The role of ART for inpatient care of PLWHA

Dr. Henry Sunpath
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HIV UNIT,
Dept of Medicine
McCord Hospital
Durban
Presented at AWACC 2010.(30/09/10)
How is the health of the inpatient units?
The inpatient unit: overwhelming demands lead to rationing of care

**Penn-Kekana, 2007 (reported at the African PC meeting in Kenya)**

- Study to see who gets good care and who doesn’t at the hospital and how care is rationed in the context of budget cuts and overwhelming demand.
- Involved over 800 hours of observation over a 2-month period in the medical wards and in casualty.
- Used a mixed team of doctors, public health specialists, and anthropologists, as well as 40 in-depth interviews with medical and managerial staff at the CHB hospital.
“It is a bit of a pot luck whether you get noticed,”
Factors that influenced whether people got care...

- Whether a person had an illness that interests a senior clinician in the hospital OR happened to get a sympathetic doctor when they arrived.

- The time of day when a person arrives at the hospital was important. Limit the number of medical admissions to 150, so if you come at 16h00 on that day, there’d be 145 patients already admitted. You’ve got to be really, really, really sick to get admitted and even then you probably won’t.

Factors that influenced the type of care...

- **Breakdown in relationship between doctors and nurses** – no longer do COMPLETE ward rounds together. Doctors write notes on the patient’s records and if the patients are lucky the nurses go and read it.

- **Care is very depersonalised.**
  Patients just don’t matter most of the time. People don’t talk to the patients. You go on these ward rounds with consultants, and they see 50 patients but probably only say a few words to each of them. Patient care is simply not how medical staff and nursing staff are evaluated,” concluded Penn-Kekana, because HIV/AIDS care is not integrated.
Why no ART preparation for inpatients?

1. No link between inpatient and outpatient programmes
HIV and AIDS services are delivered by well-funded but separate vertical programmes and people with HIV in the medical wards sometimes fall through the cracks.
“In the medical wards they feel ‘I don’t really deal with it because it’s somebody else’s problem,’”

2. Inpatient care has become a game of “MAKING BEDS”
“Finding beds for patients and then emptying the beds for the next huge influx of patients for care has become a priority at the hospital-the major concerns of the nurse managers – distracting them from other matters.
And if you look at the interns that provide most of the medical care, that’s how they are sort of evaluated, “how fast can you get the patient [out], how fast can you empty those beds?”

Sithole Z. Strategies to meet the demand for palliative care in South Africa due to the HIV epidemic. 2nd APCA Palliative Care Conference, Nairobi, Kenya, Abo147, 2007
The role of ART for inpatient care of PLWHA

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Overview of Presentation

1. *The SA 2010 guidelines*
2. ART in the setting of acute OI
3. The need for an inpatient ART provision
4. The challenges of an inpatient programme.
5. Research at McCord hospital that describe best practice models for inpatient ART initiation.
6. Other advantages of an inpatient programme for PLWHA
Eligible to start ART: SA 2010 ARV guidelines

CD₄ count <200cells/mm³ irrespective of clinical stage
CD₄ count <350cells/mm³ in patients with TB/HIV and Pregnant women
WHO stage IV irrespective of CD₄ count
MDR/XDR irrespective of CD₄
WHO Stage IV Clinical Criteria for Treatment Initiation (in absence of CD4)

- HIV wasting syndrome
- HIV encephalopathy/ADC
- *Progressive multifocal leukoencephalopathy*
- *Toxoplasmosis of the brain >1 month*
- *Cryptosporidiosis with diarrhoea/extrapulmonary*
- Disseminated Mycoses
- Candidiasis-oesophagus, trachea, bronchi, lungs
- Lymphoma
- *Recurrent severe bacterial pneumonias*
- Recurrent septicaemia
- *Symptomatic HIV associated nephropathy*
- *Symptomatic HIV associated cardiomyopathy*
WHO Stage IV Clinical Criteria for Treatment Initiation (in absence of CD4)

- **Kaposis Sarcoma**
- CNS lymphoma
- Invasive Ca cervix
- *Pneumocystis carinii pneumonia*
- *Cryptococcal meningitis*
- CMV disease of an organ other than liver, spleen or lymph nodes
- HSV infection: mucocutaneous >1 month OR visceral of any duration
- *Tuberculosis*
Conditions that require urgent ART intervention

