adherence, which could undermine the effectiveness and efficiency of the programmes. Ethically, under circumstances of restricted resources, how might the principle of distributive justice determine who benefits from the available resources and what role do personal preferences, choices and faults play in the distribution of scarce resources?

1.4 Problem Statement

Effective and efficient HAART provision is a global concern which faces a number of challenges. South Africa is scaling up HAART provision to people living with HIV in order to achieve universal access. Some of the people receiving the treatment are not actually consuming it due to various reasons (Nattrass 2004: 127-131). This problem impacts people differently through (i) restricting governmental ability to scale up and sustain HAART provision, and (ii) the emergence and spread of HIVDR. In this context, non-adherence to HAART has entrenched ethical and economic issues that remain largely unexplored.

1.5 Justification of the Study

The principal aim for HAART rollout programmes contained in the South African National Strategic Plan (NSP) 2007-2011 is to reduce HIV infection and AIDS morbidity and mortality as well as its socioeconomic impacts through provision of appropriate packages of treatment, care and support to 80% of HIV positive people and their families (DoH 2006). Life expectancy and quality of life of HIV infected individuals can be prolonged through HAART. However, successful attainment of desired outcomes is dependent on the level of commitment of all stakeholders. There is high commitment from the government to provide ART for its people. Assessing patients' commitment to medication management through adherence to therapeutic processes is vital to ensuring successful medication management. Furthermore, adherence and non-adherence assessment, together with the economic and ethical implications of these are important, considering the current cost of treatment and coverage of the ART roll out programmes. Policies are heavily influenced by economics. Economic analysis of initiating ART in South Africa was done (Nattrass 2004). However, literature on economic evaluation of the ongoing ART programmes is lacking. Literature that exists on the economic implications of non-adherence is from the developed countries where the prices of drugs are 26 times more than that of the developing countries (Downing and Kriegshaber 2008) and the cost-effectiveness cut-off points are higher than those of developing countries. Important policy decisions in developing countries on non-adherence are necessary. For one reason, such studies inform research on economic implications of non-adherence and thus could be accomplished using tariffs and prices from developing countries. Furthermore, while economics can enlighten us on the consequences of pursuing a certain path, it cannot alone inform us on which policy to pursue. Since economic institutions and policies impact people differently, ethical valuations using normative principles together with the economics may provide guidance on the best policy to follow (Wilber 1998: 572), hence the justification of this study.

1.6 Objectives

The overall aim of this study is to quantify and describe economical consequences and discuss the ethical issues related to adherence and non-adherence to HAART from the provider's perspective. More specifically, the aim of the study was attained through the following objectives:

i. Using the Markov model, to calculate the lifetime cost, effectiveness, cost effectiveness ratio, incremental cost effective ratio (ICER) of HAART treatment for adherent and non-adherent patients.

ii. To use the results obtained through objective (i) above to reflect on and analyze ethical issues concerning HAART restriction based on adherence.

iii. Conclusions reached with objective in (ii) above will be based on the review of the current state of distributive justice extending it to the provision of HAART through the following interrelated research questions:

- To what extent are public health providers morally obliged to monitor medical resources as used by individuals if distributive justice entails that the governments should provide a fair share of resources for each individual in an environment that allows each to develop and pursue his/her own concept of good?
- To what extent are communities morally obliged to correct inequalities that arise through voluntary choice or fault like non-adherence under the principle of distributive justice?
- To what extent does restriction to HAART based on adherence constitute a violation of the principles governing justice within a society that conform to such a principle?
- To what extent does restriction to HAART constitute coercion if restriction involves coercion and coercion being always morally wrong?

Chapter 2: Literature Review

2.1 Introduction

Many countries are scaling up highly active antiretroviral therapy (HAART) programmes in line with the WHO's goal of universal access by the year 2010. Such initiatives entail massive financial input. Consequently, the scaling up of ART coverage among HIV/AIDS individuals is being slowed down by lack of adequate financial and human resources in these countries which are competing with other public priorities. For example, the global budget gap was estimated at US$ 8.1 billion in 2007 and it is estimated that US$ 41 billion will be needed in 2015 to achieve universal access (WHO 2008a). The budget gap between the ideal and actual funding to achieve universal access to HAART makes rationing of HAART inevitable.

Difficult choices have to be made on who benefits from the available resources (Pieterse 2007: 514). Biomedical criteria recommended by WHO[4] are being widely used in Sub-Saharan Africa to determine eligibility for treatment. As the countries scale up the ART roll-out programmes, biomedical criteria alone may not suffice to determine eligibility as more people can be eligible but may not receive the treatment. In the light of this, Bowler and Wilson (2005: e250) developed a mathematical model of treatment which restricts HAART distribution only to cities in South Africa. They premised their argument on the finding that such distribution will cover the most number of infected people and would be effective. In Uganda, access to HAART was restricted to patients who are ARV naïve (Colebunders et al 2005: e276). These cases highlight that in the face of huge financial implications of HAART, economic and social criteria, in addition to biomedical criteria, may be required to determine eligibility (Attawell and Mundy 2003: 7). However, compelling ethical questions are raised over the fairness of any of the HAART distribution criteria or eligibility

[4] For WHO treatment guidelines, see table in Appendix C

criteria for the HAART programmes. Serious questions on who gets to benefit from the available resources and who ought to continue receiving the treatment continue to dominate HAART programmes.

The World Health Organisation and the Joint United Nations Programme on HIV/AIDS identified three core principles that should underlie the effort to fairly distribute ARVs, namely: urgency, equity, and sustainability (Macklin 2004: 5). They state that policy decisions for the fair distribution of ARVs should be based upon the following ethical principles:

(i) that like cases should be treated alike,

(ii) the utilitarian principles of maximising overall societal benefits and minimising social burden,

(iii) the egalitarian principle of equity (distributing resources, such as healthcare, equally among different groups), and

(iv) the Maximin principle (which prioritizes individuals that are least advantaged).

The pluralism of the principles guiding the fair distribution of HAART does not do justice on resolving the moral dilemma of who gets to benefit from the available resources. Instead, Daniels and Sabin (2002:4) suggest the use of procedural justice in the wake of pluralism of the principles for fair distribution. It is in this context that this research used the theoretical framework of Rawls' conception of distributive justice to reflect on ethical issues entrenched in the distribution of HAART. In this discourse, I sought the extent to which HIV/AIDS roll-out programmes are morally important to an individual and the extent of ensuing obligations placed on the individuals and health service providers.

2.2 Distributive Justice

Theories of justice date back to the days of Aristotle and Plato but they were however, mainly concerned with distribution of property in a model society (Fleischacker 2004: 7). The modern understanding of distributive justice is mainly credited to Rawls (1971) who proposed an alternative theory of distributive justice that addressed concerns raised by the weaknesses of utilitarianism in the distribution of societal goods. Distributive justice as understood in the modern sense is premised on the following according to Fleischacker (ibid: 7):

1. *Each individual, and not just societies or the human species as a whole, has a good that deserves respect, and individuals are due certain rights and protections in pursuit of that good;*
2. *Some share of material goods is part of every individual's due, part of the rights and protections that everyone deserves;*
3. *The fact that every individual deserves this can be justified rationally, in purely secular terms;*
4. *The distribution of this share of goods is practicable: attempting consciously to achieve it is neither a fool's project nor, like the attempt to enforce friendship, something that would undermine the very goal one seeks to achieve; and*
5. *The state, and not merely the private individuals or organizations, ought to be guaranteeing the distribution.*

Some of the above premises are extracted from Rawls' concept of distributive justice. In Rawls' theory of justice, his emphasis was on an individual, (as opposed to society) drawing from Kant's notion of respect for persons. Rawls also admired the scientific and mathematical character of utilitarianism and this inspired him to develop two principles which aim for an acceptable and consistent outcome. In his formulation of distributive justice, Rawls (1971: 60) held that:

1. Each person is to have an equal right to the most extensive basic liberty compatible with a similar liberty for others.
2. Social and economic inequalities are to be arranged so that they are both (a) reasonably expected to be to everyone's advantage; and (b) attached to positions and offices open to all.

Principle 1 governs the distribution of liberties and 2(a) the distribution of opportunities. Principle 2 (b) is the "difference principle"[5].

Later in chapter four I will extend the Rawlsian concept of justice to the provision of HAART, by examining the current practices and policies in the light of values and principles afforded in Rawls' theory. In particular, much investigation focussed on the adequacies and inadequacies of the use of such a theory to ground HAART programmes and resolve issues raised by non-adherence to HAART.

[5] These principles indicate what goods are to be distributed, to whom they are to be given and for what reasons they are to be distributed in such a way. This helped to clarify what utilitarians had just referred to as benefits and burdens. However, critiques of Rawls' formulation on distributive justice queried the adequacy of focusing on primary goods while disregarding what people would do with the primary good (Sen 1999:6-11, 41-43). They agreed with Rawls that individuals differ, for example, in their genetic constitutions and their environments. However, they argued that the equality of distribution of a primary good disregards an individual's capacity and efficiency to convert the good into the desired outcome. As a result, inequality results from the differential individual capacities. Another criticism to Rawls' conception argued by Anerson is that since different individuals vary, then their preferences and needs vary as well. Hence, distribution of goods should be according individuals' needs ensuring equality of welfare. With all these criticisms in mind, Daniels (1996: 179 – 207) sought to extend Rawls' theory to health care where he argued that not all preferences and needs are alike. They are subjective rather than an objective measure of well being. He proposed that distributive justice should ensure equality of opportunity where opportunity is principally concerned with the chance to pursue careers, that is, jobs and offices. He (1996: 192) wrote:

> *So equality of opportunity is strategically important: a person's well being will be measured for the most part by the primary goods that accompany placement in such jobs and offices*.

He argued that resources should be used to correct inequalities resulting from "natural lottery", that is, social factors; giving individuals opportunities to pursue careers.

2.3 Adherence

Central to this discourse's economic and ethical analysis is adherence to HAART in the context of cost-effectiveness of HAART programmes and distributive justice respectively. It is thus crucial that the dynamics of adherence to therapy are explored. Medication adherence, as the extent to which the patient takes medication in the way intended by a healthcare provider, is critical to the success of any medical intervention (Matchtinger and Bangsberg 2006). In HAART, it is one of the few alterable elements that could influence the treatment outcome, effectiveness and efficacy. As found by Nachega et al. (2007:567), a 10% increase in adherence above 50% is associated with a similar degree mean absolute increase in the proportion of patients with sustained virologic suppression. Despite its importance, in most instances where treatment is administered over long periods, the adherence rates range between 50% and 75% (Matchtinger and Bangsberg 2006). For HAART programmes, adherence to HAART averages 70% (Orrell et al. 2003: 1372). In South Africa, adherence studies have shown mean HAART adherence rates ranging from 80% to 95% depending on the method used to assess adherence and the study population (Akpomiemie 2006: 29-55; Nachega et al. 2004: 1053 -1056; Orrell et al. 2003: 1369-71).

A 95% adherence rate is a result of a patient missing a single dose of his antiretroviral in two weeks and is associated with a 1 in 5 chance of virologic failure (Akpomiemie 2006: 18). In HAART programmes, achieving above 90% adherence significantly reduces the likelihood of virologic failure and drug resistance. In addition, it provides the best chance for long-term clinical success (Harrigan *et al* 2005: 339-47). Besides clinical success, adherence to therapy is associated with lower mortality when compared to non-adherence to therapy. HAART adherence of less than 80% as measured by pharmacy claims is associated with a three-fold increase in mortality hazard among HIV-1-infected South African adults (Nachega *et al.* 2006: 82).

In the light of the above context, the proportion of patients achieving 95% adherence rates range from 63% to 88% (Nachega et al. 2004; Orrell et al. 2003:1371). This gives the non-adherent patients proportion rates between 12% and 37% (ibid). Such high proportions of patients failing to achieve 95% adherence risk failing HAART interventions. The failure would be mainly through treatment failure and emergence of HIVDR. The relationship between adherence and resistance has long been demonstrated by a number of scientists (see Bangsberg et al. 2004; Sethi et al. 2003). It was indicated that the relationship between adherence and drug resistance is not linear and varies across different drug types (ibid). It is, however, acknowledged that there is evolution of the adherence-resistance relationship. Bangsberg et al. (ibid) reported that there is now more durable and sustained viral suppression using the first line therapy[6]. This first line therapy is similar to the one currently being used in South Africa. Upon failing the first line therapy of 2NRTI and NNRTI, second line therapy is required. However first line therapy failure increases the likelihood of reduced susceptibility to some of the components of second line therapy by 23% (Wallis et al. 2010).

Safeguarding the HAART programmes against the ills of non-adherence might entail mitigating interventions such as adherence-enhancing interventions or mandatorily discontinuing non-adherent patients from HAART. The former intervention focuses on promoting pill consumption which increases adherence rate while the latter intervention is premised on the possible potential to eliminate drug resistance by not using any drugs at all.

[6] First line drug therapy include two nucleoside reverse transcriptase inhibitors (NRTI) and either a non-nucleoside reverse transcriptase inhibitors (NNRTI) or protease inhibitors (PI) (Bangsberg et al. 2004)

2.4 Adherence-enhancing interventions

Adherence is related to both structural factors (for example cost of treatment, availability of close treatment facilities and stigma) and individual factors (for example side effects of drugs and co-morbidity) (Lewis et al. 2006: 143). Of these, individual factors rather than structural factors have been the focus of many adherence interventions. The adherence interventions are aimed at increasing patients' adherence to minimal levels that are required to achieve sustained viral suppression in order to safeguard the gains of HAART. However, the efficacy of these interventions has ranged from 0% to 35% improvement in virologic suppression over a wide variety of different study periods and time lines (Freedberg et al. 2006: S113). A meta-analytic review of adherence intervention literature by Simoni et al. (2006: S23-35) reported a 1.5 times likelihood of an adult patient reaching a 95% adherence rate after the application of an adherence intervention tool.

The cost-effectiveness of HAART adherence interventions was reported to be difficult to assess as the cost of such interventions is not well defined as well as the difficulty in quantification of the long-term clinical benefits of adherence (Matchtinger and Bangsberg 2006). However, investigating the effectiveness of these interventions, Goldie et al. (2003: 632-641) found out that adherence interventions increased the QALY by 0.27 years in patients with early disease as well as reducing virologic failure by 10%. In some studies done in the US, the direct cost of adherence interventions from the provider's and societal perspectives were US$35/person/month and US$45/person/month respectively (Schackman et al. 2005: 927-937). Munakata et al. (2006: 896) using mathematical modelling also found the cost of adherence interventions to be less than US$100/person/month. Intensive nursing interventions to improve adherence in non-adherent patients were shown to have a cost-effectiveness ratio of US$14 000 per QALY gained (Freedberg et al. 2006: S113). These interventions are regarded to be cost-effective in the United States where the limit is US$50 000 per QALY gained or US$100/person/month. However, these figures are huge in the South African

context where the reasonable cost-effectiveness cut-off point is US$ 11 440 (R91 520) per QALY gained (twice the per capita GDP (Garber 2000: 181-221).

Realizing that the overall cost implications of HAART could be much more in circumstances characterized by low adherence rates, removal of barriers to adherence is then imperative. Where such barriers have been removed, and realizing the risk of HIVDR, mandatory discontinuance of therapy could mitigate the cost implications of HAART.

2.5 Mandatory Discontinuance of HAART

Fox and Goemere (2006) provide an example of a patient who was discontinued from ART due to erratic adherence to ART. The basis of discontinuance was to prevent the risk of developing HIVDR strains. The objectives of antiretroviral therapy include attaining durable suppression of viral replication of HIV that has a high mutation rate, restoration and preservation of immunologic functions and improvement of quality of life (Lucas 2005: 423). Viral suppression is attained by the use of different ARVs that inhibit various stages of HIV life-cycle including entry, replication, integration and maturation (Menendez-Arias 2010: 211). Because of the high replication rate and poor fidelity of HIV, mutations that selects viral strains resistant to ARVs in use, as well as enhancing the viral replication capacity, are selected (ibid: 211). Other mechanisms of resistance of HIV to ARV involve selective excision of the inhibitor incorporated by the polymerase during replication (ibid: 213)[7]. The triple therapy currently being used is aimed at reducing chances of treatment failure resulting from drug resistance to a particular drug. However, mutational patterns conferring resistance to combination therapy have been reported (ibid: 211). Mutational patterns that lead to resistance are encountered more often in cases of poor adherence to treatment. The risk

[7] See Menendez-Arias 2010 for in-depth discussion of mechanisms of HIV drug resistance

of multi drug HIVDR is increased in non-adherence than it is in adherent cases. Discontinuance of therapy, therefore aids in reducing the risk of developing multi drug HIVDR and its spread.

Circumstances characterized by a proportion of patients not adherent to therapy are associated with rising direct and indirect healthcare costs. In HAART, expensive treatment regimens have to be used to achieve the same level of treatment success as the adherent population[8]. As a result, the overall cost implications of HAART could be far more in circumstances characterized by low adherence rates. Given that the financial resources to bankroll HAART programmes are constrained in many countries, their governments' ability to achieve universal access would be undermined by non-adherence. It is then imperative to quantify the costs associated with low adherence to HAART. It is in this breadth that this research sought to contribute to the overall knowledge on the costs of HAART by quantifying and describing the economic consequences of non-adherence to HAART. In order to quantify these, this study was embedded in the theoretical framework of analytic models using Markov modelling as the model of choice.

