

Advanced HIV Disease in Children

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Advanced HIV Disease in Children and Adolescents

- What do we mean by advanced HIV in children?
- How does this differ from adults?
- Burden of advanced disease in children
- Guidance and examples

A case from yesterday..

- Almost 3- month old girl presented to G-Ground at Tygerberg
- Weight -3.8kg, Birth weight 2.9kg
- DC from HHH at D2 of life
- Mom=29 years G4P2.. 2 previous early infant deaths at 4 months and 3 months, last vl-26 in 2021, CD4 157, restarted ART 1 week prior to delivery.. VL at delivery pending
- Birth PCR sent and pending when baby dc, on AZT and NVP
- Breastfeeding
- Went for health visit 6/52 post-partum at Ikhwezi Clinic

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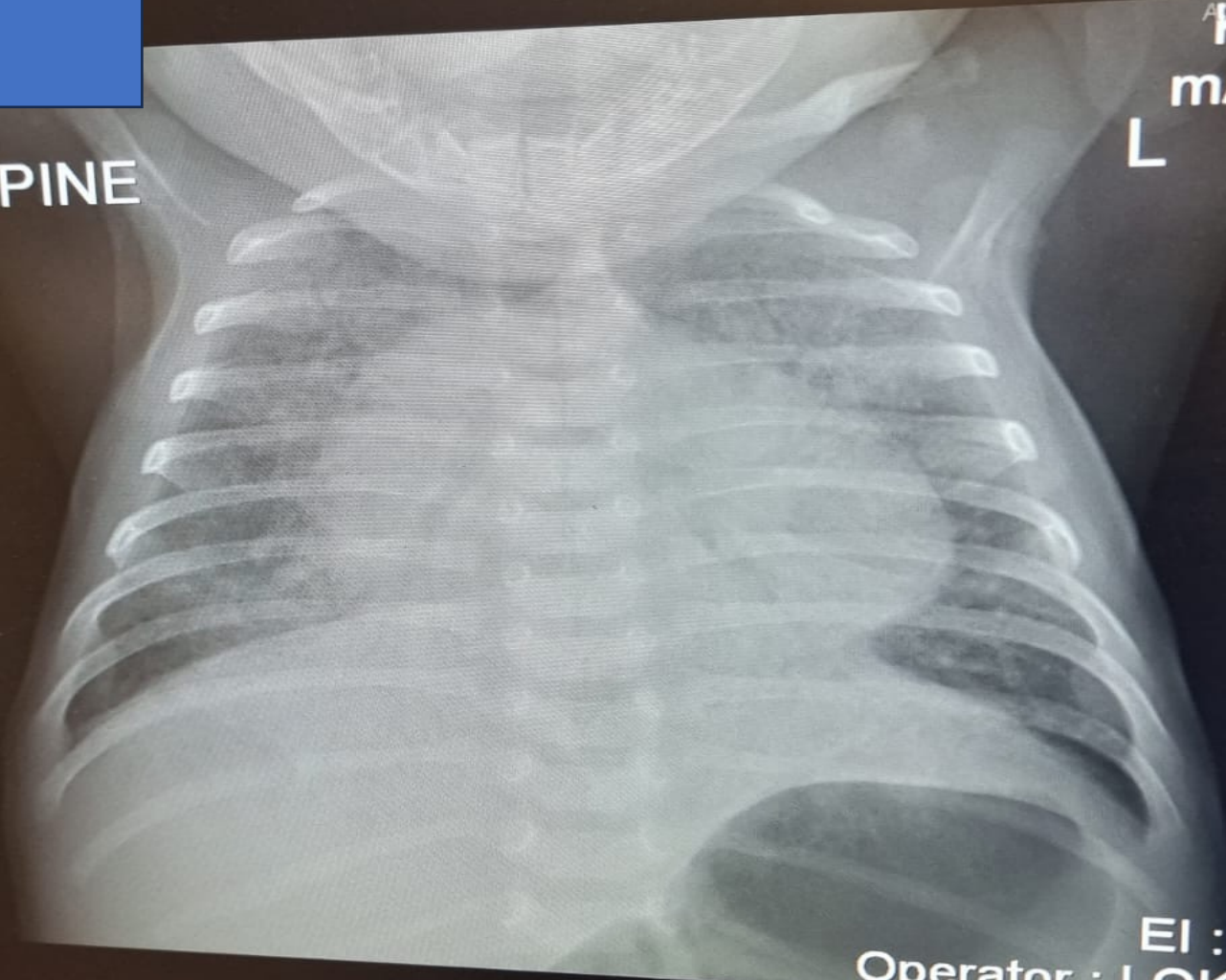
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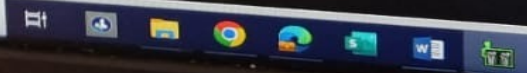
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ThinkCentre

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Advanced HIV Disease in Children and Adolescents

-Which of these children have advanced HIV disease?

- A) 3 months with severe pneumonia and CD4 count >25%
- B) 6 week growing well on +1 Z-score, CD>30%, asymptomatic, diagnosed during a PMTCT visit
- C) 2 year with moderate malnutrition and CD4 >25%
- D) 7 year on ART that presents with sores around the mouth
- E) 10 years with TB

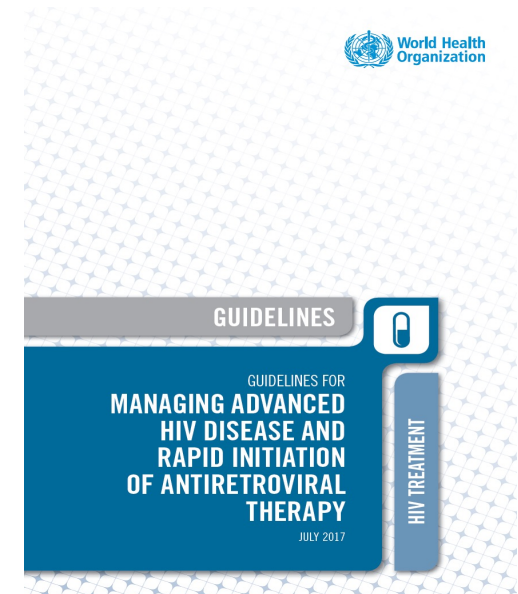
WHO guidelines for Managing Advanced HIV Disease and Rapid Initiation of ART 2017

- Advanced HIV disease is defined as CD4 count <200 cells/mm³ or WHO clinical stage 3 or 4 in children > 5 years of age
- All children <5 years old considered to have advanced disease
- Evidence that “packaged interventions” for advanced disease reduces mortality: REMSTART and REALITY

