Advanced HIV in the Democratic Republic of Congo: Free care, adapted to patient needs, is essential for survival.

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DEFINITIONS

Advanced HIV (1) (also referred to in the report as “advanced stage HIV”):

- For adults, adolescents and children over 5 years, advanced HIV is defined as a CD4 count < 200 cells/µL or World Health Organization (WHO) clinical stage 3 and 4 events at inclusion.
- All HIV positive children under 5 years old should be considered as having advanced HIV at inclusion.

CD4 count (CD4 T lymphocytes): measures the immune status of a patient. Severe immunosuppression is a CD4 count < 350 cells/µL.

ARV-naïve patient: someone who has never initiated antiretroviral therapy (ART).

ARV non-naïve or “experienced” patient: someone who has ever taken antiretroviral therapy (ART), whether currently on treatment or having interrupted treatment.

False naïve (to ART): someone who has previously been on ART but has not disclosed this.

Late presenters: naïve patients presenting at care facilities with CD4 counts < 200 cells/µL or at WHO clinical stages 3 and 4.

Prophylaxis: preventative treatment to avoid either the first occurrence of infections (primary prophylaxis) or their recurrence (secondary prophylaxis/maintenance treatment).

“Test and Treat” strategy: WHO guideline that aims to start HIV-positive people (regardless of CD4 count) on ART immediately.

Case Fatality Rate: Proportion of deaths amongst people diagnosed with a specific disease.

Homogeneous patient group (HPG): group of patients with the same main diagnosis upon admission to hospital.

PODI (Points de distribution communautaires) and clubs: differentiated models of care for the distribution of ARVs in the community.

ACRONYMS

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<thead>
<tr>
<th>Acronym</th>
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<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
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<td>ART</td>
<td>Antiretroviral Therapy</td>
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<td>ARV</td>
<td>Antiretroviral</td>
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<td>CHK</td>
<td>Centre Hospitalier de Kabinda</td>
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<td>DCIP</td>
<td>Provider Initiated Counselling</td>
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<td>DRC</td>
<td>Democratic Republic of Congo</td>
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<td>HC</td>
<td>Health Centre</td>
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<td>HGR RB</td>
<td>Roi Baudouin General Referral Hospital</td>
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<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>OI</td>
<td>Opportunistic Infection</td>
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<td>MSF</td>
<td>Médecins Sans Frontières/Doctors Without Borders</td>
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<td>OAC</td>
<td>Organisations d'assise communautaire (Community-based organisations)</td>
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<td>PICT</td>
<td>Provider-Initiated Counselling and Testing</td>
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<td>PLHIV</td>
<td>Person/People Living with HIV</td>
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<td>PNLS</td>
<td>Programme National de Lutte contre le VIH/SIDA et les IST (National Program Against HIV and STIs)</td>
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<td>PODI</td>
<td>Points de distribution communautaires (Community ART Distribution Point)</td>
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<td>RNOAC</td>
<td>Réseau National des Organisations d'Assises Communautaires (National Network of local community-based organizations)</td>
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<td>Satellite Health Centres</td>
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SUMMARY

Globally, the years 2000 to 2015 saw the number of new HIV infections fall sharply from 3.2 million to 2.1 million. The number of HIV-related deaths also decreased significantly over this period. However, in 2016 the number of annual HIV-related deaths still stood at 1 million and appeared to have plateaued, rather than declined for the previous three years. Crucially, over the past five years the proportion of people living with HIV (PLHIV) seeking treatment at advanced stages of HIV has not dropped as fast as hoped.

The Democratic Republic of Congo (DRC) has both a low HIV prevalence rate and a low level of HIV screening and treatment services. Only an estimated one in two people infected with HIV are diagnosed, and only 38% of those diagnosed are able to access ART to keep them alive. Advanced HIV disease (characterized by CD4 < 200 cells/µL) includes three categories of PLHIV: 1) those who never initiated ART, 2) those on treatment but where treatment is failing (i.e. the virus has become resistant to treatment) and 3) those who began treatment but then interrupted it (lost to follow-up).

The risk of developing advanced HIV is high at every point in the HIV care cascade: whether it be between the moment of infection and diagnosis, initiating ARV treatment, adhering to a treatment program (retention in care), or achieving an undetectable viral load.

A recent study of opportunistic infections (OIs) across the country revealed that 63% of PLHIV presented with at least one such infection. The study, by the DRC’s Programme National de Lutte contre le VIH/SIDA (PNLS) (National HIV/AIDS programme) also showed that 11% of PLHIV presented in a bedridden state at the first consultation. In Kinshasa, approximately 30% of patients present with a CD4 count under 100 cells/µL on their first visit to one of four health centres supported by MSF. At the Centre Hospitalier Kabinda (CHK) (Kabinda Hospital Centre), a MSF facility that specializes in the treatment of PLHIV, two thirds (70%) of patients are admitted with a CD4 count of under 200 cells/µL and roughly a quarter (24%) with a CD4 count under 25 cells/µL. The mortality rate in CHK’s inpatient department is extremely high. There is a mortality rate of 37% in patients needing hospital admission and 31% of these die within the first 48 hours. Together, tuberculosis (TB), cryptococcal meningitis and pneumocystis pneumonia represent 85% of diagnoses made upon admission and lead to 95% of deaths at CHK.

Several factors might explain why people seek treatment so late, as well as the high proportion of advanced HIV-related diseases in Kinshasa. The strong stigma linked to HIV is the principal reason. Certain religious leaders exacerbate this phenomenon. Poor knowledge about HIV both amongst the general population, but also amongst health workers, compounds the problem; as do the prohibitive costs associated with seeking medical help. These factors are aggravated by the wider, low prevalence context where inadequate resources are being directed towards the HIV response.

If the diagnosis and treatment of patients with advanced HIV are to be improved, measures must be taken to address their specific needs. This must occur at every level of the health care system. These measures must go hand-in-hand with a referral system governing the care of PLHIV that functions across all elements of the system. It is also essential to ensure that health care for PLHIV is free, which is in line with national policy.

Urgent steps must be taken to ensure patients with advanced HIV are diagnosed before it is too late and to ensure that they receive care suited to their particular needs. This report makes specific recommendations regarding diagnostic and treatment methods related to advanced HIV, as well as detailing the cost of hospitalizing these patients. We hope to provide future partners with the information they will need to mobilize resources to treat advanced HIV patients free of charge. This may also eventually contribute to reducing the numbers of advanced HIV admissions in Kinshasa.
ADVANCED HIV PATIENTS: LEFT BEHIND BY THE HIV RESPONSE
INTRODUCTION

Over the past twenty years the number of people newly infected with HIV worldwide has dropped substantially; falling from 3.2 million to 2.1 million between 2000 and 2015. At the same time, improved measures to treat the disease early and greater access to antiretroviral therapy (ART), have led to a significant drop in the number of HIV-related deaths. While some disparities remain, we have seen the median CD4 count at the initiation of antiretroviral therapy (the best predictor of mortality for PLHIV) rise in every region of the world. Between 2007 and 2015, the median CD4 count increased from 220 to 480 cells/µL in North America; and from 160 to 230 cells/µL in West Africa.

Nevertheless, in 2015, close to 1.1 million HIV-related deaths were recorded (2) and the decline in the number of deaths appeared to have plateaued in the three previous years (3). In addition, the number of PLHIV who seek treatment at an advanced stage of the disease does not appear to have decreased from 2010 to 2015 (4). Taking this into account, it seems increasingly evident that reaching the ambitious targets set by UNAIDS - to reduce HIV related deaths to fewer than half a million by 2020 - will be impossible.

This technical report aims to assemble the epidemiological, socio-medical, economic and operational factors affecting patients with advanced HIV in Kinshasa. It draws from the available literature, testimony of patients in hospitals supported by MSF’s Kinshasa HIV project as well as the testimony of healthcare professionals specialized in the treatment of advanced HIV. The observations of our multi-disciplinary team are intended for use by authorities in public hospitals, health care professionals, medical decision makers in the DRC’s Ministry of Health and its partners, political decision makers and the country’s major donors (the Global Fund, PEPFAR and USAID).

The aims of the report are the following:

• To describe the current circumstances of patients with advanced HIV in structures supported by MSF in Kinshasa by presenting the available data in both quantitative and qualitative terms, as well as situating this data in an international context (Chapter 1).

• To highlight the major public health problem represented by advanced HIV, and its role in the global strategy set out in the UNAIDS 90-90-90 targets.

• Suggest ways in which to identify people presenting with advanced HIV and quickly initiate them on free treatment by describing:
  o A diagnostic and therapeutic implementation package designed to identify advanced HIV patients at community, primary and hospital health care levels and get these patients into treatment (minimum requirements in terms of clinical protocols, diagnostic tests and medicines) (Chapter 2).

  o The financial cost per “homogenous patient group” (HPG). These groups represent the treatment of patients with advanced HIV disease in hospital (Chapter 3).

• To suggest a treatment model that can be implemented across all levels of health care; adapted to the specific challenges of advanced HIV, (Chapter 4).

