

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

**Constructive integration –
Changes in uptake and outcomes of reproductive health services
during the scaling up of ART and PMTCT in Thyolo District, Malawi**

by

THOMAS VAN DEN AKKER
STUDENT NUMBER: VKKTHO001

SUBMITTED TO THE UNIVERSITY OF CAPE TOWN
In partial fulfilment of the requirements for the degree

Master of Philosophy in Maternal and Child Health

**Faculty of Health Sciences
UNIVERSITY OF CAPE TOWN**

Date of submission 14 February, 2011

Supervisor: Mrs. Jawaya Shea¹, Co-supervisor: Dr. Nathan Ford²

- 1. Child Health Unit, School for Child and Adolescent Health**
- 2. Centre for Infectious Disease Epidemiology and Research**

Declaration

I, Thomas van den Akker, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature:

Signed by candidate

Date: 9 February 2011

University of Cape Town

Table of Contents

Declaration	3
Abbreviations	7
Acknowledgements	8
Executive summary	9
Background.....	9
Methods	9
Results	9
Conclusions.....	10
Introduction.....	11
The impact of HIV on health systems.....	11
The impact of HIV-programmes on reproductive health services	12
ART and PMTCT-programmes in Malawi.....	13
Literature review	15
Search strategy	15
HIV and antiretroviral therapy	15
(Prevention of) mother-to-child transmission of HIV.....	18
Reproductive health: definitions, outcome indicators and trends	20
Effects of HIV programmes on reproductive health outcomes and services.....	23
Aims and objectives.....	25
Aims:.....	25
Objectives:.....	25
Study methods.....	26
Design	26
Study period	26
Setting.....	26
Intervention/programme approach	27
Health system.....	28
Professional cadres.....	30
Antenatal care	30
Intrapartum care	30

Postpartum care.....	31
Family planning	31
Sexually transmitted infections	32
Health promotion.....	32
Outcomes.....	33
Data collection and analysis.....	34
Data sources used per study objective	34
Background of data sources.....	34
Data analysis	35
Ethics.....	35
Results.....	36
Antenatal care.....	36
Intrapartum care.....	37
Postpartum care.....	37
Treatment of sexually transmitted infections	38
Family planning.....	39
Health system	40
Governance.....	40
Financing.....	40
Infrastructure development.....	41
Procurement and supply chain management.....	41
Human resources	42
Health information systems.....	42
Service delivery and supervision.....	42
Pregnancy outcome	43
Strengths and limitations.....	49
Discussion.....	51
Conclusions	55
Recommendations	56
References	58
Annex A	66
Annex B	67

Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Care
ART	Anti-Retroviral Therapy
AZT	Zidovudine, type of antiretroviral medication
HIV	Human Immunodeficiency Virus
MoH	Ministry of Health
MSF	Médecins Sans Frontières
NVP	Nevirapine, type of antiretroviral medication
OR	Odds Ratio
PMTCT	Prevention of Mother-To-Child Transmission
STI	Sexually Transmitted Infection
WHO	World Health Organization

Acknowledgements

The principle author would like to thank all clinicians and nurses in Thyolo for their invaluable contributions to reproductive health in the district. Special thanks go out to Rumours Lumala, Emma Diggle and Sofie Scheffer (all MSF Thyolo) and to Mrs. Gamechi (Family Planning coordinator, MoH) and Mrs. Makombe (STI coordinator, MoH) for their important contributions to the collection of data used in this report, and to Marielle Bemelmans (MSF Brussels/Limbe), Ann Akesson (MSF Limbe) and Mtabeni Jemu (MoH) for their managerial and technical support.

In addition, acknowledgements go out to advocates for women, children and people living with HIV, and to all those courageous individuals within (non-) governmental organizations who are willing to stand up for the rights of the vulnerable, basing themselves on sound evidence and a strong feeling for what is right. Of these, I mention in particular my dear wife Kinke Lommerse, my inspiring friends Jos van Roosmalen, Beatrice Mwangomba and Tarek Meguid, and my supervisors Nathan Ford and Jawaya Shea.

Executive summary

Background

In recent years there has been increasing debate about the impact of scaled-up ART and PMTCT programmes on the uptake and outcomes of reproductive health services, in particular the potential detrimental effects of HIV-care on the overall capacity of fragile health systems. The objective of this study was to evaluate changes in the uptake of reproductive health services as well as the main pregnancy outcomes during the scaling up of ART and PMTCT in Thyolo District, Malawi.

Methods

Study design: retrospective descriptive district-wide cohort analysis for the period 2005 to 2009.

Setting: Thyolo District, an area with around 600,000 inhabitants, an adult HIV-prevalence of 21% and a Total Fertility Rate of 5.7 in 2004. HIV-care including ART and PMTCT was scaled up since 2004 in Thyolo District to reach district-wide coverage in 2007. HIV-care is provided at district hospital, health centre and community health post levels.

Outcomes: uptake of antenatal, intrapartum and postpartum care, family planning and treatment of sexually transmitted infections; infrastructural changes, and changes in maternal and perinatal pregnancy outcome.

Data collection and analysis: data were collected from facility antenatal, intrapartum and postpartum records, as well as from MoH and MSF databases maintained for routine programme monitoring. Chi-square tests were performed comparing the baseline year (2005) with the year of study end (2009).

Results

Uptake of peripartum care had improved markedly by the end of the five-year study period: the percentages of pregnant women who took up antenatal, intrapartum and postpartum care increased by

30%, 25% and 20% respectively. The number of family planning consultations increased by almost 50% and the number of women treated for sexually transmitted infections more than doubled.

Interactions between HIV-care and general reproductive health care had positive effects on key health system components, including governance, health financing, human resources and drug supply.

Reliable pregnancy outcome indicators for the entire observation period were difficult to obtain due to likely under-reporting of facility-based maternal and perinatal mortality. However, previously documented results from Thyolo show a reduction of facility-based severe maternal complications, including uterine rupture, between 2007 and 2009.

Conclusions

Uptake of reproductive health services and facility-based maternal outcomes increased markedly during the period of HIV scale-up. This implies that the scale up of HIV-care did not inhibit, and likely increased, uptake of reproductive health services, while quality improvements in perinatal care could still be successfully implemented. The finding that ART and PMTCT care may be successfully integrated into broader reproductive health services with satisfying outcomes is a strong argument for continued scale up of ART and PMTCT in similar settings.

Introduction

The impact of HIV on health systems

In sub-Saharan Africa, the burden of HIV illness, and the scaling up of programmes to prevent and treat HIV/AIDS, have had a considerable impact on the health systems of most countries (Chopra et al. 2009; Lawn et al. 2008). During the last 30 years, HIV/AIDS has transformed the burden of disease throughout the region (UNAIDS & WHO 2005). Public health systems that were already under-resourced to cope with existing health demands have struggled to provide adequate care to a growing influx of patients with AIDS-related opportunistic infections (Chopra et al. 2009); many patients presented with pathologies that had been uncommon before (such as cryptococcal meningitis or Kaposi's sarcoma) putting the ability of health systems to deal with these diseases to an additional test (Lawn et al. 2008).

At the same time as HIV increased the demand on health systems, it also reduced the ability of the health system to cope as health workers themselves were affected, both directly through increased HIV-related morbidity and mortality, and indirectly through increased burnout (Bemelmans et al. 2011; Yu et al. 2008). The increase in HIV-related patient burden led to a decline in the performance of health services including services for non-HIV-related illness (Samb et al. 2010; Yu et al. 2008). In other words, HIV exposed the inability of under-resourced public health systems to provide basic preventive and curative care, and this has been suggested to have contributed to an increase in maternal and infant mortality (Buve et al. 2003; Yu et al. 2008).

In the early 1990s, studies from Western countries showed that antiretroviral therapy (ART) and prevention of mother-to-child transmission (PMTCT) had the potential to dramatically reduce HIV-related mortality, including maternal mortality, and paediatric HIV-infection (Blower et al. 2000; Kim & Gilks 2005; Peckham & Gibb 1995). However, concerns about the feasibility of implementing large-scale HIV-programmes in low-income countries, meant that the provision of ART and PMTCT in high HIV-burden settings did not receive

full support from national governments and international donors until late 2003 (Kim & Gilks 2005). Initially, the scaling-up of ART and PMTCT services often occurred through specific vertical programmes that operated independently from the general health system.

The impact of HIV-programmes on reproductive health services

A comprehensive definition of reproductive health services includes antenatal, intrapartum and postpartum services as well as treatment of sexually transmitted infections (STIs) and family planning services (WHO 2010a). Several authors have expressed concerns about the potential negative effects of vertical HIV-programmes on reproductive health services and their outcomes (Both & Van Roosmalen 2010; Chopra et al. 2009; Hanefeld 2010; Hanefeld & Musheke 2009; Magoma et al. 2010). Concerns include: (1) the diversion of funding away from reproductive health towards HIV (Both & Van Roosmalen 2010; Chopra et al. 2009; Yu et al. 2008), (2) the hypothesis that scaled-up HIV-testing could reduce uptake of general reproductive health services due to HIV-related stigma (Simba et al. 2010; Turan et al. 2008), and (3) the demands on the scarce health workforce posed by these rapidly expanding HIV-programmes (Banteyerga et al. 2006; Nuwagaba-Biribonwoha et al. 2007).

However, the actual impact of these potentially negative effects on reproductive health has not been comprehensively studied or documented (Both & Van Roosmalen 2010; Brugha et al. 2010). In particular, changes in uptake and outcomes of reproductive health services within well-integrated ART/PMTCT-programmes remain unclear (Both & Van Roosmalen 2010; Kennedy et al. 2010). In the absence of documented programmatic evidence confirming or refuting these concerns, the scepticism about the benefits of large-scale HIV-programmes remains. This scepticism, in turn, has contributed to decreased political and financial support for ART and PMTCT, ultimately putting hard-won public health gains at risk (Nattrass & Gonsalves 2010).

ART and PMTCT-programmes in Malawi

Malawi is one of the countries most heavily affected by the HIV-pandemic. The HIV-prevalence rate among adults from 15 to 49 years of age was 12% in 2007 (UNAIDS 2009) with young women disproportionately affected compared to their male counterparts: the HIV-prevalence in women aged 15 to 24 years was 9% in 2010, versus 2% among men in the same age group (USAID 2010). Despite a severe lack of financial and human resources in the country's health sector, Malawi managed to scale up access to ART with marked success. By the end of 2009 at least 271,105 people had started ART, of whom 198 846 (73%) were alive and on treatment (MoH HIV department 2009). This represented almost two-thirds of the need for ART (30,000 people) at the time (MoH 2008b). This coverage figure compares favourably with Malawi's better-resourced neighbour South Africa, where ART coverage in 2009 stood at less than 40% (Adam & Johnson 2009). This difference reflects the difference in political will between both states: the Malawian government relatively quickly acknowledged the scale of the HIV-epidemic and the need for action (Kachapila 1998), whereas the South African president and minister of health supported an AIDS-denialist position until as late as 2008, casting doubt on the link between HIV and AIDS and hampering the scaling up of ART and PMTCT (Cohen 2000).

The achievements of the Malawi ART programme came after a period in which there had been no significant improvement in the uptake of other general health services including perinatal care. Despite efforts to promote antenatal care (ANC) attendance, the uptake of ANC services, for instance, did not improve between 2000 and 2004: only around 50% of all pregnant women met the recommended number of four or more antenatal visits, a mere 8% had received ANC during the first trimester of pregnancy, and around 10% had not accessed ANC at all (National Statistical Office 2005).

The low ANC-attendance was one reason why the scaling up of quality PMTCT programmes in Malawi turned out to be more challenging compared to the ART rollout. Other reasons for the delay in PMTCT scale-up include: (1) the inadequate link between general maternal and child health (MCH) services and PMTCT care: PMTCT was mostly provided separately from general MCH care (Horwood et al. 2010), (2) very

high drop-out rates of women entering into the PMTCT-programme due to the effects of stigma as well as financial and logistical constraints for women to access care (Bwirire et al. 2008; Manzi et al. 2005) and (3) an insufficiency of health workers to support MCH and PMTCT service delivery (Nakakeeto & Umaranayake 2009).

By June 2010, out of 8944 HIV-positive women in Malawi who attended ANC during the second quarter of 2010, 6345 (71%) received antiretroviral prophylaxis. This represented 35% PMTCT coverage among the estimated 18,210 HIV-positive pregnant women in the country during that quarter (MoH 2010). The majority of ART and PMTCT services is delivered within the public health system by government clinicians and nurses (Bemelmans et al. 2010).

In Thyolo, a rural district in southern Malawi, Médecins Sans Frontières (MSF) and the Ministry of Health (MoH) embarked on a district-wide scale-up of ART and PMTCT between 2003 and 2007 (Bemelmans et al. 2010). Between 2007 and 2010, ART and PMTCT were increasingly integrated into general health services, meaning that ART and PMTCT care were provided, wherever possible, at the same clinics, during the same hours, and by the same staff as general (peripartum) care. During the process of service integration, uptake of ART was maintained at steady levels and access to PMTCT further increased (Bemelmans et al. 2010).

This study examined changes in reproductive health services and outcomes in Thyolo District during the phases of scaling up and integrating HIV care into general health services. The intention was to evaluate whether the scaling up of ART and PMTCT had been detrimental to the uptake and outcomes of reproductive health services, as others had hypothesized, or had in fact been beneficial.

Literature review

This chapter presents a review of the literature related to HIV, ART, PMTCT and reproductive health.

Search strategy

A search of the Cochrane library was conducted to target systematic reviews related to 'HIV', 'antiretroviral therapy' and 'prevention of mother-to-child transmission'. In addition, a search of the Medline electronic database using the PubMed-interface was conducted using the following terms: 'HIV' AND 'ART' AND 'review', 'HIV' AND 'prevention of mother-to-child transmission' AND 'review', 'HIV' AND 'reproductive health' AND 'health systems', limiting the search to articles written in the English language and published in the highest-impact journals according to the Thomson Reuters Citation Index (Thomson Reuters 2011). In addition, an internet-search was conducted via the conference proceedings of international AIDS conferences, and Google scholar, to search for the most relevant reports and court hearings about the civil society movement for access to HIV-care.