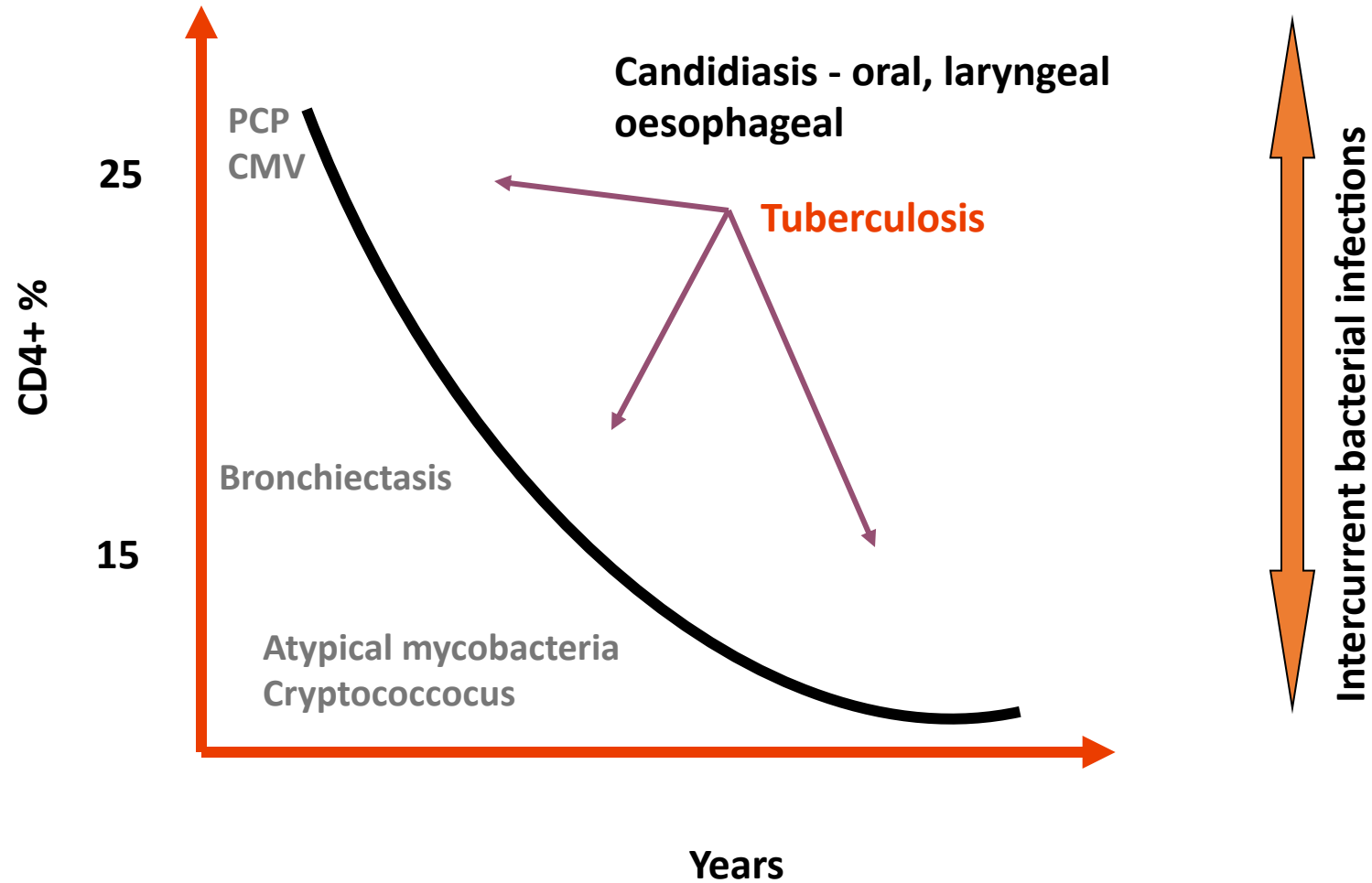
Management of advanced HIV disease

A package of interventions including screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation and intensified adherence support interventions should be offered to everyone presenting with advanced HIV disease.

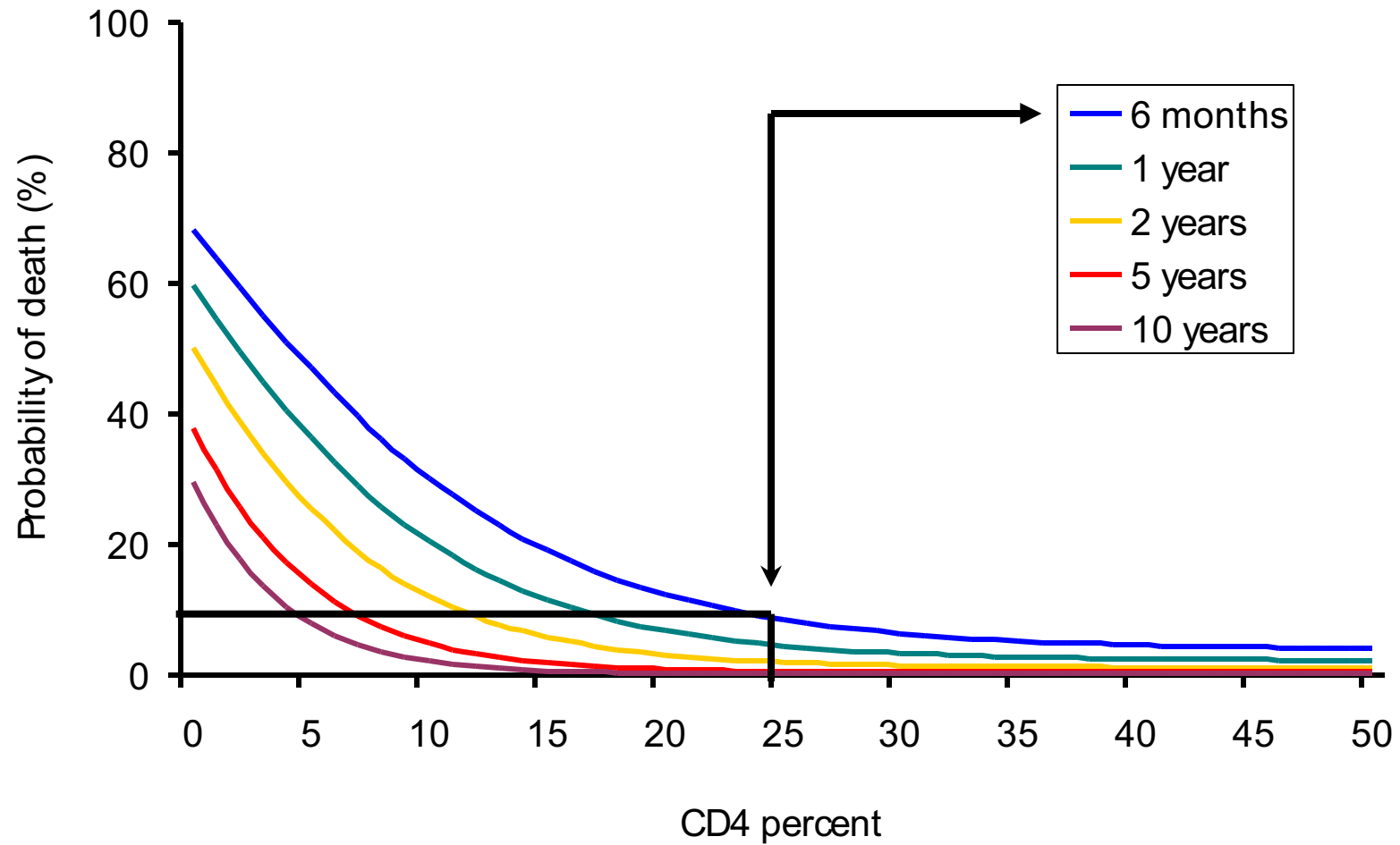
(Strong recommendation, moderate-quality evidence)



CD4% in infants with HIV



Probability of Death Within 12 Months



WHO Staging and immunological classification

- **Stage 1:** The child is generally well (asymptomatic).
- **Stage 2:** Skin rashes and “minor” infections.
- **Stage 3:** More serious infections. PTB, Oral thrush, CLD, FBC abnormalities
- **Stage 4:** OI, Cancer, Permanent organ damage due to HIV virus

SEVERITY	AGE		
	<12 Months	13-59 Months	5 + Years
None	>35%	>25%	>500 Cells/mL
Mild	25-34%	20-24%	350-499 Cell/mL
Advanced	20-24%	15-19%	200-349 Cells/mL
Severe	<20%	<15%	<200 Cells/mL

Advanced HIV disease

Clinical Staging

- **Stage 1:** The child is generally well (asymptomatic).
- **Stage 2:** Skin rashes and “minor” infections.
- **Stage 3:** More serious infections. PTB, Oral thrush, CLD, FBC abnormalities
- **Stage 4:** OI, Cancer, Permanent organ damage due to HIV virus