MSF has been engaged in responding to HIV in the DRC since 1993. Our organization is involved at the community, primary, secondary and tertiary levels of the health system. Our HIV project offers medical care to PLHIV in Kinshasa. Despite our efforts over the past fifteen years, MSF teams still confront the tragedy of advanced HIV unfolding in the city. The severity of the situation has led us to re-double our efforts to identify these patients and get them (back) onto lifelong treatment.
"The big challenge we face at CHK hospital is that these patients often arrive at a very late stage. We fight to keep them alive but often we know very little about them. Their status is often hidden from their family members who bring them in. (...) Many of these patients arrive with a CD4 count below 100. There are several reasons for this: It could be because of the ignorance of medical staff, or because the treatment is not specific enough and the patient keeps declining despite all the care we provide. It could also be because the person is suffering from self-stigmatization. These are people who know their HIV status, but they keep going from one treatment centre to another hoping for a miracle cure. The third reason is the message people hear in church: some people still believe miracles. They wait until they have lost their physical strength entirely (...)"
Chantal Meta Kadima was diagnosed with HIV in 2004. She was hospitalized at CHK in 2008 with a CD4 count of 44 cells/µL. Today she has an undetectable viral load.

“My family hid my elder son’s illness from me, then they hid my own HIV positive status from me (...) One day, I overheard a telephone conversation between my parents and my elder sister. They told her they needed to prepare coffins for my deceased son, and for me as well (...). My physical condition had become very alarming. My family kept me isolated in a room with my (younger) child. Nobody was allowed in. Sometimes a neighbour gave me food, and this went on for 4 years. One day, when I was on the way to a consultation, I fainted with my son in my arms. A woman picked up my bag and took me to the CHK. A few days later I fell into a coma that lasted two months. When I woke up, I knew nothing. I didn’t recognize anyone, I was breathing through some tubes. I could no longer eat and I weighed less than thirty kilograms. I could not even look at myself in a mirror without crying (...). My sisters had given away my belongings when I was in the coma because everyone believed I had died (...). After being in hospital for three months, I was able to leave. I had to relearn everything all over again. Even how to walk. But, with the help of the hospital staff and support groups, I began to recover slowly. This made me want to help others. That is why I started working in the PODIs. Today my viral load is undetectable. I don’t want to be ashamed about my condition any longer. I work every day and I am proud of what I have become.”
Advanced HIV In Kinshasa

The DRC’s HIV prevalence rate, estimated at 1.2% in 2014, ranks as one of the lowest in Sub-Saharan Africa (5). Nevertheless, only one in two people who contract HIV in DRC will ever be diagnosed. A mere 38% of PLHIV are on ART countrywide (Figure 1) (6).

In the capital Kinshasa (home to close to 13 million people), HIV prevalence is estimated at 1.6% (5). In 2016, the number of PLHIV receiving ART was estimated at roughly 46,000 people (7).

A study recently published of PLHIV countrywide shows that 63% arrive at health care facilities with at least one opportunistic infection (OI) and 12% are already bedridden. Pulmonary TB is the most common of these infections (48% of PLHIV are diagnosed with this disease) (8).

Figure 1 Cascade of HIV care in DRC: Goals versus Reality

Source: 2016 annual report, Programme National de Lutte Contre le SIDA et les IST (PNLS), DRC
MSF’s Kinshasa project began in 2002 with the Kabinda mobile treatment centre which subsequently moved to the CHK, where a hospital unit was set up in 2008.

Today, the CHK acts as a both a referral and training centre (for MSF and its partners). It is a private institution run by MSF that treats HIV patients free of charge. The centre consists of a hospital unit with 41 beds (on average, 160 patients are hospitalized each month with an occupancy rate of 120% and a stay of five days) and a mobile unit that provides regular treatment and follow up for 1500 patients. Situated in the Lingwala municipality, the centre caters for PLHIV from across Kinshasa. Roughly 650 patients are referred there from other health facilities.

A clinical supervision and mentorship program has been set up in conjunction with two general hospitals: Roi Baudouin Hospital General Referral Hospital (HGR RB) and the Ngaba Mother and Child Health Centre as well as at two health centres (HC): HC Kimia and HC Lisanga. The “Test and Treat” strategy is a new initiative launched in 2016 aimed at boosting the number of new diagnoses and treatment initiations.

Under the rubric of MSF’s HIV project, a decentralized, simplified HIV service delivery model is provided at multiple points at health facilities and in the community. ARVs are provided at Community Distribution Points (PODI) as well as at primary health centres and secondary health facilities.

In essence, HIV testing takes place at all MSF-supported facilities and at every level of health care as shown in Figure 2.

**Figure 2** Number of screenings and infection rate at MSF-supported structures and at community level, 1st quarter 2017

*CHK represents one entry point to care that records a 41% positive rate (amongst outpatients). Counselling sessions in the PODIs have made it possible to diagnose 10% of those screened.*
At primary health care level, a significant proportion of patients suffer from advanced HIV, despite an increase in median CD4 count at initiation stage. This increase in CD4 counts at initiation has been strongly influenced by new WHO directives governing treatment eligibility which are now part of DRC national policy. The threshold for patient eligibility for ART changed from 350 to 500 cells/µL in 2013. According to data from six health centres in Kinshasa city, the number of patients with CD4 counts under 100 cells/µL on the first visit, has remained virtually stable since 2012, at roughly one third of patients (Figure 3).

Between 2012 and 2016 at CHK, 58% of outpatients had CD4 counts under 200 cells/µL (advanced HIV), and 42% of outpatients had CD4 counts under 100 cells/µL at the start of treatment. These percentages remained roughly unchanged between 2012 and 2016.

Between 2015 and 2017, the CD4 count of patients recorded on admission at CHK was 84 cells /µL [26-244]. Over the same period, 70% of patients had CD4 counts under 200 cells /µL, 53% had CD4 counts under 100 cells/ and 24% had CD4 counts under 25 cells/µL (Figure 4) (9). During this time, the median CD4 count on admission remained unchanged, at roughly 80 cells/µL. It is higher for patients referred to CHK by MSF-supported health centers than by others (Figure 5). At HGR RB, the median CD4 count on admission in 2016 was 113 cells/µL.

![Figure 3](image3.png)

**Figure 3** Percentage of outpatients with CD4 counts ≤ 100 cells/µL at ART initiation in four MSF-supported health centers since 2016.

Roughly 30% of outpatients presented with a CD4 count ≤ 100 cells/µL during the first visit to four MSF-supported health centres in Kinshasa in 2016.

Source: Tier.net

![Figure 4](image4.png)

**Figure 4** CD4 count (cells/µL) on admission at CHK, 2015-2017 (n=1669)

On hospital admission at CHK, 70% of patients have CD4 < 200 cells/µL and 24% have CD4 < 25 cells/µL. The majority of patients are admitted with severe immunodepression.
Are patients with advanced HIV on ART? The different picture at hospital and community level

PLHIV who present with extremely low CD4 counts at an advanced stage of HIV fall into one of three categories: 1) those who have never taken any antiretroviral treatment (naïve patients) either because they have never been tested for HIV, or because they were never placed on treatment (despite having been diagnosed with HIV); 2) those who are on treatment but whose treatment is failing (the virus has become resistant to treatment and therefore treatment is no longer effective); 3) those who began treatment but later interrupted it (lost to follow-up).

The danger of developing advanced HIV is present at all stages in the cascade of HIV care; whether it be between the moment of infection and diagnosis, initiating ART, adherence to a treatment program (retention in care), or once an undetectable viral load has been achieved (as illustrated in Figure 6).

Figure 5 Median CD4 count (cells/μL) amongst patients on admission at CHK, based on center of origin, 2015-2017

The median CD4 count on hospitalization has not changed over time, remaining constant around 80 cells/μL. It is higher for patients from MSF-supported centers than for others.

Figure 6 Entry and exit doors in the cascade of HIV care

Amongst these some will present as “false naïves” whereas they should be put onto 2nd-line ART.

“False naïves”: have previously been on ART but have not disclosed this
Amongst the general population, the majority of PLHIV with advanced HIV have never initiated ART. A recent study conducted in Kenya, Malawi and South Africa showed that of PLHIV with CD4 counts below 200 cells/µL, only 32% had been on ART for six months or longer, 47% had never been diagnosed, 12% had been diagnosed but had not started ART and 9% had been on ART for less than six months (Figure 7) (10). The countries surveyed in this study are also countries with a high prevalence of HIV (5.9%, 10.8% and 11.2% for Kenya, Malawi and South Africa respectively). In a country with a low prevalence rate such as the DRC, this situation is likely to be exacerbated by the higher percentages of PLHIV with advanced HIV who have neither been diagnosed nor treated.

The majority of PLHIV admitted to hospital with advanced HIV have been exposed to ART, but either treatment is failing or they have interrupted it. Of patients hospitalized at CHK between January 2015 and April 2017, (n=2210), 71% were treatment experienced (non-naïve); 25% of all admissions had begun ART within the previous six months, and fewer than 46% of all admissions had been on ART for longer than six months before being hospitalized (Figure 8).

The median CD4 count for patients who had been on ART for longer than six months was 100 cells/µL [27-290] and for those who had been on ART for less than six months, the average was 83 cells/µL [23-217] (9).