AMONG THOSE PATIENTS BEING ADMITTED

- Cryptococcal menigitis treated with Amphotericin
- Chronic diarrhea
- PCP after acute management
- KS
- Life threatening thrombocytopenia with bleeding
- Toxoplasmosis
- HIVAN
- HIV Cardiomyopathy
- ALL ILL TB PATIENTS
Fast track: ART initiation within 2 weeks of being eligible for

1. Pregnant women eligible for lifelong ART
2. Patients with very low CD4 (<100)
3. MDR/XDR TB
4. All adults recently hospitalised with an HIV-linked condition, including TB
TB/HIV COINFECTION

• Complete 2 to a maximum of 8 weeks of TB therapy before commencing ART if the patient has CD4 count ≥ 350 cells/mm³

• In general, ART should be initiated as soon as the patient is tolerating their TB therapy; this is usually within 2-4 weeks
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ART and OIs

Two general questions

1. when to initiate ART in an ART-naïve person who develops an acute OI and

2. How ART should be managed in a person who is on ART but develops an acute OI.

ART in Acute OI (Treatment-Naïve pts)=ADVANTAGES

1. Improved immune function and faster resolution of the OI, for which effective therapy does not exist

- Cryptosporidiosis / microsporidiosis
- Progressive multifocal leukoencephalopathy (PML) may resolve or at least stabilize after the institution of effective ART
- Kaposi’s sarcoma (KS) - initiation of ART has been shown to lead to lesion resolution in the absence of therapy.


2. Preventive benefit - second OI is less likely to occur if ART is started promptly vs lengthy delay
ART in Acute OIs-Disadvantages ....

1. Poor absorption of ART in very ill pts = subtherapeutic serum levels = antiretroviral drug resistance.

2. ART toxicities - confused with disease manifestations or toxicities of drugs used for OI.

3. Drug-drug interactions among ART and anti-OI drugs may be difficult to manage.

4. Renal or hepatic dysfunction - dosing of ART drugs difficult to estimate.

5. IRIS events - manifestations that are difficult to distinguish from other clinical conditions.
ART in Acute OIs-precautions...

Alterations in renal and hepatic function related to the OI

- Distorts ART pharmacokinetics (metabolic clearance and volumes of distribution) and reduces ART efficacy and/or increases ART toxicity.

Alterations in renal and hepatic function related to the ingestion of some kinds of non allopathic therapy.

- Presents many challenges about TIME for ART and anti TB treatment.
ART and Acute OI - How soon after diagnosis

1. As soon as possible - when the early benefits of ART outweigh increased risk related other factor, Cryptosporidiosis/microsporidiosis, PML, KS and serious bacterial infections.

2. Wait for not longer than two weeks in pts with TB AND PCP.

3. How long do we wait in pts with Cryptococcosis/Toxoplasmosis?
First RCT – ACTG 5164

...Recommendations

- Unless there are other individual compelling contraindications, early initiation of ART near the time of initiation of OI treatment should be considered for most patients with an acute OI, excluding TB, Cryptococcal and other fungal diseases, Disseminated MAC disease, Toxoplasmosis.

- Other factors to be considered when making this decision are:
  - The degree of immunosuppression
  - The availability of effective therapy for the OI
  - The risk of drug interactions and overlapping drug toxicities
  - The risk of the consequences of the development of IRIS
  - The willingness of the patient to adhere to his or her drug regimens.
The immediate arm (14 days) experienced:
Fewer deaths/AIDS progressions ($p = 0.035$),

Longer time to death/AIDS progress (HR = 0.53, $p = 0.02$),

Shorter time to CD4 increase to $>100$ (11.8 vs 4.2 weeks).
No differences in grade 3/4 adverse events, adherence, hospitalizations, or IRIS (8 immediate vs 12 deferred)

Deferred arm - 8 weeks

Both arms achieved similar CD4 and viral load by week 24.
Acute OIs in ART experienced...

1. Os that occur shortly after initiating ART (within 12 weeks)
   = may be subclinical infections that have been unmasked by early IRIS
   = OIs due to advanced immunosuppression.
   = not considered to represent early failure of ART.
   Treatment for the OI should be started and ART continued.