HIV and antiretroviral therapy

In 1981, the clinical syndrome of the Acquired Immune Deficiency Syndrome (AIDS) was first reported (Gottlieb et al. 1981) and in 1983, HIV was cultured and established as the causative agent of AIDS (Barre-Sinoussi et al. 1983). When diagnostic tests became available, the enormous scale of the HIV epidemic became clear (Volberding & Deeks 2010). By end-2008, more than 33 million people were projected to be living with HIV worldwide, two-thirds of whom residing in sub-Saharan Africa (UNAIDS & WHO 2005).

HIV-infection follows sexual or parenteral exposure to HIV-containing fluids, and targets CCR5 CD4 memory T-lymphocytes ('CD4 cells'). Initial HIV-infection may be accompanied by flu-like symptoms after which the infected person enters an asymptomatic phase of varying duration, lasting between a few months and several years. Symptomatic disease often occurs when the CD4 cell count drops below 350 cells per μl . The

classic AIDS-defining events such as *Pneumocystis jirovecii pneumonia* or cryptococcal meningitis occur when the count drops below 200 cells per μl and immunity is severely compromised. However, some serious complications, such as Kaposi's sarcoma or tuberculosis –the most common opportunistic infection in sub-Saharan Africa– may also occur at higher CD4 counts (Volberding & Deeks 2010).

If no treatment is given, HIV-infection will almost inevitably lead to death of the infected person. The median survival from onset of AIDS is around 9 months in sub-Saharan Africa (Morgan et al. 1997). However, ART – usually a combination of three different drugs – can suppress the virus and regenerate CD4 count levels. ART drugs are classified according to which step in the viral life cycle they inhibit. Nucleoside analogues (e.g. zidovudine, lamivudine, stavudine and tenofovir) and non-nucleoside reverse transcriptase inhibitors (efavirenz, nevirapine) are the most common classes used in low-income countries because generic formulations are available at relatively low cost and often as fixed dose combinations (Volberding & Deeks 2010).

Despite a longstanding high demand for ART in low-income, high-prevalence countries such as Malawi, ART drugs were until recently inaccessibly expensive due to price-protecting patents held by Western pharmaceutical companies (Achmat & Simcock 2007; Heywood 2001; Waning et al. 2010). Therefore, although ART had become available in more affluent settings during the 1990s, the most heavily affected populations in low-income countries had no access to any form of this life-saving treatment (UNAIDS & WHO 2005).

Around the turn of the millennium, several civil society groups across the globe started questioning this injustice and claiming the right to antiretroviral medication (Achmat 2002a). In particular, the South African Treatment Action Campaign provided a crucial political and legal voice to people living with HIV and AIDS in Southern Africa. The Campaign sued the South African government for not providing PMTCT (Achmat 2002b), while at the same time supporting them in a case brought up by pharmaceutical industries trying to prohibit the production of generic drug formulations. This latter case against the government collapsed

(Heywood 2001) and became one of the landmark cases that help promote the right of governments to access affordable sources of cheap generic antiretroviral medicines. Similar struggles were taking place in other developing countries, including Brazil, Guatemala, India, Kenya and Thailand (Achmat & Simcock 2007; Ford 2003; Ford et al. 2007).

Despite the successes of civil society groups, it still took considerable time before governments began to scale up ART services (Waning et al. 2010). In most countries, including Malawi, this scale-up depended on access to some of the cheaper drugs, most notably Stavudine and to a lesser extent Nevirapine, that had long been replaced in more affluent settings because of their toxicity. Stavudine is commonly associated with neuropathy and lipodystrophy, and may even cause life-threatening lactic acidosis (WHO 2010d). WHO now recommends that countries move away from Stavudine-containing regimens to Tenofovir- and Zidovudine- containing treatment (WHO 2009). Due to cost implications, this has not yet happened in Malawi, nor in many other countries (MoH 2008a).

Following WHO guidelines, eligibility for ART in Malawi and in many other low-income countries is established based on either clinical criteria using the WHO staging system or immunological criteria using a CD4 cell count (MoH 2008a). The staging system was developed with the objective of facilitating ART scale-up in a simplified manner, supportive of a public health approach (WHO 2005): all individuals classified with stage 3 disease (e.g. pulmonary tuberculosis, oral candidiasis) or stage 4 disease (e.g. Kaposi's sarcoma, cryptococcal meningitis) should be started on ART regardless of CD4-count, those in stage 1 (asymptomatic) or stage 2 (mild disease) require a CD4-count to determine eligibility for ART (WHO 2009). The optimum CD4 threshold for starting ART is still subject to scientific debate (Volberding & Deeks 2010). WHO currently recommends that treatment is started at a CD4 count below 350 cells per μl , although the threshold in Malawi still stands at 250 cells per μl for all adults (except pregnant women) in order to ration care (MoH 2008a).

(Prevention of) mother-to-child transmission of HIV

In the absence of any preventive intervention, 14-23% of the HIV-positive pregnant women in non-breastfeeding (western) populations will transmit HIV to their infants, while in breastfeeding populations this mother-to-child-transmission (MTCT) rate is 25-48%. The risk of MTCT is independently associated with maternal viral load, mode of delivery, and gestational age (Sturt et al. 2010).

MTCT may occur at any of three time-points:

- (1) *in utero*: HIV is thought to infect the placenta directly and may either spread cell-to-cell or pass into the foetal circulation with maternal mononuclear cells (Sturt et al. 2010);
- (2) *intrapartum*: through contact between neonatal skin and mucosa with cervicovaginal secretions and blood; longer duration of rupture of membranes increases the risk of transmission (by approximately 2% per hour); microtransfusions during the first stage of labour may also play a role (Sturt et al. 2010);
- (3) during the breastfeeding period: associated factors include duration of breastfeeding, maternal viral load and CD4 count, breast anomalies, younger maternal age and higher parity (Horvath et al. 2009; Nicoll et al. 1995; Richardson et al. 2003; Sturt et al. 2010; WHO 2010d).

Suggested interventions to prevent maternal-to-child transmission include:

- (1) delivery by caesarean section: however, there is no benefit of this intervention when the maternal viral load is low, and complications of operative delivery, especially in low-resource settings, outweigh any possible benefit (Sturt et al. 2010);
- (2) cessation of breastfeeding: this not a practical option in most low-income countries, as no affordable and safe feeding alternatives are usually available. The WHO now recommends to continue breastfeeding up to 12 months in the presence of antiretroviral drugs (WHO et al. 2010);

- (3) antiretroviral prophylaxis by mono- [Zidovudine (AZT) or Nevirapine (NVP)], dual (AZT and NVP, but no additional benefit), or triple drug regimens (recommended by WHO for all pregnant women with CD4 counts below 350 cells per μ l also because of their own health) (WHO 2010c);
- (4) NVP-prophylaxis to the infant throughout breastfeeding, combined with maternal antiretroviral prophylaxis during pregnancy: a regimen under consideration in many countries since it recently became an option recommended by WHO for women with CD4 counts above 350 cells per μ l ('Option A'), as an alternative to continuing maternal triple-therapy throughout breastfeeding ('Option B') (WHO 2010c);

A number of other interventions have been proposed, including vaginal disinfection, vitamin A supplementation and hyperimmune HIV-immunoglobulin, but none have shown any clear benefit (Sturt et al. 2010).

WHO promotes a four-pronged approach to PMTCT with these components: (1) primary prevention of HIV-infection among women of childbearing age; (2) preventing unintended pregnancies among women living with HIV; (3) preventing HIV-infection from these women to their infants and (4) providing appropriate treatment, care and support to mothers living with HIV and their children and families (WHO 2010e).

In sub-Saharan Africa the percentage of pregnant women tested for HIV has increased from 6% in 2004 to 28% in 2008, largely due to provider-initiated testing. During the same period the percentage of HIV-positive pregnant women receiving antiretrovirals to prevent mother-to-child transmission increased from 9% in 2004 to 45% in 2008 (WHO 2010e).

In order to build on this progress made, seven strategic directions have been put forward by WHO:

- (1) strengthening commitment and leadership from partners at global, national and regional levels,
- (2) providing technical guidance,
- (3) promoting and supporting integration (with reproductive health programmes),
- (4) ensuring reliable and equitable access,

(5) supporting health systems interventions,

(6) measuring of programme performance and impact and

(7) collaborating at global, national and local level. Since sub-Saharan countries not only bear the highest HIV-burden but also the greatest challenges to making progress in maternal and child health, integration with reproductive health services is proposed in order to promote equitable and universal access to primary health care (WHO 2010e).

Reproductive health: definitions, outcome indicators and trends

WHO provides a comprehensive definition of reproductive health: 'Within the framework of WHO's definition of health as a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity, reproductive health addresses the reproductive processes, functions and system at all stages of life. Reproductive health, therefore, implies that people are able to have a responsible, satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when and how often to do so. Implicit in this are the right of men and women to be informed of and to have access to safe, effective, affordable and acceptable methods of fertility regulation of their choice, and the right of access to appropriate health care services that will enable women to go safely through pregnancy and childbirth and provide couples with the best chance of having a healthy infant' (WHO 2010a, p 1).

Based on this definition, the following types of services provided within the Malawian health system are considered to provide a comprehensive overview of available reproductive health services: antenatal, intrapartum and postpartum services, treatment of sexually transmitted infections (STIs) and family planning services.

The most commonly applied outcome indicators for the quality of antenatal, intrapartum and postpartum care are facility-based maternal mortality, severe acute maternal morbidity and perinatal mortality (Gulmezoglu et al. 2004; Pattinson et al. 2005; Shankar et al. 2008; van den Akker et al. 2011). The most

common definition of maternal mortality, and that applied throughout this study, is: 'the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes' (WHO, 2007b, p 1238). For perinatal mortality, the WHO definition is applied throughout this study: 'the death of a child during the period between the 24th week of gestation and the end of the first week of life (including stillbirths)' (WHO, 2010b, p 1). No universal definition exists for severe acute maternal morbidity. In under-resourced settings disease-specific morbidity criteria are most commonly applied because these are the most convenient (Gulmezoglu et al. 2004b). The following conditions are commonly included: (severe pre-) eclampsia, major obstetric haemorrhage (peripartum blood loss of more than one litre), severe peripartum infection, uterine rupture and/or obstructed labour (Gulmezoglu et al. 2004; Oladapo et al. 2005; van den Akker et al. 2011; van den Akker et al. 2009; Zwart et al. 2008).

In 2000, the United Nations ratified the Millennium Development Goals (MDGs) that set targets for decreasing maternal mortality by three-quarters and under-five mortality by two-thirds by 2015, compared to the 1990 levels (United Nations 2011). After a marked increase in maternal mortality between 1990 and 2000, possibly as a result of the HIV-epidemic (Bicego et al. 2002; Hogan et al. 2010), the maternal mortality figures in Malawi appear to show some improvement since the millennium ratification, possibly as a result of ART-scale-up (Hogan et al. 2010; Mayosi et al. 2009). However, the country-wide maternal mortality ratio remains a devastating 1140 per 100,000 live births in 2008 (compared to 743 per 100,000 in 1990) (Hogan et al. 2010). Malawi appears to be on track to meet the target for under-five mortality; however, progress was slow for neonatal mortality (death within the first 28 days of life; from 42 to 27 per 1000 live births between 1990 and 2004) (Bhutta et al. 2010), indicating that access to safe perinatal care remains problematic.

Since around half of the deliveries in Malawi occur outside the formal health sector, general community-based perinatal and maternal mortality figures are not reliable indicators of the quality of perinatal health

services. Facility-based figures are more suitable, but often absent or unreliable (Bhutta et al. 2010; Kongnyuy et al. 2009a; Kongnyuy et al. 2009b). Depending on the criteria are used for maternal morbidity, there are between 5 and 223 severe acute maternal morbidities for every maternal death (Say et al. 2004). Severe acute maternal morbidity is increasingly applied as an additional indicator for the quality of perinatal health care (Gulmezoglu et al. 2004; Mantel et al. 1998; Say et al. 2004; Zwart et al. 2008).

In South Africa alone, sexually transmitted infections (STIs) account for 26% of all deaths and for the loss of over five million disability-adjusted life years in 2000. Of this burden of disease, 98% was due to HIV/AIDS (Johnson et al. 2007). The HIV and conventional STI epidemics are interdependent: similar behaviours, such as frequent unprotected intercourse with multiple partners, place people at high risk of both types of infection, and conventional STIs increase the likelihood of HIV transmission (Sangani et al. 2004). According to WHO estimates, around 340 new cases of syphilis, gonorrhoea, chlamydia and trichomoniasis occurred in 1999 worldwide (WHO 2001).

Family planning has been a neglected part of health care provision in Malawi, for political and social reasons (Kirk & Pillet 1998; Lema et al. 1998). Public discourse about contraception was long considered unchaste, particularly during the autocratic Banda-reign (Yeatman & Trinitapoli 2008). Women are often not empowered to take independent decisions regarding if and when to become pregnant (National Statistical Office 2005). In recent years, access to family planning has become a more prominent issue for politicians and health managers (Meekers et al. 2007). Most modern contraceptive methods are now available in the public sector (National Statistical Office 2005; van den Akker & Lommerse 2010). Probably as a result of the liberalization of family planning, the unmet need for family planning declined from 36% in 1992 to 28% in 2004, while the total demand and percentage of demand satisfied increased from 26% to 55% between 1992 and 2004. The national total fertility rate decreased slightly between 2000 and 2004 from 6.3 to 6.0 children per woman (National Statistical Office 2005).

Effects of HIV programmes on reproductive health outcomes and services

A number of authors have highlighted the positive effects of ART/PMTCT programmes on the *quality* of general reproductive health services, describing positive outcomes such as a reduction in maternal mortality (Evjen-Olsen et al. 2009), increased syphilis testing among pregnant women (Potter et al. 2008) and improvements in the general quality of antenatal care (Delvaux et al. 2008). Others, however, have described negative effects on quality of care such as a decrease in motivation of health workers due to a higher workload (Nuwagaba-Biribonwoha et al. 2007) and more prolonged labours due to the reluctance to artificially rupture membranes to enhance delivery resulting from an often unjustified fear of increasing HIV-transmission (Nuwagaba-Biribonwoha et al. 2007).

A systematic analysis of the quality of reproductive health care in settings with high PMTCT/ART-coverage has not been performed as noted previously by others (Both & Van Roosmalen 2010; Kennedy et al. 2010). Several authors have argued that PMTCT policies have historically had too narrow a focus on the health of the child, and then primarily on HIV-specific outcomes, while underestimating the role of PMTCT in contributing to maternal health (Ginsburg et al. 2007; McIntyre 2005).