In MSF-supported hospitals in four locations (Kinshasa in the DRC, Cape Town in South Africa, Homabay in Kenya and Nsanje in Malawi) more than half of patients with advanced HIV were treatment experienced (non-naïve) as regards ART.
The same situation is observed at other hospitals supported by MSF in Africa (Figure 8). In Kenya, a hospital study showed that amongst patients with advanced HIV, 60% were already on ART; and close to half of these had been on ART for longer than six months. Of these, 44% had been classified as HIV stage 3 and 35% as stage 4. Of all patients admitted to hospital, 45% had a CD4 count < 100. Another hospital study in South Africa showed that amongst patients with advanced HIV (n=585), 64% were treatment experienced (non-naïve) (11); 45% were on ART when the study was conducted and 19% had interrupted treatment only to return six months later. Similarly, in Nsanje Hospital in Malawi, records show that 80% of hospitalized patients are treatment experienced (non-naïve) (Figure 8).

A significant proportion of patients with advanced HIV corresponds to the number of patients who temporarily interrupted treatment only to restart it after a period during which they developed clinical symptoms (12). A study of intra-hospital mortality conducted at CHK in 2014 showed that 48% of patients who interrupted treatment had done so for more than 3 months before being hospitalized (13).

Another study in South Africa in 2015 illustrates this cyclical nature of recourse to treatment. Amongst PLHIV lost to follow-up for at least six months, 34% re-accessed treatment after some time had passed, 7% were admitted to hospital and 17% were admitted to a different hospital from the referral centre (making follow-up impossible). The study also shows that the percentage of patients estimated to be lost to follow-up after five years from the start of ART is 25%, and 38% after ten years (14).

Amongst PLHIV with CD4 counts lower than 200 cells/µL, the percentage who are treatment-experienced (non-naïve) is higher than it is in the general population. Essentially, those patients who are hospitalized form part of a particular group who have access to care (even if it is late and/or insufficient) in contrast to PLHIV in the population who go undiagnosed and untreated.

Most patients with advanced HIV are likely to be found in the general population, outside the health care system.

**High morbidity and mortality amongst patients with advanced HIV**

PLHIV with advanced HIV (CD4 < 200 cells/µL) run a higher risk of mortality owing to the increased risk of OIs (15). The mortality rate in hospital at CHK is extremely high. More than one in three patients (37%) needing hospital admission die during their stay in hospital. These deaths occur during the first 48 hours of hospitalization in 31% of cases, and during the first week of hospitalization in 65% of cases. Close to half of patients (46%) hospitalized at CHK with a CD4 count lower than 100 cells/µL died while in hospital (Figure 9). Of the total number of patients who died (n=754), 71% had begun ART before hospitalization. At HGR RB, the median CD4 count of those who died was 40 cells/µL [21–81] and 38% of those who died had been ART on admission.

The post-hospitalization mortality rate is also very high, but notoriously hard to measure because of the difficulty in following up on patients after they leave hospital.

This extremely high mortality rate is also found in other hospitals in the region supported by MSF. In Homa Bay Hospital in Kenya, a 17% mortality rate in hospital amongst PLHIV was recorded in 2015. The post-hospitalization mortality rate was 30% (43% for PLHIV with CD4 counts < 100 cells/µL). In Nsanje Hospital in Malawi, in- hospital mortality amongst HIV positive patients was measured at 29% (routine hospital data, 2016) and, at Donka Hospital in Conakry, Guinea, this figure was 46% (routine hospital data, November 2016-April 2017).
Causes of death amongst patients with advanced HIV

At CHK, the principal cause of hospitalization is TB (56% of admissions), followed by bacterial and neurological infections (toxoplasmosis 12%, pneumocystis pneumonia 9%, cryptococcal meningitis 8%, pneumonitis 7%) as shown in Figure 10. The highest fatality rate is amongst patients with pneumocystis pneumonia (137 deaths per 295 admissions, or 46% of deaths) followed by Kaposi Sarcoma (29 deaths per 70 admissions, or 41% of deaths). Amongst patients diagnosed with TB, 38% died during their stay in hospital.

Why do PLHIV present late?

Qualitative research recently conducted with patients, nurses and medical personnel at CHK sought to understand why certain PLHIV seek treatment late (naïve and non-naïve patients) as well as to explore factors that influence whether people adhere to treatment or not. The results reveal the complex nature of the phenomena (Figure 11). Stigma and fear around divulging one’s HIV positive status appear to be significant factors. Another is the cost of HIV care (consultations, laboratory tests, treatment for OIs), which constitutes a major barrier for a large majority of PLHIV. It should be noted that all care and medication at MSF sites is free. In addition, the general lack of knowledge about HIV, reinforced by false messages spread by some religious leaders, negatively affects adherence to treatment. Finally, the specific context of low prevalence in the DRC (HIV is a low priority with low levels of screening and treatment) aggravates the situation. The stigmatization of PLHIV is intimately associated with poor general knowledge about HIV and this makes it even more difficult to get PLHIV into treatment, at every point in the cascade of care (Figure 12).
**Figure 11** Factors leading to the delay in seeking HIV treatment and the development of advanced HIV.

**Factors Linked to Health System**
- Low coverage of testing
- Cost of consultations, laboratory tests and treatment for opportunistic infections
- Lack of knowledge about HIV
- Stigmatisation by health-care workers
- Stockouts of ARVs and other essential medicines

**Community Level Factors**
- Religious and spiritual beliefs (some religious leaders spread false information)
- Lack of support and rejection from family members

**Individual Factors**
- Lack of knowledge about HIV
- Lack of knowledge about own HIV status and own treatment
- Self-stigmatization (fear of declaring seropositivity openly)
- Lack of means (for transport, consultations, laboratory tests, medicines for OI)

**Delay in Seeking Treatment - Advanced Stage HIV**

**Figure 12** Impact of stigmatisation and lack of knowledge on access to and retention in care.

**Stigmatisation**

**Lack of Knowledge**

**False Information**
- Spread by some religious leaders

**Testing**
- Fear of knowing own status
- Reluctance to test children
- Fear of HIV

**Treatment Initiation**
- Fear of starting treatment
- Denial of own status
- Misperceptions, feelings of worthlessness and lack of empowerment

**Retention/Adherence**
- Fear of disclosing HIV status
- Reluctance to disclose to children
- Fear of losing anonymity
- Treatment interruption
The mortality rate amongst patients with advanced HIV in hospital remains extremely high. Years of concerted effort have not succeeded in reducing these figures. The major risk factor for mortality is CD4 count: the lower the CD4 count the higher the mortality. More than half of patients hospitalized at CHK with CD4 counts ≤ 100 cells/µL died during their admission. TB, toxoplasmosis, cryptococcal meningitis and pneumocystis pneumonia are responsible for 85% of diagnoses made on admission and 95% of deaths at CHK. One in three people hospitalized for TB dies during his/her stay in hospital. Together stigma, the financial cost of care, lack of knowledge as well as the wider context of low prevalence constitute the greatest barriers to accessing treatment for PLHIV in Kinshasa.
CHAPTER 2
How mortality can be reduced
"When I found out my HIV status, I had a terrible reaction. I considered suicide. I was really desperate. I knew nothing about HIV, except that people died of it [...] Then, I became bedridden. I lost my hair. I could no longer walk. They had to carry me in to wash me. I could no longer feed myself. My first day in the hospital, I remember the welcome they gave me. The medical staff told me I had to take my medication as instructed, and that, if I believed in myself, I would make it [...] I can hardly remember anything about those two months in hospital because I lost my memory for weeks. Today, I am well. My viral load is undetectable and I have started playing football again. Even though I regret what happened, it has given me the strength and the desire to be someone respectable, and to help others who are suffering by sharing my story. Now I know a lot about HIV, and I want to pass on this information to others. This is why I became the chairperson of a support group for youth in Kinshasa."
Reducing mortality at each health care level

Interventions are necessary at every level of the health care system if we are to achieve the goals of improving 1) the quality of and access to information and 2) screening and care for people with advanced HIV. These interventions, at community level, primary health care (health centres), secondary (general hospitals) and tertiary (referral hospitals) levels, must be specifically adapted to each level. These adaptations are shown in Figure 15 and detailed in the rest of this chapter.

Community health care

The goals at community level should be: to improve information about HIV, decrease stigma, increase the number of screenings (including within the target population) and educate patients, their families and health workers about how to recognize the danger signs for advanced HIV (see list pg. 21). A strong communication strategy is needed in order to decrease stigma and improve knowledge about HIV; this is beyond the scope of this report.

Primary health care (health centres)

At primary health level, care is provided at local health centres or centres de santé. These health centres (HC) are able to treat patients in an unstable condition, whereas the more numerous satellite health centres (satHC) only treat patients in a stable condition. The satHC dispense only a minimum HIV/TB treatment package, whereas the HC offer the complete package. (Figure 13).

Secondary health care (general hospitals) and tertiary health care (referral hospitals)

Patients with advanced HIV require urgent medical attention. As the mortality rate is high, intervention must be very rapid in order to minimize the number of patient deaths. For this reason, it is crucial not to delay examinations, diagnosis and treatment.

