

ANTIRETROVIRAL THERAPY FOR ADULTS AND CHILDREN



SCALING-UP CARE AND
TREATMENT FOR HIV/AIDS
IN RURAL CAMBODIA

2002-2009





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Abbreviations



AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral therapy
ARVs	Antiretroviral drugs
FUCHIA	Follow Up and Care of HIV Infection and AIDS
HIV	Human Immunodeficiency Virus
M&E	Monitoring & Evaluation
MOH	Ministry of Health
MSF B	Médecins Sans Frontières (Belgium)
OPD	Outpatient Department
PLHIV	People Living with HIV
PMTCT	Prevention of Mother to Child Transmission
TB	Tuberculosis

Acknowledgments

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They include the Ministry of Health of Cambodia, NCHADS, the Angkor Hospital for Children, the

Provincial Health Departments of Siem Reap and Takeo, the Referral Hospitals of Takeo, Siem Reap and Sotnikum, and the health care staff working under challenging conditions in referral hospitals.

Finally, and most importantly, we acknowledge our patients and their families for their constant efforts to overcome the challenges they face living with chronic diseases and especially HIV/AIDS



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HIV/AIDS Epidemic in Cambodia

Although HIV prevalence in Cambodia is among the highest in Asia the country appears to be experiencing relative success in the fight against HIV and AIDS. After peaking at approximately 3.3% in 1997-98, HIV prevalence amongst the national adult population declined to 1.2% in 2003, and further down to 0.9% in 2006. This has been attributed to investment in and scale up of effective HIV prevention programmes and a large number of deaths among persons infected during the early years of the epidemic when life-sustaining treatment was not available. In 2007, the estimated number of adults and children living with HIV was 75.000, down from 120.000 in 2001.

Cambodia's HIV/AIDS epidemic has been concentrated among high-risk groups and largely driven by men visiting commercial sex workers. However, as correct and consistent condom use in brothels has increased and remained higher than 90 percent since 2001, HIV prevalence among brothel-based female sex workers decreased from 42.6 percent in 1998 to 33.2 percent in 1999 to 12.7 percent in 2006, a remarkable achievement. Though behavior change in terms of increased

condom use and partner reduction has clearly had an impact on the decline in incidence, this reduction has also resulted from a large number of deaths among men who were infected early in the epidemic prior to the introduction of life-saving antiretroviral therapy (ART). Prevalence of HIV infection among women visiting antenatal care (ANC) clinics also declined from a high of 2.1 percent in 1999 to 1.1 percent in 2006.

Recent (2008) data collected by the NCHADS in 22 provinces and municipalities in the country indicate that an estimated 14% of female sex workers are living with HIV, compared with 43% in 1998; 1.1% of pregnant women are estimated to be HIV-positive in 2008, as compared to 2.1% in 1998.

Though prevalence among the general population continues to decline, groups that are of higher risk of acquiring HIV, including sex workers, drug users, men who have sex with men (MSM) still need to be systematically targeted and protected, with interventions specifically tailored to their needs.

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Responses to the HIV/AIDS Epidemic in Cambodia



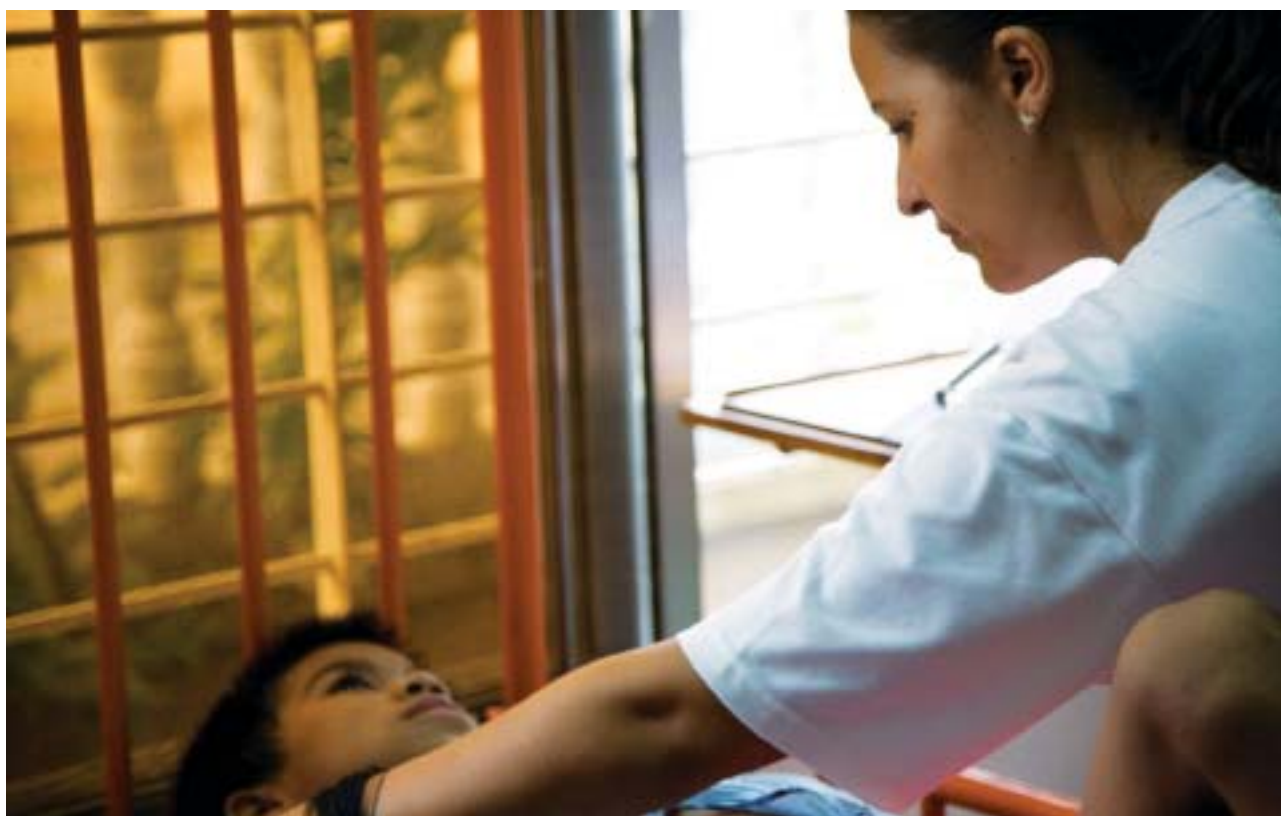
Cambodia has made considerable progress in its fight against HIV & AIDS. Factors contributing to this success are definite political commitment, a strong response from civil society and a wide range of activities by the Ministry of Health.