With regard to the *uptake* of services, several authors have hypothesized that HIV-services could prohibit women from accessing general peripartum care. Threats to uptake include: disruption of peripartum services due to off-site training courses in ART and PMTCT (Banteyerga et al. 2006), fear among women of stigma and discrimination by partners and other relatives when tested HIV-positive at the antenatal clinic (Simba et al. 2010) and fear of maltreatment by health workers upon testing HIV-positive, negatively impacting uptake of intrapartum care (Turan et al. 2008). A systematic review found no particular effects on the uptake of postpartum care, family planning or STI treatment after implementing PMTCT (Both & Van Roosmalen 2010).

In the same way that the importance of these possible negative effects on uptake and quality remains unclear, the same goes for the positive effects on the quality of reproductive health services. Although a

positive impact of PMTCT and ART care on quality could potentially enhance the uptake of reproductive health services and reduce maternal and perinatal mortality within a population, the actual occurrence of this effect has not been described. This leads the authors of the same recent systematic review to draw the conclusion that, 'PMTCT programmes miss the opportunity to contribute to the improvement of maternal health services' (Both & Van Roosmalen 2010).

In short, there is no conclusive programmatic evidence for disadvantages or benefits of ART/PMTCT-care on the uptake and outcomes of reproductive health services. The effects of scaled-up HIV-programmes on uptake and outcomes of peripartum care, family planning and STI-services remain unclear due to the limited availability of scientific reports, particularly from settings where HIV-care has been integrated with general reproductive health care (Both & Van Roosmalen 2010; Kennedy et al. 2010).

However, it is clear that considerable scepticism about the impact of scaled-up HIV-care on reproductive health services has characterized the published literature in recent times, leading WHO to stress the need for 'health system strengthening' alongside or before considering scaling up access to ART and PMTCT (Kennedy et al. 2010; WHO 2010c; WHO 2010d; WHO 2010e).

For a well-functioning health system that may provide both adequate HIV-care as well as general reproductive health care the following key components have been suggested to be necessary: governance, financing, infrastructure development, procurement and supply chain management, human resources, health information systems, service delivery and supervision (Atun et al. 2010; Harries et al. 2009; Harries et al. 2010). The interaction between 'vertical' disease-specific programmes and 'horizontal' health systems strengthening takes place at the level of each of these components. Changes in each of these key components may have an impact on the health system and on the delivery of HIV-care and reproductive health care as a result (Harries et al. 2009; Harries et al. 2010). Therefore, a description of changes in these key components caused by the scaling-up of ART/PMTCT-care may contribute to a description of their impact on the health system.

Aims and objectives

Aims:

- A. To describe the most important changes in uptake of reproductive health services and health outcomes during the scaling up of PMTCT and ART services;
- B. To assess whether this scaling up has contributed general reproductive health service delivery in Thyolo, Malawi in a positive or negative way.

Objectives:

- A. To assess uptake of the following reproductive health services:
 - a. antenatal services (with integrated PMTCT services)
 - b. intrapartum care
 - c. postpartum care
 - d. treatment of STIs
 - e. family planning services
- B. To assess health system improvements in key components of the health system
- C. To assess changes in pregnancy outcome: maternal mortality, severe acute maternal morbidity (uterine rupture, eclampsia, major obstetric haemorrhage defined as a blood loss of more than one litre around the time of delivery, severe perinatal infection) and perinatal mortality.

Study methods

This chapter presents the overall research design and methods used in the study.

Design

This was a retrospective district-wide programme analysis, or a pre- and post implementation study. This type of study design falls under the rubric of 'operational research', in which the data evaluated are routinely-collected programme data and the outcomes are directly applicable to the practical programme situation (Zachariah et al. 2009; Zachariah et al. 2010).

Study period

The study period was from 1 January 2005 to 31 December 2009.

Setting

Thyolo District is a rural area in southern Malawi with around 600,000 inhabitants, most of them subsistence farmers (National Statistical Office 2005; National Statistical Office 2008). The area has a predominantly hilly topography dominated by a number of large tea estates, with only one major tarmac road crossing the district. Access to health facilities is often difficult due to a lack of motorized transport and poor road conditions, particularly during the rainy season when the roads become muddy (Van den Akker & Lommerse 2010).

More than two-thirds of the people live in extreme poverty and the literacy rates in 2004 were 62.4% for women and 79.3% for men (National Statistical Office 2005). Although health care in government facilities and maternal care in most mission facilities are free-of-charge, lack of money for transport is one of the barriers negatively impacting on health-seeking behaviour (Blencowe et al. 2009; O'Gorman et al. 2010). Other barriers to medical care include a lack of decision-making power among women and fear of stigma

and discrimination, particularly among young women and girls (National Statistical Office 2005; O'Gorman et al. 2010).

Intervention/programme approach

Since 2003, MSF and MoH entered into a collaborative partnership to increase and maintain access to ART in Thyolo. MSF provided logistical support, technical guidance and limited human resources, while MoH provided most of the human resources and additional infrastructure as well as the medication obtained through the Global Fund. The scaling up of ART made use of a public health approach, based on task shifting, decentralization, standardized treatment and simple programme monitoring. This led to achieving the target of district-wide coverage late 2007, with 80% of the estimated need for ART fulfilled (Bemelmans et al. 2010). This 80%-target was set by MSF in line with the 80% target established by WHO and UNAIDS to define 'universal access' to PMTCT and ART (Interagency Task Team 2007; WHO & UNAIDS 2006). At the end of June 2010, there were almost 17,000 people alive on ART in Thyolo (MSF 2010).

The MSF/MoH programme for PMTCT started in 2002 at the district hospital. The medication used was single-dose nevirapine (sd NVP) as per WHO recommendation at that time (WHO 2003). In 2007, after the WHO-recommendation had changed based on new evidence regarding more effective and safer drug interventions (with lower chances of drug resistance) the regimen changed to zidovudine (AZT) from 28 weeks gestation combined with sd NVP at the onset of labour and a seven day tailing off, as well as AZT-prophylaxis to the child (WHO 2006). Since 2003, women eligible for ART for their own health have been started on a combined regimen consisting of stavudine (d4T)/lamivudine (3TC)/NVP. ART among pregnant women in Malawi is established by clinical and immunological evaluation, with (A) all those in WHO clinical stages 3 and 4 or (B) all those in stages 1 and 2 AND with a CD4 count below 350 cells/mm³ eligible for ART (until March 2010 the threshold stood at 250 cells/mm³) (MoH 2008a; WHO 2006). The newest WHO guidelines, which promote more robust and safer ART regimens as well as a continuation of ART-protection throughout the breastfeeding period, have not yet been implemented in Malawi but are currently under discussion (WHO 2010c; WHO 2010d). The Ministry of Health (MoH) is ambitious, but their ability to

implement improved protocols will depend on the willingness of international donors to provide adequate funding (IRIN Plus News 2010).

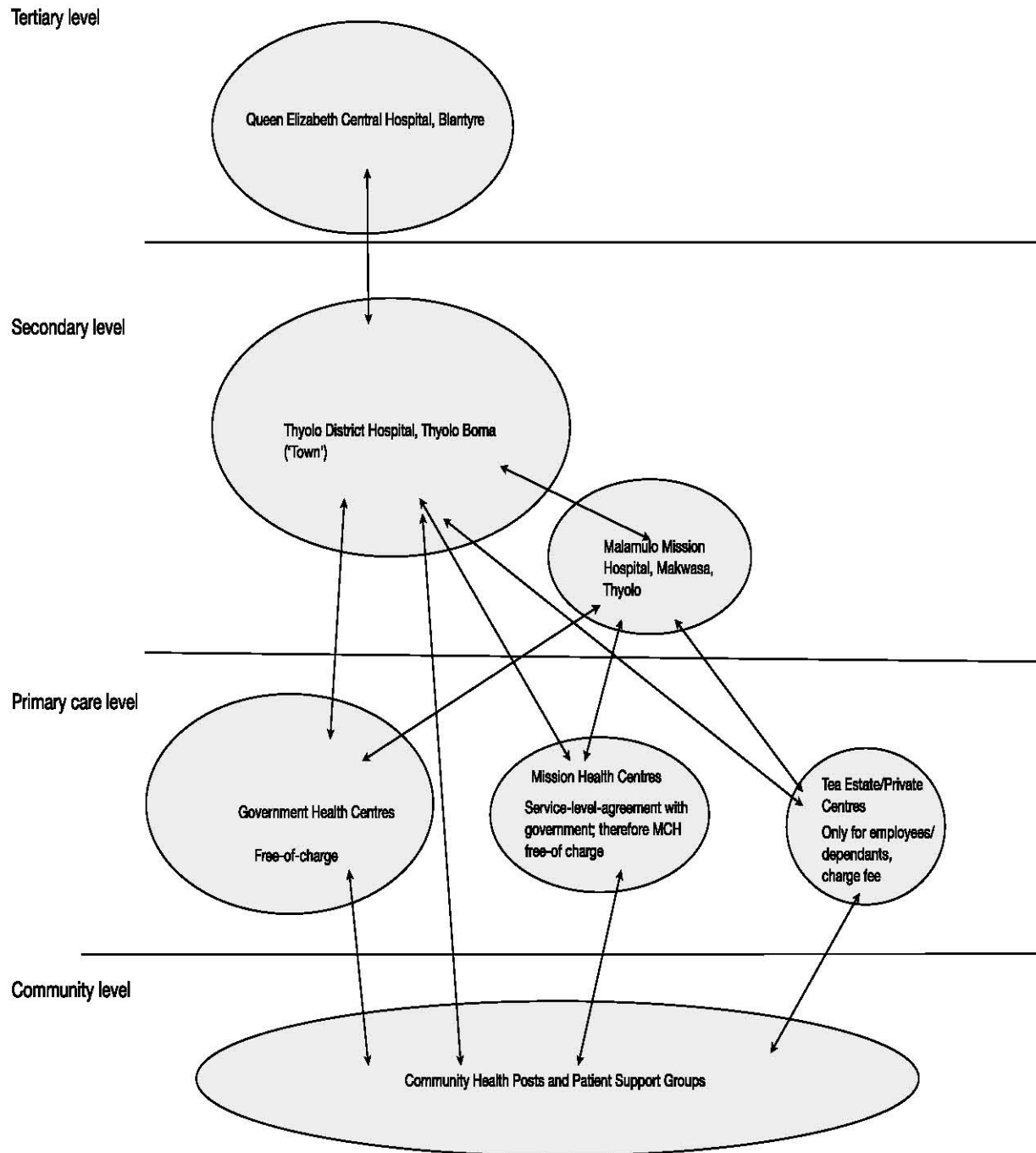
Since achieving district-wide coverage of ART and a significant increase in uptake of PMTCT, the focus of the Thyolo HIV-programme shifted to the integration of HIV-care within general health services (Bemelmans et al., 2010; MSF, 2010).

Health system

The health system in Thyolo is comprised of one district hospital (approximately 4,500 deliveries in 2009), one mission hospital (approximately 1,500 deliveries in 2009), 13 government health centres, seven mission health centres and five private centres (tea estates). In case of complications requiring emergency hospital care, transport from health centre to district hospital usually relies on a limited number of hospital ambulances, but these are poorly maintained and often unreliable. Specialist treatment and intensive care are only available at the central hospital in Blantyre, an hour's drive from Thyolo (Figure 1) (Van den Akker & Lommerse 2010).

University of Cape Town

Figure 1. Schematic representation of the health system in Thyolo District and Southern Region



Professional cadres

Registered nurse-midwives hold a degree in nursing and midwifery from the Malawi College of Nursing. In the absence of this highest-trained nursing cadre, nurse-midwife 'technicians' generally perform the same tasks as registered nurse-midwives although their education is limited to diploma level. Due to a scarcity of medical doctors, non-physician clinicians perform most of the clinical work. Medical assistants, who follow two years of professional training, are mostly based in health centres and perform non-invasive primary care including ART initiations. Clinical officers have four years of professional training and are usually based at the district hospital. They perform more advanced clinical care including surgery such as caesarean section (National Statistical Office 2005; Van den Akker & Lommerse 2010).

Antenatal care

An estimated 28,400 term pregnancies were expected to occur in Thyolo in 2009 (National Statistical Office 2005; National Statistical Office 2008). ANC protocols in Malawi generally follow WHO recommendations. Opt-out HIV testing and counselling takes place upon the first antenatal visit. Four visits are recommended, and the first visit should take place in the first trimester of gestation (National Statistical Office 2005). In Thyolo, ANC is delivered by nurse-midwife technicians at the district hospital and health centres. Since 2007, PMTCT has been provided in the general antenatal clinic with the same nurse-midwife (technician) providing both general reproductive health and PMTCT care (Van den Akker & Lommerse 2010).

Intrapartum care

At facility level, intrapartum care is provided at health centres by nurse-midwife technicians and at the district and mission hospitals by nurse-midwife technicians and registered nurse-midwives. At the district hospital, clinical officers are available in case of complications requiring invasive intervention such as caesarean section. Since 2005, one relief expatriate medical doctor with experience in obstetrics is available at hospital level to attend to serious complications occurring (Van den Akker & Lommerse 2010).

The Malawian government encourages women to deliver at formal health facilities, but still around half of the women in Malawi deliver at home, often with the assistance of a Traditional Birth Attendant (TBA) (National Statistical Office 2005). Although obstetric care in the public health system is provided free-of-charge, several barriers discourage women from accessing formal care, including socio-cultural factors, a low perceived need-benefit-ratio and physical inaccessibility. One barrier recognized by the MoH and many health workers within the Malawian health system was that women were requested to bring a cloth wrap for the newborn after delivery. Even though bringing this cloth was not a formal obligation and the MoH condemned health workers for insisting on it, some women expressed that they were afraid to come without a cloth due to shame or fear. In Thyolo, we hypothesized that providing women with a post-partum enhancement package including a baby blanket and a traditional wrap could encourage them to come for delivery at a health facility as a culturally-sensitive non-monetary incentive to enhance facility delivery (van den Akker et al. 2010).