Lumbar puncture is an important investigation for the diagnosis of meningitis, which is commonly caused by cryptococcal meningitis and TB in patients with advanced HIV.
Figure 13 Health care levels in Kinshasa

<table>
<thead>
<tr>
<th>SERVICE OFFERED</th>
<th>MINIMUM PACKAGE OF CARE</th>
<th>FULL PACKAGE OF CARE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB testing and diagnosis (using questionnaires and identifying contacts)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TB testing and diagnosis (GeneXpert and X-ray)</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>TB treatment initiation and follow-up</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HIV testing</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>ART initiation</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Counselling (by health care workers) and identification of danger signs</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Basic treatment follow-up (clinical follow-up and dispensing of ARVs)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Thorough diagnosis and follow-up: CD4, Creatinine, viral load, early diagnosis of children and TB using POC (GeneXpert) or equivalent, CrAg, TB-LAM, glucose, urine dipstick, Rapid diagnostic tests for Hepatitis B and Syphilis</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Lay counsellors provide advice and search for patients lost to follow-up</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Adapted medical care in case therapeutic failure is suspected</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

KEY:
- REFERRAL SYSTEM
- REFERRAL HOSPITALS
- HOSPITALS
- MAIN HEALTH CENTERS
- SATELLITE HEALTH CENTERS
- PODI
- COMMUNITY-BASED ORGANISATIONS
- CLUBS
Clinical guidelines for the care of PLHIV with advanced HIV

If the number of deaths amongst patients with advanced HIV is to be reduced, these patients require a range of rapid diagnostics and treatment specifically adapted to their needs. The array of care options adapted to the needs of advanced HIV patients should include:

- Advanced HIV treatment protocols
- Minimum equipment necessary for diagnosis
- Medication for the main pathologies
- Training and clinical mentoring for health workers
- Criteria for referral to hospital
- Specific guidelines for paramedics assisting patients with advanced HIV

Treatment guidelines for advanced HIV

MSF has developed a clinical manual on how to treat advanced HIV at hospital level. (16).

Danger signs

In the event that one or more of the following danger signs is observed, patients should be referred to a medical facility that is capable of treating advanced stage HIV.

- Respiratory rate > 30/min
- Saturation < 90%
- Temperature > 39°C
- Heart rate > 120/min
- Systolic BP < 90mmHg
- Moderate to severe dehydration
- Inability to walk unaided
- Neurological changes: confusion, behaviour problems, altered state of consciousness
- Other neurological symptoms: headaches, convulsions, paralysis, any other neurological symptoms or signs, including rapid deterioration of vision and sudden difficulty in speaking.

Patients, their families and health workers need to be taught to recognize these signs. A referral system for these patients needs to be clearly defined at every level of health care.

Clinical examination

It is important to gather an in-depth history of the disease in a systematic manner, beginning with the patient’s current problems and complaints.

Particular attention should always be paid to neurological and respiratory problems and diarrhea.

The following two questions are key to understanding the patient’s history regarding ART and TB medication:

**Key Question 1: Is the patient on ART?**

PLHIV taking ART should be in good health, not seriously ill and needing hospital admission. It is important to find out what has gone wrong (cf. detailed algorithm in Appendix 1). Many patients have virological failure of first line ART; this means a rapid transition to second line ART is necessary, when opportunistic infections have been diagnosed and treatment initiated. Simply treating OIs without putting the patient on an effective ART regimen will not be enough to save the patient’s life. Issues relating to adherence to treatment must be tackled at the same time that the ART regimen is being changed; as keeping a patient on an ineffective ART regimen while addressing adherence issues means the patient will die.

**Key Question 2: Is the patient on TB treatment?**

People taking TB treatment should be in good health, not seriously ill needing hospital admission. It is important to find out what has gone wrong.

A thorough clinical examination must be done; particular attention should be given to the neurological and respiratory systems. In addition, it is important to check for Kaposi’s Sarcoma, and CMV retinitis (if there has been a recent deterioration in vision).

Minimum necessary diagnostic equipment

There are a number of tests that need to be conducted immediately upon a patient’s admission with advanced HIV. To minimize the risk of death, it is crucial to ascertain the patient’s immunological status as soon as possible as well his/her diagnosis or diagnoses. The tests need to be available 24 hours a day, seven days a week. All medical personnel (clinicians, nurses and laboratory technicians) should be trained to use point-of-care tests. For tests that must be done in the laboratory, a system of rapid transmission of results to medical teams must be put in place in order to avoid any delays. The following tests are needed:

- Rapid HIV test
- CD4
- Serum CrAg (cryptococcal screening)
- TB LAM
- Rapid malaria test
- Glucose
- Hemoglobin
- Syphilis
- Hepatitis B
- Urine dipstick
**TB screening and diagnosis**

Every patient with advanced HIV needs to be systematically screened for TB. TB treatment must start immediately if the result is positive or if an empirical treatment decision is made. TB LAM is a point-of-care test that is done on admission; it is performed on a urine sample. The test must be available 24 hours a day, and is done in the ward. If the result is positive, TB treatment must be started immediately. If the result is negative, a clinical decision must be made as to whether to start empirical TB treatment.

In addition to TB LAM, samples are also taken for Xpert MTB/RIF. This is a laboratory test; it is therefore only available during laboratory working hours. It can be done on sputum, urine or samples from other body fluids.

If Xpert MTB/RIF is unavailable, sputum microscopy can be performed. However this has a low sensitivity in HIV positive patients. Additional investigations for TB diagnosis are CXR (chest Xray) and abdominal ultrasound.

**Additional tests**

If neurological symptoms and signs are present, a lumbar puncture is necessary. See appendix for details (pages 34-36).

Kidney impairment is common; all patients admitted to hospital therefor need a blood test for kidney function. If there is concern the patient has liver disease, blood tests for liver function are needed.

### ALLIED HEALTH MEASURES TO SUPPORT HOSPITALIZED PATIENTS

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>On patient’s admission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Reception and welcome of patient and persons accompanying him/her</td>
</tr>
<tr>
<td></td>
<td>• Explanation of process and hospital rules</td>
</tr>
<tr>
<td></td>
<td>• Initial assessment of patient’s needs</td>
</tr>
<tr>
<td></td>
<td>• Counselling and explanation of the importance of sharing clinical history, especially past ART and anti-TB treatment.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phase 2</th>
<th>During patient’s hospital stay (after patient is stabilized)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Follow-up evaluation of patient’s needs and evaluation of degree to which patient accepts his/her illness</td>
</tr>
<tr>
<td></td>
<td>• Support disclosure of HIV status</td>
</tr>
<tr>
<td></td>
<td>• Therapeutic education about the patient’s condition (TB/HIV), adherence assessment and support</td>
</tr>
<tr>
<td></td>
<td>• Counselling and support to caregivers who accompany the patients (including support groups)</td>
</tr>
<tr>
<td></td>
<td>• Counselling support on index testing</td>
</tr>
<tr>
<td></td>
<td>• Counselling to help patient adapt to hospital environment</td>
</tr>
<tr>
<td></td>
<td>• Diagnosis and treatment of depression</td>
</tr>
<tr>
<td></td>
<td>• Nutritional and physiological advice (physiotherapy)</td>
</tr>
<tr>
<td></td>
<td>• Palliative care</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phase 3</th>
<th>Preparing patient for discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Reinforcement of advice and counselling previously provided</td>
</tr>
<tr>
<td></td>
<td>• Agreement with patient on an adherence plan for return home</td>
</tr>
<tr>
<td></td>
<td>• Train patient to manage medication intake</td>
</tr>
<tr>
<td></td>
<td>• Explain the process of TB/HIV treatment post-hospitalization and about existing support network</td>
</tr>
<tr>
<td></td>
<td>• Conduct a socio-economic evaluation of patient, identify social support for post-hospitalization follow up</td>
</tr>
<tr>
<td></td>
<td>• Explain referral system and how to recognize danger signs to patient and accompanying persons.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In the case of a patient’s death</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Announce the death to family members</td>
</tr>
<tr>
<td>• Provide emotional support to people affected</td>
</tr>
<tr>
<td>• Identify social network</td>
</tr>
</tbody>
</table>
The importance of initiating treatment immediately

Empirical treatment must begin immediately once a patient is admitted for an OI that is amongst the most common causes of mortality (TB, pneumocystis and toxoplasmosis). Empirical treatment is initiated when there are strong causes for clinical suspicion but a diagnostic test is unavailable, or when results are delayed, or if the diagnostic tests do not allow one to exclude the diagnosis. Immunosuppression kills patients, and those with CD4 counts below 200 cells/µL have a very high mortality rate. Patients on ART for more than 6 months must be assessed for regimen failure, with viral load testing. Many patients with advanced HIV are failing first line treatment; if the viral load result can be obtained within a few days, it should be used to diagnose virological failure and the need to switch to second line treatment. If the viral load result is likely to take weeks or months, the decision to switch to second line has to be made on clinical grounds.

Medication to treat main pathologies

The list of medications necessary to treat advanced HIV are listed in Appendix 2. Several specific treatments that are not commonly used in the DRC at present are specified below:

- Liposomal amphotericin B for treatment of cryptococcal meningitis: this has fewer severe side effects than conventional amphotericin B
- Liposomal doxorubicin for treatment of advanced Kaposi's Sarcoma. This is more effective and less toxic than the more widely available combination of vincristine/bleomycin.
- For prevention of TB and other opportunistic infections, a fixed dose combination of cotrimoxazole, isoniazid and vitamin B6 will be available soon. This will reduce the pill burden compared to taking these medicines separately.