2.6 Markov Modelling

Models provide a simple framework to represent existing systems with a set of dynamic rules governing transmission processes. Markov models are used in modelling for chronic diseases as they simulate the recursive progression of disease (Sun and Faunce 2008: 316). The progression of the disease over a defined period of time (Markov cycle) is divided into specific mutually exclusive categories of the natural progression of the disease called health states. These states represent clinical and economically important stages of the disease progression where health utilities and costs are attached. Patients in each Markov state have similar costs of healthcare and similar risk of

[8] In the public sector there is one 1st line therapy and one alternate therapy (2nd line). The cheaper 1st line therapy is afforded to many HIV patients. Upon failing 1st line therapy, a patient is given the more expensive 2nd line treatment, which cost 4 times the cost of 1st line treatment.

events of importance to the disease in question (Kuntz and Weinstein 2001: 146). The progression terminates in an absorbing state where a patient cannot leave and in many cases the state is death. Transition from one state to another is through all possible and random movements whereupon each cycle has no memory of earlier cycles (Sonnerberg and Beck 1993: 322-388).

In Markov modelling, health costs and outcomes are handled concurrently. As a result, they stand as suitable tools for use in informing policy makers in decision making about healthcare interventions in question (Briggs and Sculpher 1998: 397). The ability to run a large cohort over a large number of cycles to calculate lifetime cost and outcomes gives Markov models an advantage over clinical trials in economic evaluations of medical interventions. However, Markov modelling has a limited capacity of simulating the complexities encountered in trial-based studies (Sun and Faunce 2008: 313).

Besides Markov models, economic evaluation of health interventions can be done using decision trees or clinical trials as the analytical tool. Being the simplest form of economic evaluation, decision trees are suitable for acute cases as they lack the temporal element (Fox-Rushby and Cairns. 2005:42; Drummond et al. 2005: 293-5). Trial based studies have an advantage over Markov modelling in dealing with complexities of real life. They are however limited in the number of cycles that can be done to evaluate the life time costs and outcomes (Sun and Faunce 2008: 313). While these are limitations within the Markov modelling, it however, provides more strength in enlightening policy through economic evaluations.

2.7 Conceptual Framework

The economic and ethical implications of adherence or non-adherence to HAART can be conceptualized as in the diagram below (Figure 1). The conceptual framework looks at the major

themes drawn from literature associated with adherence or non-adherence to therapy. Outstanding issues revealed in the literature which are influenced by adherence and non-adherence includes treatment outcome (recovery, treatment and death), quality of life and effectiveness of the treatment regimen (Foster et al. 2006: 1330).

2.7.1 Non-adherence and Treatment Outcomes

Non-adherence to HAART increases the chance of death three-fold compared to adherent patients (Nachega 2006: 83). This has an impact on the macro-economic picture of the country as it loses income through loss of productive persons, reduced tax base and increased number of orphans who need state support. The other treatment outcome is treatment failure due to either biological or behavioural factors-adherence. This has an impact on the overall cost of treatment because other costly treatment regimens have to be used in order to achieve the same treatment success as with first line adherent patient. As the cost of treatment is driven up by poor treatment outcome, the government's ability to provide broader access to treatment is jeopardized. Not only is the ability to provide broader access to ART compromised, but all health services would be threatened through the frequency of hospital visits from immunocompromised patients presenting with opportunistic infections utilizing resources to be used for other diseases, longer hospitalizations including possible use of intensive care (WHO 2003b).

In situations when treatment is withdrawn from non-adherent patients, it might look economical today as the individuals no longer claim the expensive 2nd line HAART. However, this might be a false economy as these individuals could present as an emergence tomorrow. If looked from the aspect that frequency of hospitalisations and clinic visits could be the same as the individual not on ART because the non-adherent individual do not benefit from the treatment, then continued supply

of HAART to non-adherent patients could have a huge impact on the overall cost of care. This argument holds for the QALYs as well articulated below.

2.7.2 Non-Adherence and QALYs

Non-adherence to treatment leads to loss of 1.2 quality adjusted life years (Munakata et al 2006: 896). This has a bearing on the cost of treatment as patients visit the hospital more often to improve the quality of life through management of the opportunistic infections. Improving QALY in the United States of America would be at an incremental cost of $29 400 (R235 200) per QALY gained (Munakata et al 2006: 896). In resource-constrained countries like South Africa, this increase in the cost of treatment undermines the government's ability to scale up access of ART as the cost of treatment of opportunistic infections of a non-adherent patient erodes the funds for provision of ART to other patients. Provision of health services in general would be seriously affected as more resources are channelled towards improving the QALY of non-adherent patients rather than improving health services.

2.7.3 Non-Adherence and HAART Effectiveness

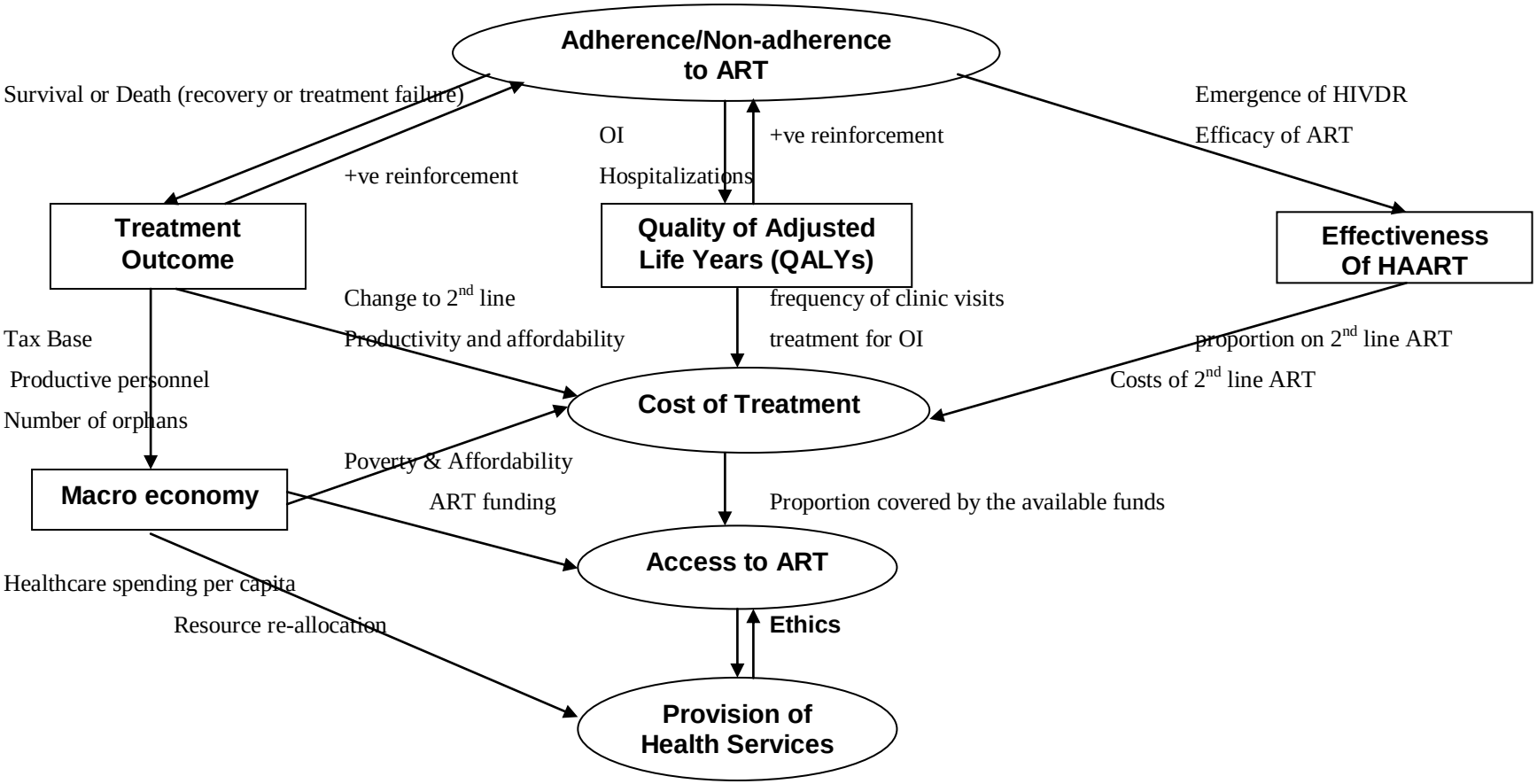
Much money and time has been spent on research to develop various drugs to manage different problematic conditions. One of the reasons behind the signing of the Trade-Related aspects of Intellectual Property Rights (TRIPS) agreement was to reward and promote research and development. The 20-year patent period is aimed at recovery of research costs. However, this recovery of research cost might not occur due to loss of treatment effectiveness. Non-adherence makes treatment non-effective as these patients develop resistance to the medication (Gardner et al. 2009: 1035). Alternative treatment methods have to be employed and these are usually more expensive than the primary treatment methods. In the case of HIV/AIDS, alternate first line or

second and third line treatment protocol might have to be used for a non-adherent patient to try and achieve the same QALY as an adherent patient. Changing the first-line treatment regimen may involve retraining healthcare providers and restocking healthcare facilities (Laxminarayan et al. 2006: 1037). The cost implications of putting a non-adherent patient on second line are the same as those of treatment failure, as outlined above. Besides these implications to the government, there are also implications to the pharmaceutical companies as they lose revenue that they were supposed to earn during the tenure of their patent protection. Furthermore, the research enterprise might be negatively affected as funds to bankroll future research are not realized. As the treatment regimen loses its effectiveness emanating from non-adherence, the ability to provide global access to treatment would therefore be unrealized.

2.7.4 Non-adherence and Access to Healthcare

Health service provisions raise issues of enormous magnitude and are sources of ethical debate. From the provider's perspective, due to limited resources, access to ART for the public is a function of cost of treatment. Although HIV/AIDS financing from the global fund has been increasing over the past 10 years, it cannot however, be predicted with a reasonable degree of certainty that it will continue to increase. This is because, for example, other factors like the economic outlook and global recession might come into play. It is vital that as much as possible should be achieved with the available restricted resources. If provision of healthcare services to non-adherent patients restricts others from accessing the primary services, then ethical theories based on distributive justice should be considered as a way in which to better apportion limited healthcare resources.

Figure 1: *Diagram conceptualizing the effects of adherence or non-adherence on treatment outcomes, effectiveness of HAART, effect of patients and the general effect on the ability to provide HAART*



Chapter 3 Economic Evaluation

Continued supply of ARVs to non-adherent patients: effect on HAART cost effectiveness

3.1 Introduction

The advent of HAART helped reduce the negative clinical and economic consequences of HIV/AIDS. This has been largely due to the increase in life expectancy, quality of life and decrease in mortality due to HIV/AIDS. Since HIV affected the most productive members of society, improvement in the life expectancy restored the tax base and productivity in manufacturing, mining and agricultural sectors, which are the major contributors to economic security and growth in African countries (Nattrass 2004: 32).

However, HAART is a chronic medication requiring adherence to stringent intake times and requirements. Suboptimal medication intake is associated with selection of the resistant HIV strains during its replication. Emergence of these strains is a threat to public health and containing the risk might be as difficult as the challenge posed by MDR- and XDR-TB. Lack of strict adherence to HAART is also associated with clinical progression to AIDS and death (Lamiraud and Moatti 2006). The effectiveness of HAART is thus under serious threat in cases of reduced drug intake.

In addition to the negative implications on health, non-adherence to HAART has potential economic implications. This is primarily because non-adherence could result in an increase in health resource utilization due to increased morbidity and side effects, loss of treatment effectiveness and increased preventable disability. Furthermore, non-adherence to HAART could reduce the confirmed cost-effectiveness of HAART therapy (Lamiraud and Moatti 2006). The potential increase in resource utilization also has a direct impact on the capacity of governments to

scale up or sustain HAART programmes. This is particularly so for governments experiencing a decline in HIV funding. This decline has been occasioned by the global economic crisis and has already affected many HAART programmes, in particular those in developing countries which are reliant on government and funded from the public and donor funds (e.g. Global Fund).

South Africa is a case in point. In 2008, this country funded 77.3 percent of the US$ 622 million total expenditure on HIV/AIDS from the domestic public funds (table 1) (WHO 2008a).

Table 1: *Domestic and International AIDS Spending by service categories and financing sources for South Africa*

Source of Funds in 2007		**Percentage**
Domestic public		77.3
International	Bilaterals	4
	Multilaterals (Global Fund)	13
	Multilaterals (UN & all other Multilaterals)	3.2
	All other internationals or source not specified	2.6

Total reported Domestic Public and International Expenditure = US$ 622 million

Source of data: UNAIDS 2008 Report on the Global AIDS Pandemic

However, with the country officially entering recession in May 2009, local and donor budget allocation for health and HIV/AIDS was substantially reduced (Assubuji and Luckscheiter 2010). For example the government budget for health was reduced resulting in a USD$123 million deficit in public health ARV programmes. Multilateral and bilateral partners that provide support to specific groups of people in HIV/AIDS programmes in South Africa, through an organized network of private providers, also experienced the ripple effects of the global economic crisis. One such

partner, TAC, reported a US$1.1 million budget deficit. The reduction in funding for bilateral partners that provide support to specific groups of people in HIV/AIDS programmes in South Africa resulted from a 10% reduction in funds approved by Global fund for round 8 funding (Hecker 2010). A further 25% reduction for round 9 funding was anticipated, with a suspension of round 10 funding in 2010. Changes in the PEPFAR funding added a further strain on the HIV management programmes.

In light of these effects of the economy on HIV programmes in various countries, UNAIDS recommended that governments should (i) conduct more rigorous evaluations to discover which interventions in prevention generate results, (ii) improve the cost-effectiveness of interventions by focusing on reducing costs in the immediate future, (iii) improve allocation of resources by ensuring budget cuts do not affect predominantly prevention areas that are crucial for reversing the course of the epidemic; (iv) expand social security nets to include people living with HIV and most affected by the epidemic; and (v) pursue options for ensuring that the HIV and AIDS response is sustainable over long-term (UNAIDS 2009).

A possible way of responding to UNAIDS suggestion (ii) outlined above would be to improve cost-effectiveness of HAART through improved adherence. Nonetheless, while the economic impact of non-adherence and subsequent resistance to treatment remains substantial, very few developing countries have assessed the extent of the impact, in particular resistance to HAART (Laxminarayan et al 2006: 1036). The effect of non-adherence and resistance on the economy is through poor health outcomes, loss of treatment effectiveness, reduced quality of life, increased preventable disability and thereby increased direct and indirect healthcare costs (Foster et al. 2006: 1330). In HAART, the rising numbers of people needing treatment for HIV/AIDS, which is not correlating to the funds available, calls for economic analysis of current interventions for efficiency and effectiveness in order to review the priorities of HIV interventions. In the light of changing HIV

treatment strategies, economic analysis would then be a priority as the costs associated with HAART change accordingly. It is then of prime importance to policy makers to re-evaluate of the priorities in the current interventions as HIV management continues to evolve.

Economic analysis through cost-effectiveness analysis is one of the principal tools for priority setting in healthcare especially when resources are scarce and are heavily dependent on the government's ability to fund (Tantivess and Walt 2006: 21). Although monetary resources can be increased through raising taxes to equal marginal social benefit, this may not be possible because of political reasons or might be economically prohibitive (Musgroove and Fox-Rushby 2006: 273).

Realizing the burden of HIV/AIDS on South Africa, loss of effectiveness of an intervention has substantial impact on the population and on the economy. In this chapter, I propose to quantify the economic effects of non-adherence to HAART.

3.2 Methods

3.2.1 Economic Evaluation Assumptions

Concerning economics, the following two broad assumptions were used to guide this research

- Non-adherence to ART leads to poor treatment outcome, loss of QALY and renders ART ineffective.
- Provision of ART treatment to non-adherent patients is not cost-effective when compared to adherent patients.

3.2.2 Study Design

This study made use of Markov modelling for cost effectiveness and cost utility analysis of ART provision to non-adherent patients and adherent patients. In healthcare analysis, this model is the

most suitable for chronic diseases that have clinically and economically important stages in its progression such as HIV/AIDS. In addition, Markov is a more convenient way of modelling the prognosis for clinical problems with an ongoing risk such as HIV/AIDS (Sonnerberg and Beck 1993).

Using secondary input data obtained from literature on the following variables; frequency of hospital visits, costs for hospitalization, laboratory tests, drugs (ARVs and prophylactic drugs for opportunistic infections), human resource costs and outcomes of adherence and non-adherence to treatment, a projection was made on the economical and treatment outcomes for a hypothetical cohort of HIV positive patients on HAART in South Africa. These input costs, for adult patients (18 years or more) from the provider's perspective, were grouped into the following costs: inpatient costs, clinic visits and ARV drug costs. Given that access to HAART for the majority of South Africa's population is a function of the government's ability to provide HAART through the public service, which provides care to 85% of the population, it is fitting that this study evaluates the implications from the provider's perspective.

3.2.3 Outcomes

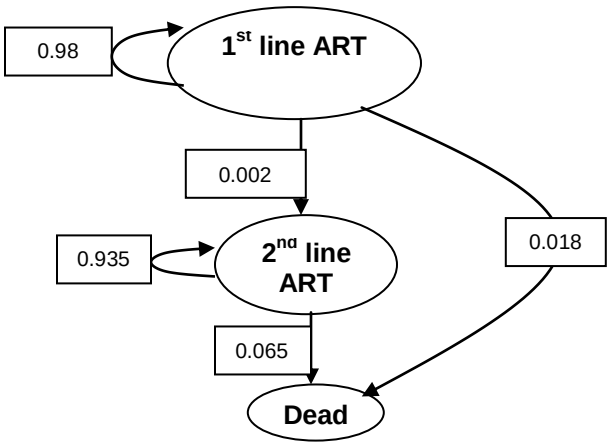
The outcomes considered in this study were the Quality Adjusted Life Years (QALYs). In this case, the use of QALYs as an outcome measurement in the cost utility analysis on HIV patients on HAART is based on the findings that QALYs present a reasonable measurement based on their well being when compared to those who are not on ART (Clearly et al. 2006). Furthermore, QALYs simultaneously integrate two outcomes, reduced morbidity (quality gains) and reduced mortality (quantity gains), into a single outcome (Drummond et al. 2005). Thus making QALYs a comprehensive outcome to use, particularly in this study where HIV positive patients adherent to treatment are likely to fair more favourably in terms of quality of life and life expectancy than those

non-adherent to treatment. In addition, the use of QALYs allows comparability of this study with other studies on the subject.

