

# Overcoming barriers to antiretroviral therapy in resource-limited settings

By

Nathan Ford

Thesis presented for the degree of  
Doctor of Philosophy  
In the  
Faculty of Health Sciences

© Nathan Ford 2010

Simon Fraser University

Summer 2010

All rights reserved. However, in accordance with the *Copyright Act of Canada*, this work may be reproduced, without authorization, under the conditions of *Fair Dealing*. Therefore, limited reproduction of this work for the purposes of private study, research, criticism, review and news reporting is likely to be in accordance with the law, particularly if cited appropriately

## Approval

**Name:** Nathan Ford

**Degree:** Doctor of Philosophy

**Title of Thesis:** Overcoming barriers to antiretroviral therapy in resource-limited settings

**Examining Committee:**

**Chair:** Dean of Graduate Studies (or designate)

---

**Dr. Michel Joffres**  
Senior Supervisor  
Professor, Faculty of Health Sciences

---

**Dr. Edward Mills**  
Supervisor, Adjunct Professor, Faculty of Health Sciences

---

**Dr. Robert Hogg**  
Supervisor  
Professor, Faculty of Health Sciences

---

**Dr. James Orbinski**  
External Supervisor  
Associate Professor, Medicine, University of Toronto

---

**Dr. Jamie Scott**  
Internal Examiner  
Professor, Faculty of Health Sciences and Molecular  
Biology and Biochemistry

---

**Dr. Thomas Kerr**  
External Examiner  
Assistant Professor, Medicine, University of British  
Columbia

Date Defended/Approved:

June 21, 2010



SIMON FRASER UNIVERSITY  
LIBRARY

## Declaration of Partial Copyright Licence

The author, whose copyright is declared on the title page of this work, has granted to Simon Fraser University the right to lend this thesis, project or extended essay to users of the Simon Fraser University Library, and to make partial or single copies only for such users or in response to a request from the library of any other university, or other educational institution, on its own behalf or for one of its users.

The author has further granted permission to Simon Fraser University to keep or make a digital copy for use in its circulating collection (currently available to the public at the "Institutional Repository" link of the SFU Library website <[www.lib.sfu.ca](http://www.lib.sfu.ca)> at: <<http://ir.lib.sfu.ca/handle/1892/112>>) and, without changing the content, to translate the thesis/project or extended essays, if technically possible, to any medium or format for the purpose of preservation of the digital work.

The author has further agreed that permission for multiple copying of this work for scholarly purposes may be granted by either the author or the Dean of Graduate Studies.

It is understood that copying or publication of this work for financial gain shall not be allowed without the author's written permission.

Permission for public performance, or limited permission for private scholarly use, of any multimedia materials forming part of this work, may have been granted by the author. This information may be found on the separately catalogued multimedia material and in the signed Partial Copyright Licence.

While licensing SFU to permit the above uses, the author retains copyright in the thesis, project or extended essays, including the right to change the work for subsequent purposes, including editing and publishing the work in whole or in part, and licensing other parties, as the author may desire.

The original Partial Copyright Licence attesting to these terms, and signed by this author, may be found in the original bound copy of this work, retained in the Simon Fraser University Archive.

Simon Fraser University Library  
Burnaby, BC, Canada

## STATEMENT OF ETHICS APPROVAL

The author, whose name appears on the title page of this work, has obtained, for the research described in this work, either:

(a) Human research ethics approval from the Simon Fraser University Office of Research Ethics,

or

(b) Advance approval of the animal care protocol from the University Animal Care Committee of Simon Fraser University;

or has conducted the research

(c) as a co-investigator, collaborator or research assistant in a research project approved in advance,

or

(d) as a member of a course approved in advance for minimal risk human research, by the Office of Research Ethics.

A copy of the approval letter has been filed at the Theses Office of the University Library at the time of submission of this thesis or project.

The original application for approval and letter of approval are filed with the relevant offices. Inquiries may be directed to those authorities.

Simon Fraser University Library  
Simon Fraser University  
Burnaby, BC, Canada

## **Abstract**

The provision of antiretroviral therapy in resource-limited settings has been one of the most ambitious global health projects to date, leading to a significant reframing of global trade rules, the establishment of new international funding mechanisms, and challenging medical and public health models. This thesis provides a summary of these major challenges. The first chapter provides an analysis of the drug policy challenges, examining the effectiveness of policy approaches to reducing the price of antiretrovirals and analyzing the role played by civil society in this struggle to increase access to treatment. Chapter two assesses efforts to overcome human resource shortage, in particular the effectiveness of task shifting. Chapter three examines the related issue of decentralization of care. Chapter four begins with an analysis of data from a treatment programme in South Africa to assess adherence to treatment over time as a prelude to a summary of emerging concerns around the quality of treatment provided to resource-limited settings. Finally, the thesis concludes with a reflection on future challenges for maintaining and sustaining access to effective treatment.

**Keywords:** antiretroviral therapy, Thailand, Africa, patents, human resources

## **Executive summary**

The last decade has seen a massive global effort to increase access to antiretroviral therapy (ART) in the developing world, leading to an estimated four million people receiving treatment by the end of 2009. This global scale up was the result of many years of political activism for treatment. Triple therapy, which revolutionized HIV/AIDS care in the West, was initially considered far too expensive for resource-limited settings and UN agencies, academics, and donors alike all argued against providing treatment in favour of prevention instead. Civil society groups, and in particular people living with HIV/AIDS themselves, were critical to breaking the deadlock. Patient groups in Thailand, Brazil, South Africa, India, Kenya, Uganda, and other high-burden countries formed alliances with health providers, nongovernmental organizations and academics in Developed countries began to argue the case that if the cost of treatment was too high, then it must come down. The most substantial price reductions came about as a result of generic drug manufacture in India, which today continues to provide over half of all antiretroviral drugs used in Africa.

The global effort to scale up antiretroviral therapy in resource-limited settings gained momentum from late 2002, as the cost of treatment fell and international funding streams were established, notably with the establishment of the Global Fund for AIDS, TB and Malaria and the US President's Emergency Plan for AIDS Relief. As programmes began to enroll increasing numbers of patients it became clear that the lack qualified health personnel, particularly in Africa, was the major bottleneck to increasing access to treatment. Whereas in Developed countries HIV/AIDS has traditionally been managed as a specialized disease, for resource-limited settings a simplified paradigm of HIV care was required, entailing a shift from a specialized medical approach to a public health approach in which the majority of clinical tasks would be undertaken by lesser-trained health cadres such as nurses.

As well as being an important strategy for overcoming the shortage of health professionals in sub-Saharan Africa, task shifting also supported equitable access to care. While doctor-led, hospital-based models of delivery were limiting capacity and promoting inequity, the shifting of

responsibilities to nurses and other health cadres promoted the decentralization of antiretroviral care to health centres in rural areas. Evidence from several countries in southern Africa has shown that patients who live a long way from health services and have to travel long distances to access antiretrovirals have greater attrition and mortality rates and compared to patients who leave closer to care.

Questions around how to maintain good adherence over time, minimize defaulting from care, and manage clinical challenges such as cumulative toxicities and treatment failure have all recently begun to bring into question the quality of care that is being provided, particularly with respect to the tolerability and efficacy of medications and the timing of treatment initiation. The challenge ahead lies in maintaining and sustaining quality care in the long term, particularly at a time of global economic crisis when donors are beginning to seriously question their commitment to funding the global AIDS response, and concerns about limited finances are being allowed to moderate evidence-informed considerations regarding how to provide effective care.

Ten years ago, the global political challenge was to start providing treatment to the thousands of people dying from HIV/AIDS every day in the developing world. Today, the challenge is to improve the response: improve access to ART for the millions of people who currently need treatment, improve the quality of care that is provided, and ensure that such care is sustained for as long as needed.

## **Dedication**

To Jan, who taught me selflessness without saying a word; to Marilyn, who advised me to just to keep going; and Sue, who supports me in all that I do and without whom none of this would have been possible.

## Acknowledgements

The work presented in this thesis describes the efforts of many people who have been engaged in the struggle to improve treatment and care for people living with HIV/AIDS over the last decade. This thesis therefore reflects the dedication and fortitude of a great number of health providers and patients who work and live in some of the most disadvantaged and challenging settings. I am grateful to all those who have allowed me to play a small part in this effort.

In Thailand, David Wilson and Paul Cawthorne taught me through their action and words the inextricable link between medicine and politics, the essential role of advocacy in improving patient care, and the importance of viewing patients not as passive swallows of pills but as equal partners in the provision of health care. In Lesotho Shraonann Lynch and Rachel Cohen spent three years directing their relentless activist energy towards a small district in the mountains of one of the poorest countries on earth, and in doing so established a district-wide antiretroviral treatment programme that has saved thousands of lives. Similarly, Eric Goemaere and Hermann Reuter fought against a decade of political denialism to establish models of HIV care that have served as an example across Africa. Far too humble to say so themselves, they are the unmeasured confounders in every description of the models of care developed in Khayelitsha and Lusikisiki; without their dedication, these programmes would never have existed. This is a long overdue thank you to all of you for the inspiration you give to me.

This PhD would not have been possible without the strong support of the faculty and staff of the Faculty of Health Sciences at Simon Fraser University who have provided unwavering support through all of my fieldwork. Thanks in particular to Jonathan Driver, Lynn Kumpala, Sheilagh MacDonald, John O'Neil and Wade Parkhouse for their flexibility, encouragement, and personal attention.

My co-supervisors, Robert Hogg and Michel Joffres, have both been impeccable supervisors for this endeavour, giving me their full backing to pursue the research where it has taken me. I know of

several beleaguered and abused students who would have completed their PhDs a long time ago if they were provided with the unobtrusively supportive environment that I have enjoyed.

Finally, the greatest thanks must go to my principal supervisor, Ed Mills. As a mentor, Ed has taught me more about epidemiology than any formal training I have received. As a colleague, he has privileged me to be involved in some of the most interesting and important research I have done. And as a friend, he has made the past few years far more enjoyable and than any PhD student ought to be permitted. Ed provided me with the impetus to get started, the knowledge to do the work, the relentless encouragement to see it through to completion, and the attentiveness to make it as good as it can be. If I took the time to thank him fully, this thesis would double in length.

## List of publications

The main body of this thesis comprises the following papers:

1. Ford N, Wilson D, Costa Chaves G, Lotrowska M, Kijtiwatchakul K. Sustaining access to antiretroviral therapy in developing countries: lessons from Brazil and Thailand. *AIDS* 2007; 21: S21-29.
2. Ford N, Wilson D, Cawthorne P, Kumphitak A, Kasi-Sedepan S, Kaetkaew S, Teemanka S, Upakaew K, Preuanbuapan C. Challenge and co-operation: ten years of civil society activism for access to HIV treatment in Thailand. *Trop Med Int Health* 2009; 14:1-9.
3. Callaghan M, Ford N, Schneider H. A systematic review of task shifting for HIV treatment and care in Africa. *Hum Resour Health* 2010; 8: 8.
4. Zachariah R, Ford N, Philips M, Lynch S, Massaquoi M, Janssens V, Harries A. Task shifting in HIV/AIDS: opportunities, challenges and proposed actions for sub-Saharan Africa. *Trans R Soc Trop Med Hyg* 2009; 103: 549-58.
5. Bedelu M, Ford N, Hildebrandt K, Reuter H. Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS care. *J Inf Dis* 2007; 196:464-468.
6. Cohen R, Lynch S, Bygrave H, Eggers E, Vlahakis N, Hilderbrand K, Knight L, Pillay P, Saranchuk P, Goemaere E, Makakole L, Ford N. Antiretroviral treatment outcomes from a nurse-driven, community-supported HIV/AIDS treatment programme in rural Lesotho: observational cohort assessment at two years. *J Int AIDS Soc* 2009; 12: 1-8.
7. Ford N, Darder M, Spelman T, Maclean E, Mills E, Boule A. Early adherence as a predictor of long-term virological suppression: five-year follow up of an observational cohort. *PLoS ONE* 2010; 5:5.
8. Ford N, Mills E, Calmy A. Rationing antiretroviral therapy in Africa — treating too few, too late. *NEJM* 2009; 36: 1808-10.

For each paper the candidate contributed to every aspect of the research, from inception to analysis, writing, redrafting and publication. The contribution of the candidate to multi-authored papers is further delineated at the end of each paper. All research was concluded within the timeframe of the PhD and publications appeared subsequent to acceptance onto the programme.

# Table of contents

	<b>Page</b>
<b>Approval</b>	ii
<b>Abstract</b>	iii
<b>Executive summary</b>	iv
<b>Dedication</b>	vi
<b>Acknowledgements</b>	vii
<b>List of publications</b>	ix
<b>Table of contents</b>	x
<b>List of figures</b>	xii
<b>List of tables</b>	xiii
<b>Introduction</b>	1
<b>Chapter 1: Improving access to antiretroviral medicines</b>	5
1.1. Introduction	5
1.2. Sustaining access to antiretroviral therapy in the less-developed world: lessons from Brazil and Thailand	7
1.2. Challenge and co-operation: civil society activism for access to HIV treatment in Thailand	22
1.4. References for Chapter 1	35
<b>Chapter 2: Overcoming the human resource crisis</b>	43
2.1. Introduction	43
2.2. A systematic review of task shifting for HIV treatment and care in Africa	45
2.3. Task shifting in HIV/AIDS: opportunities, challenges and proposed actions for sub-Saharan Africa	56
2.4. References for Chapter 2	70
<b>Chapter 3: Decentralizing HIV/AIDS care to the primary care level</b>	84
3.1. Introduction	84
3.2. Implementing antiretroviral therapy in rural communities: the Lusikisiki model of	

decentralized HIV/AIDS care	85
3.3. Antiretroviral treatment outcomes from a nurse-driven, community-supported HIV/AIDS treatment programme in rural Lesotho: observational cohort assessment at two years	94
3.4. References for Chapter 3	105
<b>Chapter 4: Improving quality of care</b>	110
4.1. Introduction	110
4.2. Early adherence to antiretroviral medication as a predictor of long-term HIV virological suppression: five-year follow up of an observational cohort	112
4.3. Rationing antiretroviral therapy in Africa — treating too few, too late	120
4.4. References for Chapter 4	124
<b>Chapter 5: Conclusions</b>	129
<b>About this PhD</b>	137
<b>Candidate's bibliography</b>	139

## List of Figures

	<b>Page</b>
Figure 1.3.1. The CCC care model _____	30
Figure 3.2.1. Enrollment into ART programs at clinics compared to the hospital	91
Figure 4.2.1. Cumulative hazard estimates for virological failure _____	117

## List of Tables

	<b>Page</b>
Table 1.2.1. Demographics, development status and HIV in Brazil and Thailand	9
Table 1.2.2. Key legal provisions improving or limiting access to medicines in Brazil and Thailand	11
Table 1.2.3. Overview of strategies to improve access to affordable medicines in Brazil and Thailand	14
Table 1.2.4. Best price of key antiretroviral drugs in Brazil and internationally	15
Table 1.3.1. Civic groups promoting access to treatment in Thailand	24
Table 1.3.2. Chronology of access to HIV treatment in Thailand	31
Table 2.2.1. Characteristics and outcomes of studies on the impact of task-shifting in HIV/AIDS care	49
Table 2.3.1. Types of task shifting commonly seen in Africa	57
Table 2.3.2. Community support ART delivery in Thyolo District, Malawi	60
Table 2.3.3. Antiretroviral treatment (ART) outcomes involving task shifting at community and health centre levels	62
Table 2.3.4. Operational research priorities for task shifting of HIV/AIDS care in sub-Saharan Africa	69
Table 3.2.1. Traditional roles of health staff in HIV/AIDS care, compared with roles of health staff in the Lusikisiki program	87
Table 3.2.2. One year outcomes at clinics and the hospital in Lusikisiki, South Africa	90
Table 3.3.1. Allocation of HIV and TB tasks at primary health care level	97
Table 3.3.2. Cumulative ART outcomes (adults and children)	100
Table 4.2.1. Baseline characteristics	116
Table 4.2.2. Associations between patient characteristics and time to viral load failure	116

## Introduction

The last decade has seen a massive global effort to increase access to antiretroviral therapy in the developing world [1]. Today, there is broad consensus that treating HIV/AIDS is an international public health priority and governments, nongovernmental organizations, academics and donors are all engaged in supporting the care and treatment of people with HIV/AIDS in some of the poorest parts of the world. National government programmes, supported by international donors and nongovernmental organizations, are today providing ART to an estimated four million people [2].

This was not always the case. Prior to 2000, HIV/AIDS was effectively considered an untreatable disease in the Developing World. Some raised arguments that antiretroviral therapy was too complicated, and that Africans could not adhere to treatment because they were unable to tell the time [3]; others raised concern about the cost-effectiveness of ART, arguing that scarce resources would be better directed at prevention efforts [4].

All that changed in 2001 when considerable political attention was directed at the price of treatment. Brazil and Thailand took the lead among Developing countries by challenging the international monopolies of antiretroviral drugs and producing generic versions for a fraction of the price of the patented equivalents [5]. In South Africa, home to the largest number of people living with HIV/AIDS, the government fought (and won) a court case against a consortium of 39 pharmaceutical companies over a law that would allow the government to source more affordable sources of antiretrovirals in neighbouring countries [6]. At the same time that the South African government won the court case against the pharmaceutical companies, Indian drug manufacturers announced that they were able to manufacture triple therapy for less than a dollar a day, setting off a price war that in ten years has reduced the price of standard triple therapy from \$US 10,000 per patient/year to under \$US100 [7].

As the price of treatment came down, serious efforts to scale up treatment began, both through the establishment of dedicated donor funding streams and increased efforts by governments and nongovernmental actors alike. While early results from small cohorts

demonstrated effectiveness comparable to that seen in developed countries [8], the scaling up of treatment on a large scale began to stretch the delivery model, both in terms of who provided care and where it was available.

The dramatic shortage of health workers in resource-limited settings proved to be one of the most important bottlenecks to delivering care, and urgent solutions were required to reduce the dependence on doctors, whose number and distribution was vastly insufficient compared to the need for treatment. At the same time, it became apparent that centralized, hospital-based models of delivery would soon become saturated while at the same time promoting inequalities in access, particularly for rural populations who lived far from hospitals.

Questions around how to maintain good adherence over time, minimize defaulting from care, and manage clinical challenges such as cumulative toxicities and treatment failure have all recently begun to bring into question the quality of care that was being provided, particularly with respect to the tolerability and efficacy of medications and the timing of treatment initiation. The challenge ahead lies in maintaining and sustaining quality care in the long term, particularly at a time of global economic crisis when donors are beginning to question their commitment to funding the global AIDS response.

### **Structure of this thesis**

This thesis examines some of the critical policy and operational challenges to the delivery of effective ART in resource-limited settings. The intention of this work has been to evaluate a range of issues relating to the delivery of ART in resource-limited settings. As such, a mixed-methods approach was taken, employing methodologies from health policy research, qualitative research, and epidemiology. The work draws on evidence and experience from a range of contexts, drawing out lessons from Thailand, Brazil and southern Africa, which all represent critical examples in the struggle to overcome barriers to providing effective antiretroviral care in some of the most disadvantaged populations in the global HIV/AIDS epidemic.

Chapter 1 comprises two papers which provide an analysis of the drug policy challenges, examining the effectiveness of approaches taken by Brazil and Thailand to reducing the price

of key antiretroviral drugs, and delineating the key role that civil society has played in this struggle to support increased access to affordable treatment for themselves and their peers.

Two papers covered in Chapter 2 review efforts to overcome human resource shortages are reviewed, in particular through an assessment of the evidence of effectiveness of ‘task-shifting’, a policy promoted by the World Health Organization and others to mobilize the capacity of lower-level health workers to undertake roles and responsibilities usually reserved for doctors [9].

The issue of decentralization of services is addressed two papers comprising Chapter 3, which assesses some examples of decentralization of antiretroviral therapy from hospital to health centres.

The two papers that comprise Chapter 4 examines some of the emerging concerns around the quality of treatment provided to resource-limited settings and outline some of the challenges for effective long-term treatment.

Finally, a concluding chapter provides an overview of some of the challenges ahead.

## **References**

1. Schwartlander B, Grubb I, Perriens J. The 10-year struggle to provide antiretroviral treatment to people with HIV in the developing world. *Lancet* 2006; 368:541–546.
2. Souteyrand Y, Akwara P, Warner Smith M, Beusenbergh M, Jashi M, Hayashi C. Scaling up access to antiretroviral therapy (ART) in low- and middle-income countries: global and regional progress in 2008. In: 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention. Cape Town, South Africa; 2009. Abstract WELB105.
3. Hogg R, Cahn P, Katabira ET, Lange J, Samuel NM, O'Shaughnessy M, Vella S, Wainberg MA, Montaner J. Time to act: global apathy towards HIV/AIDS is a crime against humanity. *Lancet* 2002; 360:1710-1.
4. Marseille E, Hofmann P, Kahn J. HIV prevention before HAART in sub-Saharan Africa. *Lancet* 2002; 359: 1851–56.

5. Ford N, Wilson D, Costa Chaves G, Lotrowska M, Kijtiwatchakul K. Sustaining access to antiretroviral therapy in developing countries: lessons from Brazil and Thailand. *AIDS* 2007 21; 4: S21-29.
6. von Schoen Angerer T, Wilson D, Ford N, Kasper T. Access and activism: the ethics of providing antiretroviral therapy in developing countries. *AIDS* 2001;15:S81-90.
7. Ford N, Calmy A, von Schoen-Angerer T. Treating HIV in the developing world: getting ahead of the drug development curve. *Drug Discovery Today* 2007; 12: 1-3.
8. Braitstein P, Brinkhof MW, Dabis F, Schechter M, Boule A, Miotti P, Wood R, Laurent C, Sprinz E, Seyler C, Bangsberg DR, Balestre E, Sterne JA, May M, Egger M; Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration; ART Cohort Collaboration (ART-CC) groups. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet* 2006; 367: 817-24.
9. WHO/UNAIDS/PEPFAR: Task Shifting: Global Recommendations and Guidelines, Geneva, 2008.

# Chapter 1: Improving access to antiretroviral medicines

## 1.1 Introduction

It is remarkable to think that just ten years ago there was no consensus on the need to provide treatment for the millions of people living with HIV/AIDS in resource-limited settings. Aside from Brazil and Thailand, the majority of high burden countries still had no national programme to support HIV AIDS care, and donor funding rarely went beyond supporting pilot demonstration programmes.

Even as late as the end of 2003, the UK government continued to argue that prevention should be prioritized over treatment [1], and many high-prevalence countries still had no national treatment plan. South Africa, the country with the greatest number of people living with HIV in the world (some 5.6 million people at the time), only introduced a national HIV/AIDS treatment plan in November 2003 [2].

The reluctance to provide ART in the early years was primarily driven by the cost of treatment. Concerns about the high price of antiretroviral medicines had been on the international agenda for several decades: at the 1988 conference in Stockholm, there was debate about how to ensure people in the Developing World could access the treatment of that time, zidovudine monotherapy, which back then was marketed at a price of US\$8000 per year [3]. Triple therapy, which revolutionized HIV/AIDS care in the West, was considered far too expensive for resource-limited settings, and UN agencies [4], academics [5], and donors alike [1] all argued against providing treatment in favour of focusing funding on prevention.

Civil society groups, and in particular people living with HIV/AIDS themselves, were critical to breaking the deadlock. Patient groups in Thailand, Brazil, South Africa India, Kenya, Uganda, and other high-burden countries formed alliances with health providers, nongovernmental organizations and health groups in Developed countries to argue the case that if the cost of treatment was too high, then it must come down [6,7]. The first paper in this Chapter assesses some of the policy avenues explored by these groups in Brazil and

Thailand, the first two resource-limited countries to achieve universal access to ART, in particular through compulsory licensing (government authorization to a third party to make a generic version of a patented drug) [8].

At the same time people living with HIV/AIDS realized that in order for their governments to provide the care that they were advocating for, both patients and health services would need to be supported. The second paper in this chapter examines how patient groups in Thailand supported health services in the roll-out of antiretroviral treatment at the same time as they challenged the government to make stronger efforts to access more affordable versions of critical medicines for HIV/AIDS [9].

## 1.2. Sustaining access to antiretroviral therapy in the less-developed world: lessons from Brazil and Thailand

*Ford N\*, Wilson D, Costa Chaves G, Lotrowska M, Kijitwanchakul K. AIDS 2007; 21: S21-29.*

### **Abstract**

**Background:** Brazil and Thailand are among few developing countries to achieve universal access to antiretroviral therapy. Three factors were critical to this success: legislation for free access to treatment; public sector capacity to manufacture medicines; and strong civil society action to support government initiatives to improve access.

**Issues:** Many older antiretroviral drugs are not patented in either country and affordable generic versions are manufactured by local pharmaceutical institutes.

**Description:** Developing countries were not required to grant patents on medicines until 2005, but under US government threats of trade sanctions, Thailand and Brazil began doing so at least ten years prior to this date. Brazil has used price negotiations with multi-national pharmaceutical companies to lower the price of newer patented antiretrovirals. However, the prices obtained by this approach remain unaffordable. Thailand recently employed compulsory licensing for two antiretrovirals, obtaining substantial price reductions, both for generic and brand products. Following Thailand's example, Brazil has issued its first compulsory license.

**Lessons learned:** Middle-income countries are unable to pay the high prices of multinational pharmaceutical companies. By relying on negotiations with companies, Brazil pays up to four times more for some drugs compared with prices available internationally. Compulsory licensing has brought treatment with newer antiretrovirals within reach in Thailand, but has resulted in pressure from industry and the US government. An informed and engaged civil society is essential to support governments in putting health before trade.

---

\* NF conceptualized the research, did the policy analysis, undertook the literature review, wrote the first draft of the paper, and contributed to all subsequent drafts.

## **Introduction**

Increasing and sustaining access to affordable antiretroviral therapy (ART) continues to pose many challenges for the developing world. Brazil and Thailand are among the few developing countries that can be said to have achieved universal access to ART [1]. The success of these two countries has depended on three positive factors: a commitment to ensuring universal access to ART with legislation giving free access to treatment; public sector capacity to manufacture medicines; and strong civil society action to challenge the lack of access to medicines and support government initiatives to improve access. This paper looks at strategies employed to improve access to key antiretroviral drugs in these two countries and reflects on the relative successes of each in order to identify factors for future success.

## **Antiretroviral rollout**

The Brazilian public health system began providing antiretroviral agents (zidovudine monotherapy) in 1991. At that time, new medicines were being clinically approved internationally and civil society groups, which have played a central role in Brazil's response to AIDS [2], started to take legal action demanding that the government supply these new drugs. This approach established the judicial basis for guaranteeing universal access to treatment for people living with HIV/AIDS within the federal constitutional right to health [3].

Nationwide access to ART was kick-started in 1996 when Brazil's Congress enacted a law requiring free treatment for individuals with AIDS. Under this law, responsibility to provide ART came under the federal government [4]. By the end of 1997, an estimated 35 900 people were receiving ART; this increased to 105 000 by 2001 and 153 000 by the end of 2004 [5]. Between 1996 and 2004 AIDS mortality was reduced by 50%, and AIDS-related hospitalizations fell by 80% [6].

Thailand began providing antiretroviral monotherapy with zidovudine in 1992, switching to dual therapy (zidovudine with either didanosine or zalcitabine) in 1995. Zidovudine became available generically in 1995, but didanosine and zalcitabine were patented and expensive. A joint evaluation by the World Bank, the World Health Organization (WHO) and the

Ministry of Public Health (MOPH) concluded that the programme was high cost and low benefit [7,8], but this economic review did not take into account the possibility of lower drug prices. In 2000, the government began providing triple therapy for individuals with HIV/AIDS, but again reliance on expensive brand drugs limited the beneficiaries to 1500 individuals.

The wide-scale provision of ART began in 2003, once government-produced generic antiretroviral drugs became broadly available, in particular the fixed-dose triple combination of stavudine, lamivudine and nevirapine (GPO-vir). In February 2003, a delegation of senior officials from MOPH and individuals living with HIV/AIDS from Thailand undertook a study visit to Brazil. This exchange, which was supported by UNAIDS, WHO, Médecins Sans Frontières and Oxfam, helped strengthen Thailand's newly established national HIV/AIDS treatment programme and supported Thailand's efforts to manufacture and procure generic antiretroviral medicines [9]. Since then, the number of individuals on ART has increased sharply from approximately 3000 at the start of 2002 to 27 000 by the end of 2003, rising to 53 000 by February 2005 [10] and 83 000 by December 2006 (see Table 1.2.1).

**Table 1.2.1. Demographics, development status and HIV in Brazil and Thailand.**

	Brazil	Thailand
Population	186.8 million	60.1 million
Human Development Index	69	74
GDP per capita	US\$8195	US\$8090
HIV prevalence (adults)	0.61%*	1%
No. of people living with HIV/AIDS (December 2006)	620 000	580 000
No. on ART	175 000 (August, 2006)	83 000 (December 2006)

ART, Antiretroviral therapy; GDP, gross domestic product. \*Estimates for 15–49 year olds for 2004 [11–13]. Sources: UNDP [11], Brazilian Ministry of Health, Thai Bureau of AIDS, TB and STI, Ministry of Public Health.

### **Generic production and treatment costs**

In both countries the local generic production of antiretroviral drugs by private (national) and state-owned pharmaceutical institutes has been essential to ensuring affordable prices for ART [14].

In Brazil, generic antiretroviral drugs are produced by a number of federal and state laboratories, the most significant being the federal public laboratory FarManguinhos. Local production of non-patented first-line drugs, coupled with price negotiations with pharmaceutical companies for newer drugs subject to patent, has helped the government steadily to reduce its average annual cost for ART, from approximately US\$4350 per patient in 1999 to US\$1517 in 2004 [15]. (Unless otherwise stated, all prices in this article are public sector prices.) Eight of the 17 antiretroviral drugs currently purchased by the government are manufactured domestically.

Thailand's Government Pharmaceutical Organization (GPO) began research and development into antiretroviral drugs (zidovudine and didanosine) in 1992. Generic zidovudine entered the market in 1995 at one-sixth the price of the originator drug. Generic didanosine was blocked in 1998 by a patent application by BMS (Bristol-Myers Squibb) [16]. GPO currently produces six antiretroviral drugs and two fixed-dose combinations in a range of dosages, which are between two (for nevirapine) and 25 (for stavudine) times cheaper than the cheapest originator equivalents. Triple therapy is currently available as a fixed-dose combination (GPO-vir) at a monthly cost of US\$360 per patient per year, compared with US\$4376 for the patented, non-fixed-dose combination drugs.

The average cost of treatment in both countries is increasing as a result of the increasing need to access newer, patented medicines.

### **Rising intellectual property protection**

Local antiretroviral manufacture in Brazil and Thailand has depended on the fact that these medicines were not patented in both countries. According to the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), developing countries were not required to grant patents on medicines until January 2005 [17]. Trade pressure, however, particularly from the United States, pushed this forward in both countries, and the TRIPS Agreement was fully implemented in Brazil in 1997 and in Thailand in 1992 (Table 1.2.2) [10,18–22].

**Table 1.2.2. Key legal provisions improving or limiting access to medicines in Brazil and Thailand**

Legal provision	Description	Practical implications		Examples	
		Brazil	Thailand	Brazil	Thailand
<i>Improves access</i>					
Compulsory licensing	Authorization given by judicial or administrative authority to third party for the use of a patented invention, without the consent	Has been used as a ‘credible threat’ in price negotiations with patent holders	Civil society has pushed for compulsory licenses since 1998. First licenses issued in 2006	Efavirenz	Efavirenz, lopinavir/ritonavir, clopidogrel
Pre-grant opposition	Provide National Patent Office with Technical information about the patentability of filed claims	Two oppositions on AIDS drugs filed by public laboratory and civil society	Thai GPO and other institutions, have opposed the granting of patents	Second patent claim for lopinavir/ritonavir. Tenofovir	Zidovudine/lamivudine (see Table 3)
Prior consent (Brazil only)	Health ministry participation (through the DRA) in analyzing pharmaceutical patent claims [18]	Strong Pharma pressures to withdraw this provision. Many patent applications are pending	---	Val-gancyclovir DRA rejected patent application on the grounds of lack of novelty and inventiveness. [19]. Case ongoing	---
<i>Limits access</i>					
Premature implementation of TRIPS	National legislation compliant with TRIPS earlier than required by WTO (2005)	Generic production restricted earlier than necessary	Generic production restricted earlier than necessary	Pharmaceutical patents started to be granted in 1997	TRIPS compliant legislation introduced in 1998
SMP	A period (2–5 years) of market exclusivity awarded to companies when registering originator brand pharmaceutical products	--	Generic production of non-patented medicines is held back for 2–5 years	---	Fluconazole [21]
Pipeline protection	Retroactive protection allowing pharmaceuticals already patented in other countries to be patented in Brazil [22]	Automatic patent protection granted without analysis of patentability requirement	---	abacavir, efavirenz, lopinavir/ritonavir, nelfinavir, amprenavir.	---

DRA, drug regulatory authority; GPO, Government Pharmaceutical Organization; SMP, safety monitoring programme; TRIPS, Trade-Related Aspects of Intellectual Property Rights

Up until the early 1980s, Brazil's intellectual property laws did not recognize patents on pharmaceutical products and processes. In response to US pressure, however, including economic sanctions, the Brazilian government passed an industrial property law [23], which was approved in 1996, the same year as the law guaranteeing free AIDS treatment [24]. The new patent law included a number of provisions that go further than required by the TRIPS Agreement (TRIPS-plus provisions). The most detrimental of these to the availability of antiretroviral medicines is the 'pipeline mechanism', which provides retroactive patent protection for medicines not yet marketed in Brazil but which have been granted patent protection elsewhere. Under this mechanism, a number of key antiretroviral drugs, including abacavir, efavirenz, lopinavir/ritonavir, nelfinavir and amprenavir were granted patent protection without any technical examination in Brazil [25,26].

As a result of concern over rising intellectual property protection, an amendment was passed in 2001 that included a number of public health flexibilities. One such mechanism, called 'prior consent', authorizes the Brazilian Drug Regulatory Authority to assess patent claims for pharmaceutical products and processes before a patent is granted [18]. This is a rare example of a government health authority playing a formal role in the examination of pharmaceutical patent applications.

Thailand has been under threat of trade sanctions from the US government to introduce strong patent protection for pharmaceuticals since 1985, even though process patents for pharmaceuticals had been introduced in the Thai Patent Act since 1979 [27–29]. Out of concern for public health, Thai academics, lawyers, non governmental organizations and health advocates formed an alliance to monitor this trade pressure, but public awareness remained low, and despite the efforts of civil society intellectual property protection has increased. In 1992, under US government pressure [30], Thailand passed a law introducing pharmaceutical product patent protection and extending patent life from 15 to 20 years. In addition, 'pipeline product protection' was introduced to provide market exclusivity for new drugs registered in Thailand that had been granted a patent elsewhere between 1986 and 1991. The provision, known as the 'Safety Monitoring Programme' allows a period of 2 years' market exclusivity (renewable on request of the pharmaceutical company) for the purposes of collecting postmarketing surveillance data (Table 2). As a safeguard, the

government created the Pharmaceutical Patent Review Board, with authority to collect economic data, including the production cost of pharmaceuticals, but the United States objected [31], and after a 1999 amendment to the Thai Patent Act the Pharmaceutical Patent Review Board was disbanded and the right to issue compulsory licences for pharmaceuticals was restricted [32]. The Safety Monitoring Programme remains in place.

