Providing Antiretroviral Therapy in Rural Zimbabwe 2002 - 2012: Lessons Learned and Future Directions

MEDECINS SANS FRONTIERES

Acknowledgements

The success of the MSF programme in Zimbabwe would not have been possible without the tireless support of the nurses in the clinics, HIV/TB counselors, doctors, laboratory staff, pharmacy staff, OPHID,Murambinda Mission Hospital staff including sister Barbara, the district and hospital management staff in Buhera, Gutu and Chikomba districts. In particular we would like to thank BHASO, DAC, Business community, ZNNP+ and Dananai for their enthusiasm and support over the years.

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For all the MSF staff that have passed through the doors of MSF-OCB Zimbabwe and who have made their contribution to the direction and outcomes of the programme.

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Last but not least we would like to pay tribute to Dr. Monica Glenshaw the then DMO and director of MMH who was instrumental for MSF to become operational in this district. Dr. Monica has encouraged the team and worked with unflinching dedication to help a population in need.

Contents

Abbreviations

1. Acquired Immuno-deficiency Syndrome	AIDS
2. Antenatal Care	ANC
3. Antiretroviral drugs	ARVs
4. Antiretroviral therapy	ART
5. Basic Education Assistance Module	BEAM
6. Department for International Development	DfID
7. Central Statistical Office	CSO
8. Canadian International Development Agency	CIDA
9. District AIDS Coordinator	DAC
10. District AIDS Action Committee	DAAC
11. Expanded Support program	ESP
12. Efavirenz	EFV
13. Estimation and Projection Package	EPP
14. Expanded Support Programme	ESP
15. Global Fund to Fight against AIDS, TB and Malaria	GFATM
16. Health Transition Fund	HTF
17. Human Immuno-deficiency Virus	HIV
18. Home-based Care	HBC
19. Information, Education and Communication	IEC
20. United Nations Joint Programme on HIV/AIDS	UNAIDS
21. Lamivudine	3TC
22. Médecins Sans Frontieres	MSF
23. Monitoring and Evaluation	M&E
24. Ministry of Health and Child Welfare	MoHCW
25. National AIDS Council	NAC
26. Opportunistic Infections	OI
27. President's Emergency Plan for AIDS Relief	PEPFAR
28. Population Services International	PSI
29. Prevention of Mother to Child Transmission	PMTCT
30. Primary care counsellors	PCCs
31. Sexually Transmitted Infections	STIs
32. Tenofovir	TDF
33. Tuberculosis	TB
34. United Nations Children Fund	UNICEF
35. United Nations Population Fund	UNFPA
36. United States Agency for International Development	USAID
37. United Kingdom Department for International Development	DFID
38. Voluntary Counselling and Testing	VCT
39. Zimbabwe Demographic and Health Survey	ZDHS

Executive Summary

Zimbabwe is a landlocked country with a population estimated at 12.4 million. During the late 1990s and 2000s political instability led to economic crisis, resulting in aggressive hyperinflation, crushing poverty and an unemployment rate of 94 percent.

The 2011 national HIV & AIDS report estimates adult HIV prevalence (15-49 years) at 13.5% and child prevalence (0-14 years) at 3.2%, making Zimbabwe one of the worst countries affected worldwide by the HIV epidemic[1,2]. The number of people living with HIV is estimated at 1,134, 919, among those 154,858 are children. Of those infected 611,264 adults and 92,454 children are in urgent need of antiretroviral therapy (ART)[1,2]. Estimated TB incidence is 742/ 100,000/ year with a case notification rate of 379/100,000/ year in 2010[3].

Médecins Sans Frontieres (MSF) has been working in Zimbabwe in collaboration with the Ministry of Health and Child Welfare (MoHCW) since 2000, and currently has continuing programme activities that include HIV, Tuberculosis (TB), drug resistant TB (DR-TB) and sexual and gender based violence (SGBV). HIV/TB projects of the Belgium MSF Section are located in the districts of Buhera, Gutu and Chikomba.

In Buhera from 2006 the strategy of using mobile teams to decentralize HIV/TB care was initiated. This has resulted in 26 sites now being able to initiate and or follow patients on antiretroviral treatment (ART). By the end of 2011, 18,495 patients were initiated on ART in Buhera district of which 13,712 remain in care. A similar process of decentralization is now being followed through a mentorship strategy in both Gutu and Chikomba[4].

This scale up of access to antiretroviral therapy has had a hugely positive impact. The percentage of patients being initiated with a CD4 <50 cells/ μl has decreased significantly from 32 % in 2005 to 12% in 2011.

The median baseline CD4 for initiation rose to 227 in 2011. Both trends suggesting that people are now testing and accessing care at an earlier stage of their illness. Outcomes are also highly satisfactory, with 86% and 80% of adults remaining in care at 12 and 24 months respectively in recent cohorts[4]. HIV /TB care has also been offered to children and adolescents at the decentralized sites.

Provision of a one stop service for TB where co-infected patients are seen by the same clinician, on the same day in the same consultation has improved indicators of TB/HIV integration with 86% of TB patients tested for HIV. ANC and PMTCT have also recently been made into a one stop service.

In December 2010 a milestone was achieved and the first patient in the programme was initiated on DR-TB treatment. From this a community model of care has been initiated, moving away from previous treatment strategies where patients would be admitted for up to two years.

The year 2011 brought a number of exciting new interventions in the programme. In line with the Zimbabwean National ART Guidelines, MSF has introduced the new first- line Tenofovir (TDF), Lamivudine (3TC) and Efavirenz (EFV) for all patients. EFV was chosen to allow a one pill, once daily fixed dose combination to be used and also to avoid the side effects associated with Nevirapine (NVP) particularly when initiating patients at higher CD4 cell counts.

In order to ensure a safe switch to TDF access to viral load has been scaled up using the dried blood spot technique and has provided data on the prevalence of virological failure in such a cohort. At first viral load 16.7 percent of routine viral load tests are > 1000 copies/ml. This initial phase of implementation has demonstrated the feasibility of scaling up viral load using DBS and routine yearly viral load is now being implemented in Buhera and Gutu districts.

Finally the new molecular diagnostic tool Xpert® MTB/RIF has been successfully implemented in three hospital laboratories. This new TB diagnostic test allows for rapid (within 2 hours) and more sensitive detection of TB and additionally identifies rifampicin resistance.

During the initial phase of implementation laboratory confirmed cases of TB increased by 64 percent[5] with a decrease in time to initiation of TB treatment from 18 days to 7 days for smear negative co-infected patients.

Building on the initial experience of scaling up access to treatment in Buhera, in 2011 MSF began support in the neighbouring district Gutu, adopting a much lighter mentoring and supervisory approach. Within the first year 1686 patients have been initiated on ART in 11 primary health clinics, including 244 children (14 percent of the cohort). Retention rates are high with 96 percent remaining in care during the first year of the programme[4]. In October 2011 this mentorship strategy was extended to Chikomba district.

Coverage however is not yet universal in the new districts and in Buhera with the challenges of providing sufficient human resources at the clinics, innovative strategies for further scale up are needed. MSF has encouraged the provision of longer ART supplies (3 months) and has shown that retention in care is good with this strategy. Community models of care may also offer an alternative to allow further scale up and improve long term retention in care.

However, in the context of the current financial retreat on HIV/TB funding, ensuring sustainability of what has already been achieved along with considering these upcoming challenges will require continued political commitment from donors and MoHCW. MSF is committed to demonstrating innovative new approaches to provision of HIV/TB care and to ensure patients living with HIV and TB continue to have access to quality care.