Advanced disease

	Clinical	CD4
> 5 years	All	All
< 5 years	3 and 4	< 200 cells

Causes of mortality in HIV+ adults and children admitted to hospital

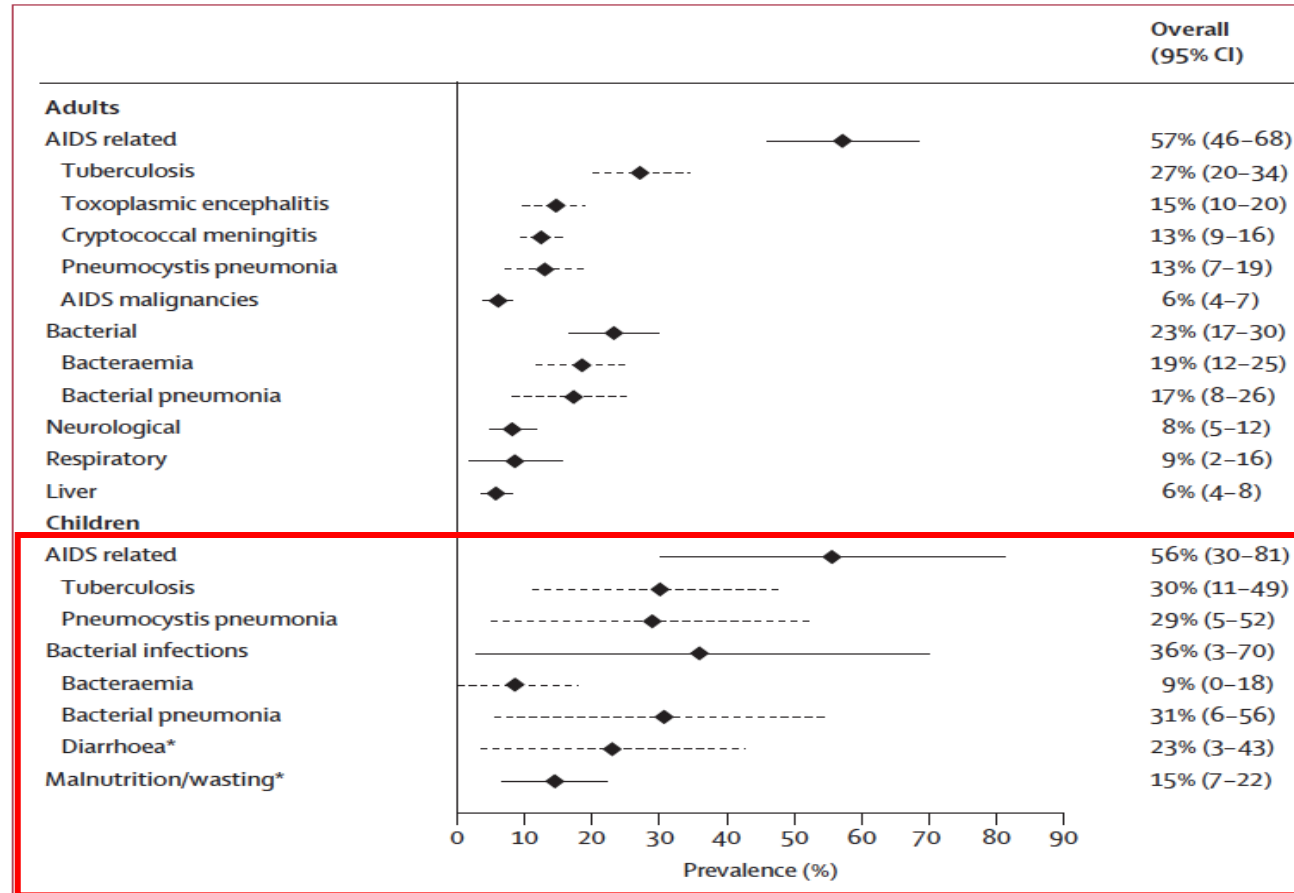


Figure 4: Causes of mortality in HIV-positive adults and children admitted to hospital
Dotted lines show specific conditions within categories. *Data from the Africa region only.

Mortality in children with HIV

Mortality risk among children < 5 years old living with HIV on ART

PEPFAR data

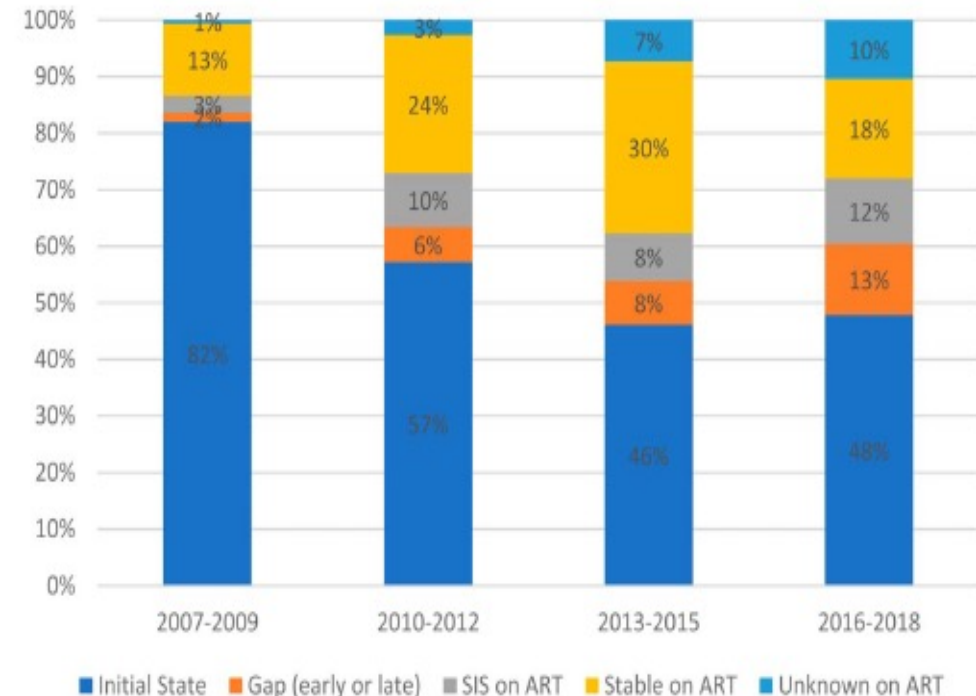
- CLHIV < 1 y on ART were more likely to die compared to PLHIV on ART 5-14 y CMR 7.6
- CLHIV 1-4 y on ART were also more likely to die compared to those 5-14 y (CMR 4.2, range 2.9-5.0),
- Average VLS among CLHIV < 1 and CLHIV 1-4 y were 78% and 72%, respectively, compared to 84%, 94%, and 96% of those 5-14, 15-49 and ≥ 50 y

Morbidity in children living with HIV

Hospitalization among infants who initiate antiretroviral therapy before 3 months of age

- Infants that started ART <3 months in Western Cape, SA 2013-2017
- 840 infants <3 months
- 69% hospitalized
- 36% - more than 1 hospitalization
- 41% - lower respiratory tract infection
- 23% - gastroenteritis

Ongoing High Prevalence of Severe Immune Suppression Among Children in South Africa



Definition of advanced disease in children: further articulated in 2020 technical brief



TECHNICAL BRIEF – JULY 2020

PACKAGE OF CARE FOR CHILDREN AND ADOLESCENTS WITH ADVANCED HIV DISEASE: **STOP AIDS**

Children > 5 years:

- WHO stage 3 or 4 or a CD4 cell count <200 cells/mm³

Children < 5 years:

- have advanced HIV disease
- “Although children younger than five years are defined as having advanced disease at presentation, those who have been receiving ART > 1 year and who are clinically stable should not be considered to have advanced disease and should be eligible for multi-month dispensing”