### **Rising drug prices**

All HIV/AIDS treatment programmes need access to newer medicines to provide treatment options in case of drug resistance or intolerance, and the need for these medicines increases over time. These newer drugs are under patent protection in the majority of countries and are far more expensive than those used in first-line regimens [33].

Brazil started to grant patents for pharmaceuticals in May 1997. Within a year, new patented medicines were included in the national AIDS programme, and these began to consume an increasing amount of the treatment budget [14]. By 2003, three newer patented drugs, lopinavir/ritonavir, nelfinavir, and efavirenz, were taking up 63% of the total ART budget. In 2005, imports accounted for 80% of government expenditures on antiretroviral drugs, and total annual expenditures are projected to increase further with the inclusion of newer drugs such as atazanavir (US\$2190 per patient/year) and emtricitabine (US\$17 000 per patient/year) in the national treatment protocol [6].

In Thailand, antiretroviral expenditure as a percentage of the national health budget is expected to increase from 6.1% in 2004 to 10.2% in 2010. According to WHO estimates, second-line therapy for one quarter of all patients will be absorbing three-quarters of the treatment budget by 2020, and the cost of ART with second-line regimens could reach US\$500 million per year if prices remain at current levels [34].

### **Efforts to ensure access to key antiretroviral drugs**

Civil society and government in both countries have fought hard to secure the availability of antiretroviral drugs, using a range of strategies and policy options to challenge and override patents (Table 1.2.3).

### *Negotiation and compromise in Brazil*

In Brazil, price negotiations, backed by the threat of compulsory licensing and local generic production, have been the main strategy used by the government to lower the price of patented antiretroviral drugs.

Between 2001 and 2003 the Brazilian government negotiated discounts on a number of patented drugs. By basing negotiations on production cost estimates calculated by

**Table 1.2.3. Overview of strategies to improve access to affordable medicines in Brazil and Thailand**

Policy approach	Drug	Action taken by	Outcome
Negotiations with pharmaceutical companies	Efavirenz	MOPH, Thailand, 2001	Merck offers price of US\$500
		MOH, Brazil, 2003	Merck offers price of US\$760
	Tenofovir	MOPH, Thailand, 2001	Gilead offers price of US\$360
	Lopinavir/ritonavir	Civil society and government, Thailand, 2006	Abbott offers price of US\$2200
	Nelfinavir	MOH, Brazil, 2003	Roche offers price of US\$1718
Challenge to patent application (pre-grant opposition)	Nelfinavir 625mg tablets	GPO, Thailand, 2005	Pending
	Nevirapine syrup	GPO, Thailand, 2006	Rejected: GPO appeals
	Zidovudine/lamivudine	Health and Development Foundation, Thailand, 2006	Successful: application withdrawn
Challenge to existing patent	Didanosine	Civil society, Thailand, 2002	Patent overturned in 2004
Compulsory license Threatened	Lopinavir/ritonavir	MOPH, Brazil, 2006	Roche offers lower price; government drops compulsory licensing
Issued	Efavirenz	MOPH, Thailand, 2006	Compulsory license issued despite objections from Merck and the US government.
	Lopinavir/ritonavir	MOPH, Thailand, 2007	Abbott offers a price of \$US1000 but threatens to withhold all new medicines unless compulsory licensing is dropped
	Efavirenz	MOPH, Brazil, 2007	

GPO, Government Pharmaceutical Organization; MOH, Ministry of Health;

MOPH, Ministry of Public Health; WHO, World Health Organization.

FarManguinhos [35] and threats to issue a compulsory licence, significant price reductions were obtained for efavirenz (73%), lopinavir/ritonavir (56%) and nelfinavir (74%). Although these percentage discounts appear impressive, the initial prices offered by pharmaceutical companies were very high (comparable to US prices) and the discounted prices obtained were still far higher than the best prices available internationally. From 2003 onwards, the price of most patented antiretroviral drugs in Brazil fell only marginally (Table 1.2.4). It was becoming clear that the government's negotiating tactic of threatening to issue compulsory licences, without ever doing so, was losing credibility.

**Table 1.2.4. Best price of key antiretroviral drugs in Brazil and internationally**

	2003			2006		
	Government price (\$US)	Best price (\$US)	Difference	Government price (\$US)	Best price (\$US)	Difference
Efavirenz	580	438	×1.3	580	220	×2.6
Lopinavir/ritonavir	3241	500	×6.5	1380	338	×4.1
Nelfinavir	1718	880	×2.0	1537	683	×2.3
Tenofovir	2905	500	×5.8	1382	500	×2.8

With increasing numbers of patients on second-line treatments, the average treatment cost had risen by over US\$1000 per patient per year to US\$2616 by 2005; the most expensive second-line drug, lopinavir/ritonavir, cost US\$3241 per patient per year.

In June 2005, the Brazilian government took a first step towards issuing a compulsory licence for lopinavir/ritonavir, announcing, in accordance with Brazilian law [36], that this was in the public interest to sustain the HIV/AIDS treatment programme. At the same time, the government gave the patent holder, Abbott, 10 days to offer a reasonable price, but in fact negotiations were protracted over 4 months, and concluded with the government agreeing on a price of US\$1380 per patient per year for the old version and US\$1518 for the heat-stable version. The discounted price obtained was still far higher than the best prices available internationally by Abbott (US\$500 per patient/year), and production cost estimates published by the WHO (US\$338 per patient/year) [37]. In addition, the Brazilian government made a number of concessions demanded by Abbott, including restricting the use of the compulsory licence, and a moratorium on future price negotiations until 2011 [38].

In December 2005, these concessions forced civil society groups (GTPI/REBRIP) together with the public attorney's office to file a civil action lawsuit against both the Brazilian government and Abbott, demanding the use of compulsory licensing for lopinavir/ritonavir. The judges have so far prevented the case from moving forward, arguing that a compulsory licence would probably result in trade retaliation from the United States while Brazil does not have capacity for local production. This is currently being challenged on the grounds that several laboratories (state-owned and private) do in fact have sufficient production capacity [25,38].

Brazil finally issued its first compulsory licence for an antiretroviral drug in May 2007 for the drug efavirenz, currently used by 75 000 patients in Brazil [39]. This followed recent negotiations with the patent holder, Merck, which was only willing to offer a 2% discount on the current price (US\$580 per patient/year), more than twice the price offered to Thailand (US\$244) after the Thai government issued a compulsory licence (see below). A generic version will be bought from India at less than US\$170 in a first stage, pending local production by public a laboratory. This move, which was forcefully opposed by Merck, represents an important change in Brazil's previous strategy of accepting industry concessions without taking further action.

### *Challenging patents in Thailand*

In Thailand, direct negotiations with pharmaceutical companies have had mixed success (Table 3). Reducing the cost of antiretroviral drugs has focused on two strategies: patent challenges and compulsory licensing.

The first successful challenge to an antiretroviral patent was made by civil society groups against a patent for didanosine. In May 2001, two patients and an AIDS nongovernmental organization filed a lawsuit against Bristol-Myers Squibb, claiming that the patent application was invalid because details of the patent had been unlawfully altered (a dose restriction in the original patent application was altered), extending the patent protection beyond the scope of the original patent application [16]. Bristol-Myers Squibb objected that patients had no legal right to challenge patents, but the court ruled that because pharmaceutical patents can lead

to high prices and limit access to medicines, patients are injured by them and can challenge their legality. This ruling has important consequences internationally, as similar cases in other countries had been thrown out on this basis. Moreover, the court eventually found in favour of the plaintiffs, opening the way for generic production. This court case strengthened the confidence of people with HIV/AIDS in fighting for access to medicines, although the direct impact in terms of access to antiretroviral drugs in Thailand was limited because by the time the legal challenge had completed its course, standard national ART regimens had been set and did not include didanosine.

In early 2006, the Health and Development Foundation of Thailand filed a legal challenge against GlaxoSmith-Kline (GSK)'s application for a patent on the zidovudine/lamivudine fixed-dose combination on the grounds of 'nothing new', arguing that the combining of two known drugs, neither of which were patented in Thailand, could not be considered sufficiently inventive to merit a patent. The cost implications of a patent would have been significant: zidovudine/lamivudine has been produced generically by the Thai GPO since 2003 at a sales price of approximately US\$276 per patient per year; the originator equivalent sales price was US\$2436 per patient per year. The same legal challenge had been filed by civil society groups in India, and activists in both countries co-ordinated their campaigns. In August 2006, several hundred HIV-positive individuals demonstrated outside GSK's offices in Bangkok and Bangalore [40]. GSK withdrew the patent application in both countries the following day, and announced that it would also withdraw applications or granted patents for this formulation in all other countries [41]. Despite this promise, however, GSK continues to seek a patent for zidovudine/lamivudine in China.

Compulsory licensing for government (non-commercial) use has recently been employed in Thailand. The first example was for efavirenz. Since 2004, supply problems had resulted in stock-outs at several hospitals. Cost was also limiting access: Merck was charging over double (US\$468 per patient/year) the price available from Indian generics (US\$216 per patient/year), and the MOPH budget was only able to cover two-thirds of the need. Following failed negotiations with Merck for a lower price, the Thai Minister of Public Health announced in November 2006 that a compulsory licence would be issued for efavirenz, a move strongly supported by civil society groups [41]. Merck responded by

offering a price of US\$288 per patient per year, but at the same time lobbied the US government and the Director General of the WHO [42] to pressure the Thai government to negotiate with Merck rather than issue a compulsory licence [43]. Despite this pressure, the Thai government has followed through with the compulsory licence, and the first supply of generic efavirenz arrived in Thailand in February 2007.

Compulsory licences were issued for two more drugs in early 2007, clopidogrel (for heart disease), and the antiretroviral drug lopinavir/ritonavir [44]. The latter followed fruitless negotiations with the manufacturer, Abbott Laboratories, between 2004 and 2006 [45].

Until 2006, the best price Abbott had offered the Thai government was US\$2967 per patient per year [46]. Under global pressure from activist groups, Abbott announced in early 2006 a price of US\$500 per year for least developed countries, but excluding middle countries such as Brazil and Thailand [47]. Following continued pressure, Abbott announced a price of US\$2200 per patient per year for a list of countries defined by the company as ‘middle-income’ countries. This is, however, more than six times the current cost of first-line ART, and far too expensive for a country such as Thailand, where the average annual wage is US\$1600 per year.

At the end of January 2007, the Thai MOPH took steps to issue a government use compulsory licence for lopinavir/ritonavir [48]. Abbott responded by offering a price of US\$2000 per patient per year (at the time a generic company was offering \$1333 per patient/year). Given that the drug costs less than US\$400 to manufacture [37] the MOPH proceeded with the compulsory licence. The company discounted the price again, to US\$1000 per patient per year for both the old and the new version of the drug, and this offer was made available to 40 ‘middle-income’ countries including Brazil.

At the same time, however, Abbott undertook an aggressive lobbying campaign to block the compulsory licensing. They announced that they would withhold registration of all new medicines from Thailand, stating that ‘Thailand has chosen to break patents on numerous medicines, ignoring the patent system. As such, we’ve elected not to introduce new medicines there’. This was despite the fact that the WHO and several governments have

confirmed that Thailand's actions are fully compliant with international law [49]. Abbott also mounted a misinformation campaign to spread false information about Thailand's compulsory licensing process, and requested that the US government pressure Thailand for allegedly 'stealing' their intellectual property; in response, the US government downgraded Thailand's trade status to a country with poor intellectual property protection. Civil society groups responded by demanding that the Thai Foreign Affairs and Commerce Ministries support the action of the Public Health Minister more actively [50].

In May 2007, a price of US\$676 per patient per year for generic heat-stable lopinavir/ritonavir was announced, after pooled procurement negotiations, together with 65 other countries, facilitated by the Clinton Foundation.

## **Discussion**

Ensuring access to affordable generic medicines has been a cornerstone of Brazil and Thailand's universal access programmes. The long-term success of these programmes will be limited unless access to newer medicines is ensured.

Middle-income countries such as Brazil and Thailand are caught in a double bind. Because they have manufacturing capacity they are heavily pressured by pharmaceutical companies, backed by the US government, to increase intellectual property protection. At the same time, they are viewed as emerging economies with rich elites representing lucrative markets, and so are excluded from differential pricing policies offered to least-developed countries. The reality, however, is that HIV/AIDS is overwhelmingly a disease of the poor. Brazil and Thailand provide ART free to patients, but public health services in these countries are unable to pay the high prices demanded by multinational pharmaceutical companies. These concerns are not limited to antiretroviral medicines, but extend to all essential medicines.

The right of governments to override patents to protect public health is clearly established in international trade law, as affirmed by the 2001 Doha Declaration on TRIPS and Public Health, and has been promoted by international institutions including the World Bank, WHO and the United Nations Development Programme. In practice, however, developing country governments have been pushed through trade pressure to implement much stricter

intellectual property protection than required under international agreements. They are also subjected to further pressure not to use public health safeguards when patents become a barrier to accessing essential medicines. Abbott's actions against Thailand are the clearest demonstration of this disregard for the public health safeguards in the patent system. Experience shows that negotiations with pharmaceutical companies alone have largely failed to secure optimal prices. By relying on this strategy, Brazil is currently paying up to four times more for second-line drugs compared with prices available internationally. Company deals have also stunted the development of local generic manufacturing capacity, and this is reflected by the fact that no new generic AIDS drug has been produced in Brazil since 2002. Thailand spent several years negotiating with companies who failed to offer reasonable prices, and this has limited treatment access for patients. By issuing compulsory licences, the Thai government has given a clear indication to generics manufacturers both in the country and abroad that generic production is worthwhile.

The importance of compulsory licensing to the sustainability of treatment programmes was highlighted by a recent World Bank evaluation of Thailand's national HIV/AIDS programme. It stated: 'Because Thailand stands to gain a great deal from bilateral agreements to reduce trade barriers with trading partners like the United States, the Royal Thai Government may be tempted to relinquish its rights to grant compulsory licences for AIDS drugs in exchange for proffered trade advantages. The report finds that the cost of such concessions would be large. For example, by exercising compulsory licensing to reduce the cost of second-line therapy by 90%, the government would reduce its future budgetary obligations by 3.2 billion discounted dollars through 2025.' [10].

Whereas many of the lessons presented in this article do not directly apply to all developing countries, the majority of whom do not currently have adequate pharmaceutical manufacturing capacity, it is clear that the compulsory licences issued by Thailand have had important international repercussions: the price offered to Thailand for efavirenz motivated the Brazilian government also to pursue compulsory licensing, and the compulsory licence for lopinavir/ritonavir forced Abbott to reduce its price in over 40 countries. Finally, by issuing compulsory licences the Thai and Brazilian government has sent a clear message to generics companies both in country and abroad that generic manufacture is worthwhile; this

will increase the availability of generic medicines that can be imported by other countries through compulsory licensing.

Brazil and Thailand are not alone in facing these challenges. India is another country with strong domestic drug production capacity. The country has a weak national HIV/AIDS program compared to Brazil and Thailand [51], but is an important exporter of generic antiretroviral drugs, currently providing approximately half of all antiretroviral medicines used in the developing world. India only met TRIPS requirements in 2005, and it remains unclear which medicines will be granted patent protection, and to what extent public health safeguards will be effective. These are critical issues for HIV/AIDS treatment programmes across the developing world.

An informed and engaged civil society is essential to supporting governments in putting health before trade, and speaking out against pressure from industry and developed country governments. As the need for newer antiretroviral drugs increases, so the efforts of civil society will be more necessary than ever.

### 1.3. Challenge and co-operation: civil society activism for access to HIV treatment in Thailand

*Ford N\*, Wilson D, Cawthorne P, Kumphitak A, Kasi-Sedepan S, Kaetkaew S, Teemanka S, Upakaew K, Preuanbuapan C. TROP MED INT HEALTH 2009; 14:1-9.*

#### **Abstract**

Civil society has been a driving force behind efforts to increase access to treatment in Thailand. A focus on HIV medicines brought civil society and nongovernmental and government actors together to fight for a single cause, creating a platform for joint action on practical issues to improve care for people with HIV/AIDS (PHA) within the public health system. The Thai Network of People with HIV/AIDS (TNP+), in partnership with other actors, has provided concrete support for patients and for the health system as a whole; its efforts have contributed significantly to the availability of affordable generic medicines, early treatment for opportunistic infections, and an informed and responsible approach towards antiretroviral treatment that is critical to good adherence and treatment success. This change in perception of PHA from 'passive receiver' to 'co-provider' of health care has led to improved acceptance and support within the healthcare system. Today, most PHA in Thailand can access treatment, and efforts have shifted to supporting care for excluded populations.

---

\* NF conceived of the study, undertook the literature review, interviewed key actors, and wrote the first draft of the paper. All other authors contributed to subsequent drafts.

## **Introduction**

Since the 1970s, health professionals in Thailand have played an important public role in health sector reform, sometimes risking their professional positions but often emerging with enhanced public standing [1]. In 1985, civic groups joined their efforts by lobbying (initially with little success) against increasingly restrictive patent legislation for pharmaceuticals, which in their view limited access to affordable medicines.

In 1998, civil society involvement in health advocacy was reinforced with the establishment of the Thai Network of People with HIV/AIDS (TNP+). Motivated by a combination of despair in front of death, a strong desire to help friends who fell ill, and anger at a system that made life-saving medicines unaffordable for the majority, people with HIV/AIDS (PHA) have developed a central role in advocacy for improved access to AIDS drugs and have also promoted a patient-centred approach to HIV/AIDS care within the public health sector. Their role is recognized by the Ministry of Public Health as central to the successful expansion of antiretroviral treatment through activities that encourage community education, reduce discrimination, provide peer support, and promote the right of government to make and use affordable generic drugs [2].

Treatment activism has brought civic groups (Table 1.3.1) together to fight for a single cause, creating a platform for joint action on practical issues to improve care within the public health system. We describe the main activities of three groups over the last decade: AIDS ACCESS Foundation, the TNP+ and Médecins Sans Frontières (MSF). Their efforts have implicated PHA in treatment activism and as co-providers of care within the public health system.

This article, written by representatives of these three groups, aims to complement recent analyses on the engagement of nongovernmental organizations (NGOs) in the provision of HIV/AIDS care in Thailand [3,4]. The aim of providing this participant-observer's perspective over the last 10 years is to contribute a rich historical analysis of the process of policy change in Thailand. Such perspectives have recently been noted as lacking in the health policy literature, particular in relation to community participation in health policy formulation [5].

**Table 1.3.1. Civic groups promoting access to treatment in Thailand**

***Governmental actors***

- The Government Pharmaceutical Organization is a state enterprise formed in 1966 to provide affordable quality medicines for the public health system. Officials from its Research and Development Institute have, together with other health professionals, taken a public stance on issues of access to medicines at some risk to their professional positions.
- The Office of Health Care Reform: In 1996, the Ministry of Public Health started a 3-year initiative to increase equity in access to health care, with patient and community involvement. The initiative identified as major concerns lack of access and affordability of drugs for HIV, both for opportunistic infections and antiretroviral therapy [9]. MSF, TNP+ and ACCESS (see below) co-operated in establishing a standard of prevention and treatment of opportunistic infections at district level.
- The National Health Security Office: The national health security scheme, promulgated in 2002, partially replaces three previous public insurance schemes and also covers those who were previously uninsured. AIDS NGOs sit on the governing board, as required under the 1997 constitution

***Nongovernmental groups established by health and other professionals***

- The Law Society, established in 1957, provides gratis defence of certain human rights cases, such as the legal challenge by PHA to the patent on the antiretroviral drug didanosine.
- The PDA, founded in 1974, provides a wide range of support for the rural poor. PDAs humorous and common sense approach has contributed significantly to HIV prevention efforts. In 2004, PDA obtained funding for antiretroviral treatment programmes, implemented by MSF and the Ministry of Public Health, for ethnic minorities and migrant workers from Laos and Myanmar.
- The Rural Doctors' Society, founded in 1978 to support rural health services, supports public health initiatives such as the formulation of a national drug policy, and acts as a watchdog to counter corruption and inappropriate administrative behaviour in the health system [1].
- The Health and Development Foundation, founded in 1983, has developed expertise in pharmaceutical and patent regulations and challenged antiretroviral patent applications and supported civil society negotiations in the US–Thailand FTAs.
- The International Law Association of Thailand, founded in 1984, provides a technical forum for discussion of the impact of patent law and international trade on Thai society.
- The CCPN was founded in 1983 to coordinate activities of nongovernmental health groups and has successfully overturned some proposed amendments to patent law on pharmaceuticals. In 1994, CCPN set up the Foundation for Consumers, which has become the leading consumer organization in Thailand.
- The Thai Red Cross AIDS Research Center began operating in December 1989 and plays a leading role with regard to prevention, counselling, treatment and research on HIV/AIDS.
- FTA Watch, a coalition of activists from academic institutions, NGOs and peoples' organizations, was formed in 2003 in response to government plans to negotiate bilateral FTA negotiations with several countries, most notably the US.

***NGOs bringing patients into the movement for access to medicines***

- The AIDS ACCESS Foundation (ACCESS), established in 1991, works with the media to promote policies to reduce discrimination. Since 2003, ACCESS has coordinated a Regional HIV/AIDS care and treatment training project (developed together with MSF and TNP+). The 'We Understand' Group was founded in January 2004 under the auspices of the AIDS Access Foundation, and is a collaboration of hospitals, NGOs, PHA groups and volunteers raising public awareness about children and youth living with HIV/AIDS.
- MSF, at the request of local NGOs, has been supporting HIV projects in Thailand since 1994. Activities include technical support, lobby for access to treatment, projects to establish a standard of care at district level (since 1997, in co-operation with the Office of Health Care Reform) and treatment projects with the Thai Ministry of Public Health. MSF, using funds from the 1999 Nobel Peace prize, the European Commission and Forum Syd, also supports coordination and infrastructure costs of TNP+ and ACCESS, as other international donors will fund activities but will not support running costs.
- The TNP+ was established in 1998 as a response to the isolation of individual PHA groups and their dependency on funding by their hospital. The founding vision of TNP+ was that PHA should be able to live with dignity and play an active role in society. By 2006 there were more than 900 PHA groups with 20

000 TNP+ members nationwide.

---

FTA, free-trade agreement; MSF, Médecins Sans Frontières; NGO, nongovernmental organization; PHA, people with HIV / AIDS; TNP+, Thai Network of People with HIV / AIDS; PDA, Population and Community Development Association.

## **Context: government, civil society and HIV/AIDS in Thailand**

Thailand's HIV epidemic began in 1984, with cases initially confined to perceived 'high-risk' groups: gay men, then injecting drug users and then commercial sex workers.

NGOs played an important role in influencing government policy related to HIV/AIDS and in 1990 succeeded in disbanding a proposed 'AIDS Bill' that required mandatory HIV testing of members of 'high-risk' groups [6]. In 1991, when more HIV cases were found in the general population, the government vigorously promoted a prevention campaign aiming at 100% condom use in commercial sex establishments [7]. The campaign is estimated to have prevented 2 million subsequent infections [8]. Nevertheless more than one million people have become infected since the epidemic began and more than 400 000 have died.

The first PHA group was established in 1990 in Bangkok. With time, more groups were established and in 1995 their contribution was officially recognized by Ministry of Public Health policy that encouraged the formation of PHA groups within the hospital system. By 2006, there were 900 PHA groups with more than 20 000 members [3] mainly supported by government funds channelled through public hospitals.

Initially, the engagement of PHA groups in HIV care was focused on social support; advocacy was constrained as groups were isolated from each other and depended on funding from their hospital. This changed with the establishment of the TNP+ in 1998. That year, the Office of Health Care Reform (Table 1) identified lack of accessible HIV treatment as a priority [9], and a pilot project to define a standard of treatment for opportunistic infections at district level was established by the Ministry of Public Health, MSF and TNP+ [10].

## **Campaigning for access to antiretroviral treatment**

Publicly funded (mono- and dual-) antiretroviral therapy was first made available for limited numbers of patients in 1992 [10]. The Ministry of Public Health began to provide triple antiretroviral therapy in 2000 but reliance on expensive brand drugs limited beneficiaries to around 1500 people [11]. Large-scale treatment only became possible later, after the Thai Government Pharmaceutical Organisation (GPO) began to produce a range of generic antiretrovirals.

The Government Pharmaceutical Organisation had begun research and development of antiretrovirals in 1992, initially for zidovudine and didanosine. Zidovudine was launched in 1995, but production of generic didanosine was blocked when a Thai patent was granted to Bristol-Myers Squibb in 1998. The patented version was prohibitively expensive and provoked the first in a series of public demonstrations against intellectual property restrictions to medicines [12].

At the end of 1999, the GPO submitted a request for a compulsory license, a request backed by public demonstrations in which over 300 PHA gathered outside the Public Health Ministry. This was the first occasion in Thailand that HIV positive people braved stigmatization to stage public demonstrations and proved to be a watershed event in terms of their awareness and self-confidence. However, under pressure from the US government [13], the Ministry of Public Health rejected the request. Activists with support from the Law Society (Table 1) then mounted a legal challenge against the patent for didanosine, claiming that the patent had been unlawfully granted [14]. After 2 years, the court ruled in favour of the plaintiffs, opening the way for generic production.

### **Campaigning for universal health care**

Prior to 2001, Thailand's public health system was accessed through three health insurance systems, but this led to significant exclusion: around three-quarters of the population lacked insurance [15] and two-thirds of those with health insurance (those holding low-income health cards) could not access the benefits to which they were entitled [16]. In 2000, civic groups drew up a petition demanding that parliament debate the introduction of universal health insurance [17]. Under the Royal Thai Government (1997) Constitution, parliament is obliged to debate any petition signed by more than 50 000 voters. TNP+ and the Rural Doctors' Society (Table 1) with their nationwide networks collected the majority of more than 60 000 signatures supporting the petition, forcing a parliamentary debate.

The National Assembly voted against the bill. However, universal health insurance became a key issue in the subsequent election campaign and, fulfilling its election promise, the Thai Rak Thai party introduced health insurance soon after winning the 2001 election, making

Thailand one of the first developing countries to provide universal healthcare coverage to their population. Antiretroviral treatment and renal dialysis were initially excluded from the benefits because of their high cost; activists were quick to point out that the constitution prohibits discrimination on account of a particular disease. In October 2001, the Thai GPO manufactured a fixed-dose medicine combination, reducing the price of this regimen from \$US 9600 to \$US 570/patient/year.

NGO networks promptly demanded government action [4], and the Minister of Public Health announced that antiretroviral drugs would be included in this universal access to healthcare policy [11]. However, it took 4 more years of campaigning before this became a reality [18].

### **Increasing the availability of treatment**

While efforts were being made to lower the cost of treatment, parallel efforts aimed at increasing its availability. The involvement of PHA in the provision of health care beyond pilot projects began in May 2000, with a Buyers' Club established by TNP+, MSF and ACCESS. While the public health system was relying mostly on brand name drugs, TNP+ purchased generic antiretrovirals from GPO and channelled these drugs to public hospitals via PHA groups; these drugs were prescribed by government doctors, paid for by patients and dispensed by PHA with supervision from the hospital pharmacists [19]. This programme established the principle of partnership at a grassroots level between NGOs and public healthcare providers, and also gave GPO its first orders for several generic antiretrovirals, thus kick starting production. The Buyers' Club was able to scale down its activities as the government programme scaled up.

Concurrently, there was a push to increase access to basic, low-cost medicines for opportunistic infections, which were poorly available prior to their inclusion in the national health insurance scheme in 2001. Surveys carried out by MSF and TNP+ in 2000 found that less than half of symptomatic PHA received co-trimoxazole prophylaxis; access to treatment for other opportunistic infections such as tuberculosis was also limited.

In November 2000, TNP+, MSF and ACCESS launched a project to increase access to

prophylaxis and treatment for opportunistic infections, referred to as the ‘AIDS can be treated’ campaign. It was considered essential that PHA should participate actively in their own treatment and care if they were to develop the knowledge and understanding necessary to stop believing that AIDS was a death sentence. Therefore, the project began by training PHA from 150 groups across the country to recognize symptomatic disease and to support each other in accessing health care. An internal evaluation 2 years after the project began found that access to correct therapeutic interventions for the commonest life-threatening opportunistic infections had increased from less than 50% before the project began to more than 80% [20].

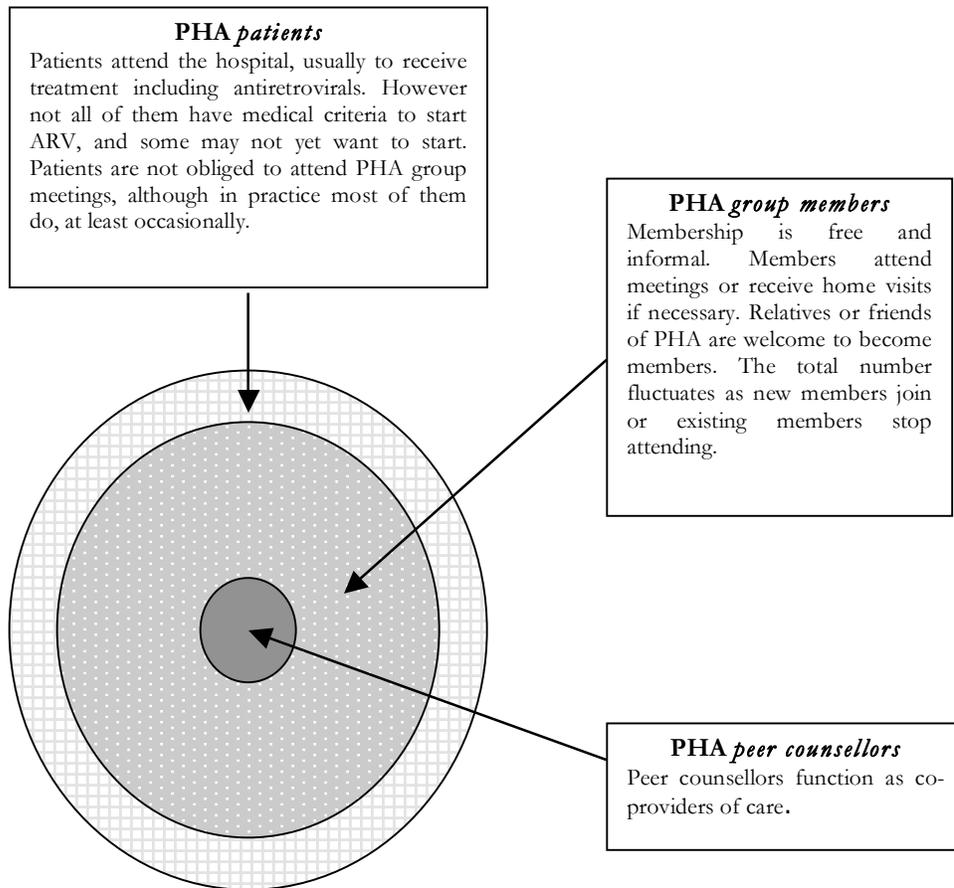
These experiences showed that with appropriate training and support PHA could develop a role as partners in provision of health care. MSF, ACCESS and TNP+ capitalized on the experiences by developing accessible health education materials and training modules; these were subsequently used to support the government’s treatment programme. The chronology of access to HIV treatment is summarised in Table 1.3.2.

### **PHA support government scale up of antiretroviral therapy**

Collaboration between civic groups and government expanded considerably in 2002 when Thailand obtained financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria for its ambitious scaling up of antiretroviral treatment. This required NGO participation at both policy decision and operational levels of the national HIV programme [4]. TNP+, MSF and ACCESS jointly developed a strategy for central involvement of PHA in the programme. A ‘Comprehensive and Continuous Care Centre’(CCC Centre) model (Figure 1.3.1) was developed in which PHA activists, working within the hospital system, provide accessible care and support, activities that formal health providers have limited capacity to undertake [4,20].

Most PHA group members in Thailand are farm labourers, factory workers or unemployed with only primary education. PHA members working in CCC Centres, in addition to appropriate training to develop their knowledge and skills in provision of care, also need ongoing practical support with such matters as record keeping, teamwork and coordination with the hospital. The training and support is provided by TNP+, MSF and ACCESS.

**Figure 1.3.1. The CCC care model**



In addition to providing care and support, the CCC Centres are an attempt to ensure a central involvement of grassroots PHA in the government rollout of antiretroviral therapy. The group must have sought permission from the hospital director, been assigned a room in the hospital to do their work, and hospital staff must have agreed that the PHA can join their HIV care and treatment team. One activist can normally manage a caseload of 15 to 20 clients. Activists are expected to recognize common side effects of antiretroviral drug regimens available in their hospital, support prevention and treatment of three common opportunistic infections (TB, *Pneumocystis carinii* pneumonia and cryptococcal meningitis) and to be able to provide ‘first aid’ for symptoms such as fever and diarrhoea, and evaluate treatment adherence. A support team, staffed by members of TNP+, ACCESS and MSF provides training, together with ongoing support for transparent financial management,

timely submission of reports, record keeping and problem solving within the CCC Centre teams. One support team member can manage around 25 CCC Centres. This support model is a good investment in terms of treatment success and life expectancy [21].

**Table 1.3.2. Chronology of access to HIV treatment in Thailand**

1984	First Thai HIV case
1985	Process patents introduced under United States Government pressure
1988	Increase in numbers of HIV cases in at risk groups (injecting drug user and commercial sex worker)
1990	Bill proposed to introduce mandatory HIV testing for people suspected of belonging to an 'at risk' group. Disbanded under civil society pressure. First PHA group (Wednesday Friends) established by Thai Red Cross
1991	Sentinel surveillance first detected a significant level of HIV in the general population (3% amongst army conscripts) prompting a national campaign promoting 100% condom use in commercial sex establishments
1995	Ministry of Public Health introduces policy to encourage formation of PHA groups within the hospital system
1998	TNP+ established. MSF, ACCESS and TNP+ begin working together on supporting access to ART, and join the first public demonstrations in Thailand against high prices of ART, organized by the Thai Consumer Foundation
1999	MSF wins Nobel Peace Prize; donates some of the prize money to TNP+ for infrastructure development. MSF, ACCESS and TNP+ and other civil society organizations support a request by the Thai GPO to the Minister of Public Health to issue a Compulsory License for didanosine (Request refused.)
2000	MSF start to provide ART in Thailand in one of the organization's first treatment programmes TNP+, MSF and ACCESS launch campaign to increase access to opportunistic infection medication ART Buyers Club established
2001	Universal health insurance scheme introduced. ART and treatment for renal failure are initially excluded. Civil Society lobbies for inclusion of all treatments. NGOs and PHA appointed to various National Health Security Office subcommittees. In October, the GPO manufactures a fixed-dose combination of ARV (GPO-vir). Following NGO lobbying for government action, minister of Public Health announces that GPO production capacity would be increased and that antiretroviral drugs would be included in the universal access to healthcare policy. CCC Centre model, with PHA as co-providers of care, piloted in two public district hospitals, under MSF supervision.
2002	Thai government includes GPO-vir in national ART programme, and scales up treatment nationwide PHA file legal claim against Bristol Myers Squibb and the Dept. of IP, contesting the Thai didanosine patent in the IP Court. The Thai Law Society, the Health and Development Foundation, MSF and ACCESS support this action. CCC Centre model agreed by TNP+ and first 30 centres established in public hospitals, with Global Fund support, to provide formal role for PHA in health system. Health and Development Foundation files pre-grant opposition to zidovudine + lamivudine patent application which is withdrawn following demonstrations by PHA in Thailand and India.
2003	180 CCC Centres functioning across the country
2004	Didanosine patent overturned in IP court.
2005	ART included in universal health insurance scheme.
2006	TNP+ wins UNAIDS Red Ribbon Award. Zidovudine + lamivudine patent application withdrawn following civil society challenge Compulsory licence issued for efavirenz 10 000 protestors mobilize against the US–Thai FTA. World Bank study concludes CCC Centre model is cost-effective and recommends compulsory licensing as an option to control ART costs National Health Security Office agrees to fund an additional 70 CCC Centres, establishing government support for patients as co-providers of care
2007	Minister of Public Health issues Compulsory License for the antiretroviral drug efavirenz, supported by civil society
2008	Minister of Public Health issues Compulsory License for the antiretroviral drug lopinavir / ritonavir, supported by civil society. MSF hands over HIV / AIDS care and treatment activities to local partners, but continues advocacy for access to medicines.

