COMMON EMERGENCY PRESENTATIONS IN HIV

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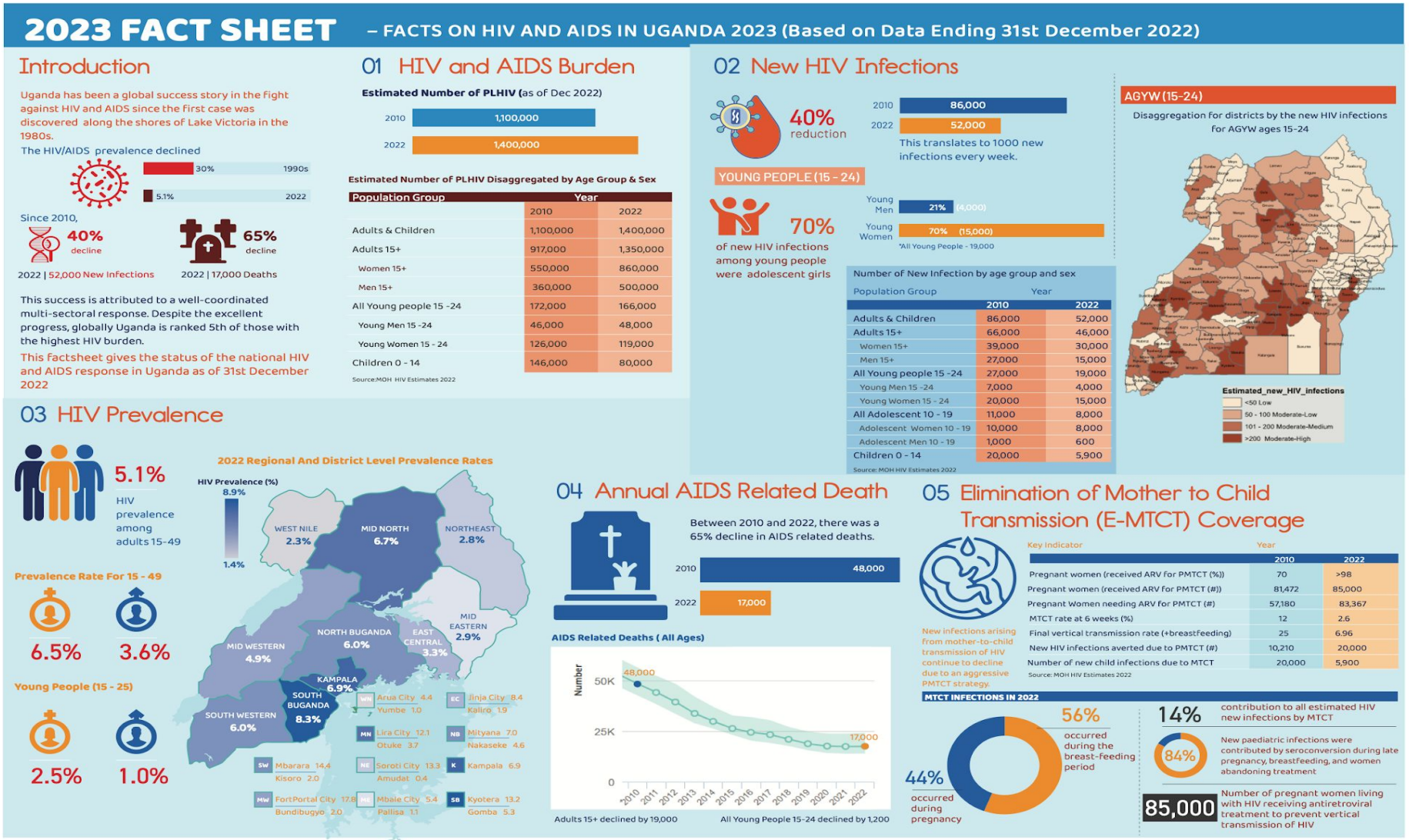
CHANGING HIV LANDSCAPE