NCHADS, established in 1999, is the HIV/AIDS focal point within the Ministry of Health (MOH), with responsibility for recommending and implementing policies and strategies for the health sector response to the HIV epidemic. In addition, to coordinate a multi-sectorial approach involving ministries beyond the MOH, the government established the National AIDS Committee in 1993, which was succeeded in 1999 by the National AIDS Authority (NAA), comprising 26 line Ministries, the Cambodian Red Cross and 24 provinces and with responsibility for formulating and monitoring

the national response to HIV & AIDS. Currently, the National AIDS Authority is administering the National Strategic Plan for a Comprehensive & Multi-sectorial Response to HIV/AIDS from 2006–2010, while NCHADS administers the Strategic Plan for HIV/AIDS and STI Prevention and Care in the Health Sector from 2008–2010. The goals of the current strategies are to reduce new infections of HIV, provide care and support to people living with and affected by HIV/AIDS, and alleviate the socioeconomic and human impact of AIDS on the individual, family and the community.

The civil society response in Cambodia is coordinated through the HIV/AIDS Coordinating Committee, an umbrella body with a membership of approximately 90 nongovernmental organizations (NGOs).

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MSF in Cambodia: Towards Chronic Diseases Care for HIV/AIDS Care

Médecins Sans Frontières (MSF) has been active in Cambodia since 1989. MSF chose primarily to work strengthening public health services in the periphery, and its programs were redirected progressively from supporting provincial hospitals to district hospitals and health centers and managing intermittent emergencies.

MSF started working in January 1995 to support a private not-for-profit clinic in Phnom Penh, focusing on primary health care for vulnerable urban groups, prevention of HIV transmission and empowerment of sex workers. In 2001, the clinic (located in Svay Pak red-light district) was handed over to two local NGOs. In 1996, MSF also started up STD clinics providing similar services in brothel areas in Banteay Meanchey province on the Thai border in Poipet and Sisophon and in Siem Reap town. The activities of the two clinics in Banteay Meanchey province were

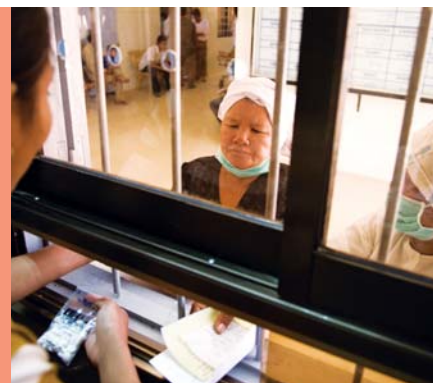
handed over to the government and to local and international NGOs in 2001. The project in Siem Reap was handed over to an international NGO in 2002.

In March 2002, MSF opened a chronic diseases clinic in Siem Reap Provincial Hospital. At that time there was a limited understanding of the concept of chronic diseases in the country. A common approach was proposed to include care for both HIV and other chronic diseases (diabetes and hypertension) in the same location, and by the same staff. They would respond to the needs of different chronic disease patients in providing continuity of care, long-term adherence and social support. Besides providing care, another objective was to reduce discrimination of PLHA by including other diseases that could benefit from the same type of patient-centered approach.

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Scaling-up of ART within a Chronic Disease Model



In 2002, Médecins Sans Frontières (MSF) and the Cambodian Ministry of Health established chronic disease clinics (CDC) to integrate care for diabetes and hypertension with HIV/AIDS in two provincial capitals, Takeo and Siem Reap. Both locations were selected for this pilot programme because they are large provincial centers with referral hospitals.