Human resources

The requirements in terms of human resources at each level of health care are outlined below.

- Community level: Patient support groups and associations. It is crucial, above all, to educate and train people involved in PODI, clubs and organisations d'assises communautaires (OAC) (community-based organisations), as well as their supervisors (about screening, ARV distribution and what to do in the event that danger signs are detected).
- Primary health care
  - Satellite health centre (minimum package of care): nurses and/or pharmacists. Nurses are trained to do screenings, counselling (both before and after testing) and to recognize danger signs. They can decide to refer patients to a main health centre or to a hospital.
  - Main health centre (full package of care): counsellors, nurses, pharmacists, laboratory technicians. Clinical staff are trained and mentored in the treatment and follow-up of PLHIV, including screening and treatment for OIs.
- Secondary health care: hospital counselling or PICT (provider-initiated counselling and testing): health personnel (doctors, nurses, pharmacists, laboratory technicians) are trained to treat PLHIV with advanced HIV.

In main health centres and hospitals, clinicians are trained as part of a mentorship programme. This programme has two components: 1) weekly training sessions for all hospital personnel and 2) professional discussions between the mentor and the person being mentored. Theirs is a relationship of mutual trust where information is shared. The goal is to improve the quality of treatment for PLHIV. The mentor accompanies the trainee (the person being mentored) to all consultations and on ward rounds.

Referral criteria

At each level of care, referral criteria are defined by the need to orient patients towards a health facility adapted to their needs. Patients tested at community level are referred to a health centre for treatment and follow-up. Patients who are ill, and who need clinical investigations on a more frequent and specialized level, are referred to a main health centre where they can access a complete range of treatment options.

If danger signs are observed and hospitalization is necessary, patients are referred to a general hospital.

Specific allied health guidelines for advanced HIV

Psychological and physiological support are vital elements in the provision of quality treatment to patients with advanced HIV in hospital. For more detail see box: “Allied health measures to support hospitalized patients” (previous page).

Note

In order to improve both the screening and treatment of patients with advanced HIV, it is important to intervene at all levels of health care and ensure that a referral system exists between these levels. The care offered should also be specifically adapted to each level (cf. Figure 13). As the hospital mortality rate of advanced HIV patients is extremely high, it is crucial that treatment be specifically adapted to their needs and rapid. It is also important to initiate empirical treatment for OIs which are the most frequent causes of death.
CHAPTER 3
Cost of hospital treatment for advanced HIV

MSF doctor, Dr. Pulchéry helps Dr. Zola, a doctor at Roi Baudouin General Hospital to interpret chest X-rays of a patient suspected of having contracted tuberculosis.
"Since our partnership with MSF began, we have opened a (new) service and the way treatment is administered in hospital has improved significantly. HIV patients had to pay for treatment before, but they no longer have to. From the first consultation until discharge, everything is now free of charge. We also benefit from ongoing training. By strengthening the capacities of our teams through theoretic and practical training, we have been able to improve the way we manage people living with HIV-AIDS.

I remember one HIV patient who developed a terrible case of herpes and was incapacitated by it. She did not follow advice on taking her medication but hid herself in her home because she was so ashamed. Eventually she came to hospital. Luckily that day the MSF team were with us on a ward tour when we came across her case. After sharing our experience and knowledge, we decided on a treatment together. One week later, all her lesions had disappeared as if by magic! She was able to stand up and began walking whereas she hadn’t been able to before. She left hospital walking and smiling."
In order to improve access to treatment, it is essential to ensure that PLHIV are provided with care free of charge. This is in line with national policy. Free care is *de facto* being provided for patients at CHK, where it is managed and financed by MSF. By contrast, free treatment for patients who are admitted to other hospitals necessitates a compensation mechanism meant to reimburse hospitals.

Despite a national policy which provides free treatment for PLHIV, the reality is that public facilities charge these patients either the partial or total cost of care (except for certain services such as ART), which these facilities justify by arguing that they are underfunded by the government. Two simulations based on tariffs applied in Kinshasa hospitals suggest that the average cost of hospitalization (for a patient) is between USD160 and USD280 for one hospitalization of a PLHIV. This cost is prohibitive for the majority of patients.

MSF financed a study aimed at estimating the real cost of hospital treatment for PLHIV in three MSF supported facilities: CHK, HGR RB and the Ngaba Mother and Child Health Centre. The goal was to propose a tariff structure for treatment as well as a method of reimbursement for partner facilities using donor funding. This study was the subject of a detailed report, the results of which (for HGR RB) are outlined below (17).

Reference data used in the study was drawn from a national survey of hospital costs in in France and adapted to the context of care of PLHIV in the DRC. This methodology made it possible to estimate the average cost of treatment for one patient depending on the type of hospital stay, and by grouping patients into “homogenous patients groups” (HPG) according to their principal hospitalization diagnosis using hospitalization statistics (cf. HPG detailed in table 1). Each HPG was associated with a syndrome or disease. For example, a patient hospitalized with pulmonary TB (principal diagnosis) and presenting with malaria would be classed in HPG1. Four diseases were exempted from this classification: TB, meningitis, cryptococcal meningoitis and septicemia. A combination of two of these four diagnoses would lead to a classification in HPG8.

Hospital stays at HGR RB in 2016 were classified according to this system. Table 1 shows the number of cases and their distribution, average length of stay (ALOS), estimated cost of treatment of PLHIV (total cost and unit cost) as well as a proposed unit tariff per stay.

Based on these estimations, the cost of one hospital stay for HPG1 for one LOS (length of stay) of nine days at HGR RB represents a total cost of USD278. This amount is USD247 if it does not include food, and USD136 if it does not include meals or laboratory tests.

Reimbursement by a partner who provides medicines and laboratory tests should be set at a base cost of USD136 per stay for HPG1. A partner who wishes to pay for the totality of treatment costs (including meals, medicines and laboratory tests) should reimburse the hospital to the amount of USD10 804 per month minimum (for 32 patients hospitalized for an average stay of one month). This cost includes medical treatment and nursing based on care protocols. Attention should be paid to ensure that the hospital is capable of sourcing medicines and laboratory inputs specifically for treating PLHIV.

It is suggested that 10% more be added to costs obtained at HGR RB per HPG as this creates a financial incentive (i.e. a reimbursement tariff that is higher than cost) in line with the idea of paying for a quality service, and also to ensure that unexpected costs are covered.
Table 1 Estimated cost of treatment for PLHIV per homogeneous patient group (HPG) at Roi Baudouin Hospital in 2016

<table>
<thead>
<tr>
<th>HPG</th>
<th>Respiratory disorders: Pulmonary TB</th>
<th>Respiratory disorders: Others</th>
<th>Neurological disorders: Cryptococcosis</th>
<th>Neurological disorders: Others</th>
<th>Digestive disorders: (chronic diarrhea etc.)</th>
<th>Septicemia</th>
<th>Unrelated disorders (cardiac, renal etc.)</th>
<th>Multiple pathologies</th>
<th>Others (malaria, severe secondary effects etc.)</th>
<th>Severe anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case distribution (%) in 2016</td>
<td>39.1%</td>
<td>10.1%</td>
<td>4.5%</td>
<td>11.7%</td>
<td>14.5%</td>
<td>1.1%</td>
<td>2.5%</td>
<td>1.1%</td>
<td>10.0%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Nb cases in 2016</td>
<td>148</td>
<td>38</td>
<td>17</td>
<td>44</td>
<td>55</td>
<td>4</td>
<td>9</td>
<td>4</td>
<td>38</td>
<td>18</td>
</tr>
<tr>
<td>Average duration of stay</td>
<td>9</td>
<td>10</td>
<td>7</td>
<td>10</td>
<td>9</td>
<td>16</td>
<td>6</td>
<td>8</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>TOTAL COST (USD)</td>
<td>41 143</td>
<td>11 415</td>
<td>19 737</td>
<td>20 047</td>
<td>15 604</td>
<td>1 696</td>
<td>2 236</td>
<td>1 888</td>
<td>14 520</td>
<td>1 368</td>
</tr>
<tr>
<td>TOTAL COST excl. meals (USD)</td>
<td>36 536</td>
<td>10 093</td>
<td>19 326</td>
<td>18 515</td>
<td>13 896</td>
<td>1 466</td>
<td>2 040</td>
<td>1 772</td>
<td>12 949</td>
<td>1 117</td>
</tr>
<tr>
<td>TOTAL COST excl. meals &amp; meds &amp; lab (USD)</td>
<td>20 096</td>
<td>5 759</td>
<td>1 772</td>
<td>6 583</td>
<td>7 452</td>
<td>1 007</td>
<td>901</td>
<td>512</td>
<td>6 752</td>
<td>1 017</td>
</tr>
<tr>
<td>UNIT COST (per stay) excl. meals &amp; meds &amp; lab (USD)</td>
<td>135.6</td>
<td>150.5</td>
<td>103.9</td>
<td>148.5</td>
<td>135.6</td>
<td>241.5</td>
<td>95.1</td>
<td>122.8</td>
<td>178.1</td>
<td>61.4</td>
</tr>
<tr>
<td>Proposed Unit tariff (per stay) (USD)</td>
<td>149</td>
<td>166</td>
<td>114</td>
<td>163</td>
<td>149</td>
<td>266</td>
<td>105</td>
<td>135</td>
<td>196</td>
<td>68</td>
</tr>
</tbody>
</table>

**Annual total**: 379 129 654 117 708 51 951

**Monthly average**: 32 10 804 9 809 4 329

**KEY**: HPG: Homogenous Patient Group, USD: United States Dollar

Source: Etude de coûts, Hospitalisation PVVIH à Kinshasa, RDC (17)

**NOTE**

A partner wishing to pay for the total cost of hospital care (including meals, medication and laboratory charges) would have to reimburse a minimum of USD10 804 per month (for an average of 32 patients hospitalized a month) according to a lump-sum payment system.