- Significant strides
- Largely due to successful HIV programing

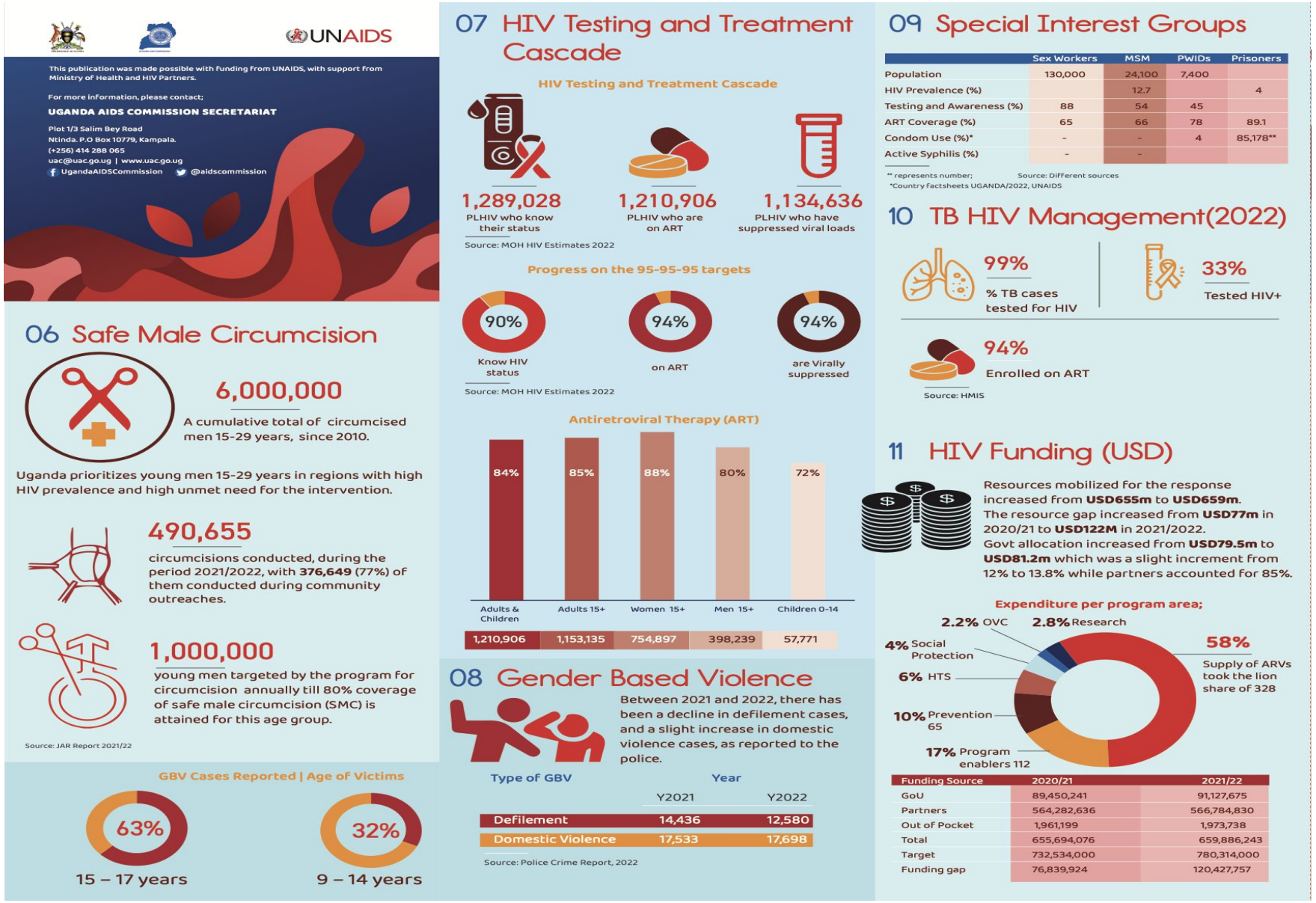


https://uac.go.ug/media/attachments/2024/01/23/hiv-aids-factsheet-2023.pdf

- Still more work to be done

?95-95-95 targets

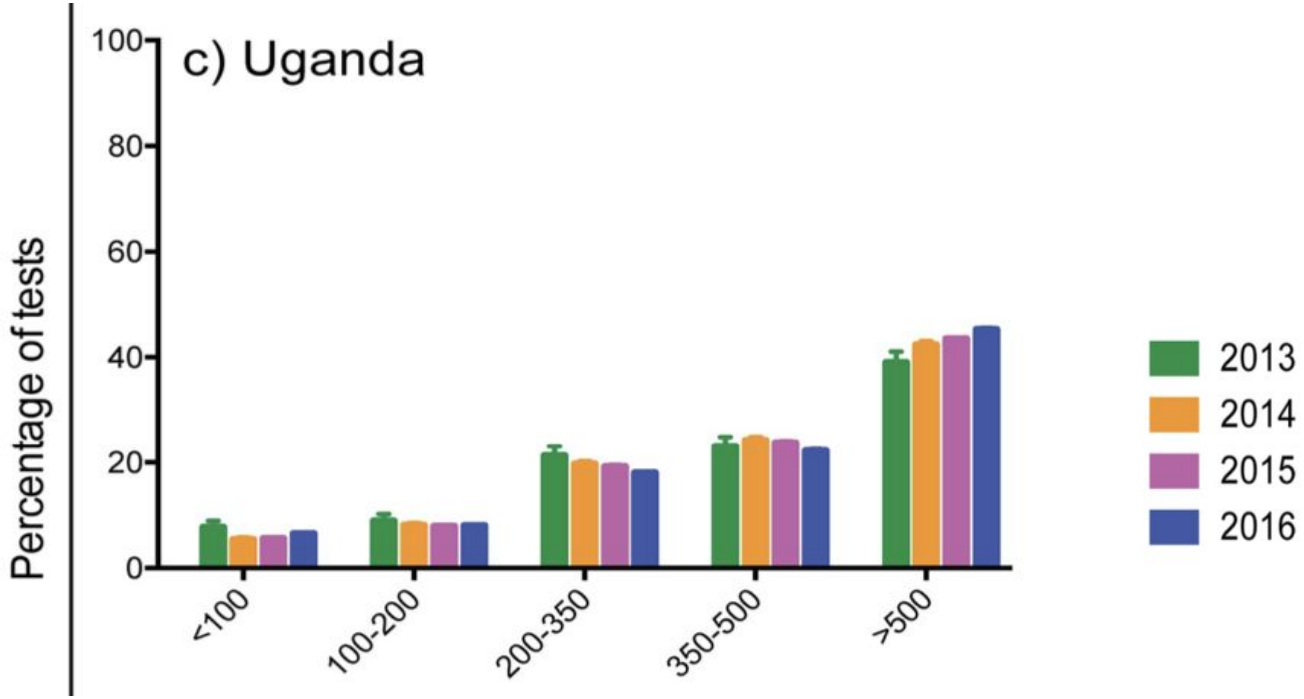
- Funding



https://uac.go.ug/media/attachments/2024/01/23/hiv-aids-factsheet-2023.pdf

- Advanced HIV disease persists

CD4 < 200
WHO stage III/IV defining illness
Children < 5years



https://doi.org/10.1371/journal.pone.0226987

- High in-hospital mortality ~26%

- Nearly 2/3 of patients presenting with AHD are ART experienced

https://doi.org/10.1186/s12879-024-09112-7

- Patients with AHD are more likely to present with emergencies

Primary HIV infection

Asymptomatic
- Acute retroviral syndrome

Clinical stage 1

Asymptomatic
- Persistent generalized lymphadenopathy

Clinical stage 2

- Moderate unexplained weight loss
- Recurrent respiratory infections
- Herpes Zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

Clinical stage 3

- Unexplained severe weight loss
- Unexplained chronic diarrhoea for >1 month
- Unexplained persistent fever for >1 month
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary Tuberculosis
- Severe presumed bacterial infections
- Acute necrotizing ulcerative stomatitis, gingivitis or peridontitis
- Unexplained anaemia
- Neutropenia
- Chronic Thrombocytopenia