Postpartum care

Postnatal visits are advised at one and six weeks after delivery. The physical and mental states of the mother are assessed by taking a short history and performing vital signs measurements and a focused physical examination. The infant is weighed and examined and breastfeeding is observed, and appropriate feeding advice given accordingly. Postpartum care is provided by nurse-midwife technicians at health centre level and by registered nurse midwives at district hospital level. The visit at six weeks should be integrated with the provision of family planning services and neonatal care including immunization (National Statistical Office 2005; Van den Akker & Lommerse 2010).

Family planning

Increasingly, and in accordance with current national policy, contraception is made readily accessible in all outpatient departments in Thyolo District, both for HIV-positive and HIV-negative people (MSF 2010; Van den Akker & Lommerse 2010). The most commonly applied methods are injectable contraceptives (Depo-Provera®, more than 90%) and oral contraceptives (Lo-Feminal®, around 5%). An average of 1500 women

per year since 2005 underwent a bilateral tubal ligation. Intra-uterine contraceptive devices are available but rarely used due to cultural beliefs. Contraceptive implants (Norplant®) are used by a minority of mostly higher-educated women (e.g. family of health workers).

Sexually transmitted infections

In 1992, the Malawi Government adopted the Syndromic Management Approach for the treatment of STIs that also forms the basis for STI treatment in Thyolo. This implies that a number of syndromes are treated according to guidelines described in easy-to-use flowcharts. These syndromes are: cervical cancer, genital ulcer disease, urethral discharge, abnormal vaginal discharge, lower abdominal pain in women, scrotal swelling, inguinal bubo, balanitis and neonatal conjunctivitis (WHO 2007). HIV-positive patients in Thyolo are actively screened and referred for treatment of these conditions (Van den Akker & Lommerse 2010). Although patients are encouraged to bring their sexual partners for STI treatment, active contact tracing is not done.

Health promotion

All women attending STI care are actively encouraged to have themselves tested for HIV. In turn, all women attending HIV-care are supposed to be asked whether they have STI-related complaints and treated if this is the case. Women attending HIV-care should be encouraged to use condoms. However, some health workers, especially those in catholic mission health centres, have embraced the 'abstinence-adagio' and are reluctant to offer condoms during consultations. In general, it is a challenge to convince health workers to offer more reliable contraceptive measures in addition to condoms. Recently, efforts have been undertaken to improve family planning health promotion, in particular to HIV-positive women, as well as the uptake of antenatal care, particularly in the first trimester, to all women. Women attending STI treatment and HIV-care are encouraged to bring their husbands to the clinic during subsequent visits for assessment and treatment. Lastly, all client-health worker contacts are supposed to be entry points for HIV-prevention. Conventional STI contacts are used to provide health promotion messages on the prevention of STI transmission.

Outcomes

We chose 2005 as the baseline year and 2009 as the outcome year. Outcomes collected were:

Uptake indicators:

- (1) antenatal uptake data (first visit, four visits, uptake of HIV-testing, PMTCT-uptake)
- (2) uptake of intrapartum care
- (3) uptake of postpartum care (only for the one-week visit, data for the six-week visit are not recorded)
- (4) uptake of STI treatment
- (5) number of family planning visits as a proxy for the uptake of contraceptive measures

Outcome indicators:

- (1) facility-based maternal mortality, perinatal mortality and severe acute maternal morbidity
- (2) PCR-HIV test outcome among children born to PMTCT-mothers

In addition, we described the major changes in the key components of the health system as detailed on page 24: governance, financing, infrastructure development, procurement and supply chain management, human resources, health information systems, service delivery and supervision (Atun et al. 2010; Harries et al. 2009; Harries et al. 2010b).

Data collection and analysis

Data sources used per study objective

In order to achieve objective A (to assess the uptake of reproductive health services) data were collected from facility-records (MoH, mission and private facilities), the HMIS database and the MSF database (PMTCT-uptake) maintained for routine programme monitoring. To achieve objective B (to assess health system improvements) data were retrieved from the same databases, as well as from the MSF annual report in 2010 (MSF 2010), earlier studies conducted in Thyolo (Bemelmans et al. 2011; van den Akker et al. 2009; van den Akker et al. 2011; Jouquet et al. 2009) and from a local situation analysis of maternal and child health services which was primarily based on MoH-data (van den Akker & Lommerse 2010). To achieve objective C (to assess pregnancy outcome) data were retrieved from the HMIS, the MSF database (PCR-outcome data) and from previous studies (van den Akker et al. 2009; van den Akker et al. 2011).

Background of data sources

The HMIS database is managed by the district health office and contains data on peripartum care delivery (uptake of antenatal, intrapartum and postpartum care) and the main pregnancy outcome indicators (maternal and perinatal mortality, maternal morbidity).

Facility-records include information on the uptake of STI care and family planning services. Unfortunately, there are no reliable data on repeat visits for family planning or on STI treatment outcome, nor on the uptake of treatment among partners of STI patients. Data from facility records were collected by a dedicated MSF staff member with experience in data collection, and by the family planning and STI coordinators from the District Health Office (DHO). All data were crosschecked by senior MSF and DHO staff.

The MSF database is managed by experienced staff with a background in epidemiology or information technology and contains information on the uptake of ART, PMTCT and peripartum care. Quality control is

regularly performed on both the MSF and the MoH databases by verifying sentinel information contained in databases with facility records intermittently.

In addition to routinely collected clinic data, data were used from the '4M-study' (study of maternal mortality and maternal morbidity in Thyolo) that was conducted in the district between September 2007 and September 2009. The 4M-study had the objective to evaluate the effects of obstetric audit and feedback on the occurrence of maternal mortality and severe acute maternal morbidity. All instances of maternal mortality and severe acute maternal morbidity were included in this study. In line with several other international studies disease-specific criteria were used to define severe acute maternal morbidity (Gulmezoglu et al. 2004; Zwart et al. 2008), as these criteria are the most convenient in low-resource settings: (1) uterine rupture, (2) eclampsia, (3) major obstetric haemorrhage (estimated blood loss more than one litre or two or more units of blood transfused), (4) severe infection that required medical or surgical treatment, (5) any other condition that the clinician found severe acute morbidity.

Data analysis

From all these sources, data relevant for this study were entered into a separate, password-protected Microsoft Excel sheet. Analysis was performed using IBM® SPSS® Statistics version 15 and OpenEpi (www.openepi.com) software packages. Two-by-two tables were constructed to compare baseline and outcome values for each uptake indicator. For all analyses, a P-value of <0.05 was considered significant.

Ethics

Permission was obtained from the Faculty of Health Sciences Human Research Ethics Committee of the University of Cape Town, South Africa (See Annex A). In addition, this study has met the Medecins Sans Frontieres' Ethics Review Board-approved criteria for analysis of routinely-collected programme data (See Annex B).

Results

The absolute number of people presenting at antenatal, intrapartum and postpartum services all markedly improved comparing the beginning (2005) and end (2009) of the observation period. Based on the estimated numbers of pregnant women per year, there was a marked increase in the uptake of peripartum care.

Antenatal care

The number of women who attended at least one antenatal visit increased from 15,655 in 2005, to 25,310 in 2009. In 2005, there were an estimated 25,052 pregnant women; in 2009 there were projected to be 28,384 (National Statistical Office 2005; National Statistical Office 2008). This means that the uptake of ANC went up from 62.5% in 2005, to 89.2% of pregnant women in 2009 (OR 4.95, 95%CI 4.73-5.18, $p < 0.001$). The number of women who attended at least four antenatal visits as recommended by WHO went up from 3391 in 2008, to 4694 in 2009 (OR 1.41, 95%CI 1.34 – 1.48, $p < 0.001$). The number of HIV-tests performed in pregnant women between 2005 and 2010 increased from 4133 to 23,081. There may have been repeat tests in the same women throughout the same pregnancy, especially since we started emphasizing re-testing in 2009.

In 2005, 936 women received single-dose nevirapine (NVP) for PMTCT, out of an estimated 5260 HIV-positive pregnant women that year (HIV-prevalence 21%, number of pregnant women 25,050). In 2009, 2922 women received an improved PMTCT regimen including zidovudine (AZT) from 28 weeks gestation, out of an estimated 5960 pregnant women (HIV-prevalence 21%, number of pregnant women 28,380). This means that the uptake of PMTCT care almost tripled (OR 2.89, 95% CI 2.64-3.15, $p < 0.001$).

Intrapartum care

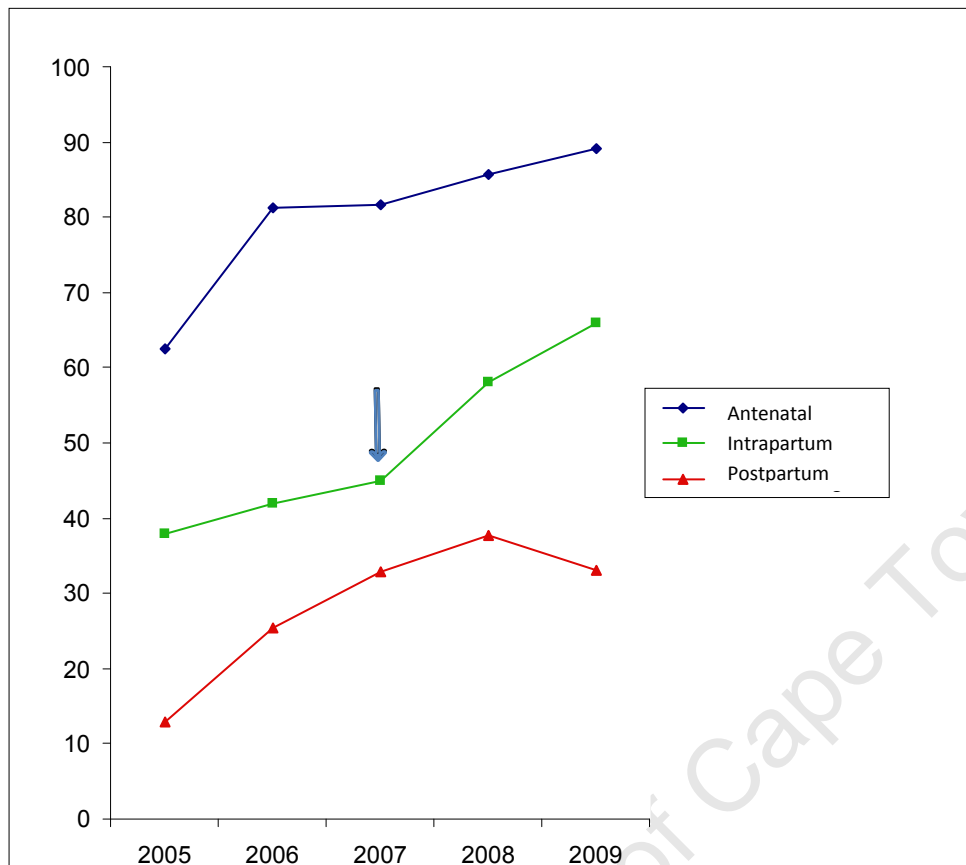
In the two-year period between late 2007 and late 2009, before and after implementation of the incentive that included soap, a baby blanket and a traditional wrap, the number of deliveries in health facilities throughout the district almost doubled (van den Akker et al. 2010). In figure 2, the sharp increase in deliveries after implementation of the incentive (indicated with an arrow) is visible.

Postpartum care

In 2005, 3253 women came for a postnatal visit at around one week after delivery. This number gradually increased reaching a peak of 10,470 in 2008, with a slight decline thereafter (for unknown reasons) to 9401 women in 2009. This represents an increase in the uptake of postpartum care of 20% among pregnant women between 2005 and 2009 (OR 3.32, 95% CI 3.18 – 3.47, $p < 0.001$).

Figure 2 shows the increases in uptake for antepartum, intrapartum and postpartum care between 2005 and 2009, calculated as women receiving any antepartum, formal intrapartum and postpartum care as percentages of the total number of pregnant women.

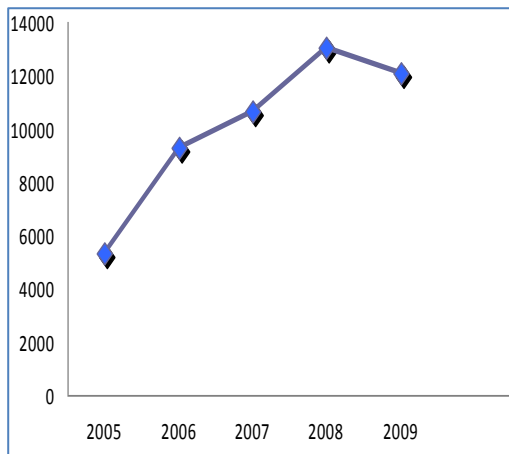
Figure 2. Increase in uptake of peripartum care between 2005 and 2009.



Treatment of sexually transmitted infections

Between 2005 and 2009, the number of women receiving treatment for STIs increased from 5345 to 12,117 (population exposed 140,000 and 150,000 women of reproductive age respectively). This means that the uptake of STI treatment doubled during the period of observation (OR 2.18, 95% CI: 2.12-2.26), $p < 0.001$ (figure 3).

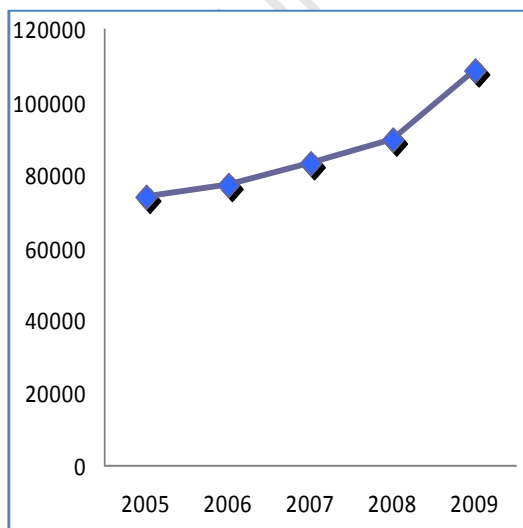
Figure 3. Number of women receiving STI treatment.



Family planning

The number of family planning consultations at medical facilities in Thyolo district increased from 73,625 in 2005 to 108,427 in 2009, an increase of 47% (Figure 4). This includes consultations in the public as well as the private sector. While it is not known how many of these consultations were repeat consultations nor for how many women, it is clear that uptake of modern contraceptive methods shows a marked increase throughout recent years.