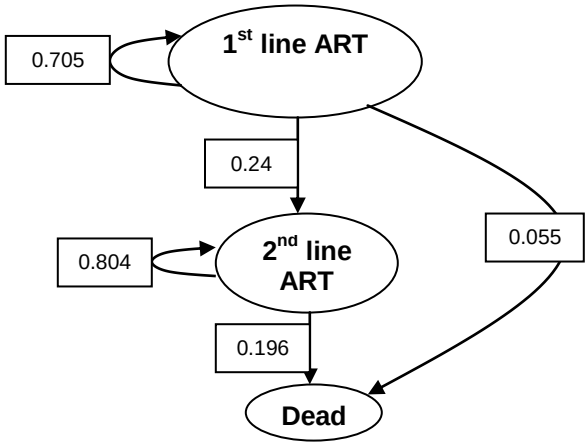
3.2.4 Model Description

The Markov modelling to be used in this study was done using TreeAge Software (2009). Two Markov bubbles were created according to adherence to HAART, which are the adherent bubble and non-adherent bubble[9]. Entrance into the Markov states was a function of biomedical criteria of CD4+ <200 cells/dL. The model used for this study had three health states as defined by 1st line HAART, 2nd line HAART and death as shown in figure 2 below. Transition from one health state to another within the cycle was a function of clinical, virological responsiveness to ART and the natural history of progression of the disease, and was considered independent of previous health states. The cycles terminated in the absorbing state, in this case is death.

Adherent Model



Non-Adherent Model



[9] For the purpose of this study, adherent bubble would constitute individual whose adherence to HAART is >80% and the non-adherent bubble containing individuals whose adherence to HAART is <80%. This is based on the finding by Bangeberg et al. (2004) that resistance to ART is higher at adherence rates less than 80% when compared to more than 80%.

Figure 2: *A flowchart showing probabilities in the adherent and non-adherent proportion Markov states during the first year of ART. See table 2 below for variables used in the construction of this flowchart and their references.*

Adherent proportion Markov states	Non-adherent proportion Markov states
• Patients on 1st line treatment	- Patients on 1st line treatment
• Patients on 2nd line treatment	- Patients on 2nd line treatment
• Dead	- Dead

Costs and QALYs for each associated Markov state where computed into the model for the length of the Markov cycle. In this model QALYs were modelled using a 1 year Markov cycle. The model was run over 20 cycles for both strategies, after which lifetime costs and lifetime outcomes (QALYs) were calculated. The cost-effectiveness ratio was calculated as the incremental cost per QALY gained, comparing the strategy for adherent proportion with that for non-adherent proportion.

3.2.5 Markov Tree

The tree below was constructed for modelling using TreeAge[10].

[10] © TreeAge Pro 2009

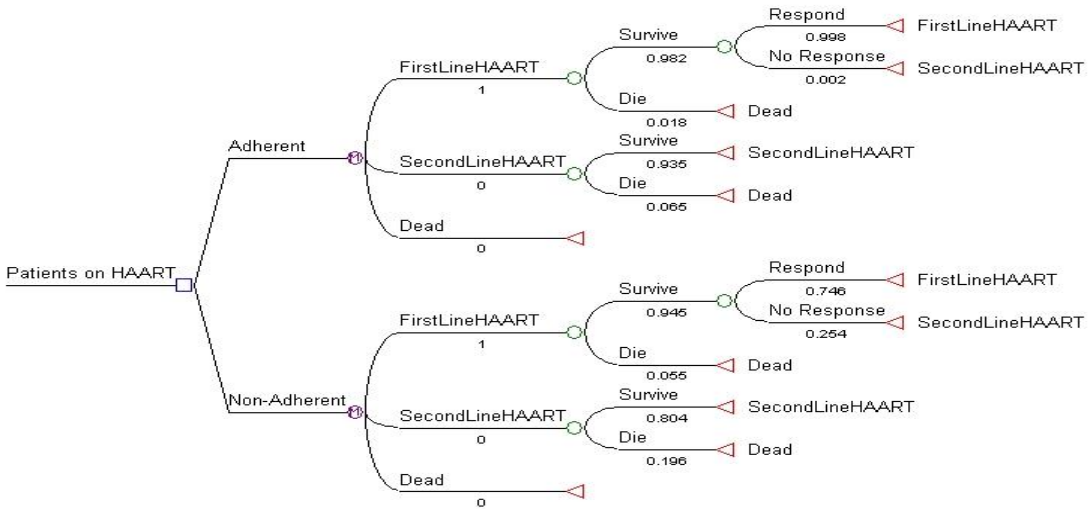


Figure 3: *Markov tree showing transitions between Markov Health States*

3.2.6 Detailed Baseline input for modelling

Table 2: *Baseline input data for modelling*

Input Parameter	Value	Range	Source(s)
Adherence:			
Typical adherence rates		80-95%	
Proportion of those on ART who are adherent	0.565		Nachega et al. 2004; Orrell et al. 2003
Proportion of those on ART who are non-adherent	0.435		Nachega et al. 2004; Orrell et al. 2003
Costs (US$)			
1st Line ART drugs	346.21	128.82-460.42	ASPEN & ABBOTT**
2nd Line ART drugs	782.67		ASPEN & ABBOTT**
In-patient cost for adherent patient	335.50*	280-399	Badri et al. 2006
In-patient cost for non-adherent patient	2054*	1884-2239	Badri et al. 2006
Out-patient cost for adherent patient	269*	251-289	Badri et al. 2006
Out-patient cost for non-adherent patient	181*	162-219	Badri et al. 2006
Utilities			
Adherent	0.80	0.73 - 1	Louwagie et al. 2007; Jelsma et al. 2005
Non-adherent	0.69	0.66 - 1	Louwagie et al 2007; Jelsma et al. 2005
Transition Probabilities			
Probability of transitioning to Second line ART within 12 months			

Adherent	0.002	0.001-0.006	Cleary et al. 2006
Non-adherent	0.24	0.1-0.6	Rosenblum et al. 2009; Bangsberg et al. 2006
Probability of transitioning to dead Markov State within 12 months			
Adherent			
First line ART	0.018	0.017-0.020	Cleary et al. 2006; Nachega et al. 2006: 10
Second line ART	0.065	0.062-0.068	Fox et al. 2009
Non-Adherent			
First line ART	0.055	0.051-0.060	Nachega et al. 2006
Second line ART	0.196	0.185-0.203	Nachega et al. 2006
Discount Rate (%)	6	3-10	van der Merwe 2004

*the cost was an average of the Non-AIDS group and the AIDS group

** Prices obtained through personal communication with A. Beatie.

At the time of the study, there was no generic substitute for Tenofovir on the market and the prices of the drug are expected to drop dramatically due to the generic substitution of tenofovir.

For first line drugs, the cost was calculated on a current treatment regimen for new patients, which has tenofovir, lamivudine and nevaripine. The cost range provided in the table was calculated for the alternative treatment regimen which included stavudine and efavirenz instead of tenofovir and nevirapine.

3.2.7 Markov Modelling Assumptions

In this study, it was assumed that there is insignificant transition between the two Markov bubbles: the Adherent Markov cycle bubble and the Non-Adherent Markov cycle bubble. Parruti et al. (2006) reported that the incidence of adherence failure remained fairly stable at 10% every 6 months up to 24 months follow up and a 5% decline thereafter. Such evidence is lacking in the context of South Africa, hence the assumption.

The full therapeutic benefit of ART is not achieved in non-adherent HIV positive patients as they fail to achieve the minimal inhibitory concentration of the drug. Furthermore, development of HIVDR makes the consumption of ARVs non-effective. It was therefore assumed that the frequency of hospital visits and days of hospitalization of a non-adherent HIV positive patient are similar to those of HIV positive patient not on ART.

3.2.8 Discounting

Individuals receiving benefits might prefer to have money and resources now, rather than in the future. In order to reflect such time preference by societies, both lifetime costs and QALYs are discounted (Walker and Kumarayanake 2002). Discount rates that best capture this societal rate of time preference can be reflected by the interest rate on risk free investments such as government bonds (Drummond et al. 2005). However, other discount rates used have been chosen based on the rate used by the Finance Ministry of the country under investigation (Walker and Kumarayanake 2002) or rates of 3% and 5% which are conventional with economic guidelines. For this study the discount rate used was 6% per annum as provided by the Reserve Bank of South Africa inflation target rates (van der Merwe 2004).

3.2.9 Sensitivity Analysis

Wide range of literature sources used for input data in Markov modelling have inherent variances and deviations. These multiple sources and inaccurate information derived from expert opinion create uncertainties in the simulations (Sun and Faunce 2008: 320, Torrance et al. 1996). Sensitivity analysis is often employed to overcome these uncertainties and to allow for generalisability of results of patients who have different characteristics (Briggs et al. 1994: 95-104). In this study, one

way sensitivity analysis was done on the cost of antiretroviral drugs and on cost of care (hospitalizations and outpatients' visits).

3.3 Results

Table 3 shows the lifetime costs and the lifetime strategies for the two strategies under study. The decision analysis model predicted that lifetime costs for initiating ART in an HIV positive adult adherent to therapy would be much lower (discounted: approximately US$10,000) than the cost of initiating ART in a non-adherent patient (discounted: approximately $15,000). However, non-adherence to therapy resulted in a net loss of 4.55 QALYs relative to initiating therapy for an adherent adult patient. Initiating ART in a non-adherent patient was associated with an incremental cost of US$ 4, 991. Adherence to therapy was associated with an incremental cost-effectiveness ratio that was cost saving

Table 3: *Undiscounted Cost-effectiveness of HAART for the Adherent and Non-adherent populations*

	Cost US$	Incremental Cost (US$)	Effectiveness QALYs	Incremental Eff.(Yrs)	C/E US$/Yr	Incr C/E (ICER)
Adherent	15, 983		13.36		1, 196	
Non-adherent	19, 569	3, 586	4.76	-8.6	4, 111	(Dominated)

Table 4: *Discounted Cost-effectiveness of HAART for the Adherent and Non-adherent*

	Cost US$	Incremental Cost	Effectiveness QALYs	Incremental Eff./Yrs	C/E US$/Yr	Incr C/E (ICER)
Adherent	9, 771		8.18		1, 195	
Non-adherent	14.762	4, 991	3.62	-4.55	4, 074	(Dominated)

3.3.1 Sensitivity

One way sensitivity analysis indicated that results were not sensitive to cost of 1st line drugs and 2nd line drugs, where sensitivity is indicated by variations in ICER greater or equal to 10%. Varying the cost of in-patient care for non-adherent patients influenced results. When the cost of in-patient care for non-adherent patients was reduced to $500 for example, adherence to therapy was more costly and more effective. The additional cost required for each QALY gained was US$696.

Table 5: *Sensitivity analysis on cost of 1st line HAART Drugs*

Cost of Care US$	Strategy	Cost US$	Incr Cost US$	Eff, QALYs	Incr Eff Yrs	C/E US$/Yr	Incr C/E (ICER)
120	Adherent	7, 489		8.18		916	
	Non-Adherent	14, 200		3.62		3, 919	(Dominated)
320	Adherent	9, 509		8.18		1, 163	
	Non-Adherent	14, 697		3.62		4, 056	(Dominated)
520	Adherent	11, 529		8.18		1, 410	
	Non-Adherent	15, 194		3.62		4, 194	(Dominated)
720	Adherent	13, 548		8.18		1, 657	
	Non-Adherent	15, 691		3.62		4, 331	(Dominated)
920	Adherent	15, 568		8.18		1, 904	
	Non-Adherent	16, 188		3.62		4, 468	(Dominated)

Table 6: *Sensitivity analysis on cost of 2nd line HAART Drugs*

Cost of Care US$	Strategy	Cost US$	Incr Cost US$	Eff, QALYs	Incr Eff Yrs	C/E US$/Yr	Incr C/E (ICER)
400	Adherent	9, 725		8.18		1, 190	
	Non-Adherent	13, 702		3.62		3, 782	(Dominated)
600	Adherent	9, 749		8.18		1, 192	
	Non-Adherent	14, 256		3.62		3, 934	(Dominated)
800	Adherent	9, 773		8.18		1, 195	
	Non-Adherent	14, 809		3.62		4, 087	(Dominated)
1000	Adherent	9, 798		8.18		1, 198	
	Non-Adherent	15, 362		3.62		4, 240	(Dominated)
1200	Adherent	9, 822		8.18		1, 201	
	Non-Adherent	15, 915		3.62		4, 393	(Dominated)

Table 7: *Sensitivity analysis in patient care for non-adherent*

Cost of Care US$	Strategy	Cost US$	Incr Cost US$	Eff, QALYs	Incr Eff Yrs	C/E US$/Yr	Incr C/E (ICER)
500	Non-adherent	6, 602		3.62		1, 822	
	Adherent	9, 771	3, 170	8.18	4.55	1, 195	696
100	Non-adherent	9, 227		3.62		2, 547	
	Adherent	9, 771	544	8.18	4.55	1, 195	120
1500	Adherent	9, 771		8.18		1, 195	
	Non-Adherent	11, 853		3.62		3, 271	(Dominated)
2000	Adherent	9, 771		8.18		1, 195	
	Non-Adherent	14, 478		3.62		3, 996	(Dominated)
2500	Adherent	9, 771		8.18		1, 195	
	Non-Adherent	17, 104		3.62		4, 721	(Dominated)

3.4 Discussion

While the world has witnessed improved global funding for HIV/AIDS, such improvement has been associated with minimal general improvement in the well being of people living with HIV/AIDS (Blinderman 2009: 106). Such lack of improvement was thought to be the effect of non-adherence, among other factors. Adherence to treatment is one of the essential elements for a successful HAART programme. Achieving the required levels of adherence has remained a challenge for the chronic condition of HIV/AIDS. Failure to attain these minimum adherence levels has been associated with an increase in morbidity and mortality (Nachega et al. 2006); disability and impaired quality of life; and direct and indirect healthcare costs (Lamiraud and Moatti 2006). Details on the potential economic implications of non-adherence to HAART have remained very limited, especially its implications for developing countries. It was in this context that this study sought to calculate the cost effectiveness implication of non-adherence to therapy using mathematical models.

Starting ART in adherent patients is consistently less costly than initiating therapy in non-adherent patients. However, effectiveness of non-adherence to therapy compared to adherence to therapy is lower. Undiscounted lifetime cost of HAART for an adherent and non-adherent patient was US $ 15 983 and US $ 19 589 respectively. The lifetime cost for an adherent patient is with the reference range of one study by Cleary et al. (2009). She reports the undiscounted lifetime cost of US $ 13 191 (11 167 – 16 056). Similarly, an undiscounted effectiveness of 13.36 QALYs for an adherent patient obtained in this study is within Clearly et al.'s (ibid) reference range 12.9 (11.1 – 15.2). Looking at the incremental cost-effectiveness ratio; adherence to therapy dominates non-adherence, thus suggesting that adherence to therapy is both less costly and more effective. In South Africa, there are very few studies on cost-effectiveness providing HAART to non-adherent patients which have been conducted. As a result I cannot compare the ICER obtained for this study with that of

other interventions so as to judge relative cost-effectiveness. The ICER in this study for adherent proportion was cost saving. As the cost-effectiveness threshold varies among countries, and given that no such clear guidelines for cost-effectiveness threshold exists in South Africa, the reasonable limit would be twice the per capita GDP (Garber 2000: 181-221). The GDP for South Africa in the year 2009 was US$ 5 823 (IMF 2010), thus giving US$ 11 646 (R91 520) per QALY gained as the cost-effectiveness threshold. The threshold of US$ 11 646 can be considered as the maximum amount society would be willing to pay to purchase an additional unit of health. In this regard, the cost per QALYs for starting HAART in the adherent patient proportion and non-adherent patient proportion revealed that initiating HAART in the adherent patients proportion would be very cost-effective while doing so in the non-adherent patients proportion would not be cost-effective.

The decision to initiate therapy or to continue therapy for adherent or non-adherent patients also influences efficiency in the allocation of resources as well as equity in access of these resources. Looking at efficiency first, this study shows that a significant proportion of the healthcare budget will be devoted to the ARV intervention if ART is initiated and continued for the non-adherent patients. This discriminates against other competing health needs for which cost-effectiveness may even be greater. Thus therapy for the non-adherent patients may impact negatively on allocative efficiency. Where a decision such as this one has to be made in the face of great scarcity, it might be more economically reasonable to restrict HAART access only to adherent patients.

Initiating and continuing therapy for non-adherent patients has been shown to be associated with greater unmet needs. This is hugely attributed to increased drugs costs and hospitalization costs in the face of restricted HAART programmes budget.

Decisions to continue therapy for the non-adherent patients exacerbate inequalities in HAART programmes as the continued supply of expensive drugs and hospitalizations of non-adherent

patients quickly exhausts the available HAART funds when compared to the context where access to therapy is restricted to adherent patients only. It then becomes difficult to decide who gets therapy thus augmenting inequity in access to services. Equity was identified by WHO as one of the major ethical principles that should underlie HAART distribution. It thus follows that measures addressing non-adherence to therapy would help to address equity issues.