Elysée is a counsellor who works with patients at CHK. She often organizes activities for the children.
CHAPTER 4
Recommended model of free care for advanced HIV patients in Kinshasa

The CrAg test is an antigen test that enables the detection of cryptococcal disease in the blood, and also cryptococcal meningitis.
"At CHK, we receive people from all over. These patients have often been stigmatized and marginalized. They do not have the money to get treated because medication is very expensive. If this facility didn’t exist, I think it would be a disaster (...) At CHK we can’t keep up with the demand. We have a current capacity of 41 beds and sometimes we have 65 patients hospitalized at one time! Other centres capable of treating advanced HIV need to be opened urgently, so that we can treat just those patients who need specialized care for advanced HIV. Decentralization can help ensure advanced HIV patients are treated before they require hospitalization, by referring stable patients to health centres and PODI."
“I was very thin, so thin that my bones were stuck to my skin. I wasn’t sleeping at the hospital and I went back and forth every day, but I never had to be carried on anybody’s back. Even though I staggered as I walked to the hospital, I wanted to walk on my own. People would look at me in the street, and they could tell that I was sick […] I had many relapses. I was hospitalized seven times at CHK, almost twice a year between 2006 and 2012. The longest I was in hospital was 3 months. I suffered a lot, but today I’m well, and this is why I give my time to support patients who are hospitalized and who don’t have anybody to be their confidant. This allows me to help other patients and give them advice. The last time I was hospitalized, a light went off in my head. […] I decided that I needed to strengthen myself mentally and live more positively. I didn’t want to be at the mercy of what people think about me and my disease anymore. I had to battle against stigmatization. Today, I am proud of myself; of the people I have met along my journey, and of my life, which has become pleasant. If people insult me, I don’t let that kind of thing bother me anymore. The mental strength that I have managed to gain has improved my health enormously.”

Mundele Angélique was born in 1974. She was hospitalized almost twice a year between 2006 and 2012 at CHK. Today, she is a carer, providing support and counselling for unaccompanied patients at CHK. She is pictured with her husband, Jean de Dieu.
**Recommendations**

MSF’s experience in Kinshasa has enabled us to identify the main pillars of a strategy to treat patients with advanced HIV and to reduce the mortality rate of PLHIV. Specific objectives and associated activities, are explored below.

**Objective 1: Ensure coordination of treatment for advanced HIV at national level.**
- Draw up national guidelines for the treatment of advanced HIV
- Put in place a national “advanced HIV working group” (see objective 4)

**Objective 2: Ensure patients living with HIV have access to treatment**
- Reduce stigma linked to HIV in Kinshasa by:
  - Organizing communication campaigns against stigmatization
  - Using social networks to inform and educate the youth
  - Organizing information and education sessions in health structures, OAC (community-based organisations) and the PODI
  - Organizing information and education sessions in the community
- Ensure treatment is free for patients by:
  - Implementing a flat-rate payment system to hospitals
  - Implementing a payment system to health centres
  - Enhancing the role of patients activists in the follow-up of free access to care for HIV patients

**Objective 3: Implement a referral system at the level of health zones and in Kinshasa city**
- Conduct a study of the socio-economic and medical context of each zone de santé (health zone)
- Identify HC and SatHC
- Train personnel in health facilities within a mentorship programme
- Educate patients, their families and health personnel to recognize advanced HIV danger signs
- Organize meetings in the central offices of the zones de santé (health zones) to ensure the smooth functioning of the system

**Objective 4: Improve the quality of care for patients with advanced HIV**
- Offer a minimum package of care in the satHC and a full package of care in the main HC in order to ensure fast diagnoses and early treatment for OIs
- Offer a complete treatment package in general referral hospitals
- Technical recommendations:
  - Conduct CD4 counts systematically at initiation
  - Make rapid diagnostic tests available (CrAg and TB LAM)
  - Integrate free treatment services for HIV and TB
- Put a mentoring system in place in hospitals (training and accompanying health personnel)
- Organize clinical exchanges between different hospitals and health centres
- Put in place an “advanced HIV working group” with the following specific goals:
  - to organize technical meetings with multiple partners to revise protocols and to agree on referral criteria and algorithms
  - to ensure that hospital care is free for PLHIV
  - to develop training sessions on offering free hospital treatment to patients with advanced HIV
  - to put in place psychosocial and educational components of hospital care
  - to ensure physiotherapy is part of hospital care
  - to reinforce pediatric treatment by organizing a specific workshop on the subject

**Objective 5: Promote a supply system for medicines to treat OI and laboratory tests at HC and referral hospitals**
- Organize technical meetings about the medical supply system and to ensure stock outs are avoided
- Organize multi-stakeholder quantification meetings
- Train staff in hospitals and health centres on managing the stock of medicines for OIs.
- Develop controls to ensure medicines are used correctly
One man’s journey through advanced HIV

Despite a very high mortality rate amongst PLHIV with advanced stage HIV, rapid, well adapted treatment can save the lives of many; as the following case illustrates.

**Day 1** G is brought into CHK in a very frail state. He is severely wasted, in a state of confusion, and has trouble breathing. After a series of rapid diagnostic tests, he is diagnosed with HIV and TB and quickly taken to the TB isolation ward where he is to spend several days.

**Day 2** He is started on TB treatment within 24 hours. The priority is to treat the TB first, with ART starting a few days later to begin reconstituting his immune system.

**Day 3** He remains in the TB isolation ward but has regained consciousness. Treating TB, severe infections and correcting any kidney failure can result in significant improvements within a few days.

**Day 4** He is started on TB treatment within 24 hours. The priority is to treat the TB first, with ART starting a few days later to begin reconstituting his immune system.

**Day 5** G. is still severely weak, and needs help moving and with personal hygiene. A nurse assistant offers him hygiene care.

**Day 6** He remains in the TB isolation ward, but has regained consciousness. Treating TB, severe infections and correcting any kidney failure can result in significant improvements within a few days.

**Day 7** Smiling and making eye contact is a strong indication for health staff that a patient is recovering: small improvements can be significant.

**Day 8** He is started on TB treatment within 24 hours. The priority is to treat the TB first, with ART starting a few days later to begin reconstituting his immune system.

**Day 9** The physiotherapist takes G. for a walk outside. Mobility is very important for advanced HIV patients who may have been bed ridden for a long time.

**Day 10** G. is deemed ready for discharge as he has received a clear diagnosis, started treatment and is showing good overall functional improvement. He remains extremely sick however; and post-hospitalization care is critical to ensure he is able to stay on treatment and fully recover.

“I am pleased to be feeling better and to be able to leave hospital. Now I can walk by myself and I think I am able to go home by myself. My desire is to move forward and not to return to hospital again.” (G’s statement the day he was discharged).
Acknowledgements:

The authors would like to express our warmest thanks to the patients and personnel at HGR RB and CHK, as well as MSF’s project and coordination staff in Kinshasa, all of whom made the writing of this report possible.

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References

## ADVANCED HIV – SERIOUSLY ILL PATIENTS

### DEFINITION OF ‘SERIOUSLY ILL’:
- One or more danger signs

### MORTALITY IS HIGH:
- Do not delay investigations and management

### COMMON CAUSES OF MORTALITY: SEE BOX
- Often there is more than one cause
- Investigations and management focus on these causes

### TAKE A GOOD HISTORY
- Start with the presenting complaint
- Always ask about neurological and respiratory symptoms, and diarrhea
- Ask the 2 key questions [see right]

### EXAMINE THE PATIENT
- Reassess vital signs
- Specifically assess neurological and respiratory systems, and assess for dehydration
- Look for KS (skin, palate)
- Look for CMV retinitis if recent deterioration in vision