Figure 4. Increase in family planning consultations in Thyolo.



Health system

We follow the key components of the health system where the interaction between 'vertical' disease-specific programmes and 'horizontal' health system strengthening takes place (Atun et al. 2010; Harries et al. 2009; Harries et al. 2010).

Governance

The interaction between the District Health Office and MSF was generally found to increase the transparency of the decision-making process. Every year, one larger joint planning meeting and several smaller meetings between MSF and MoH health managers were organized, during which both the priorities in HIV-care and those in reproductive health and other general health care services were addressed. The difference in administrative years between the government (starting in the middle of the calendar year) and MSF (following the calendar year) allowed for the tracking of budgets of each of these groups and allocating funds appropriately in order to jointly address priorities.

Financing

A costing study for the Thyolo HIV-programme identified ART costs and costs of other essential drugs as the main cost driver behind the ART/PMTCT-programme: US\$158 out of US\$237 annual direct treatment costs per patient on ART were spent on medication, and two-thirds of the treatment costs per patient went into ART alone. ART has been provided by the Global Fund. Consultation costs contributed only 13% to the total annual cost per patient. District-wide ART-coverage was achieved at US\$2.5 additional spending per Thyolo inhabitant, and was found to lie well within estimated basic health package costs (Jouquet et al. 2009).

The financial support for the delivery incentive came from MSF, using money from the ART/PMTCT programme at a cost of seven US\$ per woman. In Thyolo District, with 30,000 deliveries per year, the maximum cost if every woman accessed the package, would be US\$210,000 per year. This would increase the cost of the essential health package by about US\$0.3 per head per year, which is affordable in this setting (van den Akker et al. 2010).

Infrastructure development

Four maternity waiting homes were built at peripheral health centres throughout the district in 2007 and 2008. These waiting homes started being used early 2009. Four maternal and child health units of health centres were renovated in 2008. These constructions and renovations were all supported with funds from MSF's HIV/AIDS programme budget (MSF 2010; Van den Akker & Lommerse 2010).

Five facilities were upgraded to provide full Basic Emergency Obstetric Care services, including the possibility to perform vacuum extraction, administer magnesium sulphate and intravenous antibiotics and perform manual vacuum aspirations. This involved both upgrading of existing buildings and equipment, as well as training of health staff. The upgrading was financed by both MoH and MSF, using both general funds and HIV-funds.

Procurement and supply chain management

In general, effective procurement and supply chain management are major challenges in Malawi, which cannot be discussed in detail here. The poor functioning of the procurement system, including the functioning of the central medical stores which are responsible for the supply of all drugs in the public health system, was a major reason for the Global Fund to reject the country's national strategic application in February 2010 (Nyasa Times 2011). At district level, supply systems of MSF and MoH have been integrated into one general procurement and supply system, and combined efforts have been undertaken to enhance performance.

The availability of essential medications within the health system improved thanks to investments in second- and third-line antibiotic regimens supported by funding from the HIV/AIDS programme. For instance, higher-quality antibiotics became available for the treatment of STIs including third-generation cephalosporines.

Human resources

Despite the launching of an Emergency Human Resource Plan in 2004, the number of health workers did not increase much in Thyolo in recent years. The only measurable improvement was at the district hospital where the number of hospital clinical officers went up from 11 in April 2007 to 19 in April 2010. However, no increases were seen in other cadres or in health centres (Van den Akker & Lommerse 2010). One important initiative in the district that has most certainly contributed to increased availability of existing health staff was the implementation of a dedicated and confidential staff clinic providing general primary care including ART to all staff and their first-degree relatives (Bemelmans et al. 2011).

Health information systems

Basic information on MSF and MoH databases was given in the chapter on data collection (page 34). The information collection tools for HIV and general reproductive health care still function rather independently. A sustainable and comprehensive computerized health information system is not currently in place, although the government is currently exploring different systems (Baobab Health Partnership 2011).

Service delivery and supervision

Together with efforts to increase uptake, measures to improve the quality of peripartum care were taken. A system of rigorous obstetric audit was implemented and supervision of all delivery rooms by senior staff increased (van den Akker et al. 2011; Van den Akker et al. 2009). Supervision of antenatal and postpartum services and infrastructure also increased and was performed by a joint team of senior MSF and MoH health workers and managers. Audit results are described in the section on maternal and perinatal pregnancy outcome.

Pregnancy outcome

Out of 503 children whose mothers had received PMTCT at any of the peripheral health centres and who were tested by Polymerase Chain Reaction (PCR) in 2009, 47 (9.3%) tested positive. The data, unfortunately, do not specify at what age the HIV-test was performed. Among 670 children born to mothers who had attended PMTCT at the district hospital, 30 (4.5%) were tested HIV-positive.

The District Health Management Information System (HMIS) reported between 14 and 20 deaths per year for the years 2005 to 2009 (Table 1). However, the 4M-study to maternal mortality and morbidity in the district conducted between September 2007 and September 2009 counted 29 inclusions for maternal mortality alone in the year 2008 (Van den Akker et al. 2009). This suggests that the reliability of the maternal mortality data in the HMIS is poor due to under-reporting.

Reported perinatal deaths varied between 212 in 2007 to 129 in 2009. However, in 2010 (after the study period ended), following efforts to improve recording and reporting of perinatal mortality there were 159 perinatal deaths reported in the first six months only (table 1). This leads us to suspect that data for previous years do not reflect true perinatal mortality. Due to these reliability concerns, perinatal mortality was not included as an indicator of quality of care in our district.

Table 1. Maternal and perinatal mortality reported at HMIS. Comparison with the 4M-inclusions indicates that there is gross underreporting of maternal mortality; the high number of perinatal mortality in 2010 is likely to be due to more stringent data collection.

Data	Maternal deaths reported to HMIS	4M-study	Perinatal deaths reported to HMIS
2005	14		N/A
2006	15		159
2007	14	8 (September – December only)	212
2008	20	29	183
2009	12	9 (January – August only)	129
2010			159 (January-June only!)

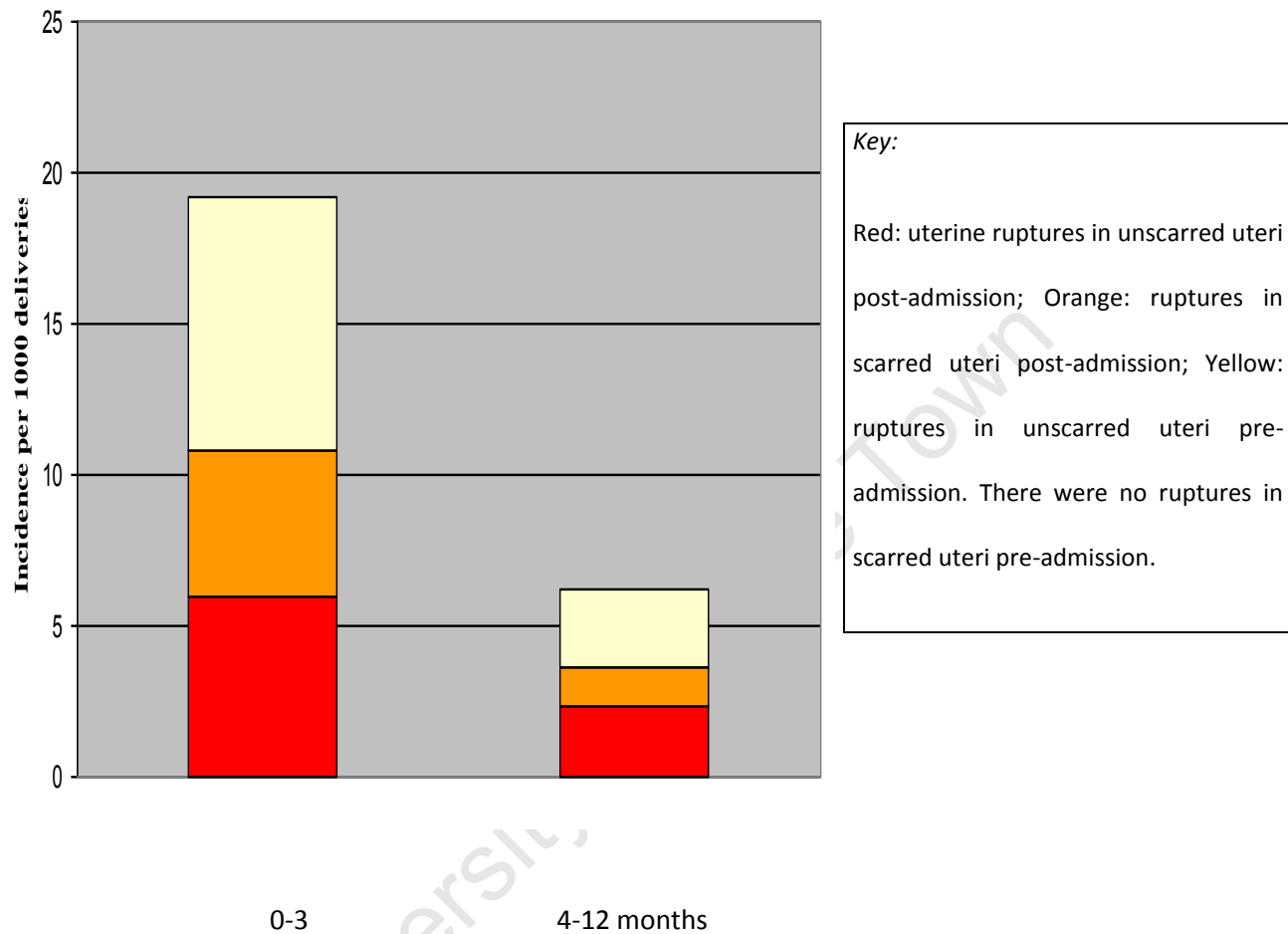
Data for maternal morbidity reported to the district health office before September 2007 were also considered unreliable due to substantial underreporting. For instance, only 16 uterine ruptures were reported to HMIS for all of 2005, whereas the prospective 4M-study identified 19 ruptures in the first three months of the study alone (Van den Akker et al. 2009). We consider that the 4M-study gives accurate insight into facility-based maternal mortality and severe acute maternal morbidity between September 2007 and September 2009. Based on 4M-study results, we were able to document improvements in maternal pregnancy outcome for Thyolo District Hospital and other facilities (van den Akker et al. 2011; van den Akker et al. 2009). The results are detailed as follows.

Over the two years, 386 women with serious complications were included in the study. Among these, 46 women died and 340 sustained severe acute maternal morbidity (Case Fatality Rate: 11.9%). Forty-five cases were audited in plenary; care for 30 cases was assessed to be substandard by more than half of the available staff (van den Akker et al. 2011).

During the first three months of the 4M-study period, a particularly high incidence of uterine rupture of almost 20 per 1000 hospital deliveries was observed. This was thought to be due to poor adherence to local standards. Therefore, several audit sessions were organized. At the request of hospital staff a larger session involving two external obstetricians-gynaecologists was held following which recommendations were put forward and implemented, including refresher training (funded by MSF with 'HIV-funds'), increased on-the-job coaching and supervision by seniors, and follow-up visits to peripheral centres. The incidence of uterine rupture decreased by 68% (OR 0.32; 95% CI, 0.16-0.63) to 6.1 per 1000 deliveries over the next 9 months (Figure 5). The overall case fatality rate was 11.4%, and the perinatal mortality rate was 829 per 1000 live births (Van den Akker et al. 2009). Throughout the second year of study, the incidence of uterine rupture further decreased to 3.7 per 1000 hospital deliveries (van den Akker et al. 2011).

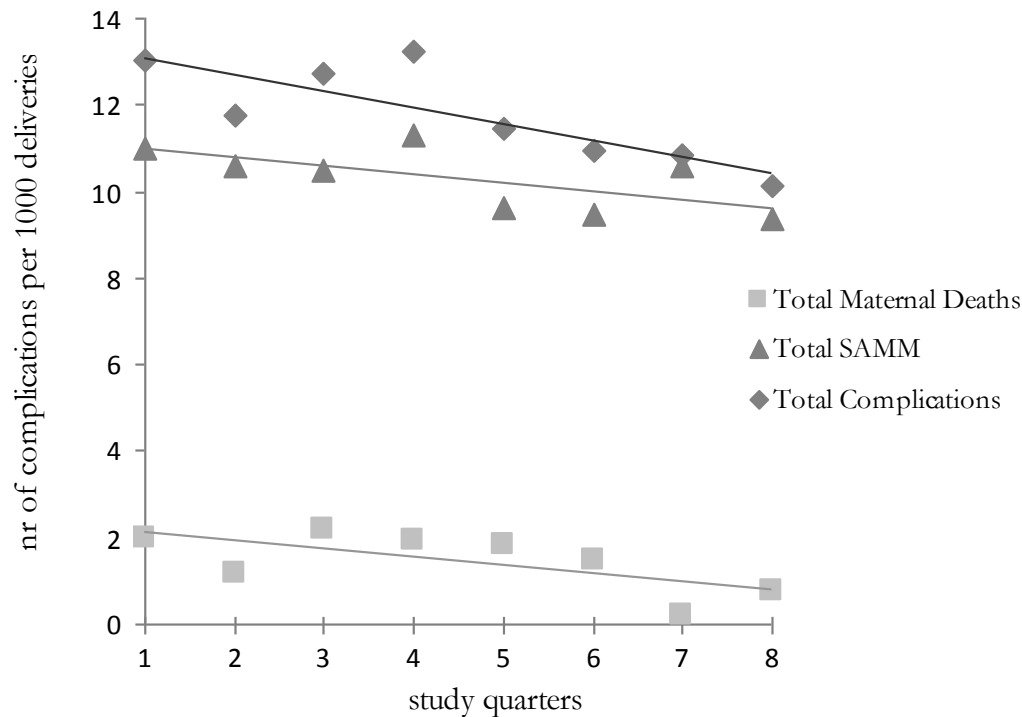
University

Figure 5. Incidence and type of uterine rupture before and after audit aimed at uterine rupture in Thyolo District Hospital (Van den Akker et al. 2009)



In addition to this assessment of uterine rupture, the total number of severe acute maternal morbidity and mortality cases were analysed during the two-year period in which audit of a variety of mortality and morbidity cases was performed. A plot of severe maternal complications (severe acute maternal morbidity and mortality) showed a reduction in the number of complications during the two-year study period from 13.5 to 10.4 per 1000 deliveries (figure 6) (van den Akker et al. 2011).