MSF reference material can be downloaded at **www.msf.org.za/publications/reports-and-publications**

Introduction

Country Background

Zimbabwe is a landlocked country bordered by Mozambique, South Africa, Botswana, Zambia and Namibia at the western tip. The population is estimated at 12.4 million. Bountiful in agricultural produce and rich in mineral wealth it was once known as the bread basket of Africa. During the late 1990s and 2000s political instability led to economic crises, resulting in aggressive hyperinflation, crushing poverty and an unemployment rate of 94 percent. Basic infrastructure and services collapsed, resulting in food shortages and deterioration of the country's health system in 2008-2009[6].

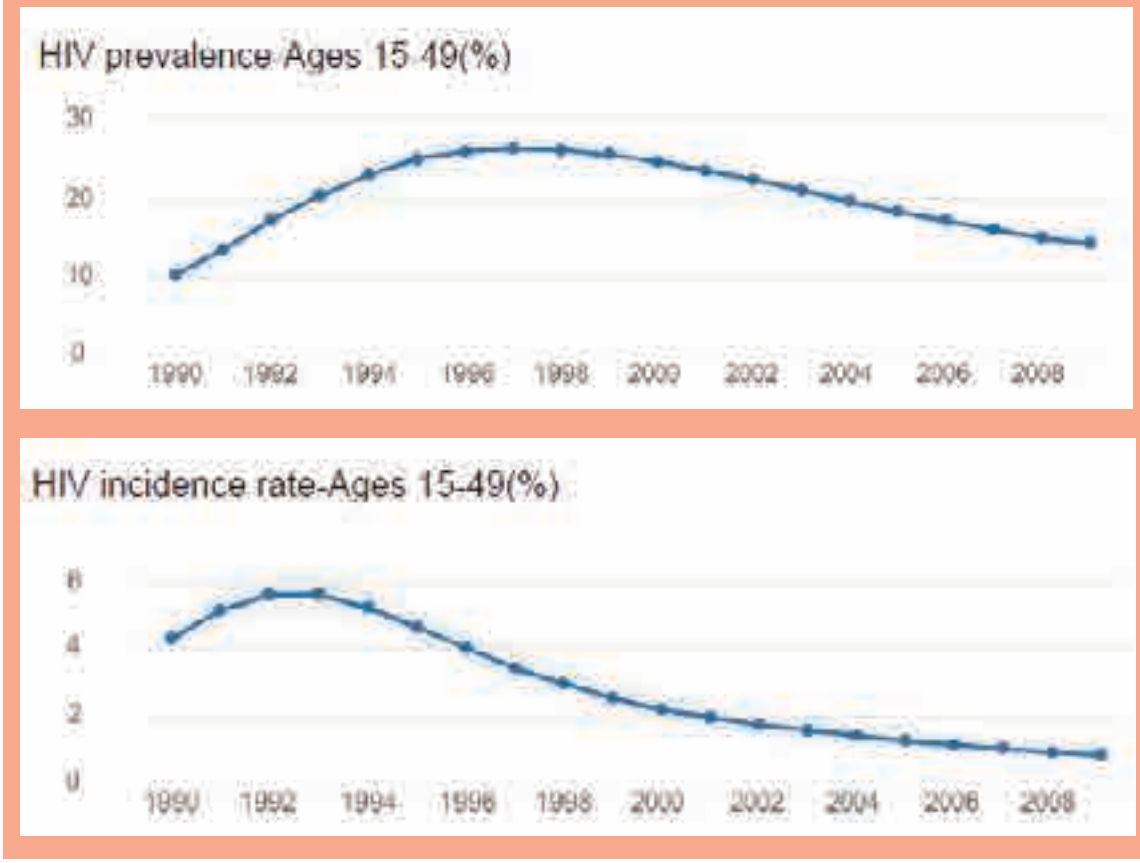
The healthcare system is overwhelmed with the needs of the 1.2 million people living with HIV, while outbreaks of cholera, measles and typhoid have become a reality. Today the average life expectancy at birth in Zimbabwe is among the worst in the world, at 49 years[7]. Maternal mortality is reported as 960 per 100,000 and infant mortality as 57 per 1,000 live births[8].

In early 2009 a new power-sharing government was established in Zimbabwe. Since then the country's economy has gradually improved with the introduction of the USD. Regardless of this development, the medical needs of the Zimbabwean people remain pressing.

HIV/TB In Zimbabwe

Despite significant declines in HIV incidence in the past few years (Figure 1) the current HIV prevalence rate at 13.5 percent continues to make Zimbabwe one of the worst affected countries in the world[9]. It is also ranked 17th of the 22 high-burden TB countries in the world.

Figure1: HIV Prevalence and Incidence (*UNAIDS Epidemiological Factsheet 2011)*



The 2011 national HIV & AIDS report estimates adult prevalence in those > 15 yrs at 13.5 percent and children (0-14 yrs) at 3.2 percent . The number of people living with HIV is estimated at 1,134, 919, among those 154,858 are children. Of those infected 611,264 adults and 92,454 children are in need of ART. The total number of people on ART at the end 2011 stood at 408,665[2]. A 2010 ART outcome study showed survival rates of 91 percent, 78 percent, 69 percent and 64 percent at 6, 12, 24 and 36 months respectively[10]. Estimated TB incidence is 742/ 100,000/ year with a case notification rate of 379/100,000/ year in 2010.

Zimbabwe has been credited by many observers for having its own dedicated resources to address the HIV epidemic. Most significant of these resources has been the National AIDS Trust Fund (NATF) where a 3 percent levy is made on taxes paid by formal sector workers and their employers[11]. Other main donors include The Global Fund for HIV, TB and Malaria, EU, DFID, PEPFAR, ESP/HTF and NAC/ Government of Zimbabwe.

In 2010 Zimbabwe adopted the latest WHO guidelines moving to an initiation threshold of CD4 < 350 cells/ μl, introducing a Tenofovir based first- line regimen and the introduction of PMTCT Option A[12].

The following report outlines the work of MSF-OCB providing comprehensive HIV/TB care over the last eight years across three districts.

Time Line of MSF Belgium in Zimbabwe

2002: Launch of Nutrition intervention in Buhera
2004: Opening of OI clinic in Murambinda Mission Hospital
2006-2007: Decentralization of HIV/TB care to 22 clinics through mobile teams
2008-2009: Fast scaling up of ART initiations; increasing to 4 mobile teams and 7 staff per team
2010: Implementation of WHO recommendation to initiate at CD4< 350.
2011-2012: Scale up of integration with MOH; Introduction of TDF/3TC/EFV; Scale up access to Viral Load; Introduction of Xpert® MTB/RIF and MDR TB treatment; Start Out Of District project.