### DANGER SIGNS

<table>
<thead>
<tr>
<th>Key Question 1: Is the patient on ART?</th>
<th>DANGER SIGNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients on ART should be doing well, and not seriously ill: What has gone wrong?</td>
<td></td>
</tr>
<tr>
<td>- {d} How long has the patient been on ART?</td>
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<tr>
<td>- &lt; 3 months: TB is very common during this time - ‘unmasking TB’ &gt; 6 months: is there treatment failure?</td>
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<tr>
<td>- The majority of seriously ill patients nowadays with advanced HIV are failing first line treatment and need rapid switch to second line treatment</td>
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<tr>
<td>- If this is not addressed, treating opportunistic infections alone will not save the patient’s life</td>
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<tr>
<td>- Adherence issues must be addressed at the same time as changing regimen; staying on a failed regimen means the patient will die</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Key Question 2: Is the patient taking TB treatment?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients on TB treatment should be doing well, and not seriously ill: what has gone wrong?</td>
</tr>
<tr>
<td>- Respiratory rate &gt; 30/min</td>
</tr>
<tr>
<td>- Temperature &gt; 39°C</td>
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<tr>
<td>- Heart rate &gt; 120/min</td>
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<tr>
<td>- Systolic BP &lt; 90mm Hg</td>
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<tr>
<td>- Saturation &lt; 90%</td>
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<tr>
<td>- Unable to walk unaided</td>
</tr>
<tr>
<td>- Altered mental state: confusion, strange behaviour, reduced level of consciousness</td>
</tr>
<tr>
<td>- Any other neurological problem: headache, seizures, paralysis, difficulty talking, cranial nerve problems, rapid deterioration in vision.</td>
</tr>
<tr>
<td>- Renal failure and abnormal sodium and potassium levels are common, and are often asymptomatic</td>
</tr>
<tr>
<td>- ‘Bloodstream’ infections</td>
</tr>
<tr>
<td>- Meningitis</td>
</tr>
<tr>
<td>- Urinary tract infections</td>
</tr>
<tr>
<td>- Hypoglycaemia</td>
</tr>
<tr>
<td>- Renal failure</td>
</tr>
<tr>
<td>- Sodium/potassium abnormalities</td>
</tr>
<tr>
<td>- Liver disease</td>
</tr>
<tr>
<td>- Drug side effects: find out all the medication the patient is taking</td>
</tr>
</tbody>
</table>

### DISSEMINATED TB IS THE MOST COMMON CAUSE OF MORTALITY:
- All patients need investigating for TB, and rapid initiation of treatment if indicated.

- 1. ART failure
- 2. Neurological disease – Big 3:
  - TB
  - Cryptococcal meningitis
  - Toxoplasmosis
- 3. Respiratory Disease – Big 3:
  - Pneumocystis pneumonia
  - Pulmonary TB
  - Bacterial pneumonia
- 4. Severe diarrhoea:
  - Renal failure and abnormal sodium and potassium levels are common, and are often asymptomatic
- 5. Other bacterial infections:
  - ‘Bloodstream’ infections
  - Meningitis
  - Urinary tract infections
- 6. Common non-infectious causes:
  - Hypoglycaemia
  - Renal failure
  - Sodium/potassium abnormalities
  - Liver disease
  - Drug side effects: find out all the medication the patient is taking

### KEY QUESTION 1: IS THE PATIENT ON ART?

Questions to ask:
- How long has the patient been on TB treatment?
- Was TB proven? Rifampicin sensitive?
- Is the admission due to drug adverse effects?
- Did the patient improve on TB treatment? If not – see algorithm ‘Patients deteriorating or not improving on TB treatment’

### KEY QUESTION 2: IS THE PATIENT TAKING TB TREATMENT?

Questions to ask:
- How long has the patient been on ART?
- Was TB proven? Rifampicin sensitive?
- Is the admission due to drug adverse effects?
- Did the patient improve on TB treatment? If not – see algorithm ‘Patients deteriorating or not improving on TB treatment’

### RESPIRATORY RATE  > 30/min
- Temperature > 39°C
- Heart rate > 120/min
- Systolic BP < 90mm Hg
- Saturation < 90%
- Unable to walk unaided
- Altered mental state: confusion, strange behaviour, reduced level of consciousness
- Any other neurological problem: headache, seizures, paralysis, difficulty talking, cranial nerve problems, rapid deterioration in vision.

### Respiratory Disease – Big 3:
- Pneumocystis pneumonia
- Pulmonary TB
- Bacterial pneumonia

### Common non-infectious causes:
- Hypoglycaemia
- Renal failure
- Sodium/potassium abnormalities
- Liver disease
- Drug side effects: find out all the medication the patient is taking

### Source:
HIV / TB Clinical Manual. Hospital level. MSF May 2017 (18)
### INVESTIGATIONS: TAKE SAMPLE IMMEDIATELY AND COLLECT RESULTS IMMEDIATELY

If the patient is to be referred to a higher level of care, conduct as many investigations as possible at the initial facility, and start management.

#### BASIC PACKAGE OF POINT-OF-CARE TESTS:

These should be available 24/7, and all clinical, nursing and lab staff trained in their use.

- HIV Testing
- CD4
- Serum CrAg
- TB LAM
- Rapid malaria test
- Glucose
- Haemoglobin
- Urine dipstick

#### CHEST X RAY

**TB**
- Miliary TB
- Pleural effusion, pericardial effusion
- Lymphadenopathy
- Pulmonary infiltrate

**Pneumocystis pneumonia**
- Ground glass pulmonary infiltrate

**Bacterial pneumonia**
- Consolidation, air bronchograms

#### ALL PATIENTS NEED INVESTIGATION FOR TB:

**TB LAM:**
- **TB LAM positive:** start TB treatment
- **TB LAM negative:** TB is not excluded! Continue investigations, start empiric TB treatment if indicated (see Management section)

**GeneXpert:**
- Sputum: spontaneous or induced
- Non-sputum samples: urine*, CSF*, ascites* pus
- **GeneXpert positive:** start TB treatment
- **GeneXpert negative:** TB is not excluded! Continue investigations, start empiric TB treatment if indicated (see Management section)

**OTHER INVESTIGATIONS FOR TB:**

**Sputum microscopy:**
- If GeneXpert unavailable

**CXR:** see left

**Abdominal ultrasound:**
- Lymphadenopathy
- Ascites
- Hepatosplenomegaly

**Centrifuge urine, CSF, ascites and pus otherwise sensitivity is very low.**

#### LUMBAR PUNCTURE

**Indications for LP:**
- Any neurological symptoms or signs
- Serum CrAg positive
- LP should be done before antibiotics are started unless this will delay the first dose; the sample can be stored in a fridge overnight

**Baseline investigations:**
- CrAg
- Cell count and differential (lymphocyte count, neutrophil count)
- Protein, glucose
- Gram stain for bacteria: Streptococcal pneumoniae: gram positive cocci in pairs/chains
- Neisseria meningitidis: gram negative diplococci
- GeneXpert*
- If unable to do an LP or if there is an inevitable delay (e.g. referral is necessary for LP), empiric treatment may be necessary
- See Management section: Neurological Disease

#### BLOOD TESTS

- Creatinine, sodium, potassium
- Full blood count
- VDRL
- Jaundice or hepatomegaly: bilirubin, ALT, hepatitis B

#### DOES THE PATIENT HAVE A BACTERIAL INFECTION?

**Look for any of the following:**
- Temp > 38 degrees or < 35 degrees
- HR > 120, or RR > 30
- White cell count <4 or > 12
- Other causes possible: Acute onset of symptoms suggests bacterial infection. If in doubt, start antibiotics if seriously ill. Diagnosis can be reviewed upon further results
- **Look for the source** (pneumonia, meningitis, UTI; bloodstream infections are also common)
- **Take blood culture**, using sterile technique; other relevant tests, e.g. urine dipstick, urine culture

**REMEMBER:** All neurological signs are Danger Signs

Take before antibiotics are started unless this will delay the first dose.
MANAGEMENT: START WITHOUT DELAY

Start empiric treatment [highlighted text] for diseases where clinical suspicion is high, but there is no diagnostic test available, there is an unavoidable delay with results, or if diagnostic test cannot exclude the disease. Start second line ART if CD4<200 and suspected treatment failure.

GENERAL MANAGEMENT

Hypoglycemia
- Give 50mLs of 50% dextrose, monitor PoC glucose 4 hourly until hypoglycaemia has resolved for 24 hours.

Dehydration and/or renal impairment:
- Intravenous fluids and electrolyte replacement [NaCl or Ringer’s lactate], at least 3L per day if tolerated.
- Beware nephrotoxic drugs; see renal algorithm.
- If chronic watery diarrhoea is the cause, start empiric treatment for Isospora belli infection.
- If vomiting, start regular IV antiemetics

Liver impairment:
- Beware hepatotoxic drugs; see liver algorithm

Anemia:
- HB < 5g/dl: transfuse, give oxygen
- HB < 8g/dl and tachypnoea or active bleeding: transfuse
- Assess for likely cause; see anaemia algorithm

Is bacterial infection likely?
- Start empiric antibiotics according to local guidelines
- Review all antibiotic prescriptions every 48 hours to assess if IV drugs can be changed to oral, or if antibiotics can be stopped; see bacterial infection algorithm.