ART, antiretroviral therapy; CCC, Comprehensive and Continuous Care; FTA, free trade agreement; GPO,

Government Pharmaceutical Organisation; MSF, Médecins Sans Frontières; NGO, nongovernmental organization; PHA, people with HIV/AIDS; TNP+, Thai Network of People with HIV/AIDS; IP, Intellectual Property.

As of mid-2008, antiretroviral treatment was available at all government hospitals, with 180 000 PHA under treatment. One-third (327) of hospitals had established CCC centres, each with 3-10 PHA activists. A Ministry of Public Health/World Bank study estimated that systematically providing PHA peer support in treatment sites throughout Thailand would increase the cost per life year saved by less than \$US 40 (triple-therapy costs \$US 360/year) [10].

Initially, the CCC Centres were financed by the Global Fund (95%) and MSF (5%), but an external review of the health sector response to HIV/AIDS in Thailand recommended that community-based organizations should be more effectively financed by domestic sources [22]. From 2006 Global Fund money was matched by the National Health Security Office, which has since committed to supporting all individual CCC Centre costs from 2009, when the current Global Fund grant expires. But the National Health Security Office has not yet agreed to cover support costs of the support teams, raising doubts about how to maintain the quality of the services they provide.

### **Further efforts to increase access to medicines**

Civic groups continued pressing for wider access to medicines. An important victory was gained in 2006 when 500 people protested outside the offices of GlaxoSmithKline in Bangkok, forcing withdrawal of a patent application for the drug combination of lamivudine + zidovudine [23].

Eight years after the GPO requested a compulsory licence for didanosine, the Thai government finally issued compulsory licenses in 2007 and 2008, including for the second-line antiretroviral lopinavir–ritonavir. This followed a WHO evaluation forecasting that the cost of antiretroviral therapy with second-line regimens could cost the country US\$ 500 million/year by 2020 unless action was taken against drug prices [24].

In addition to these actions against specific patents, civil society groups have worked to promote public health within trade negotiations by mobilizing against US trade pressure for further restrictions via the US–Thai free trade agreement (FTA) [23]. In 2006, nearly 10 000 protesters gathered outside the venue of the free-trade talks demanding, in line with UN recommendations, that Thailand should not accept any further reinforcement of intellectual property protection proposed in the FTA [24]. In response, the Thai Government declared that demands by the United States for Thailand to tighten up drug patenting were ‘unacceptable’ [25].

### **Expanding support to other countries/diseases**

In 2003, ACCESS, MSF and TNP+ set up a project to train participants from Vietnam, Cambodia and Laos, later expanding to Nepal, Myanmar and Yunnan (southern China). While these countries have wide differences in their level of access to HIV/AIDS care and nature of their civil society, it has been possible to modify and apply some lessons learned in Thailand in all of these other countries, notably the need to develop a broad network of health workers and NGO staff to ensure ongoing support for PHA.

In 2007, ACCESS and TNP+ expanded the scope of their work by helping patients with chronic renal failure to lobby for access to treatment, and the next year the National Health Security Office began discussing plans to include renal dialysis in the health insurance scheme. This reflects a broader understanding among both government and NGO that access to expensive medicines is not a problem limited to HIV/AIDS drugs: the Thai government has also investigated the possibility to source generic versions of medicines for cancer, cardiovascular and neuropathic drugs and antibiotics [26].

### **Conclusions**

This paper provides a participant-observers’ perspective of the role of civil society activism for access to HIV treatment in Thailand. Such ‘insider’ perspectives carry the risk of certain biases, in particular in relation to the issues the researcher focuses on and the framing of lessons-learned towards policy-relevant conclusions rather than generalizable, theoretical themes. We acknowledge that such biases exist in this account, and do not claim this to be a

historical perspective of all actors involved in the policy-setting process. Nevertheless, participant observation holds a critical place in health policy analysis as it allows for a degree of access to information, understanding of culture and authenticity that is not readily available to an external researcher [27].

As our account illustrates, PHA have made an essential contribution to overall provision of treatment and care in Thailand, to the point that some have concluded that the scale up and sustainability of antiretroviral therapy (ART) in Thailand would not have been possible without the engagement of civil society networks [4]. The role of these groups has been one of both co-operation (providing concrete support for patients and for the health system as a whole) and challenge (advocating for increased access to treatment as a human right). Their efforts contributed substantially to the availability of affordable generic medicines, early treatment for opportunistic infections and an informed and responsible approach towards antiretroviral treatment that is supportive of good adherence and treatment success.

Since 1990, the role of PHA in providing peer support has been increasingly accepted and encouraged in Thailand. A change in perception of PHA from ‘passive receiver’ to ‘co-provider’ of health care came about due to their own action, with significant support from local and international NGOs. Improved acceptance of and support for PHA by the healthcare system followed. A few years ago, health care for PHA was mainly provided by specialist centres; today, nearly every hospital in Thailand accepts its responsibility to provide care for PHA and the gap between doctors and patients has been markedly reduced, with over one third of all hospitals including a formal role for PHA through the CCC model. Increased control over their own health has also brought benefits for PHA in terms of self-image, confidence, and dignity. Empowerment has come from the recognition that many of the barriers to care – lack of access to affordable medicines, lack of national drug supply and lack of peer support – are barriers they have been able to overcome themselves. These successes have firmly established the role of patients not just as beneficiaries of the health system, but stakeholders in its development.

With Thailand virtually reaching the goal of universal access to antiretroviral treatment, the access to medicines crisis that TNP+ confronted in 1998 is largely resolved. But access for

unregistered groups, principally ethnic minorities and migrant populations, who account for more than 2 million people in Thailand, remains very limited. Specific vulnerabilities make these groups at high risk from contracting HIV/AIDS. Other high-risk groups such as sex workers and injecting drug users continue to have difficulty accessing the health system [28]. TNP+ and ACCESS are advocating to extend the reach of the public ART system to these marginalized groups, and have negotiated with the Thai government to ensure that a proportion of the Global Fund grant goes towards supporting these groups.

Successful campaigning for access to affordable medicines has depended on strong working relationships between PHA, academics, NGOs, key government officials and journalists who have been willing to take the time to understand complex issues. This activism has been supportive of, rather than antagonistic towards, government: pushing the government to increase availability of affordable antiretrovirals, and then providing practical support to the implementation of treatment programmes when the medicines become available.

However, with first-line treatment available nationwide and with PHA taking a formal role in policy formulation, there is no longer a single urgent common cause for which to fight. Challenges now faced by Thai civic groups, and which need to be prioritized, include lack of a once-daily first-line regimen, of fixed-dose combinations of ART for children and of TB medication, of wider access to second-line treatment, treatment for Hepatitis C and harm reduction programmes for injecting drug users. Perhaps most pressing, however, is how to maintain the quality of CCC Centre services if funding for their support system is withdrawn.

## 1.4 References to Chapter 1

### 1.1 Introduction

1. Boseley S. Government u-turn on AIDS crisis. *Guardian* 26 November 2003.
2. Operational Plan for Comprehensive HIV and AIDS Care, Management and Treatment for South Africa. National Department of Health, South Africa 19 November 2003.
3. Ford N, Calmy A, von Schoen-Angerer. Treating HIV in the developing world: getting ahead of the drug development curve. *Drug Discovery Today* 2007; 12: 1-3.
4. Creese A, Floyd K, Alban A, et al. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. *Lancet* 2002; 359: 1635–42.
5. Marseille E, Hofmann P, Kahn J. HIV prevention before HAART in sub-Saharan Africa. *Lancet* 2002; 359: 1851–56.
6. Schoen Angerer T, Wilson D, Ford N, Kasper T. Access and activism: the ethics of providing antiretroviral therapy in developing countries. *AIDS* 2001; 15: S81-90.
7. Ford N. Patents, access to medicines, and the role of nongovernmental organisations. *J Generic Medicines* January 2004; 1: 137-145.
8. Ford N, Wilson D, Costa Chaves G, Lotrowska M, Kijtiwatchakul K. Sustaining access to antiretroviral therapy in developing countries: lessons from Brazil and Thailand. *AIDS* 2007; 21: S21-29.
9. Ford N, Wilson D, Cawthorne P, Kumphitak A, Kasi-Sedepan S, Kaetkaew S, Teemanka S, Upakaew K, Preuanbuapan C. Challenge and co-operation: ten years of civil society activism for access to HIV treatment in Thailand. *TROP MED INT HEALTH* 2009; 14: 1-9.

### 1.2 Sustaining access to antiretroviral therapy in the less-developed world: lessons from Brazil and Thailand

1. World Health Organization. 3 by 5 progress report. Geneva: WHO; March 2006.
2. Levi GC, Vitoria MA. Fighting against AIDS: the Brazilian experience. *AIDS* 2002; 16:2378–2383.
3. Scheffer M, Salazar AL, Grou K. Medicines through court: a study on access to new medicines and examinations to HIV/AIDS in Brazil by using legal actions. *Serie legislacao3*. Ministerio da Saude, Brasilia. Available at: <http://www.saberviver.org.br/pdf/>

remedio\_via\_justica.pdf

4. Oliveira MA, Esher A. Universal access to treatment for people living with HIV and AIDS in Brazil. In: Bermudez JAZ, Oliveira MA, Esher A, editors. Acceso a medicamentos: derecho fundamental, papel del estado. Rio de Janeiro: ENSP; 2004. pp. 233–250.
5. Galvao J. Access to antiretroviral drugs in Brazil. *Lancet* 2002; 360:1862–1865.
6. Anon. Response magazine, 2005: experiences of the Brazilian AIDS programme. Brasilia: Ministry of Health, Brazilian Program for STD/AIDS; 2005.
7. Kuanusont C. An antiretroviral program: Thailand's experience. In: van Praag E, Fernyak S, Katz AM, editors. The implications of antiretroviral treatments. WHO/ASD/97.2. Geneva: World Health Organization; 1997: pp. 109–113.
8. Prescott N. Economic analysis of antiretroviral treatment options in Thailand. In: Proceedings of the Third International Conference on AIDS in Asia and the Pacific. Chiang Mai, Thailand, 17–21 September 1995. pp. 88–98.
9. UNAIDS. Strengthening national response in ART provision through exchange visits and technical network development between Thailand and Brazil. Report of the Thai Delegation. UNAID/WHO/MSF/Oxfam, StarChine Creation, Bangkok, June 2003; 53.
10. Revenga A, Over M, Masaki E, Peerapatanapokin W, Gold J, Tangcharoensathien V, Thanprasertsuk S. The economics of effective AIDS treatment: evaluating policy options for Thailand. Washington, DC, USA: The World Bank; 2006.
11. United Nations Development Programme. Human development report. New York: United Nations; 2006.
12. Ministry of Health. Epidemiological Bulletin, 2006.
13. Ministerio da Saude. Monitoraids, 2006. Available at: [www.aids.gov.br](http://www.aids.gov.br)
14. Bermudez JAZ, Oliveira MA. Essential medicines and AIDS care in Brazil: recent lessons learnt. In: Improving access to care in developing countries: lessons from practice, research, resources and partnerships. Joint United Nations Programme on HIV/AIDS (UNAIDS)/WHO/French Ministry of Foreign Affairs; 2002.
15. Granjeiro A, Teixeira L, Bastos FI, Teixeira P. Sustainability of Brazilian policy for access to antiretroviral drugs. *Rev Saude Publica* 2006; 40.
16. Ford N, Wilson D, Bunjumngong O, von Schoen Angerer T. The role of civil society in protecting public health over commercial interests: lessons from Thailand. *Lancet* 2004; 363: 560–563.

17. World Trade Organization. Frequently asked questions about TRIPS. Which countries are using the general transition periods? Available at: [http://www.wto.org/english/tratop\\_e/trips\\_e/tripfq\\_e.htm#Transition](http://www.wto.org/english/tratop_e/trips_e/tripfq_e.htm#Transition)
18. Oliveira MA, Chaves GC, Epsztejn R. Brazilian intellectual property legislation. In: Jorge A, Bermudez M, Auxiliadora O, editors. Intellectual property in the context of the WTO TRIPS Agreement: challenges for public health. Rio de Janeiro: Escola Nacional de Saude Publica; 2004.
19. Basso M. Intervention of health authorities in patent examination: the Brazilian practice of the prior consent. *Int J Intellectual Property Manage* 2006; 1: 54–74.
20. Chaves GC, Oliveira MA. A proposal for measuring the degree of public health sensitivity of patent legislation in the context of the WTO TRIPS Agreement. *Bull WHO* 2007; 85: 49–56.
21. Von Schoen-Angerer T, Limpananont J. US pressure on less-developed countries. *Lancet* 2001; 358: 245.
22. Velasquez G, Boulet P. Globalization and access to drugs – perspectives on the WTO/TRIPS Agreement. WHO/DAP/98.9 revised. Geneva: WHO; 1999.
23. Brazil, 1996. Act 9.279, May 14 1996. Establishes rights and obligations related to industrial property. Brasilia: Diario Oficial da Uniao of May 15 1996.
24. Brazil, 1996. Act 9.313, November 13 1996. Establishes free medicines distribution to individuals with HIV and AIDS. Brasilia: Diario Oficial da Uniao of November 14 1996.
25. Working Group on Intellectual Property (GTPI) of the Brazilian Network for the Integration of Peoples (Rebrip), 2006. Why Brazil pays more for important medicines to public health? Available at: [http://www.abiaids.org.br/media/patentes\\_GTPI.pdf](http://www.abiaids.org.br/media/patentes_GTPI.pdf)
26. Medecins Sans Frontieres. Drug patents under the spotlight: Sharing practical knowledge about pharmaceutical patents. Geneva: MSF; May 2003. Available at: <http://www.accessmed-msf.org/documents/Patent%20report%20.pdf>.
27. The Economist Intelligence Unit. Thailand country report: 2<sup>nd</sup> quarter 1998. London: EIU; 1999.
28. Limpananont J. Thailand: the impact of pressure from the US – patents, pills and public health: can TRIPS deliver? London: Panos; 2002, pp. 41–43.
29. Kuanpoth J, Limpananont J, Narintarakul K, Silarak B, Taneewuth S, Lianchamroon W, et al. Free Trade Agreements and their impact on Developing Countries: the Thai

- experience. Nonthaburi, Thailand: FTA Watch; September 2005.
30. Aongsonwang S. Pharmaceutical patent law: a law by transnational companies – Thailand's experience. Paper presented at NGO meeting on compulsory licensing of essential medical technologies. Geneva, 1999.
  31. Office of the United States Trade Representative. National trade estimate report on foreign trade barriers. Washington, DC: US Trade Representative; 1999.
  32. Wilson D, Cawthorne P, Ford N, Aongsonwang S. Global trade and access to medicines: AIDS treatments in Thailand. *Lancet* 1999; 354: 1893–1895.
  33. Calmy A, Pascual F, Shettle S, de la Vega FG, Ford N. The Lancet Red: a missed opportunity. *Lancet* 2006; 36: 1063.
  34. World Health Organization. External review of the health sector response to HIV/AIDS in Thailand. New Delhi: MOPH, WHOSEA; August 2005.
  35. Bermudez JAZ, Oliveira MA, Chaves GC. 2004. The WTO TRIPS Agreement and challenges for public health. In: Bermudez JAZ, Oliveira MA, Esher A, editors. Access to medicines: fundamental right, the role of the State. Rio de Janeiro: ENSP; 2004, pp. 69–88.
  36. Later changed through the Decree 4.830, September 4th 2003.
  37. Pinheiro E, Vasan A, Kim JY, Leed E, Guimier J-M, Perriens J. Examining the production costs of antiretroviral drugs. *AIDS* 2006; 20: 1745–1752.
  38. Fortunak JM, Antunes OAC. ARVs production in Brazil – an evaluation. 2006. Available at: <http://www.abiaids.org.br/media/ARV.pdf>
  39. Astor M. Brazil AIDS drug negotiations break down. Associated Press, 4 May 2007.
  40. Anon. HIV drug fears. Hundreds rally at Glaxo office. UK firm's move for patent on Combivir is 'a threat to access of cheap medicines'. *Nation*, 8 August 2006. Available at: <http://www.gsk.com/media/archive.htm>.
  41. Cawthorne P, Dayal A. Thailand still shows the way on HIV/AIDS. *Nation*, 2 December 2006.
  42. Cawthorne P, Ford N, Limpananont J, Tienudom N, Purahong W. WHO must defend patients' interests, not industry. *Lancet* 2007; 369: 974–975.
  43. Gerhardsen TIS. Thailand compulsory license on AIDS drug prompts policy debate. Intellectual Property Watch, 23 December 2006. Available at: [http://www.ipwatch.org/weblog/index.php?p=499&res=1024\\_ff&print=0](http://www.ipwatch.org/weblog/index.php?p=499&res=1024_ff&print=0)
  44. Facts and evidences on the ten burning issues related to the government use of patents

- on three patented essential drugs in Thailand. Issued by the Ministry of Public Health and the National Health Security Office, Nonthaburi, Thailand, February 2007.
45. Open Letter to Miles White, CEO of Abbott, 15 March 2006.
46. Steinbrook R. Thailand and the compulsory licensing of efavirenz. *N Engl J Med* 2007; 356: 544–546.
47. Wong-Anan N. Thailand issues more compulsory drugs licences. Reuters, 25 January 2007.
48. Wongruang P. Move to break drug patents lauded. *Bangkok Post*, 3 February 2007.
49. Cawthorne P, Ford N, Wilson D, Kijtiwathakul K, Purahong V, Tianudom N, Nacapew S. Access to drugs: the case of Abbott in Thailand. *Lancet Infect Dis* 2007; 7: 373–374.
50. Anon. Status downgrade: outrage grows at US trade pressure. *Nation*, 3 May 2007.
51. Over M, Heywood P, Gold J, Gupta I, Hira S, Marseille E. Prevention and treatment in India: modeling the costs and consequences. Washington, DC: World Bank; 2004.

### **1.3 Challenge and co-operation: civil society activism for access to HIV treatment in Thailand**

1. Bamber S. The Thai medical profession and political activism in the Thai political economy. In: *Political Change in Thailand: Democracy and Participation* (ed K Hewison) Routledge, London, 1997. pp. 233–250.
2. Kunaratanapruk S. Research Challenges for Scaling up Antiretroviral Treatment: Experience From Thailand. Presentation by the Deputy permanent secretary of the Thai MOPH. Ministerial Summit on Health Research, Mexico City, 18 November 2004.
3. Lyttleton C, Beesey A, Sitthikriengkrai M. Expanding community through ARV provision in Thailand. *AIDS Care* 2007. 19: 44–53.
4. Tantivess S, Walt G. The role of state and non-state actors in the policy process: the contribution of policy networks to the scale-up of antiretroviral therapy in Thailand. *Health Policy Planning* 23 2008: 328–338.
5. Gilson L, Raphaely N. The terrain of health policy analysis in low and middle income countries: a review of published literature 1994–2007. *Health Policy Planning* 2008. 23: 294–307.
6. World Bank. *Thailand's Response to AIDS: Building on Success, Confronting the Future*. World Bank, Washington, DC, 2000.

7. Rojanapithayakorn W, Hanenberg R. The 100% condom program in Thailand. *AIDS* 1996. 10: 1–7.
8. UNAIDS. Evaluation of the 100% Condom Programme in Thailand. UNAIDS, Bangkok, 2000. [http://data.unaids.org/Publications/IRC-pub01/JC275-100pCondom\\_en.pdf](http://data.unaids.org/Publications/IRC-pub01/JC275-100pCondom_en.pdf), accessed 12/10/2008.
9. Nitayarumphong S. Health Care Reform: At the Frontier of Research and Policy Decisions. Ministry of Public Health, Nonthaburi, 1996.
10. Revenga A, Over M, Masaki E, Peerapatanapokin W. The Economics of Effective AIDS Treatment: Evaluating Policy Options for Thailand. World Bank, Washington, 2006.
11. Phanuphak P. Antiretroviral treatment in resource-poor settings: what can we learn from the existing programmes in Thailand? *AIDS* 2004; 18: S33–S38.
12. Limpananont J. Thailand: The Impact of Pressure From the US. Patents, Pills and Public Health: Can TRIPS Deliver? Panos, London, 2002, pp 41–43.
13. Hecklinger RE. Letter from former US ambassador to Thailand, to the US Secretary of State, November 1999. <http://www.lists.essential.org/pipermail/iphealth/2003-march/004416.html>.
14. Ford N, Wilson N, Bunjumngong O, von Schoen-Angerer T. The role of civil society in protecting public health over commercial interests: lessons from Thailand. *Lancet* 2004; 360: 560–563.
15. United Nations Development Programme. The Role and Experiences of PLHIV Networks in Securing Access to Generic ARV Medicines. ANP+/UNDP, Bangkok, 2007.
16. Phromporn P, Wibulpolprasert S. Health Insurance Systems in Thailand. Health systems Research Institute, Nonthaburi, 2002.
- 17 International Labour Organisation. Lessons From Thailand – Involvement of People Living With HIV/AIDS in Treatment Preparedness. ILO, Bangkok, 2008.
18. Kiatying-Angsulee N, Sringernyuang L, Haritavorn N. Beyond the Targets: Assessment of Public and Private ARV Treatment Programs. Thailand Country Working Paper. HAI Europe, Amsterdam, 2006.
19. Kreudhutha N, Donmon B, Uppakaew K et al. Experience of a community-based antiretroviral Buyers' Club in Thailand. *WHO Essential Drugs Monitor* 2006; 34: 10–11.
20. Kumphitak A, Kasi-Sedapan S, Wilson D et al. (2004) Perspectives and Practice in Antiretroviral Treatment: Involvement of People Living With HIV / AIDS in Treatment

Preparedness in Thailand. Case Study. WHO, Geneva, 2005.

21. Over M, Revenga A, Masaki E et al. The economics of effective AIDS treatment in Thailand. *AIDS* 2007; 21: S105–S116.

22. Ministry of Public Health, Thailand & World Health Organisation. External review of the health sector response to HIV / AIDS in Thailand. WHO Regional Office for South-East Asia, 2005.

23. Ford N, Wilson D, Costa Chaves G, Lotrowska M, Kijtiwatchakul K. Sustaining access to antiretroviral therapy in developing countries: lessons from Brazil and Thailand. *AIDS* 2007; 21: S21–S29.

24. Ministry of Public Health, Chulalongkorn University, United Nations Programme for HIV / AIDS, United Nations Development Programme & World Health Organization. Free Trade Agreements and Intellectual Property Rights: Implications for Access to Medicines. World Health Organization, Bangkok, 2005.

25. Hongthong P, Thalang J. Thai–US FTA Talks: Stumbling Block. Nation, Bangkok, 2006.

26. Cawthorne P, Ford N, Limpananont J, Tienudom N, Purahong W. WHO must defend patients' interests, not industry. *Lancet* 2007; 369: 974–975.

27. Walt G, Shiffman J, Schneider H, Murray S, Brugha R, Gilson L. 'Doing' health policy analysis: methodological and conceptual reflections and challenges. *Health Policy and Planning* 2008; 23: 308–317.

28. Ainsworth M, Beyrer C, Soucat A. AIDS and public policy: the lessons and challenges of “success” in Thailand. *Health Policy* 2003; 64: 13–37.

## Chapter 2: Overcoming the human resource crisis

### 2.1. Introduction

The global effort to scale up ART gained momentum from late 2002 as the cost of treatment fell and international funding streams were established, notably with the establishment of the Global Fund for TB, AIDS, and the US President's Emergency Plan for AIDS Relief (PEPFAR) [1].

As programmes began to enroll increasing numbers of patients, so it became rapidly clear that the lack of qualified health personnel, particularly in Africa, would prove to be a major bottleneck to increasing access to treatment. As early as 2004, public health experts were beginning to raise attention to the human resource crisis in Africa [2].

In well-resourced Western countries HIV/AIDS has traditionally been managed as a specialized disease requiring a broad range of clinicians such as infectious disease specialists, dermatologists, oncologists, nephrologists, and pharmacologists. In contrast, the high-HIV prevalence countries of Africa which account for a dominant proportion of the global AIDS burden have a critical shortage of the most basic essential health staff: countries like Malawi, where adult HIV prevalence is around 10%, have almost 100 times fewer doctors per population compared to the UK [3]. This crisis is partly driven by proactive recruitment of health personnel by Developed countries, a practice that has been framed as an international crime [4].

It therefore became apparent that a simplified treatment paradigm was required in resource-limited settings, entailing a shift from a specialized medical approach to a public health approach in which the majority of clinical tasks would be undertaken by lower health cadres such as nurses [5].

Given the vast numbers of lives being lost to HIV/AIDS every day, such task shifting strategies had to be employed outside of a formal evidence base; rather than waiting for

randomized trial data to demonstrate that nurses could perform as well as doctors in the prescribing of antiretrovirals, operational research was conducted to assess the effectiveness of such a strategy at the same time as it was being rolled out as national policy.

Substantial evidence has now accumulated around the effectiveness of different modalities of task shifting, and this evidence is compiled in the first paper of this chapter that provides a systematic review of the evidence for task shifting [6]. The second paper in this chapter examines some of the policy implications of task shifting strategies, and provides some direction for future research in this field [7].

## 2.2. A systematic review of task shifting for HIV treatment and care in Africa

*Callaghan M, Ford N\*, Schneider H. Hum Resour Health 2010; 8: 8.*

### **Abstract**

**Background:** Shortages of human resources for health (HRH) have severely hampered the rollout of antiretroviral therapy (ART) in sub-Saharan Africa. Current rollout models are hospital-and physician-intensive. Task shifting, or delegating tasks performed by physicians to staff with lower-level qualifications, is considered a means of expanding rollout in resource-poor or HRH-limited settings.

**Methods:** We conducted a systematic literature review. Medline, the Cochrane Library, the Social Science Citation Index, and the South African National Health Research Database were searched with the following terms: task shift\*, balance of care, non-physician clinicians, substitute health care worker, community care givers, primary healthcare teams, cadres, and nurs\* HIV. Grey literature was searched online, and conference proceedings searched for abstracts.

**Results:** We found 2960 articles, of which 84 were included in the core review. 51 reported outcomes, including research from 10 countries in sub-Saharan Africa. The most common intervention studied was the delegation of tasks (especially initiating and monitoring HAART) from doctors to nurses and other non-physician clinicians. Five studies showed increased access to HAART through expanded clinical capacity; four concluded task shifting is cost effective; nine showed staff provided equal or better quality of care; studies on non-physician clinician agreement with physician decisions was mixed, with the majority showing good agreement.

**Discussion:** Task shifting offers high-quality, cost-effective care to more patients than a physician-centered model. The main challenges to implementation include adequate and sustainable training, support and pay for staff in new roles, the integration of new members

---

\* NF supported the literature review, undertook the methodological quality assessment and contributed to drafting and finalization of the manuscript.

into healthcare teams, and the compliance of regulatory bodies. Task shifting should be considered for careful implementation where HRH shortages threaten rollout programmes.

### **Introduction**

Sub-Saharan Africa suffers from the world's most pronounced human resources for health (HRH) crisis: 36 of the 57 countries that now face health worker shortages are in Africa [1]. These shortages intensify – and are intensified by – the HIV/AIDS pandemic. Much interest has recently been paid to how to streamline HIV care, both to offer high-quality care to patients and expand access to care. One response to this shortage has been the reassignment of clinical roles by shifting tasks to different cadres of health workers: nurses may become involved in prescribing drugs, lay counsellors involved in testing, new cadres may be introduced to perform specific tasks, and patients may be engaged to take over some elements of their own care. The objective is a streamlined, rationalized chain of care that relieves pressure on each worker involved while maintaining quality standards for patients and increasing access to interventions.

Task shifting is not a new phenomenon. In 19<sup>th</sup>-century France, *Officiers de Santé* [2] were an officially recognized and commonly used class of non-physician health care worker, while in China, 'Barefoot doctors' were widely deployed across the country in the mid-20<sup>th</sup> century [3]. In Africa, non-physician clinicians (NPCs) have long been trained across the continent to fill various roles [4-6]. Systematic reviews from various areas of health care provision support the general conclusion that good health outcomes can be achieved by task shifting to nurses [7] and lay- or community health workers [8-10].

The potential for task shifting in HIV care was elaborated by the World Health Organization's 2004 publication of Integrated Management of Adult and Adolescent Illness guidelines which recommended that nurses and clinical aids be trained to provide primary care for HIV [11]. In 2008, this was expanded and formalized by joint WHO/UNAIDS/PEPFAR guidelines for the implementation of task shifting [12] as an immediate way to address staff shortages while delivering good quality care. However, the rapidly emerging evidence from sub-Saharan Africa, where task shifting is seen as most relevant, has not been systematically reviewed. This is important, as task shifting has been the subject of some debate. Critics have argued that task shifting has become a 'bandwagon'

that is uncritically championed at the expense of ignoring existing health cadres, whose low pay and poor working conditions drive high attrition [13]. Several commentators have noted that even though this approach may be able to provide increased quality care for HIV-positive patients, task shifting should not be a substitute for investments in health care systems more generally [14-17], and that even the best staffing models will be inadequate in areas with an absolute shortage of all levels of staff [18]. Concern has also been expressed that shifting additional HIV tasks to lower cadres could risk competing with other service priorities [19-20], particularly given the overall shortage of nurses [21]. In some areas, community health workers already ‘fill in’ for nurses when the latter are unavailable [22-23].

These concerns underscore the need for careful, critical analysis, particularly where task shifting policies re-write the job descriptions of some cadres. If task shifting is already widespread in practice, if not in policy, the process should be formalized and rationalized for the long-term. This includes ensuring staff competencies and adequate working conditions [24]. This perspective takes for granted the unavoidable necessity of task shifting, and focuses on the need for a timely and logical policy response.

## **Methods**

We developed a search strategy combining the following search terms: (task shift\*) AND (balance of care OR non-physician clinician OR substitute health worker OR community care giver OR primary health care team OR cadres OR nurs\*) AND (HIV). Using these terms, we searched the following databases from inception up to May 2009: Medline via PubMed, Social Science Citation Index, the South African National Health Research Database, and the Cochrane Library. The abstract databases of the following two international AIDS conference databases were searched: all International AIDS Society Conferences (up to Cape Town, July 2009), all Conferences on Retroviruses and Opportunistic Infections (up to Montreal, February 2009), and all HIV/AIDS Implementers Meetings (up to Windhoek, June 2009) This search was complemented by reviewing the bibliographies of relevant papers and grey literature reviews, and personal communication with researchers in the field. Where abstracts identified in the search were known to be subsequently published, the reference was updated accordingly.

Our review included all articles that detailed approaches to task-shifting for the delivery of HIV care in Africa. Abstracts were initially screened by one reviewer (MC) and agreement for final inclusion was sought with other authors (HS, NF).

While the search methodology was systematic, the paucity and heterogeneity of the results prevent the drawing of ‘systematic’ conclusions on any particular task shifting practice. We therefore subsequently organized the findings within the context of current debates about task shifting as policy and practice according to five main themes: efficiency; access; quality of care; health outcomes; and team dynamics.

## **Results**

Our initial search yielded 2960 articles of which 84 were included in the core review. These included articles reporting outcomes (51), review articles (15), opinion pieces and position papers (12), papers elaborating theories and models (13), and policy analysis studies (6). Of those that reported outcomes, 25 were original articles (Table 2.2.1); the rest were supplementary presentations of the same study or programme.

### *Efficiency*

We found evidence that task shifting increases programme efficiency. A number of studies have quantified time saved by implementing task shifting on the assumption that delegating tasks gives senior clinical staff more time to deal with complicated patients. Time savings are an important outcome for HIV care and could help in addressing bottlenecks in treatment. A large study in Rwanda assessed time savings from nurse-initiated and monitored ART and concluded that such task shifting at the national level would result in a 183% increase in doctor capacity for non-HIV related tasks [25-6]. Reductions in waiting times and loss-to-follow-up have also been observed in task shifted HIV care models [27-30].

Doctor salaries can be the single-largest cost of running an ARV clinic. One South African study found that doctor salaries constituted roughly 42% of all clinic costs, including utilities and supplies [31]. Reducing dependence on doctors for ART could reduce clinic operating costs, or increase patient load for the same cost. A study comparing total average annual clinic-level cost per ART patient in Uganda and South Africa found that mean costs were

almost a third less in the former (\$US331 vs \$US 892) and concluded that task-shifting may have helped to reduce clinic costs and improve overall efficiency [32].

**Table 2.2.1. Characteristics and outcomes of studies on the impact of task-shifting in HIV/AIDS care**

Study	Setting	Study design	Intervention	Outcomes
Apondi et al, 2007 [65]; Tugume et al 2009 [66].	Uganda (rural)	Cohort	'Field officers' provide home-based ART	Cumulative outcomes at 4 years showed excellent adherence (96.8% were >95% adherent) and <1% defaulting. Social improvements: reduced stigma, stronger family and community relationships
Bedelu et al, 2007 [40].	South Africa (rural)	Cohort	Decentralized, nurse-initiated ART	Loss-to-follow-up was clinics 2% at clinics compared to 19% at hospital for comparable virological and immunological outcomes.
Bolton-Moore et al, 2007 [50]	Zambia (urban)	Cohort (paediatric)	Nurse- and clinical officer-initiated paediatric ART	Decentralization allows for dramatically scaled-up rollout; cumulative 3-year mortality (8.3%) and defaulting (5.4%)
Chiambe et al, 2009 [42].	Kenya (urban and rural)	Cohort	Lay health care workers supporting basic clinic tasks and adherence counselling	Enrollment increased from 1,176 to 39,900 patients within 3 years
Cohen et al, 2009 [55].	Lesotho (rural)	Cohort	Nurse-initiated ART	Favourable outcomes at 12 months among adults (9.3% mortality, 2.5% defaulting) and children (5% mortality, 2% defaulting)
Jaffar et al, 2009 [59].	Uganda (rural)	RCT	Home vs clinic-based ART delivery	Similar outcomes of mortality and viral suppression in home-based and faculty-based ART
Shumbusho et al, 2008 [47].	Rwanda (rural)	Concordance study	Nurses trained in ART initiation	Discordance between eligibility and initiation <1% (n=343)
Torpey et al 2008 [27].	Zambia	Cohort (quantitative and qualitative analysis)	Lay-workers used as 'adherence supporters'	Lay adherence supporters reduced loss-to-follow-up from 15% to 0%; reduced wait times
Van Griensven et al, 2008 [57].	Rwanda (urban)	Cohort	Nurse-initiated paediatric ART	84% retention and 83% viral suppression at 2 years
Wood et al, 2009 [45].	South Africa (urban)	RCT	Doctor vs nurse-initiated ART	Non-inferiority according to virological failure, toxicity, adherence, and mortality.
Zachariah et al, 2007 [62].	Malawi (rural)	Cohort	Community support vs no support	26% increase in survival; 98% reduction in loss to follow up.