Figure 6. Regression lines of maternal mortality, morbidity and total complications, calculated per 1000 health facility deliveries.



Individual case reviews showed a particularly high number of maternal infections amongst cases of severe acute maternal morbidity and maternal mortality. Maternal infections had replaced haemorrhage, traditionally the major cause of poor maternal outcome, as the most common cause of maternal mortality. HIV-infection seems to play an important role in this shift: more than 30% of women sustaining severe acute maternal morbidity and 40% of women who died were HIV-positive (van den Akker et al. 2011).

Numerous recommendations resulting from audit were implemented, and many of which were partially supported by HIV programme funds. Therefore, although reliable information on facility-based maternal and perinatal indicators before 2007 is not available, the 4M-outcome data show that despite marked increases in the uptake of peripartum care and the resulting increase in patient burden on the health

system, maternal pregnancy outcome improved. This improvement was most likely a result of simultaneous investments into the quality of care using audit and feedback, (refresher) training, increased supervision by senior staff, improved infrastructure and investments towards district-wide provision of BEmOC (van den Akker et al. 2011; van den Akker et al. 2009).

Strengths and limitations

This study is based on operational research data from a routine programme review. This approach has several strengths and limitations that deserve mentioning.

The main strength of this approach is that the data are all derived from 'real programme' inputs and outputs, and as such provide a credible picture for programme planners who are concerned about on-the-ground inputs and outputs. While randomized trials have the distinct advantage of controlling for potential confounding factors in order to allow for a valid and precise estimate of the true effect of a particular intervention, the conditions of randomized trials (highly resourced, focusing on a single intervention with considerable attention paid to limiting loss to follow up) are very rarely approximated in an operational context, particularly a setting such as rural Malawi (Zachariah et al. 2009).

However, this approach carries with it a number of important limitations. First, we relied on programme data that had been routinely collected for programme tracking. Proper recording and storing of data is often a challenge in under-resourced settings since it is usually not given high priority (Wagaarachchi et al. 2001). Maternal morbidity as well as perinatal and mortality mortality all seemed substantially underreported at the District Health Management Information System and we had to resort to 'independent' study data for reliable pregnancy outcome indicators. However, all the other data used in this analysis for the period 2005 to 2009 are considered reliable for several reasons. First, data reported at HMIS and MSF were regularly crosschecked with facility records. Second, data on peripartum care, family planning and STI treatment all showed very clear trends without any major 'outliers'. Finally, all data were verified by senior data staff with experience in data collection and monitoring.

Second, as this study did not attempt to investigate causal relationships but rather a number of programme indicators evolving during the period when PMTCT and ART were scaled up, some may argue that the RH

improvements described may have happened *despite* rather than *because of* investments in PMTCT and ART. However, where possible, this study attempts to show which initiatives were implemented with money allocated to HIV, thus allowing for the tentative conclusion that taking HIV funding has broadly benefitted the overall health system and contributed tremendously to the reproductive health improvements summarized in this report. At the very least these findings show that scaling up PMTCT and ART does not necessarily pose a hindrance to improvements in other health priorities.

The generalizability of these findings to other districts may be limited due to the fact that the scaling-up of ART and PMTCT and the investment in reproductive health services in Thyolo received considerable support from MSF. Although many districts receive various levels and forms of NGO-support, not all of them may have the same means to achieve the positive trends described in this report.

The data about the uptake of reproductive health services included data from mission and private facilities, in addition to government clinics. However, the changes in the key components of the health system were largely based on results of the collaboration between MSF and MoH and therefore apply primarily to public health facilities and should not automatically be inferred to include mission and private facilities. In fact, improvements in these parts of the health system may have lagged behind.

Although it was previously documented that the uptake of formal delivery care was not larger in mission facilities compared to other facilities following the implementation of the enhancement package, the signing of service-level-agreements between the DHO and mission facilities may have had some additional positive impact on the uptake of care (van den Akker et al. 2011). Other factors that may have contributed to the increased uptake of peripartum care include increased investment in community awareness of safe peripartum practices by the Ministry of Health and other partners as well as efforts by the government to discourage women from delivering with TBAs. These factors may have had some impact on the described increases in uptake (van den Akker et al. 2011; van den Akker & Lommerse 2010).

Discussion

This is one of the first district-wide studies that attempted to comprehensively describe the effects of the PMTCT and ART rollout on general reproductive health service uptake and outcomes. The findings suggest that this scale-up, provided that it is planned with the general health system in mind may benefit reproductive health in a broader sense, in addition to increasing survival among the HIV-positive and reducing vertical transmission.

Uptake of peripartum care, family planning and STI treatment all improved significantly during the scale-up of HIV-care in Thyolo. This shows that: (1) the integration of opt-out HIV testing and counselling and PMTCT care within the general peripartum services did not prohibit more women from accessing care as others had feared (Simba et al. 2010; Turan et al. 2008), (2) despite the fact that considerable human and material resources were allocated to HIV-care, the health care system was still able to accommodate a larger number of patients attending general reproductive health care, and (3) the fact that the uptake of reproductive health services increased markedly during the period of the ART/PMTCT scale-up suggests that the rollout of HIV-care may have been an important driver behind the increased uptake.

The increases in service uptake happened without any identifiable decrease in quality of care. Maternal and perinatal pregnancy outcomes were difficult to obtain for the entire study period, but the positive outcomes of the 4M-study show that – at least between 2007 and 2009 – facility-based maternal pregnancy outcomes improved significantly (van den Akker et al. 2011; van den Akker et al. 2009). This is an important finding that contradicts, at least for Thyolo district, claims that fragile health systems in sub-Saharan Africa are not able to upgrade their performance in the absence of adequate material and human resources.

The tremendous increase in the uptake of ANC may have been the result of several factors, including: (1) increased health promotion efforts to all women, including HIV-positive women, (2) increased quality of antenatal care due to increased supervision, easy access to HIV testing and counselling, integrated PMTCT with a combined regimen, and (3) improved impression of health services in general, due to improvements in intrapartum care, increased availability of ART and increased availability of health staff (partly as a result of the staff clinic). The increase in women coming for at least four antenatal visits may have been due to an increase in the number of women coming for PMTCT-care who are urged to come every month for their ART or AZT-refills, although clinic records do not differentiate between PMTCT and non-PMTCT women among those coming for a fourth visit. The number of women coming for four or more antenatal visits before 2008 were not recorded. Increased health promotion and improvements in quality of care are also the likely contributors to the increased uptake of postpartum care, family planning services and STI treatment.

It is important to note that the quality improvements described are measures that have been implemented at programme level. Whether these measures have actually raised quality in the eyes of people accessing care would require additional qualitative research. Semi-structured in-depth interviews and a focus group discussion conducted earlier among health workers in Thyolo showed that health staff were generally satisfied with the way obstetric audit sessions were conducted. Staff found audit a useful and satisfactory activity, particularly because of its educational value. Audit clearly had become part of the professional routine in this district hospital with limited availability of material and human resources (Bakker et al. 2011).

It is not clear why the number of women accessing STI treatment went down between 2008 and 2009. An optimistic interpretation would be that access to ART and health promotion messages given alongside supplementation of ART may have reduced the incidence of STIs. Available data, unfortunately, do not specify HIV-positive versus HIV-negative or 'on-ART' versus 'not-on-ART'. A negative interpretation would

be that the reduction was due to several shortages of STI-drugs that occurred in 2009 due to logistical and financial problems within the government supply chain.

An important explanation for the favourable outcomes described in this report lies in the fact that PMTCT and ART were delivered in an integrated manner, through the public health system, by health staff in the same clinics used for general health care. This means that HIV testing and counselling, PMTCT and ART care could be accessed by patients at the same place and time they received their general peripartum care. This will favourably affect losses to follow-up of those accessing PMTCT and ART and will, at the same time, improve the credibility of the general health services. The fact that PMTCT and ART are readily available should one be tested HIV-positive, could potentially have a positive effect on women's decision to seek care. The fact that PMTCT and ART were provided at the general clinic also forced both MoH and MSF health managers to keep the general health system in mind while planning the scale-up, and increased effective and transparent joint governance of the health system. Initially, MSF brought in some extra human resources to facilitate the scaling up. Where these staff used to work independently from the rest of the system providing HIV-care only, they have recently been incorporated in the general system providing general peripartum care. These MSF service providers are gradually reduced. Even with these 'external' providers from outside the public health system, Thyolo had no more human resources in the health sector than any other district in Malawi in recent years. The central government is likely to have adjusted allocations of staff to Thyolo as a compensation mechanism for the presence of MSF.

It is understandable that those concerned with the general health of women and children have grown apprehensive of the substantial resources devoted to HIV-care in many places. Similar investments were unlikely to have been made towards providing comprehensive maternal and child health care in the pre-HIV era. In some places, it may appear that HIV/AIDS draws resources away from the public health sector. However, it may well be that the financial situation of the local public health sector would be in an even more deplorable state without the influx of HIV-money. Although the findings presented here are context-dependent and should be seen in complement with study results from other settings, they suggest that it

may be beneficial, for the health of both HIV-positive and the HIV-negative women, to try and tackle different health priorities together by applying similar means, and by making use of what is available.

University of Cape Town

Conclusions

During the period of ART/PMTCT scale-up in Thyolo District, uptake of antenatal, intrapartum and postpartum care, family planning services and STI treatment all increased significantly. Infrastructure available for reproductive health care improved, partly as a result of the influx of HIV funding. Although data for some indicators were difficult to obtain, pregnancy outcomes appear to have improved during the period of scaling up HIV-services. The number of children born to mothers that received PMTCT services who tested HIV-positive at six weeks of age was low and, in addition, an independent study of maternal mortality and morbidity in Thyolo showed a reduction in severe maternal complications between 2007 and 2009 after implementing systematic obstetric audit and feedback. The implementation of recommendations coming from audit was partly made possible by the availability of HIV-funding. Based on these findings, it can be concluded that ART/PMTCT scale-up in Thyolo has very likely contributed to the increased uptake of general reproductive health care, while the performance of the reproductive health care services did not decline, and likely improved as a result of investments in quality.

Recommendations

1. Since ART and PMTCT rollout in high-prevalence HIV-countries may well be accompanied by other positive reproductive health outcomes, the scale-up should remain a public health priority for national governments, non-governmental actors and international donors. Concerns that the rollout would be detrimental to general reproductive health services in terms of uptake and outcome are understandable, but not necessarily justified. This study shows that, provided the general health system is taken into consideration while planning the scale-up, increased access to HIV care may also enhance the uptake of general reproductive health services without a negative effect on health outcomes. The question should not be *whether* to rollout but rather *how* to roll out.

2. Weaknesses within the general health system should be considered during the rollout of ART and PMTCT and investments in HIV-services should also address these weaknesses within the general health system within which HIV-services are delivered. Underlying this recommendation is the understanding that sustainable HIV-care is not possible without a well-functioning system to deliver it. Investments towards strengthening the general health care system will benefit both the ART/PMTCT scaling-up as well as uptake and quality of general health services, including reproductive health. The findings of this report indicate that investments in a district health system may produce significant improvements in reproductive health outcomes, provided they are well planned.

3. Maternal mortality and HIV should be tackled together by the same interventions rather than separately. The ART rollout should be promoted as an essential element of primary maternal care and during the ART scale-up, pregnant women should be considered a priority group. ART will reduce MTCT, promote women's health and survival and, in this way, also improve the health outcomes of their children.

4. More evidence is needed to demonstrate the effects of scaled-up HIV care on general health services and outcomes, especially within well-integrated HIV-programmes. Since it is difficult to generalize findings from Thyolo automatically to other settings, the findings of this report should encourage others who developed similar or different initiatives elsewhere to document and publish their experiences.

5. The increased uptake of reproductive health services that would hopefully result in the improvement of women's health should form a basis for poor women in low-income countries and civil society groups representing them to enhance advocacy for women's right to health care. The barriers for poor young women to acquire a joint political force are manifold, and those concerned with maternal and child health should not consider their job done once basic care has been provided but encourage women to organize themselves and help them break down these barriers. In this way, uptake of health care and improvements in quality of care should enhance women's dignity and their chances to acquire a space within the political and legal arena (Meguid 2010).

University of Cape Town

References

- Achmat, Z 2002a, 'The XIV International AIDS Conference: treatment access as a human right', *Positively Aware*, vol. 13, no. 5, pp. 32-35.
- Achmat, Z 2002b, 'South Africans win MTCT court case', *WORLD*, no. 129, p. 6.
- Achmat, Z & Simcock, J 2007, 'Combining prevention, treatment and care: lessons from South Africa', *AIDS*, vol. 21, Suppl. 4, p. S11-S20.
- Adam, MA & Johnson, LF 2009, 'Estimation of adult antiretroviral treatment coverage in South Africa', *South African medical journal*, vol. 99, no. 9, pp. 661-667.
- Atun, R, Weil, DE, Eang, MT & Mwakyusa, D 2010, 'Health-system strengthening and tuberculosis control', *Lancet*, vol. 375, no. 9732, pp. 2169-2178.
- Bakker, W, van den Akker, T, Mwangombwa, B, Khukulu, R, Van Elteren, M & Van Roosmalen, J 2011, 'Health workers' perceptions of obstetric audit in Thyolo, Malawi', submitted.
- Banteyerga, H, Kidanu, A & Stillman, K 2006, 'The systemwide effects of the global fund in Ethiopia: final study report', USAID, Partners for Health Reform Plus. Retrieved February 8, 2011, from <http://www.healthsystems2020.org/content/resource/detail/1402/>
- Baobab Health Partnership. Health Information Systems. Retrieved February 1, 2011, from <http://baobabhealth.org/>
- Barre-Sinoussi, F, Chermann, JC, Rey, F, Nugeyre, MT, Chamaret, S, Gruest, J, Dautet, C, Axler-Blin, C, Vezinet-Brun, F, Rouzioux, C, Rozenbaum, W & Montagnier, L 1983, 'Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)', *Science*, vol. 220, no. 4599, pp. 868-871.
- Bemelmans, M, van den Akker, T, Pasulani, O, Tayub, NS, Hermann, K, Mwangombwa, B, Jalasi, W, Chiomba, H, Ford, N & Philips, M 2011, 'Keeping health staff healthy: evaluation of a workplace initiative to reduce morbidity and mortality from HIV/AIDS in Malawi', *Journal of the International AIDS Society*, vol. 14, no. 1, p.1.
- Bemelmans, M, van den Akker, T, Ford, N, Philips, M, Zachariah, R, Harries, A, Schouten, E, Hermann, K, Mwangombwa, B & Massaquoi, M 2010, 'Providing universal access to antiretroviral therapy in Thyolo, Malawi through task shifting and decentralization of HIV/AIDS care', *Tropical medicine & international health*, vol. 15, no. 12, pp. 1413-1420.
- Bhutta, ZA, Chopra, M, Axelson, H, Berman, P, Boerma, T, Bryce, J, Bustreo, F, Cavagnero, E, Cometto, G, Daelmans, B, de Francisco, A, Fogstad, H, Gupta, N, Laski, L, Lawn, J, Maliqi, B, Mason, E, Pitt, C, Requejo, J, Starrs, A, Victora, CG & Wardlaw, T 2010, 'Countdown to 2015 decade report (2000-10): taking stock of maternal, newborn, and child survival', *Lancet*, vol. 375, no. 9730, pp. 2032-2044.
- Bicego, G, Boerma, JT & Ronsmans, C 2002, 'The effect of AIDS on maternal mortality in Malawi and Zimbabwe', *AIDS*, vol. 16, no. 7, pp. 1078-1081.