Box 1. Screen, Treat, Optimize and Prevent AIDS

Screen*

TB

- Screen for TB using a clinical algorithm^b followed by X-ray when indicated and if available
- Use the following diagnostic tests to confirm TB as applicable:^c
 - Rapid molecular diagnostic (Xpert® MTB/RIF or Ultra) on (induced) sputum, stool, gastric aspirate or nasopharyngeal aspirate or other extrapulmonary samples if relevant
 - Lateral flow urine lipoarabinomannan (LF-LAM) assay^d

Cryptococcal infection among adolescents

- Serum or plasma or blood cryptococcal antigen screening followed by lumbar puncture if positive or symptomatic

Malnutrition

- Weight-for-height
- Height-for-age
- Mid-upper arm circumference among children 2–5 years old

Treat

TB, severe pneumonia, severe bacterial infections, cryptococcal meningitis and severe acute malnutrition according to WHO guidelines

Optimize

Rapid antiretroviral therapy start – within seven days with optimal regimens*
Antiretroviral therapy counselling

Prevent

Bacterial infections and *Pneumocystis pneumonia*
■ Co-trimoxazole prophylaxis

TB

■ TB preventive treatment

Cryptococcal meningitis among adolescents
■ Fluconazole pre-emptive therapy

Vaccinations

- Pneumococcal vaccine
- Human papillomavirus
- Measles
- BCG



* Screening refers to screening and diagnostics throughout this publication.

^b See Fig. 3 in *Guidance for national tuberculosis programmes on the management of tuberculosis in children* (9).

^c A negative test result does not exclude TB in children living with HIV in whom there is a strong clinical suspicion of TB.

^d See Table 2 and the text for recommendations.

* Unless TB or cryptococcal disease is diagnosed (10).

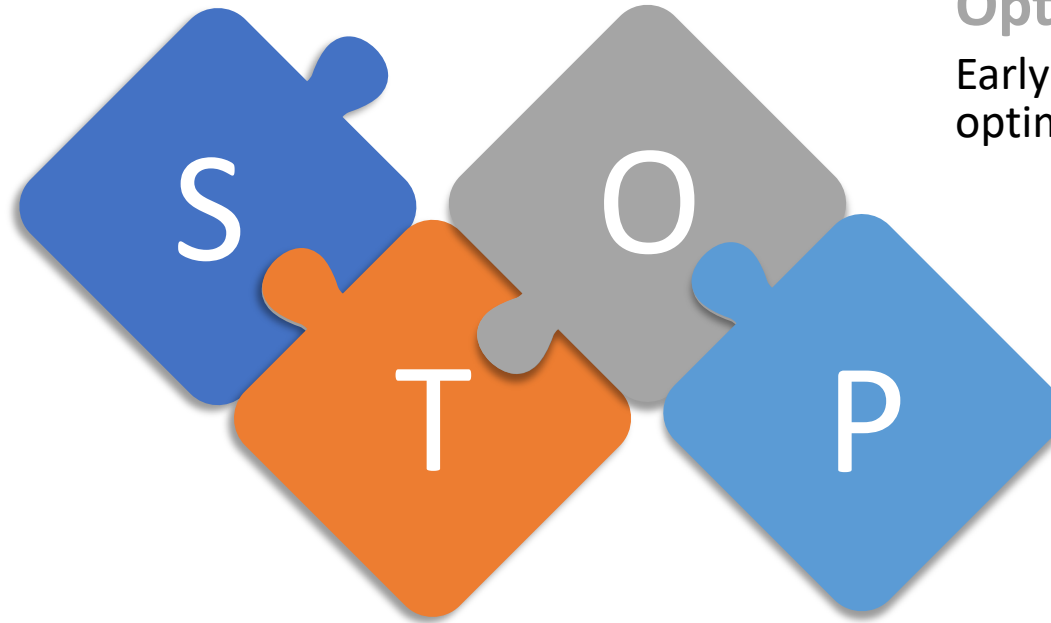
Addressing advanced HIV disease

Screen

For TB, cryptococcal disease

Treat

For TB, cryptococcal disease, severe pneumonia and blood stream infections



Optimize

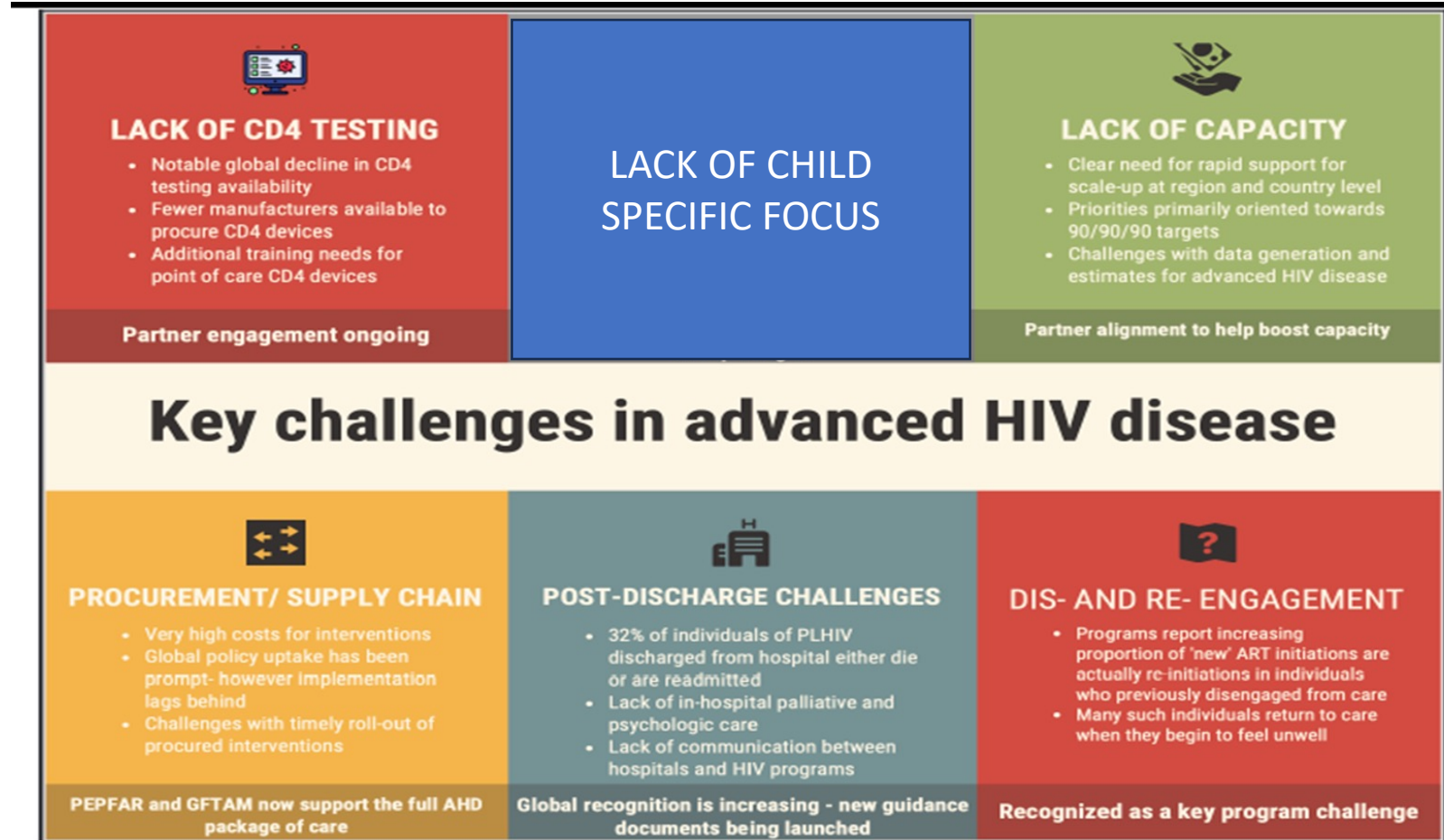
Early ART initiation within 7 days, optimal regimen, counselling

Prevent

TB, PJP, cryptococcus, pneumonia and catch-up immunizations

We need to Stop AIDS!