The initial goals of the ART part of MSF's program were modest, as it aimed to deliver treatment and achieve good adherence and treatment outcomes in a small cohort. However, with increasing evidence of the feasibility of ART in the country, MSF decided to scale up the services through the CDC model and by 2009 more than 4.000 PLHIV were under care. MSF worked to improve the efficiency of ART delivery for patients, strengthened government capacity, and achieved MSF's and the government's scale-up goals through a collaborative approach. It also was the first step towards a future handover of MSF's involvement once the integrated services were functioning well with strong government involvement.

These clinics were the first ones providing pro-phylaxis, treatment and care for PLHA in both provinces, and in fact the first outside Phnom Penh. As they soon became known for providing good quality of health service, they attracted patients not only from the provinces where they were situated but also from surrounding provinces with limited services, in case of Siem Reap mainly from Banteay Meanchey, Battambang and Oddar Meanchey provinces and in Takeo from Kampot province.

Early on the number of registered patients increased rapidly but it was still possible to meet the growing demand by gradually adding more human resources. By 2004 the CDCs were approaching their limits in capacity to manage the number of patients enrolled.

In response, in 2005 MSF decided not to open more clinics but to actively support the Ministry of Health, NGOs or other organizations to start and scale up ART. At about the same time, NCHADS began to open OI/ART clinics throughout the whole country. As the MoH staff had limited practical experience of care and treatment of HIV, MSF offered technical and material support as well as on-the-job training over a defined period of time.





Chronogram of the HIV programs 1996-2009

STI prevention in Poipet and Sisophon in 1996-2001

AIDS care through CDC model in Siem Reap, 2002-2009

AIDS care through CDC model in Takeo, 2003-2009

ART in Kampong Trach, Kampot province Nov 2005 to March 2007

ART in Poipet: 2006

ART in Samrong, Odormeanchey, Dec 2006 to Dec 2007

Handover of CDC to MoH, 2007-2009

Components of the Programs

- *Antiretroviral (ARV) therapy for adults*
- *Pediatric HIV/AIDS care & treatment*
- *Diagnosis, treatment and prophylaxis of opportunistic infections*
- *HIV/TB co-infection management*
- *Infectious Diseases Department (IPD)/In-patient Department (IPD)*
- *Cervical Cancer Screening (SCC) among HIV+ women*
- *Counselling & Psychosocial support*
- *Nutritional support for HIV and co-infected patients and Home Based Care*

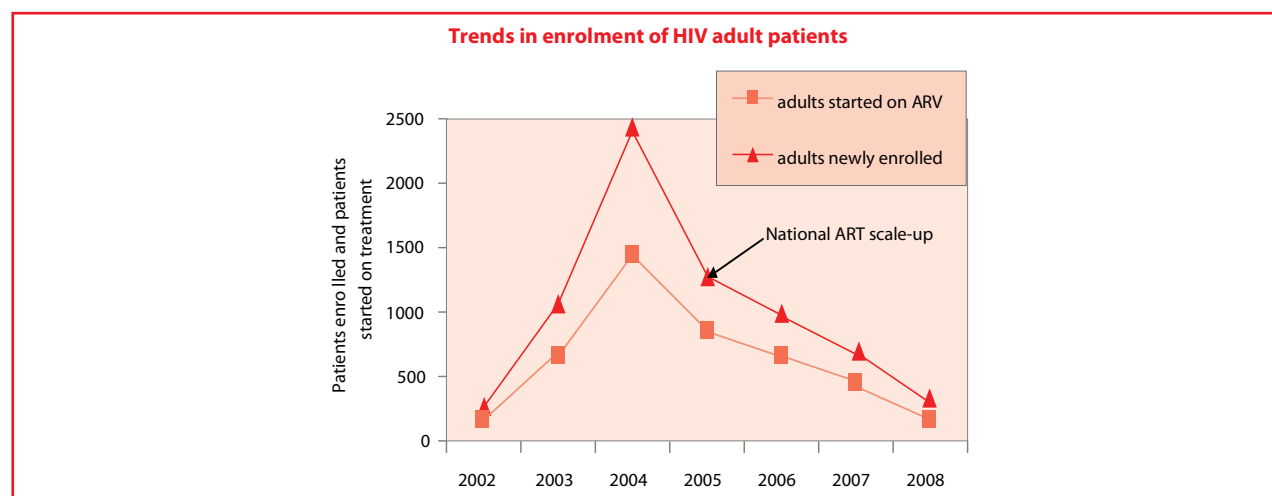
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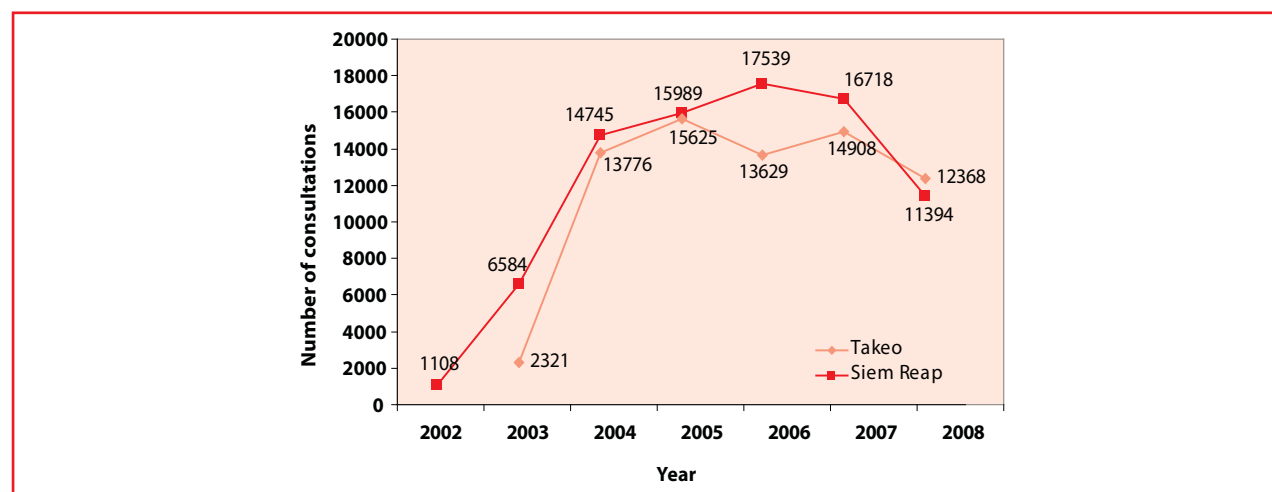
Antiretroviral (ARV) therapy for adults