Clinical stage 4

- HIV Wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection
- Oesophageal candidiasis
- Extra-pulmonary Tuberculosis
- Kaposi Sarcoma
- Cytomegalovirus
- Central Nervous system toxoplasmosis
- HIV Encephalopathy
- Extra-pulmonary Cryptococcus
- Disseminated non-tuberculosis mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Candida of trachea, bronchi or lungs
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis
- Recurrent nontyphoidal *Salmonella* bacteraemia
- Lymphoma
- Invasive cervical cancer
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy
- Symptomatic HIV-associated cardiomyopathy
- Reactivation of American trypanosomiasis

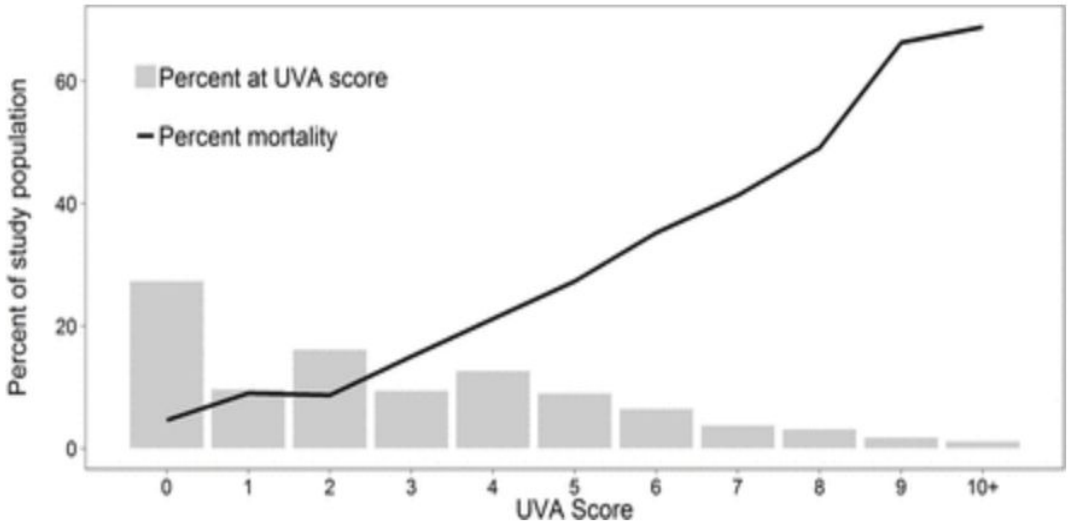
• Progressive multifocal leukoencephalopathy

EMERGENCY PRESENTATIONS

1. **Sepsis**

- 2.3x increased risk of death

- How do you recognize sepsis in a patient?
  - SIRS, MEWS
  - qSOFA
  - UVA



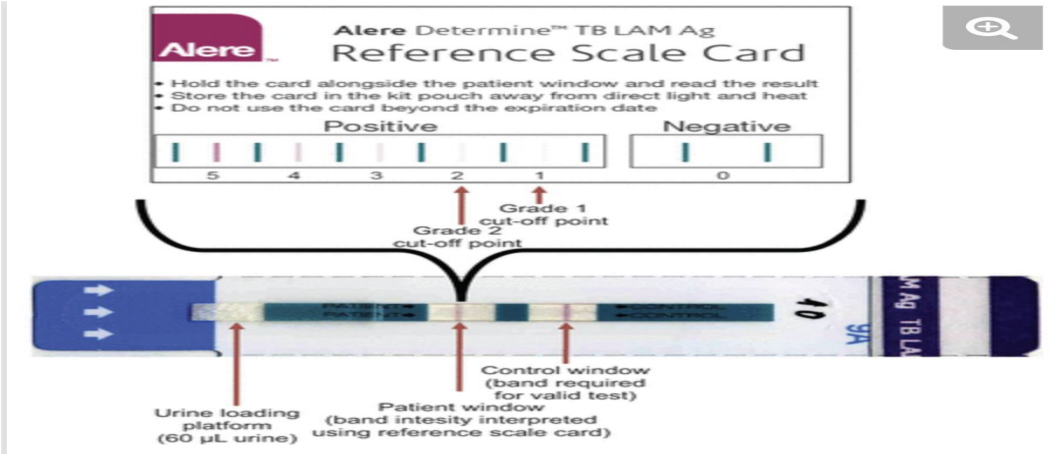
	Adapted MEWS*		qSOFA		UVA	
	Cut-off	Points	Cut-off	Points	Cut-off	Points
Respiratory rate (breaths/min)	15–20	1	≥22	1	≥30	1
	21–29 or <9	2				
	≥30	3				
Altered mental status (Glasgow Coma Scale <15)	Present	2	Present	1	Present	4
Systolic blood pressure (mm Hg)	81–100	1	≤100	1	<90	1
	71–80 or ≥200	2				
	≤70	3				
Temperature (°C)	≥38.5	1			<36	2
	<35	2				
Heart rate (beats/min)	101–110 or 41–50	1			≥120	1
	111–129 or <40	2				
	≥130	3				
Oxygen saturation (%)					<92	2
HIV seropositivity					Present	2