### *Access*

Efficiencies make possible increased access and affordability. Several studies have reported an increase in access to counselling and testing through task shifting and the “up-training” of clinic staff [33-7]. In Botswana, the training of nurses to prescribe and dispense antiretroviral therapy increased uptake of antiretroviral therapy, with nearly 20,000 patients receiving treatment at rural clinics as of December 2007 [38]. In Zambia intensive training in a task shifted model of ART rollout was able to expand treatment access substantially without compromising quality of care [39]. In Lusikisiki, South Africa, district-wide access to ART was achieved within 2 years with a task-shifted model of care [40]. Similar scale up has been reported in Mozambique [41], Kenya [42], and Swaziland [43]. Finally, a costing study from Malawi found that district-wide access to ART using a non-physician model of care was achieved for an additional \$2.5 per capita, well within the estimated minimal basic health package costs (WHO) [44].

### *Quality of care*

Provider performance is a crucial indicator, since lower-level cadres who require constant supervision, or who under- or over-refer patients, will save neither time nor money, nor improve the health of their patients. Several studies have evaluated task shifting against a ‘gold standard’ of care.

We identified only one randomized controlled trial that directly compared the effectiveness of doctors and nurses for HAART delivery in sub-Saharan Africa. This study found that nurse-managed ART was non-inferior to doctor-managed ART in urban clinics in Johannesburg and Cape Town, South Africa: both treatment arms had similar outcomes of viral suppression, adherence, toxicity and death [45]. A study done in the Democratic Republic of Congo looked at concordance between doctor and nurse decisions to initiate ART and found 95% agreement on ART initiation [46]. Similarly in Rwanda, nurses performed extremely well, accurately determining ART eligibility for >99% of patients [47]. In Mozambique, patients seen by mid-level workers (with 2.5 years training) were almost 30% more likely to have CD4 counts done at 6 months post ART initiation than those seen

by doctors, and were 44% less likely to be lost to follow-up. There were no significant differences in mortality, CD4 counts done at 12 months, or adherence rates [48]. Finally, a study from Malawi found that the training of lay workers as pharmacy assistants reduced prescribing errors by 25% by unburdening the system [49].

### *Health Outcomes*

Several studies have assessed patient health outcomes in HIV services where tasks have been shifted to nurses and lay workers, against internationally accepted standards. A study of nurse initiated and managed paediatric ART in Zambia showed good clinical outcomes [50]. Similarly, a study of a primarily nurse-driven ART program in Kampala, Uganda, reported very good clinical outcomes after 2 years [51]. In each of these examples, the high level of performance of task-shifted workers has occurred in a context of in-depth training and ongoing support. The need for ongoing training was highlighted by a study in Mozambique where expert clinicians oversaw the work of mid-level providers and found errors in antiretroviral management in over 40% of cases; errors were associated with duration since pre-service training [52].

A decentralized programme in rural South Africa involved mainstreaming uncomplicated HIV care to lower-level cadres (specifically, nurses and ‘adherence counsellors’) in clinics [40]. In a cohort study of 1025 patients, loss-to-follow-up at the ‘decentralized’ clinics was 2.2%, compared with 19.3% at the relatively centralised hospital, and patients with CD4 >200 was 87.1% compared with 14.2%. Other programmes in South Africa have reported similarly good outcomes for patients managed by non-physician health workers [53]. Nurse-managed programmes in Lesotho [54-5] and Rwanda [56-8] have also reported highly satisfactory outcomes in terms of mortality and retention-in-care for both adults and children.

Home-based care, treatment support, and other extra-clinical services provided by lay health workers have been shown to be effective in sub-Saharan Africa. A randomized trial in Uganda [59] comparing home-based and facility-based care found similar rates of viral load suppression, failure and mortality. A community-based program offering home-based ART through lay providers in Uganda achieved excellent outcomes without recourse to regular

clinic visits [60]. Adherence to antiretroviral therapy improved after the introduction of lay counsellors and field officers [60-61], with a study from Malawi showing that patients who were offered community support had significantly better survival and retention-in-care rates compared to patients who did not receive such support [61]. In one Malawian study [62], however, community health workers did a comparatively poorer job of identifying eligible patients for ART compared to clinicians, pointing to the limits of which tasks can be shifted, and underlining the need to address the question of what tasks can be delegated, and to whom

Non-medical patient outcomes have also been measured in task-shifted models of care. In Uganda, the implementation of home-based ART through community health workers is associated with positive social outcomes, including an increase in social and family support and strengthened relationships [63-66].

### *Team Dynamics*

The process of task shifting can influence the social dynamics within clinics. An ethnographic study of a task shifted ART scale-up program in Cameroon [67] found a pervasive tension between nurses and community health workers, and ambiguity around the definitions of roles and hierarchies within the clinic. It concluded that task shifting policies must anticipate this problem and clearly delineate processes and responsibilities for existing and newly created health cadres.

One recent South African study [68] suggested that task shifting leads not only to higher job satisfaction among staff, but to lower workload and usage of sick leave. The same study, however, reported higher staff turnover and poorer physical state of premises at task-shifted clinics. A qualitative survey done in rural Uganda found that almost all clinic staff interviewed (97%; n=37) strongly agreed or agreed that peer health workers improved the care of patients, and 86% strongly agreed or agreed that peer health workers had made their own jobs easier [69]. In a structured survey conducted among 62 national/provincial managers and HIV clinic staff in Mozambique, respondents indicated that NPCs should initiate ART for adults (100%), pregnant women (95%), and patients with TB (83%) [70]. In an evaluation of a programme in Uganda and Zambia where lay counsellors provide basic

triage, intensive adherence support and assist in the provision of ART, their performance was rated as good or very good by 97% of health providers who were interviewed (n=42); acceptability was also 97% [71].

The importance of ongoing training has been highlighted by qualitative interviews. Community health workers in South Africa [72] report a desire for better training and supervision to meet the formidable challenges posed by the synergy of HIV, TB and poverty. Similarly, a study done in Zambia found that additional training needs were identified by almost 85% of lay counsellors [73].

Finally, task shifting is recognized as a valuable way to take increase patient involvement in care [74]. People living with HIV/AIDS represent a largely ‘untapped pool’ of treatment supporters who will continue to grow apace with prevalence and are more likely to remain in their communities than more mobile higher-cadre health workers [75]. Their involvement as active participants in health care delivery will require the negotiation of new power dynamics between patients and care givers and training and supervision where appropriate.

### **Assessment of methodological quality of studies**

We undertook an assessment of methodological quality for the original studies reporting quantitative outcomes included in this review (webappendix) to assess all studies on criteria relating to methodological quality. These included: sampling, methodology (comparative design or not, including randomization), use of objective outcomes, and discussion on sources of bias and generalizability of findings. Of the 25 original studies included in this review, 11 included a comparative approach; for 2 studies randomization was done. The majority of studies (21) used objective outcome measures. Twelve studies were published as full peer review articles (the rest appeared as conference abstracts), allowing for a more complete assessment. Among these, all employed an appropriate statistical analysis, but only half (6) discussed potential sources of bias. The majority (11) included discussion about the generalizability of findings.

### **Discussion and conclusion**

The challenges facing Africa's health care system in responding to the human resource crisis urgently require policies and practices based on robust, policy-relevant evidence [76]. Although formal cost effectiveness studies have not been done, the available evidence for task shifting in HIV care supports the conclusion that it is both effective and economical [77]. Non-physician health care workers are able, with careful training and supervision, to deliver equal and sometimes better results than doctors; similarly there is now considerable evidence regarding the possibility of shifting tasks from professionals or mid-level workers to lay or community health workers. Further, task shifted models of care may foster other beneficial outcomes in the socio-cultural sphere. Perhaps most importantly, task shifting can substantially expand access to HIV interventions, even in under-serviced areas.

This literature review found that studies to date are marked by substantial heterogeneity [78-9], and identified several gaps in current research on task shifting. In particular, more research is needed on how the social dynamics in health care teams may be affected by task-shifting policies, as are broader approaches to assessing the outcomes of certain aspects of task shifting, including the management of HAART by cadres lower than nurses. In this regard, while data emerging from randomized controlled trials are important, it is unlikely that this approach is the most appropriate as such complex studies are unlikely to yield data in time to inform such a rapidly changing environment. Nevertheless, our assessment of methodological quality highlights some considerations for improving the design and analysis of future studies. Another important gap relates to the analysis of professional, regulatory and other barriers to policy change in specific contexts.

This review used a comprehensive search strategy that included multiple databases and grey literature sources. The fact that over half of the studies that comprised the core of this review are not yet published in peer-reviewed journals is both strength and a limitation of this review. The aim of systematic reviews is to assemble data from both published and unpublished sources to minimize publication bias. However, the inclusion of unpublished studies may lead to the reporting of problematic information that would otherwise be noted during peer reviews.

Policies on task shifting must be considered in context. Decisions of exactly which type of task shifting (involving doctors, nurses, community health workers, or patients) to implement will also have to be made according to each country context where task shifting will involve a different set of politics, professional and social dynamics, and resource and training needs. This will determine, in line with available evidence, which cadres can reliably perform which tasks, where to set performance thresholds, and how to ensure the best fit with existing roles and scopes of practice. The importance of processes surrounding task shifting are a recurring theme in the literature: appropriate integration into staff structures, adequate pay, and ongoing support and supervision, all require careful attention. More broadly, task shifting has to be engaged within broader health system goals of building access, equity and responsiveness; and where task shifting involves the mobilisation of community health workers, to questions of community participation and accountability [80].

There appears to be consensus that task shifting alone will not solve human resources problems in HIV services, or in health care more generally, in areas with substantial staff shortages and failing health systems. Indeed, health care worker shortages remain a major impediment to the scale-up of antiretroviral therapy in sub-Saharan Africa. Nor should task shifting be considered simply as a means of saving money: while it makes for more efficient uses of clinical resources, in contexts of worker shortages task shifting is primarily a means of extending access to quality care to a greater number of people. Ultimately, task shifting may offer cost-effectiveness rather than cost-savings, and will require strong government leadership to ensure that an enabling regulatory framework, and adequate training and financing [80].

In conclusion, our literature review finds that task shifting is a viable and rapid response to sub-Saharan Africa's human resources crisis in HIV care. Carefully focused action is needed at this stage, not to determine whether task shifting is possible or effective, but to define the limits of task shifting and determine where it can have the strongest and most sustainable impact.

## 2.3. Task shifting in HIV/AIDS: opportunities, challenges and proposed actions for sub-Saharan Africa

*Zachariah R, Ford N\*, Philips M, Lynch S, Massaquoi M, Janssens V, Harries A. Trans R Soc Trop Med Hyg 2009; 103: 549-58.*

### **Abstract**

Sub-Saharan Africa is facing a crisis in human health resources due to a critical shortage of health workers. The shortage is compounded by a high burden of infectious diseases; emigration of trained professionals; difficult working conditions and low motivation. In particular, the burden of HIV/AIDS has led to the concept of task shifting being increasingly promoted as a way of rapidly expanding human resource capacity. This refers to the delegation of medical and health service responsibilities from higher to lower cadres of health staff, in some cases non-professionals. This paper, drawing on Médecins Sans Frontières'(MSFs) experience of scaling-up antiretroviral treatment in three sub-Saharan African countries (Malawi, South Africa and Lesotho) and supplemented by a review of the literature, highlights the main opportunities and challenges posed by task shifting and proposes specific actions to tackle the challenges. The opportunities include: increasing access to life-saving treatment; improving the workforce skills mix and health-system efficiency; enhancing the role of the community; cost advantages and reducing attrition and international 'brain drain'. The challenges include: maintaining quality and safety; addressing professional and institutional resistance; sustaining motivation and performance and preventing deaths of health workers from HIV/AIDS. Task shifting should not undermine the primary objective of improving patient benefits and public health outcomes.

---

\* NF contributed to the conceptualization of the study, undertook the literature review, co-wrote the first draft of the paper, and contributed to all subsequent drafts.

## Introduction

At the end of 2006 the WHO estimated that there are 57 countries facing critical shortages of health workers. Over half of them (36) are in Africa and an additional 2.4 million doctors and nurses are needed to meet the Millennium Development Goals [1]. In sub-Saharan Africa the situation constitutes a human resource crisis due to significant emigration of trained professionals; difficult working conditions; poor salaries; low motivation and a high burden of infectious diseases, particularly HIV/AIDS, among the workforce [1-3]. Sub-Saharan African countries are hardest hit in terms of emigration of trained health staff, both to South Africa as well as to countries in the West. Malawi, for example, has two doctors per 100 000 population, which is 10 times below the WHO minimum standard, while South Africa has 77 doctors per 100 000 population. In Western countries that attract health workers from countries such as Malawi the availability of doctors is even higher at 256 per 100 000 in the USA, 214 in Canada and 230 in the United Kingdom. Similarly, the number of nurses per 100 000 population is 59 in Malawi compared with 937 in the USA, 995 in Canada and 1212 in the United Kingdom [4,5].

**Table 2.3.1 Types of task shifting commonly seen in Africa [13].**

Type of task shifting	Definition	Example
Type I	The extension of the scope of practice of <i>non-physician clinicians</i> in order to enable them to assume some tasks previously undertaken by more senior cadres, e.g. doctors	Clinical officers deciding eligibility and prescribing ART (Malawi)
Type II	The extension of the scope of practice of <i>nurses</i> and <i>midwives</i> in order to enable them to assume some tasks previously undertaken by senior cadres	Nurses treating opportunistic infections and prescribing ART (Botswana, Ethiopia, Uganda, Malawi)
Type III	The extension of the scope of practice of <i>community health workers</i> or <i>lay providers</i> in order to enable them to assume some tasks previously undertaken by more senior cadres	Community health workers providing ART counseling and HIV testing (Uganda, Rwanda, Malawi)
Type IV	<i>People living with HIV/AIDS</i> , trained in self-management to assume some tasks related to their own care	Provision of basic HIV support, treatment adherence and psychosocial support.
Type V	The extension of the scope of practice of other cadres that do not traditionally have a clinical function, e.g. <i>pharmacists, laboratory technicians, administrators, record clerks</i>	Record clerks filling in basic patient information at HIV clinics (Malawi)

The scale-up of antiretroviral treatment (ART) in sub-Saharan Africa has highlighted the human resource challenge of delivering and sustaining this life-saving intervention [6-8]. Consequently, the delegation of medical and health service duties from higher to lower cadres or new cadres, known as task shifting, is increasingly promoted as a coping mechanism for general and specific human resource shortages. Table 2.3.1 on the previous page classifies different types of task shifting commonly seen in Africa.

The concept is not new and has been employed in the past to support a range of health service demands. Examples include surgical technicians in Mozambique [9]; nurse-anaesthetists and clinical officers in Malawi, Ghana, Tanzania and Zambia [2,10]; and the deployment of community health workers in multiple countries [11]. Over half the countries in sub-Saharan Africa have recourse to non-physician clinicians [12]. Recently, task shifting has gained considerable momentum, with the WHO releasing specific guidelines and recommendations on task shifting [13]. In as much as task shifting raises many potential opportunities for the health system, there are associated challenges which need to be addressed to ensure that this mechanism does not undermine the primary goal of improving patient benefits and public health outcomes.

This paper, drawing on Médecins sans Frontières (MSF's) experience of scaling up ART in three sub-Saharan African countries (Malawi, South Africa and Lesotho), and supplemented by a review of the literature, highlights the main opportunities and challenges posed by task shifting and proposes specific actions to tackle the challenges.

### **Opportunities presented by task shifting**

#### *Improves access to life-saving treatment and improves survival*

The task-shifting process requires the development of standardized protocols, including simplified clinical guidelines, simplified recording and reporting systems and simplified monitoring and evaluation. These measures facilitate the decentralisation of interventions to lower levels of the health system, and are associated with improved access, increased national coverage and better geographical equity, the latter parameters being of key importance in ART scale-up efforts.

This is illustrated in Malawi, where the national ART scale-up plan launched in 2004 involved non-physician clinicians providing ART [7,14]. By September 2007, 130 488 patients had been started on ART at 154 health facilities (Ministry of Health ART Quarterly Report: Results up to 30 September, 2007). Task shifting, coupled with a simplified and standardized public health approach and strong supervision, made it possible to scale up ART with acceptable quality standards resulting in many lives saved [7].

In Malawi, Lesotho and in Lusikisiki, South Africa, nurses initiated and managed ART at rural primary health clinics with support from mobile medical teams who provided clinical mentoring. This enabled access for patients who otherwise might not have received the treatment they needed. When task shifting from doctors to nurses was reversed in Lusikisiki patient enrolment rates dropped precipitously [15].

*Optimizes skills of the health worker team to cope with growing patient loads*

Task shifting stimulates the creation of multidisciplinary teams with a better strategic skills mix [16]. For example, a model of HIV care in which nurses initiate ART and doctors supervise and manage complex cases is being promoted by the WHO [13]. In Botswana [17], Mozambique [18], Malawi (A.D. Harries, unpublished observations), Lesotho and the Democratic Republic of Congo (N. Ford, unpublished observations), this strategy has met with success: nurses have reduced the dependence on doctors by taking on clinical tasks such as determining ART eligibility; prescribing first-line regimens; and managing follow-up and common side-effects of medication, while senior clinicians manage complicated cases. An overview of how a team of health staff, community workers and people living with HIV/AIDS either changed their roles or took up new roles within a multidisciplinary team is given by the HIV/AIDS programme in Lusikisiki, South Africa [19].

*Engages the community to address health needs*

Communities are increasingly recognized as an underexploited resource in the delivery of ART. Community health workers have had a significant positive impact, particularly on reducing mortality linked to childhood pneumonia [20], malaria [21] and tuberculosis (TB) [22]. In HIV care the deployment of lay counsellors has resulted in a dramatic uptake of

HIV testing services in Thyolo, Malawi, [23] Lusikiski, South Africa [19], and Lesotho [8]. Communities can also contribute in a comprehensive manner to ART delivery as seen in Malawi (Table 2.3.2) [23,24] Community workers also have a positive influence on health-seeking behaviour among people with HIV/AIDS, help to reduce stigma and discrimination [24,25] and often play a critical role in adherence support [26]. People with HIV/AIDS have also been effectively mobilized as partners in the provision of care. One programme that trained people with HIV/AIDS to screen for signs and symptoms of immune deficiency and to refer people to hospital if they were not on prophylaxis resulted in a 40% increase in those receiving co-trimoxazole and fluconazole prophylaxis [27].

**Table 2.3.2. Community support for ART delivery in Thyolo District, Malawi [24].**

Component	Specific activities
Management of opportunistic infections	Home-based diagnosis and management supervised by community nurses  Symptomatic treatment for diarrhoea, fever, oral candida and common skin conditions  Monthly supply of CTX prophylaxis for individuals too ill to travel to health facilities
Recognition and referral of individuals with risk signs to community nurse or hospital	Referral of patients with worsening signs of dehydration despite oral rehydration, persistent difficulty in swallowing despite medication for oral thrush, reduced level of consciousness, progressive worsening of headache, increased breathlessness despite CTX prophylaxis, cough >3 weeks, focal palsies, violet discoloration of palate or skin
Adherence counselling	One-to-one supportive counselling for CTX and ART
Counselling on drug reactions and early referral	Early recognition and referral of individuals having possible drug reactions to ART, CTX or anti-TB treatment
Defaulter tracing	Active tracing of individuals who do not attend scheduled follow-up visits or drug collection appointments
Nutritional support	Distribution and monitoring of supplementary dry rations to malnourished patients
Support to family caregivers	FCG's provide HIV education; counselling on ART, CTX and anti-TB treatment; early recognition of possible drug reactions; nutritional supplementation and palliative care
Community mobilization and awareness	Various forms of information, education and communication as well as vocational and income-generating activities

CTX: co-trimoxazole prophylaxis; FCG: family caregivers

*May provide cost benefits for patients and health systems*

Both the cost of initial training and the remuneration of medical assistants and clinical officers are lower than for doctors, especially as the education and pre-service training periods are shorter. Data from five sub-Saharan African countries show that training time and costs for non-physician clinicians are lower than for doctors [12] and they can be as much as 10 times less expensive, with comparable performance, as seen in Mozambique [9]. A simplified approach might also rationalise the use of diagnostic tests and sophisticated equipment [28], although this potential advantage might be negated by individuals with weaker clinical acumen who would have an increased reliance on such tests and equipment. While these costs do not include the cost of systems adaptations to support task shifting, such as supervision and a strong referral system, the overall costs are likely to remain lower, particularly at the lower end of the health cadre spectrum.

From a patient perspective, travel and indirect costs are also expected to be lower since people generally live a shorter distance from a nurse- or medical assistant-run facility than a doctor-based facility [2]. Travel costs have been associated with a high rate of defaulting from HIV care [29]. It should be recognized, however, that cost saving alone is not a valid reason for task shifting, as in-service training and supervision may negate much of the saving made by switching to lower cadres. Above all, compromising on quality of care should not be tolerated at any cost.

*Increases retention and reduces the risk of international 'brain drain'*

Task shifting can meet specific needs by establishing new cadres that are better retained in rural and hardship areas because their qualifications are generally not recognized internationally. The 'brain drain' of health staff from Africa to developed countries is a major factor contributing to the current human resource crisis, and this local specificity supports staff retention [3]. A follow-up study of a task-shifting programme to engage non-physician clinicians in obstetric care in Mozambique found that after 7 years around 90% of non-physicians were still working in the district hospital while almost all of the doctors had left [30]. Finally, task shifting can be expected to support the retention of existing cadres by

reducing burnout and increasing morale through more efficient team management of patient case-loads.

## Challenges and proposed actions

### 1. *Quality of care and safety*

Evidence from Lusisiki in South Africa and Thyolo in Malawi showed that the use of nurses (Type II task shifting) [19] and community cadres (Type IV task shifting) [24] in the delivery of ART significantly improved overall ART outcomes (Table 2.3.3).

**Table 2.3.3. Antiretroviral treatment (ART) outcomes involving task shifting at community and health centre levels.**

	Thyolo district, Malawi <sup>a</sup> [24].		P-value <sup>c</sup>	Lusisiki, South Africa <sup>b</sup> [19]		P-value <sup>c</sup>
	With CHWs <i>n</i> (%)	Without CHWs <i>n</i> (%)		Health centres <i>n</i> (%)	Hospital <i>n</i> (%)	
Placed on ART	895	739		595	430	
Alive and on ART	856 (95.6)	560 (75.8)	<0.01	482 (81)	289 (67.2)	<0.01
Died	31 (3.5)	115 (15.6)	<0.01	100 (16.8)	58 (13.5)	0.15
Lost to follow-up	1 (0.1)	39 (5.3)	<0.01	13 (2.2)	83 (19.3)	<0.01
Stopped	7 (0.8)	25 (3.4)	<0.01	--	--	
CD4 count at 12 months						
Determined				348 (58.5)	81 (18.8)	<0.01
≥200 cells/mm <sup>3</sup>	--	--		303 (87.1)	61 (75.3)	0.08
	--	--				
Viral load at 12 months						
Determined				296 (49.7)	41 (9.5)	<0.01
<400 copies/ml	--	--		265 (89.5)	32 (78)	0.33
	--	--				

NA: not available. a Thyolo district: patients registered between April 2003 and December 2004. b Lusisiki district: patients registered between January 2004 and June 2005. c X<sup>2</sup> test.

Thus, from a public health perspective, the use of task shifting for HIV/AIDS care at two relatively new levels of the health system (health centres and the community) did not compromise quality but, on the contrary, was associated with significantly better ART outcomes.

There is a wealth of supportive evidence from outside HIV care. In a study comparing medical assistants with doctors and looking at the quality of child care in Malawi, doctors, medical assistants and nurses were found to have a similar level of diagnostic ability when examining children under 5 years of age [31]. One study looking specifically at the delivery of HIV services found that the quality of HIV care provided by non-physician clinicians was similar to that provided by medical doctors who were HIV experts, and better than that provided by medical doctors who were not HIV experts [32]. In Mozambique a detailed assessment of over 10 000 surgical interventions by medical assistants showed that quality (measured in terms of complication rates) was effectively identical to interventions by doctors [9]. A study in Benin showed that higher percentages of children with diarrhoea received oral rehydration therapy and more children with fever were appropriately treated with a recommended antimalarial drug by nursing aides than by nurses (intermediate) or physicians (worst performance) [33,34].

These findings show the important contribution of nonprofessional health workers (Type IV task shifting) to achieving child survival goals, not because they can perform clinical tasks better than professionals (they almost certainly cannot) but because they may adhere more strictly to simple clinical practice guidelines.

### *Proposed actions*

Patients, health staff and policymakers should be involved in setting measurable targets and indicators for an acceptable level of quality for a given intervention. Such targets and indicators can serve as benchmarks for supervision, monitoring and evaluation of specific interventions, which in turn serve to protect patients and providers. Evidence and experience suggest that inappropriate curricula, poor supervision and weak regulatory mechanisms affect the quality of care provided by any cadre. Examples include the poor ability of medical and nursing graduates in Ghana and Tanzania to deliver quality family

practice [2] and medical assistants persisting with unconventional treatment patterns after in-service training [35].

Strong supportive supervision and continuous education are proven strategies to improve patient outcomes [36]. In Malawi, Lesotho and Lusikisiki MSF provided theoretical and practical training for nurses, introduced tools adapted for nurses and provided on-site clinical mentoring, with good associated patient outcomes [8,19,24].

Accreditation of individuals and sites is one way to ensure that health workers have the necessary skills and capacity for specific interventions and that these are maintained over time. If standards are not met accreditation should be suspended or removed, as is practiced in Malawi for the delivery of ART [14]. Registration of health workers by a licensing or regulatory authority legitimizes a cadre and ensures institutional responsibility for the performance of that particular cadre.

## ***2. Resistance to task shifting***

Experience shows that task shifting may not be readily accepted by various professions. Doctors and pharmacists have objected to the delegation of their tasks to what they perceive as ‘half-baked doctors’ [12]; nurses have resisted taking on doctors’ roles without commensurate salary increases [2]; professional groups have objected to a potential loss of earnings where remuneration includes a fee-for-services component [37], professional councils and associations have in some instances resisted delegation of tasks to lower cadres [8,38] and finally, the additional supervisory responsibilities that come with shifting tasks from higher to lower cadres have also met with resistance.

Informal task shifting, as an *ad hoc* response to need rather than as an explicit policy, may result in the proliferation of new cadres with vague or overlapping responsibilities, which are then questioned by existing staff, policy-makers and the patients themselves, as seen in Tanzania [2].

## ***Proposed actions***

Key questions relating to task shifting include: what tasks are needed to deliver a particular intervention; which personnel currently undertake these tasks; what are their annual productivity and attrition rates and who could safely do these tasks instead?

Once tasks have been defined, appropriate training (pre- or in-service), clear job descriptions and remuneration packages need to be established [38]. Inter-cadre relationships can be improved by consulting with existing cadres prior to and during the process of task shifting. Clear delineation of professional boundaries and responsibilities are needed to foster teamwork.

Coordination and consultation from the outset with key regulatory bodies such as medical and nursing councils, as well as with relevant government ministries (health, education, labour), are essential. Finally, as legal changes in regulatory frameworks can take years to be enacted, approaches that use other policies to create an enabling environment such as changes in strategic plans, the passing of ‘executive orders’ or granting ‘temporary pilot status’ to programmes engaged in task shifting may be more expedient, especially if the package of services to be delivered is urgent as is the case for ART. Particularly in rural areas informal task shifting occurs out of necessity among limited health staff struggling with an overwhelming burden of patients. Care must be taken not to ban such initiatives that may occur outside existing regulatory frameworks but contribute to delivering effective care.

### ***3. Motivation, retention and performance***

Poor salaries have been a key factor behind job dissatisfaction and the migration of nurses from sub-Saharan Africa to Western countries [39-41] where one in five nurses trained in sub-Saharan Africa currently work. Low salaries also have an impact on patient care. For example in Malawi, participation in workshops is more lucrative than doing clinical work: by attending a 5 day training course a nurse can increase her basic monthly salary by 25-40%. The plethora of workshops and per diems (which provide untaxed top-ups for low salaries) acts as a perverse incentive, encouraging absenteeism from health facilities, which increases the workload for the remaining staff. A survey in Nigeria found that 45% of staff supplemented their income privately [42]. Poor working and living conditions of staff are also important issues, particularly in rural areas. In a report from Lusikisiki, South Africa,

where a third of all nursing posts were vacant, only one-third of the 12 existing clinics had electricity, barely 8% had running water and half lacked nursing accommodation [8]. Finally, the lack of supportive supervision and opportunities for professional and career development affect staff morale, motivation and job satisfaction.

### *Proposed actions*

Health workers must receive a decent salary that constitutes a living wage and that is commensurate with their responsibilities. Although task shifting may be seen as a pragmatic method to deal with staff shortages there is a real potential for exploiting vulnerable workers who might continue to be paid only for work for which they are qualified. Payment must therefore be linked to the level of responsibility and increasing workload associated with task shifting. If this is not taken into consideration it could affect the long-term viability of task shifting. There is an urgent need to lift national spending limits imposed by finance ministries and international finance institutions such as the International Monetary Fund so that governments can increase salaries. Performance-related allowances have been shown to be both feasible and effective [44] and should be encouraged. An incentive package to attract individuals to rural areas is needed and should include good housing; better work-related infrastructure and equipment; transport (e.g. motorcycles); hardship or rural allowances and arrangements or subsidies for school and boarding.

Regular supervision visits are critical for maintaining staff motivation. The use of token benefits such as certificates of excellence in ART delivery in Malawi [14] and the Yellow Star award programme in Uganda [45] that recognize performance according to set standards are highly appreciated by health staff as indicators of official recognition.

Since the qualifications of substitute health workers may not be accredited by universities, introducing mechanisms to advance professionally is essential for motivating lower cadres of health workers.

#### *4. Livelihoods of lay health workers*

Lay counsellors and community-based volunteers have become the backbone of many care and support activities linked to HIV/AIDS and TB in sub-Saharan Africa, but the

appointment of these cadres is often considered to be a temporary measure, without any longer-term perspective [46].

Where their status remains that of an unpaid volunteer, a threshold is likely to be reached where the volunteers will have to choose between time dedicated to service support and time required to make a living. Most of the existing evidence demonstrates that lack of payment or other appropriate commensurate incentive(s) results in progressive deterioration in activity rates and high dropout rates of community workers [47-49]. There is virtually no evidence to show that volunteerism can be sustained for long periods [47].

### *Proposed actions*

Community groups should not become a ‘dumping ground’ for responsibilities that should fall under the mandate of public services (24,50,51). Some countries in sub-Saharan Africa, facing serious shortages of human resources in the health sector and high HIV prevalence, have introduced remunerated HIV-dedicated lay cadres. In Malawi the health surveillance assistant is a community cadre that has been fully integrated within the national system of service delivery and receives payment from government. Similarly, the post of paid community HIV/AIDS worker could be developed to support the work of community health workers and both cadres could work together, thus sustaining community health and HIV-specific activities without jeopardizing the livelihoods of individuals who live in communities that are living in or on the limits of poverty.

### *5. Health of medical personnel*

Death from HIV/AIDS is a major contributor to healthcare worker shortages in sub-Saharan Africa [52]. In Malawi it is estimated that over 10% of all health workers had died of AIDS by 1997 [53]. A survey carried out in all district and main mission hospitals in the same country found a 2% annual death rate among key healthcare workers, with AIDS and TB being the most common causes [54]. Death from HIV/AIDS accounted for up to 40% of all the attrition of nurses in Zambia [55] and was the main reason for the attrition of health workers in Lesotho [8]

### *Proposed actions*

Occupational health services and staff policy guidelines that cover HIV prevention and care would go a long way towards keeping staff in good health. Access to voluntary counseling and HIV testing services; isoniazid prophylaxis for nosocomial TB; co-trimoxazole prophylaxis; post-HIV exposure prophylaxis and ART and TB care should be available to all health staff and their families. Evidence from Malawi on offering ART to health workers showed that at least 250 health workers' lives were saved due to ART, representing the equivalent of 1000 health worker days per week, the number required to implement the national ART programme [56]. An additional benefit is the reduction in absenteeism due to illness or to attend colleagues' funerals.

### *6. Operational research in task shifting*

There are limited data and evidence for how task shifting influences the quality, safety, acceptability, cost, management and impact of interventions in sub-Saharan Africa. Such information is required to inform and guide policy.

#### *Proposed actions*

Table 2.3.4 lists some of the main operational research priorities for task shifting of HIV/AIDS care in sub-Saharan Africa. Countries, organisations and academic institutions need to make efforts towards finding answers to these pressing questions.

### **Conclusions**

Task shifting must be seen as part of an overall strategy that includes tangible measures to increase, retain and sustain existing and new cadres of staff [57]. In addition to task shifting, the crumbling health systems of sub-Saharan Africa badly need an increased human resource pool that is flexible, motivated and able to respond to the increasing disease burden and the changing landscape of public health needs. What is demanded of the medical profession is flexible pragmatism to safeguard both quality and safety and to prioritize patient needs above those of the profession.

**Table 2.3.4. Operational research priorities for task shifting of HIV/AIDS care in sub-Saharan Africa**

<b>Issue</b>	<b>Examples</b>	<b>Study approach</b>
<i>Quality and safety</i>		
How does task shifting to different cadres influence the quality of care?	ART initiation and follow-up of adults and children on first-line regimens by nurses or nurse assistants	Cohort outcomes: enrolment rates, adherence, biological outcome; comparative performance studies (case-control, comparative cohort, RCT)
<i>Acceptability</i>		
Do societal and cultural values and preferences influence the choice of cadres for task shifting and skills mix?	Community view on the role of hospital vs. the health centre and on the ability of lay workers to perform clinical tasks	Qualitative survey
How do patients and the community perceive being treated by a lower cadre?	Community acceptance of care managed by non-physicians	Qualitative survey
What are the perceptions of health staff, particularly in relation to confidence and satisfaction with a new skills mix?	Doctor acceptance of nurse initiation of ART; nurses accepting higher levels of responsibility in clinical care	Qualitative survey
<i>Health system impact</i>		
Is task shifting cost effective?	What is the cost benefit of moving towards nurse-initiated ART?	Comparative cost analyses
Assessment of payment and incentive structure(s) to ensure commitment and long-term sustainability	To what extent do non-remunerative incentives support staff retention?	Qualitative surveys, retention studies
Cost differences between vertical and integrated approaches to HIV management	Cost benefit of providing HIV care at primary care level	Comparative cost analyses
<i>Public health impact</i>		
Does introducing task shifting improve earlier access and service efficiency	Does the introduction of task shifting increase ART initiation rates	Comparative analysis of programme data over time
What is the overall impact of task shifting on scaling-up HIV/AIDS interventions?	How does task shifting affect ART enrolment rates at the population level?	Enrolment, retention in care, coverage

ART: Antiretroviral treatment; RCT: randomized controlled trial.