Admissions of HIV-positive adults in Takeo and Siem Reap HIV/AIDS programs; 2002-2008.



Scaling up of HIV services at Siem Reap and Takeo chronic disease clinics (consultations by year, 2002-2008)



Baseline characteristics of adults started on ART in Takeo and Siem Reap, from 2002-2009

Age at start (years), median (IQR)	35 (30-40)
Women, n (%)	2114 (50.9%)
Clinical WHO-stage on admission	
WHO stage I	567 (13.7%)
WHO stage II	772 (18.7%)
WHO stage III	1865 (45.1%)
WHO stage IV	928 (22.5%)
Baseline Body Mass Index on admission, kg/m ² , median (IQR)	19 (17.4-20.9)
Baseline CD4 count on admission, cells/mm ³ , median (IQR)	80 (22-212)
Initial ART regimen	
d4T/3TC/NVP	3295 (79.3%)
d4T/3TC/EFV	672 (16.2%)
AZT/3TC/NVP	117 (2.8%)
AZT/3TC/EFV	26 (0.6%)
Other	40 (0.1%)
Median treatment duration (IQR) in months	26.4 (11.7-43.5)

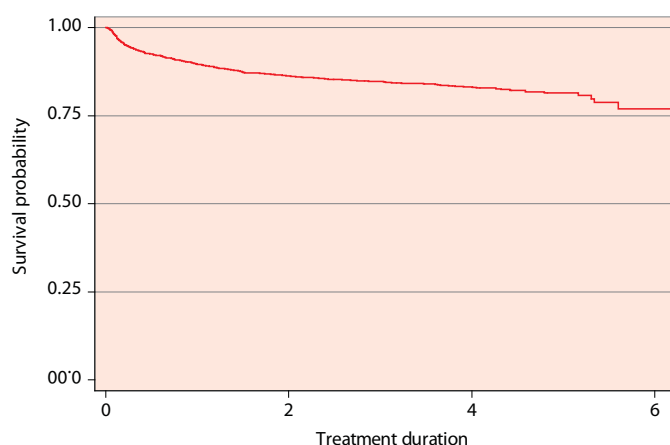
Retention and attrition for patients on ART in Takeo and Siem Reap provinces; 2002-2008.

Retention in care	3565 (85.9%)	37.1
Alive and on ART	1759 (42.4%)	18.2
Transferred out	1806 (43.5%)	18.8
Attrition from care	585 (14.1%)	6.0
Lost to follow-up	203 (4.9%)	2.0
Dead	382 (9.2%)	4.0

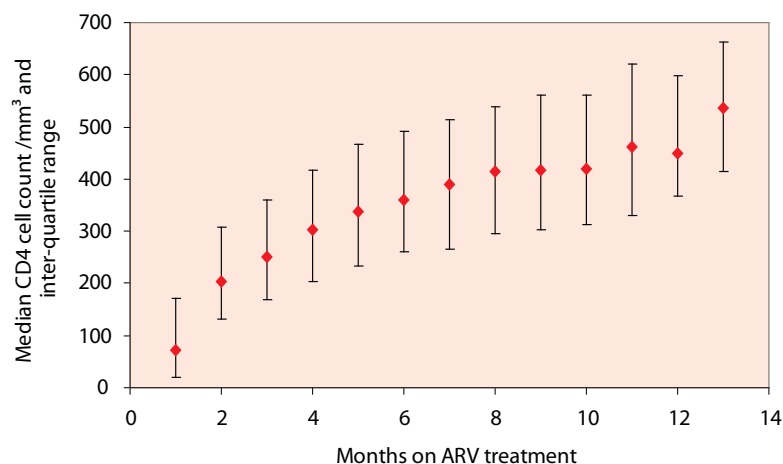
Immunological and clinical outcomes of patients on ART