Blencowe, H, Kerac, M & Molyneux, E 2009, 'Safety, effectiveness and barriers to follow-up using an 'early discharge' Kangaroo Care policy in a resource poor setting', *Journal of tropical pediatrics*, vol. 55, no. 4, pp. 244-248.

Blower, SM, Gershengorn, HB & Grant, RM 2000, 'A tale of two futures: HIV and antiretroviral therapy in San Francisco', *Science*, vol. 287, no. 5453, pp. 650-654.

Both, JM & Van Roosmalen, J 2010, 'The impact of Prevention of Mother to Child Transmission (PMTCT) programmes on maternal health care in resource-poor settings: looking beyond the PMTCT programme--a systematic review', *BJOG: an international journal of obstetrics and gynaecology*, vol. 117, no. 12, pp. 1444-1450.

Brugha, R, Simbaya, J, Walsh, A, Dicker, P & Ndubani, P 2010, 'How HIV/AIDS scale-up has impacted on non-HIV priority services in Zambia', *BMC Public Health*, vol. 10, p. 540.

Buve, A, Kalibala, S & McIntyre, J 2003, 'Stronger health systems for more effective HIV/AIDS prevention and care', *The international journal of health planning and management*, vol. 18 Suppl 1, p. S41-S51.

Bwirire, LD, Fitzgerald, M, Zachariah, R, Chikafa, V, Massaquoi, M, Moens, M, Kamoto, K & Schouten, EJ 2008, 'Reasons for loss to follow-up among mothers registered in a prevention-of-mother-to-child transmission program in rural Malawi', *Transactions of the Royal Society of Tropical Medicine and Hygiene*, vol. 102, no. 12, pp. 1195-1200.

Chopra, M, Lawn, JE, Sanders, D, Barron, P, Abdool Karim, SS, Bradshaw, D, Jewkes, R, Abdool, KQ, Flisher, AJ, Mayosi, BM, Tollman, SM, Churchyard, GJ & Coovadia, H 2009, 'Achieving the health Millennium Development Goals for South Africa: challenges and priorities', *Lancet*, vol. 374, no. 9694, pp. 1023-1031.

Cohen, J 2000, 'AIDS meeting: South African Leader Declines to Join the Chorus on HIV and AIDS', *Science*, vol. 289, no. 5477, p. 222a.

Delvaux, T, Konan, JP, Aké-Tano, O, Gohou-Kouassi, V, Bosso, PE, Buve, A & Ronsmans, C 2008, 'Quality of antenatal and delivery care before and after the implementation of a prevention of mother-to-child HIV transmission programme in Cote d'Ivoire', *Tropical medicine & international health*, vol. 13, no. 8, pp. 970-979.

Evjen-Olsen, B, Olsen, OE & Kvale, G 2009, 'Achieving progress in maternal and neonatal health through integrated and comprehensive healthcare services - experiences from a programme in northern Tanzania', *International journal for equity in health*, vol. 8, p. 27.

Ford, N 2003, 'Public health and company wealth', *BMJ*, vol. 326, no. 7402, p. 1296.

Ford, N, Wilson, D, Costa, CG, Lotrowska, M & Kijtiwatchakul, K 2007, 'Sustaining access to antiretroviral therapy in the less-developed world: lessons from Brazil and Thailand', *AIDS*, vol. 21 Suppl 4, p. S21-S29.

Ginsburg, AS, Hoblitzelle, CW, Sripipatana, TL & Wilfert, CM 2007, 'Provision of care following prevention of mother-to-child HIV transmission services in resource-limited settings', *AIDS*, vol. 21, no. 18, pp. 2529-2532.

Gottlieb, MS, Schroff, R, Schanker, HM, Weisman, JD, Fan, PT, Wolf, RA & Saxon, A 1981, 'Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency', *The New England journal of medicine*, vol. 305, no. 24, pp. 1425-1431.

Gulmezoglu, AM, Say, L, Betran, AP, Villar, J & Piaggio, G 2004, 'WHO systematic review of maternal mortality and morbidity: methodological issues and challenges', *BMC medical research methodology*, vol. 4, p. 16.

Hanefeld, J 2010, 'The impact of Global Health Initiatives at national and sub-national level - a policy analysis of their role in implementation processes of antiretroviral treatment (ART) roll-out in Zambia and South Africa', *AIDS Care*, vol. 22 Suppl 1, pp. 93-102.

Hanefeld, J & Musheke M 2009, 'What impact do Global Health Initiatives have on human resources for antiretroviral treatment roll-out? A qualitative policy analysis of implementation processes in Zambia', *Human resources for health*, vol. 7, p. 8.

Harries, AD, Jensen, PM, Zachariah, R, Rusen, ID & Enarson, DA 2009, 'How health systems in sub-Saharan Africa can benefit from tuberculosis and other infectious disease programmes', *The international journal of tuberculosis and lung disease: the official journal of the International Union against Tuberculosis and Lung Disease*, vol. 13, no. 10, pp. 1194-1199.

Harries, AD, Zachariah, R, Tayler-Smith, K, Schouten, EJ, Chimbwandira, F, Van Damme, W & El-Sadr, WM 2010, 'Keeping health facilities safe: one way of strengthening the interaction between disease-specific programmes and health systems', *Tropical medicine & international health*, vol. 15, no. 12, pp. 1407-1412.

Heywood, M 2001, 'Debunking 'Conglomo-talk': A Case Study of the Amicus Curiae as an Instrument for Advocacy, Investigation and Mobilisation', *Proceedings of: Health, Law and Human Rights: Exploring the Connections*.

Hogan, MC, Foreman, KJ, Naghavi, M, Ahn, SY, Wang, M, Makela, SM, Lopez, AD, Lozano, R & Murray, CJ 2010, 'Maternal mortality for 181 countries, 1980-2008: a systematic analysis of progress towards Millennium Development Goal 5', *Lancet*, vol. 375, no. 9726, pp. 1609-1623.

Horvath, T, Madi, BC, Iuppa, IM, Kennedy, GE, Rutherford, G & Read, JS 2009, 'Interventions for preventing late postnatal mother-to-child transmission of HIV', *Cochrane database of systematic reviews*, no. 1, p. CD006734.

Horwood, C, Haskins, L, Vermaak, K, Phakathi, S, Subbaya, R & Doherty, T 2010, 'Prevention of mother to child transmission of HIV (PMTCT) programme in KwaZulu-Natal, South Africa: an evaluation of PMTCT implementation and integration into routine maternal, child and women's health services', *Tropical medicine & international health*. Epub ahead of print.

Interagency Task Team on prevention of HIV infection in pregnant women, mothers and their children 2007, 'Guidance on global scale-up of the prevention of mother-to-child transmission of HIV. Towards universal access for women, infants and young children and eliminating HIV and AIDS among children', WHO, Geneva.

IRIN Plus News 2010, 'Malawi moves to adopt WHO guidelines', Retrieved December 29, 2010, from <http://www.plusnews.org/Report/asp?Reportid=89266>

Johnson, L, Bradshaw, D & Dorrington, R 2007, 'The burden of disease attributable to sexually transmitted infections in South Africa in 2000', *South African medical journal*, vol. 97, no. 8 Pt 2, pp. 658-662.

Jouquet, G, Bemelmans, M, Massaquoi, M, Arnould, L, Mwagomba, B, Bauernfeind, A & Philips, M 2009, 'Cost analysis of an ARV programme reaching universal access in Thyolo, Malawi', *Proceedings of the fifth conference of the International AIDS Society*, Cape Town.

Kachapila, L 1998, 'The HIV/AIDS epidemic in Malawi', *International nursing review*, vol. 45, no. 6, pp. 179-181.

Kennedy, CE, Spaulding, AB, Brickley, DB, Almers, L, Mirjahangir, J, Packel, L, Kennedy, GE, Mbizvo, M, Collins, L & Osborne, K 2010, 'Linking sexual and reproductive health and HIV interventions: a systematic review', *Journal of the International AIDS Society*, vol. 13, p. 26.

Kim, JY & Gilks, C 2005, 'Scaling up treatment--why we can't wait', *The New England journal of medicine*, vol. 353, no. 22, pp. 2392-2394.

Kirk, D & Pillet, B 1998, 'Fertility levels, trends, and differentials in sub-Saharan Africa in the 1980s and 1990s', *Studies in Family Planning*, vol. 29, no. 1, pp. 1-22.

Kongnyuy, EJ, Mlava, G & van den Broek, N 2009a, 'Criteria-based audit to improve women-friendly care in maternity units in Malawi', *The journal of obstetrics and gynaecology research*, vol. 35, no. 3, pp. 483-489.

Kongnyuy, EJ, Mlava, G & van den Broek, N 2009b, 'Facility-based maternal death review in three districts in the central region of Malawi: an analysis of causes and characteristics of maternal deaths', *Women's health issues: official publication of the Jacobs Institute of Women's Health*, vol. 19, no. 1, pp. 14-20.

Lawn, SD, Harries, AD, Anglaret, X, Myer, L & Wood, R 2008, 'Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa', *AIDS*, vol. 22, no. 15, pp. 1897-1908.

Lema, VM, Mtimavalye, LA & Msiska, FS 1998, 'Socio-demographic characteristics of family planning clients and their possible influence on contraception in Malawi', *East African medical journal*, vol. 75, no. 1, pp. 41-46.

Magoma, M, Requejo, J, Campbell, OM, Cousens, S & Filippi, V 2010, 'High ANC coverage and low skilled attendance in a rural Tanzanian district: a case for implementing a birth plan intervention', *BMC pregnancy and childbirth*, vol. 10, p. 13.

Mantel, GD, Buchmann, E, Rees, H & Pattinson, RC 1998, 'Severe acute maternal morbidity: a pilot study of a definition for a near-miss', *British journal of obstetrics and gynaecology*, vol. 105, no. 9, pp. 985-990.

Manzi, M, Zachariah, R, Teck, R, Buhendwa, L, Kazima, J, Bakali, E, Firmenich, P & Humblet, P 2005, 'High acceptability of voluntary counselling and HIV-testing but unacceptable loss to follow up in a prevention of mother-to-child HIV transmission programme in rural Malawi: scaling-up requires a different way of acting', *Tropical medicine & international health*, vol. 10, no. 12, pp. 1242-1250.

Mayosi, BM, Flisher, AJ, Lalloo, UG, Sitas, F, Tollman, SM & Bradshaw, D 2009, 'The burden of non-communicable diseases in South Africa', *Lancet*, vol. 374, no. 9693, pp. 934-947.

McIntyre, J 2005, 'Maternal health and HIV', *Reproductive health matters*, vol. 13, no. 25, pp. 129-135.

Meekers, D, van Rossem, R, Silva, M & Koleros, A 2007, 'The reach and effect of radio communication campaigns on condom use in Malawi', *Studies in family planning*, vol. 38, no. 2, pp. 113-120.

Meguid, T 2010, *The possibility of public interest litigation in Malawi to clarify national and international responsibilities to fulfil the right to (maternal) health*. Dissertation for a master's in international human rights law, University of Oxford.

MoH 2008a, *Guidelines for the use of antiretroviral therapy in Malawi, 3rd edition*. Lilongwe, Malawi.

MoH 2008b, *HIV and Syphilis Sero-Survey and National HIV Prevalence and AIDS Estimates Report for 2007 (Surveillance Survey Report)*. Lilongwe, Malawi.

MoH 2010, *Quarterly HIV Programme report HIV Testing and Counselling, Prevention of Mother to Child Transmission, Antiretroviral Therapy, Treatment of Sexually Transmitted Infections*. Lilongwe, Malawi.

MoH HIV department 2009. *Quarterly Report Antiretroviral Treatment Programme in Malawi with Results up to 31st December 2009*. Lilongwe, Malawi.

Morgan, D, Maude, GH, Malamba, SS, Okongo, MJ, Wagner, HU, Mulder, DW & Whitworth, JA 1997, 'HIV-1 disease progression and AIDS-defining disorders in rural Uganda', *Lancet*, vol. 350, no. 9073, pp. 245-250.

MSF 2010, *Annual Report Malawi Mission, Thyolo Project 2010*. MSF Operational Centre Brussels.

Nakakeeto, ON & Umaranayake, L 2009, 'The global strategy to eliminate HIV infection in infants and young children: a seven-country assessment of costs and feasibility', *AIDS*, vol. 23, no. 8, pp. 987-995.

National Statistical Office 2005. *Malawi Demographic and Health Survey 2004*. Lilongwe.

National Statistical Office 2008. *2008 Population and Housing Census*. Lilongwe.

Nattrass, N & Gonsalves, G 2010, 'AIDS funds: undervalued', *Science*, vol. 330, no. 6001, pp. 174-175.

Nicoll, A, Newell, ML, van Praag, E, Van de Perre, P & Peckham, C 1995, 'Infant feeding policy and practice in the presence of HIV-1 infection', *AIDS*, vol. 9, no. 2, pp. 107-119.