Providing comprehensive HIV/TB care in Buhera District 2004-2012

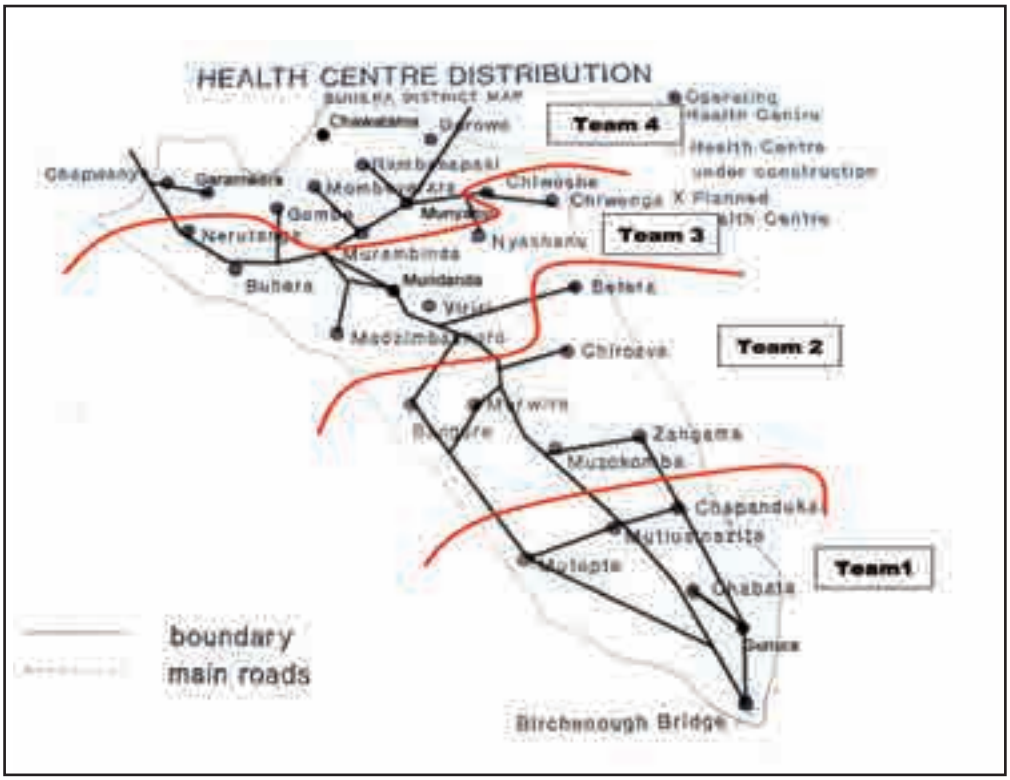
Buhera is located in Manicaland Province. Murambinda is a rural growth point located 240 km from Harare in Buhera district. It has a population of around 240,000. At the start of the project in Buhera the HIV prevalence rate was amongst the highest in the country at 18.6%[13].

Opportunistic Infection Clinic - Decentralization

In 2004 MSF constructed the Opportunistic Infections (OI) clinic at Murambinda Mission Hospital (MMH). When it was opened it was independently run by MSF staff. Treatment of opportunistic infections was offered along with the introduction of ART.

Over the span of one year (2006-2007) the project decentralized to 22 sites using 2 mobile teams. The decentralization strategy was driven by the economic instability at that time making access to a centralised health facility difficult due to the high cost of transport as well as lack of fuel. Hence during this period of instability loss to follow up rates doubled[14].

To ensure weekly visits to each clinic and to answer to the increasing workload, two additional mobile teams, each with seven staff (1 doctor, 2 nurses, 2 counselors, 1 Nurse Aide and 1 dispenser) were introduced in 2008. 3 teams being based in Murambinda and 1 in Birchenough Bridge.



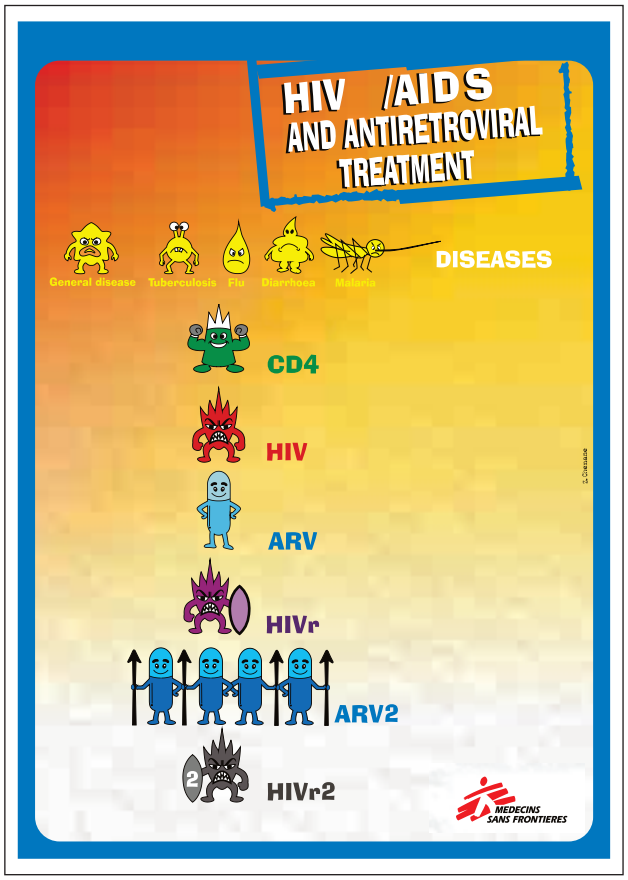
"Map of Buhera District"

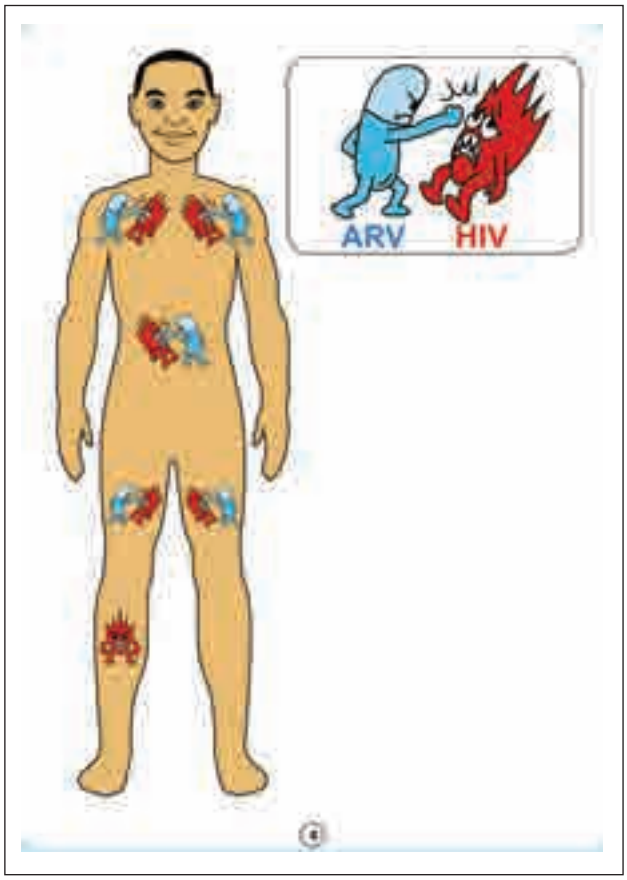
Laboratory support was given to two laboratories in the district, 1 at Murambinda Mission Hospital and 1 at Birchenough Bridge Hospital. Support consisted of provision of human resources, laboratory equipment for haematology, biochemistry, TB diagnosis , HIV monitoring and ongoing supply of reagents. Specimen collection and result delivery was provided via the mobile teams.

Essential to the programme has been the training of counselors and the development of visual tools to aid both adult and paediatric counseling. Patients are counseled prior to ART initiation (3 sessions) at week 2, month 1,3,6, and 12. After month 12 counseling is triggered by signs of poor adherence (missed pills, late appointments) or by clinical, immunological or virological failure. Specific paediatric counseling tools aid the counselors through the process of disclosure for children growing up with HIV[15].

"MSF Mobile Team Buhera"

"OI Clinic in Murambinda Mission Hospital"





"The MSF HIV/AIDS and Antiretroviral Treatment Counseling Flipchart "

Adult Antiretroviral Therapy Programme Outcomes

Through decentralization and the mobile team strategy rapid scale up of ART was possible (Figure 2). By 2009 80 percent coverage had been reached at a CD4 threshold of < 200 cells/μl and by mid 2010 a coverage of > 80 percent at a CD4 threshold of < 350 cells/μl. By the end of 2011 MSF had 18, 495 patients ever initiated on ART in Buhera district of which 13,712 patients currently remain in care[4].

The percentage of patients being initiated with a CD4 <50 CD4 cells/μl decreased significantly from 32% in 2005 to 12% in 2011 (Figure 3), whilst the median baseline CD4 for initiation rose to 227 in 2011(Figure 4). Both trends suggest that people are now testing and accessing care at an earlier stage of their illness[4].