CD4 count (cells/mm ³), median (IQR)	72 (21-171)	203 (131-309)	251 (169-359)	337 (233-466)	389 (266-513)
Weight (kg), median (IQR)	47.0 (42.0-53.0)	51.0 (45.5-57.0)	52.0 (47.0-57.5)	52.0 (46.0-58.0)	52.0 (47.0-59.0)

Kaplan-Meier survival curve for adults on ART



Immunological recovery of adults on ART; 2002-2008; Takeo and Siem Reap



Overall, by the end of 2008, 150 adults (3.6%) had a viral load >1000copies/ml detected after a median treatment time of 28 months (IQR: 18-40mo). 138 patients have been started on

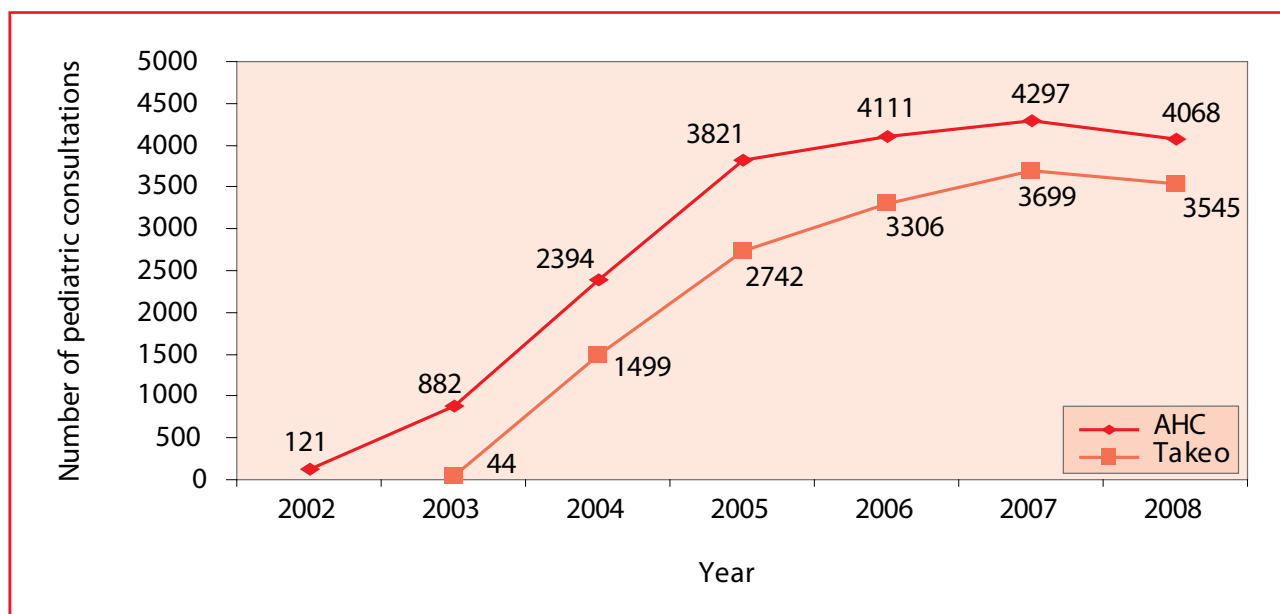
second line therapy. By December 2008, 1753 patients started on ART were alive and in care, 1806 had been transferred out, 382 had died, and 203 had defaulted.

Pediatric HIV/AIDS Care



Pediatric HIV/AIDS care was always a high priority for MSF in its effort to support the national program. The collaboration with partners (MoH

and Angkor Hospital for Children, in Takeo and Siem Reap respectively) resulted in satisfactory clinical outcomes amongst



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Baseline characteristics of children started on ART

	<18 months	18-59 months	≥60 months	Total
Number of children started on ART	43	307	422	772
Gender				
Femaled	20 (46.5%)	142 (46.2%)	202 (47.9%)	364 (47.1%)
WHO stage				
unspecified	2	19	46	67
stage 1	8	60	87	155
stage 2	1	44	45	90
stage 3	21	154	197	372
stage 4	11	30	47	88
CD4 cells/mm³, median (IQR)	740 (502-1099)	408 (206-676)	128 (34-288)	229 (70-462)
CD4%, median (IQR)	17.0 (12.8-22.0)	12.7 (7.4-17.0)	6.7 (2.6-13.2)	10.3 (4.4-15.7)
Initial ART regimen				
3TC+D4T+NVP	39 (90.7%)	268 (87.3%)	353 (83.6%)	660 (85.5%)
3TC+D4T+EFV	2 (4.6%)	23 (7.5%)	56 (10.5%)	81 (10.5%)
3TC+AZT+NVP	1 (2.3%)	15 (4.9%)	12 (3.6%)	28 (3.6%)
other	1 (2.3%)	1 (0.3%)	1 (0.3%)	3 (0.1%)

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The following table summarizes the characteristics of the pediatric HIV/AIDS cohorts, at both clinics supported by MSF, and shows basic cumulative mortality, LTFU, and transferred-out rates. Accurate mortality data on pediatric patients not started on ART are not available, as active surveillance system and systematic tracing of defaulters (not on

ART) were not fully in place. In Angkor Children's Hospital a Home Based Care component is very active and tracing of children defaulters is well organized. Tracing is also well organized in Takeo, by the MSF team in collaboration with other NGOs, and this is reflected in the satisfactory, very low LTFU rates among both groups of children.