2. OIs occurring >12 weeks after initiation of ART among patients with suppressed HIV RNA levels and sustained CD4+ counts >200 cells/μL
   = May represent a form of IRIS as opposed to incomplete immunity
   Therapy for the OI should be started and ART continued.
Acute OIs in ART experienced..

3. OI occurs in the setting of virologic failure

OI therapy should be started, ARV resistance testing may be performed, and the ART regimen modified for possible virologic control.

4. Data is lacking with regard to the optimal management of patients who develop OIs in the context of discordant immunologic and virological responses.

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What is the current trajectory for patients after OI in the medical wards?

Is early ART a possible goal and for whom?
Background: Is ACTG relevant to Resource-Poor Settings?

Shortage of ART treatment capacity and long pre-ART training = difficulty transitioning patients between inpatient and outpatient care = delay of ART for weeks to months.
What happens to patients after acute OI in SA? - A prospective pilot study -

What are the characteristics of inpatients with acute OI (most HIV-infected patients with acute OI are admitted)?

What is the rate of ART uptake after discharge?
What is the rate of death after discharge?

What baseline characteristics predict ART uptake by six months after acute OI?
How do the most advanced (CD4<50/mm3) HIV-infected patients fare in the setting of ART scarcity?

What happens to patients after acute OI in SA?

- A prospective pilot study -

Figure 2: Patient Flow:

55 Subjects Screened

49 (89%) Enrolled

4 (8%) Lost to Follow-up

45 (92%) 6M Follow-up Complete

1 Five subjects did not endorse “readiness to initiate ART” and 1 subject had not disclosed HIV status to an emergency contact.
What happens to patients after acute OI in SA?

- A prospective pilot study -

Table 1: Baseline Characteristics

<table>
<thead>
<tr>
<th>At the time of admission:</th>
<th>N = 49</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female — no. (%)</td>
<td>24 (49%)</td>
</tr>
<tr>
<td>Time since HIV diagnosis — median</td>
<td>2.9 months</td>
</tr>
<tr>
<td>Subjects with no prior OIs — no. (%)</td>
<td>33 (67%)</td>
</tr>
<tr>
<td>Acute opportunistic infection — no. (%)</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Pulmonary,</td>
<td>14 (28%)</td>
</tr>
<tr>
<td>Extrapulmonary(^2)</td>
<td>18 (38%)</td>
</tr>
<tr>
<td>PCP</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>3 (6%)</td>
</tr>
<tr>
<td><em>T. gondii</em></td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (8%)</td>
</tr>
</tbody>
</table>
What happens to patients after acute OI in SA?
- A prospective pilot study -

Figure 3: Patient Trajectory After Discharge

- 20 (41%) Initiated ART *
- 13 (27%) Died Prior to ART
- 12 (24%) Alive, Remain Pre-ART
- 4 (8%) Lost to follow-up
- 49 Patients Enrolled

* 1 patient died during ART
What happens to patients after acute OI in SA?
-A prospective pilot study-

Conclusions:
- After inpatient treatment for OI, we observed poor ART uptake (41%) and high mortality (21%) among HIV-infected patients.
- Among those who died, median time to death was 95 days, and among those who initiated ART, median time to ART was 82 days.
- The patients with the most advanced disease (CD4 count <50/mm³) were least likely to initiate ART by 6 months.
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Challenges for an in patient ART programme

1. Very ill patients admitted to a hospital with unique challenges as multiple co morbid illnesses—may be complex to manage
2. High pill burden and toxicities/interactions of drugs
3. Identifying treatment supporter AND handing patients to the next level of care for follow up.
4. Ethical issues: Difficulty in getting patients cooperation/consent and need to involve family.
5. Controversies around disease specific management guidelines eg. CCM/TB

When should we treat CCM with ART?

CROI 2008; Abstract 1010

• Prospective evaluation in Botswana of patients admitted with CM and those with IRIS CM (included only those with no prior episode of CM prior to ART) and comparison with pre-ART patients with CM.
• Mortality during inpatient therapy differed =patient presented with IRIS (8%) vs those not yet initiated ART (21%).
• CM IRIS may not be highly lethal, potentially supporting early initiation of ART in CM


Initiate ART between 2 and 4 weeks after starting amphotericin-based treatment. = a reasonable approach until ongoing trials provide more information about the best way to stagger these two lifesaving therapies.