Outcomes are highly satisfactory, with up to 86% and 80% of adults remaining in care at 12 and 24 months respectively (Figure 5) . Overall mortality rate was **8.8/100** person-years (95% confidence interval 8.1-9.5) and overall loss to follow-up rate was **9.5/100** person-years (95% confidence interval 8.8-10.3)[14] .

These outcomes compare favourably with a systematic review of HIV cohorts from 39 countries in sub- Saharan Africa that reported lower retention rates at 12 months (77% v 86%) and 24 months (76% v 80%)[16]. These retention rates are achieved thanks to four main strategies of the programme.

Provision of free care, decentralisation (taking the treatment to the patient), task shifting responsibilities to lower cadres and the implementation of a comprehensive adherence, defaulter tracing and community-support strategy[14].

Of particular note the introduction of decentralized ART services resulted in significant improvements in retention compared with centralized care. Patients seen at decentralized sites were 72% more likely to be retained in care at 24 mths on ART than those at centralized sites (Adjusted Hazard Ration (AHR) 0.28; 95% CI 0.17-0.48)[14].

Figure 2: Enrollment in Care and on ART 2005-2011

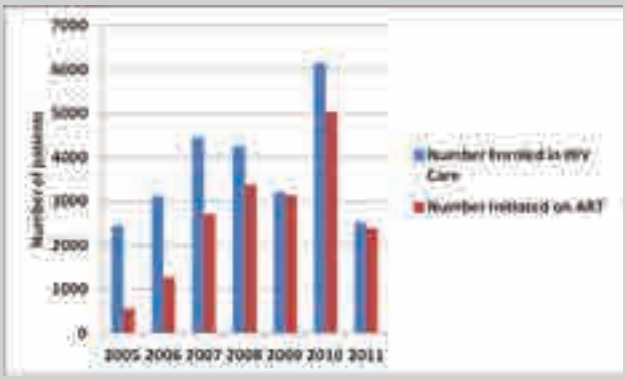


Figure 3: Proportion Baseline CD4 < 50 cells/μl by year

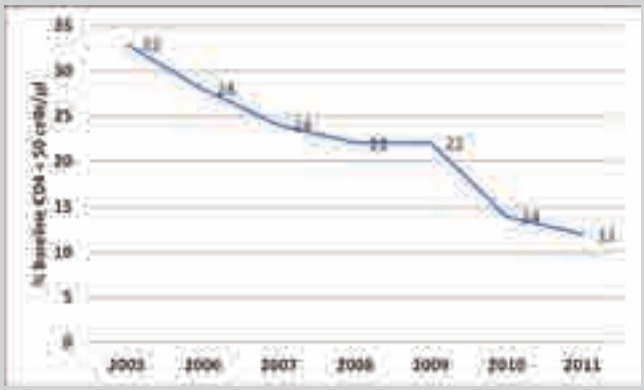


Figure 4: Median Adult Baseline CD4 (IQR) by year

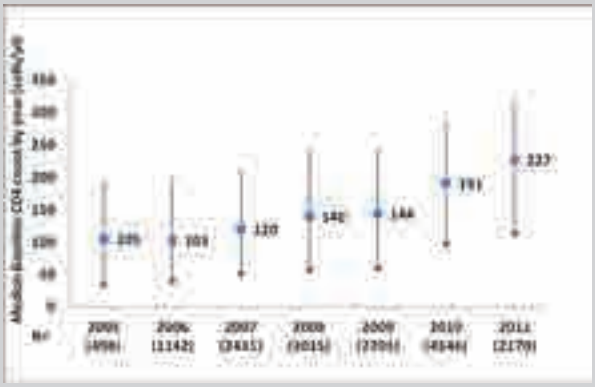
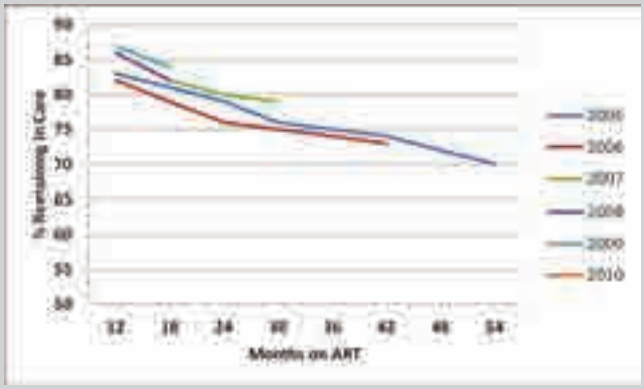


Figure 5: Cohort Outcomes 2005-2009



Paediatric and Adolescent Antiretroviral Programme Outcomes

Early infant diagnosis with DBS was decentralized in 2010 allowing for early identification of HIV positive children and initiation on ART (Figure 6)[4]. Paediatric HIV care was provided through the mobile teams with initiation performed by a doctor and follow up by nurses. In addition specific paediatric counseling strategies and support groups have been developed to aid the disclosure process and providing support to both the children and their carers.

Mortality in the paediatric cohort was 7.7 (95%CI 3.5-17), 1.4 (95%CI 0.0-4.3) and 4.0 (95%CI 2.3-6.9) per 100 person years in the age groups ≤ 2 years, 2.1-5 years and 5.1-9 years respectively. Rates of loss to follow up were 23 (95%CI 14.6-36.9), 2.8 (95%CI 1.3-6.3) and 4.3 (95%CI 2.6-7.3) per 100 person years in the age groups ≤ 2 years, 2.1-5 years and 5.1-9 years respectively (Figure 7). The high rates of loss to follow up in the ≤ 2 years age group most likely reflects both a survival bias in the older age groups and misclassification of death as loss to follow up in the ≤ 2 years age group[17].

"Group Education for Young Adolescents"

Figure 6: Paediatric Initiations By Year

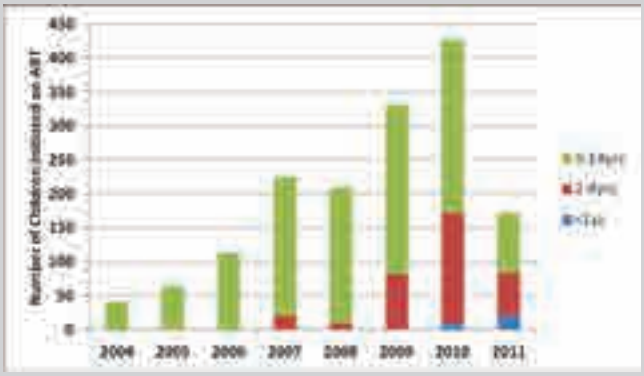


Figure 7: Paediatric Retention in Care

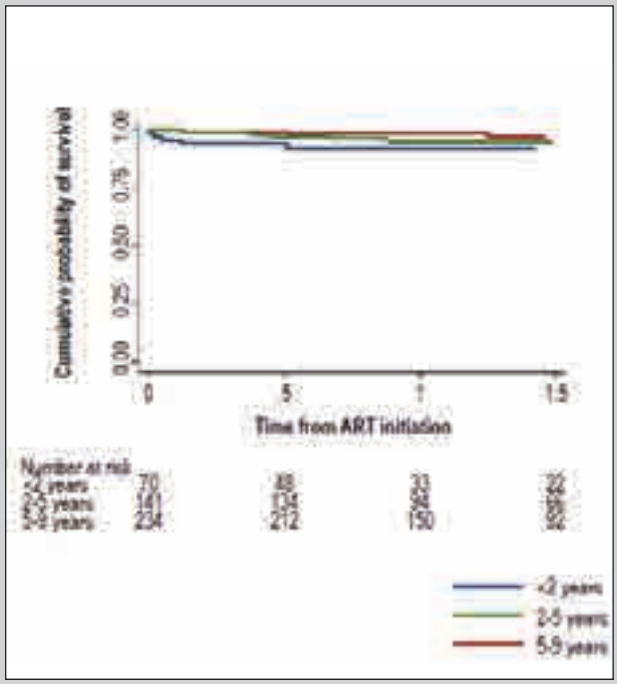
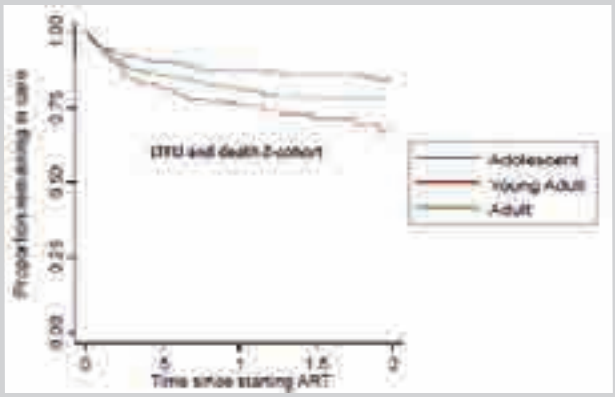