General Data of Pediatric HIV cohorts in Siem Reap and Takeo in 2008

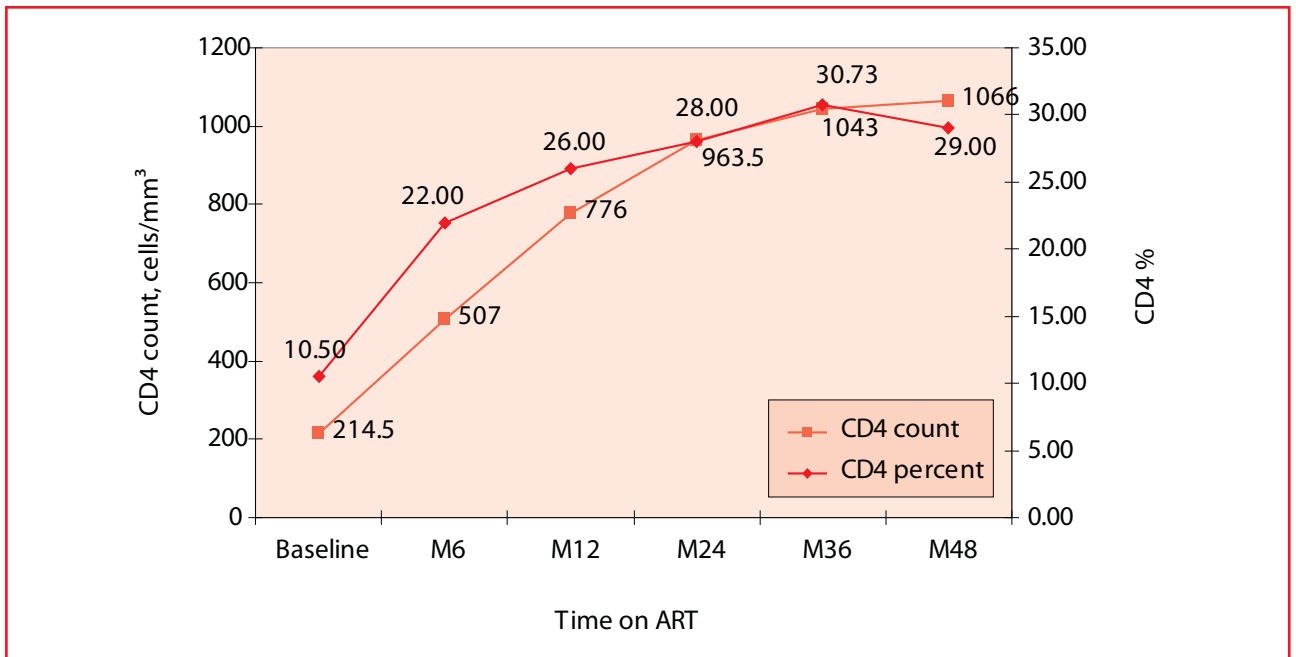
Years 2002- 2008	Pediatric HIV cohort		
	AHC-SRP	Takeo	Total
Total consultations	19691	14835	34526
New cases HIV	985	502	1487
Active cohort HIV, Dec 08	414	226	640
New cases on ART	507	289	796
Active cohort ART, Dec08	129	206	335
Patients on 2nd line	37	17	54
Died on ART, cum Nb	28	16	44
LTFU not on ART, cum Nb	269	99	368
LTFU on ART, cum Nb	13	3	16
Transferred-out on ART, cum Nb	52	44	96

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Immunological recovery (CD4-gain) among children on ART



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Diagnosis & treatment of opportunistic infections



Treatment for opportunistic infections among HIV/AIDS patients, mainly tuberculosis and cryptococcus meningitis, was provided and prophylaxis for PCP and cryptococcal meningitis were started according to national guidelines to all eligible patients.

Even though TB was the main cause of morbidity and mortality among patients, MSF diagnosed and treated a wide range of disorders including oral candidiasis, pneumonia, pulmonary TB, recurrent upper respiratory tract infections, Herpes Zoster and minor mucocutaneous manifestations, which were the most frequently occurring OIs.