## 2.4. References for Chapter 2

### 2.1 Introduction

1. Schwartlander B, Grubb I, Perriens J. The 10-year struggle to provide antiretroviral treatment to people with HIV in the developing world. *Lancet* 2006; 368:541–546.
2. Kober K, Van Damme W. Scaling up access to antiretroviral treatment in southern Africa: who will do the job? *Lancet*. 2004; 364: 103-7.
3. World Health Statistics 2007. WHOSIS (WHO Statistical Information System).
4. Mills EJ, Schabas WA, Volmink J, Walker R, Ford N, Katabira E, Anema A, Joffres M, Cahn P, Montaner J. Should active health worker recruitment from sub-Saharan Africa be viewed as a crime? *Lancet* 2008; 371: 685–88.
5. Harries A, Schouten E, Libamba E. Scaling up antiretroviral treatment in resource-poor settings. *Lancet* 2006; 367: 1870–72.
6. Callaghan M, Ford N, Schneider H. A systematic review of task-shifting for HIV treatment and care in Africa. *Human Resources for Health* 2010; 8: 8.
7. Zachariah R, Ford N, Philips M, Lynch S, Massaquoi M, Janssens V, Harries A. Task shifting in HIV/AIDS: opportunities, challenges and proposed actions for sub-Saharan Africa. *Trans R Soc Trop Med Hyg* 2009; 103: 549-58.

### 2.2 A systematic review of task shifting for HIV treatment and care in Africa

#### References

1. WHO/UNAIDS/PEPFAR: Task Shifting: Global Recommendations and Guidelines, Geneva, 2008.
2. Heller J. *Officiers de Sante: The second-class doctors of Nineteenth-Century France.* *Medical History* 1978, 22:1.
3. Sidel V. The barefoot doctors of the People's Republic of China. *New England Journal of Medicine* 1972; 286: 1292-1300.
4. Mullan F, Frehywot S. Non-physician clinicians in 47 sub-Saharan African countries. *Lancet* 2007; 370: 2158-63.
5. McPake B, Mensah K. Task-Shifting in health care in resource-poor countries. *Lancet* 2008; 372: 870-1.

6. Samb B, Celletti F, Holloway J, Van Damme W, De Cock KM, Dybul M. Rapid Expansion of the health workforce in Response to the HIV Epidemic. *New England Journal of Medicine* 2007; 357: 2510-14.
7. Laurent M, Reeves D, Hermens R, Braspenning J, Grol R, Sibbald B. Substitution of Doctors by Nurses in Primary Care. *Cochrane Database of Systematic Reviews*. 2005; 1: CD004015.
8. Lehmann U, Sanders D. Community health workers: what do we know about them? The state of evidence on programmes, activities, costs and impact on health outcomes of using community health workers. Geneva: World Health Organization: Evidence and Information for Policy, 2007.
9. Lewin SA, Dick J, Pond P, Zwarenstein M, Aja G, van Wyk B, Bosch-Capblanch X, Patrick M: Lay health workers in primary and community health care. *Cochrane Database of Systematic Reviews*. 2005; 1: CD004015.
10. Laurent M, Reeves D, Hermens R, Braspenning J, Grol R, Sibbald B. Substitution of doctors by nurses in primary care. *Cochrane Database of Systematic Reviews* 2004; 4: CD001271.
11. World Health Organization. Integrated Management of Adolescent and Adult Illness. Geneva: WHO, 2004.
12. World Health Organization. Treat, train, retain. Task shifting: Global recommendations and guidelines. Geneva, 2007.
13. Zelnick J, O'Donnell M. Expansion of the health workforce and the HIV epidemic. *New England Journal of Medicine* 2008; 358: 1639-40.
14. Philips M, Lynch S, Massaquoi M, Janssens V, Harries A. Task Shifting for HIV/AIDS: Opportunities, Challenges and Proposed Actions for sub-Saharan Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2009; 103: 549-58.
15. Gaede B. Rural ARV Provision – Policy implications for accelerated ARV rollout. *Southern African Journal of HIV Medicine* 2006: 23-5.
16. Schneider H, Blaauw D, Gilson L, Chabikuli N, Goudge J. Health systems and Access to antiretroviral drugs for HIV in Southern Africa: service delivery and human resources challenges. *Reproductive Health Matters* 2008; 14: 12-23.
17. Philips M, Zachariah R, Venis S. Task shifting for antiretroviral treatment delivery in sub-Saharan Africa: not a panacea. *Lancet* 2008; 371: 682-4.

18. Ojikutu B. The realities of antiretroviral rollout: overcoming challenges to successful programmatic implementation. *Journal of Infectious Disease* 2007; 196: S445-8.
19. van Rensburg DH, Steyn F, Schneider H, Loffstadt L. Human resources development and antiretroviral treatment in Free State Province, South Africa. *Human Resources for Health* 2008; 6: 15.
20. Yu D, Souteyrand Y, Banda MA, Kaufman J, Perriens JH. Investment in HIV/AIDS programs: does it help strengthen health systems in Developing Countries? *Global Health* 2008; 4: 8.
21. Calpin-Davies PJ, Akehurst RL. Doctor-nurse substitution: the workforce equation. *Journal of Nursing Management* 1999; 7: 71-9.
22. Doherty TM, Coetzee M. Community health workers and professional nurses: defining the roles and understanding the relationships. *Public Health Nursing* 2005; 22: 360-265.
23. Schneider H, Hlophe H, van Rensburg D. Community health workers and the response to HIV/AIDS in South Africa: tensions and prospects. *Health Policy and Planning* 2008; 23: 179-87.
24. Stilwell B, Wilson A, McCaffery J. Non-physician clinicians in sub-Saharan African countries. *Lancet* 2008; 371: 1578.
25. Chung J, O'Brien M, Price J, Shumbusho F. Quantification of physician-time saved in a task shifting pilot program in Rwanda. *AIDS 2008 - XVII International AIDS Conference*. Abstract no. WEAB0205
26. O'Brien ME, Chung J, Binagwaho A. Nurse delivery of HIV care: Modeling the impact of task-shifting on physician demand. In Press (personal communication).
27. Torpey KE, Kabaso ME, Mutale LN, Kamanga MK, Mwango AJ, Simpungwe J, Suzuki C, Mukadi YD. Adherence support workers: a way to address human resource constraints in antiretroviral treatment programs in the public health setting in Zambia. *PLoS ONE* 2008; 3: e2204.
28. Udegboka N, Moses John H. Reduction of client waiting time through task shifting in Northern Nigeria. 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. Abstract CDD091.
29. McGuire M, Goossens S, Kukasha W, Ahoua L, Le Pailh M, Munger A, Kabwinja A, Mpunga J, Chazel E, Jeannin A, Szumilin E, Kamoto K, Harries A. Nurses and medical

- assistants taking charge: task-shifting HIV care and HAART initiation in resource-constrained and rural Malawi. Oral Abstract Session: AIDS 2008 - XVII International AIDS Conference: Abstract WEPE0106.
30. Kosgei R, Wools-Kaloustian K, Braitstein P, Sidle J, Sang E, Gitau J, Sitienei J, Owino R, Tierney W, Mamlin J, Kimaiyo S, Siika A. Express Care: a clinician–nurse model for the management of high volume HIV clinics in Western Kenya. Oral Abstract Session: AIDS 2008 - XVII International AIDS Conference: Abstract WEAX0102.
31. Harling G, Bekker LG, Wood R. Costs of a Dedicated ART Clinic. *South African Medical Journal* 2007; 97: 8.
32. Stearns B, Evans D, Lutung P, Wagner G, Ryan G, Aledort J. Primary estimates of the costs of ART care in South Africa and Uganda. AIDS 2008 - XVII International AIDS Conference: Abstract MOPE0706.
33. Bussmann C, Rotz P, Ndwapi N, Baxter D, Bussmann H, Wester CW, Ncube P, Avalos A, Mine M, Mabe E, Burns P, Cardiello P, Makhema J, Marlink R Strengthening healthcare capacity through a responsive, country-Specific, training standard: the KITSO AIDS training program’s support of Botswana’s national antiretroviral therapy rollout. *Open AIDS Journal* 2008; 10: 6.
34. Gimbel S, Durao Mola O, Assan A, Manjate R, Sheer K. Rolling out ART in Mozambique 2003-2006: task shifting and decentralization. HIV/AIDS Implementers’ Meeting, Kigali, Rwanda, 16-19 June 2007. Abstract 90: 2007.
35. Koenig SP, Leandre F, Farmer P. Scaling up HIV treatment programmes in resource-limited settings: The rural Haiti experience. *AIDS* 2004; 18: S21-5.
36. Massaquoi M, Zachariah R, von Pilar U. Task-Shifting in HIV/AIDS Care in a rural district of Malawi: some successes and lessons learned from Thyolo. AIDS 2008 – XVII International AIDS Conference. Abstract WEAB0202.
37. Giorgis B, Bekele R, Tafesse M, Admassu A, Alemu A, Berhanu S, Merdassa G, Tizazu G, Zewde A, Melaku Z. Point of service rapid HIV testing: a key strategy for scaling-up of provider-initiated counseling & testing. HIV/AIDS Implementers’ Meeting Windhoek, Namibia. June 10-14, 2009. Abstract 700.
38. Hulela E, Puvimanasinghe J, Ndwapi N, Ali A, Avalos A, Mwala P, Gaolathe T, Seipone K. Task shifting in Botswana: empowerment of nurses in ART roll-out. AIDS 2008 – XVII International AIDS Conference. Abstract WEPE0108.

39. Morris MB, Chapula BT, Chi BH, Mwangi A, Chi HF, Mwanza J, Manda H, Bolton C, Pankratz DS, Stringer JS, Reid SE. Use of task-shifting to rapidly scale-up HIV treatment services: experiences from Lusaka, Zambia. *BMC Health Services Research* 2009; 9: 5.
40. Bedelu M, Ford N, Hilderbrand K, Reuter H. Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS Care. *J Inf Dis* 2007; 196: S464-8.
41. Assan A, Mussa A, Ramirez L, McKinney M, Nelson L. Task shifting mechanisms for scaling up HIV services in Mozambique. AIDS 2008 - XVII International AIDS Conference. Abstract MOPE0798.
42. Chiambe G, Kulzer J, Nyabiage L, Bukuzi E, Penner J, Cohen C. Maximizing human resources by involving lay health workers in HIV service delivery in Kenya. 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. Abstract TUPED091.
43. Mareverwa J, Bhembe B, Kamiru H, Shabangu P, Kim J, Mccollum A, Mccollum D, Sibandze M, Mahuma O, Adler M, Amzel A, Pittman R, Henderson F. Impact of task-shifting and joint efforts in the provision of care and antiretroviral treatment to infants and children in a resource constrained setting. AIDS 2008 - XVII International AIDS Conference: Abstract LBPE1151.
44. Jouquet G, Bemelmans M, Massaquoi M, Arnould L, Mwagomba B, Bauernfeind A, Philips M. Cost analysis of an ARV care programme reaching universal access in Thyolo, Malawi. 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. Abstract TUAD105.
45. Wood R, Fox M, Conradie F, Cornell M, Dehlinger M, Heiberg C, Ingram C, Ive P, Orrell C, Panchia R, Rassool M, Stevens W, Truter H, van der Horst C, Zeinekcer J, McIntyre J, Sanne I. Nurse management is not inferior to doctor management of antiretroviral naïve HIV infected patients. Conference Abstract, 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. July 22 2009. Abstract LBPED03.
46. Van Rie A, Mbonze N, Tillerson K, Kitenge F, Roger I, Vanden Driessche K, Behets F. A nurse-centered primary health care model for HIV care of patients with active

tuberculosis: antiretroviral treatment initiation decision-making. 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. Abstract TUPED133.

47. Shumbusho F, Turate I, Price J, Lowrance D, Binagwaho A. Task shifting to achieve universal access to HIV Care: evaluation of a pilot program of antiretroviral treatment service delivery by nurses in Rwanda. 2008 HIV/AIDS Implementers meeting, Kampala, Uganda. Abstract 621.

48. Gimbel-Sherr K, Augusto O, Micek M, Gimbel-Sherr S, Tomo M, Pfeiffer J, Gloyd S. Task shifting to mid-level clinical health providers: an evaluation of quality of ART provided by tecnicos de medicina and physicians in Mozambique. AIDS 2008 - XVII International AIDS Conference: Abstract WEAX0105.

49. Shulman D, Jobarteh K, Makani E, Mtewa S, Mapwelemwe A, Manjomo A, Crocker J, Joseph K. Task-shifting in the pharmacy: a framework for expanding and strengthening services in rural Malawi. 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. Abstract CDD094.

50. Bolton-Moore C, Mubiana-Mbewe M, Cantrell RA, Chintu N, Stringer EM, Chi BH, Sinkala M, Kankasa C, Wilson CM, Wilfert CM, Mwangi A, Levy J, Abrams EJ, Bulterys M, Stringer JS. Clinical outcomes and CD4 cell response in children receiving antiretroviral therapy in primary health care facilities in Zambia. *Journal of the American Medical Association* 2007; 298: 1888-99.

51. Chang LW, Alamo S, Guma S, Christopher J, Suntok T, Omasete R, Montis JP, Quinn TC, Juncker M, Reynolds SJ. Two-year virologic outcomes of an alternative AIDS care model: evaluation of a peer health worker and nurse-staffed community-based program in Uganda. *Journal of Acquired Immune Deficiency Syndrome* 2009; 50: 276–282.

52. Assan A, Mudender F, Brentlinger P, Vallejo J, Bacon O, Martinez P, Ghee A, Branigan E, Smith M. Task-shifting in Mozambique: evaluating antiretroviral therapy as newly implemented by mid-level health professionals. Task-shifting in Mozambique: evaluating antiretroviral therapy as newly implemented by mid-level health professionals. AIDS 2008 - XVII International AIDS Conference. Abstract MOPE0790.

53. Tootla F, Buhlungu N, Okongo B, Farthing C, Ritchey G, Khanlou H, McKellar M. Successful task shifting at an antiretroviral therapy (ART) clinic in South Africa: a good clinic model for resource-limited settings. 4th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Sydney. Abstract CDB287.

54. Anon. Nurse-driven, community-supported HIV/AIDS treatment at the primary health care level in rural Lesotho. Médecins Sans Frontières, Johannesburg, 2009.
55. Cohen R, Lynch S, Bygrave H, Eggers E, Vlahakis N, Hilderbrand K, Knight L, Pillay P, Saranchuk P, Goemaere E, Makakole L, Ford N. Antiretroviral treatment outcomes from a nurse-driven, community-supported HIV/AIDS treatment programme in rural Lesotho: observational cohort assessment at two years. *J Int AIDS Soc* 2009; 12: 23.
56. Shumusho, F. Task shifting to achieve universal access to HIV care and treatment services in Rwanda: a nurse-centered ART program at three rural health centres. 2008 HIV Implementers' Meeting, Kampala, Uganda, 3-7 June 2008. Abstract 621.
57. Van Griensven J, De Naeyer L, Uwera J, Asiimwe A, Gazille C, Reid T. Success with antiretroviral treatment for children in Kigali, Rwanda: experiences with health center/nurse-based care. *BMC Paediatrics* 2008; 8: 39.
58. Shumbusho F, van Griensven J, Lowrance D, Turate I, Weaver MA, Price J, Binagwaho A. Task shifting for scale-up of HIV care: evaluation of nurse-centered antiretroviral treatment at rural health centers in Rwanda. *PLoS Med* 2009; 6: 10.
59. Jaffar S, Amuron B, Foster S, Birungi J, Levin J, Namara G, Nabiryo C, Ndemi N, Kyomuhangi R, Opio A, Bunnell R, Tappero JW, Mermin J, Coutinho A, Grosskurth H; Jinja Trial Team. Rates of virological failure in patients treated in a home-based versus a facility-based HIV-care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial. *Lancet* 2009; 374: 2080-9.
60. Mermin J, Were W, Ekwaru JP, Moore D, Downing R, Behumbiize P, Lule JR, Coutinho A, Tappero J, Bunnell R. Mortality in HIV-infected Ugandan adults receiving antiretroviral treatment and survival of their HIV-uninfected children: a prospective cohort study. *Lancet* 2008; 371: 752-9.
61. Weidle PJ, Wamai N, Solberg P, Liechty C, Sendagala S, Were W, Mermin J, Buchacz K, Behumbiize P, Ransom RL, Bunnell R. Adherence to antiretroviral therapy in a home-based AIDS care programme in rural Uganda. *Lancet* 2006; 368: 1556-7. 20
62. Alamo-Talisuna S. Task shifting, a strategy to overcome the human resource crisis in HIV/AIDS programs in Uganda. 4th IAS Conference on HIV Pathogenesis, Treatment and Prevention. Abstract CDB281

63. Zachariah R, Teck R, Buhendwa L, Fitzgerald M, Labana S, Chinji C, Humblet P, Harries A. Community support is associated with better antiretroviral treatment outcomes in a resource-limited rural district in Malawi. *Trans R Soc Trop Med Hyg* 2007; 101: 79-84.
64. Tweya H, Nsona D, Weigel R, Phiri S, Jahn A. Effectiveness of screening for ART eligibility by non-medical HIV testing counsellors. XVII International AIDS Conference, Mexico, 3-8 August, 2008. Abstract WEAB0203.
65. Apondi R, Bunnell R, Awor A, Wamai N, Bikaako-Kajura W, Solberg P, Stall RD, Coutinho A, Mermin J. Home-based antiretroviral care is associated with positive social outcomes in a prospective cohort in Uganda. *Journal of Acquired Immune Deficiency Syndrome* 2007; 44: 71-6.
66. Tugume G, Jjuko G, Ssali L. Task shifting - an approach for expanding quality and cost effective community antiretroviral therapy. 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. Abstract CDD077.
67. Tantchou Yakam JYC, Gruénais M-E. Involving new actors to achieve ART scaling-up: difficulties in an HIV/AIDS counselling and testing center in Cameroon. *International Nursing Review* 2009; 56: 50-7.
68. Tobi P, George G, Schmidt E, Renton A. Antiretroviral treatment and the health workforce in South Africa: how have ART workers been affected by scaling up? *Tropical Medicine and International Health* 2008; 13: 1452-8.
69. Arem H, Nakyanjo N, Kagaayi J, Mulamba J, Laks R, Nakigozi G, Serwadda D, Quinn T, Gray R, Bollinger R, Reynolds S, Chang L. Peer health workers and AIDS care in Rakai, Uganda: a mixed methods process evaluation of a cluster-randomized trial. 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. Abstract CDD100.
70. Sherr K, Manjate R, Gimbel S, Pfeiffer J, S. Gloyd S. Policymaker and clinician perspectives towards task shifting for HIV care and treatment in Mozambique: a cross-sectional study. 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, 2009. TUPED129.
71. Hiner C, Mwale G, Parsons M, Adair M, Reis P, Hughes R. Evaluation of a task-shifting program implemented to increase access to ART in Uganda and Zambia. *AIDS 2008 – XVII International AIDS Conference: Abstract MOPE0097.*
72. Suri A, Gan K, Carpenter S. Voices from the field: perspectives from community

health workers on health care delivery in KwaZulu-Natal, South Africa. *Journal of Infectious Diseases* 2007; 196: S505-11.

73. Sanjana P, Torpey P, Schwarzwald A, Simumba C, Kasonde P, Nyirenda L, Kapanda P, Kakungu-Simpungwe M, Kabaso M, Thompson C. Task-shifting HIV counselling and testing services in Zambia: the role of lay counsellors. *Human Resources for Health* 2009; 7: 44.

74. Chang LW, Kagaayi J, Nakigozi G, Packer AH, Serwadda D, Quinn TC, Gray RH, Bollinger RC, Reynolds SJ. Responding to the human resource crisis: peer health workers, mobile phones, and HIV care in Uganda. *AIDS Patient Care and STDs* 2008; 22: 173-4.

75. Kober K, Van Damme W. Expert Patients and AIDS Care: A Literature review on expert patient programmes in high-income countries, and an exploration of their relevance for HIV-AIDS care in low-income countries with severe human resource shortages. March 2006. Available at: [www.equinetafrica.org/bibl/docs/KOBaids.pdf](http://www.equinetafrica.org/bibl/docs/KOBaids.pdf)

76. Labonte R, Torgerson R. Interrogating globalization, health and development: towards a comprehensive framework for research, policy and political action. *Critical Public Health* 2005; 15: 157-79.

77. Dovlo D. Using mid-level cadres as substitutes for internationally mobile health professionals in Africa: a desk review. *Human Resources for Health* 2004; 2: 7.

78. Scott A, Vale L. Increased General Practice Workload due to a primary care led National Health Service: the need for increased evidence to support rhetoric. *British Journal of General Practice* 1998; 48: 1085-8.

79. Swider SM. Outcome effectiveness of community health workers: An integrative literature review. *Public Health Nursing* 2002; 19:11-20.

80. Lehmann U, Van Damme W, Barten F, Sanders D. Task shifting: the answer to the human resource crisis in Africa? *Human Resources for Health* 2009; 7: 49.

### **2.3 Task shifting in HIV/AIDS: opportunities, challenges and proposed actions for sub-Saharan Africa.**

1. WHO. *The World Health Report 2006. Working together for health.* Geneva: World Health Organization; 2006.

2. Dovlo D. Using mid-level cadres as substitutes for internationally mobile health professionals in Africa. A desk review. *Human Res Health* 2004; 2: 1-12.

3. Dovlo D. Taking more than a fair share? The migration of health professionals from poor to rich countries. *Plos Med* 2005; 2:e109.
4. WHO. World Health Statistics 2007. Geneva: World Health Organization; 2007. <http://www.who.int/whosis/whostat2007/en/index.html>
5. Samb B, Celletti F, Holloway J, van Damme W, de Cock KM, Dybul M. Rapid expansion of the health workforce in response to the HIV epidemic. *N Engl J Med* 2007; 357: 2510-4.
6. Van Damme W, Kober K, Laga M. The real challenges for scaling up ART in sub-Saharan Africa. *AIDS* 2006; 20: 653-6.
7. Harries AD, Schouten EJ, Libamba E. Scaling up antiretroviral treatment in resource-poor settings. *Lancet* 2006; 367: 1870-2.
8. Médecins Sans Frontières. Help wanted. Confronting the healthcare worker crisis to expand access to HIV/AIDS treatment. Lausanne: Médecins Sans Frontières; 2008. <http://www.msf.org/msfinternational/invoke.cfm?component=report&objectid=AD90630F-15C5-F00A-25723C556AA2E57E&method=full.html>
9. Vaz F, Bergstrom S, Vaz M, Langa J, Bugalho A. Training medical assistants for surgery. Policy and practice. *Bull World Health Organ* 1999; 77: 688-91.
10. White SM, Thorpe RG, Maine D. Emergency obstetric surgery performed by nurses in Zaire. *Lancet* 1987; 2: 612-3.
11. Berman PA, Gwatkin DR, Burger SE. Community-based health workers: head start or false start towards health for all? *Soc Sci Med* 1987; 25: 443-59.
12. Mullan F, Frehywot S. Non-physician clinicians in 47 sub-Saharan African countries. *Lancet* 2007; 370: 2158-63.
13. WHO. Treat Train Retrain. Task shifting: Global recommendations and guidelines. Geneva: World Health Organization; 2007.
14. Libamba E, Makombe S, Harries AD, Chimzizi R, Salaniponi FM, Schouten EJ, Mpazanje R. Scaling up antiretroviral therapy in Africa: learning from tuberculosis control programs: the case of Malawi. *Int J Tuberc Lung Dis* 2005; 9: 1062-71.
15. Department of Health. HIV/AIDS and STI strategic plan for South Africa, 2007-2011. Pretoria: Department of Health, 2007.
16. Buchan J, Dal Poz MR. Skill mix in the health care workforce: reviewing the evidence. *Bull World Health Organ* 2002; 80: 575-80.

17. Miles K, Clutterbuck DJ, Seitio O, Sebego M, Riley A. Antiretroviral treatment roll-out in a resource-constrained setting: capitalizing on nursing resources in Botswana. *Bull World Health Organ* 2007; 85: 555-60.
18. Gimbel-Sherr SO, Micek MA, Gimbel-Sherr KH, Koepsell T, Hughes JP, Thomas KK, Pfeiffer J, Gloyd SS. Using nurses to identify HAART eligible patients in the Republic of Mozambique: results of a time series analysis. *Human Res Health* 2007; 5: 1-9.
19. Bedelu M, Ford N, Hilderbrand K, Reuter H. Implementing antiretroviral therapy in rural communities: The Lusikisiki model of decentralized HIV/AIDS care. *J Infect Dis* 2007; 196: S464-8.
20. Sazawal S, Black RE. Effect of pneumonia case management on mortality in neonates, infants and preschool children: a meta-analysis of community-based trials. *Lancet Infect Dis* 2003; 3: 547-56.
21. Kidane G, Morrow RH. Teaching mothers to provide home treatment of malaria in Tigray, Ethiopia: a randomized trial. *Lancet* 2000; 356: 550-5.
22. Lewin SA, Dick J, Pond P. Lay health workers in primary and community health care. *Cochrane Database Syst Rev* 2005; 1: CD004015.
23. Zachariah R, Teck R, Buhendwa L, Labana S, Chinji C, Humblet P, Harries AD. How can the community contribute in the fight against HIV/AIDS and tuberculosis? An example from a rural district of Malawi. *Trans R Soc Trop Med Hyg* 2006; 100: 167-75.
24. Zachariah R, Teck R, Buhendwa L, Fitzgerald M, Labana S, Harries AD. Community support is associated with better antiretroviral treatment outcomes in a resource-limited rural district in Malawi. *Trans R Soc Trop Med Hyg* 2007; 101: 79-84.
25. Zachariah R, Spielmann MP, Harries AD, Nkhoma W. Motives, sexual behaviour and risk factors associated with HIV in individuals seeking voluntary counselling and testing in a rural district of Malawi. *Trop Doct* 2003; 33: 88-91.
26. Coetzee D, Boule A, Hildebrand K, Asselman V, van Cutsem G, Goemaere E. Promoting adherence to antiretroviral therapy: the experience from a primary care setting in Khayelitsha, South Africa. *AIDS* 2004; 18(Suppl 3): S27—31.
27. Kumphitak A, Kasi-Sedapan S, Wilson D, Ford N, Adpoon P, Kaethaew S, et al. Perspectives and practice in antiretroviral treatment: Involvement of people living with HIV/AIDS in treatment preparedness in Thailand. Geneva: World Health Organization; 2004.

28. Calmy A, Klement E, Teck R, Berman D, Pécoul B, Ford N. Simplifying and adapting antiretroviral treatment in resource-poor settings: a necessary step to scaling up. *AIDS* 2004; 18: 2353-60.
29. Deribe K, Hailekiros F, Biadgilign S, Amberbir A, Beyene BK. Defaulters from antiretroviral treatment in Jimma University Specialized Hospital, southwest Ethiopia. *Trop Med Int Health* 2008; 13: 328-33.
30. Pereira C, Cumbi A, Malalane R, Vaz F, McCord C, Bacci A, Bergstrom S. Meeting the need for obstetric care in Mozambique: work performance and histories of medical doctors and assistant medical officers trained for surgery. *BJOG* 2007; 114: 1530-3.
31. Lin Y, Franco LM. Assessing malaria treatment and control at peer facilities in Malawi. Quality Assurance Project Case Study. Bethesda, MD: Quality Assurance Project; 2000. <http://www.qaproject.org/pubs/PDFs/BIMI.PDF>
32. Wilson IB, Landon BE, Hirschhorn LR, McInnes K, Ding L, Marsden PV, Cleary PD. Quality of HIV care provided by nurse practitioners, physician assistants and physicians. *Ann Int Med* 2005; 143: 729-36.
33. Rowe AK, Onikpo F, Mama M, Cokou F, Deming MS. Management of childhood illness at health facilities in Benin: Problems and their causes. *Am J Public Health* 2001; 91: 1625-35.
34. Rowe AK, Lama M, Onikpo F, Deming MS. Risk and protective factors for two types of error in the treatment of children with fever at outpatient health facilities in Benin. *Int J Epidemiol* 2003; 32: 296-303.
35. Ofori-Adjei D, Arhinful D. Effect of training on the clinical management of malaria by medical assistants in Ghana. *Soc Sci Med* 1996; 42: 1169-76.
36. Chopra M, Munro S, Lavis J, Vist G, Bennett S. Effects of policy options for human resources for health: an analysis of systematic reviews. *Lancet* 2008; 371: 668-74.
37. James CD, Hanson K, McPake B, Balabanova D, Gwatkin D, Hopwood I. To retain or remove user fees? Reflections on the current debate in low- and middle-income countries. *Appl Health Econ Health Policy* 2006; 5: 137-53.
38. Daviaud E, Chopra M. How much is not enough? Human resource requirements for primary health care: A case study from South Africa. *Bull World Health Organ* 2008; 86: 46-51.

39. Sibbald B, Chen J, McBride A. Changing the skill-mix of the healthcare workforce. *J Health Serv Res Policy* 2004; 9: S28-38.
40. Lanata C. Human resources in developing countries. *Lancet* 2007; 369: 1238-9.
41. Vujicic M, Zurn P, Diallo K, Adams O, Dal Poz MR. The role of wages in the migration of health care professionals from developing countries. *Human Res Health* 2004; 2: 3.
42. McCoy D, Bennett S, Witter S, Pond B, Baker B, Gowe J, Chand S, Ensor T, McPake B. Salaries and incomes of health workers in sub-Saharan Africa. *Lancet* 2008; 371: 675-81.
43. Rowe AK, de Savigny D, Lanata CF, Victora CG. How can we achieve and maintain high-quality performance of health workers in low-resource settings? *Lancet* 2005; 366: 1026-35.
44. Harries AD, Salaniponi FM, Nunn PP, Raviglione M. Performance-related allowances within the Malawi National Tuberculosis Control Programme. *Int J Tuberc Lung Dis* 2005; 9: 138-44.
45. Egger D, Ollier L. Strengthening management in low-income countries: Lessons from Uganda. Geneva: World Health Organization; 2007.
46. Schneider H, Hlophe H, Rensburg D. Community health workers and the response to HIV/AIDS in South Africa: tensions and prospects. *Health Policy Plann* 2008; 23: 179-87.
47. Lehmann S, Sander D. Community health workers. What do we know about them. Geneva: World Health Organization; 2007.
48. Walt G, Heggenhougen K. Are large-scale volunteer community health worker programmes feasible? The case of Sri Lanka. *Soc Sci Med* 1989; 29: 599-608.
49. Kironde S, Khasen S. What motivates lay volunteers in high burden but resource-limited tuberculosis control programmes? Perceptions from the Northern Cape Province, South Africa. *Int J Tuberc Lung Dis* 2002; 6: 104-10.
50. Lehman U, Friedman I, Sander D. Review of the utilization and effectiveness of community-based health workers in Africa. Global Health Trust, Joint Learning Initiative on Human Resources for Health and Development (JLI), JLI Working Paper 4-1; 2004.
51. Knippenberg R, Alihonon E, Soucat A. Implementation of the Bamako Initiative: strategies in Benin and Guinea. *Int J Health Plann Manage* 1997; 12: 29-47.
52. Feeley F. Fight AIDS as well as the brain drain. *Lancet* 2006; 368: 435-6.
53. UNAIDS. AIDS in Africa: country by country. Geneva: Joint United Nations Programme on HIV/AIDS; 2000.

54. Harries AD, Hargreaves NJ, Gausi F, Kwanjana JH, Salaniponi FM. High death rates in health workers and teachers in Malawi. *Trans R Soc Trop Med Hyg* 2002; 96: 34-7.
55. Tawfik L, Kinoti S. The impact of HIV/AIDS on health systems and the health workforce in sub-Saharan Africa. Washington, DC: US Agency for International Development (USAID) Bureau for Africa; 2003.
56. Makombe SD, Jahn A, Tweya H, Thambo L, Yu JK, Hedt B, Weigel R, Nkhata A, Schouten EJ, Kamoto K, Harries AD. A national survey of the impact of rapid scale-up of antiretroviral therapy on health-care workers in Malawi: effects on human resources and survival. *Bull World Health Organ* 2007; 85: 851-7.
57. Philips M, Zachariah R, Venis S. Task shifting for antiretroviral treatment in sub-Saharan Africa: not a panacea. *Lancet* 2008; 371: 682-4.

## **Chapter 3: Decentralizing HIV/AIDS care to the primary care level**

### **3.1. Introduction**

Task shifting has been shown to be an effective strategy for overcoming the dire shortage of health professionals in sub-Saharan Africa. It has also supported equitable access to care. Doctors are unevenly distributed across southern Africa, and for the most part are located in hospitals in cities: rural parts of South Africa for example have 14 times fewer doctors than the national average [1] while over half of Mozambique's doctors are working in the capital city, Maputo [2]. Health policies that insist on doctor-based provision of antiretroviral therapy are, by default, policies that limit access to treatment to hospitals in cities.

Patients who live a long way from health care services and have to travel long distances to access antiretrovirals have been found to have greater attrition and mortality rates compared to patients who live closer to care; the cost and time required to travel such distances has been associated with poorer adherence [3] and higher rates of defaulting from care [4]. The decentralization of antiretroviral care to health centres in rural areas is therefore essential to improving both access and equity.

This chapter presents operational research evidence of the effectiveness of providing antiretroviral therapy at the primary care level in two high HIV burden countries in southern Africa: South Africa [5] and Lesotho [6]

### 3.2. Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS Care

*Bedelu M, Ford N\*, Hildebrandt K, Reuter H. J Inf Dis 2007; 196 :464-468.*

#### **Abstract**

**Background:** Health worker shortages are a major bottleneck to scaling up antiretroviral therapy (ART), particularly in rural areas.

**Programme approach:** In Lusikisiki, a rural area of South Africa with a population of 150,000 serviced by 1 hospital and 12 clinics, Médecins Sans Frontières has been supporting a program to deliver human immunodeficiency virus (HIV) services through decentralization to primary health care clinics, task shifting (including nurse-initiated as opposed to physician-initiated treatment), and community support.

**Discussion and evaluation:** This approach has allowed for a rapid scale-up of treatment with satisfactory outcomes. Although the general approach in South Africa is to provide ART through hospitals – which seriously limits access for many people, if not the majority of people – 1-year outcomes in Lusikisiki are comparable in the clinics and hospital. The greater proximity and acceptability of services at the clinic level has led to a faster enrollment of people into treatment and better retention of patients in treatment (2% vs. 19% lost to follow-up). In all, 2200 people were receiving ART in Lusikisiki in 2006, which represents 95% coverage.

**Conclusions:** Maintaining quality and coverage will require increased resource input from the public sector and full acceptance of creative approaches to implementation, including task shifting and community involvement.

---

\* NF designed and undertook the study, wrote the first draft of the paper, and contributed to all subsequent drafts. The study is based on routinely collected data.

## **Background**

The chronic shortage of health care workers is recognized as one of the major bottlenecks to health care provision, and scaling up treatment is no exception [1]. The impact is most devastating in rural areas, where the human-resource crisis is most acute [2]. For the past 3 years, Médecins Sans Frontières (MSF) has been supporting a program to provide care and treatment for people with HIV/AIDS in the local service area of Lusikisiki, one of the poorest and most densely populated rural areas of South Africa.

The Lusikisiki subdistrict comprises 150,000 inhabitants serviced by 1 hospital and 12 clinics. The HIV infection prevalence is high, with almost one-third (31%) of women who present at antenatal care clinics testing positive. A lack of staff within the health system is a major problem. With just 5 physicians per 100,000 people, Lusikisiki's physician-to-patient ratio is 14 times lower than the national average [3]. Approximately one-half of all nursing posts remain vacant. In addition, a chronic lack of auxiliary staff adds to nurses' workloads. In this article, we describe how the integration of HIV care and treatment into primary health care in Lusikisiki overcame some of the challenges of working in a resource-limited rural area, to achieve good treatment coverage and clinical outcomes [4].