Figure 8: Retention in Care Adolescents, Young Adults and Adults



Around 2 million adolescents (Age 10-19) and 3 million youth (Age 19-24) are estimated to be living with HIV worldwide. In Zimbabwe, mathematical modelling estimates that deaths among untreated slow progressors will increase from 8,000 per year in 2008 to a peak of 9,700 per year in 2014. Hence, identifying these children and addressing their needs once on treatment is an essential challenge for ART programmes across the region. HIV prevalence in 2009 in the 15-24 age group was 7.7% in females and 2.9% in males[18].

Outcomes among patients aged 10-19 years (adolescents), 19.1-24 years (young adults) and 24.1-29 years (older adults) who were initiated on ART between 2004 and 2008 were analysed from the Buhera programme. 898 patients were included in the analysis and median duration on ART was 468 days. There was a higher risk of death in both young adults (Adjusted Hazard Ratio (aHR) 2.85, 95% CI 0.45-17.8) and adults (aHR 5.16, 95% CI 1.44-18.53). The overall hazard for attrition (combining death and loss to follow) in young adults was twice that of adolescents (aHR 2.2, 95% CI 1.37-3.36) (Figure 8)[18].

This highlights the young adult group as being at highest risk of being lost from care compared to adolescent and adults. During focus groups carried out in Buhera context specific challenges to retention in care for the young adult group highlighted: the transition out of education, the need to move away in order to seek work (moving to an urban setting or moving across a border to South Africa or Botswana) and entering into more serious relationships and marriage where new disclosure was needed.

Adapting adherence support and service delivery models for this group should be a priority to avoid treatment interruptions, development of resistance and increased morbidity within this group.

From Implementers to Mentors

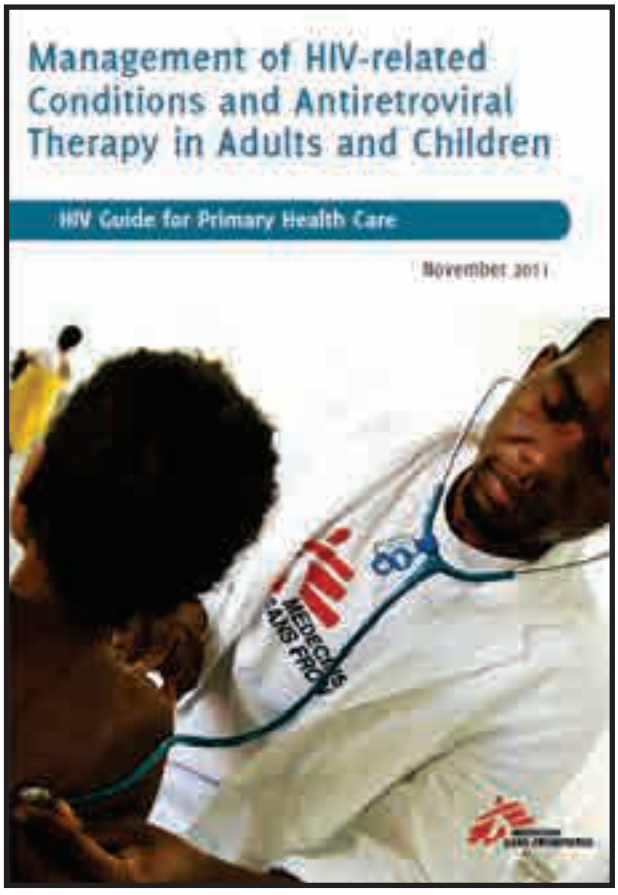
Since 2010 increasing responsibility for HIV and TB activities was handed over to MoHCW staff. Following renovations works carried out in Murambinda Mission Hospital in 2011, integration of HIV care into general OPD activities was achieved by moving the OI/ART services from the specialist OI clinic to the outpatient department at the Hospital.

At the primary health care clinics spreading of patients from 1 day (the mobile team day) to 5 days per week allowed MoHCW nurses to take a stronger role in HIV management. Nurse Aids were trained in dispensing and primary counsellors recruited from the community and trained in collaboration with MoHCW.

The process of increasing the capacity of MoHCW in the provision of HIV care was developed through the use of the project management dashboard. Tools such as the integrated HIV/TB supervision tool, HIV guide for primary health care and the counselors toolkit also facilitated the mentoring process.

After evaluation using the dashboard monitoring tool, MSF mobile teams have now gradually reduced their human resources with the aim to provide mentorship and support for second line and difficult clinical cases.

Material used by MSF to help integration and mentoring can be downloaded at www.msf.org.za/publications/reports-and-publications.



HIV Guide for Primary Health Care

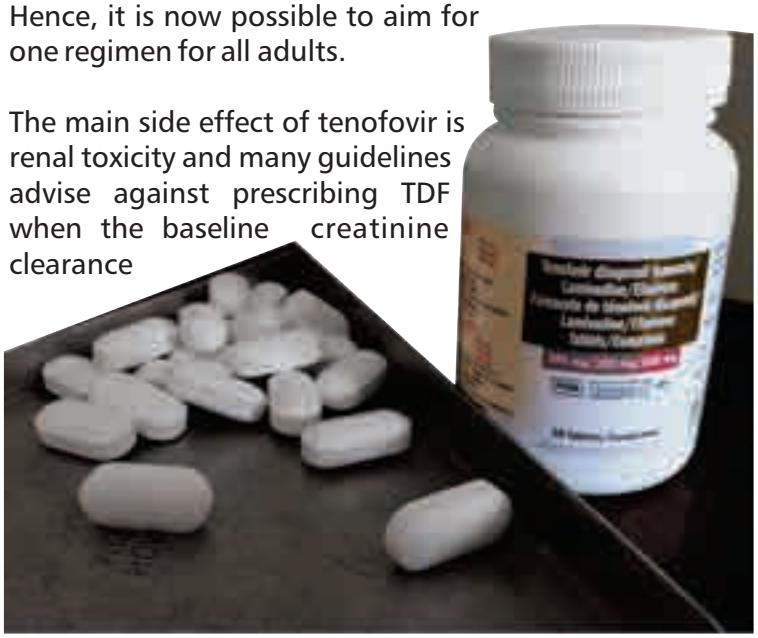
Counsellor's Tool Kit

Introducing New Drugs and New Diagnostics

Introducing a Tenofovir Based First Line

In 2010 following the recommendations of WHO, the Zimbabwean MoHCW adopted a Tenofovir (TDF) based first-line. Based on previous experience in both Lesotho and South Africa MSF opted to combine TDF with Lamivudine (3TC) and Efavirenz (EFV), allowing for a one pill, once a day regimen. The lower toxicity of Tenofovir compared with Stavudine is a huge advantage, making nurse based ART-initiation and follow-up of patients on treatment much easier. For patients, side effects such as neuropathy and liposdystrophy no longer occur and the one pill once a day regimen aids adherence. WHO has also recently released guidance on the safety of EFV in pregnancy which now allows its use in pregnancy and women of child bearing age[19]. Hence, it is now possible to aim for one regimen for all adults.