Treatment with amphotericin had to be combined with the management of raised intracranial pressure.


TB/HIV Coinfection...

- Are we starting ART early enough?

- Are we starting TB therapy early enough?

Reducing Mortality in Seriously-ill Patients with HIV and Smear-negative Pulmonary Tuberculosis, KwaZulu-Natal, South Africa...

CDC/MRC/McCords/St Marys hosp....Holtz,Rustomjee,Sunpath,Ross

Presented at SA TB Conference 2010.
Diagnostic utility in an **WHO algorithm cohort** compared to an **observed standard practice cohort** in patients admitted to three hospitals in KwaZulu-Natal, South Africa.

**Inclusion criteria** were age ≥ 15 years, HIV-infection, signs of being clinically seriously-ill, cough ≥ 2 weeks, radiographic abnormalities consistent with TB, and at least two negative sputum smears.

Screened 6,196 seriously-ill patients and enrolled 338 HIV-infected SNPTB suspects for **the standard practice cohort**, and screened 3,424 seriously-ill patients and enrolled 187 SNPTB suspects for the **algorithm cohort**.
Results ...

- Proportion on **antiretrovirals**, 17% versus 15%, respectively \((P = 0.61)\).

- **Seven days after admission**, 27% \((50/187)\) of algorithm patients were still hospitalized, compared to 38% \((130/338)\) of standard practice patients \((\text{Risk ratio [RR]} \ 0.70, \ 95\% \ 	ext{Confidence Interval [CI]} \ 0.53–0.91)\).

- **Eight weeks after admission**, 83% \((156/187)\) of algorithm patients were still alive, compared to 68% \((230/338)\) of standard practice patients \((\text{RR} \ 1.23, \ 95\% \ 	ext{CI} \ 1.11-1.35)\).

Start TB treatment soon after admission

Only 47% of the standard practice patients were given anti-tuberculosis treatment.

The WHO algorithm had a statistically significant impact on not only lowering the risk of hospitalization at 7 days after admission by 30%, but also significantly improving the “risk” of survival at 8 weeks after admission by 23%.

- Early integration arm (within the first 2 months of TB treatment)
- Late integration arm (after completing the 2 months intensive phase of TB treatment. )
- Mortality rate of 11.6 per 100 person-years in the sequential arm compared to the mortality rate of 5.1 per 100 person-years in the integrated arms.
SAPIT...

- Recommended starting ART early (within 2 months) after initiation of anti tuberculosis treatment irrespective of CD4 count.

- Many patients are admitted to the wards with disseminated TB and will be greatly benefited from an inpatient ART programme.\(^5\)
A total of 661 HIV-infected, ART-naive patients with smear-positive TB and CD4 counts <200 cells/mm³ (median, 25 cells/mm³) were randomized to initiate efavirenz + d4T + 3TC either 2 weeks or 8 weeks after starting a standard four-drug regimen for TB.

**At 1 year, overall mortality was 34% lower in the early-ART group than in the late-ART group,**

A multivariate analysis confirmed that late receipt of ART was an independent predictor of death.

IRIS occurred more than twice as often in the early-ART group but was manageable in most patients.

Among survivors, the virologic efficacy of ART was excellent in both groups.
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BEST PRACTICE MODELS... Background

1. SUBACUTE CARE WARD/ "STEP DOWN CARE " UNITS --LINKED TO AN ACUTE CARE MEDICAL WARD /HOSPITAL

2. Multidisciplinary teams in the acute care wards that help expedite ART initiation – preparation and follow up
Case presentation

- 28 Year Old, HM
- 17/06 Pregnant – 20/40
- CD4 count = 25
- P/W – LOW, cough x 3/52
- Sputum for AFB - negative
- Had gen cutaneous K S lesions
- Cervical L N
- Extensive vaginal warts
Ref to PMTCT
RPR – Pos (1 : 1) FTA Abs – positive
Treated for late syphilis
CXR -(R) upper zone consolidation and
(R) Pleural effusion
Diagnostic tap failed
Started on empiric TB treatment at presentation to PMTCT
Gynae wards