Incidence of opportunistic infections in the MSF supported clinics

<i>Main OI diagnosed</i>	<i>Number (% of all new diagnoses)</i>
<i>Candidiasis</i>	3119 (14.2%)
<i>Bacterial pneumonia</i>	2270 (10.3%)
<i>Tuberculosis</i>	2146 (9.8%)
<i>Upper Respiratory Tract Infection</i>	1444 (6.6%)
<i>Herpes zoster</i>	821(3.7%)
<i>Severe bacterial infection</i>	751(3.4%)
<i>Extra-pulmonary cryptococcosis</i>	143(0.6%)
<i>Cytomegalovirus infection</i>	59(0.3%)
<i>Pneumocystis pneumonia</i>	64(0.3%)
<i>Oral hairy leukoplakia</i>	52(0.2%)
<i>Herpes simplex</i>	102(0.5%)

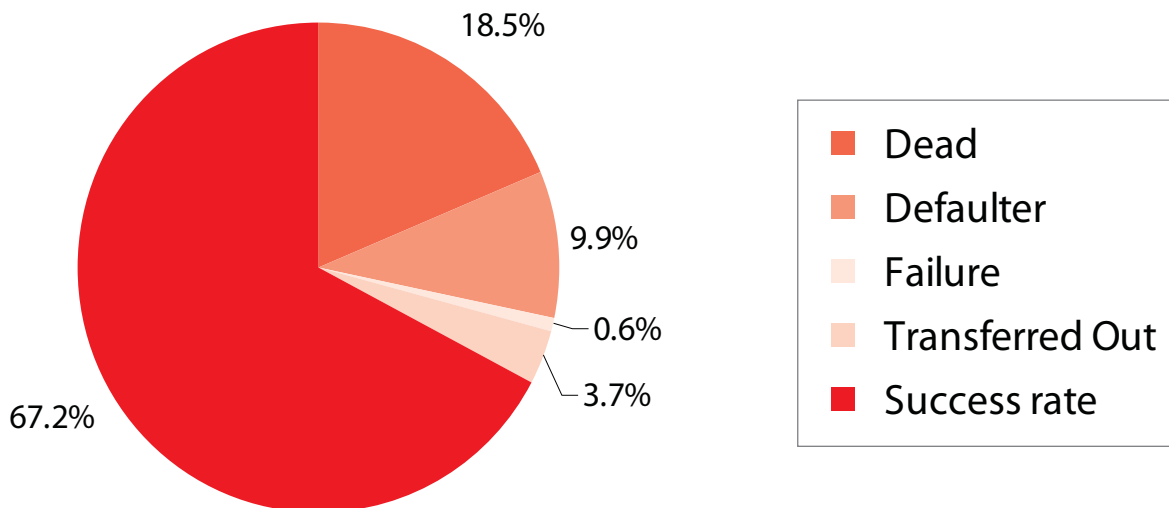


HIV/TB co-infection

Cambodia has a high and growing incidence of TB, making timely diagnosis of TB/HIV co-infection critical. The program addressed this through clinical protocols which emphasized early detection through symptom screening, sputum

examination and chest X-ray. TB/HIV co-infected patients were usually managed by MSF CDC, but some were referred to the nearest health centers where they easily accessed care provided by the national program.

TB treatment outcomes for HIV+ adults; Takeo; 2002-2007



IPD/IDD patients



Quality of care among HIV-positive hospitalized patients was reflected in acceptable mortality rates among this group at 7.14% and 10% in Takeo and Siem Reap respectively. TB, ARV-associated toxicities, chronic diarrhoea and cryptococcal meningitis were the main causes for hospitalization during the period, as shown in the table below.

MSF was involved in the Infectious Diseases departments from 2005 to 2008. It focused mostly on providing technical support to improve the quality of care and follow up of the patients hospitalized, specifically by trainings of clinical staff, nutritional support to eligible patients and provision of most drugs and medical materials.

IPD/IDD data in 2008			
<i>IPD activities 2008</i>	<i>Siem Reap</i>	<i>Takeo</i>	<i>Total</i>
<i>Admissions</i>	491	400	891
<i>Discharges</i>	319	372	691
<i>Av. Length of stay (days)</i>	ND	8.45	
<i>Bed occupancy rate (%)</i>	61.16%	50%	
<i>Mortality (cum CFR)</i>	7.14%	10%	
<i>Diagnosis at discharge</i>			
<i>Crypto meningitis</i>	27	15	42
<i>PTB</i>	106	53	159
<i>EPTB</i>	113	34	147
<i>PCP</i>	25	6	31
<i>Chronic diarrhea</i>	49	17	66
<i>Drug adverse events</i>	98	14	112
<i>Others</i>	252	136	388

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Cervical Cancer Screening among HIV positive women

A pilot cervical cancer screening among HIV+ women attending the two MSF supported clinics revealed a high yield of 41/540 (7.5%) women with cervical abnormalities requiring treatment. Based on these findings and on the lessons learnt from the experience, it was decided to expand cervical cancer screening, on a systematic basis, to all eligible HIV+ women enrolled in the cohorts. The systematic screening,

which was based on the one-stop-service strategy with VIA and cryotherapy, started in July 2008 and was completed in April 2009. During this period the clinics were in the process of being handed over to the Ministry of Health. Since MSF was gradually disengaging from the clinic activities, not all eligible women could be screened.