The main side effect of tenofovir is renal toxicity and many guidelines advise against prescribing TDF when the baseline creatinine clearance



Patients experience with TDF

- Joyce Bimha (36) Garamwera Clinic "The first 2 days were difficult as I experienced nightmares and dizziness. But now, a month after initiation, I feel good; the side effects are gone."

- Mary Nhongodya (VHW Garamwera) - "Piritsi iri rakandirerukira zvekuti sezvo ndichingonwa kamwe pazuva. I find the drug very easy; it's a once a day affair."

- Stella Mushowe "It's a good drug I take it only once a day unlike Triviro. I never experienced any side effects."

is < 50ml/min. In Buhera an analysis of baseline renal function of ART naïve HIV positive patients showed that 9% of those eligible for ART had a baseline CrCl < 50ml/min, the risk being 5.5 times higher in those aged > 40 years[20]. In the absence of creatinine monitoring these potential risks should be considered.

TDF has already been shown to be a cost effective regimen[21]. As more countries worldwide adopt a TDF based regimen, significant decreases in price have already been seen and with the hope of further generic manufacturers of the triple fixed dosed combination with EFV soon appearing on the market, further price decreases can be expected.

Introducing Viral Load

Routine virological monitoring for HIV positive patients on ART is important for detecting early virological failure, preventing the development of drug resistant mutations, identifying patients in need of intensive adherence support, and accurately diagnosing treatment failure. Through these clinically advantageous outcomes, the use of first-line drugs may be preserved and transmission of both drug sensitive and drug resistant viral strains may be limited. Driven initially by the need to check for virological failure prior to switching to TDF, in 2012 MSF adopted routine yearly viral load (VL) monitoring.

The logisitics required to send whole blood samples for large numbers of patients to a centralized laboratory were not feasible. Due to these challenges it was decided to move to performing VL on dried blood spots (DBS) using the NucliSENS® platform. Initially blood was drawn in EDTA tubes at clinic level and the DBS cards prepared by the laboratory but in order that patients could have this test performed on any day at the clinics, rather than only on the day of specimen collection, nurses have now been trained to prepare the samples. Ongoing supervision of this task shifting is essential.

In 2010, where viral load was only being performed on whole blood to confirm either clinical or immunological failure, only 286 viral loads were performed (Figure 9)[22]. In 2011 with the introduction of DBS this increased to 2,783 samples and in 2012 approximately 1,000 samples are being processed every month. In total over 11,000 samples have now been tested.

A preliminary analysis performed in Buhera has shown overall, in those with no signs of immunological failure or side effects, 16.7% of the cohort to have a viral load >1000 copies/ml.

A 1000 copies/ ml threshold was used as the lower threshold for action on a DBS sample.

For all patients whose first viral load is >1,000 copies /ml an intensive adherence intervention is given (3 sessions over 3 months) after which a second viral load is performed. Analysis of these follow up viral loads is ongoing.

Those with a second viral load >5,000 copies will be assessed for possible switch to second line therapy. As shown in many other studies many patients with clinical or immunological failure were in fact not virologically failing and hence were not switched unnecessarily to a second line regimen (Figure 10).

At present DBS samples are sent to South Africa for analysis each sample costing SAR 200 (~23USD). In 2012 MSF plans to work closely with the MoHCW to further scale up access to viral load at national level in Harare. As with Tenofovir, as more countries in the region look to scale up access to viral load, prices for this important monitoring tool will be driven down.

"Before we had access to routine viral load, it was challenging to determine which patients were failing treatment. Also we had patients who had a drop in CD4 count, which is a marker for possible failure, but in more than 60 per cent of patients this was not confirmed with increased viral load. So it shows that CD4 - which most projects are using in low-resource settings - is actually quite a bad predictor of failure.

When we have a patient with an increased viral load we know something is wrong. Either the patient is not taking their drugs or the drugs are not working, so what we do is work with the counselor over three months. We do what we call enhanced adherence where we try to find out what can be the underlying reasons why a patient is not taking their medication and we try to see where we can support the patient in taking their medication better.

For a patient, it's a good thing if you know your viral load is undetectable. It means the medication is working and the chances of becoming healthy in the long run are high, so it can really motivate patients to keep taking their medication.

"MSF Doctor in Murambinda"

Figure 9: Number of Viral Load Tests Performed in Buhera District 2010-2011

Figure 10: Proportion of Viral Load Tests > 1000 copies/ml (Buhera VL Database)

	N =2186	>1000 copies/ml	95% CI
Clinical failure	45	33.3%	19.4-47.3
Immunological Failure (>30% drop CD4)	466	34.3%	30.0-38.7
Side effects	568	11.6%	9.0-14.3
Routine switch to TDF	1107	16.7%	14.5-18.9

Introducing Xpert® MTB/RIF

Xpert® MTB/RIF is a new molecular diagnostic tool, developed to increase detection and shorten time to diagnosis of sputum-smear-negative (SSN) tuberculosis in addition to detecting Rifampicin resistance. Results are available within 2 hours opposed to traditional culture methods that may take several months to process.

In April 2011, Médecins Sans Frontières (MSF) in collaboration with the MoHCW implemented two Xpert® MTB/RIF systems in Buhera district at district laboratory level. Logistical preparations were made to ensure a stable electrical power supply and air conditioning to maintain the temperature at levels below 30°C necessary for optimum instrument operation. Feedback from laboratory staff is positive; preparation of samples is not complicated and once used as the first diagnostic test workload is reduced.

During an initial parallel phase where Xpert® MTB/RIF was performed in parallel with smear, a 64% increase in laboratory confirmed TB was seen compared to microscopy using auramine staining[5]. This increase in sensitivity will allow more patients to be initiated by nurses at clinic level based on a positive Xpert® MTB/RIF result even when smear is negative. Case finding however did not increase. Comparing the period after implementing Xpert® MTB/RIF with the period before, the proportion of TB notifications that were smear positive (33% versus 27%), smear-negative (48% versus 49%), sputum not tested (11% versus 12%), and extra-pulmonary (8% versus 12%) did not change significantly[23].

This is likely to be due to strong implementation of the previous smear negative diagnostic algorithm, provision of transport and CXR fees and the weekly presence of a doctor at each clinic to initiate smear negative cases. The impact on casefinding in settings where MSF support was not present before Xpert® MTB/RIF has been implemented will be assessed. Time to initiation of TB treatment was however significantly reduced for smear negative cases with the introduction of Xpert® MTB/RIF, decreasing from 18 to 7 days at decentralized sites[23]. This has the potential to reduce morbidity in individuals and reduce the risk of TB transmission to others.

Since introduction of Xpert® MTB/RIF in April 2011, 21 cases of MDR TB have been diagnosed. Early identification and provision of MDR treatment for these patients is of benefit for the patient but also will serve to reduce cross infection in the community.

Xpert® MTB/RIF is now being used as first test for TB diagnosis in Buhera and a third machine has been recently installed in Gutu Mission Hospital.

A cost effectiveness study of Pre- & Post-Xpert TB diagnosis from patient and provider perspective was carried out in Buhera in June 2012. The sensitivity analyses show that the Post-Xpert intervention is more cost effective then the Pre-Xpert intervention at the present price of Xpert catridge at 11.7 USD[24].