- c/o – wheeze & obstructive symptoms with stridor
- CXR – No improvement – suspect Pulm KS –
- Started on ARVs 11.07.2008 – D4t/3TC/NVP
- **Sent to Siyaphila**
- 24/40 gestation – wheezing and Dyspnoeic
- Positive skin biopsy for KS –
Oncology – needs bronchoscopy
Exclude other infection by pleural tap.
18.08.2008 – Tracheostomy at IALCH bec of upper airway obstruction
Progressive dyspnoea. Sent back to acute care wards
Had spontaneous pre term labour at 30 wk gestation
Terminal care

- BIOPSY - VALLECCULAR LESION = CONFIRM KS

- PROGRESSIVE DYSPNOEA and GREAT ANGUISH OVER IMPENDING DEATH

- MORPHINE CONTINUED TILL DEMISE ON 20 SEPTEMBER (3 months after admission)

- FULLY SUPPORTED THROUGHOUT BY THE INTERDISCIPLINARY TEAM OF CLINICIANS, PSYCHOSOCIAL AND SPIRITUAL CARE TEAMS,
Mc Cord- Siyaphila (SYP) - in patient unit for subacute care and chronic care
Opportunities for care of PLWHA among those admitted to an inpatient care unit.

1) Multisystem disorders with variable presentations create indistinct boundaries between cure and palliation.

2) Higher proportion of emotive issues - like sexuality, reproduction guilt, loss of vitality, loss of productivity and death take time to sort out
HIV palliative care: A paradigm shift

**Former Allocation of Resources**

- Active disease-specific Rx
- Palliative Rx

**Current Allocation of Resources in Developed Countries**

- Active disease-specific Rx
- Palliative Rx

**Proposed Allocation of Resources in Developing Countries**

- Active disease-specific Rx
- Palliative Rx

Source: U.S. Department of Health and Human Services - Palliative Care in Resource Poor Settings
SIYAPHILA HEALTHCARE

- **Clinical Care**: Providing clinical care to restore and maintains the immune status and mitigate the physical consequences related to HIV/AIDS disease. A *key component is initiating patients on ART*.

- **Spiritual Care**: A team competent in spiritual care addresses the major life events that cause people living with HIV/AIDS to question themselves, their purpose and their meaning in life.
• **Psychological Care:** A psychologist and visiting psychiatrist addresses the non-physical suffering of people living with HIV/AIDS and that their family members. The team assesses cognitive disorders and AIDS related dementia prior to starting ART and again after two months of therapy.

• **Social Care:** The social workers team assists individuals and family members in maintaining linkages to and use of care, preventing HIV infection and ensuring adherence to treatment. This also includes provision of support group services.

• **Physical Rehabilitation:** Physical therapy and nutritional interventions are the key elements of successful rehabilitation.
End of Life Care: The purpose of end of life care is to ensure good quality of life through symptom management and supportive care through the patient’s terminal phase of HIV/AIDS illness and bereavement counseling for the family.

HIV Counseling Services: A team of dedicated HIV counselors is involved in ART literacy training before and after ART initiation.

Community Support and Follow up: Patients who do not initiate ART at Siyaphila are followed up by linking them to different care providers and programmes in the area of their residence.
TERMINAL CARE ...

- End stage **renal disease** with multiple co-morbidities
- Advanced s **malignancies** (Kaposi’s sarcoma. Lymphoma, cancer of the Cervix)
- Intractable **cardiac failure** with cardiomyopathy; pulmonary hypertension with poor prognosis
- Severe **bacterial infections**/ surgical sepsis
- Other patients – Team discussion / discussion with specialist care clinicians
Unanswered questions:

1. What is the most practical way to “fast-track” patients for expedited ART in resource-limited settings? Syphilis experience at McCord Hospital

2. What are the long-term outcomes for patients who receive early ART during OI therapy?
Case Management and Clinical Outcomes of Patients Living with HIV/AIDS and Admitted to a District State-aided Hospital in Durban, South Africa in 2006-2007

H.Sunpath / C.Edwin / Murphy...
Aim

To describe the clinical conditions, inpatient case management and outcomes of patients that received ART with those not on ART (ART and non-ART cohort)

To use the observations together with evidence in the literature as a basis to discuss best practice models of care for SUBACUTE /STEP DOWN CARE.
Objectives

- Measure **inpatient prevalence** of AIDS defining conditions in the subacute care facility.