Challenges



Research Gaps

COMMENTARY

The hard part we often forget: providing care to children and adolescents with advanced HIV disease

- How many children die after discharge and how many are readmitted?
- Ultimate package of care not only at start but post discharge
- Diagnostics
- Treatment – do we have the right dose of valganciclovir?
 - appropriate antibiotics for resistant bacterial organisms
 - fixed dose combinations with ethambutol
- Prevention – TB vaccine, optimal TPT regimens including FDCs, prevention of bacterial infections beyond cotrimoxazole

Case 1

Age: 4 month old

Gender: male

Family circumstance: born before arrival, mom booked late in pregnancy,
2-day history of cough, blocked nose and fast breathing

Not known to be HIV positive

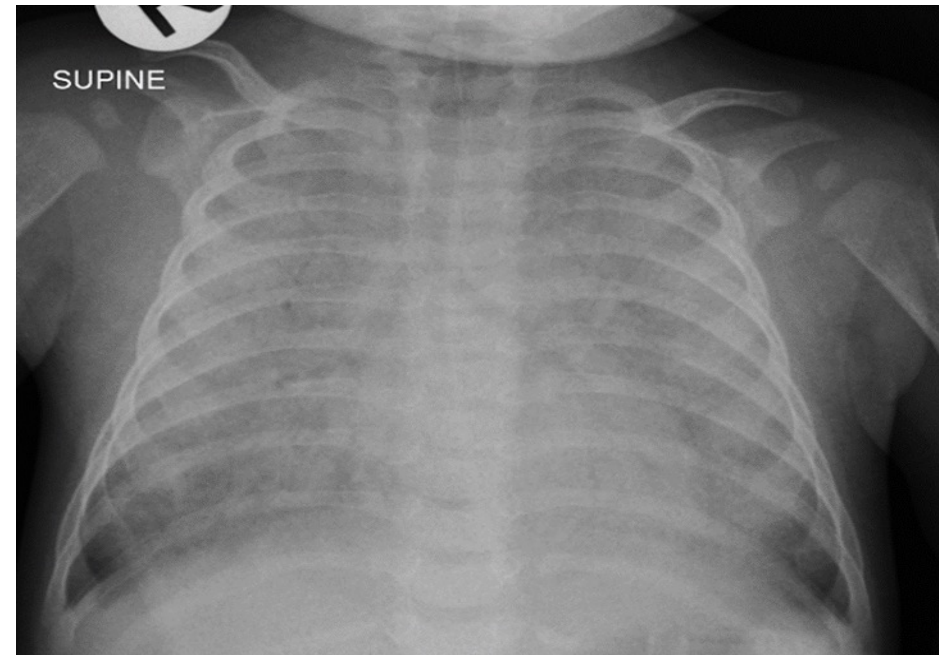
Clinical examination

Tachypnoeic

SC and IC recession

Crackles bilaterally

hepatosplenomegaly



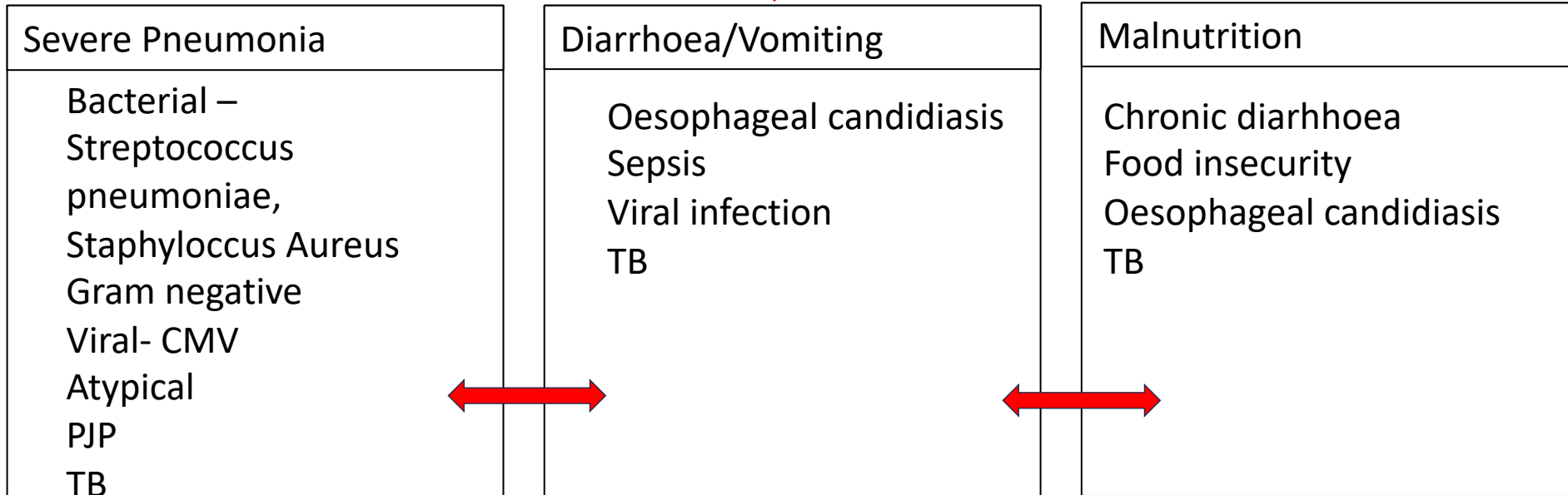
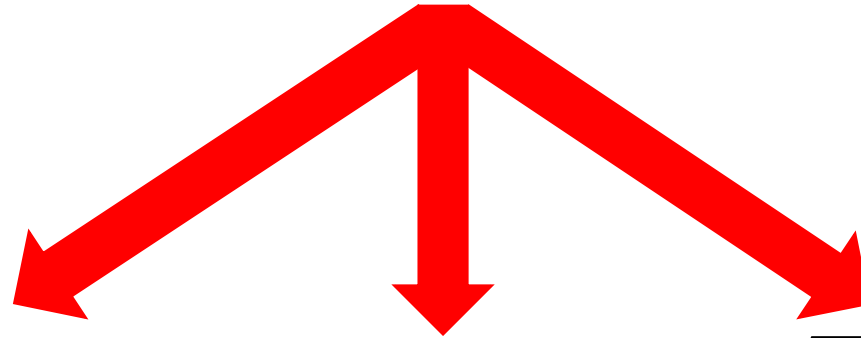
Questions

1. How would you manage this child further
2. What antibiotics if any would you start?
3. Does this child have advanced hiv disease
4. What strategies could have prevented this child from becoming so ill
5. What options do you have if the child has low saturations? (Discuss supplemental oxygen and non-invasive ventilation)



Baby of 2 – 3 months old

Undiagnosed



Case 1

- S** – early diagnosis of HIV, PJP and CMV diagnostics?
- T** – high dose cotrimoxazole, valganciclovir, prednisone, antibiotics, CPAP, invasive ventilation
- O** – early ART start
- P** – vaccinate on ART, cotrimoxazole, TPT

Key challenges

Early diagnosis of difficult to reach women and infants

Access to non-invasive ventilation like CPAP

Treatment – access to valganciclovir, steroids

Often unable to make a definitive Diagnosis of PJP but treat for polymicrobial pneumonia