## **Approaches to support clinic-based care**

The World Health Organization promotes the role of primary health care and community-led care in the delivery of antiretroviral therapy (ART) in resource-limited settings [5]. In keeping with these principles, the delivery of HIV services in Lusikisiki was achieved through decentralization to primary health care, task shifting within services, and strong community support.

### ***Decentralization and task-shifting***

The provision of treatment at the clinic level inevitably resulted in a significant increase in the number of service users within a system that was already chronically understaffed and poorly equipped. Although overall utilization of clinic services increased almost 2-fold since the start of the program (from 16,465 service users in April 2004 to 28,191 service users in April 2006), the number of professional nurses (30) did not increase. This near doubling of the workload would have been impossible to manage without task shifting. With appropriate

training, mentoring, and supervision, it was possible to delegate the running of the ART program to primary health care nurses and community health workers. Table 3.2.1 provides a description of some of the changes in the roles of clinic and support personnel in the Lusikisiki program. As much responsibility as possible was delegated to lower-level health care workers while ensuring that professional medical oversight was provided to maintain quality control.

**Table 3.2.1. Traditional roles of health staff in HIV/AIDS care, compared with roles of health staff in the Lusikisiki program.**

Category	Traditional roles	Roles in the Lusikisiki program
Physicians	Conduct patient consultations: OIs, staging, ART initiation Visiting physician does not interact with clinic staff	Mobile visit: sees only problem cases Supervise clinics and mentor nurses and counselors Serve as part of a multidisciplinary team, including service users
Pharmacists	Manage drug supply Oversee prescriptions	Hospital pharmacist: provide mentoring to pharmacist assistants
Nurses	Support physician Conduct VCT Prepare individuals for ART Monitor ART recipients Collect data Manage drug supply Supervise community caregivers	Manage OIs Perform clinical staging Initiate and monitor ART Supervise clinic staff Manage drug supply Supervise adherence counselors
Adherence counsellors	Not utilized	Prepare individuals for ART Empower ART recipients Run ART support groups Collect data (ART registers) Mentor community caregivers Trace individuals who default
Pharmacist's assistants	Not utilized or play a limited role (dispense drugs only under strict pharmacist supervision at the hospital)	Manage drug supply Dispense drugs Check adherence Identify individuals who default
Community caregivers	Promote health Directly observe treatment (including recall of individuals who default)	Run HIV support groups
Support groups, committees, activists, people with HIV/AIDS	Not utilized	Prepare individuals for and monitor adherence to ART Promote health in community Recall individuals who default React to bottlenecks Advocate for better service delivery

ART, antiretroviral therapy; OI, opportunistic infection; VCT, voluntary counseling and testing.

### *Training and mentoring through mobile teams*

All clinics received regular physician support via a mobile team visit to support the overall health services. In addition, these mobile teams provided training and mentoring of nurses in HIV management, including prevention of mother-to-child transmission, management of opportunistic infections, and ART. This was reinforced through on-the-job training, which also included patient management skills, such as examination, history taking, and counseling. Tuberculosis (TB) is the major cause of death among people with HIV/AIDS in South Africa; according to Statistics South Africa (the government statistical agency) [6], 150,000 people died of TB in 2001 alone. In the Lusikisiki program, 82.5% of patients with TB are found to be HIV positive; therefore, a particular emphasis was placed on developing a high suspicion for TB and making a clinical diagnosis when smear results are negative or extrapulmonary TB is present.

Systems improvement and quality control were overseen by the mobile team (comprising 1 physician and 1 nurse), using a program-evaluation tool that looks at specific outcomes of the different components of HIV care on a quarterly basis. The whole clinic team was brought together to identify the strengths and weaknesses and to decide on priorities for the following quarter.

### *Creating new capacity*

The role of adherence counselors extended far beyond counseling. With training and mentoring, these auxiliary/lay workers were able to support many of the key processes required to run a clinic-based HIV service, including service-user support, treatment preparedness, facilitation of support groups, and arrangement of follow-up visits, as well as teaching people receiving ART to package pillboxes, addressing problems in adherence, and collecting and collating statistics. High commitment was maintained by means of weekly meetings and workshops (and, it should be acknowledged, by the tenacious commitment of key individuals). Adherence counselors also worked with other community actors: volunteer workers (community caregivers), other support groups, adherence and clinic committees, and treatment activists. They also undertook all aspects of voluntary counseling and testing, with nurse supervision. Previously, this was solely the responsibility of the nurses, but, with this increased capacity, the number of people tested has increased 14-fold in the past 3 years (4874 tests performed in 2002 vs. 18,809 performed in 2005).

Engaging the community in HIV/AIDS care is a proven way to enhance program quality, in terms of clinical outcomes, adherence rates, and retention [7]. In Lusikisiki, the community interacted with HIV services in a number of ways. General support groups provided peer support for disclosure and testing and performed home visits when problems were identified. ART support groups prepared people for treatment, provided support for adherence and managing adverse effects, and traced and supported individuals who defaulted. A clinic committee represented service users in the case of complaints, advocated for better infrastructure and drug supply, and monitored HIV program and condom distribution in the community. An adherence committee followed up with nonadherent patients and served as arbitrator if a clinic team could not decide on the readiness of a person for ART. Finally, individual service users provided important support to other members of the community through learning about HIV and sharing their experiences.

Initially, some nurses doubted the capacity of community health workers, but their participation in clinical discussions and patient management was encouraged by the supervising physician. Eventually, nurses began to appreciate the benefits of having some of their workload shared by community health workers.

### **Outcomes of integrating HIV services into clinic care**

The approach taken in Lusikisiki has allowed for rapid scale-up of treatment coverage in a short time with good outcomes. A cohort analysis of people who have been receiving treatment for 12 months shows satisfactory immunological recovery and viral suppression (Table 3.2.2). The data presented allow comparison of outcomes in the hospital and the clinics. Hospital-based ART is generally promoted in South Africa, as in many countries, with a progressive down-referral of patients to the clinics in some areas. Our aim was to show that satisfactory outcomes can be achieved when treatment is initiated at the clinic level. Routine program monitoring showed no difference between the sex ratio among patients attending the clinics and that among patients attending the hospital. The proportion of patients enrolling who had CD4 cell counts  $<50$  cells/mm<sup>3</sup> was 19.2% (95% confidence interval [CI], 17.1%–21.3%) in the clinics and 26.3% (95% CI, 23.1%–29.0%) in the hospital ( $P=0.0002$ ). This indicates that the patients enrolling in the hospital had disease that was at a

more advanced stage.

The greater proximity and acceptability of services at the clinic level has led to faster enrollment of people receiving treatment and better patient retention. Only 2% of people were lost to follow-up in the clinics, compared with 19% at the hospital. This higher dropout rate at the hospital may be explained by several factors: a higher early mortality, people having to travel farther, less preparation of ART recipients, and less-effective follow-up of individuals who default (adherence counselors are not employed at the hospital). There is no statistical difference between the recorded mortality rates in the hospital and the clinics; however, the percentage of individuals remaining in care was lower in the hospital (67%) than in the clinics (81%). Although the mortality rate among those lost to follow-up cannot be known, it is expected to be high.

**Table 3.2.2. One year outcomes at clinics and the hospital in Lusikisiki, South Africa.**

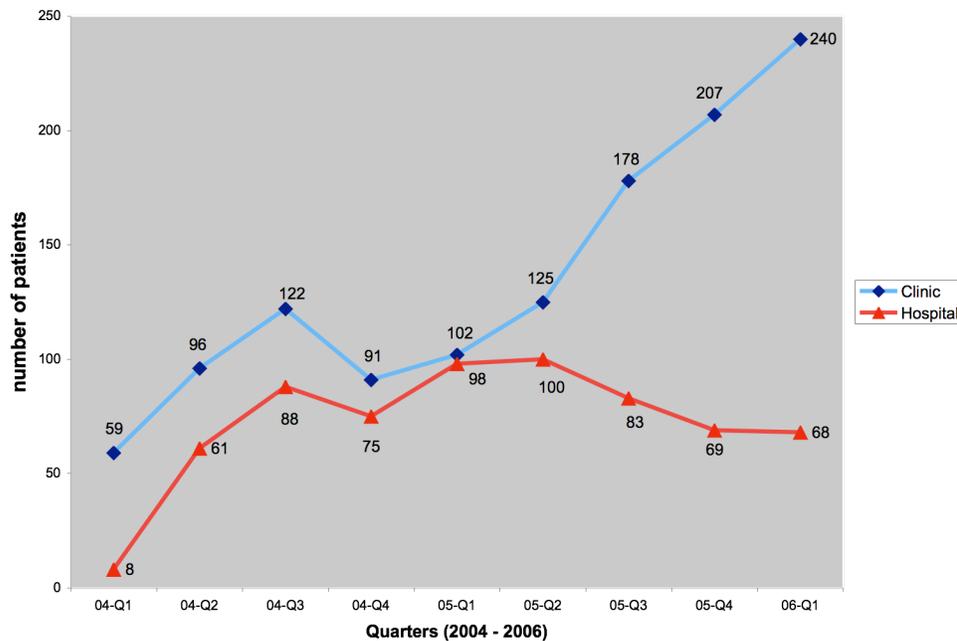
Outcome	Patients at clinics		Patients at hospital		P
	No.	Percentage (95% CI)	No.	Percentage (95% CI)	
Started ART	595	100.0	430	100.0	---
Continued to receive ART	482	81.0 (77.6–84.1)	289	67.2 (62.5–71.6)	<0.001
Died	100	16.8 (13.9–20.1)	58	13.5 (10.4–17.1)	0.147
Lost to follow-up	13	2.2 (1.2–3.7)	83	19.3 (15.7–23.4)	<0.001
CD4 cell count at 12 months	348	58.5 (54.4–62.5)	81	18.8 (15.3–22.9)	<0.001
Determined >200 cells/mm <sup>3</sup>	303	87.1 (83.1–90.4)	61	14.2 (6.5–24.2)	0.008
Viral load at 12 months	296	49.7 (45.7–53.8)	41	9.5 (6.9–12.7)	<0.001
Determined <400 copies/mL	265	89.5 (85.5–92.8)	32	78.0 (62.4–89.4)	0.033

N.B. Sample includes all patients who enrolled between January 2004 and June 2005 to receive antiretroviral therapy (ART) and who had completed at least 12 months of treatment by July 2006. All analyses done in Stata version 8.0

Enrollment initially increased at a similar pace at the clinics and hospital. After 1 year, enrollment at the hospital reached a plateau and then began to decline, suggesting a saturation of services. In contrast, enrollment in the clinics continued to increase (Figure 1). This is likely a result of clinics offering multiple service points and clinic services being integrated into general consultations.

By mid-2006, there were 2200 people receiving ART in Lusikisiki. According to modeling done for 2005, the program had achieved universal coverage for the subdistrict [4, 8]. At this level of coverage, people arriving at the clinics with HIV/AIDS were far less sick than previously noted. In the inception phases of the program, many people were very ill. This “catch-up of the backlog” is reflected in the statistics: in early 2004, 50% of service users at the hospital and 40% of those at clinics arrived with CD4 cell counts  $<50$  cells/mm<sup>3</sup>; by the end of 2005, the number of patients with CD4 cell counts  $<50$  cells/mm<sup>3</sup> had decreased to 16% at both the hospital and clinics. Because people were arriving with a better immune status, clinical management was less time consuming, so that more patients could be seen.

**Figure 3.2.1. Enrollment into ART programs at clinics compared to the hospital.**



N.B.: Graph shows the number of patients newly enrolled into ART programs for each quarter (i.e., numbers are not cumulative).

## Conclusions

The primary health care approach to providing HIV services in Lusikisiki had achieved nearly universal coverage within 2 years without compromising quality of care. Integration

and task shifting helped to spread the workload among the staff, while decentralization helped to spread the load among different clinics. Outcome data show that treatment can be initiated at the clinic level with very satisfactory outcomes and that initiation at clinics allows for more rapid enrollment than does initiation done only at the hospital. Because clinics are part of the local community, they are more user friendly, so people seek treatment earlier and continue to receive treatment longer.

The shortage of nurses in rural areas is a critical issue. A number of potential ways to improve nurse recruitment and retention have emerged from the Lusikisiki experience: these include: (1) ensuring an adequate budget for a full complement of clinic staff; (2) recruitment of adequate administrative staff (drivers, clerks, and pharmacist's assistants), to ensure that nurses' time is optimized toward direct patient care rather than being consumed by nonnursing tasks; (3) accreditation and increased remuneration of nurses trained and experienced in HIV care; (4) acknowledging the great disparity between non-urban settings by paying maximum rural allowances to staff working in the most challenging rural areas, like Lusikisiki; and (5) building and renovating nursing accommodations to meet acceptable standards.

The creation of new capacity has been an important aspect of increasing service efficiency and improving outcomes. In particular, the low rate (2%) of loss to follow-up in clinics can largely be attributed to the work of the adherence counselors. Although the critical role played by adherence counselors is recognized by clinic staff and service users, their function is not supported by Department of Health staffing structures; instead, they are employed by a local community-based organization. Our experience shows that, far from being a detriment to health care services, as some have suggested [9], the provision of ART is having a positive effect on the general quality of primary health care. Improvements in drug supply, diagnostic services, monitoring, staff training, and infrastructural improvements all contribute to improving general primary health care. The strong community ownership of and participation in health care delivery have also been major benefits in supporting the general quality of health services.

Nongovernmental organizations are a valuable source of technical and financial input, but

perhaps their greatest contribution is their political freedom to promote innovation. The importance of MSF's role in Lusikisiki was not the provision of human and financial resources—which is a time-limited and unsustainable contribution—but, rather, the mobilization of expertise and fostering of partnerships to develop innovative approaches to delivering HIV services, to strengthen the system, and to enhance the quality of care. After a gradual handover of responsibilities and resources over a period of 18 months, MSF left Lusikisiki, in October 2006.

Some of the approaches utilized in the Lusikisiki program, such as nurse initiation of treatment, are hampered by a lack of clear policy guidance. Others, such as lay counselor testing, are inconsistent with current policy. However, in practice, these approaches are broadly recognized as an effective way to respond to the overwhelming need for comprehensive HIV care and treatment, including ART. Ensuring sustainability will require increased resource input from the public sector and full acceptance of the creative approaches to implementation, including task shifting and community involvement.

### **3.3. Antiretroviral treatment outcomes from a nurse-driven, community-supported HIV/AIDS treatment programme in rural Lesotho: observational cohort assessment at two years**

*Cohen R, Lynch S, Bygrave H, Eggers E, Vlabakis N, Hilderbrand K, Knight L, Pillay P, Saranchuk P, Goemaere E, Makakole L, Ford N\*. J Int AIDS Soc 2009; 12: 1-8.*

#### **Abstract**

**Introduction:** Lesotho has the third highest HIV prevalence in the world (an adult prevalence of 23.2%).

**Programme approach:** We describe two-year outcomes of a decentralized HIV/AIDS care programme run by Doctors Without Borders/*Médecins Sans Frontières*, the Ministry of Health and Social Welfare, and the Christian Health Association of Lesotho in Scott catchment area. Outcome data are described through a retrospective cohort analysis of adults and children initiated on ART between 2006 and 2008.

**Discussion and Evaluation:** Overall, 13,243 people have been enrolled in HIV care (5% children), and 5376 initiated on ART (6.5% children), 80% at primary care level. Between 2006 and 2008, annual enrolment more than doubled for adults and children, with no major external increase in human resources. Twelve-month outcomes were satisfactory in terms of mortality (11% for adults; 9% for children) and loss to follow up (8.8%). At 12 months, 80% of adults and 89% of children were alive and in care, meaning they were still taking their treatment; at 24 months, 77% of adults remained in care.

**Conclusion:** The successful two-year outcomes are further evidence that HIV/AIDS care and treatment can be provided effectively at the primary care level. The programme highlights how improving HIV care strengthened the primary health care system, and validates several critical areas for task shifting that are being considered by other countries in the region, including nurse-driven ART for adults and children, and lay-counselor supported

---

\* NF conceived of the paper, undertook the research, wrote the first draft of the paper, and contributed to all subsequent drafts.

testing and counselling, adherence and case management.

## **Introduction**

Lesotho has the third highest HIV prevalence in the world (after Swaziland and Botswana), at 23.2% among adults aged 15 to 49 [1], and is the poorest of the three countries, ranking 138 out of 177 nations on the Human Development Index [2]. More than half of Lesotho's 1.8 million inhabitants live below the poverty line [2]. According to the latest available census data, Lesotho's population is declining drastically, largely as a result of HIV/AIDS [3,4].

The high HIV prevalence can be explained largely by Lesotho's dependence on migrant labour: the heavy reliance on remittances from miners employed in South Africa, by some estimates, accounts for almost 60% of Lesotho's gross domestic product [5]. One in every three male wage earners works in South Africa. This dependence on migrant labour - characterised by unsafe and unhealthy working conditions [6], overcrowded living quarters, long periods away from family and community, and easy access to commercial sex work [7,8] - is driving the dual epidemics of HIV and tuberculosis (TB).

An estimated 270,000 people are living with HIV/AIDS in the country, and between 80,000 and 85,000 of these are estimated to be in clinical need of antiretroviral therapy (ART) [9]. HIV/AIDS is having a devastating impact on all aspects of Basotho society, including health, education, agriculture and general economic development. It is the leading cause of mortality, accounting for 56% of deaths among children under five [10], and is responsible for a more than 20 year drop in life expectancy over the past two decades - to as low as 36 years, according to recent statistics [11]. Approximately 18,000 people die annually of AIDS-related complications, representing 1% of the entire population [12].

In addition to its HIV/AIDS epidemic, Lesotho also has the fourth highest TB incidence in the world (635 per 100,000 people per year [13]); according to estimates from the Lesotho National Tuberculosis Programme, up to 90% of TB patients are also infected with HIV. The high co-infection rate, the historically weak TB programme, and the presence of multidrug and extensively drug resistant (M/XDR) TB in every province in neighbouring South Africa has created conditions for a dire drug-resistant (DR) TB problem in Lesotho:

10% of patients with smear-positive TB in Lesotho are estimated to have multidrug-resistant TB [14].

The Government of Lesotho has shown strong commitment to addressing HIV/AIDS and TB. However, health care delivery has been severely limited by major resource constraints, in particular a dire shortage of professional health workers: there are just five doctors and 62 nurses per 100,000 inhabitants in Lesotho (neighbouring South Africa has 74 doctors and 393 nurses per 100,000 inhabitants) [15]; 80% of doctors in Lesotho are visiting foreigners, mainly from other parts of Africa, awaiting certification to practice in South Africa; around a quarter of nurses leave their posts to seek work elsewhere; and another quarter of nurse attrition is due to death.

In January 2006, Médecins Sans Frontières (MSF) and the Ministry of Health and Social Welfare (MOHSW) launched a joint pilot programme to provide decentralized HIV/AIDS care and treatment at the primary health care level. The programme, which relies on a nurse-driven approach, was launched in what was formerly called Scott Hospital Health Service Area, a rural health zone straddling Maseru and Mafeteng districts, with a population in the catchment area of approximately 200,000 people.

This article describes the development, evolution and main outcomes of the first three years of this programme.

### **Programme approach**

The decentralized model of care developed in Scott catchment area covers one 102-bed district hospital and 14 basic, rural health centres, each staffed only by nurses. These nurses are responsible for providing all primary health care and for integrating a full range of HIV/AIDS services, including HIV testing and counselling (HTC), prevention of mother to child transmission (PMTCT) services, TB and HIV care, and antiretroviral therapy, into the package of primary health care offered at the health centre level.

At the start of the programme, approximately 30,000 people were estimated to be living with HIV/AIDS in Scott catchment area. Knowledge of clinical management of HIV was limited and few drugs to treat opportunistic infections were available; ART was not available at all.

**Table 3.3.1. Allocation of HIV and TB tasks at primary health care level**

<b>District level</b>	<b>Tasks</b>
Public health nurse	<ul style="list-style-type: none"> <li>– Carries out monthly visits to health centres</li> <li>– Conducts quarterly supervision visits</li> <li>– Provides refresher trainings</li> </ul>
Doctor	<ul style="list-style-type: none"> <li>– Provides clinical mentorship at health centres (and OPD) during bi-weekly clinic visits</li> <li>– Provides referral support for complicated cases</li> <li>– Prescribes ART for non-ARV naïve patients</li> <li>– Manages patients suspected to have TB IRIS</li> <li>– Makes clinical decision about switching to second-line therapy, as needed</li> <li>– Formally admits patients to hospital and provides inpatient care</li> </ul>
<b>Health centre level</b>	
<b>Nurse clinician</b> MOHSW minimum staffing: 1 per health centre	<ul style="list-style-type: none"> <li>– Initiates and manages first-line ART for adults and children</li> <li>– Interprets chest x-rays to diagnose smear negative TB using the smear negative algorithm</li> <li>– Initiates second-line ART in the case of treatment failure, after doctor's approval</li> <li>– All of the below</li> </ul>
<b>Professional nurse</b> MOHSW minimum staffing: 1 per health centre	<ul style="list-style-type: none"> <li>– Initiates and manages first-line ART for adults and children</li> <li>– Makes a presumptive diagnosis of severe HIV disease in children &lt;18 months</li> <li>– Refers patients to hospital</li> <li>– Initiates TB treatment for patients newly initiated on ART</li> <li>– All of the below</li> </ul>
<b>Trained nurse assistant</b> MOHSW minimum staffing: 2 per health centre	<ul style="list-style-type: none"> <li>– Initiates and manages first-line ART for adults and children</li> <li>– Stages HIV+ adults and children according to WHO classification</li> <li>– Manages opportunistic infections</li> <li>– Initiates cotrimoxazole as prophylaxis</li> <li>– Prepares children's caregivers to provide ART</li> <li>– Provides education and counselling on feeding options for HIV+ pregnant women</li> </ul>
<b>HIV/TB lay counsellor (adherence)</b> Recommended minimum staffing: 1 per health centre	<ul style="list-style-type: none"> <li>– Provides preparatory counselling before patients are initiated on ART</li> <li>– Provides ART and TB treatment adherence counselling</li> <li>– Identifies TB and ART defaulters and mobilises community-based health workers to trace them</li> <li>– Facilitates support groups and provides health talks on pertinent topics (e.g., ANC and PMTCT, HTC, TB, ART)</li> <li>– Counsels pregnant women on PMTCT and testing schedule for infants</li> <li>– Schedules appointments for HIV patients, including: labs, counselling, refills and clinical exams, according to national guidelines</li> <li>– Assists in recording basic information in registers and compiling monthly reports, including pre-ART, ART, HTC, PMTCT, TB suspect, and general TB registers</li> </ul>
<b>HIV/TB lay counsellor (HTC)</b> Recommended minimum staffing: 1 per health centre	<ul style="list-style-type: none"> <li>– Provides HIV testing and counselling for adults and children via rapid tests</li> <li>– Collects dried blood spots for PCR testing of infants, after training</li> <li>– Provides TB and STI screening and refers to nurse accordingly for all HIV+ patients</li> <li>– Weighs patients, carries out basic cough triage and other clinic support tasks</li> <li>– Provides sputum production education, fills out lab specimen request forms, collects and prepares lab samples for transport</li> </ul>
<b>Community-based health worker</b>	<ul style="list-style-type: none"> <li>– Traces TB treatment and ART defaulters</li> <li>– Provides education and encourages uptake of HIV- and TB-related services</li> <li>– Refers symptomatic patients to health centre</li> <li>– Carries out awareness-raising activities</li> </ul>

Building on MSF's previous experience in South Africa [16], nurses were supported to initiate and manage HIV care and ART at the health centres. Unlike South Africa, the Lesotho health authorities encouraged task shifting to enable all levels of nurses with diagnosing, prescribing and dispensing powers; this model was readily accepted by the MOHSW for replication throughout the country (Table 3.3.1).

To equip nurses with the skills to meet these new responsibilities, intensive in-service theoretical and practical training was provided on management of HIV-related conditions and ART. This included quarterly "out-of-service" trainings, each lasting one week, which were clinical trainings adapted from the World Health Organization's (WHO's) Integrated Management of Adolescent and Adult Illness (IMAI) [17].

Targeted trainings were also provided on the basis of weaknesses identified via pre- and post-test evaluations and in-service support and supervision visits. These covered specific issues, such as drug management, monitoring and evaluation, laboratory investigations, diagnosis of smear-negative TB, DR-TB, infection control, family planning, isoniazid prophylaxis, PMTCT, and paediatric ART. In addition, a number of clinical support tools were developed, including a nurse-oriented guideline for HIV management [18], an algorithm for the diagnosis of smear-negative TB [19], and standardised protocols and flowcharts for basic clinic procedures.

Each clinic is staffed by just one or two nurses (often, they are nursing assistants with just two years of training), who provide a full range of primary care activities. Their work is supported by a doctor or an experienced nurse clinician, who visits on a weekly or bi-weekly basis to provide clinical mentorship for nurses on such issues as: the diagnosis and management of complicated HIV-related conditions, antiretroviral (ARV) side effects, and other clinical challenges; referral support for complicated cases; and assistance with general clinic management, including monitoring and evaluation tasks.

Nurse workload is high. An assessment in August 2006 found that nurses were carrying out up to 45 consultations per day, far greater than the WHO recommended maximum of 30

consultations per day (excluding HIV consultations). Acknowledging that the ever-increasing need for ART could not be met due to scarcity of doctors, nurses and other professional health staff, MSF and Scott Hospital established a cadre of HIV/TB lay counsellors to reinforce capacity to deliver HIV and TB services.

In contrast to traditional models of community-based health worker support, these lay counsellors (typically people living openly with HIV/AIDS) are facility based, receive structured training in HIV and TB and counselling, have clear task descriptions, and are compensated for their work, receiving 39 to 55 maloti (US\$5-7) per day. As of July 2009, there were a total of 42 facility-based lay counselors working across the catchment area.

Lay counsellors manage HTC services and provide pre- ART preparatory counselling, and ART and TB treatment adherence support. They also carry out general clinic support tasks, including tracking of patients who are eligible for ART but have not yet been started, and organising ART and TB defaulter tracing. One of the challenges they face, and an important barrier to adherence, is that many Basotho move temporarily or semi-permanently to South Africa in search of work. Clinic staffers, including counsellors, try to respond to their clients' needs by detailing HIV clinical history in patient-held records, providing two to three month refills, and helping the client's continuity of care by discussing what facilities provide ART care in the area in South Africa to which they are moving.

## **Discussion and Evaluation**

### *ART outcomes*

ART was introduced at the primary care level in Scott catchment area in March 2006. As of July 2009, 13,243 people had been enrolled in HIV care (5% children), and 5376 initiated on ART (6.5% children), 80% at primary care level. Overall, four in five people were initiated at the health centre level. Enrolment has increased substantially year to year, while the proportion of adults arriving sick (with a CD4 count of less than 50 cells/mm<sup>3</sup>) has halved, from 22.2% in 2006 to 11.9% in 2008, an indication that people are seeking treatment earlier.

Outcomes for the first two years were satisfactory, with 80% of patients still alive and in care

(i.e., still receiving ART) at 12 months, and 76.5% of patients remaining in care at 24 months (Table 3.3.2). These data compare favourably with outcomes from other programmes in Africa: a systematic review of HIV cohorts from 13 countries in sub-Saharan Africa reported lower retention rates at six months (79% vs 89% in Scott catchment area), 12 months (75% vs 80%) and 24 months (61.6% vs 77%) [20].

Although long-term follow-up data are still limited, the fact that three in four patients were still in care at two years is particularly encouraging and likely reflects the positive impact of two main programme principles, both of which have been associated with better retention in care: the decentralization of services to provide care close to people's homes, and the provision of free care [21-23].

**Table 3.3.2. Cumulative ART outcomes (adults and children)**

	<b>Adults</b>	<b>Children</b>
<b>Total enrolled</b>	<b>4061</b>	<b>244</b>
<b>12 months</b>		
Cumulative lost-to-follow up	185 (8.8%)	2 (1.6%)
Cumulative died	234 (11.1%)	11 (8.9%)
Cumulative transferred	63	5
<b>Cumulative remaining in care at 12 months</b>	<b>1691 (80.1%)</b>	<b>110 (89.4%)</b>
<b>24 months</b>		
Cumulative lost-to-follow up	76 (9.4%)	1 (2.1%)
Cumulative died	114 (14.1%)	5 (10.4%)
Cumulative transferred	32	6
<b>Cumulative remaining in care at 24 months</b>	<b>618 (76.5%)</b>	<b>40 (87.5%)</b>

Outcomes in children are also highly satisfactory, with 89.4% remaining in care at 12 months and 87.5% at 24 months. These data compare favourably with other programmes in southern Africa (Rwanda: 95% [24]; Malawi: 72% [25]) and data from multicentric cohorts (14 countries: 89% [26]). This provides strong evidence that the provision of ART to children by nurses at the primary care level is feasible and effective (Table 2), and does not require the presence of paediatric specialists. The steady increase in enrolment of children - annual enrolment more than doubled in two years, from 54 in 2006 to 116 in 2008 - reflects an increase in confidence and skill of nurses to initiate treatment in children, although this remains an important challenge in the programme.

### *Innovations to support the expansion and quality of HIV services*

Given the extreme poverty and the shortage of health staff in Lesotho, the national HIV/AIDS programme is notable for having introduced a range of innovations that are still absent from the policies of its better resourced neighbours. In 2007, national ART guidelines were revised to raise the threshold of initiation from CD4 counts of less than 200 cells/mm<sup>3</sup> to less than 350 cells/mm<sup>3</sup>. The guidelines included a number of treatment innovations, including tenofovir disoproxil fumarate in first-line therapy for adults, a state-of-the-art PMTCT protocol that includes triple therapy for mothers, and early infant diagnosis by DNA polymerase chain reaction testing and initiation of ART for all HIV-positive infants less than 12 months.

Similarly, while many countries in southern Africa have been reluctant to endorse nurse initiation of ART despite the fact that it is recommended by the World Health Organization, Lesotho has permitted nurse initiation since 2006 and it was incorporated formally into the Lesotho National Treatment Guidelines in 2008 [27]. Finally, while the engagement of lay counsellors to support HTC, adherence support and other essential services is still not endorsed by many countries, in Lesotho it has clearly facilitated the expansion of care and contributed to empowering people living with HIV/AIDS.

The early introduction of these innovations is in stark contrast to neighbouring South Africa, where tenofovir is not authorised for routine use in first-line treatment in the public sector. Initiation is delayed until 200 cells/mm<sup>3</sup> (for asymptomatic patients), and nurse initiation and lay counsellor administration of HIV rapid tests is stymied: both are provided for in the regulatory framework, but approval has not been forthcoming from the national level.

### *Strengthening primary health care to address leading causes of death*

There has been considerable debate about the extent to which interventions to address HIV have supported the delivery of primary health care. In such debates, it is important to first consider the burden of disease and how HIV is affecting general health indicators. In Lesotho, HIV/AIDS has contributed to a major increase in mortality – it accounts for at least 60% of all deaths in the country [28] – and decrease in life expectancy and overall negative population growth over the past two decades.

Whereas in previous years, the leading causes of infant and under-five mortality were neonatal and diarrhoeal diseases, 56% of deaths in children are now HIV related [29]. In order to have an impact on childhood mortality in Lesotho, therefore, the most important interventions are to: treat HIV-positive pregnant women, thereby reducing the risk of vertical transmission; facilitate early diagnosis of HIV in infants; and initiate treatment as soon as possible for infants who are HIV infected.

By integrating comprehensive HIV/AIDS services into the primary health care package, existing health systems in Scott catchment area were better able to address the leading cause of mortality among adults and children (HIV/AIDS itself). In addition, the inputs needed to support HIV services - such as improving nurses' clinical management skills, strengthening laboratory capacity, reinforcing the drug supply system, improving general infrastructure, and strengthening programme management capacity - were, by design, to the benefit of the entire primary health care system in the catchment area.

Clinical management skills of MOHSW nurses in facilities in Scott catchment area were improved through intensive out-of-facility training and in-service clinical mentorship. Training of nurses improved diagnostic and management skills in other common presentations at primary care level (authors' observations). The syndromic management of sexually transmitted infections, diarrhoea and reproductive tract infections, and improved monitoring of children, including assessment of malnutrition, were additional areas, alongside HIV, where the quality of management was improved. A survey done by MSF in 2007 among 47 health centre and hospital nurses trained in HIV/AIDS found that almost all (46) said they felt improved morale and confidence since acquiring skills and tools to provide HIV/AIDS care and treatment.

Scott Hospital's laboratory, serving the hospital and health centres, was improved through additional equipment, technical and management training, and additional human resources initially paid for by MSF and now absorbed by Scott Hospital. A mobile specimen collection system enabled clinic patients to forego costly trips to the hospital and allowed nurses and patients to have more timely results. The government, in collaboration with another

nongovernmental organization, has recently started to implement this system independent of MSF.

Drug supply and management were improved through training and supervision, structural improvements to increase storage capacity, and subsidising additional human resources at the Scott Hospital pharmacy (initially paid for by MSF and now absorbed by Scott Hospital).

Substantial infrastructure improvements have been made to expand capacity for an increased volume of patients, improve patient flow and clinic organization, and address deplorable working conditions for health staff. Priorities were identified through basic audits and discussions with staff and included: providing essential equipment (such as stethoscopes, thermometers and syringes); improving organisational capacity with basic furniture and supplies (such as additional benches, cabinets and patient files and folders); improving conditions (for example, by upgrading radios and providing coal and other materials for heating during winter months); and perhaps most importantly, improving infection control and occupational health practices. The most important addition relating to occupational health was the provision of HIV services for health workers, in light of the fact that death due to HIV has been cited as the number one reason for health care worker attrition in the country [30].

Finally, programme management capacity has been improved. Mobile medical teams have supported improved data recording and reporting, and a simplified cohort monitoring tool was developed using restricted indicators in order to produce quarterly outcomes and empower nurses with feedback about the services they are providing so that they can make necessary improvements to enhance quality of care. Individual clinics are assessed through a quarterly TB/HIV clinic supervision tool, which measures both process and outcome indicators. Supervision visits are now carried out jointly by MSF, Scott Hospital, and district health management teams.

## **Conclusions**

The MSF-supported programme in Scott catchment area provides further evidence that HIV care and treatment can be provided effectively at the primary care level, to the benefit of

primary health care services. It also validates several critical areas for task shifting that are being piloted in many countries in southern Africa and beyond, including nurse-driven ART for adults and children, and lay counsellor-supported testing and counselling, adherence and case management. In addition to rapidly increasing coverage of ART and related services, the programme has managed to incorporate some of the latest national and international guidelines for PMTCT and ART that support important improvements in quality of care. Given Lesotho's severe resource constraints, the aim of the MSF-supported programme in Scott was to develop a model that was replicable and sustainable in the long term, while meeting ambitious early targets for ART enrolment and ensuring quality of care.

The first phase of the programme, designed for three years, has come to a close and the project has entered a hand-over phase, during which MSF will gradually transfer all responsibilities to the MOHSW and other local health authorities and partners. The real test of whether the objectives of sustainability and replicability of the model have been met will come after the programme has been fully handed over. The ongoing success of a similarly decentralized model of care in rural South Africa that was handed over to the government more than three years ago gives cause for optimism [16].