- Determine the **duration of stay and time taken** for different stages of care for different clinical conditions viz. admission, discharge and ART start times.

- Determine the **clinical outcomes** of patients with different clinical conditions a
Mc Cord- Siyaphila(SYP)- in patient unit for subacute care and chronic care
432 Referred for immediate ART

405 Evaluated for immediate ART

32 ART -experienced

171 Patients initiated early ART

160 Survived to hospital discharge

11 Died during early inpatient ART

234 Patients did not initiate early ART

179 Survived to hospital discharge

55 Died prior to discharge
<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>33%</td>
</tr>
<tr>
<td>Extra pulmonary</td>
<td>29%</td>
</tr>
<tr>
<td>Cryptococcus meningitis</td>
<td>17%</td>
</tr>
<tr>
<td>Pneumocystis jirovecii pneumonia</td>
<td>7%</td>
</tr>
<tr>
<td>Chronic diarrhoea (&gt;14 days)</td>
<td>2%</td>
</tr>
<tr>
<td>Toxoplasmosis gondii</td>
<td>1%</td>
</tr>
<tr>
<td>HIV associated nephropathy</td>
<td>1%</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
<td>1%</td>
</tr>
<tr>
<td>Other</td>
<td>0%</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>62%</td>
</tr>
</tbody>
</table>

*Acute Opportunistic Infection or Complication*
Table: Outcomes by opportunistic infection among patients enrolled in the subacute ward from December 2006 and November 2007 for early inpatient ART

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>N</th>
<th>Mortality during ART initiation no. (%)</th>
<th>IRIS event No. (%)</th>
<th>Time from admission to ART (median/mean days) *</th>
<th>Time from admission to discharge (median/mean days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All infections</td>
<td>162</td>
<td>8 (5%)</td>
<td>7 (4%)</td>
<td>14 / 16</td>
<td>18 / 21</td>
</tr>
<tr>
<td>Pulmonary tuberculosis</td>
<td>60</td>
<td>3 (5%)</td>
<td>2 (3%)</td>
<td>13 / 15</td>
<td>17 / 20</td>
</tr>
<tr>
<td>Extra pulmonary TB</td>
<td>28</td>
<td>1 (4%)</td>
<td>2 (7%)</td>
<td>12 / 15</td>
<td>17 / 19</td>
</tr>
<tr>
<td>Tuberculous meningitis</td>
<td>22</td>
<td>2 (9%)</td>
<td>1 (4%)</td>
<td>14 / 18</td>
<td>18 / 21</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>23</td>
<td>2 (9%)</td>
<td>2 (9%)</td>
<td>18 / 19</td>
<td>22 / 24</td>
</tr>
<tr>
<td><em>P. jirovecii</em> pneumonia</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>16 / 16</td>
<td>19 / 21</td>
</tr>
<tr>
<td>Chronic diarrhoea</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>16 / 16</td>
<td>19 / 20</td>
</tr>
<tr>
<td><em>Toxoplasmosis gondii</em></td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>21 / 21</td>
<td>25 / 25</td>
</tr>
<tr>
<td>Other infection</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>13 / 13</td>
<td>18 / 17</td>
</tr>
<tr>
<td>Acute OI</td>
<td>no. (%)</td>
<td>ART(171)</td>
<td>nonART(234)</td>
<td></td>
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<tr>
<td><em>Tuberculosis</em></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>60 (35)</td>
<td>80 (34%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extra pulmonary</td>
<td>28 (16)</td>
<td>47 (20%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cryptococcus meningitis</td>
<td>23 (14)</td>
<td>46 (20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumocystis pneumonia</td>
<td>15 (9)</td>
<td>18 (7)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Chronic diarrhea (&gt;14 days)</td>
<td>6 (4)</td>
<td>7 (3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxoplasmosis gondii</td>
<td>5 (3)</td>
<td>4 (2)</td>
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<td></td>
</tr>
<tr>
<td>HIV associated nephropathy</td>
<td>3 (1)</td>
<td>3 (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4 (2)</td>
<td>3 (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N/S</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean baseline CD4 cells/uL) 55.0 84.0 (<0.01)

Early mortality prior to discharge 11 (6) 55 (24) <0.001
In Summary...