Uncertainty in drug costs did not change the picture of the results. Sensitivity analysis for both first line and second line treatment was associated with an ICER that was cost saving for the adherent patients. However, sensitivity analysis for cost of in-patient care was associated with robust results as the ICER significantly varied, ranging from cost saving to US$700 per QALYs gained. Such robustness of results is vital in their interpretation as the sensitivity of lifetime costs and outcomes reported in this study cannot be generalized to other settings (Cleary et al. 2006). This is the case, for example, in settings where costs of ARVs are high and inefficiency in healthcare setting results in markedly different inputs and outputs and consequently different costs per in-patient days.

There are some limitations with this study that can be addressed in future research. These include use of the provider's perspective. It has been suggested that a societal perspective which includes direct non-healthcare costs should be considered (ibid). Such costs can significantly impact universal access and adherence. The interpretation of the ICER is also challenging in South Africa due to the lack of cost-effectiveness studies, and also a lack of government policy on cost-effectiveness threshold (Badri et al. 2006: e4). Generally comparison with other studies would have allowed better assessment of the study.

3.5 Conclusion

This study has provided evidence on costs and benefits of the two strategies. It has indicated that initiation and continuance of therapy to non-adherent patients is not a cost-effective intervention in South Africa. Although to make a decision on such grounds is admittedly complex without policies on willingness to pay and additional cost-effectiveness studies, which with appropriate funding and willingness could be researched further. A trade off between costs and benefits are crucial in deciding which strategies to implement particularly in the context of major resource constraints, potential inequity in access to care, and reduced efficiency in allocation of resources. Uncertainty due to key parameters used in this study plays a major role in influencing the generalizability of results and robustness. Further research should be conducted using better quality data so that decisions may be made based on robust results. However, I have shown the idea and application has merit.

The findings in this chapter expose ethical issues concerning treatment of non-adherent patients which I will discuss in the following chapter (Chapter four). In it, I will use findings from this chapter to discuss the suggestion that there is merit in considering that HAART be restricted only to adherent patients.

Chapter 4 Ethical Analysis

To Treat or Not To Treat: HAART, Non-adherence and Justice

4.1 Introduction

The field of medicine is changing rapidly. New technologies and therapies are continuously being introduced. Though the means to the ends of medicine are rapidly changing, the ends in themselves remain fairly constant and universal, that is for the "good" of the individual seeking medical attention (Pellegrino and Thomasma 1993: 53). Healthcare systems are designed to promote the end of medicine as evidenced when possible by the normal functioning of the individual. This is achieved through provision of opportunities to meet the end. As Savulescu (1998a: 216) puts it, "the good of healthcare is a state of affairs which provides people with the best chance or opportunity to achieve what is for them the best life". This statement draws from the idea that disease confers some sort of disability to individuals which restricts opportunities to realize his or her rational plan of life. This is also the belief of Daniels (1996: 10) writing: "the central idea is that disease and disability restrict the range of opportunities individuals have open to them, whereas healthcare protects it."

The pace of development of new medical technologies and therapies is occurring within a context characterized by increasing unwillingness to finance rising health costs (Lamb 1989: 33). In developing countries, the failure of financial mechanisms to keep pace with medical technological and therapeutic developments can be exemplified by the management of HIV/AIDS. The management of HIV evolved from monotherapy in 1986, to dual therapy in 1992 and now involves triple therapy. Triple therapy has 1st line to about 4th line regimens. Treatment advances have always been beyond the reach of many at the time. Financing for treatment also has remained problematic.

Globally in 2001, only 16% of the target funds to fight the pandemic were raised through the Global Fund. In 2009, the budget deficit was not any better. It is therefore inevitable that acute ethical problems rise. Moreover, it is important that the responsibility for decision-making over healthcare financial priorities is justly distributed (ibid).

In light of the above, economic reasoning at best tell us the effects of pursuing different policies; but it cannot, without guidance of normative analysis, recommend which policy to pursue. Economic reasoning has much to contribute to the development of ethical policy as important concerns are consequences of alternative arrangements and trade-off margins (Hurley 2001: 234). It is in this context that the purpose of this chapter is to use the economic analysis results from the previous chapter to reflect on some ethical issues concerning the continued use of new therapies (that is 2^{nd}, 3^{rd} or 4^{th} line treatment regimens) in treating individuals who were not adherent to treatment.

The ethical issues concerning access to healthcare have been analysed in literature from a rights perspective and theoretical perspective (use of ethical theories like Kantianism, virtue and utilitarianism). However, for this chapter, I reflect on some ethical issues concerning the continued use of new therapies using Rawls' theory of justice.

I will extend the Rawlsian concept of justice to the provision of HAART, by examining the current ART distribution practices and policies. The use of Rawls concept of justice should not be construed as a total acceptance of his theory and rejection of other concepts of justice. Rather, it should be viewed as a reflection into some of the adequacies and inadequacies of such a theory to ground HAART programmes. The use of Rawls theory stems from the widespread attention his theory has received and its use in many economic policy formulations. Besides Rawls theory of

justice, applied (clinical) ethics will also be used to analyse the suggestion that there is merit in considering that HAART be restricted only to adherent patients.

In reflecting and analysing the suggestion that there is merit in considering that HAART be restricted only to adherent patients, I acknowledge that during the course of therapy, some non-adherent individual could be enlightened and might decide to redeem themselves by becoming adherent. As in the assumption used in the previous chapter, such transitions are assumed not to take place. In this way, I deliberately avoid ethical issues concerning such individuals. As a result, this discourse is limited in scope to ethical issues embodied in individuals being not adherent to therapy out of *choice*.

4.2 Distributive Justice

Distributive justice concerns the allocation of resources amongst diverse members of society fairly. Fair distribution usually considers the total amount of goods to be allocated, the procedures used for distribution and the pattern resulting from the distribution.

Because all societies have limits on their wealth and resources, the question grappled within distributive justice concerns how to allocate goods (resources) fairly. This raises questions concerning in what a "fair share" should consist.

Some people say that equity and need should determine the distribution of goods. Equity includes the idea that people who make a greater contribution on their society should receive more benefits than those who did not or those who contribute less. If needs is the basis for distribution of goods, those who need more of a benefit or resource will receive more. Another view is the allocation of

goods according to social utility, in other words, the distribution of benefits would be determined by the best interests of society as a whole.

Different sorts of distribution advance different social goals. Equal distribution of goods is premised on the ideas that equality fosters group identity, as a motivation to produce, and that basic and essential needs are met for all members of society.

Amongst the most influential scholars writing on justice and distributive justice was John Rawls. Briefly, Rawls conceives justice to be that all social primary goods (liberty and opportunity, income and wealth as the basis of self respect) should be distributed equally. Rawls' rider to this is that it holds unless an unequal distribution of any or all of these goods is to the advantage of the least favoured members of society.

Rawls argues that each person's good is that which is needed for him or her to execute a rational long-term life plan under reasonable circumstances. Since each individual has his or her own life-plan, what is good may vary from person to person. Rawls (1971: 232) writes, "the good is the satisfaction of rational desire." He also considers that what is right is set out in the social contract people have in society as that which is fair (Rawls 1958: 178). He writes:

> "Persons engaged in a just, or fair, practice can face another member openly and support their respective positions … it is in this notion of the possibility of mutual acknowledgement of principles by free persons who have no authority over one another which makes the concept of fairness fundamental to justice (ibid: 179)."

Rawls' conception of that which is right as fairness is determined by the "veil of ignorance". The veil of ignorance is a procedure of reasoning which purports to reduce or discard personal bias when it comes to fair distribution of goods.

Rawls asks us to imagine a social contract developed by self-interested (but non-existent) individuals who are all acting under the veil of ignorance, that is, social or economic status they will inherit at their birth. He then argues that a just and fair society is the type of society these non-existents would argue as the best society in which to be born. This is, of course, because these non-existents do not know what type of genetic, physical or social circumstances – the innate differences – they will be faced with upon birth.

Another argument in Rawls' social contract is that, free and equal citizens situated in a "well-ordered society" who are morally motivated by their sense of justice can accept and generally comply with the same principles of justice. Regarding the principles of justice, Rawls invites us to a criterion of justice, as a solution to the problem of social justice. It ranks feasible alternative basic structures by the minimum representative lifetime share of primary goods each of them tends to generate.

The Difference Principle

The principle allows allocation that does not conform to strict equality so long as the inequality has the effect that the least advantaged in society are materially better off than they would be under strict equality. Advocates of this principle argue that we should change our policies and laws to raise the position of the least advantaged in society. Distributive principles vary in numerous dimensions:

- In what is subject to distribution (income, wealth, healthcare, jobs, etc.)
- In the nature of the subjects of the distribution (natural persons, groups, reference classes, etc.)

- On what basis distribution should be made (equity, maximization, according to individual character, etc.).

Broadly grouped (1971 and 1993), Rawls' two principles govern distribution of index goods of powers and prerogatives of offices and positions of responsibilities; income and wealth; and social bases of self-respect. His two principles read:

1. Each person has an equal claim to a fully adequate scheme of equal rights and liberties, which scheme is compatible with the same scheme for all; and in this scheme the equal political liberties, and only those liberties, are to be guaranteed their fair value
2. Social and economic inequalities are to satisfy two conditions: (a) they are to be attached to positions and offices open to all under conditions of fair equality of opportunity; and (b) they are to be to the greatest benefit of the least advantaged members of society (Rawls 1993: 5-6).

Given the above context of distributive justice, I shall reflect on ethical issues concerning distribution of HAART in healthcare. More specifically, I will analyse the suggestion that there is merit, under justice theory, in considering that HAART be restricted only to adherent patients.

4.3 HIV, Health and Human Function

The justifying principle of the ends of medicine is morally enshrined in the "good" of the person seeking treatment. This moral end may be grounded in different ways such as the Kantian [1785](1983) moral notion of respect for persons or in the liberal belief as indicated by Mill [1869](1993) that the individual knows his or her best interests better than anyone else. Another perspective of the good gravitates towards essentialism or the notion that human life has certain central defining features. In her list of important functions in human life, Nussbaum (1992: 214-

223) identifies the shape of the human form of life and basic human functional capabilities to which we aspire[11]. Some of the basic functional capabilities that she referred to in theory of good are also described as basic needs by Daniels (1981: 153) who writes:

> "Human *course-of-life* needs would include food, shelter, clothing, exercise, rest, companionship, a mate (in one's prime), and so on."

For Rawls, the 'good' is taken to be the desire for primary goods such as self-respect and liberty, powers and opportunities, and income and wealth. Good is determined by "what is for him rational plan of life given reasonably favourable circumstances" (Rawls 1971: 347).

What is called a "thin theory of good" is determined by the individual's purposes, causes and intentions in life. Rawls (1971: 349) points out that:

> "Indeed, even rational plans for life which determine what things are good for human beings, the values of human life so to speak, are themselves constrained by the principles of justice."

Thus we can see that the principles of justice are far-reaching, even into healthcare as a part of normal functioning.

[11] The basic human functional capabilities as proposed by Nussbaum (1992: 221) are: 1.Being able to live to the end of a complete human life, as far as is possible; not dying prematurely, or before one's life is so reduced as to be not worth living. 2. Being able to have good health; to be adequately nourished; to have adequate shelter; having opportunities for sexual satisfaction; being able to move from place to place. 3. being able to avoid unnecessary and non-beneficial pain and to have pleasurable experiences. 4. Being able to use the five senses; being able to imagine, to think, and to reason. 5. Being able to have attachments to things and persons outside ourselves; to love those who love and care for us, to grieve at their absence, in general, to love, grieve, to feel longing and gratitude. 6. Being able to form a conception of the good and to engage in critical reflection about the planning of one's own life. 7. Being able to live for and with others, to recognize and show concern for other human beings, to engage in various forms of familial and social interaction. 8. Being able to live with concern for and in relation to animals, plants, and the world of nature. 9. Being able to laugh, to play, to enjoy recreational activities. 10. Being able to live one's on life and nobody else's; being able to live one's own life in one's very own surroundings and context.

Normal human functioning is key to individuals in the original position. The individuals should be "normal, active and fully cooperating members of society over the course of a complete life" (Rawls 1993: 20). In this regard, it is assumed that "physical needs and psychological capacities are within normal range so that questions of healthcare and mental capacity do not arise" (Rawls 1971: 83). Thus, these individuals should be of good physical, mental and social well-being. Lack of such well-being curtails their basic liberties and reduces the "normal range" of opportunities available for the individual to develop a rational life plan. Normal [opportunity] range is defined as "the array of life plans reasonable persons [in a given society] are likely to construct for themselves" (Daniels 1985: 33). This range is very much relative to a given society, including key features of its historical development, technological development, and level of material wealth (Fleck 1989: 303).

Handicaps to an individual's physical, social and mental well-being are typical in HIV infection. HIV/AIDS reduces individual's abilities and capabilities; and hence opportunities and productivity[12]. Socially, the individuals are disadvantaged as they may be marginalised or discriminated because of stigma attached to the condition (Skinner and Mfecane 2004: 160). Although it might be illegal and immoral, certain jobs refuse employing individuals who are HIV positive, thus individuals' ability for social positions is undermined (NAT 2003; see *Hoffman v South African Airway case*[13]). As HIV weakens one's health, this means that virtually all opportunities for life plans in a normal range are lost or severely constrained (Fleck 1989: 303). Not only are opportunities restricted, but also their basic liberties such as freedom of association[14] and freedoms specified by liberty and integrity of the person[15] (Audard 2007: 95).

---

[12] For example, HIV/AIDS infected individuals are prone opportunistic infections. Much time and money is spent in hospitals through hospitalizations or clinic visits. Economic productivity is reduced through time spent out of work due to illness.

[13] *Hoffmann v South African Airways* 2000 (2) SA 628 (W)

[14] Persons living with HIV/AIDS are discriminated based on HIV status in their admission to organizations of employers or trade union and continuation as members and participation in their activities. This is against the

The goals of HAART are to preserve life through achieving a durable suppression of viral replication of HIV that has a high mutation rate, the restoration and preservation of immunologic functions and the improvement of quality of life (Lucas 2005: 423). Achieving these would be for the "good" of the individual as it restores normal or near normal functioning. In this way HAART contributes to the realization of the individual's intermediate and ultimate ends such as liberty, opportunity, income and self respect.

4.4 HAART and Rawls's First Principle

The provision of basic healthcare can be seen as affording a condition necessary for the full autonomy of citizens, thereby protecting their inalienable basic rights and liberties which then afford individuals equality in opportunities. This follows the notion that basic liberties are productive conditions for opportunities (Van Parijs 2003). The opportunities are good as they retain their value as a means to prolonging a good rationally planned life (Savulescu 1998a:219). Regarding HIV/AIDS in South Africa, the question that arises would be whether provision of HAART falls under the provision of basic healthcare[16]. The WHO suggests that HAART is basic healthcare (WHO 2008b). In assuming that HAART is basic healthcare HAART programmes would be a *priori* committed to bringing citizens across a threshold of good functioning necessary

---

International Labour Organization (ILO) instruments on freedom of association and collective bargaining (UNAIDS 1996).

[15] In some countries, people living with HIV/AIDS are subject to being quarantined, detention in special colonies and isolation. Such coercive measures restrict individual's freedoms specified by liberty and integrity of the person. There is no public health justification for such deprivation of liberty. In addition to the above coercive measures, some countries, sectors, and companies subject people to a compulsory HIV testing. This can constitute a deprivation of liberty and a violation of the right to integrity of person. This is more prevalent in government institutions like military force, prisons, etc. The right to physical integrity requires that testing be voluntary and based on informed consent (UNAIDS 1996)

[16] Increasingly literature reports are found which point to primary health care including HIV/AIDS clinical services. See for example Price et al. 2009 and Mukherjee 2003.

for basic rights and liberties, and would be governed by Rawls' (1971: 60) first principle which states that:

> "Each person is to have an equal right to the most extensive basic liberty compatible with a similar liberty for others."

Under the first principle, HAART provision as a basic healthcare service would be required to be brought within the reach of every member of society (Shelton 1978: 168). This would be more inclined to the "test and treat" policy being advocated by some sectors in health (de Bruyn and Conradie 2010). In such a case, healthcare (HAART) would not be treated only as a social good but also as a basic liberty (Green 1976: 112). This egalitarian concept, where each member would be guaranteed an equal right despite position or background, is contained within the WHO's principles underlying the effort to fairly distribute HAART (Macklin 2004: 5). Furthermore, providing HAART under this principle would be aimed at achieving a certain minimal level of functionality for every constituent of society in keeping with the claim to basic liberties.

The end of HAART under Rawls first principle is affording normal human function for patients (species-typical) as a way to protect their basic rights and liberties. In this context, therapy has to bring "physical needs and psychological capacities" needs to within normal range regardless of the cost. But the pursuit of species-typical functioning for some classes can be enormously costly - and probably achieved only at the cost of limiting resources for other classes of patients (Callahan 1996: 9). Given that the first principle is not subject to trade-offs between basic rights and liberties and issues of economic efficiency, the cost of such requirements could prove too expensive, especially for poor countries, and could exhaust resources left for application of Rawls' second principle (Audard 2007: 97). Furthermore, this strong egalitarian account of healthcare justice is not truly in synch to the vagaries of healthcare systems or to the pace of scientific advancements (Fleck 1989: 302).