Case 2: 18 month boy with chronic diarrhoea, malnutrition and fever



Clinical Evaluation and Current Challenges

Clinical presentation

Not wanting to play

Cold

Rash

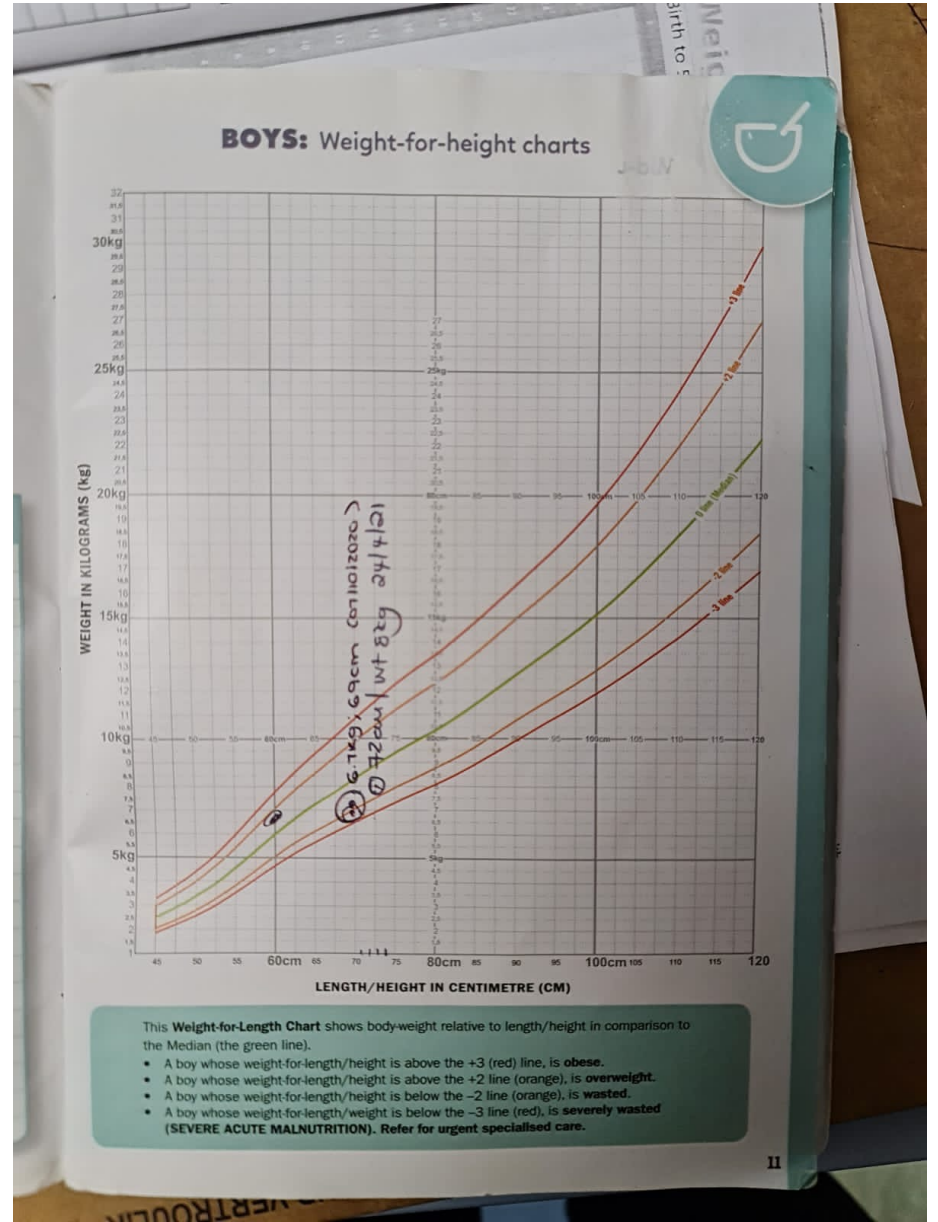
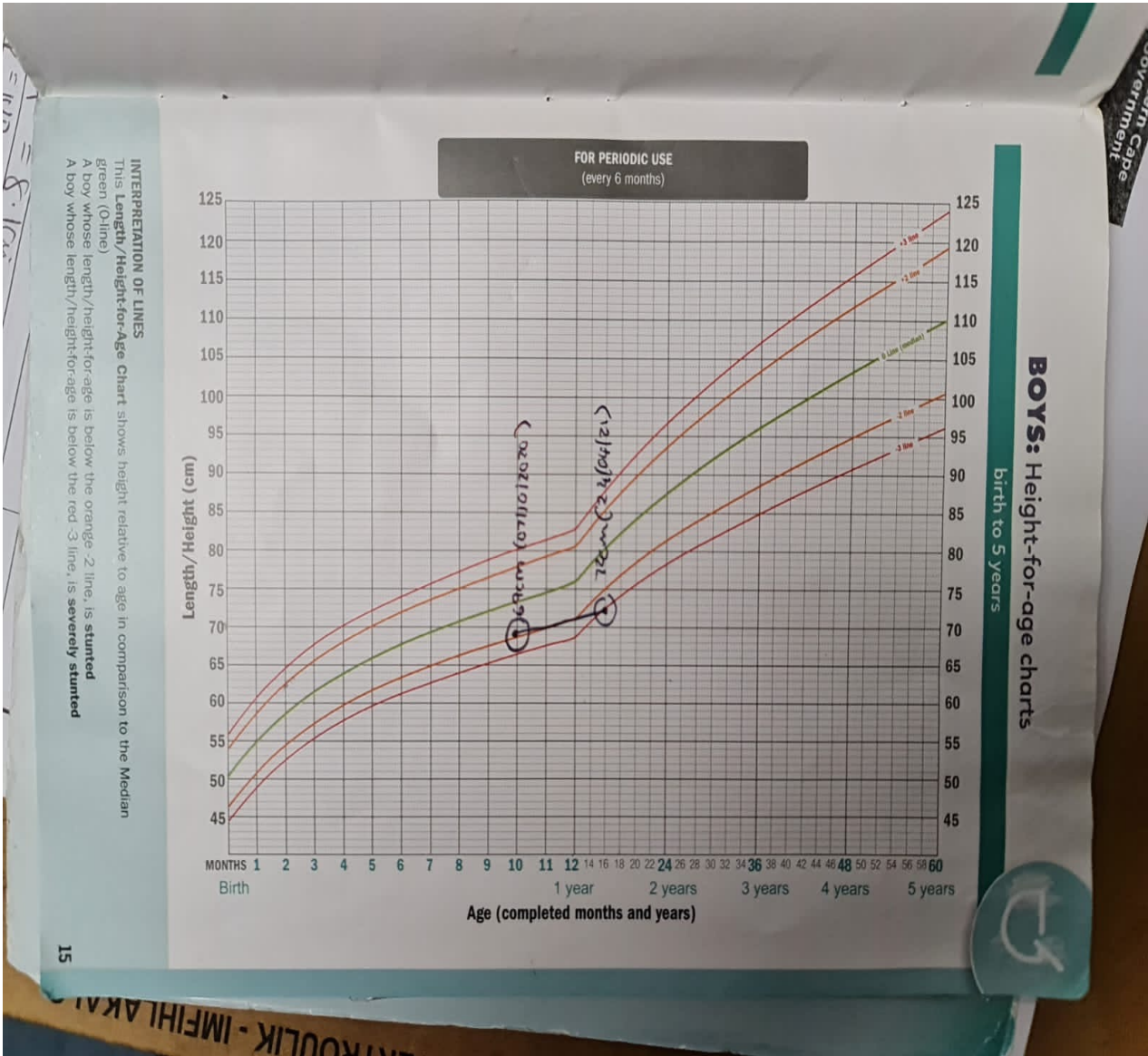
Not eating