Introducing Stabilization Tubes

At the primary health care clinics samples are collected once per week. Therefore patients often have to return on the day of specimen collection. To avoid these repeat visits for patients we evaluated the use of BD CD4 Vacutainer stabilization tubes to assess whether blood collected in stabilization tubes and stored at room temperature for several days, gave similar CD4 results to blood collected in EDTA tubes and tested the same day according to the standard method BD FACSCount™ cytometer

EDTA tube samples were tested on arrival in the laboratory (Day 0), and the remaining sample was discarded. Stabilization tube samples were tested on arrival in the laboratory, and were stored in racks at room temperature and retested on Days 3, 5, and 7. Twenty of the samples were stored an extra week and retested on Day 14.

Our study showed that CD4 measured in EDTA tube and CD4 stabilization tube specimens were comparable. Measures in the stabilization tubes stored at room temperature remained stable over the following 14 days (Figure 11)[25]. As such CD4 stabilization tubes could really help in scaling up access to CD4 count in rural health facilities.

Figure 11 Accuracy of CD4 and haemoglobin results on samples stored in Stabilization Tubes for 7 days!

Figure 1a: CD4

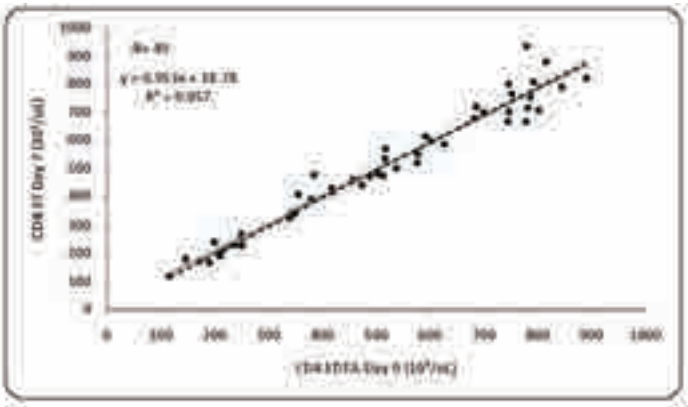


Figure 1b: Haemoglobin

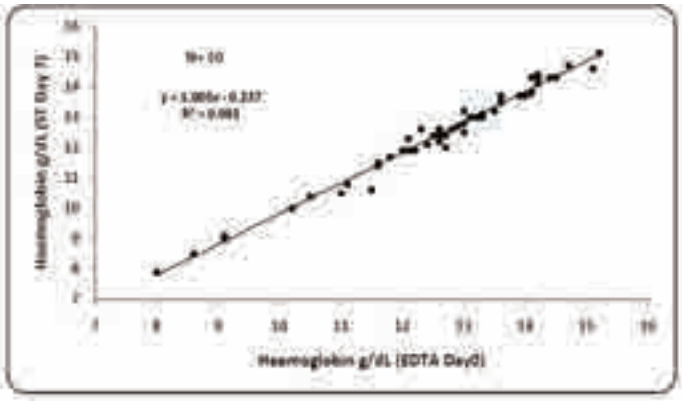


Figure 2a: CD4

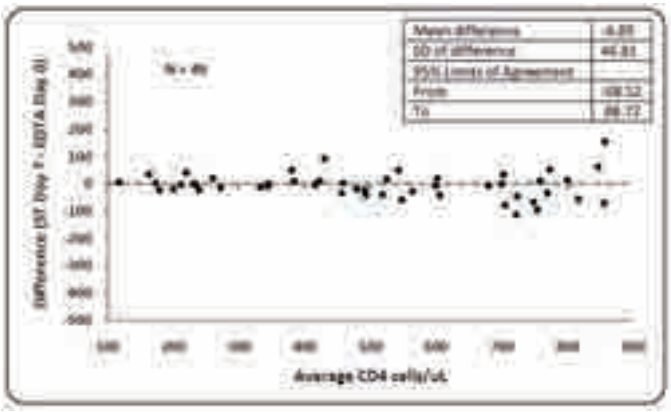


Figure 2b: Haemoglobin

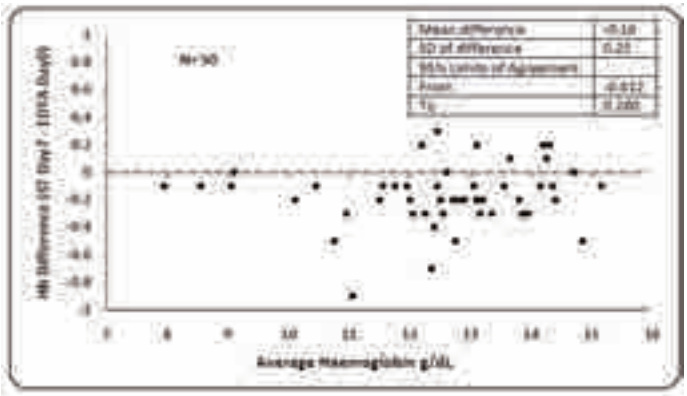


Figure 3a: CD4

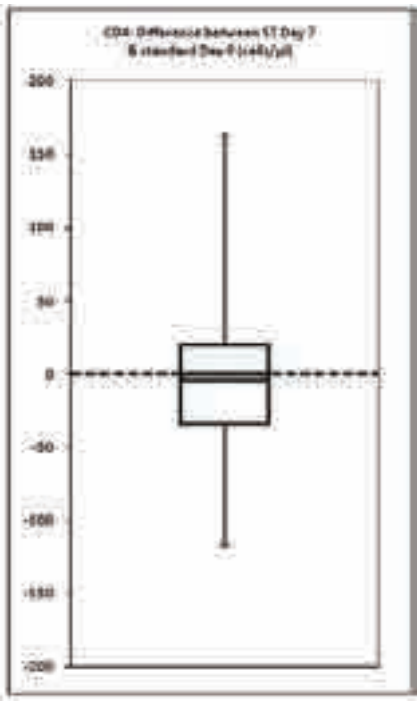


Figure 3b: Haemoglobin

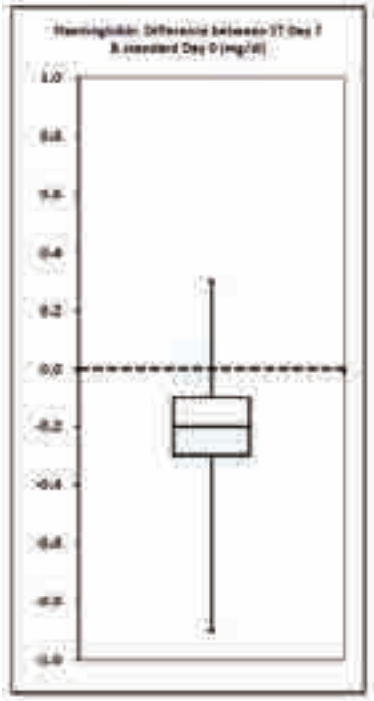


Figure 1: Linear correlation of ST Day 7 vs EDTA Day 0 results

Figure 2: Bland-Altman plots of agreement between ST Day 7 & EDTA Day 0 results

Figure 3: Box-plots showing difference between ST Day 7 & EDTA Day 0 results in quartiles!

Integrating TB, MDRTB and PMTCT

TB/HIV

HIV patients are at higher risk of developing tuberculosis compared to the general population and TB remains the most frequent cause of death among persons living with HIV. In Buhera 86% of TB patients are co-infected with HIV. At all clinics cough triage is implemented, as well as routine TB screening for all HIV patients and HIV testing for all TB suspects. Diagnosis including access to CXR has been provided free of charge and in 2011 Xpert® MTB/RIF has been introduced for TB diagnosis.

TB notifications rose from 2005 until 2008 and have remained constant up until 2011(Figure 12). 1,613 TB cases were initiated on TB treatment in 2010 with a treatment success rate of 77%[26].

For HIV/TB co-infected patients a "one stop service" is provided. This ensures both TB and HIV treatment and counseling services are provided on the same day, in the same clinic and by the same nurse and counsellor . This "one stop" approach has led to improved indicators of TB/HIV integration.