In HAART, species-typical functioning might require provision of 1st line treatment or 2nd – 4th line treatment in the case of treatment failure. However, treatment failure can come about due to a personal *choice* not to take the medication as prescribed. Thus, after initial distribution of 1st line HAART to achieve normal or near normal function, failure to adhere to treatment might lead to resistance to 1st line HAART. This would result in a further claim on society to provide 2nd line treatment as a basic liberty under the first principle. Such claims would limit HAART's availability to other persons needing the treatment. This further claim on society due to an individual's fault or *choice* is called "social hijacking" (Daniels 2008: 67, 168). Daniels argues that the societal obligation to assure everyone access to healthcare as a matter of justice is not unlimited in scope (ibid).

Accepting the finality of justice in this case would be irrational as the principle would be "impossible and too costly to implement and you can change as a consequence of disutility", thus contradicting the rationality of the concept of justice (Audard 2007: 136). Rawls also noted that the first principle can be applied only if reasonable economic and social conditions are attained, not in desperate situations where survival is at stake (Rawls 2001: 47; Audard 2007: 97).

4.5 HAART and Rawls's Second Principle

Although Rawls omitted health and healthcare from his list of primary goods, he later sought to see how health might be incorporated into his framework in his book *Political Liberalism*. The distribution of healthcare would be guided by Rawls' second principle. The second principle holds that (Rawls 1993: 5-6):

> Social and economic inequalities are to satisfy two conditions: (a) they are to be attached to positions and offices open to all under conditions of fair equality of opportunity; and (b) they are to be to the greatest benefit of the least advantaged members of society

The difference principle is secondary to the principle of fair equality of opportunity.

The aims of the second principle are creation of wealth and economic efficiency (Audard 2007: 98). Wealth creation and economic efficiency involves healthy individuals. Healthcare can therefore provide normal functioning of individuals thereby affording a platform for equality for opportunities contained in the first part of Rawls' second principle. Healthcare institutions are created through tax payer funds (donor funded institutions are excluded in this case because their function is not a matter of justice but of benevolence, charity and care (Livnat 2003: 507). They are a result of the cooperative efforts of the citizens of a country.

Distribution of healthcare is therefore not an allocative justice concept but rather that of distributive justice as the bundle of goods is obtained through cooperative efforts. The creation of the goods of healthcare comes with claims attached and these claims are founded on justice (Kukathas and Pettit 1990: 66). Its distribution would therefore permit deviation from equal distribution if it improved the health and well-being of the least advantaged (Hurley 2001: 235).

Regarding HAART, the normal functional range is not limited to the same level in the infected individuals. It is not conceived as the binary oppositions of disease and health as HIV/AIDS is a chronic condition with different health states throughout the person's lifetime. Integrating HAART into Rawls' framework would entail use of HAART in those individuals whose clinical picture (CD4 <200) indicates a tendency towards a greater disability. Furthermore, these individuals are subject to social and economic inequalities as indicated above. Most of the individuals with a CD4 >350 do not show signs of immune system compromise. Their clinic visits and hospitalizations are

limited. They spend much of their time being productive in the different sectors of the economy. Prioritizing those most affected would effect an increase in the proportion of productive people and a resulting increase in the tax base.

Since benefits and rewards are governed by a just/equitable and efficient social scheme where people's talents work for the benefit of all (Audard 2007:104), more wealth would be created and financial resources would then be available to commit to healthcare. It is plausible then for resources to be committed to those showing signs of immunodeficiency as it would be economically efficient and to everyone's advantage. Furthermore, in many developing countries the most HIV afflicted are poor and the marginalized. The "natural lottery" and social misfortune further reduces the normal range of goods available to these individuals. The moral price of not protecting these weak members of society would be unacceptable.

Now let us look at the justification for giving 2nd or 3rd or 4th line treatment in cases of treatment failure. Treatment failure occurs when an individual deteriorates both clinically and virologically whilst they are on HAART. When it occurs, the individual needs the more costly 2nd or 3rd or 4th line drugs to achieve durable viral suppression. This non-suppression could result from biological or individual factors. Audard (2007: 106) argued that if a negative consequence is not a result of *choice*, but of *bad luck*, then it is no longer a matter of justice but of care and assistance. It is plausible therefore to say that if treatment failure is due to biological factors, giving 2nd or 3rd or 4th line treatment is a matter of care. If it is a result of individual factors, such as non-adherence to therapy and alcoholism then it would be a matter of justice. Those individual who fail on treatment end up worse-off if 2nd or 3rd or 4th line treatment is not given as they succumb to the deleterious effects of HIV outlined above. Looking at non-adherence to HAART in the context of behavioural factors leading to treatment failure, it may often be a matter of *rational choice* or patient's subjective valuation of HAART therapies (Lemiraud and Moatti 2006). But distributive justice

does not recommend any intervention to correct inequalities arising from voluntary *choice* or *fault* of those who end up the least advantaged, so long as it is proper to hold individuals responsible for choice or fault that led to the inequality. It would suffice then to say that in a society subscribing to the principles of justice, the more costly treatment interventions are not recommended for non-adherent individuals.

Regarding costs of HAART, cost containment interventions and efficiency are of importance in HAART because efficiency is a necessary, but not sufficient, condition of equity (ibid: 145). Justice holds that society should enhance our efficiency, permit our talents to flourish and make us more secure. This is critical in societies where resources are constrained and where inefficiency would result in others being denied their portion of the good (Savulescu 1998b: 233). Justice would then resolve these first order conflicts (*ibid*).

Rawls' second principle underscores the importance of effectiveness and efficiency. He held that under the difference principle, society has to "aim at the highest point of the most effectively designed scheme of cooperation." (Rawls 2001: 63). If HAART programmes are governed by the principles of justice then such programmes should be efficient; where efficient systems are those that "... ensures social cooperation and stability in the long run, not only because the least advantaged are better off in terms of their own expectations, but because they are a part of a fairer scheme of cooperation" (Audard 2007: 145).

Using the results from the previous chapter, non-adherence to treatment, which could be a *rational choice*, is associated with lifetime costs that are one and a half times more than those who are adherent to medication. This is largely due to the costs of hospitalizations and 2nd or 3rd or 4th line treatment to those who have failed 1st line treatment. From these results, it can be said that giving lifetime treatment to two non-adherent individuals would deny one adherent individual of lifetime

treatment. But justice as in the second principle requires *reciprocity*, where in a scheme of cooperation, society works and develops so as to "contribute to others' good as well as their own" (Rawls 2001: 75)[17].

The arguments above deliberately avoid using cost-effectiveness as a measure for efficiency. Rather they use lifetime cost because of ethical issues surrounding the use of such as a guide for resource distribution. It is argued that life years or QALYs used in cost-effectiveness analysis may fail to capture public preferences for spending the limited resource (Gold et al. 1996: 31). However, if the society is a scheme of cooperation in the original position, and the parties are behind a veil of ignorance, they would be unaware of their preferences but subject *to circumstances of justice*. Use of cost-effectiveness as a measure of efficiency would therefore be acceptable. Under such, non-adherence to treatment which is less cost-effective when compared to adherence would be less acceptable.

4.6 Autonomy and Tyranny of Majority

Application of Rawls' concept of justice to healthcare is not without objections and criticisms. It is contended that the use of a structural ideal of justice in governing the societal goods would interfere with people's lives as it cannot be realized without such interference (Nozick 1974: 163). The upshot of such interference would then be limitation of individuals' autonomy, liberty or rights. It can therefore be viewed as a "tyranny of majority" as it forces individuals to act according to

[17] This may be supported by other moral theorists such as Hume (1911: 135) who expresses the same moral commitment. He writes:

> If it be allowed that particular consequence of a particular act of justice may be hurtful to the public as well as individuals, it follows that every man in embracing that virtue must have an eye to the whole plan or system, and must expect the concurrence of his fellows in the same conduct

Since non-adherence to treatment cannot be universalized as in Kant's [1785](1983) categorical imperative and such consequence is does not contribute to the individuals' good or that of others, then it would be unjust to give new therapies to the non-adherent proportion.

maxims of the majority in the ideal society. Extending this objection to HAART, it can be contended that withholding or withdrawing treatment based on adherence to treatment is an interference with an individual's private transaction and is a coercive[18] way in which the government is pushing a citizen to act in a particular valued way. The central argument in this objection can be framed in the following way:

P1: Restriction of access to HAART is coercive

P2: Coercion is unjust

C: It is unjust to restrict access HAART

Conclusions reached above are based much on the acceptability of the second premise. Coercion is argued to be morally wrong because it does not show respect for persons and thus a respect for individual autonomy. If justice as *fairness* is a result of a fair procedure and respecting persons' equality and autonomy, then coercion would be unjust because coercion lacks respect for autonomy which is an accomplice of justice. The theory of justice is argued to give rise to conflicts that can only be settled, if settled at all, by coercion (Jackson 1978: 732). In that sense people are free but cannot choose what they want. Thus justice would impose constrains on autonomy (Savulescu 1998b: 235).

However, it is argued that the purpose of governments is not to push citizens into acting in certain valued ways; instead, it is directed to make sure that all human beings have the necessary resources and conditions for acting in those ways (Nussbaum 1992: 225). Choosing not to take medication when it is available can be likened to a person with food who can always choose to fast; a person who has access to subsidized university education who can always decide to do something else

[18] The word *coercion* "comes from the Latin verb *arcere*, to shut in, also the root of the word *incarceration*, and implies physical force to produce or change behaviour" (Powers 2007: 126). It is an action, or lack of action thereof, that forces other individual to respond in an involuntary manner. The definition of coercion is, however, context specific. In this discourse, it is taken to imply an intentional constrain on a set of options available to an individual. Drawing from this, coercion would be a replacement of an individual's preference and values with the common values pursed by society (Blake 2002: 272).

instead. Thus even if a person is encouraged to eat or go to college because of the grave consequences of contrary actions, his choice not to takes precedence. These are also the sentiments shared by libertarians such as J S Mill who holds that "All errors he is likely to commit against advice and warning are far outweighed by the evil of allowing others to constrain him to what they deem his good" Mill [1869](1993: 41).

Counter-arguments against the above are premised on the understanding that our freedom is limited by the constraints of cooperative social existence (Savulescu 1998b: 233). In this way of thinking, it is argued that autonomy is not an end in itself. There is an interpersonal dimension to autonomy, called "relational autonomy" (van Bogaert and Ogubanjo 2006). The principle of autonomy is both self-legislating and other-legislating: if my actions are guided by a universally applicable moral rule (Kant's principle of universalisation), I expect the other to follow the same rule in relevant similar circumstances (ibid). Respect for autonomy would therefore imply acting in a way that would allow others act autonomously as well. As Rawls puts it, our autonomy is within the framework of the principles of justice whose aim is "to combine into one conception of totality of conditions that we are ready, upon due reflection, to recognize as reasonable in our conduct with regard to one another" (Rawls 1971: 587). If not taking HAART (non-adherence) when given the chance would restrict other individuals from having access to a similar chance, then non-adherence is unjust. Also, by being non-adherent out of *choice*, then a person may expect others to follow the same action.

The purpose of withholding or withdrawing treatment from non-adherent individuals under justice principles is aimed at the protection of the HAART programmes rather than deny individuals of their liberty/autonomy. This was emphasised by Jackson (1979: 736) when he wrote:

> "The one clear qualification logged in the discussion of coercion of the intolerant is that it cannot be taken in the name of increasing liberty, but only to safeguard the existing domain of a just constitution. Were there justice in the use of coercion to advance liberty, it would

> mean diminishing of the liberty of some citizens by coercion in order to increase the liberty of others. Some persons (the coerced) would be treated as the means to the ends of others (the newly freed, perhaps). Treating persons as means in such calculus is categorically repudiated in the foundations of the theory."

Since non-adherence to treatment threatens the stability of HAART programmes, Rawls' theory of justice permits an extent of coercion, which in this case is restricting access to HAART. Such limitation to autonomy or rather liberty would be acceptable as it would enhance the equal freedom enjoyed by all.

The above arguments justify limitation of autonomy to enhance other liberties under Rawls' theory of justice. Yet, it can be contended that non-adherent individuals are not fully autonomous (because they are ill) and therefore cannot be part of the social contract whose citizens are "normal, active and fully cooperating members of society over the course of a complete life" (Rawls 1993: 20). In this, autonomy is taken as an attitude a person takes guided by his or her faculty of reason towards influences that motivate him or her. The influences are determined whether or not they are considered full autonomy in the light of three obstacles to it: incompetency, coercion and ignorance (Illingworth 1990: 67).

Coercion has been considered above. Incompetency and ignorance can be viewed in the context of principlism that is in the ambit of informed consent in medical fraternity. Educating individuals would enhance their autonomy. If it can then be shown that non-adherent individuals are competent or well informed, it can be argued that they can be citizens in Rawls' social contract and subject to its principle, hence justifying limitation of individual autonomy for enhancement of other freedoms.

In HAART programmes, patients undergo at least two counselling sessions before therapy initiation. A wide spectrum of matters is discussed including the importance of adherence to the

prescribed treatment. Treatment is only started when individuals are deemed ready as indicated by their willingness to adhere to treatment. During therapy, choosing not to take the medication as prescribed would therefore be not as a result of incompetency as these patients are educated about the conditions. Moreover, the education process is not a once-off process but is continuous. Non-adherence would therefore be a matter of choice and not incompetence.[19]

In spite of the education given to individuals to augment autonomy through competency, other social events can foster restricting autonomy. This is evident in situations characterised by a hostile family environment. For example, fear of domestic violence and divorce might force women not to disclose their status or that they are taking HAART. It can thus be argued that such individuals who are not adherent to ART are not doing so autonomously because it is restricted out of fear. However, such fears cannot adequately justify that the individuals are not fully autonomous. It only serves to point out that *circumstance* affects autonomous *choice*. In HAART programmes there are social support structures, including counselling that has been mentioned. These programmes assist individuals in addressing all other issues pertaining to life and health. These are adequate to manage issues of domestic violence, divorce, etc., and hence restore full autonomy to those individuals. Given all this, the above argument is flawed and non-adherent individuals could be subject to Rawls' principles under the idea of social cooperation.

4.7 Restricting access to non-adherent HAART patients: Let them die?

An argument could be made that withholding or withdrawing treatment from non-adherent HAART patients can be likened to letting them to die. This is similar to Young's (1771) argument on the

[19] See Fox and Goemere (2006) who give an example of the services that were provided before discontinuing HAART on certain individual.

poor; that they should not be helped as they will die anyway (Baugh 1983: 77). The killing and letting die distinction has dominated the ethical debate for decades. It has been widely referred to in debates on euthanasia.

Killing has been intuitively regarded as morally worse than letting someone die. Some philosophers, however, contend that there are no moral differences between the acts of killing and of letting someone die. One such philosopher is Rachels who used the "Bare Difference" argument to show moral equivalence in killing and letting die. In the argument, he used the *Smith and Jones case*[20] to assert that killing and letting die are morally indistinct as they result in a similar consequence. In this interpretation the motives could be the same and a defence of lack of causality is represented as a gross pervasion of moral reasoning. Harris (1995: 10-11) also added that we are equally morally responsible for both our positive actions and our negative actions, bringing about a moral indistinction between killing and letting die. But Green (1980: 204) argued that the "killing and letting die can be distinguished in terms of causal role of the agent and the distinction is inherently relevant to the determination of the extent of moral responsibility of the agent."

[20] In brief, Rachels' (1986: 111-14) bare difference argument begins by acknowledging that, guided by certain reasons; a particular act killing may be morally inferior to a particular act of dying. He, however, argues that regardless of the reason, the difference in killing and letting die is not among the actions.

In illustration the bare difference, Rachels used a scenario involving two individuals that had similar conditions except one. In the scenario, Smith and Jones stand to gain a large inheritance if anything should happens to their respective six-year old cousins. The only difference is that Smith drowns his cousin in the bath (Smith kills his cousin) while Jones watches his cousin drown in the bath after having slipped accidentally (Jones lets his cousin die). Jones would, however, have gone into the bath with the intention to kill his cousin when notices that his cousin is drowning. In both case, Smith and Jones gain their respective inheritances (ibid: 112).

From the above scenario, Rachels argues that if the killing and letting die distinction is morally important, then Jones' behaviour is less reprehensible than Smith's. Intuitively we do not agree with that for the reason that they both had a similar motive. Furthermore, their actions or lack of action thereof resulted in similar consequences (death of their respective cousins and gaining the inheritance).

If we extend Green's (ibid) proposal of the causal role of the agent to distinguish between cases of killing and letting die, generally we realize that withdrawing HAART from non-adherent patients could be regarded as letting this patient die rather than killing the patient. This would be so as the withdrawal of HAART would mean a refrain from continuing to prevent the patient's death and thus the patient dies. The patient's death is a result of the infection or acquired disease and not by societal withdrawal of HAART. In such a case, society would not have killed the patient but simply let the patient die[21].

Extending justice to the killing and letting die distinction, Dinello (1971: 86) believed that "the killing and letting die distinction can have a moral significance at least in situations in which one must choose between the lives of two persons." This connects justice to the moral significance of the killing/letting die dichotomy (Foot 1977: 101).

In the management of HIV/AIDS, lack of adequate resources makes it necessary to make a choice between those who adhere to therapy (and have a better prognosis) and those who are non-adherent (and have a poor prognosis). Withdrawing second line treatment from a non-adherent patient would result in an earlier death of the patient but also could benefit four other adherent individuals on first line treatment.