However, a number of critical clinical and programme-level challenges remain to be addressed. Clinical challenges include: continuing enrolment rates for ART care to keep up with ever increasing needs without compromising quality of care; increasing nurse confidence and skills for paediatric care; increasing the role of lay counsellors to screen stable patients on ART; promoting community-based PMTCT; and continuing to improve diagnosis and management of TB, including smear-negative, extra-pulmonary and DR-TB, as it is the leading cause of death among HIV-positive individuals in the programme and in Lesotho more generally.

At the programme level, key challenges include: ensuring minimum necessary staffing levels, ongoing training and clinical mentorship; assuring an uninterrupted supply of essential HIV medicines, including ARVs; and boosting programme management.

Partly in recognition of the success of the Scott programme, the Government of Lesotho is

reviewing the policies for scaling up task shifting at the national level. Special attention needs to be paid to guaranteeing the long-term engagement of the HIV/TB lay counsellors in health service support. In 2009, efforts were made by numerous international nongovernmental organizations working in Lesotho to harmonize their policies for engagement of lay counsellors across the country and to provide recommendations, evidence and input to the MOHSW regarding establishment of a national standard for remuneration, training and core responsibilities of lay counsellors as a first step towards their recognition as a formal health cadre.

Finally, efforts must continue to strengthen the primary care services to accommodate the ever-increasing numbers of patients who need to be initiated on ART in the years to come. Out-of-facility models of care have been found to be effective in other parts of southern Africa [31] and will likely need to be developed to provide support for stable patients with good adherence as a way to make treatment follow up less burdensome for patients and the health system.

### **3.4. References for Chapter 3**

#### **3.1 Introduction**

1. Ford N, Reuter H, Bedelu M, Schneider H, Reuter H. Sustainability of long-term treatment in a rural district: the Lusikisiki model of decentralized HIV/AIDS care. *Southern African J HIV Med* 2006; 17-20.
2. Médecins Sans Frontières. Help wanted. Confronting the healthcare worker crisis to expand access to HIV/AIDS treatment. Geneva: Médecins Sans Frontières; 2008. <http://www.msf.org/msfinternational/invoke.cfm?component=report&objectid=AD90630F-15C5-F00A-25723C556AA2E57E&method=full.html>
3. Rosen S, Fox M, Gill C. Patient Retention in Antiretroviral Therapy Programs in Sub-Saharan Africa: A Systematic Review. *Plos Medicine* 2007; 4: 1-11.
4. Mills EJ, Nachege JB, Bangsberg DR, Singh S, Rachlis B, Wu P, Wilson K, Buchan I, Gill CJ, Cooper C. Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. *PLoS Med* 2006: e438
5. Bedelu M, Ford N, Hildebrandt K, Reuter H. Implementing antiretroviral therapy in rural

communities: the Lusikisiki model of decentralized HIV/AIDS care. *J Inf Dis* 2007; S3: 464-468.

6. Cohen R, Lynch S, Bygrave H, Eggers E, Vlahakis N, Hilderbrand K, Knight L, Pillay P, Saranchuk P, Goemaere E, Makakole L, Ford N. Antiretroviral treatment outcomes from a nurse-driven, community-supported HIV/AIDS treatment programme in rural Lesotho: observational cohort assessment at two years. *J Int AIDS Soc* 2009; 12: 1-8.

### **3.2 Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS Care**

1. Van Damme W, Kober K, Laga M. The real challenges for scaling up ART in sub-Saharan Africa. *AIDS* 2006; 20: 653-6.

2. Padarath A, Chamberlain C, McCoy D, Ntuli A, Rowson M, Loewenson R. Health personnel in Southern Africa: confronting maldistribution and brain drain. Discussion paper 3.

3. Harare, Zimbabwe: Equinet, 2003.

3. United Nations Human Development Report. Country fact sheet: South Africa, 2006 4.

Medecins Sans Frontieres. Achieving and sustaining universal access to antiretrovirals in rural areas: the primary health care approach to HIV services in Lusikisiki, Eastern Cape. Cape Town, South Africa: Medecins Sans Frontieres, 2006. Available at: [http://www.msf.org.za/docs/lusikisiki\\_final\\_report\\_2006.pdf](http://www.msf.org.za/docs/lusikisiki_final_report_2006.pdf).

5. World Health Organization (WHO). Health worker shortages and the response to AIDS. Geneva: WHO, 2006.

6. Statistics South Africa. Mortality and causes of death in South Africa: findings from death notification, 1997-2003. Statistical release PO309.3. Pretoria, South Africa: Statistics South Africa, 2005.

7. Zachariah R, Teck R, Buhendwa L, Labana S, Chinji C, Humblet P, Harries AD. How can the community contribute in the fight against HIV/AIDS and tuberculosis? An example from a rural district in Malawi. *Trans R Soc Trop Med Hyg* 2006; 100: 167-75.

8. Actuarial Society of South Africa. ASSA2003 AIDS and demographic model. Available at: <http://www.assa.org.za/aidsmodel.asp>.

9. McCoy D, Chopra M, Loewenson R, Aitken JM, Ngulube T, Muula A, Ray S, Kureyi T, Ijumba P, Rowson M. Expanding access to antiretroviral therapy in sub-Saharan Africa: avoiding the pitfalls and dangers, capitalizing on the opportunities. *Am J Public Health* 2005;

### **3.3. Antiretroviral treatment outcomes from a nurse-driven, community-supported HIV/AIDS treatment programme in rural Lesotho: observational cohort assessment at two years**

1. UNAIDS. Report on the Global AIDS Epidemic UNAIDS, Geneva; 2006. Annex 1: Lesotho Country Profile.
2. United Nations Development Programme: Human Development Report 2009. UNDP, New York, 2009.
3. Kingdom of Lesotho, Bureau of Statistics: Shrinking Population [http://www.statssa.gov.za/assd\\_dec2007/Presentations/Day%203\\_Wednesday%205%20Dec%2007/Session%209/lesotho.ppt](http://www.statssa.gov.za/assd_dec2007/Presentations/Day%203_Wednesday%205%20Dec%2007/Session%209/lesotho.ppt).
4. Health Economics & HIV/AIDS Research Division (HEARD). Reviewing "Emergencies" in HIV and AIDS-affected Countries in Southern Africa: Shifting the Paradigm in Lesotho University of KwaZulu-Natal, 2008.
5. Furin J, Behforuz H, Shin S, Mukherjee J, Bayona J, Farmer P, Kim J, Keshavjee S. Expanding global HIV treatment: case studies from the field. *Ann NY Acad Sci* 2008; 1136: 12-20.
6. Akugizibwe P. The dark heart of mining. AIDS and Rights Alliance for Southern Africa. *The Times of South Africa* 2009.
7. Campbell C, Williams B. Beyond the biomedical and behavioural: towards an integrated approach to HIV prevention in the southern African mining industry. *Soc Sci Med* 1999; 48: 1625-1639.
8. Meekers D. Going underground and going after women: trends in sexual risk behaviour among gold miners in South Africa. *Int J STD AIDS* 2000; 11:21-26.
9. WHO/UNAIDS. Report on the Global AIDS Pandemic 2008 [<http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/default.asp>]. WHO, Geneva Annex 2.
10. Anon World Health Statistics. World Health Organization, Geneva, 2008.
11. US Department of State: Background Note: Lesotho. Bureau of African Affairs, Washington, 2009.
12. UNAIDS/WHO/UNICEF. Epidemiologic Fact Sheet on HIV and AIDS: Core Data on

Epidemiology and Response. Geneva, 2008.

13. WHO: TB Country Profile. Lesotho. Geneva 2008 14. Satti H, Seung K, Keshavjee S, Furin J: Extensively drug-resistant tuberculosis, Lesotho. *Emerg Infect Dis* 2008; 6: 992.

15. World Health Organization. Human Resources for Health. Geneva, 2007

16. Bedelu M, Ford N, Hildebrandt K, Reuter H: Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS care. *J Inf Dis* 2007; 196: 464-468.

17. World Health Organization: Chronic HIV Care with ARV Therapy and Prevention. IMAI/IMCI WHO, Geneva, 2004.

18. MSF. Guide for Nurses: management of HIV-related conditions and antiretroviral therapy in adults and children at primary health care level. Khayelitsha 2005.

19. Saranchuk P, Goemaere E, Meintjes G. A nurse-based algorithm for earlier diagnosis of smear-negative pulmonary tuberculosis in HIV-infected adults. IUATLD Conference, Cape Town 2008. Abstract PS-71976-10.

20. Rosen S, Fox M, Gill C. Patient Retention in Antiretroviral Therapy Programs in Sub-Saharan Africa: A Systematic Review. *Plos Medicine* 2007; 4: 1691-1701.

21. Maskew M, MacPhail P, Menezes C, Rubel D: Lost to follow up - contributing factors and challenges in South African patients on antiretroviral therapy. *SAMJ* 2007; 97: 853-7.

22. Zachariaha R, Van Engelgem I, Massaquoi M, Kocholla L, Manzi M, Suleh A, Phillips M, Borgdorff M. Payment for antiretroviral drugs is associated with a higher rate of patients lost to follow-up than those offered free-of-charge therapy in Nairobi, Kenya. *Trans Roy Soc Trop Med Hygiene* 2008; 102: 288-293.

23. Boulle A, Bock P, Osler M, Cohen K, Channing L, Hilderbrand K, Mothibi E, Zweigenthal V, Slingers N, Cloete K, Abdulla F. Antiretroviral therapy and early mortality in South Africa. *Bull World Health Organ* 2008; 86: 657-736.

24. Griensven J, Naeyer L, Uwera J, Asimwe A, Gazille C, Reid T. Success with antiretroviral treatment for children in Kigali, Rwanda: experience with health center/nurse-based care. *BMC Pediatrics* 2008; 8: 39.

25. The Malawi Paediatric Antiretroviral Treatment Group. Antiretroviral therapy for children in the routine setting in Malawi. *Trans Roy Soc Trop Med Hygiene* 2007; 101: 511-516.

26. O'Brien D, Sauvageot D, Olson D, Schaeffer M, Humblet P, Pudjades M, Ellman T,

Zachariah R, Szumilin E, Arnould L, Read T. Treatment outcomes stratified by baseline immunological status among young children receiving nonnucleoside reverse-transcriptase inhibitor-based antiretroviral therapy in resource-limited settings. *Clinical Infectious Diseases* 2007; 44: 1245-8.

27. MOHSW. Draft Lesotho National ART Guidelines. Maseru, 2007-2008.

28. World Health Organization: Mortality Country Fact Sheet, Lesotho, 2006.

29. Health Economics & HIV/AIDS Research Division (HEARD). Reviewing "Emergencies" in HIV and AIDS-affected Countries in Southern Africa: Shifting the Paradigm in Lesotho University of KwaZulu-Natal; 2008: 54.

30. Schwabe C, McGrath E, Lerotholi K. Lesotho human resources consultancy: health sector human resources needs assessment. Medical Care Development International, Silver Spring, Maryland, 2004.

31. Jaffar S, Amuron B, Foster S, Birungi J, Levin J, Namara G, Nabiryo C, Ndembu N, Kyomuhangi R, Opio A, Bunnell R, Tappero JW, Mermin J, Coutinho A, Grosskurth H; Jinja Trial Team. Rates of virological failure in patients treated in a home-based versus a facility-based HIV-care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial. *Lancet*. 2009 Dec 19;374(9707):2080-9. Epub 2009 Nov 24.

## Chapter 4: Improving quality of care

### 4.1 Introduction

The early years of delivering ART in resource-limited settings were an emergency response to major mortality: at the time it was argued that AIDS was a humanitarian emergency, like floods and famines, and deserved the recognition as a disaster in its own right [1].

In order to provide effective, affordable care as quickly as possible to the millions in need adaptations to the Western model of care were required in order to simplify the treatment regimens and delivery models to the realities of resource-limited settings [2]. Strong cases were made for a public health approach to HIV/AIDS that meant focusing on those patients who were waiting for treatment, even if it was at the expense of those who developed drug resistance and side-effects and required more complicated case-management and newer but more expensive medications [3].

Until recently, the level of CD4 indicating ART differed between Developed and Developing countries. European and US guidelines recommend ART initiation at a CD4 cell threshold of 350 cells/mm<sup>3</sup> (moderate immunodeficiency). This was originally based on concerns related to the accumulative risks of toxicity and drug resistance [4]. Such concerns have diminished in recent years as newer medicines have become available with fewer toxicities and better potency (reducing the chance of resistance development). The availability of these newer medicines, together with studies that have increased the understanding of the risks of developing life-threatening illnesses over time if ART is initiated at a low CD4 count have shifted the risk-benefit equation [4]. Recent evidence from European cohorts show that starting ART earlier (at least 350 cells/mm<sup>3</sup>) results in significant survival gains [5].

Guidelines for Developing countries have recently been revised in line with Developed world recommendations. Treatment guidelines issued by the International AIDS society in

August 2008 state that “the core principle underlying these guidelines, namely pathogenesis-directed therapy with regimens designed to achieve full virologic suppression with minimal toxicity and maximal simplicity, is applicable to the developing world.” [6] and the latest World Health Organization antiretroviral treatment guidelines for resource-limited settings released at the end of 2009 recommend a move towards earlier initiation at 350 cells/mm<sup>3</sup> [7].

In addition, as developing country cohorts matured, so the limits of an emergency, public health approach for a chronic, lifelong disease, became apparent [8]. The inevitable challenges of how to manage long-term toxicities and drug resistance [9] began to call into question the standard of care provided to people in resource-limited settings.

This chapter examines some of these emerging challenges to improving the quality of care provided in resource-limited settings. The first paper, based on an analysis of data from a primary care programme in South Africa, shows that early adherence is predictive of long-term patient outcomes, demonstrating that, while models of care need to be developed to support ART care over time, the initial early investment in adherence counseling and support is an effective way to maximize the likelihood of treatment success in the longer term [10]. The second paper provides a broader critique of the level of care, making the case that, in light of new clinical evidence, the basic essential package of care needs to be reviewed [11].

## 4.2. Early adherence to antiretroviral medication as a predictor of long-term HIV virological suppression: five-year follow up of an observational cohort

Ford N\*, Darder M, Spelman T, Maclean E, Mills E, Boulle A. *PLoS ONE* 2010; 5:5.

### Abstract

**Objective:** Previous studies have demonstrated a cross-sectional relationship between adherence and virological suppression. We assessed the predictive value of baseline adherence to antiretroviral medication in determining long-term virological failure.

**Design:** We assessed baseline adherence via an adherence questionnaire administered to all consenting patients attending antiretroviral clinics in Khayelitsha township, South Africa, between May 2002 and March 2004. Virological status was ascertained after five years of follow up and multivariate analysis was used to model associations of baseline variables and medication adherence with time to viral suppression or failure.

**Results:** Our adherence cohort comprised 207 patients, among which 72% were female. Median age was 30 years and median CD4 count at initiation was 55 cells/mm<sup>3</sup>. We found no statistically significant differences between baseline characteristics and early adherence groups. Multivariate analysis adjusting for baseline CD4 and age found that patients with suboptimal baseline adherence had a hazard ratio of 2.82 (95% CI 1.19- 6.66, p= 0.018) for progression to virological failure compared to those whose baseline adherence was considered optimal.

**Conclusions:** Our longitudinal study provides further confirmation of adherence as a primary determinant of subsequent confirmed virological failure, and serves as a reminder of the importance of initial early investment in adherence counseling and support as an effective way to maximize long-term treatment success.

---

\*NF designed the study, executed the analysis, wrote the first draft of the paper, and contributed to all subsequent drafts.

## **Introduction**

The widespread availability of antiretroviral therapy (ART) has changed the course of HIV infection in developed countries, and comparable benefits are observed in resource-limited settings. The provision of effective ART is increasingly understood to be critical for both medical and a public health reasons. Maintaining virological suppression is an important objective for both the individual (reduced morbidity and mortality) and at the population level (reduced resistance [1] and transmission [2]).

A mixture of biologic factors such as virus type, host immunology, disease status and genetics, together with characteristics of medications such as drug potency, toxicity, formulation, and pharmacology can influence adherence and therapeutic success. Thus, virological failure may result from suboptimal adherence, poor drug potency, drug resistance, or a combination of these factors [3].

Amid these multiple explanations, sub-optimal adherence to medication has been recognized as one of the main patient-mediated risk factors for treatment failure [3] and several studies have demonstrated a cross-sectional relationship between adherence and virological suppression [4-7]. It is unknown whether patient-mediated factors may predict poor adherence, and thus poor virological suppression, in the long-term. We aimed to assess this relationship in a longitudinal study to determine the predictive value of baseline adherence in determining virological failure over time.

## **Methods**

### *Study Setting and data sources*

Our study includes patients enrolled in an HIV treatment programme, in Khayelitsha township, South Africa. ART was first provided through a pilot demonstration project in May 2001, with initial capacity to provide ART for 180 adults. By the end of 2007, the service had cumulatively enrolled over 7000 adults onto ART as part of the routine programme [8].

We used data derived from a baseline adherence questionnaire done in Khayelitsha township during the early phase of antiretroviral provision in 2002. This adherence study was conducted at a time when the ability of people in Africa to adhere to antiretroviral medication was questioned, a hypothesis that has since been found to be unsupported by evidence [9].

The adherence survey included all consenting patients enrolled onto antiretroviral therapy at primary care clinics in Khayelitsha township, South Africa between May 2002 and March 2004. Self-reported adherence was assessed by a dedicated study team unrelated to the provision of clinical care using a modified version of the AIDS Clinical Trials Group questionnaire [10] that was forward- and back-translated and piloted prior to administration. We assessed adherence one and three months after initiation of ART and considered patients as highly adherent if they reported  $\geq 95\%$  adherence to medication; otherwise, adherence was considered as suboptimal.

Baseline and outcome data were collected as standard indicators for monitoring and evaluation in the Khayelitsha programme. Viral load (NucliSens EasyQ HIV-1 assay (bioMerieux, Boxtel, The Netherlands) and CD4 count (single-platform panleucogating method) were assessed at baseline and every six months according to manufacturer's instructions. Virological failure was defined as two consecutive HIV RNA levels greater than 5000 copies/ml, in accordance with national guidelines. Mortality ascertainment is corrected through linkages with the South African vital registration system [8]. The duration of follow-up for this study was five years.

### *Statistical analyses*

Descriptive analyses were based on percentages and frequencies for categorical variables and medians and interquartile ranges (IQR) for continuous variables. Continuous variables were assessed for skew and as all demonstrated non-normality they were compared using the Wilcoxon rank-sum test. Proportions were compared using the  $\chi^2$  test and, in the case of small numbers, the Fisher's Exact test. We used Nelson-Aalen cumulative hazards estimates to describe time to confirmed virological failure per adherence group, as this method provides an appropriate summary for failure events [11]. Univariate cox regression was used

to model the individual associations of baseline variables and medication adherence with time to viral suppression or failure; variables were stratified into discrete categories as follows: early adherence (<95% or ≥95%), baseline CD4 (<50 cells/mm<sup>3</sup> or ≥50 cells/mm<sup>3</sup>), sex (male or female), HAART regimen (efavirenz- or nevirapine-based), and age (per 10 years). Multivariate models of associations with virological failure included variables associated with poor adherence in univariate analysis adjusted for potential confounders identified a priori. Hazard proportionality was assessed by analysis of scaled Schoenfeld residuals. All reported p values are exact and 2-tailed, and for each analysis p<0.05 was considered significant. All analyses were performed using STATA version 11.0 (StataCorp, College Station, Texas).

All aspects of data collection (adherence questionnaire, analysis of routine cohort data and the linkage to the national death registry) were approved by the University of Cape Town Research Ethics Committee. As the data were based on routinely collected data and anonymized, informed consent was not sought.

## **Results**

Our adherence cohort comprised 207 patients, among whom 149 (72%) were female. The median age at ART initiation was 30 years (IQR 28-37) years and the majority (80%) received an efavirenz-based regimen. Median CD4 count at initiation was 55 cells/mm<sup>3</sup> (IQR 20-115 cells/mm<sup>3</sup>) and median HIV-1 RNA levels at initiation was 5.03 log<sub>10</sub> copies/mL (IQR 4.3 – 5.5 log<sub>10</sub> copies/mL). Our early adherence assessment found that 181 (87%) patients were considered highly adherent. We found no statistically significant differences between baseline characteristics and early adherence groups (Table 4.2.1).

In our univariate analysis suboptimal early adherence was the only association with virological failure (hazard ratio 2.72, 95%CI 1.16-6.31, p=0.02) (Table 4.2.2). In multivariate analysis we adjusted for baseline CD4 and age as these have been found to be associated with virological failure in larger studies from the same population [8]; this analysis found that patients with suboptimal baseline adherence had a hazard ratio of 2.82 for progression to virological failure compared to those whose baseline adherence was considered optimal

(95% CI 1.19- 6.66, p= 0.018). Cumulative hazard estimates by adherence category are described in Figure 4.2.1.

**Table 4.2.1. Baseline characteristics**

	Patients with adherence $\geq$ 95% (n=181)	Patients with adherence <95% (n=26)	p
Sex, n (%)			
Male	50 (28)	8 (31)	0.74
Female	131 (72)	18 (69)	
Age, median (IQR)	31 (8-37)	30 (IQR 26-32)	0.147
Baseline CD4, Median (IQR)	51 (19-121)	59.5 (23-102)	0.71
Baseline VL, median (IQR)	110,000 (20,000-320,000)	155,550 (97,000-300,000)	0.19
Regimen, n (%)			
EFV	144 (80)	21 (81)	0.24*
NVP	36 (20)	4 (15)	
Other	1 (1)	1 (4)	
Prior TB			
Yes	87 (48)	11 (42)	0.58
No	94 (52)	15 (58)	

\* Fishers exact; EFV – efavirenz; NVP – nevirapine; TB – tuberculosis; VL viral load; IQR – interquartile range

**Table 4.2.2. Associations between patient characteristics and time to viral load failure**

Predictor variable	Failures n, %	Univariate		Multivariate	
		HR (95% CI)	p	HR (95% CI)	P
Adherence					
>95%	25 (78.1%)	1	0.020	1	0.010
<95%	7 (21.9%)	2.72 (1.17-6.31)		3.07 (1.30-7.22)	
Sex					
Male	12 (27.5%)	1	0.12	1	0.086
Female	20 (62.5%)	1.79 (0.87-3.68)		1.89 (0.91-3.91)	
Age					
20-29	15 (46.9%)	0.98 (0.93-1.03)*	0.35		
30-39	13 (40.6%)				
40-49	2 (6.3%)				
50-59	2 (6.3%)				
Baseline CD4					
$\leq 0.5 \times 10^9$ cells/L	17 (53.1%)	1	0.52	1	0.345
$> 0.5 \times 10^9$ cells/L	15 (46.9%)	0.79 (0.39-1.60)		0.71 (0.35-1.45)	
Regimen					
NVP	6 (18.7%)	1	0.87		
EFV	26 (81.3%)	1.08 (0.44-2.94)			

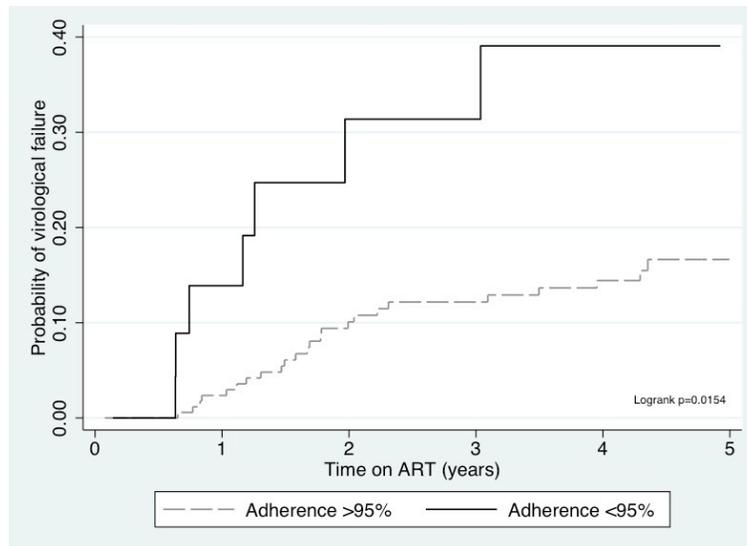
\* per category; EFV – efavirenz; NVP – nevirapine

schoenfelds p=0.12

## Discussion

Our longitudinal study provides further confirmation of adherence as a primary determinant of subsequent confirmed virological failure, reinforcing the findings of previous studies that associate adherence with viraemia at a single point in time concurrent to or soon after the adherence measures [12].

Figure 4.2.1. Cumulative hazard estimates for virological failure



We found that early adherence was a more important predictor of long-term virological suppression than prognostic variables such as CD4 and drug regimens, a phenomenon also observed in better-resourced settings [13]. Patients initiating ART and surviving the first three months of therapy typically have improved survival outcomes in the long term if they can maintain optimal adherence [14].

The use of routine viral load monitoring in South Africa enables the exploration of associations with confirmed virological failure. The confirmation of failure, subsequent to a period of adherence optimization, has been shown to identify patients with a high probability of multi-class drug resistance [15].

Our study was not able to distinguish whether the association between virological failure and early adherence was due to the early adherence being a marker of long term sup-optimal adherence, or due to ongoing viral replication under selective drug pressure in the early

months on ART. Nevertheless, the association we describe validates the structured adherence interventions that are commonplace in the public health approach to ART, including facility-based counseling [16], and the use of early viral load testing to identify patients who might benefit from further adherence-promoting interventions [17].

Several issues need to be considered with respect to the external validity of our findings. First, there is no agreed definition of what constitutes sub-optimal adherence. We applied a conservative cut-off of 95% partly because the drug regimens used did not include boosted protease inhibitors, and partly because of the expectation of poor adherence. Nevertheless, the fact that the majority of our cohort (87%) was considered to be highly adherent is consistent with other findings that display, on average, good adherence within large patient populations [18]. Second, the use of self-reports in assessing medication adherence is subject to information (recall) bias. There is no gold standard for medication adherence, but studies from similar settings in southern Africa have found that self-report can provide a reliable measure compared to other methods [19], especially when administered by independent researchers rather than members of the clinical team. Finally, our adherence cohort was established during the early phase of the programme when most patients were severely immuno-compromised at the start of ART, as indicated by low median baseline CD4. In general baseline CD4 at ART initiation is today much higher than in previous years, both in this cohort [8] and other cohorts [20]. Low baseline CD4 has been found to be associated with virological failure [21], although the extent to which this relates to poor adherence is not known. The patients we describe had to take treatment at least twice daily, at least two different tablets, and often with uneven dosing. They were at relatively high risk of haematological and hypersensitivity reactions [22]. While great strides have been made in improving access to treatments in South Africa, we remain far from providing optimal treatments for patients from an adherence perspective.

As ART programmes mature and lessons emerge over time, concern is growing around the challenges of sustaining long-term adherence [23]. Our study serves as a reminder that a patients' initial experience with antiretroviral medication is critically important. Thus while models of care need to be developed to support ART care over time, the initial early

investments in adherence counseling and support is an effective way to maximize the likelihood of treatment success in the longer term.

### **4.3. Rationing antiretroviral therapy in Africa — treating too few, too late**

*Ford N\*, Mills E, Calmy A. NEJM 2009; 36: 1808-10.*

The past 6 years have seen striking advances in access to antiretroviral therapy in Africa. From 2002 onward, the international drive to scale up antiretroviral treatment gained considerable momentum, most notably with the establishment of the Global Fund to Fight AIDS, Tuberculosis, and Malaria, the “3 by 5” Initiative of the World Health Organization (WHO), and the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR). Today, an estimated 3 million people in the developing world are receiving antiretroviral therapy.

The momentum has now begun to wane, with various groups arguing that the focus on AIDS has had its day and that health care funding should now be redirected to other areas, such as maternal and child health and primary care. But before the international community gives up on prioritizing care for patients with HIV infection, we believe that on-the-ground discussions must address not only whether enough has been done to scale up treatment but also whether the treatment that patients are receiving is good enough.

The standard approach to HIV treatment in Africa is to wait until people are visibly sick, treat them with effective but poorly tolerated drugs, and then wait until they are sick again before switching regimens. There are several problems with this approach.

The first is that too few people are receiving treatment. The 3 million people receiving antiretroviral therapy are usually said to account for about 30% of the need for such treatment, but even this rate reflects the use of stringent eligibility criteria that have been abandoned in wealthier countries.

---

\* NF conceptualized and wrote the first draft of the paper, and contributed to all subsequent drafts.

Second, we are waiting until people are symptomatic before they are treated. In most African countries, patients begin receiving treatment when the CD4+ count falls below 200 cells per cubic millimeter, at which point most patients already have symptomatic and severe (WHO stage 3 or 4) infection. In the United States and Europe, treatment is initiated earlier — as soon as the CD4+ count reaches 350 cells per cubic millimeter — and increasingly, experts are arguing that even that is too late.

In many patients in Africa, the CD4+ count takes only about a year to decline from the cutoff for such early initiation to that for the later initiation now practiced in developing countries [1]. Although delaying therapy may mean saving money on drugs during this period, the long-term cost of such delays is increased substantially by the need for more intensive clinical care, decreased income, and likely regimen switches. Cost is thus no longer a tenable justification for delaying therapy. More important, recent observational data [2] show that the risk of death increases by 69% when the initiation of therapy is delayed until the CD4+ count drops below 350 cells per cubic millimeter. Patients' immunologic nadir — how low their CD4+ count is allowed to drop — is predictive of the degree of benefit they will obtain from future antiretroviral therapy. Although guidelines for low-income settings recommend initiating treatment when a patient's CD4+ count drops below 200 cells per cubic millimeter, patients frequently begin receiving therapy even later, on average when the CD4+ count is just over 100 cells per cubic millimeter. Enrolling patients in treatment programs earlier is a priority [3].

There are also important public health costs. For one thing, a policy of late initiation encourages the spread of tuberculosis. One recent study estimated that patients starting antiretroviral therapy at a CD4+ count below 200 cells per cubic millimeter have more than three times the risk of tuberculosis of those who begin therapy earlier [4]. Moreover, late initiation compromises the potential effect of antiretroviral therapy on HIV transmission by allowing patients to remain viremic longer. One study estimated that starting treatment earlier would reduce HIV transmission by 56% [5]. However, if the current guidelines for the initiation of therapy in the West were adopted in developing countries, several million more people would be eligible for care, and the treatment gap would widen even further.

Another concern is that in most developing countries, patients are receiving drugs with major tolerability issues. The majority of treatment programs in Africa use an antiretroviral regimen based on stavudine. There are a number of sound reasons for using this drug, including the fact that it forms part of a simple, affordable, fixed-dose combination. However, the drug's severe side-effects have rendered it all but obsolete in the West. A tenofovir-based regimen would be preferable, but the use of tenofovir has largely been limited by its cost.

Furthermore, not only should initial treatment begin earlier in developing countries, but when the first-line regimen fails, patients should also be switched earlier to another regimen. In the Western world, evaluations of viral load and genotyping are performed regularly, and the drug regimen is altered at the first sign of virologic resistance. In Africa, access to viral-load assessment is extremely limited, and patients must wait until immunologic or clinical deterioration is manifested before being switched to new drugs, which reduces future treatment options and increases the risk of transmission.

It should be acknowledged that although there are outstanding clinical questions regarding the optimal time for initiating and switching treatments, the overriding rationale behind current guidelines for antiretroviral therapy is rationing — limiting the number of people who must be treated, providing the cheapest available drugs, and delaying shifts to more expensive drugs for as long as possible. But as other experts have argued, rationing on the basis of clinical criteria alone is an inherently flawed way of prioritizing the needs competing for scarce resources [6].

The drive to scale up antiretroviral treatment in Africa has encouraged a public health approach that promotes reaching the greatest number of patients with the simplest, most affordable regimens. We would argue that treating people when they are less sick with drugs that are less toxic and providing a simple tool for monitoring adherence and detecting treatment failure would be entirely consistent with this approach and would improve access to care by facilitating the decentralization of services from the hospital level to the clinic. Newer, more potent drugs should be considered for inclusion in treatment guidelines, rather

than being reserved for use in salvage regimens for a minority of patients in the West. The better the drug, the simpler the treatment, and the fewer treatment switches will be necessary. Viral-load monitoring should be expanded to reinforce adherence and ensure that treatment failure is detected as early as possible.

Taking this new approach will require a reorientation of the organization and support of HIV care programs. A policy of earlier initiation of therapy could help to streamline services that are currently overwhelmed, by prioritizing clinic care according to patients' health needs. Clinic services could be primarily used by patients who are clinically sick, whereas patients with stronger immunity could, after initial consultation, receive follow-up medication and care in the community. In this way, a policy of earlier initiation of therapy could help to streamline services that are already overwhelmed by the competing needs of patients with various levels of illness.

Earlier treatment and regimen switching would initially require additional investment by national governments and the international community (in particular, PEPFAR and the Global Fund), but it might well turn out to be cheaper in the long run, as the need for managing clinical complications is reduced and the rate of new infections falls. The initial provision of antiretroviral therapy in the late 1990s ultimately led to massive cost savings, thanks to the avoidance of hospitalizations and opportunistic infections; in this way, Brazil alone is estimated to have saved more than \$1 billion in 4 years. At the same time, increased demand forced the cost of medicines down considerably, from more than \$10,000 per patient per year to less than \$100. The same dynamic can be expected for a policy of early starting and switching, provided that there are clear messages to manufacturers and ministries of health to support expanded access to better drugs and diagnostics.

The battle to start providing antiretroviral therapy in the developing world has been won. The battle to provide the best care we can is just beginning.

## 4.4. References for Chapter 4

### 4.1. Introduction

1. Stabinski L, Pelley K, Jacob S, Long J, Leaning J. Reframing HIV and AIDS. *BMJ* 2003; 7423: 1101–03.
2. Calmy A, Klement E, Teck R, Berman D, Pécoul B, Ferradini L, Ford N. Simplifying and adapting antiretroviral treatment in resource-poor settings: a necessary step to scaling up. *AIDS* 2004; 18: 2353-60.
3. Harries A, Schouten E, Libamba E. Scaling up antiretroviral treatment in resource-poor settings. *Lancet* 2006; 367: 1870–72.
4. Phillips AN, Gazzard BG, Clumeck N, Losso MH, Lundgren JD. When should antiretroviral therapy for HIV be started? *BMJ* 2007: 76-78.
5. When To Start Consortium. Timing of initiation of antiretroviral therapy in AIDS-free HIV-1-infected patients: a collaborative analysis of 18 HIV cohort studies. *Lancet* 2009; 373: 1352-63.
6. Hammer SM, Eron JJ Jr, Reiss P, Schooley RT, Thompson MA, Walmsley S, Cahn P, Fischl MA, Gatell JM, Hirsch MS, Jacobsen DM, Montaner JS, Richman DD, Yeni PG, Volberding PA; International AIDS Society-USA. Antiretroviral Treatment of Adult HIV Infection 2008 Recommendations of the International AIDS Society–USA Panel. *JAMA* 2008; 300: 555-570.
7. World Health Organization. Rapid advice: antiretroviral therapy for HIV infection in adults and adolescents – November 2009. World Health Organization, Geneva, Switzerland, 2009.
8. Boule A, Orrel C, Kaplan R, Van Cutsem G, Mc Nally M, Hilderbrand K, Myer L, Egger M, Coetzee D, Maartens G, Wood R, International Epidemiological Databases to evaluate AIDS in Southern Africa collaboration. Substitutions due to antiretroviral toxicity or contraindication in the first 3 years of antiretroviral therapy in a large South African cohort. *Antivir Ther* 2007; 12: 753-60.
9. Ellman T, Ford N. Scaling up antiretroviral treatment in resource-poor settings. *Lancet* 5 August 2006; 368: 445-446.
10. Ford N, Darder M, Spelman T, Maclean E, Mills E, Boule A. Early adherence to antiretroviral medication as a predictor of long-term HIV virological suppression: five-year

follow up of an observational cohort. PLoS ONE 2010; 5:5.