Nuwagaba-Biribonwoha, H, Mayon-White, RT, Okong, P & Carpenter, LM 2007, 'Challenges faced by health workers in implementing the prevention of mother-to-child HIV transmission (PMTCT) programme in Uganda', *Journal of public health (Oxford, England)*, vol. 29, no. 3, pp. 269-274.

Nyasa Times. 2011. *Global Fund rejects Malawi's funding proposal again*. Retrieved 2 January, 2011, from <http://mwnyasatimesbnl.com/global-fund-rejects-malawi-s-funding-proposal-again-14493.htm>

O'Gorman, DA, Nyirenda, LJ & Theobald, SJ 2010, 'Prevention of mother-to-child transmission of HIV infection: views and perceptions about swallowing nevirapine in rural Lilongwe, Malawi', *BMC public health*, vol. 10, p. 354.

Oladapo, OT, Sule-Odu, AO, Olatunji, AO & Daniel, OJ 2005, '"Near-miss' obstetric events and maternal deaths in Sagamu, Nigeria: a retrospective study', *Reproductive health*, vol. 2, p. 9.

Pattinson, RC, Say, L, Makin, JD & Bastos, MH 2005, 'Critical incident audit and feedback to improve perinatal and maternal mortality and morbidity', *Cochrane database of systematic reviews*, no. 4, p. CD002961.

Peckham, C & Gibb, D 1995, 'Mother-to-child transmission of the human immunodeficiency virus', *The New England journal of medicine*, vol. 333, no. 5, pp. 298-302.

Potter, D, Goldenberg, RL, Chao, A, Sinkala, M, Degroot, A, Stringer, JS, Bulterys, M & Vermund, SH 2008, 'Do targeted HIV programs improve overall care for pregnant women?: Antenatal syphilis management in Zambia before and after implementation of prevention of mother-to-child HIV transmission programs', *Journal of acquired immune deficiency syndromes (1999)*, vol. 47, no. 1, pp. 79-85.

Richardson, BA, John-Stewart, GC, Hughes, JP, Nduati, R, Mbori-Ngacha, D, Overbaugh, J & Kreiss, JK 2003, 'Breast-milk infectivity in human immunodeficiency virus type 1-infected mothers', *The Journal of infectious diseases*, vol. 187, no. 5, pp. 736-740.

Samb, B, Desai, N, Nishtar, S, Mendis, S, Bekedam, H, Wright, A, Hsu, J, Martiniuk, A, Celletti, F, Patel, K, Adshead, F, McKee, M, Evans, T, Alwan, A & Etienne, C 2010, 'Prevention and management of chronic disease: a litmus test for health-systems strengthening in low-income and middle-income countries', *Lancet*, vol. 376, no. 9754, pp. 1785-1797.

Sangani, P, Rutherford, G & Wilkinson, D 2004, 'Population-based interventions for reducing sexually transmitted infections, including HIV infection', *Cochrane database of systematic reviews*, no. 2, p. CD001220.

Say, L, Pattinson, RC & Gulmezoglu, AM 2004, 'WHO systematic review of maternal morbidity and mortality: the prevalence of severe acute maternal morbidity (near miss)', *Reproductive health*, vol. 1, no. 1, p. 3.

Shankar, A, Bartlett, L, Fauveau, V, Islam, M & Terreri, N 2008, 'Delivery of MDG 5 by active management with data', *Lancet*, vol. 371, no. 9620, pp. 1223-1224.

Simba, D, Kamwela, J, Mpembeni, R & Msamanga, G 2010, 'The impact of scaling-up prevention of mother-to-child transmission (PMTCT) of HIV infection on the human resource requirement: the need to go beyond numbers', *The international journal of health planning and management*, vol. 25, no. 1, pp. 17-29.

Sturt, AS, Dokubo, EK & Sint, TT 2010, 'Antiretroviral therapy (ART) for treating HIV infection in ART-eligible pregnant women', *Cochrane database of systematic reviews*, no. 3, p. CD008440.

Thomson Reuters 2011. *Journal citation reports*. Retrieved 31 January, 2011, from: http://thomsonreuters.com/products_services/science_products/a-z/journal_citation_reports/

Turan, JM, Miller, S, Bukusi, EA, Sande, J & Cohen, CR 2008, 'HIV/AIDS and maternity care in Kenya: how fears of stigma and discrimination affect uptake and provision of labour and delivery services', *AIDS Care*, vol. 20, no. 8, pp. 938-945.

UNAIDS 2009, *AIDS Epidemic update 2009*. Retrieved 2 February, 2011, from <http://www.unaids.org/en/dataanalysis/epidemiology/2009aidsepidemicupdate/>

UNAIDS & WHO 2005, *AIDS epidemic update 2005. Joint United Nations Programme on HIV/AIDS (UNAIDS)*. Geneva. Retrieved 2 February, 2011, from <http://www.unaids.org/epi/2005/>

United Nations 2011, *Millennium Development Goals*. Retrieved 31 January, 2011, from <http://www.un.org/millenniumgoals/>

USAID 2010, *Malawi HIV/AIDS health profile*. Retrieved 28 January, 2011, from http://www.usaid.gov/our_work/global_health/aids/Countries/africa/malawi_profile.pdf

van den Akker, T, Radge, G, Mateyu, A, Mwagomba, B, Bemelmans, M & Reid, T 2011, 'Can non-monetary incentives increase health facility deliveries? - The experience in Thyolo District, Malawi', *International Health*, vol.3, pp.66-68.

van den Akker, T, Van Rhenen, J, Mwagomba, B, Lommerse, K, Vinkhumbo, S & van Roosmalen, J 2011, 'Reduction of maternal mortality and severe maternal morbidity in Thyolo District, Malawi: the impact of obstetric audit', *PLoS One*. In press.

van den Akker, T & Lommerse, K 2010, *Towards health care without borders. A situation analysis of health services in Thyolo District with an emphasis on maternal and child health and in light of the anticipated reduced involvement of MSF*. Assignment for M.Phil (MCH), University of Cape Town.

van den Akker, T, Mwagomba, B, Irlam, J & van Roosmalen, J 2009, 'Using audits to reduce the incidence of uterine rupture in a Malawian district hospital', *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, vol. 107, no. 3, pp. 289-294.

Volberding, PA & Deeks, SG 2010, 'Antiretroviral therapy and management of HIV infection', *Lancet*, vol. 376, no. 9734, pp. 49-62.

Wagaarachchi, PT, Graham, WJ, Penney, GC, Caw-Binns, A, Yeboah, AK & Hall, MH 2001, 'Holding up a mirror: changing obstetric practice through criterion-based clinical audit in developing countries', *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, vol. 74, no. 2, pp. 119-130.

Waning, B, Kyle, M, Diedrichsen, E, Soucy, L, Hochstadt, J, Barnighausen, T, & Moon, S 2010, 'Intervening in global markets to improve access to HIV/AIDS treatment: an analysis of international policies and the dynamics of global antiretroviral medicines markets', *Global health*, vol. 6, p. 9.

WHO 2001, *Global prevalence and incidence of selected curable sexually transmitted infections: overview and estimates*. Geneva. Retrieved 8 February, 2011, from: http://www.who.int/reproductivehealth/publications/rtis/HIV_AIDS_2001_2/en/index.html

WHO 2003, *Strategic approaches to the prevention of HIV-infection in infants. Report of a WHO, meeting held 20-22 March, 2002, in Morges, Switzerland*. Geneva. Retrieved 31 January, 2011, from <http://www.who.int/hiv/pub/mtct/strategic/en/>

WHO 2005, *Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for surveillance*. Geneva. Retrieved 31 January, 2011, from <http://www.who.int/hiv/pub/guidelines/casedefinitions/en/>

WHO 2006, *Antiretroviral drugs for treating pregnant women and preventing HIV-infection in infants: towards universal access. Recommendations for a public health approach. 2006 version*. Geneva. Retrieved 31 January, 2011, from <http://www.who.int/hiv/pub/mtct/antiretroviral/en/>

WHO 2007a, *Global strategy for the prevention and control of sexually transmitted infections: 2006-2015. Breaking the chain of transmission*. Geneva. <http://www.who.int/reproductivehealth/publications/rtis/9789241563475/en/> (accessed 31 January, 2011).

WHO 2007b, *International Statistical Classification of Diseases and Related Health Problems, 10th revision*. Geneva.

WHO 2009, *Rapid advice: antiretroviral therapy for HIV-infection in adults and adolescents*, WHO, Geneva.

WHO 2010a, http://www.who.int/topics/reproductive_health/en/ (accessed 2 December, 2010).

WHO 2010b, <http://www.who.int/ceh/indicators/perinatalmortality.pdf> (accessed 2 December, 2010).

WHO 2010c, *Antiretroviral drugs for treating pregnant women and preventing HIV-infection in infants. Recommendations for a public health approach. 2010 version.* Geneva.

WHO 2010d, *Antiretroviral therapy for HIV-infection in adults and adolescents. Recommendations for a public health approach.* Geneva.

WHO 2010e, *PMTCT strategic vision 2010-2015. Preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals. Moving towards the elimination of paediatric HIV.* Geneva.

WHO & UNAIDS 2006, *Progress on global access to HIV antiretroviral therapy. A report on '3 by 5' and beyond.* Geneva.

WHO, UNAIDS, UNFPA, & UNICEF 2010, *Guidelines on HIV and infant feeding 2010. Principles and recommendations for infant feeding in the context of HIV and a summary of evidence.* Geneva.

Yeatman, SE & Trinitapoli, J 2008, 'Beyond Denomination: The Relationship between Religion and Family Planning in Rural Malawi', *Demographic research*, vol. 19, no. 55, pp. 1851-1882.

Yu, D, Souteyrand, Y, Banda, MA, Kaufman, J & Perriens, JH 2008, 'Investment in HIV/AIDS programs: does it help strengthen health systems in developing countries?' *Global health*, vol. 4, p. 8.

Zachariah, R, Harries, AD, Ishikawa, N, Rieder, HL, Bissell, K, Laserson, K, Massaquoi, M, van Herp, M & Reid, T 2009, 'Operational research in low-income countries: what, why, and how?' *The Lancet infectious diseases*, vol. 9, no. 11, pp. 711-717.

Zachariah, R, Tayler-Smith, K, Ngamvithayapong-Yana, J, Ota, M, Murakami, K, Ohkado, A, Yamada, N, van den Boogard, W, Draguez, B, Ishikawa, N & Harries, AD 2010, 'The published research paper: is it an important indicator of successful operational research at programme level?' *Tropical medicine & international health*, vol. 15, no. 11, pp. 1274-1277.

Zwart, JJ, Richters, JM, Ory, F, de Vries, JI, Bloemenkamp, KW & van Roosmalen, J 2008, 'Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population-based study of 371,000 pregnancies', *BJOG: an international journal of gynaecology and obstetrics*, vol. 115, no. 7, pp. 842-850.

Annex A

UNIVERSITY OF CAPE TOWN



Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6626 • Facsimile [021] 406 6411
e-mail: lamees.cmjedi@uct.ac.za

20 October 2010

HREC REF: 492/2010

Dr T Van Den Akker
Paediatrics, Red Cross

Dear Dr Van Den Akker

PROJECT TITLE: CONSTRUCTIVE INTEGRATION-THE EFFECTS OF PMTCT/ART PROGRAMME ON GENERAL REPRODUCTIVE HEALTH AND REPRODUCTIVE HEALTH SERVICES IN THYOLO, MALAWI

Thank you for submitting your new study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the FHS HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until 28 October 2011.

Please send us an annual progress report (website form FHS 016) if your research continues beyond the approval period. Alternatively, please send us a brief summary of your findings so that we can close the research file.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSE HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.

temjedi

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Annex B

PRINCIPLE INVESTIGATOR: THOMAS VAN DEN AKKER, MSF BRUSSELS OPERATIONAK CENTRE BELGIUM, THYOLO PROJECT, MALAWI MISSION

COUNTRY: MALAWI

SITE: THYOLO

TITLE: Constructive integration – The effects of PMTCT and ART programmes on general reproductive health services in Thyolo, Malawi

COUNTRY: MALAWI

SITE: THYOLO

1. Studies/articles are based on routinely-collected program data.

This is the case in our study. We are only using routinely-collected programme data.

2. They are either descriptive/evaluative or targeted evaluations.

This is a retrospective analysis of program data We will evaluate a number of reproductive health indicators. Our study is a targeted evaluation of reproductive health services and outcomes (during the ART/PMTCT scale-up).

3. Confidentiality is respected; no individual patient identifiers are revealed or used.

This applies to our study. All our data are de-identified and no information can be traced back to individuals.

4. Harm is minimal but acknowledged where relevant.

Our study does not involve any specific harm to patients.

5. Potential benefits to both the program and the community are described. Since the goal is publication, the relevance to a wider audience is described.

Benefits to the programme:

practical knowledge about the effects of the ART/PMTCT scaling up on general/reproductive health services; this knowledge may in particular contribute importantly to the MSF exit strategy (which areas need more or less attention?)

Benefits to the community:

If the hypothesis is confirmed that during the scale-up reproductive health indicators also improved, this has important repercussions for our advocacy; our results will help refute negative attention for scaled-up HIV-programmes and help to ensure continued donor involvement; this to the benefit of the Thyolo community

Relevance to a wider audience:

As clearly described in the research protocol there is widespread lack of knowledge on the topic; our study will help to fill this gap at least partly; our findings on RH changes during the scale-up will be of major importance to other settings with high HIV-prevalence/scale-up.

5. Collaborative involvement and, if applicable, authorship from a local authority or partner (Ministry of Health, DHO, other NGO) is encouraged. If relevant and possible, consultation with a body representing the community is desirable.

MoH has been actively involved in study conceptualization and design. One of the authors will be a DHO staff. We did not consider consultation with the community relevant for the moment.

This is to certify that the study entitled Constructive integration – The effects of PMTCT and ART programmes on general reproductive health services in Thyolo, Malawi satisfies the MSF ERB's ethics criteria for studies using routinely-collected data.

Dr Rony Zachariah MBBS,PhD,DTM&H,DCH
Operational research coordinator

MSF Operational Centre Brussels
MSF Luxembourg
68 Rue de Gasperich
L-1617, Luxembourg
20/10/2010

Dr Tony Reid
A.J. Reid, MD MSc FCFP
Medical Editor,

Note: If challenged by the journal, authors would be responsible for demonstrating that their study met these criteria.