This is similar to the "spare parts" case cited by Green (1980: 200), "a physician can kill a patient to obtain organs for transplantation into five others who will otherwise die." Withdrawing treatment from a non-adherent patient would be to let the patient die so that the four other adherent patients could survive. In such a case, the non-adherent patient would be used as a means to an end for the

[21] It is interesting to consider that many of the ethical dilemmas we face today are from technological advances. Most of the new technologies are expensive and of greater benefit to individual than to population health. Ethical issues concerning organ transplantation highlights another context of dilemmas associated with technological advances (Callahan 1996: 9).

adherent patient. Such measures would be unjust as they contradict the notion of justice as fairness where "justice as *fairness* is a result of a fair procedure and respecting persons' equality and autonomy". Treating persons as means to an end for others would be failure to respect that person's equality. However, there is pluralism of conditions leading to the withdrawal of HAART from non-adherent patients. A non-adherent patient would have enjoyed the initial claim on society. Their personal failure to utilize their allocated resource is in the first place what makes them claim further more expensive resources. It can be said then that their individual fault results in them using others as means to their own ends. This is because they consume HAART that could have saved 3 other patients had they remained adherent. It is in such a case that O'Neil (1978: 125) argued that loss should lie where it falls in the initial "natural lottery". She wrote:

> "There exists a random procedure for distributing the evil of death the fairness of which we have come to accept: the 'natural lottery' of fate. This is not to say we consider it wrong to interfere with nature's processes in order to save lives. It is only when we are at the point when we must choose between one person's death and another's we find that there already exists the randomization involved in letting the loss lie where it falls. To introduce another lottery or some other method for choosing at this point is unfair to the winner of the initial 'lottery'."

The result of letting nature take its toll in this case could imply that once an individual is offered HAART and then the individual by *choice* does not adhere to it, then he or she forfeits the opportunity.

Extending Rawls' ideas to letting the non-adherent patients die would entail "social control and regulation of necessary unequal outcomes of apparently free *choices*, not about eradicating them" (Rawls 1971: 88). This therefore means that inequalities resulting from non-adherence to treatment, which could be a *choice* and not a *circumstance*, ought to be corrected but not necessarily eliminated. However, such a transaction would not result in the overall advantage of the least

advantaged as more resources are committed to a smaller segment of the least advantaged (non-adherent patients). This would contradict the second principle. Rawls's second principle cannot, therefore, be applied in this case.

4.8 Risk, Precaution and Prevention

HAART has been used as a public health intervention in both primary and secondary HIV prevention programmes. Its use as a preventative method was based on the findings that the number of new secondary cases generated was proportional to the duration of infectiousness, contact rate and transmission probability (Garnnett and Anderson 1996: 137). HAART thus reduces all three variables of the transmission dynamic formula given below (McCormick et al. 2007; Garnnett and Anderson 1996: 137).

$$R_o = Dc\beta$$ where:

R_o = the number of secondary cases generated

β = Probability of transmission

c = Contact rate

D = Duration of infectiousness

The use of HAART in this regard can be taken as a duty in risk management that is anticipating and taking precautionary measures to prevent or minimize unacceptable harms. In context, conflicts arise in risk management when one's private behaviours expose others to the risk of harm posed by HIV. This private transaction is well defined when one chooses not to adhere to HAART which increases the duration of infectiousness and the risk of generating new cases. Resolution of such conflicts call on the use on normative arguments since risk management cannot be separated from public policy and ethics (Perri 2000: 139).

In HAART programmes where one chooses not to adhere to treatment, the unwanted hazards resulting from such include development of HIVDR, loss of effectiveness of HAART and increased risk of development of multi drug HIVDR. Risk management in this given situation entails use of adherence-enhancing interventions or mandatory discontinuance of HAART where the former fail. The latter risk management intervention is tangled with ethical issues. Normative argument for minimizing the risks of non-adherence to therapy through withdrawal of HAART from non-adherent patients can be formulated as below:

P1: Restriction of an individual's liberty is morally acceptable when failure to do so could result in harm to other members of society

P2: Non-adherence to HAART harms the other members of society

C: It is morally acceptable to restrict access to HAART in non-adherent persons

The first premise (P1) is a risk management premise because it is ground on consequentialist foundations. Restriction of an individual's liberty where it is perceived to result in harm to others is precautionary as it is an anticipatory preventative action. Physically harming or defrauding other members of society is supposed to be everyone, regardless of religious or cultural beliefs. On harm, the moral justification of weak paternalistic action to prevent harm to others is entrenched in J.S. Mill's (1806-1873) harm principle. It entails that:

> "the sole end for which mankind are warranted to, individually or collectively, in interfering with the liberty of action of any of their number, is self-protection. That the only purpose for which power can be rightfully exercised over any member of a civilized community, against his will, is to prevent harm to others. His own good, either physical or moral, is not sufficient warrant[22]."

[22] Similar principles were contained in Hume's (1911) arguments on justice where he insisted that:

Use of such arguments was instrumental in the passing of legislation prohibiting drunken driving, public smoking and commercial sex work. Some liberals express reservations in the use of restrictive laws to control private transactions and foster certain virtues to individuals. Others accept weaker tools which involve persuasion to cultivate the required virtues (Perri 2000: 143). Weaker tools are argued not to infringe liberty in a way similar to coercion. It is argued that for instance, information, advice, education, deception, incentives, manipulation, and behavioural modification do not equally infringe on liberty (Childress 1981: 566). In health, such weaker tools include fines or taxes, for example tobacco tax in order to discourage smoking.

The use of weaker tools like taxes and fines is difficult to extend to HAART for non-adherent patients. Non-adherence as a health-risk behaviour cannot be easily taxed in the same way as tobacco taxes for smokers. Furthermore, use of taxes creates certain unfairness as some risk behaviours do not deserve subsidy, such as failing to exercise and therefore cannot be taxed even though there exists clear evidence correlating the behaviour to a health state (Veatch 1974: 8-9). Thus the use of taxes to prevent harm to self and others cannot be categorical as it cultivates discrimination.

If liberty, in the frame of justice as fairness, used in HAART is regarded not as a defense of vested interests, but rather regarded to mean "the liberation of society from the injustices of preventable disability and early death" (Beauchamp 1999: 109), then P1 would be true and the conclusion above sound. The premise would be seen in the light of Beauchamp's (ibid) argument that:

> extending life and health to all persons will require some diminution of personal choices, but that such restrictions of personal choices are not only fair and do not constitute an

---

> the safety of people is the supreme law; all other particular laws are subordinate to it and depend on it. And if, in the common course of thing, they be followed and regarded, it is only because public safety and interest demand so equal and impartial an administration.

> abridgement of fundamental liberties, they are a basic sign and imprint of just society and a guarantee of that most basic of all freedom – protection against man's most ancient fore.

Much of the second premise's acceptability is not hinged on the availability of sound scientific evidence but rather on the probability of occurrence of such harm. This makes the premise a risk management premise.

Regarding non-adherence to HAART, it could be argued that there is no connection between non-adherence to HAART and harm to others. In this argument, it could be said that if an individual chooses not to take medication as prescribed, the individual would harm self, and not others members of society. It follows that HIVDR strains develop in non-adherent individual not in members of society. It could be, however, conceived that there is harm to others if an individual is non-adherent to therapy. Matchtinger and Bangsberg (2006) reported that non-adherence is a significant public health threat. It (non-adherence) accelerates the development and transmission of the drug-resistant virus. Moreover, each new carrier of the HIV infection is a potential locus for further social contamination (Bayer 1986: 171). In this context, it could be argued that the risk of releasing a resistant strain into society exposes other members of society to possible harm. This could warrant intervention by society. Given that the erratic uptake of HAART is associated with the emergence of HIVDR strains, restricting access to non-adherent individuals could reduce the risk.

Counter-arguments make reference to the disease's mode of contagion. The mode of infection assures that those at risk are those whose actions contribute to their risk of infection, chiefly through intimate sexual contact and shared hypodermic needles (Mohr 1987: 38). It could therefore be argued that claims referring to non-adherent patients as a public health threat are unfounded. Individuals harmed are those with risky behaviours and harm to self does not constitute harm per se.

This is seen in the legal maxim *volenti non fit injuria* translated as 'to one who consents no harm is done' (Illingworth 1990: 27). If the most important value that contributes to the good of society is individual freedom, and that non-adherence to HAART harms self, then restricting access to HAART based on non-adherence would restrict an individual's liberty.

The justification of discontinuance of the supply of HAART to non-adherent patients could be drawn from the other conceivable harms to other members of society that result from self harm. Economic harm could be such harm to society. From the previous chapter, we found out that the lifetime treatment of a non-adherent patient would be at the cost of two other adherent patients. In countries where resources are constrained, affording HAART to a non-adherent patient would mean limiting access of two individuals not on treatment. In this context, an adherent individual's freedom is restricted by the liberty of a non-adherent individual.

Public funds are used to finance HAART programmes. These funds are limited in many developing countries. Given this, economic harm associated with non-adherence of a patient is endured by society through increased taxation and a rise in medical care premiums. Restricting access to HAART in this case would not be an attempt to foster certain virtues in the non-adherent individuals. Rather it could be an attempt to recover marginal costs associated with HAART (Beauchamp 1999: 102-3).

If the most important value that contributes to the good of society is individual freedom, and that non-adherence to HAART economically harms others, then restricting access to HAART based on non-adherence would be morally acceptable.

There is a conceivable tragedy of self harm that might lead to death when one decides not to adhere. Beauchamp (ibid) believes that preventable 'death and disability' are public goods that should not

be subject to the vagaries of the market concept of justice or subject only to the concept of liberty. He held that the moral responsibilities to prevent those diseases and illnesses which can be prevented are contained in the concept of justice. This concept does not identify health issues within the private domain.

The goal of precaution (as found in risk management) is public health itself: the good of disease and disability prevention to afford equality of opportunity (Perri 2000). In a well ordered society where there is dependence on the order, intolerance risks the instability of society and precautionary interventions ought to be implemented to prevent the risk. The risk in the stability of HAART programmes is high due to non-adherence to HAART. Paternalistic measures such as withdrawal of HAART could be of merit. The merit stems from the need to protect viability, stability and sustainability of just/equitable institutions or programmes and of just/fair societies.

Rawls' second principle distributes goods to the advantage of those less advantaged. Such distribution can be seen as to have the lowest risk of unwanted hazards. In HAART programmes, individuals with a low CD4 count have a high viral load and transmission probability (Nattrass and Geffen 2005: 66). Prioritising the least advantaged (in terms of low CD4 count) would have a greater impact on reducing the generation of new secondary cases when compared to instances prioritising those with a greater CD4. In this context, apportioning HAART to the least advantaged under the second principle may not only improve their functionality and economic picture but could prevent the harms to society posed by generation of new secondary cases.

4.9 Conclusion

The ethical significance of healthcare stems from the reasoning that ill health and injury are unpredictable and sometimes beyond the control of the individual. Ill-health represents a time of

considerable vulnerability and dependency on others (Hurley 2001: 235). However, ill-health is not always beyond an individual's control because it can result from factors within the control of the individual. These factors may include, for example, obesity, reckless driving, skipping of a regular investigation such as Pap smear and skipping regular treatment as in non-adherence. Nevertheless, distribution of healthcare should be fair. Pluralism of healthcare needs coupled with inadequate resources are some factors which make it difficult to apportion a fair healthcare treatment for all. This difficulty is furthered by *self-inflicted health problems*. Theories of justice have been used to inform ethical dilemmas embodied in the distribution of healthcare (Persad et al. 2009: 429).

The use of Rawls' theory of justice to solve the moral issues pertinent in the distribution of HAART is useful though not adequate alone. HAART as a basic liberty or *priori* to Rawls' first principle is met with fundamental sustainability problems. The financial implications of the strict egalitarian "test and treat" policy under the first principle are huge and unsustainable. Such a policy can be changed based on the disutility of the policy, thereby contradicting the rationality of the concept of justice. The second principle allows for the use of "baby steps" in HAART provision instead of the "one giant step" required by the first principle. Its use is to bring the least advantaged individuals to an acceptable level of functioning so that they can compete for the opportunities available to other normal functioning individuals. The least advantaged group in Rawls concept of justice excludes those individuals who end up in that position as a matter of *choice* rather than *circumstance* after the initial distribution of the resources.

Withdrawal of treatment from non-adherent individuals has merit under Rawls' principles. Such a coercive measure can be just/fair as it is necessary to sustain the societal and the programme's stability. In addition it contains cost elements thereby bestowing economic efficiency to HAART

programmes[23]. From a liberal and risk management point of view, it can be viewed as just/equitable as it is necessary as a precautionary intervention to prevent economic harm to other members of society. The harm results from use of more expensive new therapies by non-adherent individuals.

As it has been used by WHO, Rawls' theory of justice is a key consideration in resolving moral issues concerning the initial distribution of HAART. It is also of merit in restricting HAART access to only adherent patients as a means to maintain the stability of HAART programmes and of society at large. Criticisms to using Rawls' theory for healthcare are premised on societal interference with private transaction, which results in the loss of liberties or right to privacy. However, freedom and liberty enjoyed by all members of society is enhanced through protection of the stability of just/equitable institutions. Such protection could involve interference with private transaction. In the context of this research report, I have suggested that restriction of HAART access only to adherent patients could have merit.

[23] The goals of Rawls' second principle are wealth creation and economic efficiency.

Chapter 5 Concluding Remarks

5.1 Introduction

The burden of HIV/AIDS in South Africa is huge. HAART has been key to reducing the burden. However, new challenges continue to emerge. Universal access to HAART, which is crucial in reducing new secondary cases generated to close to zero, is being curtailed by lack of adequate resources. Priorities on who benefits from the available resources were set. Treatment guidelines currently available prioritized individuals in WHO stage III and IV or individuals with a CD4+ <200 cells/dL. Despite such interventions, the incidence of new secondary cases continues to rise. This has been attributed among other reasons to the emergence of drug resistant virus (HIVDR). Drug resistance has been long associated with biological and behavioural factors. Poor adherence to therapy is one such behavioural factor. Connected to poor adherence to therapy would therefore be loss of efficacy of drugs, poor treatment outcomes and increased direct and indirect health outcomes.

In the wake of the new challenges posed on HAART programmes, analysis of the current programmes with the goal of finding response options that are effective and sustainable becomes necessary. This stems from the necessity, in priority setting, to include "the cost of increased resistance against the backdrop of the benefits of using the drug in treating infections and preventing their further spread to uninfected individuals" (Laxminarayan et al. 2006: 1037). In as much as it is potentially possible to eliminate drug resistance by not using any drugs at all (*ibid*), a decision prioritizing certain interventions on particular diseases may in fact conceal a decision about which population to treat since some diseases may be more common among some groups (Childress 1981:561-7). Such could be true in HIV/AIDS which tends to affect the poor and marginalized in developing countries.

Macro-allocation of health resources requires a consideration of both economic and ethical issues (Zembaty 1981: 521). In as much as HAART has been offered in an atmosphere shrouded in mystery and unaccountability, cost effectiveness analysis helps in placing HAART programmes in the context of burden of disease and priority setting. The cost effectiveness used in economic evaluation is crucial in clarifying the concept of access which is central to distributive justice arguments. In addition, cost effectiveness is central in identifying ethically acceptable arrangements premised on concepts of equity and efficiency embodied in some theories of justice (Hurley 2001: 239). A consideration of economic and ethical issues in HAART posed by the new challenges to the programme (non-adherence) yielded the findings outlined below.

5.2 Major Findings

The economic analysis of HAART programmes in South African public sector revealed that non-adherence to therapy was associated with huge costs of care and less effectiveness when compared to adherence. It was also correlated to a 56 per cent loss of QALYs. The overall lifetime cost of therapy of a non-adherent individual was 1.5 times that of an adherent individual. In this light, lifetime provision of the HAART to two non-adherent individuals would deny one adherent individual of a similar opportunity. Given that non-adherence to therapy can be a matter of *choice* rather than *circumstance*, provision of HAART to non-adherent individuals would have ethical issues embodied in it. Such moral issues could be analyzed from a justice perspective.

The use of Rawls' theory of justice to underpin an ethically justifiable distribution of HAART provides a useful framework. It permits unequal distribution of the treatment in a way that reduces the risk of a crisis caused by HIV/AIDS while at the same time improving the general welfare of society. In addition, the theory of justice has principles ensuring efficiency, stability and viability of

just/equitable institutions, as well as sustainability of just/equitable interventions. These are of unequivocal importance in HAART as AIDS is a chronic condition requiring life-long medication. In order to maintain HAART stability and sustainability, Rawls permits some kind of coercion. Such morally justified coercive measures include restricting access to HAART in non-adherent patients. These reduce the risk of non-adherent individuals harming others economically and also enhance freedom enjoyed by all.

Despite providing an acceptable framework for the just/equitable distribution of HAART, Rawls' theory of justice fails to address some fundamental distributive issues pertinent in developing countries. Its relevance in developing countries is severely limited by the constrained resources, which make the first principle non-applicable to HAART distribution. Furthermore, although the second principle prioritizes the least advantaged class, it fails to provide a just/equitable framework for micro-allocation of resources. Such micro-allocation issues are exemplified by having to make a choice on who benefits from a single resource where two or more individuals are eligible to receive treatment (they are all in the same least advantaged category – those with a CD4 <200 cell/dL). This scenario is more pertinent to developing countries that have many people on the waiting lists to receive HAART. The use of adherence to determine the beneficiary of HAART has been proposed but cannot be morally justified using Rawls' theory.

5.3 Policy Recommendations

Failure to effectively use HAART as a primary or secondary prevention intervention could result in a crisis. The use of rescue medicine in the crisis intervention can only produce marginal returns (Childress 1981: 561-7). HAART adherence is therefore of significant importance economically and clinically. Non-adherence to therapy would reverse the clinical and economic gains achieved through HAART. Although restricting access to HAART only to adherent patients can be

economically and morally justified, it could be politically unpopular. Such a form of intervention can be likened to earlier governmental policies that denied treatment by questioning the association between HIV and AIDS. In the light of the country's political history and the findings that the most HIV afflicted are the poor and the marginalized, restricting access could be construed to be discriminatory and targeting the poor black majority. Given this, interventions to improve adherence to treatment could be significant in reversing the clinical and economic consequences of non-adherence to HAART. As health administrators review strategic plans to curb HIV transmission and treatment, it is vital that they factor in the costs associated with adherence improvement interventions in a drive to safeguard the effectiveness of HAART.