11. Ford N, Mills E, Calmy A. Rationing antiretroviral therapy in Africa — treating too few, too late. NEJM 2009; 36: 1808-10.

#### **4.2. Early adherence to antiretroviral medication as a predictor of long-term HIV virological suppression: five-year follow up of an observational cohort**

1. Gill VS, Lima VD, Zhang W, Wynhoven B, Yip B, Hogg RS, Montaner JS, Harrigan PR. Improved virological outcomes in British Columbia concomitant with decreasing incidence of HIV type 1 drug resistance detection. Clin Infect Dis 2010; 50: 98-105.

2. Granich R, Gilks C, Dye C, De Cock K, Williams B. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet 2009; 373: 48-57.

3. Friedland GH. HIV medication adherence. The intersection of biomedical, behavioral, and social science research and clinical practice. J Acquir Immune Defic Syndr 2006; 43: S3–S9.

4. Arnsten JH, Demas PA, Farzadegan H, Grant RW, Gourevitch MN, Chang CJ, Buono D, Eckholdt H, Howard AA, Schoenbaum EE. Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. Clin Infect Dis 2001; 33: 1417–1423.

5. Nachega JB, Hislop M, Dowdy DW, Chaisson RE, Regensberg L, Maartens G. Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes. Ann Intern Med 2007; 146: 564–573.

6. Martin M, Del Cacho E, Codina C, Tuset M, De Lazzari E, Mallolas J, Miró JM, Gatell JM, Ribas J. Relationship between adherence level, type of the antiretroviral regimen, and plasma HIV type 1 RNA viral load: a prospective cohort study. AIDS Res Hum Retroviruses 2008; 24: 1263–1268.

7. Garcia R, Badaró R, Netto EM, Silva M, Amorin FS, Ramos A, Valda F, Brites C, Schooley R. Cross-sectional study to evaluate factors associated with adherence to antiretroviral therapy by Brazilian HIV-infected patients. AIDS Res Hum Retroviruses 2006 ; 22: 1248-52.

8. Boule A, Van Cutsem G, Hilderbrand K, Cragg C, Abrahams M, Mathee S, Ford N, Knight L, Osler M, Myers J, Goemaere E, Coetzee D, Maartens G. Seven-year experience of

a primary care antiretroviral treatment programme in Khayelitsha, South Africa. *AIDS* 2010; 24: 563-72.

9. Mills EJ, Nachega JB, Buchan I, Orbinski J, Attaran A, Singh S, Rachlis B, Wu P, Cooper C, Thabane L, Wilson K, Guyatt GH, Bangsberg DR. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. *JAMA* 2006; 296: 679-90.

10. Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B, Wu A. Self-reported adherence to antiretroviral medications among participants in HIV clinic trials: the AACTG adherence instruments. *AIDS Care* 2009; 12: 255-66.

11. Colosimo, E, Ferreira F, Oliveira M, Sousa C. Empirical comparisons between Kaplan-Meier and Nelson-Aalen survival function estimators. *J Statistical Computation Simulation* 2002; 72: 299-308.

12. Ahoua L, Guenther G, Pinoges L, Anguzu P, Chaix ML, Le Tiec C, Balkan S, Olson D, Olaro C, Pujades-Rodríguez M. Risk factors for virological failure and subtherapeutic antiretroviral drug concentrations in HIV-positive adults treated in rural northwestern Uganda. *BMC Infect Dis* 2009; 9: 81.

13. Wood E, Hogg RS, Yip B, Harrigan PR, O'Shaughnessy MV, Montaner JS. Effect of medication adherence on survival of HIV-infected adults who start highly active antiretroviral therapy when the CD4+ cell count is 0.200 to 0.350 x 10<sup>9</sup> cells/L. *Ann Intern Med* 2009; 139: 810-6.

14. Braitstein P, Brinkhof MW, Dabis F, Schechter M, Boulle A, Miotti P, Wood R, Laurent C, Sprinz E, Seyler C, Bangsberg DR, Balestre E, Sterne JA, May M, Egger M; Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration; ART Cohort Collaboration (ART-CC) groups. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet* 2006; 367: 817-24.

15. Orrell C, Walensky RP, Losina E, Pitt J, Freedberg KA, Wood R. HIV type-1 clade C resistance genotypes in treatment-naive patients and after first virological failure in a large community antiretroviral therapy programme. *Antivir Ther* 2009; 14: 523-31

16. Coetzee D, Hildebrand K, Boulle A, Maartens G, Louis F, Labatala V, Reuter H, Ntwana N, Goemaere E. Outcomes after two years of providing antiretroviral treatment in Khayelitsha, South Africa. *AIDS* 2004; 18: 887-895.

17. Calmy A, Ford N, Hirschel B, Reynolds SJ, Lynen L, Goemaere E, et al. HIV viral load monitoring in resource-limited regions: optional or necessary? *Clin Inf Dis* 2007; 44: 128-34.
18. Ford N, Nachega J, Engel M, Mills E. Directly observed antiretroviral therapy: a systematic review and meta-analysis of randomized clinical trials. *Lancet* 2009; 374: 2064–71.
19. Oyugi JH, Byakika-Tusiime J, Charlebois ED, Kityo C, Mugerwa R, Mugenyi P, Bangsberg D. Multiple validated measures of adherence indicate high levels of adherence to generic HIV antiretroviral therapy in a resource-limited setting. *J Acquir Immune Defic Syndr* 2004; 36: 1100-2.
20. The ART-LINC Collaboration of the International Databases to Evaluate AIDS (IeDEA). Antiretroviral therapy in resource-limited settings 1996 to 2006: patient characteristics, treatment regimens and monitoring in sub-Saharan Africa, Asia and Latin America. *Trop Med Int Health* 2008; 13: 870–879.
21. Boulle A, van Cutsem G, Hilderbrand K, Cragg C, Abrahams M, Matthee S. Good outcomes on ART sustained at five years in Khayelitsha in spite of massive scale up. 5th IAS Conference on HIV Pathogenesis and Treatment, Cape Town, 2009. Abstract no. WEPED211.
22. Boulle A, Orrel C, Kaplan R, Van Cutsem G, McNally M, Hilderbrand K, Myer L, Egger M, Coetzee D, Maartens G, Wood R; International Epidemiological Databases to Evaluate Aids in Southern Africa Collaboration. Substitutions due to antiretroviral toxicity or contraindication in the first 3 years of antiretroviral therapy in a large South African cohort. *Antivir Ther* 2007; 12: 753–760.
23. Byakika-Tusiime J, Crane J, Oyugi JH, Ragland K, Kawuma A, Musoke P, Bansberg D. Longitudinal antiretroviral adherence in HIV<sup>+</sup> Ugandan parents and their children initiating HAART in the MTCT-Plus family treatment model: role of depression in declining adherence over time. *AIDS Behav* 2009; 13 (Suppl 1): 82–91.

#### **4.3. Rationing antiretroviral therapy in Africa — treating too few, too late**

##### **References**

1. Lawn SD, Harries AD, Anglaret X, Myer L, Wood R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. *AIDS* 2008; 22: 1897-908.

2. Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, Justice AC, Hogg RS, Deeks SG, Eron JJ, Brooks JT, Rourke SB, Gill MJ, Bosch RJ, Martin JN, Klein MB, Jacobson LP, Rodriguez B, Sterling TR, Kirk GD, Napravnik S, Rachlis AR, Calzavara LM, Horberg MA, Silverberg MJ, Gebo KA, Goedert JJ, Benson CA, Collier AC, Van Rompaey SE, Crane HM, McKaig RG, Lau B, Freeman AM, Moore RD; NA-ACCORD Investigators. Effect of early versus deferred antiretroviral therapy for HIV on survival. *N Engl J Med*. 2009; 360: 1815-26.
3. ART-LINC Collaboration of International Databases to Evaluate AIDS (IeDEA). Antiretroviral therapy in resource-limited settings 1996 to 2006: patient characteristics, treatment regimens and monitoring in sub-Saharan Africa, Asia and Latin America. *Trop Med Int Health* 2008; 13: 870-9.
4. Moreno S, Jarrin I, Iribarren JA, Perez-Elías MJ, Viciano P, Parra-Ruiz J, Gomez-Sirvent JL, Lopez-Aldeguer J, Gutierrez F, Blanco JR, Vidal F, Leal M, Rodríguez Arenas MA, Del Amo J; CoRIS-MD. Incidence and risk factors for tuberculosis in HIV-positive subjects by HAART status. *Int J Tuberc Lung Dis* 2008;12:1393-400.
5. Auvert B, Males S, Puren A, Taljaard D, Caraël M, Williams B. Can highly active antiretroviral therapy reduce the spread of HIV? A study in a township of South Africa. *J Acquir Immune Defic Syndr* 2004; 36: 613-21.
6. Persad G, Wertheimer A, Emanuel EJ. Principles for allocation of scarce medical interventions. *Lancet* 2009; 373: 423-31.

## Chapter 5: Conclusions

The concluding Chapter of this thesis is divided into three sections. The first section provides a synopsis of the main contributions to knowledge provided by this work; the second section summarizes limitations and gaps; and the final section looks at the main challenges that lie ahead for increasing and sustaining antiretroviral therapy in future years.

### Synopsis

The papers upon which this thesis is built aim to address some of the major barriers to scaling up antiretroviral therapy in resource-limited settings over the last decade. A mix of research approaches were taken to describe the diversity of challenges faced, employing methods from health policy research, qualitative research, and clinical and public health epidemiology.

The first contribution of this thesis is synthetic: to draw together some of the major issues in an attempt to broadly assess the main policy and practice challenges faced in scaling up antiretroviral therapy. While improving clinical practice and programme design requires rigorous and detailed analysis of specific aspects of treatment provision, the challenge for policy makers and donors lies in understanding in broad terms the main challenges: a clinical trial may be the best method for assessing drug efficacy, but provides little guidance as to how to ensure that the drug is affordable and available in a setting of health worker scarcity.

The second contribution is the provision of evidence that informs approaches to overcoming particular issues, in particular in relation to the effectiveness of policy options for reducing the price of medicines and task shifting and decentralization of care. These issues continue to be ongoing challenges to scaling up ART as discussed below.

The final contribution is to provide some direction for future research and practice, in particular with relation to task shifting and decentralization of care.

### **Limitations and gaps in the thesis**

In attempting to describe the diversity of challenges to scaling up ART in resource-limited settings, a range of methodologies have been employed. Each is associated with inherent limitations.

The first chapter addressed the challenge of promoting access to affordable medicines using health policy analysis to assess the effectiveness of various policy tools, and document the case of civil society in Thailand. In the first paper, a health policy analysis was done, drawing on information provided through key information interviews and public documents. As such, no analysis was done (such as thematic analysis) which might have otherwise allowed for a more profound framing of the issues. In the second paper, the ‘participant-observer’ method was used, engaging members from different civil society groups to provide reflection around the content of the paper. This method is acknowledged to be biased towards providing an account from a particular perspective, but this risk of subjectivity is the price paid for an account supported by a degree of access to information that is not easily accessible to external researchers [1].

In the second chapter, a systematic review was undertaken to assess the impact of task shifting to overcome human resource shortages. Systematic reviews are subject to potential for publication bias that favours the publication of positive results [2]. To try and minimize this risk, a range of databases was searched and key authors contacted for further information. Second, the search identified a broad range of studies that were regrouped into themes; these themes involved a deliberate choice on the part of the researchers and other themes could have been chosen that would have resulted in a different framing of the evidence. The second paper in this chapter combines a literature review with operational research data in order to define policy and operational research priorities. This paper contains inherent investigator biases associated with non-systematic reviews, and should be more understood as an expert review.

Chapter three presents operational research data from two routine HIV/AIDS care programmes to describe the impact of decentralized HIV/AIDS care services in terms of

clinical outcomes and patient retention in care. An essential difference between programme data derived from operational research and classic cohort studies is that no methods of random sampling have been used to recruit participants, which strictly speaking carries a risk of invalidating subsequent statistical inferences regarding generalizability [3]. Moreover, the inferences derived from the analysis of routinely collected data are subjected to limitations in terms of both the type of data available for analysis (limited of covariates) and a host of unmeasured and uncontrolled confounders. Such limitations also apply to the survival analysis presented in Chapter four. Nevertheless, programmatic data have contributed enormously to our understanding of the evolution of trends and challenges faced by HIV/AIDS treatment programmes in settings where controlled experiments are extremely challenging [4], and the value of operational research is being increasingly recognized [5,6].

Scaling up of treatment was only possible once donors and affected countries agreed to start funding treatment and an analysis of funding trends over the last decade would have been an appropriate complement to this thesis. The successes and failures of national and international funding mechanisms has been the subject of numerous articles [7-10] and at least one PhD thesis [11]. The current threat to the sustainability of global financing for antiretroviral treatment is discussed in the next section. Another gap arises from the choice of case studies. The assessment of policy options to reduce drug prices in particular would benefit from a broader geographical scope, including other Developing countries on the one hand (notably India [12], South Africa [13], and Kenya [14]) and Developed countries on the other (notably Canada [15]). Finally, in trying to assess the main broad barriers related to antiretroviral provision, this thesis inevitably suffers from a lack of detail regarding determinants of programme effectiveness such as treatment adherence [16], survival [17], and retention in care [18], each of which could make the subject of a separate thesis.

### **Looking forward**

Almost a decade ago, one prevailing view among policy makers and donors was that antiretroviral therapy (ART) was not an option for the Developing world. At the same time as Western countries were beginning to appreciate the major reductions in illness and death that ART could provide [19], the provision of ART was argued to be too costly and too

complex for Developing countries [20, 21], and might even do harm to health services that were overburdened and under-resourced [22].

Yet with three million people dying each year, mostly in Africa, withholding ART was considered simply unacceptable by a growing number of Activists, academics, clinicians and patients. Global inaction against HIV/AIDS was labeled as a crime against humanity [23]. A growing international movement fought against the high cost of treatment and in just a few years succeeded in reducing the price of ART to a fraction of its original price [24]. Small pilot programmes that carefully selected a few dozen patients for treatment were rapidly swept away by demand and these pilot programmes rapidly evolved into district wide programmes treating thousands of people [25]. Treatment outcomes were evaluated and found to be as good [26] and in some cases better than [27] in Western settings. The model of ART care was adapted from a resource-intensive individualized approach to a public health programme [28] that could be delivered by nurses at the clinic and community level [29]. Contrary to early fears, ART delivery was after careful analysis found to be supportive of health system strengthening [30].

Yet despite these major advances, it seems that most of the lessons of the last decade are rapidly being forgotten.

The high cost of treatment is again cited as a reason to accept sub-optimal care. The latest WHO guidelines recommend replacing older drugs long-abandoned in the West with more durable and less toxic alternatives, but because these newer drugs are more expensive, Developing countries are reluctant to make the change [31]. Instead of pushing for cheaper versions of preferred treatments, policy advisors are equivocating [32].

Similarly, several studies have shown important benefits to starting treatment earlier, including one randomized trial which found that starting treatment earlier was associated with a four-fold decrease in mortality and a two-fold decrease in incident tuberculosis [33]. But lowering the threshold for initiation means that several million more people become eligible for ART, and while this may be clinically desirable, it is not politically supported at a time when many Western donors are trying to get out of funding HIV/AIDS programmes.

As a result, just as the early benefits of ART were ignored in favour of cheaper interventions despite a clear mortality cost, this latest evidence is being swept aside by major funders who defend a policy of delaying treatment in order to ration resources [34]. International advisors are suggesting that treatment numbers should simply be frozen: bluntly put, no new patients until existing patients have died [35].

Five years ago the international community committed to a goal of achieving universal access to antiretroviral therapy by 2010 [36]. Not only have we failed to achieve that goal; the sustainability of gains made to date are under threat from multiple sides. Clinics are reporting major stock ruptures of antiretrovirals due in part to insufficiencies in Global Fund financing [37]; similarly, Uganda has reported similar stock ruptures just as PEPFAR announced that it will not provide any increased funding for HIV/AIDS care in the country [38].

The global apathy towards HIV/AIDS that in 2002 was labeled as a crime against humanity is once again being allowed to dominate under the pretense of insufficient global resources. What has changed in the last decade is that today we know that treating HIV/AIDS on a large scale is entirely possible. We know that the price of treatment can be reduced; we know that simple, adapted models of delivery can support treatment provision even in highly under-resourced areas; and we know that major savings can be made by health systems that invest early. Improving the basic package of care can limit side-effects delay the need for patients to switch to more expensive second-line regimens, while treating earlier will potentially yield massive public health benefits in terms of reduced transmission of HIV and other diseases [39]

A decade ago, those in the international community who did not support the scale up of ART in Africa could argue that it was untested. Today, the latest clinical and public health evidence is being sidelined by donors who are willing to save costs by promoting a standard of care that would be unacceptable in their own countries. Those who argue today we should limit our support for ART provision do so in the full knowledge of what works and how to get there. That is surely an even greater crime.

## References

1. Walt G, Shiffman J, Schneider H, Murray SF, Brugha R, Gilson L. 'Doing' health policy analysis: methodological and conceptual reflections and challenges. *Health Policy Plan* 2008; 5:308-17.
2. Dickersin K, Min YI, Meinert CL. Factors influencing publication of research results. Follow-up of applications submitted to two institutional review boards. *JAMA* 1992; 267:374-8.
3. Mendenhall W, Ott L, Schaeffer R. *Elementary survey sampling*. Belmont, CA. Wadsworth, 1971.
4. Ford N, Mills EJ, Zachariah R, Upshur R. Ethics of conducting research in conflict settings. *Confl Health* 2009; 3: 7.
5. Zachariah R, Ford N, Draguez B, Yun O, Reid T. Conducting operational research within a nongovernmental organization. The example of Médecins Sans Frontières. *International Health* 2010; 2: 1-8.
6. Zachariah R, Harries AD, Ishikawa N, Rieder HL, Bissell K, Laserson K, Massaquoi M, Van Herp M, Reid T. Operational research in low-income countries: what, why, and how? *Lancet Infect Dis* 2009; 11:711-7.
7. Schwartlander B, Grubb I, Perriens J. The 10-year struggle to provide antiretroviral treatment to people with HIV in the developing world. *Lancet* 2006; 368: 541–546.
8. Smith R, MacKellar L. Global public goods and the global health agenda: problems, priorities and potential. *Global Health* 2007; 3: 9.
9. Lu C, Schneider MT, Gubbins P, Leach-Kemon K, Jamison D, Murray CJL. Public financing of health in developing countries: a cross-national systematic analysis. *Lancet* 2010; 375: 1375-87.
10. Ooms G, Derderian K, Melody D. Do we need a world health insurance to realise the right to health? *PLoS Med* 2006; 3: e530.
11. Ooms G. The right to health and the sustainability of health care: Why a new global health aid paradigm is needed. Doctoral thesis submitted to the Faculty of Medicine and Health Sciences, Ghent University, 2008.
12. Bhattacharya R. Are developing countries going too far on TRIPS? A closer look at the new laws in India. *Am J Law Med* 2008; 34: 395-421.

13. Saslow EL. Compulsory licensing and the AIDS epidemic in South Africa. *AIDS Patient Care STDS* 1999; 13 : 577-84.
14. Ford N. Patents, access to medicines, and the role of nongovernmental organisations. *J Generic Medicines* January 2004; 2: 137-145.
15. Cohen-Kohler JC, Esmail LC, Cosio AP. Canada's implementation of the Paragraph 6 Decision: is it sustainable public policy? *Global Health* 2007; 3: 12.
16. Mills EJ, Nachega JB, Bangsberg DR, Singh S, Rachlis B, Wu P, Wilson K, Buchan I, Gill CJ, Cooper C. Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. *PLoS Med* 2006; 3:e438.
17. Bisson GP, Gaolathe T, Gross R, Rollins C, Bellamy S, Mogorosi M, Avalos A, Friedman H, Dickinson D, Frank I, Ndwapi N. Overestimates of survival after HAART: implications for global scale-up efforts. *PLoS ONE* 2008; 3:e1725.
18. Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. *PLoS Med* 2007; 4:e298.
19. Hogg RS, Yip B, Kully C, Craib KJ, O'Shaughnessy MV, Schechter MT, Montaner JS. Improved survival among HIV-infected patients after initiation of triple-drug antiretroviral regimens. *CMAJ* 1999; 160: 659–65.
20. Marseille E, Hoffman PB, Kahn JG. HIV prevention before HAART in sub-Saharan Africa. *Lancet* 2002; 359: 1851–56.
21. Creese A, Floyd K, Alban A, Guinness L. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. *Lancet* 2002; 359: 1635–42.
22. McCoy D, Chopra M, Loewenson R, Aitken JM, Ngulube T, Muula A, Ray S, Kureyi T, Ijumba P, Rowson M. Expanding access to antiretroviral therapy in sub-Saharan Africa: avoiding the pitfalls and dangers, capitalizing on the opportunities. *Am J Public Health* 2005; 95: 18-22.
23. Hogg R, Cahn P, Katabira E, Jange J, Samuel N, O'Shaughnessy M, Vella S, Wainbrg M, Montaner J. Time to act: global apathy towards HIV/AIDS is a crime against humanity. *Lancet* 2002; 360: 1710-1.
24. von Schoen Angerer T, Wilson D, Ford N, Kasper T. Access and activism: the ethics of providing antiretroviral therapy in developing countries. *AIDS* 2001; 15: S81-90.
25. Fox RC, Goemaere E. They call it "patient selection" in Khayelitsha: the experience of Médecins Sans Frontières-South Africa in enrolling patients to receive antiretroviral treatment for HIV/AIDS. *Camb Q Healthc Ethics* 2006; 15: 302-12.

26. Braitstein P, Brinkhof MW, Dabis F, Schechter M, Boulle A, Miotti P, Wood R, Laurent C, Sprinz E, Seyler C, Bangsberg DR, Balestre E, Sterne JA, May M, Egger M; Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration; ART Cohort Collaboration (ART-CC) groups. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet* 2006; 367: 817-24.
27. Mills EJ, Nachega JB, Buchan I, Orbinski J, Attaran A, Singh S, Rachlis B, Wu P, Cooper C, Thabane L, Wilson K, Guyatt GH, Bangsberg DR. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. *JAMA* 2006; 296: 679-90.
28. Harries AD, Schouten EJ, Libamba E. Scaling up antiretroviral treatment in resource-poor settings. *Lancet* 2006; 367: 1870-72.
29. Callaghan M, Ford N, Schneider H. A systematic review of task shifting for HIV treatment and care in Africa. *Human Resources for Health* 2010; 8: 8.
30. Anon. Venice statement: global health initiatives and health systems. *Lancet* 2009 374; 9683: 10-12.
31. Ford N, Calmy A. Improving first-line antiretroviral therapy in resource-limited settings. *Curr Opin HIV AIDS* 2010; 1: 38-47.
32. Anon. Officials say switching to tenofovir or AZT would double the country's ARV budget. *IRIN*, December 13, 2009.
33. Ford N. Highlights of the International AIDS Society Conference. *Lancet Infectious Diseases* 2009; 9: 528.
34. Stockman F. US seeks to rein in AIDS program Overseas clinic costs have tripled to \$7b in 6 years. *Boston Globe*, 11 April 2010.
35. US Centres for Disease Control. Memo to Ugandan Ministry of Health. 29 October 2009.
36. G8 Summit Communiqué, Paragraphs 15-18, Gleneagles, July 2005.
37. Anon. Southern Africa: preparing for the worst. *IRIN/Plus News* 1 March 2010.
38. Mugenyi P. Flat-line funding for PEPFAR: a recipe for chaos. *Lancet* 2009; 374: 292.
39. Ford N, Calmy A, Hurst S. When to start antiretroviral therapy in resource-limited settings: a human rights analysis. *BMC International Health and Human Rights* 2010; 10: 6.

## About this PhD

Prior to undertaking this PhD I had worked with the medical aid agency Médecins Sans Frontières (MSF) for eight years in a variety of settings. MSF is not a research organization, however it frequently finds itself in situations where there is no clear evidence for how to act, and there is a sense within the organization that being a pioneer carries a responsibility to document and disseminate experiences. Before the advent of antiretroviral therapy in Africa, MSF's involvement in research was limited to evaluations of simple interventions and data arising from routine needs assessments. MSF was one of the first organizations to begin treating HIV in resource-limited settings. The early years were about lobbying for access to simple drugs and diagnostics and demonstrating that treatment was possible, but from 2007 onwards (the period of this PhD) there was a need to document the experience of going to scale. The research skills I have gained during this PhD have been directly applied to this effort.

The following research methodology was acquired and applied during the course of this PhD: health policy analysis [1], systematic reviewing and meta-analysis [2-4], quality evidence assessment [5] and regression and survival analysis [6]. With these skills I have been able to address clinical and public health research questions that, just a few years ago, I could not even conceive. While not all of the papers have been included in this thesis, they are all the direct result of teaching received from my supervisors or courses taken for this PhD, and I am very grateful for having been encouraged to develop research skills that I had previously assumed were beyond my abilities.

Some of the research generated by this PhD has contributed directly to informing policy. The work relating to task shifting and decentralization of care has fed into national treatment guideline revisions undertaken by several national governments in southern Africa. It has also indirectly contributed to encouraging colleagues at MSF to improve the quality of operational research done by the organization.

Good research is also collaborative research. Through this PhD I have been fortunate to be able to develop a network of excellent colleagues, and become involved in a broader range of research questions that I would previously have considered beyond my scope of

knowledge and experience [7,8]. These collaborations are as important as the knowledge I have gained, and I have no doubt that they will continue for a long time to come.

## References

1. Ford N, Wilson D, Cawthorne P, Kumphitak A, Kasi-Sedepan S, Kaetkaew S, Teemanka S, Upakaew K, Preuanbuapan C. Challenge and co-operation: ten years of civil society activism for access to HIV treatment in Thailand. *TROP MED INT HEALTH* 2009; 14: 1-9.
2. Callaghan M, Ford N, Schneider H. A systematic review of task-shifting for HIV treatment and care in Africa. *Human Resources for Health* 2010; 8: 8.
3. Ford N, Nachega J, Engel M, Mills E. Directly observed antiretroviral therapy: a systematic review and meta-analysis of randomized clinical trials. *Lancet* 2009; 374: 2064–71.
4. Ford N, Mofenson L, Krazner K, Medu L, Frigati L, Mills E, Calmy A. Safety of efavirenz in first-trimester of pregnancy: a systematic review and meta-analysis of outcomes from observational cohorts. *AIDS* 2010 [accepted].
5. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; 336: 924-6.
6. Ford N, Darder M, Spelman T, Maclean E, Mills E, Boulle A. Early adherence as a predictor of long-term virological suppression: five-year follow up of an observational cohort. *PLoS ONE* 2010; 5:5.
7. Mills EJ, Schabas WA, Volmink J, Walker R, Ford N, Katabira E, Anema A, Joffres M, Cahn P, Montaner J. Should active health worker recruitment from sub-Saharan Africa be viewed as a crime? *Lancet* 2008; 371: 685–88.
8. Palmer A, Tomkinson J, Phung C, Ford N, Joffres M, Fernandes K, Zeng L, Lima V, Montaner J, Guyatt G, Mills E. Does the ratification of human rights treaties affect population health? *Lancet* 2009 373; 9679: 1987-92.

## Candidate's bibliography

The following is a full list of HIV/AIDS related publications produced during the period of this PhD.

1. Ford N, Wilson D, Costa Chaves G, Lotrowska M, Kijtiwatchakul K. Sustaining access to antiretroviral therapy in developing countries: lessons from Brazil and Thailand. *AIDS* 2007; 21: S21-29.
2. Bedelu M, Ford N, Hildebrandt K, Reuter H. Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS care. *J Inf Dis* 2007; 196: 464-468.
3. Janssens B, Van Damsme W, Raleigh B, Gupta J, Khem S, Soy Ty K, Vun MC, Ford N, Zachariah R. Offering integrated care for HIV/AIDS, diabetes and hypertension within chronic disease clinics in Cambodia. *Bulletin World Health Organ* 2007; 85: 880-5.
4. Janssens B, Raleigh B, Seithabot S, Akao K, Te V, Gupta J, Vun M, Ford N, Nouhin J, Nerrienet E. Effectiveness of HAART in children: evaluation at 12 months in a routine programme in Cambodia. *Paediatrics* 2007; 120: 1134-40.
5. Boule A, Ford N. Scaling up antiretroviral therapy in developing countries: what are the benefits and challenges? *Sex Transm Inf* 2007; 83: 503-505.
6. Heiden D, Ford N, Wilson D, Rodriguez W, Margolis T, Janssens B, Bedelu M, Tun N, Goemaere E, Saranchuk P, Sabapathy K, Smithius F, Luririka E, Drew L. CMV: the neglected disease in the AIDS pandemic. *Plos Medicine* 2007; 4: 12:1-7.
7. Mills EJ, Schabas WA, Volmink J, Walker R, Ford N, Katabira E, Anema A, Joffres M, Cahn P, Montaner J. Should active health worker recruitment from sub-Saharan Africa be viewed as a crime? *Lancet* 2008; 371: 685-88.
8. Ford N, Gray A, Venter F. Tough choices: Tenofovir, tenders and treatment. *Southern African J HIV Med* 2008: 8-10.
9. van Roey J, von Schoen-Angerer T, Ford N, Calmy A. How developing world concerns need to be part of drug development plans: a case study of four emerging antiretrovirals. *Drug Discovery Today* 2008; 13: 601-5.
10. Boule A, Hilderbrand K, Menten J, Coetzee D, Ford N, Matthys F, Boelaert M, Van der Stuyft P. Exploring HIV risk perception and behaviour in the context of antiretroviral treatment: results from a township household survey. *AIDS Care* 2008; 20: 771-81.

11. Lynch S, Lethola P, Ford N. International nurse migration and HIV/AIDS. *JAMA* 2008; 300: 1024.
12. Zachariah R, Ford N, Philips M, Lynch S, Massaquoi M, Janssens V, Harries A. Task shifting in HIV/AIDS: opportunities, challenges and proposed actions for sub-Saharan Africa. *Trans Roy Soc Trop Med Hygiene* 2009; 103: 549-58.
13. Wilson D, Kache Keiluhua A, Kogrum S, Reid T, Serirat N, Ford N, Kyaw Kyaw M, Talangsri P, Taochalee N. HIV-1 viral load monitoring: an opportunity to reinforce treatment adherence in a resource-limited setting in Thailand. *Trans Roy Soc Trop Med Hygiene* 2009; 103: 601-6.
14. Cooper C, Mills E, Wabwire B, Ford N, Olupot-Olupot P. Chronic viral hepatitis may diminish the gains of HIV antiretroviral therapy in Sub-Saharan Africa. *Int J Infect Dis* 2009; 13: 302-6.
15. O'Brien DP, Mills C, Hammel C, Ford N, Pottie K. Universal access: what does it mean? Challenges in bringing HIV care to isolated and conflict affected populations in the Republic of Congo. *Conflict & Health* 2009; 3: 1.
16. Ford N, Wilson D, Cawthorne P, Kumphitak A, Kasi-Sedepan S, Kaetkaew S, Teemanka S, Upakaew K, Preuanbuapan C. Challenge and co-operation: ten years of civil society activism for access to HIV treatment in Thailand. *Trop Med Int Health* 2009; 14: 1-9.
17. Ford N. Treating AIDS in complex emergencies: the need for clear policy consensus. *Progress in Development Studies* 2009; 9: 55-61.
18. Ford N, Mills E, Calmy A. Rationing antiretroviral therapy in Africa — treating too few, too late. *NEJM* 2009; 36: 1808-10.
19. Decroo T, Panunzi I, Dores C, Maldonado F, Biot M, Ford N, Chu K. Lessons learned during down referral of antiretroviral treatment in Tete, Mozambique. *J Int AIDS Soc* 2009; 12: 1-5.
20. Simon S, Chu K, Frieden M, Candrinho B, Ford N, Schneider H, Biot M. An integrated approach to community health worker support for HIV/AIDS and TB care in Mozambique. *BMC Int Health Hum Rights* 2009; 9: 13.
21. Mills E, Ford N, Mugenyi P. Expanding HIV care in Africa: making men matter. *Lancet* 2009; 374: 275-6.

22. Caluwaerts C, Maendaenda R, Maldonado F, Decroo T, Biot M, Ford N, Chu K. Risk factors and true outcomes for lost to follow-up individuals in an antiretroviral treatment program in Tete, Mozambique. *Int Health* 2009; 1: 97-101.
23. Cohen R, Lynch S, Bygrave H, Eggers E, Vlahakis N, Hilderbrand K, Knight L, Pillay P, Saranchuk P, Goemaere E, Makakole L, Ford N. Antiretroviral treatment outcomes from a nurse-driven, community-supported HIV/AIDS treatment programme in rural Lesotho: observational cohort assessment at two years. *J Int AIDS Soc* 2009; 12: 1-8.
24. Mills E, Ford N, Singh S, Ewayo O. Providing antiretroviral care in conflict settings. *Current HIV/AIDS reports* 2009; 6: 201-209.
25. Ford N, Nachega J, Engel M, Mills E. Directly observed antiretroviral therapy: a systematic review and meta-analysis of randomized clinical trials. *Lancet* 2009; 374: 2064–71.
26. Ford N, Calmy A. Improving first-line antiretroviral therapy in resource-limited settings. *Curr Opin HIV AIDS* 2010; 1: 38-47.
27. Mills EJ, Ford N, Nabiryo C, Cooper C, Montaner J. Ensuring sustainable antiretroviral provision during economic crises. *AIDS* 2010;24: 341-3.
28. Boule A, Van Cutsem G, Hilderbrand K, Cragg C, Abrahams M, Mathee S, Ford N, Knight L, Osler M, Myers J, Goemaere E, Coetzee D, Maartens G. Seven-year experience of a primary care antiretroviral treatment programme in Khayelitsha, South Africa. *AIDS* 2010; 24: 563–572.
29. Chu K, Boule A, Ford N, van Cutsem G. Nevirapine-associated early hepatotoxicity: incidence, risk factors, and associated mortality in a primary care ART programme in South Africa. *PLoS ONE* 2010; 5: 1-6.
30. Zachariah R, Ford N, Draguez B, Yun O, Reid T. Conducting operational research within a nongovernmental organization. The example of Médecins Sans Frontières. *Int Health* 2010; 2: 1-8.
31. Ford N, Calmy A, Hurst S. When to start antiretroviral therapy in resource-limited settings: a human rights analysis. *BMC Int Health Hum Rights* 2010; 10: 6.
32. Callaghan M, Ford N, Schneider H. A systematic review of task shifting for HIV treatment and care in Africa. *Hum Res Health* 2010; 8: 8.

33. Ford N, Mofenson L, Krazner K, Medu L, Frigati L, Mills E, Calmy A. Safety of efavirenz in first-trimester of pregnancy: a systematic review and meta-analysis of outcomes from observational cohorts. *AIDS* 2010. 14 May 2010 [Epub ahead of print]