- Baseline characteristics in both groups were similar. The groups had similar presenting opportunistic infections.
- **Mortality before discharge from the Siyaphila was four times lower in the ART cohort** (6%) compared to the non-ART cohort (24%) \( (p< 0.05) \)
- All 3 **deaths from PCP** occurred in the non-ART cohort. None of the patients who were started on PCP treatment and ART during the inpatient stay died
Mortality - cryptococcal meningitis

- Cryptococcal meningitis was the leading cause of death (15 out of 55 deaths; 26%) in the non-ART cohort.
- 15 out of 43 patients with cryptococcal meningitis in the non-ART cohort (48%) died.
- 2 of the 23 patients with cryptococcal meningitis in the ART cohort (8.6%) died.
Retrospective analysis of the ART programme – inpatient initiation and clinic follow up
382 Initiated immediate ART

- 97 Died during 24-week follow-up
  - 22 Died during inpatient ART initiation
  - 80 Died after ART initiation and discharge
  - 19 Changed service provider before 24 weeks
- 19 Were lost to follow-up
- 247 Assessed at 24 weeks
### Clinical characteristics

<table>
<thead>
<tr>
<th>Median baseline CD4 count (cells/ul) [IQR]</th>
<th>33 [12-78]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline CD4 cell count category (%)</td>
<td></td>
</tr>
<tr>
<td>0-49 cells/ul</td>
<td>224 (62)</td>
</tr>
<tr>
<td>50-99 cells/ul</td>
<td>65 (18)</td>
</tr>
<tr>
<td>100-199 cells/ul</td>
<td>52 (15)</td>
</tr>
<tr>
<td>200-349 cells/ul</td>
<td>18 (5)</td>
</tr>
</tbody>
</table>

#### Acute OI — no. (%)

- Pulmonary tuberculosis | 147 (39)
- Extrapulmonary tuberculosis (including meningitis) | 96 (25)
- Cryptococcal meningitis | 40 (10)
- Chronic diarrhea (>14 days) | 35 (9)
- Bacterial pneumonia | 11 (3)
- *Toxoplasmosis gondii* | 9 (2)
- *Pneumocystis jirovecii* pneumonia | 5 (1)
- HIV-associated kidney disease | 4 (1)
- Other cause for admission in ART-eligible patient | 20 (5)
- Undiagnosed OI | 15 (3)
### Timing of ART initiation

<table>
<thead>
<tr>
<th>Days from admission with OI to ART by category, no. (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-7 days</td>
<td>181 (47)</td>
</tr>
<tr>
<td>8-14 days</td>
<td>105 (26)</td>
</tr>
<tr>
<td>15-21 days</td>
<td>62 (16)</td>
</tr>
<tr>
<td>&gt;21 days</td>
<td>14 [11-18]</td>
</tr>
</tbody>
</table>

#### 24-week Virologic Outcomes

<table>
<thead>
<tr>
<th>Intent-to-treat (ITT) viral suppression &lt;400 c/mL no., (%)</th>
<th>206 (57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>As-treated (AT) viral suppression &lt;400 c/mL no., (%)</td>
<td>206 (93)</td>
</tr>
</tbody>
</table>

#### 24-week Immunologic Outcomes

| Median CD4 count improvement (cells/ul) (IQR) | 100 (48-188) |

#### 24-week Vital Outcomes

<table>
<thead>
<tr>
<th>Overall mortality (%)</th>
<th>97 (25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality prior to discharge in the step-down facility</td>
<td>20/102</td>
</tr>
<tr>
<td>Mortality after discharge</td>
<td>77/102</td>
</tr>
<tr>
<td>Among patients who died, median days to death, (IQR)</td>
<td>33 (9-95)</td>
</tr>
</tbody>
</table>

#### 24-week Program Outcomes

<table>
<thead>
<tr>
<th>Loss to follow-up (%)</th>
<th>19 (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changed service provider (%)</td>
<td>19 (5)</td>
</tr>
</tbody>
</table>