A just/equitable framework for distribution of HAART could be provided by Rawls theory. However, when used alone in developing countries like South Africa, it is insufficient as its success relies on, for example, sufficient monetary and human resources. Its use in healthcare and HAART should be limited to the provision of normal functionality and affordance of stability to just/equitable institutions where conditions that characterised by sufficient monetary and human resources.

5.4 Study Limitations

This study was limited by the lack of adequate information on non-adherent patients. Many assumptions where made where such information was lacking and that could have an effect on the conclusion deduced from the results.

5.5 Areas of Further Research

Recommendations above suggest the use of adherence enhancing intervention in order to safeguard the effectiveness of HAART programmes. The cost-effectiveness of such intervention remains unknown in the South African setting. Exploration of this could provide critical information in establishing priorities for allocation of funds within the healthcare budget or within the HAART strategic plan budget.

In the same regard, it is of essence to reflect on the ethical issues concerning the use of adherence enhancing interventions in resource constrained countries from a justice perspective. Such investigation would help understand the values which society upholds and ought to encourage.

REFERENCES

Akpomiemie, G. 2006. Measurement of and factors affecting patients' adherence to antiretroviral therapy in Helen Joseph Hospital, Johannesburg Dissertation submitted in partial fulfilment of the requirement of the degree Masters in Public Health. Faculty of Health Sciences School of Public Health. University of the Witwatersrand, 17 November 2006.

Assubuji, P., Luckscheiter, J. 2010. The global economic crisis and South Africa. *Perspectives*, 3.09: 1.

Attawell, K., Mandy, J. 2003. Provision of antiretroviral therapy in resource-limited settings: a review of experience up to August 2003. London: DFID Health Systems Resource Centre.

Audard, C. 2007. *John Rawls*. Stockfield: Acumen Publishing Limited.

Badri, M., Maartens, G., Mandalia, S., Bekker, L-G., Penrod, J. R., Platt, R. W., Wood, R., Beck, E. J. 2006. Cost-Effectiveness of Highly Active Antiretroviral Therapy in South Africa. *Plos Medicine* (online) 3(1): e4. Retrieved September 9, 2009. Available at: www.plosmedicine.org

Bangsberg, D. R., Moss, A. R., Deeks, S. G. 2004. Paradoxes of adherence and drug resistance to HIV antiretroviral therapy. *Journal of Antimicrobial Chemotherapy*, 53(5): 696-99.

_____., Acosta, E. P., Gupta, R., Guzman, D., Riley, E. D., Harrigan, P. R., Parkin, N., Deeks, S. G. 2006. Adherence–resistance relationships for protease and non-nucleoside reverse transcriptase inhibitors explained by virological fitness. *AIDS*, 20(2)*:*223–231.

Baugh, D. A. 1983. Poverty, Protestantism and Political Economy: English Attitude Towards the Poor, 1660 - 1800. In: *England's rise to greatness*. S. Baxter (Ed.). Berkeley: University of California Press.

Bayer, R. 1986. AIDS, Power and Reason. *The Milbank Quarterly*, 64 (1): 171.

Beauchamp, D. E. 1999. Public Health as Social Justice. In: *New Ethics for the Public's Health*. D. E. Beauchamp, B. Steinbock (Eds.). New York: Oxford University Press: 101-109.

Bell, C., Devarajan, S., Gersbach, H. 2003. The Long-run Economic Costs of AIDS: Theory and An Application to South Africa. [Unpublished]. Retrieved June 16, 2008. Available at: http://www.popline.org/docs/1542/281969.html

Bennett, D. E., Bertagnolio, S., Sutherland, D., Gilks, C. F. 2008. The World Health Organization's global strategy for prevention and assessment of HIV drug resistance. *Antiviral Therapy*, 13: 1–13.

Bhorat, H., van der Westhuizen, C. 2008. Economic growth, poverty and inequality in South Africa: the First Decade of Democracy. Conference Paper: The Regulatory Environment and its Impact on the Nature and Level of Economic Growth and Development in South Africa. Retrieved May 25, 2010. Available at: http://www.commerce.uct.ac.za/Research_Units/DPRU/Conference2008/Conference2008_Papers/Carlene1995_2005%20growth%20&_poverty_28march_updated.pdf

Bisson, G. P., Gross, R., Bellamy, S., Chittams, J., Hislop, M., Regensberg, L., Frank, I., Maartens, G., Nachega, J. B. 2008. Pharmacy Refill Adherence Compared with CD4 Count Changes for

Monitoring HIV-Infected Adults on Antiretroviral Therapy. *Plos Medicine* (online) 5(5): e109. Retrieved September 9, 2009. Available at: www.plosmedicine.org

Blake, M. 2002. Distributive Justice, State Coercion, and Autonomy. *Philosophy and Public Affairs*, 30(3): 257-296.

Blinderman, C. 2009. Palliative care, Public health and Justice: Setting Priorities in Resource Poor Countries. *Developing World Bioethics*, 7(7): 105-110.

Bowler, S. M., Wilson, P. D. 2005. Designing Equitable Antiretroviral Allocation Strategies in Resource Constrained Countries. *PloS Medicine* online 2 (2): e50. Retrieved May 6, 2008. Available at: http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0020050

Briggs, A., Sculpher, M., Buxton, M. 1994. Uncertainty in the economic evaluation of health care technologies: the role of sensitivity analysis. *Health Economics*, 3(2): 95-104.

_____., Sculpher, M. 1998. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics*, 13: 397-409.

De Bruyn, G. Conradie, F. 2010. An end to AIDS pandemic: Test and Treat? *Research Newsletter* (online). Retrieved April 18, 2010. Available at: http://web.wits.ac.za/Academic/Health/Research/e-News/January2010/RNBabySteps.htm

Callahan, D. 1996. Is Justice Enough? Ends and Means in Bioethics. *The Hastings Centre Report*, 26(6): 9-10.

Childress, J. F. 1981. Who Shall Live When Not All Can Live? In: *Biomedical Ethics.* T. A. Mappes, J. S. Zembaty (Eds.). New York: McGraw-Hill Inc.: 561-7.

Chigwedere, P., Seage III, G. R., Gruskin, S., Lee, T. H. 2008. Estimating the lost benefits of antiretroviral drug use in South Africa. *Journal of Acquired Immune Deficiency Syndrome*, 49(4): 410-415.

Cleary, S. M., McIntyre, D., Booule, A. M. 2006. The cost-effectiveness of Antiretroviral Treatment in Khayelitsha, South Africa – a primary data analysis. *Cost Effectiveness and Resource Allocation*, 4: 20.

_____., Mooney, G., McIntyre, D.2009. Equity and efficiency in HIV-treatment in South Africa: the contribution of mathematical programming to priority setting. *Health Ecomonics,* (online). Retrieved May 28, 2010. Available at: http://www3.interscience.wiley.com/cgi-bin/fulltext/122580765/PDFSTART

Colebunders, R., Kamya, M., Semitala, F., Castelnouvo, B., Katabira, E., McAdam, K. 2005. Free Antiretrovirals Must Not Be Restricted Only To Treatment-Naïve Patients. *PloS Medicine* (online) 2 (10). Retrieved June 7, 2008. Available at: doi:10.1371/journal.pmed.0020276

Daniels, N. 1981. Health care needs and distributive Justice. *Philosophy and Public Affairs,* 10(2): 147-179.

_____. 1985. *Just Health Care*. Cambridge: Cambridge University Press.

_____. 1996. *Justice and Justification: Reflective Equality in Theory and Practice.* New York: Cambridge University Press: 179-207.

_____, Sabin, J. E. 2002. *Setting Limits Fairly: Can We Learn to Share Medical Resources?* New York: Oxford UP.

_____. 2008. *Just health: meeting health needs fairly*. New York: Cambridge University Press: 67, 168.

Dinello, D. 1971. On Killing and Letting Die. *Analysis*, 31: 86.

(DoH) Department of Health. 2004. National Antiretroviral Treatment Guidelines. Pretoria: Department of Health. Retrieved June 18, 2008. Available at: http://www.doh.gov.za/docs/factsheets/guidelines/artguide04-f.html

_____. 2006. HIV and AIDS and STI Strategic Plan For South Africa, 2007-2011. Pretoria: Department of Health. Retrieved February 20, 2008. Available at: http://www.doh.gov.za/docs/misc/stratplan-f.html

_____. 2010. Clinical Guidelines for the Management of HIV & AIDS in Adults and Adolescents. Pretoria: Department of Health. Retrieved April 9, 2010. Available at: http://www.doh.gov.za/docs/

Downing, M., Kriegshaber, J. 2008. Pharmaceutical Pricing for ARV Drugs in South Africa. Pharma Report. Retrieved April 4, 2009. Available at: http://kelley.iu.edu/CBLS/files/DowningKriegshaberG400PharmaReport2.pdf

Drummond, M. F., Sculpher, M. J., Torrance, G. W., O'Brien, B. J. 2005. *Methods for the economic evaluation of health care programmes.* Oxford New York: Oxford University Press: 277-307.

Feely, F., Connelly, P., Rosen, S. 2007. Private Sector Provision and Financing of AIDS treatment in Africa: Current Developments. *Current HIV/AIDS Reports*, 4: 192-200.

Fleck, L. M. 1989. Just health care (II): is equality too much? *Theoretical Medicine*, 10: 301-310.

Fleischacker, S. 2004. *A Short History of Distributive Justice.* London: Harvard University Press.

Foot, P. 1977. Euthanasia. *Philosophy and Public Affairs*, 6: 101.

Foster, S., Laing, R., Melgaard, B., Zaffran, M. 2006. Ensuring Supplies of Appropriate Drugs and Vaccines. In: *Disease Control Priorities in Developing Countries*. D. T. Jamison, J. G. Breman, A. R. Measham, G. Alleyne, M. Claeson, D. B. Evans, P. Jha, A. Mills, P. Musgrove (Eds.). New York: Oxford University Press: 1323-1337.

Fox, M., Ive, P., Long, L., Maskew, M., Sanne, I. 2009. High rates of Survival, Immune Reconstitution and Virologic Suppression on Second-Line Antiretroviral Therapy in South Africa. *Journal of Acquired Immune Deficiency Syndrome*, 00(0).

Fox, R. C., Goemere, E. 2006. They Call It "Patient Selection" in Khayelitsha: The Experience of Medecins Sans Frontieres-South Africa in Enrolling Patients to Receive Antiretroviral Treatment for HIV/AIDS. *Cambridge Quarterly of Healthcare Ethics*, 15: 302-312.

Fox-Rushby, J. A., Cairns, J. 2005. *Economic evaluation*. Berkshire: Open University Press: 42.

Freedberg, K. A., Hirschhorn, L. R., Schackman, B. R., Wolf, L. L., Martin, L. A., Weinstein, M. C., Goldin, S., Paltiel, A. D., Katz, C., Goldie, S. J., Losina, E. 2006. Cost-Effectiveness of an Intervention to Improve Adherence to Antiretroviral Therapy in HIV-Infected Patients. *Journal of Acquired Immune Deficiency* Syndrome, 43:S113–S118.

Garber, A. M. 2000. Advances in cost-effectiveness analysis of health interventions. In: *Handbook of Health Economics, volume 1A.* C. J. Cuyler, J. P. Newhouse (Eds.). Amsterdam: Elsevier: 181-121.

Gardner, E. M., Burman, W. J., Steiner, J. F., Anderson, P. L., Bangsberg, D. R. 2009. Antiretroviral medication and the development of class-specific antiretroviral resistance. *AIDS*, 23(9): 1035-1446.

Garnnett, G. P., Anderson, R. M. 1996. Antiviral therapy and the transmission dynamics of HIV-1. *Journal of Antimicrobial Chemotherapy*, 37: 135-150.

George, G., Quilan, T. 2009. 'Health Management' in the Private Sector in the Context of HIV/AIDS: Progress and Challenges Faced by Company Programmes in South Africa. *Sustainable Development*, 17: 19-29.

Gold, M. R., Patrick, D. L., Torrance, G. W., Fryback, D. G., Hadorn, D. C., Kamlet, M. S., Daniels, N., Weinstein, M. C. 1996. Identifying and valuing outcomes. In *Cost-Effectiveness in Health and Medicine*. M. R. Gold, J. E. Siegel, L. B. Russell, M. C. Weinstein (Eds.). New York: Oxford University Press: 83–134.

Green, O. H. 1980. Killing and letting die. *American Philosophical Quarterly*, 17(3): 195-204.

Goldie, S. J., Paltiel, A. D., Weinstein, M. C., Losina, E., Seage III, G. R., Kimmel, A. D., Walensky, R. P., Sax, P. E., Freedberg, K. A. 2003. Projecting the cost-effectiveness of adherence interventions in persons with human immunodeficiency virus infection. *American Journal of Medicine*, 115(8): 632-641.

(Gov SA) Government of South Africa (2010) 'Budget speech of Honourable Dr A Motsoaledi, MP, Minister of Health, delivered to the National Assembly, Parliament of the Republic of South Africa. Retrieved July 15, 2010 Available at: http://www.doh.gov.za/docs/sp-f.html

Green, R. 1976. Health care and Justice in Contract Theory Perspective. In: *Ethics and Health Policy*. R. M. Veatch, R. Branson (Eds.). Cambridge: Ballinger: 112.

Harrigan, P. R., Hoggs, R. S., Dong, W. W. Y., Yip, B., Wynhoven, B., Woodward, J., Brumme, C. J., Brumme, Z. L., Mo, T., Alexander, C. S., Montaner, J. S. G. 2005. Predictors of HIV drug resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy. *Journal of Infectious Diseases*, 191: 339-47.

Harris, F. 1995. Euthanasia and the Value of Life. In: *Euthanasia Examined: Ethical, Clinical And Legal Perspectives*. J. Keown (Ed.). New York: Cambridge University Press: 10-11.

Hassim, A., Heywood, M., Berger, J. 2007. *Health and Democracy: A Guide to Human Rights, Health Law and Policy in Post-Apartheid South Africa*. Tokai, Cape: Siberlink.

Hecker, H. 2010. Effects of the Global Economic Crisis: Examining the Impact on HIV and AIDS Funding. *NGO Pulse,* [internet]. Available at: www.ngopulse.org. Accessed 18 May 2010.

(HST) Health Systems Trust. 2009. *District Health Barometer 2007/08*. Westvile: Health Systems Trust.

Hume, D. 1911. *A Treatise on Human Nature*. London: Dent: 94-95

Hurley, J. 2001. Ethics, economics, and public financing of health care. *Journal of Medical Ethics*, 27(4): 234-239.

Illingworth, P. 1990. *AIDS and The Good Society*. London: Routlegle: 22-102.

(IMF) International Monetary Fund. 2010. *World Economic Outlook Database*. Retrieved June 18, 2010. Available at: http://www.imf.org/external/data.htm

Jackson, M. W. 1979. The Least Advantaged Class in Rawls's Theory. *Canadian Journal of Political Science,* XII(4): 728-746.

Jelsma, J., Maclean, E., Hughes, J., Tinise, X., Darder, M. 2005. An investigation into health-related quality of life of individuals living with HIV who are receiving HAART. *AIDS care*, 17(5): 579-588.

(UNAIDS) Joint United Nations Programme on HIV/AIDS. 1996. Second International Consultation on HIV/AIDS and Human Rights. Geneva: UNAIDS. Retrieved May 28, 2008. Available at: http://data.unaids.org/publications/irc-pub03/3797_en.html

_____. 2006. Annex 2: HIV/AIDS Estimates and Data, 2005. In: *2006 Report On The Global AIDS Epidemic*. Retrieved April 9, 2008. Available at: http://data.unaids.org/pub/GlobalReport/2006/2006_GR_ANN2_en.pdf

_____. 2008. *2008 Report on the global AIDS epidemic*. Geneva: CH: UNAIDS. Retrieved May 5, 2009. Available at: http://data.unaids.org/pub/GlobalReport/2008/jc1511_gr08_executivesummary_en.pdf

_____. 2009. *Update on the Impact of the Economic Crisis: HIV Prevention and Treatment Programmes*. Geneva: CH: UNAIDS. Retrieved May 6, 2010. Available at: http://data.unaids.org/pub/Report/2010/economiccrisisandhivandaids61_en.pdf

Kant, I. [1785] 1993. *Metaphysics of Morals*. Mary Gregor (trans.) New York: Oxford University Press.

Katzestein, D., Lega, M., Moatti, J. 2003. The evaluation of the HIV/AIDS Drug Access Initiatives in Cote D'Ivoire, Senegal and Uganda: how access to antiretroviral can be feasible in Africa. *AIDS,* 17 (3):S1-S4.

Kukathas, C., Pettit, P. 1990. *Rawls: A Theory of Justice and its Critics*. Oxford: Blackwell Publishers.

Kuntz, K. M., Weinstein, M. C. 2001. Modelling in Economic Evaluation. In: *Economic Evaluation in Health Care: Merging Theory with Practice*. M. Drummond, A. McGuire (Eds.). Oxford: Oxford University Press: 141-71.

Lamb, D. 1989. Priorities in health care: reply to Lewis and Charny. *Journal of Medical Ethics*, 15(1): 33-34.

Lamiraud, K., Moatti, J-P. 2006. Economic implications of nonadherence to highly active antiretroviral treatment in HIV patients. *Expert Opinion in Pharmacotherapy*, 7(2).