Variables and values in adapted MEWS, qSOFA and UVA scores

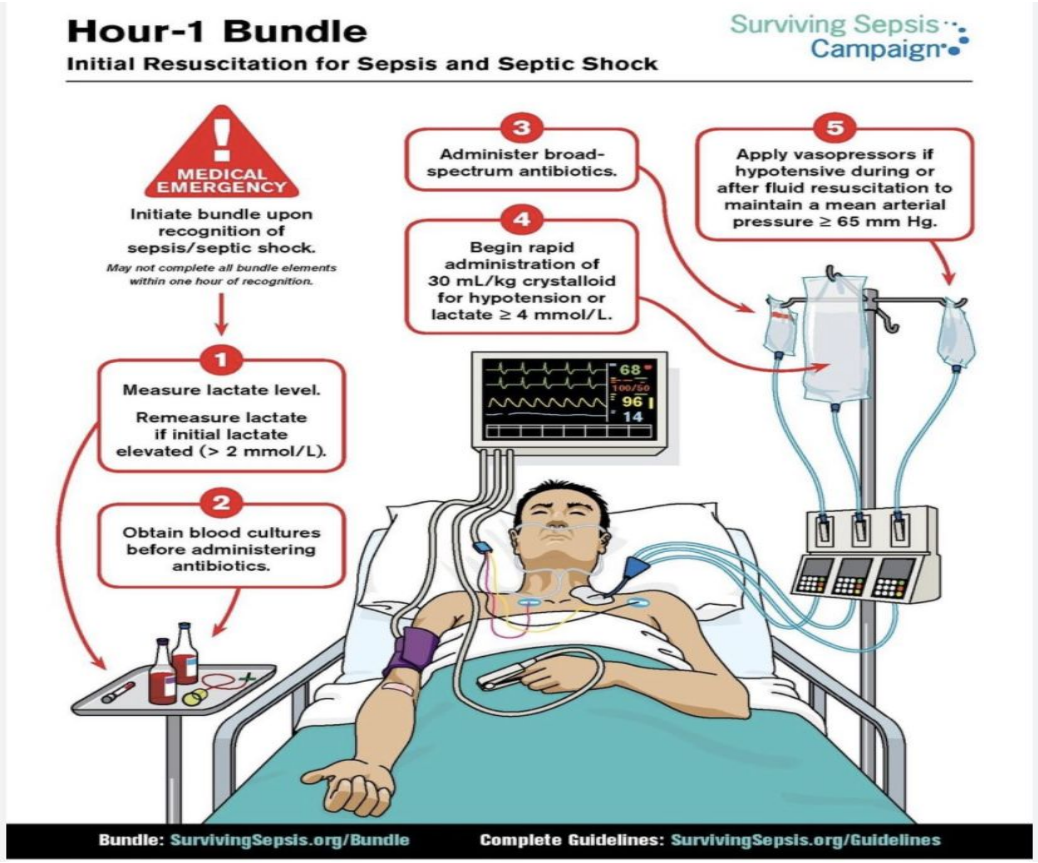
Moore CC, Hazard R, Saulters KJ, *et al*
Derivation and validation of a universal vital assessment (UVA) score: a tool for predicting mortality in adult hospitalised patients in sub-Saharan Africa
BMJ Global Health 2017;**2:**e000344.