Respiratory Danger Signs:
- RR > 30 or saturation < 90%
- Oxygen by face mask or nasal prongs

Start empiric treatment immediately for:
- Pneumocystis pneumonia: cotrimoxazole (960mg/4kg body wt, plus prednisone initially 40mg bd)
- Bacterial pneumonia: see local guidelines
- TB: if immediate investigations positive, or empiric treatment indicated [see below]

Evidence of respiratory disease but no Danger Signs:
- CXR if available; see ‘Investigations: CXR’
- CXR not available; consider empiric treatment for:
  - Pneumocystis pneumonia [dyspnoea, dry cough]
  - Bacterial pneumonia [acute onset, crepitations]
  - TB: if investigations positive, or empiric treatment indicated

Clinical indications for immediate empiric TB treatment:
1. CNS TB is likely:
   - Neurological symptoms/signs with evidence of TB elsewhere or clinical presentation is suggestive
2. Clinical presentation strongly suggests TB, and investigations not available or cannot exclude TB
   - Peripheral lymph nodes
   - Night sweats, weight loss, fever, cough
   - Pleural effusion, pericardial effusion or ascites and no other more likely cause
3. CXR evidence of TB (see ‘Investigations - CXR’)
4. Patient is seriously ill (any danger signs), patient is deteriorating, or patient is not improving 3 days after hospital admission

RESPIRATORY DISEASE

Respiratory Danger Signs:
- RR > 30 or saturation < 90%
- Oxygen by face mask or nasal prongs

Start empiric treatment immediately for:
- Pneumocystis pneumonia: cotrimoxazole (960mg/4kg body wt, plus prednisone initially 40mg bd)
- Bacterial pneumonia: see local guidelines
- TB: if immediate investigations positive, or empiric treatment indicated [see below]

NEUROLOGICAL DISEASE

Treat for Cryptococcal meningitis (CCM)*
- CSF CrAg positive
- Serum CrAg positive, and LP not possible or unavoidable delay, and any neurological symptoms/signs
- No CrAg available and any neurological symptoms/signs

Treat positive serum CrAg, and not for CCM**
- Serum CrAg positive and CSF CrAg negative
- Serum CrAg positive, and LP not possible or unavoidable delay, and no neurological symptoms/signs

Treat for CNS TB (TB treatment plus prednisone 1.5mg/kg):
- Suggestive LP (mostly lymphocytes, and/or high protein)
- Neurological symptoms or signs with evidence of TB elsewhere, or clinical presentation suggestive
- CSF GeneXpert positive

Treat for Toxoplasmosis (cotrimoxazole 960mg/8kg body wt)
- CD4 < 200 or unknown and new onset neurology:
  - Focal neurology (eg hemiplegia)
  - Altered mental state, or new headache and no alternative diagnosis

Treat for Bacterial Meningitis (see local guidelines):
- Acute onset of meningitis symptoms
- Meningococcal meningitis: non-blanching petechiae
- CSF: neutrophil predominance and/or CSF microscopy shows bacteria on gram stain, and/or high protein

If there is no evidence to support bacterial meningitis (neutrophils in CSF) and an alternative diagnosis found (for example CCM), antibiotics can be stopped.

If LP not available or unavoidable delay – and any neurological symptoms or signs:
- Acute onset of symptoms: treat for bacterial meningitis
- Serum CrAg positive or not available: treat for CCM
- Treat CNS TB and/or toxoplasmosis: see above

* amphotericin B plus fluconazole 800mg
** Fluconazole alone; 800mg if CSF CrAg negative, 1200mg if unable to do serum CrAg
> Treat as above for 14 days; continue fluconazole according to protocol in MSF/HIV handbook.
**APPENDIX 2**

**List of medications**

### List of essential medications to treat Opportunistic Infections

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug Name</th>
<th>Dose/Route</th>
<th>Notes/Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NEUROLOGY</strong></td>
<td></td>
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</tr>
<tr>
<td>BACTERIAL Meningitis</td>
<td>Ceftriaxone</td>
<td>100mg/kg/day</td>
<td>As loading dose and then 80 mg/kg/day in IV</td>
</tr>
<tr>
<td>CRYPTOCOCCAL Meningitis</td>
<td>Combination of Liposomal Amphotericin B 3mg/kg/day and Fluconazole 100mg/kg/day PO for 14 days; then Fluconazole 400mg/day for 8 weeks. Alternative treatment: Combination of Liposomal Amphotericin B 3mg/kg/day and Fluconazole 800mg/day PO for 14 days; then Fluconazole 400mg/day for 8 days</td>
<td></td>
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</tr>
<tr>
<td>Meningeval Tuberculosis</td>
<td>National Protocol: 2HRZE + 10 RH</td>
<td>Prednisolone: Prednisolone 2-4 mg/kg in children and 1.5 mg/kg in adults (standard dose 60 mg/day) for 4 weeks then decreasing dose for 2 weeks. Vitamin B6: 50 mg/day</td>
<td></td>
</tr>
<tr>
<td>Cerebral Toxoplasmosis</td>
<td>Primary therapy → 8 WEEKS: Sulfadiazine 960 mg/kg/day in 2 doses PO, Pyrimethamine 2mg/kg/day in 2 doses for 2 days then 1 mg/kg/day/day, Folic acid: 10 mg/day. Secondary therapy → 4 WEEKS: Cotrimoxazole 60 mg/kg/day and Folic Acid 5 mg/day (less favorable owing toCTX resistance)</td>
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<tr>
<td><strong>DIARRHEA</strong></td>
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<tr>
<td>Acute Diarrhea</td>
<td>Cotrimoxazole</td>
<td>960 mg 2x/day for 5 days</td>
<td></td>
</tr>
<tr>
<td>Isospora belli</td>
<td>Cotrimoxazole</td>
<td>960 mg 4x/day for 10 days then 2x/day for 3 weeks</td>
<td></td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>ARV Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strongyloides</td>
<td>Albendazole</td>
<td>400 mg 2x/day for 7 days</td>
<td></td>
</tr>
<tr>
<td>CytoMegalovirus</td>
<td>Valganciclovir</td>
<td>450mg 2x/day for 21 days</td>
<td></td>
</tr>
<tr>
<td>Amebiasis</td>
<td>Metronidazole</td>
<td>400 mg 3x/day for 10 days</td>
<td></td>
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<tr>
<td>MAC</td>
<td>Azithromycin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Giardiasis</td>
<td>Metronidazole</td>
<td>2g/day for 3 days</td>
<td></td>
</tr>
<tr>
<td>Diarrhea of bacterial</td>
<td>Cotrimoxazole</td>
<td>800 mg 2x/day for 5 days</td>
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<tr>
<td><strong>PULMONARY</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Pulmonary Tuberculosis</td>
<td>National protocol: 2HRZE + 4RH for initial treatment; and 2 SRHEZ + 1 RHEZ + 5 RHE in case of relapse. MSF Recommendations: 3HRZE + 5 RHE. Vitamin B6 50 mg/day.</td>
<td>Prednisolone 40 mg 2x/day for 5 days, 40 mg 1x/day for 5 days, 20 mg 1x/day for 11 days. Folic Acid 5mg/day</td>
<td></td>
</tr>
<tr>
<td>Pneumocystis Jiroveci</td>
<td>Cotrimoxazole</td>
<td>120 mg/kg/day for 21 days</td>
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</tr>
<tr>
<td><strong>BACTERIAL Pneumonia</strong></td>
<td>Ceftriaxone</td>
<td>1g/day for 7 days</td>
<td></td>
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<tr>
<td>Pulmonary Cryptococcus</td>
<td>Fluconazole</td>
<td>200mg 1g/day (after exclusion of meningitis)</td>
<td></td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>Emergency ARV Treatment and Chemotherapy: Liposomal Doxorubicin IV 0.8mg/kg/day. Alternative chemotherapy: BLEOMYCINE 15 mg IV AND Vincriistine 2 mg IV</td>
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<tr>
<td><strong>DERMATOLOGY</strong></td>
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<tr>
<td>Bacillary Angiomatosis</td>
<td>Dapsone</td>
<td>100mg 2x/day for 2 months</td>
<td></td>
</tr>
<tr>
<td>Dermal Candidiasis</td>
<td>Micronazole cream</td>
<td>4g for 7-10 days</td>
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</tr>
<tr>
<td>Condyloma (warts)</td>
<td>Podophyllin</td>
<td>25% for 2 weeks</td>
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<tr>
<td>Dermatophyoses (ringworm)</td>
<td>Whitfield's 3x 1 application/day for 2-3 weeks</td>
<td></td>
<td></td>
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<tr>
<td>PPE (pruritic papular eruption)</td>
<td>Chlorpheniramine 4mg for 10 days</td>
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<tr>
<td>GALE</td>
<td>Benzyl Benzadote Lotidrin Persistent cases: Ivermectin</td>
<td></td>
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<tr>
<td>Herpes Zoster and Simplex</td>
<td>Acyclovir (Dosage according to severity)</td>
<td></td>
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</tr>
<tr>
<td>Cutaneous Kaposi Sarcoma</td>
<td>ARV Treatment then Chemotherapy if eligible (confer pulmonary KS)</td>
<td></td>
<td></td>
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<tr>
<td><strong>SYRPHILIS</strong></td>
<td>Dapsone</td>
<td>100mg 2x/day for 14 days</td>
<td></td>
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<tr>
<td>Oral candidosis</td>
<td>NYSTATIN Oral Suspension 4x1ml/day for children</td>
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<td></td>
</tr>
<tr>
<td>Oesophageal candidosis</td>
<td>Fluconazole</td>
<td>200mg 1x/day for 14 days; Children: Fluconazole 3mg/kg/day for 21 days</td>
<td></td>
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<tr>
<td><strong>OTHER</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>Treat according to etiology</td>
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<tr>
<td>Hepatitis C</td>
<td>Sofosbuvir + Daclatasvir</td>
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