Laxminarayan, R., Bhutta, Z. A., Duse, A., Jenkins, P., O'Brien, T., Okeke, I. N., Pablo-Mendez, A., Klugman, K. P. 2006. Drug Resistance. In: *Disease Control Priorities in Developing Countries*. D. T. Jamison, J. G. Breman, A. R. Measham, G. Alleyne, M. Claeson, D. B. Evans, P. Jha, A. Mills, P. Musgrove (Eds.). New York: Oxford University Press: 1031-1052.

Lewis, M. P., Colbert, A., Erlern, J., Meyers, M. 2006. A qualitative study of persons who are 100% adherent to antiretroviral therapy. *AIDS Care*, 18(2): 140-148.

Livnat, Y. 2003. Benevolence and Justice. *The Journal of Value Inquiry*, 37: 507–515..

Louwagie, G. M., Bachmann, M. O., Meyer, K., Booysen, F. R., Fairall, L. R., Heunis, C. 2007. Highly active antiretroviral treatment and health related quality of life in South African adults with human immunodeficiency virus infection: A cross-sectional analytical study. *BMC Public Health*, 7: 244.

Lucas, G. M. 2005. Antiretroviral adherence, drug resistance, viral fitness and HIV disease progression: a tangled web is woven. *Journal of Antimicrobial Chemotherapy*, 25(4): 413-423.

Mabandu, P., Parker, F. 2009. Healthcare in reverse. *Mail & Guardian*, 12 July 2009. Retrieved, April 18, 2010. Available at: http://www.mg.co.za/article/2009-07-11-healthcare-in-reverse

Macklin, R. 2004. *Ethics and equity in access to HIV treatment: 3 by 5 initiative*. Geneva: World Health Organization. Retrieved June 4, 2009. Available: http://www.who.int/ethics/en/background-macklin.pdf .

Matchtinger, E. L., Bangsberg, D. R. 2006. Adherence to HIV Antiretroviral Therapy. In HIV Insite Knowledge Base Chapter, [internet]. Available at: http://hivinsite.ucsf.edu/InSite. Accessed 14 May 2008.

Matjila, M. J., Hoosen, A. A., Stoltz, A., Cameron, N. 2008. STIs, HIV and AIDS and TB: Progress and Challenges. Westivile: Health Systems Trust. Retrieved April 9, 2010 Available at: http://www.hst.org.za/uploads/files/chap6_08.pdf

McCormick, A. W., Walensky, R. P., Lipsitch, M., Losina, E., Hsu, H., Weinstein, M. C., Paltiel, A. D., Freedberg, K. A., Seage III, G. R. 2007. The Effect of Antiretroviral Therapy on Secondary Transmission of HIV among Men Who Have Sex with Men. *Clinical Infectious Diseases*, 44(8): 1115–1122.

Menendez-Ariaz, L. 2010. Molecular basis of human immunodeficiency virus drug resistance: An update. *Antiviral Research*, 85:210–231.

Mill, J. S. [1869] 1993. *On Liberty and Utilitarianism*. New York: Bantam Books.

Mohr, R. D. 1987. AIDS, Gays and State Coercion. *Bioethics*. 1 (1): 35-50.

Mukherjee, J. 2003. HIV-1 care in resource-poor settings: A view from Haiti. *The Lancet*, 362: 994-995.

Munakata, J., Benner, J. S., Becker, S., Dezzi, C. M., Hazard, E. H., Tierce, J. C. 2006. Clinical and Economic Outcomes of Nonadherence to Highly Active Antiretroviral Therapy in Patients with Human Immunodeficiency Virus. *Medical Care*, 44(10): 893-899.

Musgroove, P., Fox-Rushby, J. 2006. Cost-Effectiveness Analysis for Priority Setting. In: *Disease Control Priorities in Developing Countries*. D. T. Jamison, J. G. Breman, A. R. Measham, G. Alleyne, M. Claeson, D. B. Evans, P. Jha, A. Mills, P. Musgrove (Eds.). New York: Oxford University Press: 271-285.

Nachega, J. B., Stein, D. M., Lehman, D. A., Hlatshwayo, D., Mothopeng, R. E., Chaisson, R. E., Karstaedt, A. S. 2004. Adherence to antiretroviral therapy in HIV infected adults in Soweto, South Africa. *AIDS Research and Human Retroviruses*, 20(10): 1053 -1056.

_____., Hislop, M., Dowdy, D. W., Lo, M., Omer, S. B., Chalsson, R. E., Regensberg, L., Maartens, G. 2006. Adherence to Highly Active Antiretroviral Therapy by Pharmacy Claims Predicts Survival in HIV-infected South African Adults. *Journal of Acquired Immune Deficiency Syndrome*, 43 (1): 78-84.

_____., Hislop, M., Dowdy, D. W., Chalsson, R. E., Regensberg, L., Maartens, G. 2007. Adherence to Nonnucleoside Reverse Transcriptase Inhibitor-Based HIV Therapy and Virologic Outcomes. *Annals of Internal Medicine*, 147(11): 564-73.

(NAT) National Aids Trust. 2003. *Examples of HIV/AIDS Discrimination Fact Sheet 3*. Retrieved May 28, 2010. Available at: http://www.heart-intl.net/HEART/Stigma/Comp/AreadofHIVdiscrimination.pdf

Nattrass, N. 2004. *The Moral Economy of AIDS in South Africa*. Cape Town: Cambridge University Press: 127-131, 171-4.

_____., Geffen, N. 2005. The impact of reduced drug prices on the cost-effectiveness of HAART in South Africa. *African Journal of AIDS Research*, 4(1): 65–67.

_____. 2007. Disability and welfare in South Africa's age of unemployment and AIDS. In: *State of the Nation: South Africa 2007*. R. Southall, J. Daniel (Eds). Cape Town: Human Sciences and Research Council.

Ndhlalambi, M. 2009. Strengthening the Capacity of Traditional Health Practitioners to Respond to HIV/AIDS and TB in Kwazulu Natal, South Africa. *AMREF Case Studies*. Retrieved July 28, 2010. Available at: http://www.amref.org/silo/files/strengthening-the-capacity-of-traditional-health-practitioners.pdf

Nozick, R. 1974. *Anarchy, State and Utopia.* New York: Basic Books.

Nussbaum, M. 1992. Human Functioning and Social Justice: In Defense of Aristotelian Essentialism. *Political Theory*, 20(2): 202-246.

Oberholzer, R. 2007. Perceptions of taxation: a comparative study of different population groups in South Africa. Dissertation submitted in fulfilment of the requirements for the degree doctor of

commerce. Faculty of economics and management sciences. University of Pretoria, August 2007. Available at: http://upetd.up.ac.za/thesis/available/etd-05192008-170854/unrestricted/00front.pdf Accessed on 5 November 2010.

O'Neil, R. 1978. Killing, Letting Die and Justice. *Analysis*, 38(3): 124-125

Orrell, C., Bangsberg, D. R., Badri, M., Wood, R. 2003. Adherence is not a barrier to successful antiretroviral therapy in South Africa. *AIDS*, 17: 1369-75.

Parruti, G., Manzoli, L., Toro, P. M., D'Amico, G., Rotolo, S., Graziani, V., Schioppa, F., Consorte, A., Alterio, L., Toro, G. M., Boyle, B. A. 2006 Long-Term Adherence to First-Line Highly Active Antiretroviral Therapy in a Hospital-Based Cohort: Predictors and Impact on Virologic Response and Relapse. *AIDS Patient Care and STDs*, 20(1): 48-57.

Pellegrino, E. D., Thomasma, D. C. 1993. *The Virtues in Medical Practice.* New York: Oxford University Press: 51-65.

Perri, 6. 2000. The morality of managing risk: paternalism, prevention and precaution, and the limits of proceeduralism. *Journal of Risk Research*, 3(2): 135-165.

Persad, G., Wertheimer, A., Emanuel, E. J. 2009. Principles for allocation of scarce medical interventions. *Lancet*, 373(9661): 423-431.

Pieterse, M. 2007. Healthcare Right, Resources and Rationing. *South African Law Journal*, 124 (3):514-536.

(PCAS) Policy Coordination and Advisory Services in the Presidency. 2008. *Towards A Fifteen Year Review.* Retrieved July 28, 2009. Available at: http://www.info.gov.za/view/DownloadFileAction?id=89475

Powers, P. 2007. Persuasion and Coercion: A Critical Review of Philosophical and Empirical Approaches. *HEC Forum*, 19(2): 125-143.

Price, J. E., Leslie, J. A., Welsh, M., Binagwaho, A. 2009. Intergrating HIV clinical services into primary health care in Rwanda: a measure of quantitative effects. *AIDS Care*, 21(5): 608-614.

Rachels, J. 1986. *End of Life: Euthanasia And Morality*. Oxford: Oxford University Press: 5-6, 111-123.

Rawls, J. 1958. Justice as Fairness. *The Philosophical Review*, 67(2): 164-194.

_____. 1971. *A Theory of Justice*. Harvard: Harvard University Press.

_____. 1993. *Political Liberalism.* New York: Columbia University Press.

_____. 2001. *Justice as Fairness: A Restatement*. Harvard: Harvard University Press.

Rosenblum, M., Deeks, S. G., van der Laan, M., Bangsberg, D. R. 2009. The Risk of Virologic Failure Decreases with Duration of HIV Suppression, at Greater than 50% Adherence to Antiretroviral Therapy. *Plos ONE* (online) 4(9): e7196. Retrieved March 28, 2010. Available at: www.plosone.org

Savulescu , J. 1998a. Consequentialism, Reason, Value and Justice. *Bioethics*, 12(3): 212-235.

_____. 1998b. The cost of refusing treatment and equality outcome. *Journal of Medical Ethics*, 24(4): 231-236.

Schackman, B. R., Finkelstein, R., Neukermans, C. P., Lewis, L., Eldred, L. 2005. The cost of HIV medication adherence support interventions: Results of a cross-site evaluation. *AIDS Care*, 17(8): 927-/937.

Selegid, M. J. 2007. Ethics and Resistance. *Bioethics*, 21(4): 218-229.

Sen, A. K. 1999. *Commodities and Capabilities*. Oxford: Oxford University Press: 6-11, 41-43.

Sethi, A. K., Celentano, D. D., Gange, S. J., Moore, R. D., Gallant, J. E. 2003. *Clinical infectious Diseases*, 37(8): 1112-8.

Shelton, R. L. 1978. Human rights and distributive justice in health care delivery. *Journal of medical ethics*, 4: 165-171.

Simoni, J. M., Pearson, C. R., Pantalone, D. W., Marks, G., Crepaz, N. 2006. Efficacy of Interventions in Improving Highly Active Antiretroviral Therapy Adherence and HIV-1 RNA Viral Load: A Meta-Analytic Review of Randomized Controlled Trials. *Journal of Acquired Immune Deficiency* Syndrome, 43: S23-S35.

Skinner, D., Mfecane, S. 2004. Stigma, discrimination and the implications for people living with HIV/AIDS in South Africa. *Journal of Social Aspects of HIV/AIDS*, 1(3): 157-164.

Sonnerberg, F., Beck, J. 1993. Markov models in medical decision-making: A practical guide. *Medical Decision Making*, 13: 322-388.

(SSA) Statistics South Africa. *Quarterly Labour Force Survey Q1 2010*. Retrieved May 13, 2010. Available at: http://www.statssa.gov.za/keyindicators/QLFS/Press/Q1_2010_Press_Statement.pdf

Sun, X., Faunce, T. 2008. Decision-analytical modelling in health-care economic evaluations. *European Journal of Health Economics*, 9: 313-323.

Tantivess, S., Walt, G. 2006. Using cost-effectiveness to inform policy: the case of antiretroviral therapy in Thailand. *Cost Effectiveness and Resource Allocation*, 4:21.

Torrance, G. W., Siegel, J. E., Luce, B. R. 1996. Framing and Designing Cost-effectiveness Analysis. In: *Cost-Effectiveness in Health and Medicine.* M. R. Gold, J. E. Siegel, L. B. Russell, M. C. Weinstein (Eds). New York/Oxford: Oxford University Press: 54-79.

Van Bogaert, D. K., Ogubanjo, G. A. 2006. *Autonomy And Rights*. [Unpublished].

Van der Merwe, E. J. 2004. *Inflation targeting in South Africa. Occasional Paper 19*. Pretoria: South African Reserve Bank. . Retrieved June 4, 2010. Available: http://www.reservebank.co.za/internet/Publication.nsf/

Van Parijs, P. 2003. The Difference Principles. In: *The Companion to Rawls*. S. Freeman (Ed). Cambridge: Cambridge University Press: 200-236.

Veatch, R. M. 1974. Who Should Pay for Smokers' Medical Care? *Hastings Centre Report*, 4: 8-9.

Walensky, R. P., Wood, R., Weinstein, M C., Martinson, N. A., Losina, E., Fofana, M. O., Goldie, S. J., Divi, N., Yazdanpanah, Y., Wang, B., Paltiel, D., Freedberg, K. A. 2008. Scaling Up Antiretroviral Therapy in South Africa: The Impact of Speed on Survival. *Journal of Infectious Diseases*, 197(9): 1324–1332.

Walker, D., Kumarayanake, L. 2002. Allowing for differential timing in cost analysis: discounting and annualization. *Health Policy and Planning*, 17(1): 112-118.

Wallis, C., Sanne, I., Ventor, F., Mellors, J., Stevens, W. 2010. Varied Patterns of HIV-1 Drug Resistance on Failing First-Line Antiretroviral Therapy in South Africa. *Journal of Acquired Immune Deficiency Syndrome*, **53**(4): 480-4.

Wang, W., Sulzbach, S., De, S. 2010. Utilization of HIV-Related services from the Private Health Sector: A Multi-Country Analysis. *Demographic and Health Research*, **67**.

Wilber, C. 1998. Economics and Ethics. In *The Elgar Handbook to Economic Methodology.* J. B. Davis. D. W. Hands, U. Maki (Eds). Edward Elgar Publishing: 572

World Bank 2009. World Development Indicators Database. Retrieved May 9, 2010. Available at: http://data.worldbank.org/country/south-africa

(WHO) World Health Organisation. 2010. *Antiretroviral therapy for HIV infection in adults and adolescents: recommendation for a public health approach.* Geneva: WHO Publications. Retrieved

November 5, 2010. Available at:
http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf

_____. 2008a. *Towards Universal Access: Scaling up priority HIV/AIDS interventions in health sector: Progress Report 2008.* Geneva: WHO Publications.

_____. 2008b. *Health Action in Crisis: Annex 4: HIV/AIDS and Complex emergencies.* Geneva: WHO Publications. Retrieved July 15, 2010. Available at:
http://www.who.int/hac/techguidance/tools/disrupted_sectors/module_04/en/index6.html

_____. 2003a. *Treating 3 million by 2005: Making it happen*. Geneva: World Health Organization. Retrieved January 4, 2008. Available:
http://www.who.int/3by5/publications/documents/en/3by5StrategyMakingItHappen.pdf

_____. 2003b. *Adherence to Long-Term Therapies: Evidence for Action.* Geneva: World Health Organization. Retrieved May 18, 2009. Available at:
http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf

Zembaty, J. S. 1981. Social Justice and Health Care. In: *Biomedical Ethics*. T. A. Mappes, J. S. Zembaty (Eds.). New York: McGraw-Hill Inc.: 516-522.

APPENDICES

Appendix A

Antonyms

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretrovirals
CD4	Cluster Differentiation 4
GDP	Gross Domestic Product
dL	Decilitre
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immune-deficiency Virus
HIVDR	Human Immune-deficiency Virus Drug Resistance
ICER	Incremental Cost-Effectiveness Ratio
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
OI	Opportunistic Infections
PI	Protease Inhibitors
QALYs	Quality of Adjusted Life Years
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

Appendix B

University
of the Witwatersrand,
Johannesburg

Human Research Ethics Committee (Medical)
(formerly Committee for Research on Human Subjects (Medical)

Secretariat: Research Office, Room SH10005, 10th floor, Senate House • Telephone: +27 11 717-1234 • Fax: +27 11 339-5708
Private Bag 3, Wits 2050, South Africa

Ref: W-CJ-100127-1

27/01/2010

TO WHOM IT MAY CONCERN:

Waiver: This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical).

Investigator: **Dr Richard Chawana Student no 331986**

Project title: **Risk management in HIV/AIDS: ethical and economic issues concerning the restriction of HAART access only to adherent patients.**

Reason: This study is an analysis of literature in the public domain. There are no humans involved.

UNIVERSITY OF THE WITWATERSRAND
PROF PE CLEATON - JONES
HREC (MEDICAL)
2010 -01- 27
JOHANNESBURG

Professor Peter Cleaton-Jones
Chair: Human Research Ethics Committee (Medical)

copy: Anisa Keshav, Research Office, Senate House, Wits

Appendix C

Table 8: criteria for Art initiation in specific populations

Target population	Clinical condition	Recommendation
Asymptomatic individuals (including pregnant women)	WHO clinical stage 1	Start ART if CD4 ≤350
Symptomatic individuals (including pregnant women)	WHO clinical stage 2	Start ART if CD4 ≤350
	WHO clinical stage 3 or 4	Start ART irrespective of CD4 cell count
TB and hepatitis B coinfections	Active TB disease	Start ART irrespective of CD4 cell count
	HBV infection requiring treatment*	Start ART irrespective of CD4 cell count

* The current standard definition of chronic active hepatitis in industrialized countries is mainly based on histological parameters obtained by liver biopsy, a procedure not usually available in the large majority of resource-limited settings. A global definition of chronic active hepatitis for resource-limited settings based on clinical and more simple laboratory parameters is under discussion.

Source: WHO 2010