Add weight height

Weight: 8.34kg

Height: 73.3cm

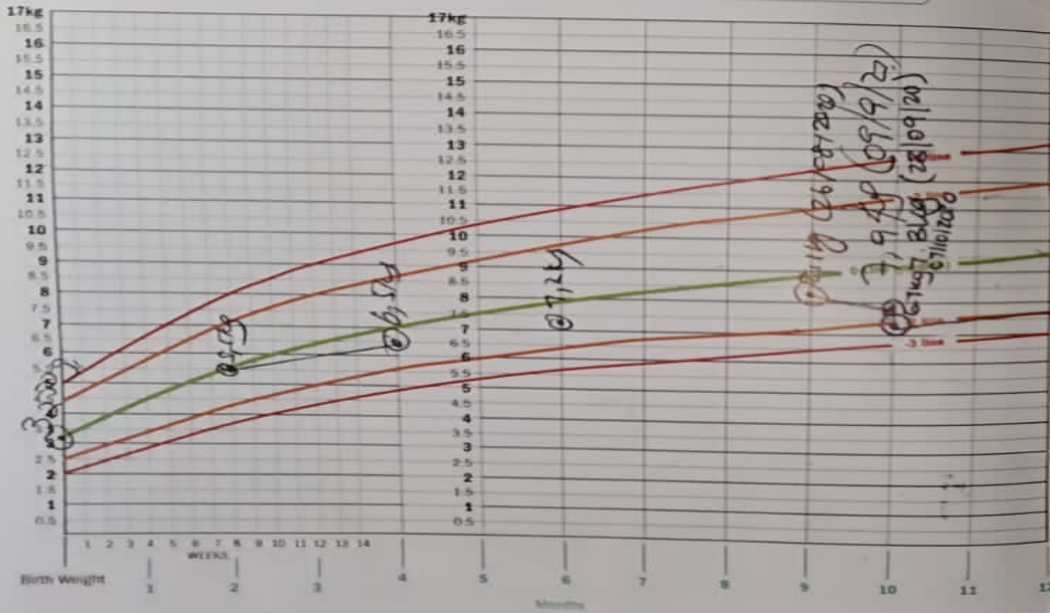
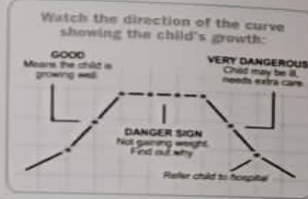
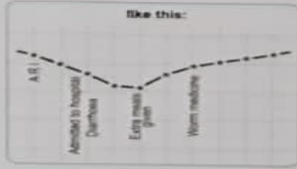
MUAC: 13.5 cm



BOYS: Weight-for-age charts

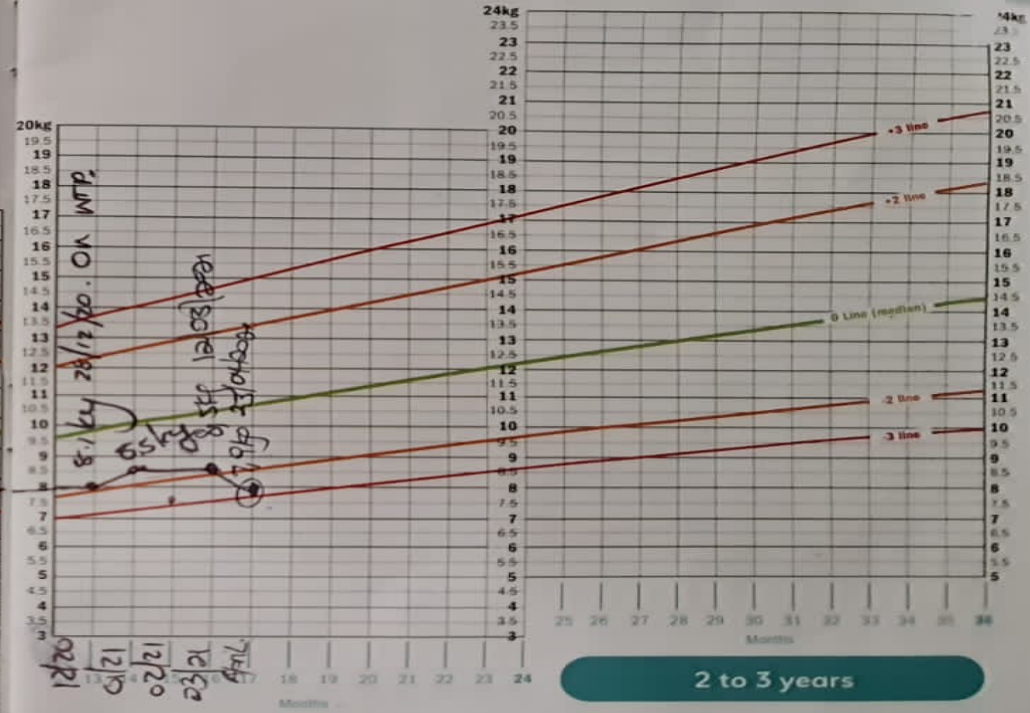
Write on the chart

Any illness e.g. diarrhoea, ARI, etc.
Admission to hospital.
Suckle introduced.
Breastfeeding stopped.
Start of next child, etc.



Birth to 1 year

BOYS: Weight-for-age charts



1 to 2 years

2 to 3 years

Interpretation of lines:

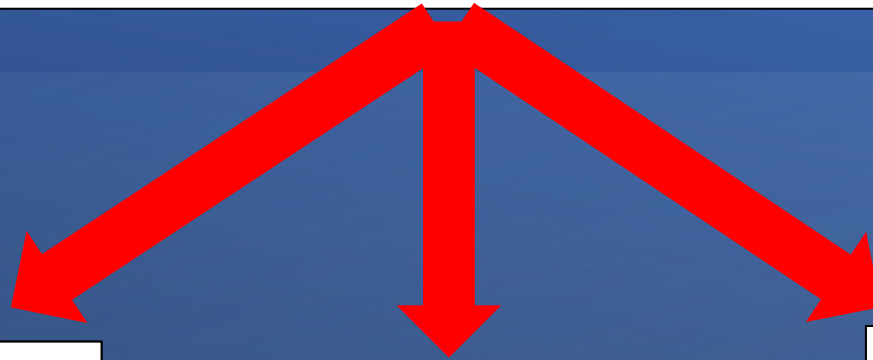
- This Weight-for-Age Chart shows body-weight relative to age in comparison to the Median (green 0-line).
- A boy whose weight-for-age is below the orange -2 line, is underweight.
- A boy whose weight-for-age is below the red -3 line, is severely underweight.
- If his line crosses a z-score line and the shift is away from the median, this may indicate a problem or risk of a problem.
- If his line shifts away from his birth trend line, this may indicate a problem or a risk of a problem.

Questions

1. How would you manage this child further-
Would you start antibiotics, if yes what empiric antibiotic therapy?
2. When would you start ART?
3. Does this child have advanced HIV disease
4. What strategies could have prevented this child from becoming so ill



The Unwell Child 1– 5 years old



Severe bacterial infection

- Older studies show high rates of bacteraemia in first 3 months on ART
- More recently 6% of children admitted with HIV and malnutrition had a +BC on admission
- HAIs :gram negative and ESBL