In the course of HIV care, MSF realized that there was an opportunity to address the unmet need of cervical cancer screening in a population of women at high risk. Although the screening programme was shown to be feasible, the use of the PAP smear technique limited its effectiveness due to the complexities of obtaining confirmatory biopsy and treatment in this setting.

We have found that the Pap test-based strategy for cervical cancer screening for HIV-positive women in two provincial hospital clinics in Cambodia was actually resource-demanding and challenging to implement even when targeting regular HIV-clinic attendees.

The use of VIA and cryotherapy will allow bypassing the need for cytology-based screening thereby minimizing referrals and repeated consultations, for at least a majority of HIV-positive women in resource-constrained countries. However, research is urgently needed to confirm the safety and effectiveness of this screen-and-treat strategy for HIV+ women.



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Psychosocial counseling support



Counselors were recruited since the first days of the projects, although when the clinics started counselors were not yet a recognized part of the Cambodian health system and trained psychologists were and still are rare. Thus, counselors were either nurses or staff members recruited after an evaluation of appropriate personal skills.

In both clinics, a team of counselors provided a series of services complementary to the medical consultations for HIV/AIDS patients. Their principal objectives were to encourage drug adherence and healthy lifestyle changes with information and psychosocial support. The long-term aim was to provide patients with the means (knowledge and confidence) to assume more responsibility in the management of their disease. Peer-support groups were established for antiretroviral users and, these groups provided an essential continuation of the work of the

counselors and doctors. Over the years subjects incorporated into the counseling schedule included: TB counseling, family planning, cervical cancer screening, transferring of the patients, and nutritional advice.

During the lead-up to transferring care from MSF to MoH, several new initiatives were undertaken. The Takeo pediatric counseling team added information on second line ART treatment for children and during the same period MoH counselors started being integrated into the team. MoH nurses were identified by the pediatric team leader to receive training on the counseling process: training and support on how to provide emotional support for children and caretakers, and how to use new tools. Counseling training for orphanage staff was also provided after an operational research study found that orphan status was associated with treatment failure.

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Nutritional support for HIV and co-infected patients and Home Based Care

Initiatives for improving the nutritional support for HIV and TB patients were started over time; a simplified protocol was written and shared with HBC partners at both projects. In Siem Reap the HBC component was organized via a network where MSF was involved mainly providing technical support to partners. At monthly network meetings with HBC NGOs MSF carried out training for staff on HIV/AIDS counseling, on ART and on the practical aspects of the nutritional protocol. In Takeo, the nutritional program for malnourished HIV-AIDS patients was only implemented in 2008.

In the middle of 2008 MSF reviewed the nutritional program/protocol, and integrated new activities that put more effort on patient's follow up (including support for the medical appointments, training, and standard rations).

Outcomes for 2008 were not satisfactory. Some improvement was observed with adults but was not seen with children, probably due to lack of strict follow up (home visits). After MSF withdrawal, the nutrition program for HIV-AIDS children will probably be integrated in the overall national program for in-patients in the hospitals.

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Decentralization of MSF-supported care and Handover of chronic diseases



Decentralization and transfer of patients started in Kampong Trach (Kampot province) in 2005, followed by Poipet (Banteay Meanchey province) in 2006, Samraong (Oddar Meanchey province) in 2007 and was completed by the end of 2007.

In the past two years (2007 and 2008), while the National Program for HIV/AIDS has consolidated

its financial capacity and strengthened a standardized approach for OI/ART clinics, the need for MSF to remain in the field of HIV/AIDS has decreased considerably. We, therefore, developed a schedule to withdraw gradually from our main sites in Takeo and Siem Reap with a final deadline put at mid 2009.

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Recommendations

- *International donors, aid organizations and the scientific community should not be complacent, despite the success stories of the fight against HIV/AIDS in Cambodia*
- *Prevention activities targeting most-at-risk populations (MARPs), and PMTCT urgently need action*
- *There is an increasing need for an expanded ARV drug formulary to cover the needs of alternative first line regimens (toxicity, intolerance) and 2nd line regimens*
- *While the ARV supplies remain constant and reliable around the country, more efforts should be made to support the logistic aspects of the drug procurement*
- *Viral load measurements should soon become part of the routine laboratory monitoring of patients on ART as increasing evidence show the low sensitivity of CD4 count monitoring for early detection of treatment failure*
- *Laboratory follow-up should be quality assured for all OI/ART sites (including biochemistry, microbiology and serology)*
- *We suggest further investigation of the one-stop-service approach for the cervical cancer screening among HIV+ women*
- *Financial barriers to hospitalization should be removed and immediate access to in-patient care should be guaranteed for all, especially for TB patients*
- *Interventions to improve patient self-empowerment are essential for program success and treatment adherence and peers should play a major role in the OI/ART clinics*
- *Operational research should be promoted as a means of improving the quality of care*

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Petros Isaakidis, Marie-Eve Raguenaud, Vantha Te, Tray Chhraing, Kazumi Akao, Varun Kumar, Sopheap Ngin, Eric Nerrienet, Rony Zachariah. High survival and treatment success sustained after two and three years of first-line ART for children in Cambodia (under peer review)

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