

## Supplemental Digital Content 1: Study Definitions.

### A. Case Definitions for World Health Organization Clinical Algorithm for Symptomatic HIV Infection in Infants

#### Oral Thrush (either of 2 types):

1. Pseudomembranous: Creamy white-to-yellow soft small plaques on red or normally coloured mucosa which can be scraped off
  2. Membranous: Red patches on the tongue, palate, or lining of the mouth, usually painful or tender
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#### Severe Pneumonia (eg severe or very severe):

1. **Must** have either
    - a. cough
    - b. difficulty breathing
  2. **Must** have at least **one** of the following:
    - a. chest indrawing
    - b. stridor (obstructed breathing)
    - c. at least one IMCI general danger sign
      - Severe respiratory distress (fast breathing  $\geq 70$ ; head nodding; grunting; or nasal flaring)
      - Lethargy
      - Unconscious ( $\text{BCS} \leq 3$ )
      - Not able to drink
      - Not able to breastfeed
      - Vomiting everything
      - Presence or history of convulsions during current illness
      - Responding to antibiotics?
      - Oxygen saturation  $\leq 90\%$
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#### Severe Sepsis

1. **Must** be **< 2 months old** (eg “young infant”)
2. **Must** have either:
  - a. high temperature  $\geq > 37.5$  degrees celcius (axillary) **or** **38** degrees celcius (oral; auricular; or rectal)
  - b. low temperature  $\leq 35.9$  degrees (oral; auricular; rectal; or axillary)
3. **Must** have any **one** severe sign including:
  - a. fast breathing
    - i.  $\geq 60$  breaths/minute in infant younger than **2 months of age**
    - ii.  $\geq 50$  breaths/minute in infant between **2 months and 12 months of age**
  - b. chest indrawing
  - c. bulging fontanelle
  - d. lethargy
  - e. reduced movement
  - f. not feeding
  - g. not sucking breastmilk

- h. Presence or history of convulsions during current illness
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### **Presumptive Pneumocystis Jirovecii Pneumonia (PCP)**

1. **Must** qualify as **Severe** or **Very Severe Pneumonia** according to **IMCI** guidelines
  2. **Must** have fast breathing
    - i.  $\geq 60$  breaths/minute in infant younger than **2 months of age**
    - ii.  $\geq 50$  breaths/minute in infant between **2 months and 12 months of age**
  3. **Must** have **one** of the following:
    - **bilateral** interstitial infiltrates on chest radiograph
    - lung examination clear to auscultation or with **bilateral** chest findings
    - **Hypoxemia** (oxygen saturation  $< 90\%$ )
    - Does not respond to antibiotic therapy (defined as after **2 days**)
    - Respiratory distress out of proportion to lung findings
    - **Slow** response to high-dose cotrimoxazole
    - Severe malnutrition
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### **Severe acute malnutrition**

1. **Must** have either
    - a. weight-for-height  $< 69\%$
    - b. mid-upper arm circumference (MUAC)  $< 11$  cm
    - c. oedema of both feet (at least)
  2. **Must** have continued weight loss **or** no weight gain after **2 weeks** of standard therapy
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### **Presumptive esophageal candida**

1. **Must** have any **one** of the following:
    - a. Presence of oral thrush
    - b. Food refusal
    - c. Difficulty/crying when feeding
  2. **Must** respond to treatment after **2 days**
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### **Extrapulmonary Mycobacterium Tuberculosis**

1. **Must** have lymph node enlargement  $> 2$  weeks
2. Lymph nodes **must** be **painless**, “**cold**,” and **localized** in **one** region
3. **Must** have response to standard TB therapy after **1 month**
4. *May* have draining sinuses (not required)

5. Lymph nodes *may* be “matted”
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### **Definitive Diagnosis of Cryptococcal meningitis**

1. **Must** have isolation of *Cryptococcus neoformans* in CSF or positive cryptococcal antigen test (CRAG) in CSF **or** blood.
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### **Presumptive Kaposi’s Sarcoma**

1. **Must** have typical appearance in skin or oropharynx of persistent, **initially** flat, patches with a **pink or blood-bruise** colour.
  2. *May* have nodular skin lesions
  3. *May* have diffuse lymphadenopathy
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### **Presumptive toxoplasmosis of the brain**

1. Onset **must** be at age > 1 month
2. **Must** have fever **and** either headache, focal neurological signs, or convulsions.
3. **Must** respond to therapy within **10** days to specific therapy.

#### **A. High-risk for Tuberculosis:**

A child with a positive tuberculin skin test, known or suspected tuberculosis contact, WHO-defined non-severe, severe, or very severe pneumonia, abnormal chest radiograph suggesting tuberculosis, or WHO-defined moderate or severe malnutrition. A positive tuberculin skin test was defined as  $\geq 5$ mm skin induration in HIV-infected or severely malnourished children, or  $\geq 10$ mm skin induration in HIV-exposed patients.

## **Supplemental Digital Content 2. World Health Organization clinical algorithm for symptomatic HIV infection in infants**

Child who is HIV antibody positive, less than 18 months of age, and fulfills either criteria A or B.

A. Presence of two of the following three conditions:

- i. oral thrush
- ii. WHO-defined severe or very severe pneumonia
- iii. severe sepsis in an infant younger than 2 months

B. Presence of one of the following AIDS-specific conditions:

- i. *Pneumocystis jirovecii* pneumonia
- ii. esophageal candidiasis
- iii. treatment unresponsive severe acute malnutrition
- iv. extra-pulmonary tuberculosis disease
- v. Kaposi Sarcoma
- vi. cerebral toxoplasmosis (with onset after one month of age)
- vii. cryptococcal meningitis