Tuberculosis

Malnutrition/Diarrhoea

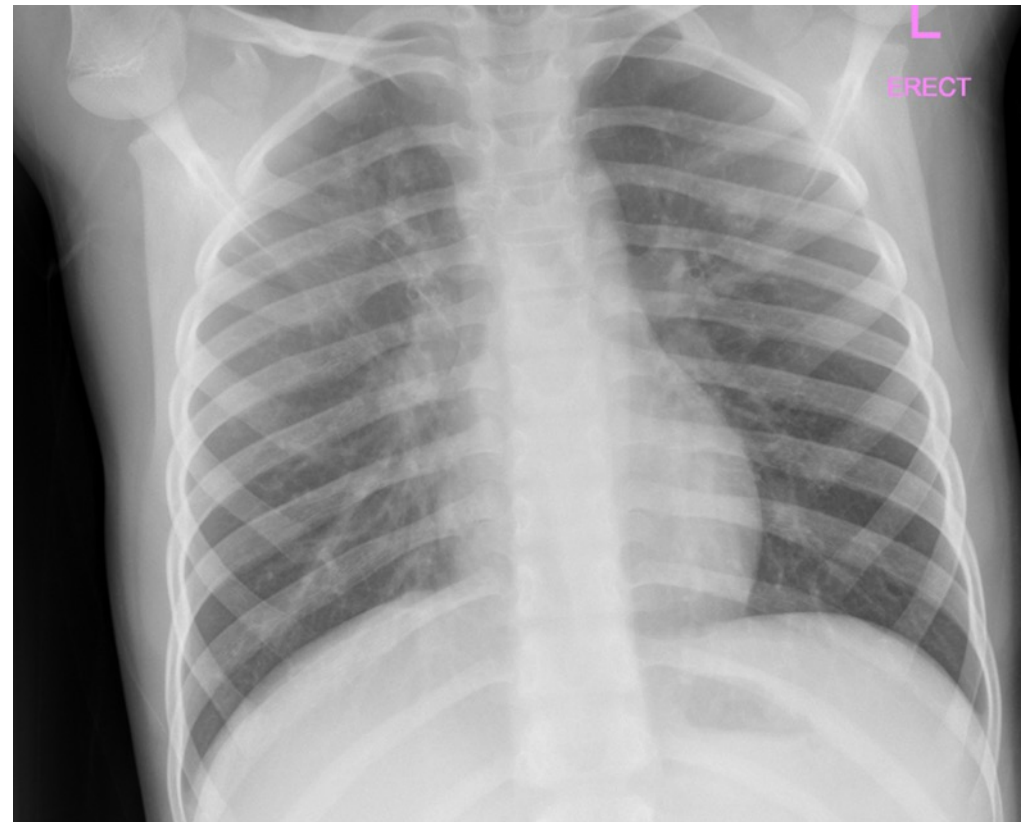
- WHO 10 steps
- RCTs in SA children showed a short delay in ART initiation resulted in faster viral suppression and improved immune recovery
- Study from Kenya can start in 48 hrs
ART initiation within 7 days

Case 2

- S** – screen for malnutrition and TB, access to blood microscopy, culture and sensitivity.
- T** – appropriate antibiotics, electrolyte management, fluid therapy, WHO 10 steps, rapid ART initiation
- O** – ongoing adherence counselling, social worker intervention
- P** – social interventions

Case 3: 11-year-old “well” boy

- Diagnosed in March 2021 at an OUTPATIENT clinic as had lost some weight
- Mom was unaware of her diagnosis
- His CD4 was 220 cells/mm³
- Screened for TB – CXR normal, sputa gene Xpert and culture negative
- Started ART April 2021, no TPT
- Presented at clinic in May 2021 with vomiting, no fever or other clinical signs



Questions

1. How tests would you request?
2. What could be happening?
3. Does this child have advanced hiv disease?
4. What strategies could have prevented this child from becoming so ill?

Case 3

CSF findings:

- Glucose 0.5
- Protein 1.53
- P=0 L=348 E=0
- Cryptococcal antigen negative
- Gene X-pert positive !
- Started on tuberculous meningitis therapy

The "Well" Older Child



IRIS

Drug toxicity

Non-adherence.....



Case 4

- 10-year-old boy weight, 24kg
- DX HIV In August 2022, started ART 5 days later
- CD4 count 7
- Also diagnosed with Rif mono resistant TB started on levofloxacin, bedaquilline, linezolid, clofazimine, terizidone October 2022
- Treated for eosophageal candida for 3 weeks with oral fluconazole in November
- Seizures in December 2022..
- Presented to our clinic in December 2022 in a wheelchair, with headache and vomiting.. Was supposed to attend our MDR TB clinic but got lost and attended HIV clinic

Questions

1. How tests would you request?
2. What could be happening?
3. Does this child have advanced hiv disease?
4. What strategies could have prevented this child from becoming so ill?

Case 4

- LP CSF: L= 66, protein marginally raised, glucose 2.5, culture positive for cryptococcus neoformans
- CT brain: multiple tuberculomas, no hydrocephalus
- December VL = LDL

The "Seriously ill" Older Child



Tuberculosis

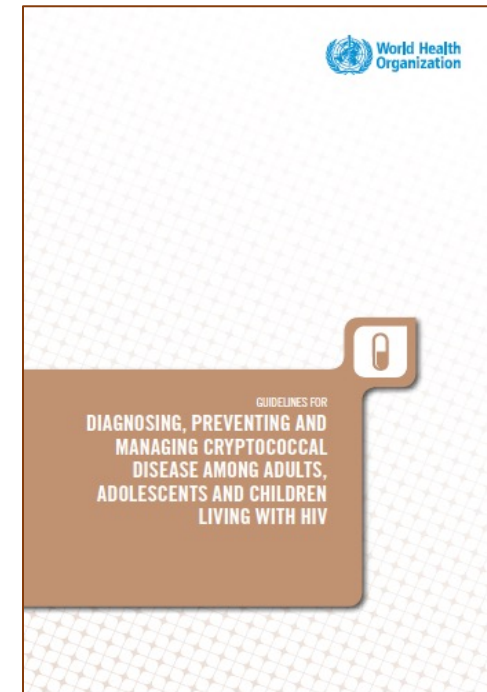
Cryptococcal Meningitis

Other OI



Cryptococcal Disease

<https://www.youtube.com/@sharecm>



Which of these children have advanced HIV disease?

- A) 3-month-old with severe pneumonia and CD4 count >35%
- B) 6-week-old growing well on + ART, 5% symptomatic, diagnosed during pregnancy
- C) 2-year-old with TB and CD4 count 5%
- D) 7-year-old with a few impetigo
- E) 10-year-old with TB

ALL OF THEM !!

MCQs

- Question 1-
- **Which of these children has advanced HIV disease**
- A) 3 months with severe pneumonia and CD4 count >25%
- B) 6 week growing well on +1 Z-score, CD>30%, asymptomatic, diagnosed during a PMTCT visit
- C) 2 year with moderate malnutrition and CD4 >25%
- D) 10 yearl old with TB
- E) all of the above

MCQs

- Question 2-
- **The definition of advanced HIV disease in children is:**
- A) any child with HIV less than 5 years old and any child older than five years with CD4 <200 or WHO Stage 3 or 4 disease
- B) all children less than 10 regardless of CD4 count
- C) All children less than 5 and must have CD4 count less than 200
- D) Any child older than 5 with a CD4 count of less than 500

MCQs

- Question 3:

In HIV-exposed or HIV infected infants less than 6 months that present with severe pneumonia the following is the recommended (if available in your setting)

- A) High dose cotrimoxazole, ampicillin, gentamicin, ganciclovir
- B) Ampicillin and gentamicin
- C) Ampicillin gentamicin and amphotericin B
- D) Bactrim and ganciclovir only
- E) Bactrim prophylaxis and ampicillin, gentamicin, ganciclovir

MCQs

- Question 4
- The most common cause of mortality in children < 5 years with HIV in our setting is
- A) Cryptococcal meningitis
- B) Candida
- C) Bacterial infections
- D) TB
- E) gastroenteritis
-

MCQs

- Question 5;
- Which of the following statements regarding cryptococcal disease in children is the most correct
- A) fluconazole for 4 weeks is the best treatment
- B) flucytosine is readily available at all clinics
- C) cryptococcal meningitis is rare in children younger than 5 years of age
- D) children don't get cryptococcal meningitis

Conclusions

- Children and Adolescents can present with AHD in many ways
- We already have a package of care that we can implement BUT
- Advanced disease is not just PJP, TB, CMV and cryptococcal disease
- Children with HIV can be at risk at any point- even if on ART for a long time
- We need more than ART