### Serious IRIS Events

<table>
<thead>
<tr>
<th>IRIS events, no. (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>14/17</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>2/17</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>1/17</td>
</tr>
<tr>
<td>IRIS-associated deaths</td>
<td>5 (1)</td>
</tr>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----</td>
</tr>
<tr>
<td><strong>All subjects</strong></td>
<td>382</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>184</td>
</tr>
<tr>
<td>Male</td>
<td>198</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>≤ 39 years</td>
<td>234</td>
</tr>
<tr>
<td>&gt; 40 years</td>
<td>148</td>
</tr>
<tr>
<td><strong>Admitting opportunistic infection</strong></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>342</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>40</td>
</tr>
<tr>
<td><strong>Initial CD cell count</strong></td>
<td></td>
</tr>
<tr>
<td>0-49 cells/ul</td>
<td>224</td>
</tr>
<tr>
<td>≥ 50 cells/ul</td>
<td>135</td>
</tr>
<tr>
<td><strong>IRIS in initial six months</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>365</td>
</tr>
<tr>
<td>Present</td>
<td>17</td>
</tr>
<tr>
<td><strong>Days to ART initiation</strong></td>
<td></td>
</tr>
<tr>
<td>≤ 21</td>
<td>301</td>
</tr>
<tr>
<td>&gt; 21</td>
<td>62</td>
</tr>
</tbody>
</table>
In Summary...

- The median number of days to early ART after initial treatment for OI was 14 (IQR 11-18).
- During 24 weeks of follow-up, 4% experienced a serious IRIS event; 1% (n=5) experienced an IRIS-associated death.
- At 24 weeks, as-treated and intention-to-treat virologic suppression was 57 and 93% respectively
- The median improvement in CD4 cell count was 100 cells/ul.
Conclusions...mortality at six months doubled with ART initiation >3 weeks

- The 24-week mortality was 25% and loss to follow-up was 5%.

- In this clinically advanced population, independently associated with early mortality was time to ART initiation of ≥21 days after OI (OR: 2.1, 95% CI: 1.2-4.0, P=0.016) compared with <21 days.
Other reports of inpatient ART care


Antiretroviral therapy could even be commenced in the sickest patients as demonstrated in a retrospective study conducted in Brazil. PCP was the commonest infection. Mortality rates were high both in the ICU (55%) and six months after admission (69%).

After adjustment for potential confounders, the use of ART in the ICU (whether initiated then or previously) was associated with a 50% reduction in 6-month mortality; the benefit was statistically significant only if ART was used within the first 4 days after ICU admission.
ICU

Mortality rates were high both in the ICU (55%) and six months after admission (69%). After adjustment for potential confounders, the use of ART in the ICU (whether initiated then or previously) was associated with a 50% reduction in 6-month mortality.

The benefit was statistically significant only if ART was used within the first 4 days after ICU admission.
CONCLUSIONS

- We have ART freely available IN EVERY HOSPITAL, and the potential to save lives daily
- We know what OIs are prevalent in the wards of SA hospitals and we have antimicrobials for their treatment
- We need clinicians trained in the intergration of care even at specialist care centres.
- We need beds and a supportive team to take the patients onto ART with good treatment support and follow up
References

- Clifford DB, Yiannoutsos C, Glicksman DM et. al. HAART improves prognosis in HIV-associated progressive multifocal leukoencephalopathy.
References

- Foley, K et al. U.S. Palliative Care in Resource Poor Settings. Department of Health and Human Services – Health Resources and Service Administration, Clinical Guide to Supportive and Palliative Care for HIV/AIDS 2003 Ed.


- World Heath Organization website (www.who.org)
Acknowledgements

• The MCH management – for making the care of the most ill patients a priority in the wards.
• Dr. Christina Edwin and the interdisciplinary team at the MCH-Siyaphila programme for saving innumerable lives.
• The patients who have been our precious inspiration
• To all our colleagues in the HIV Medicine fraternity in SA and Internationally who have supported us academically and by their own example.
• To Loving South Africa – for their valuable funds that help us extend the stay of some patients so that we can help them remain alive until discharge.
• The national ARV roll out programme and the 2010 guidelines!