Figure 12: TB Notifications 2004-2011

Community Model of Care for MDR TB

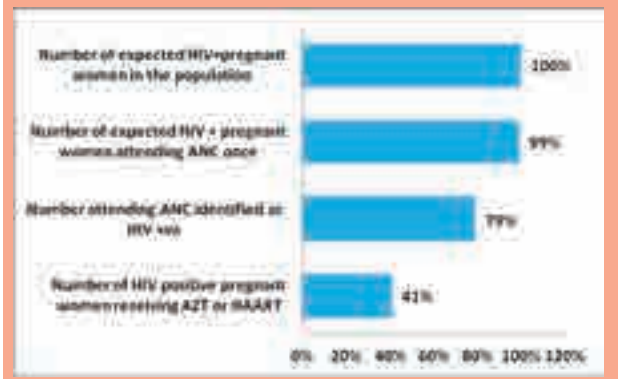
In Buhera district 39 patients have been diagnosed with MDR TB since December 2009. The MDR treatment programme began in December 2010. To date twenty patients have been initiated on treatment and 17 remain in care. Patients are not hospitalized and treatment is provided at the community level. Patients are encouraged to attend their local clinic for the daily injections of kanamycin, but if too far a mobile MDR community team provides this service at home. Basic infection control measures are put in place with patients encouraged to sleep in a separate room at home, keeping windows open and using a surgical mask when with others.

PMTCT

Together with the partners OPHID and MoHCW, MSF is fighting for better outcomes for the most vulnerable patients: the unborn babies. Option A as recommended in the WHO 2010 guidelines is implemented in the whole of Buhera. However due to previous restrictions on nurse initiation, ANC and PMTCT were not fully integrated, pregnant women requiring triple therapy being referred for initiation on the MSF mobile team day.

An analysis of the PMTCT cascade in a sample of clinics indicated two important " leaks" in the cascade. Despite ANC attendance being high, because 14% of pregnant women were not tested and 48% not initiated on a PMTCT intervention, of all expected HIV positive pregnant women in the population only 41% received a PMTCT intervention (Figure 13)[27]. By ensuring defaulter tracing for all pregnant women both on triple therapy and AZT and by fully integrating ANC and PMTCT allowing nurses to initiate triple therapy it is hoped coverage will increase.

Figure 13: PMTCT Cascade from 12 Clinics in Buhera District



"The Light Approach"
- Supporting HIV/TB care in other districts

In 2010 MSF conducted a rapid assessment in the neighboring district Gutu. This showed at least 900 patients from Gutu were receiving their treatment in Buhera, whilst Gutu district itself had only 1500 patient on ART. In January 2011 MSF decided to begin support to MoHCW in Gutu through support to Gutu Mission Hospital and 11 primary health care clinics using a 'lighter' approach than that used in Buhera.

This lighter approach, using only 1 mobile team with 3 staff (1 doctor, 1 nurse and 1 counsellor) visiting health centers on a 2 weekly basis, aims at decentralizing HIV/TB services to facilities with sufficient staffing levels using a mentoring approach from the start. A mentorship dashboard was developed by the team to allow easy assessment of progress of the nurses and counselors and to determine when support visits from the team could be reduced.

Within the first year of support 1,686 patients have been initiated on ART in 11 primary health clinics, including 244 children (14% of the cohort). Decentralization allowed 744 patients from Gutu who were on ART treatment in other districts to access treatment in the clinic closest to their home.

Retention rates are high with 96% remaining in care during the first year of the programme. In addition all sites were able to follow up patients after 6 months of mentoring and 4 sites were capable to perform all ART services independently after 12 months mentoring. Those sites have now been weaned to monthly supervision visits, enabling the team to start mentoring new sites[4].

A similar decentralization project using the mentoring approach was launched in Chikomba District in October 2011. This project supports HIV/ TB care at Sadza district hospital and 8 primary health care clinics, working in close collaboration with MoHCW staff in each clinic. In this district, which already has 2 MoHCW mobile teams, MSF's main aim is to share experience on the 'mentoring' approach , allowing health centers to become independent from mobile team visits.

Key elements that have made this light approach successful have been a very motivated mobile team committed to mentoring; a strong and committed district health management team with strong human resource management skills and a commitment to performing supervision visits; decentralizing HIV/TB care to health facilities with sufficient staff from the start (minimum 2 nurses and 1 primary counselor); a motivated local NGO - such as BHASO in Gutu -encouraging support group formation, peer education, stigma reduction and defaulter tracing.

Strategic objective	Operational objectives	Indicators	Clinic A	Clinic B	Clinic C	Clinic D	Clinic E	Clinic F
By June 2011 in 6 clinics in Buhera district MoH is providing quality comprehensive HIV/TB care with ongoing MSF mentorship	Accreditation	Clinic to be accredited for follow up and initiation of ART						
	Outcomes	% of all follow up patients seen by MoH						
		% of target adult initiations performed by MoH						
		% of target Children ART initiation by MoH						
		RIP						
		LTFU						
		Supervision score						
	HR Nurses	2 Nurses able to follow up all pre art and Art patients 4 nurses for BBH and Buhera						
		2 Nurses are able to initiate ART 4 nurses for BBH and Buhera						
		2 nurses able to follow up TB 4 nurses for BBH and Buhera						
		2 nurses are able to initiate TB 4 nurses for BBH and Buhera						
		2 nurses able to carry out full PMTCT 4 nurses for BBH and Buhera						
	HR counsellors	1 MoH PC counselor to provide health promotion VCT, HIV, TB						
	HR admin	Observations,registration and filing to be performed by MoH						
	Drug supply	ARV and OI order to be done by MoH						
		All drugs to be dispensed by MoH						
	Lab services	All specimens to be taken by MoH staff						
	M and E	MoH staff to fill pre ART, ART PMTCT and TB registers						
		Monthly reports to be filed by MoH on time						
	Programme management	Joint clinical supervision with MoH to be performed monthly						
		Joint clinic supervision tool with MoH to be performed quarterly						

Future Directions

With the substantial achievements of decentralization and the introduction of a TDF based first-line simplifying provision of ART for staff and patients alike, significant scale up of treatment has been achieved in Buhera and is now starting in Gutu and Chikomba. Coverage however is not yet universal in the new districts and in Buhera with the challenges of providing sufficient human resources at the clinics, innovative strategies for further scale up are needed.

MSF has encouraged the provision of longer ART supplies (3 months) and has shown that retention in care is good with this strategy. With the introduction of viral load the possibility of reducing clinical consultations to once a year with a 3 monthly pharmacy refill could further reduce workload for clinic staff. Community models of care such as the community ART groups demonstrated by the MSF programme in Mozambique[28] or the adherence clubs in Khayelitsha may also offer an alternative model of care to allow further scale up and improve long term retention in care.

MSF will continue to offer routine Viral Load (M3, M12, M24, M36.....) in the supported districts and will support scale up of VL diagnostic capacity in the country through provision of a NucliSENS® platform and 4 Laboratory Scientists at NMRL. Routine Viral load goes hand in hand with improved detection of patients adhering poorly to treatment, offering enhanced adherence counselling sessions, as well as correct switching of those patients eligible for second line treatment; all indicators for quality of care. In addition MSF will continue to ensure the importance of screening for OI's such as cryptococcal meningitis and providing treatment in patients presenting with severe immunosupression, a group who despite high coverage in Buhera still represents 12% of patients presentings to MSF supported clinics.

However in the context of the current financial retreat on HIV/TB funding, ensuring sustainability of what has already been achieved, along with considering these upcoming challenges will require continued political commitment from donors and the MoHCW / Government of Zimbabwe. MSF is committed to demonstrating innovative new approaches to provision of HIV/TB care and will continue to lobby donors to ensure patients living with HIV and TB continue to have access to quality HIV/TB care.

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