- What is the cause of sepsis in the HIV population?

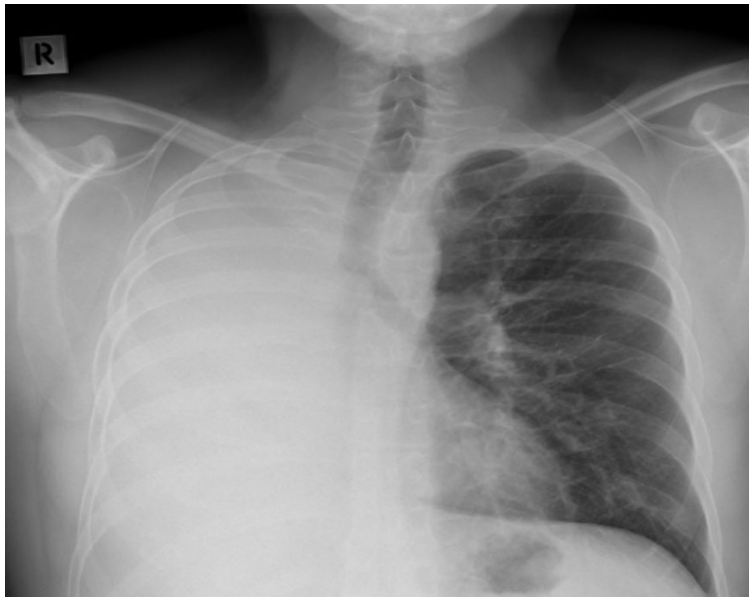
1. ***M.tuberculosis***
2. Non-typhoidal salmonellae
3. Malaria
4. S. pneumoniae



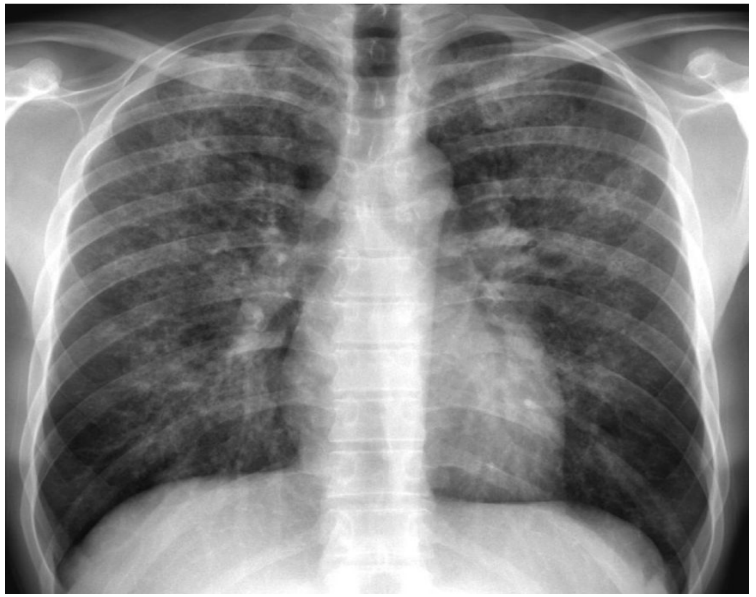
- What do you do for a septic patient?



2. **Respiratory Infections**



- Cough, fever, dyspnea may progress to respiratory failure
- Aetiology; **Mtb**, bacterial, fungal
- Investigations: CXR key
- Important to identify & treat complications ~ hypoxic RF, Effusions



- **PJP** – high index of suscpicion
  - hard to diagnose ~ BAL sample, CXR
  - treat with high dose CTX, steroids for severe disease

3. **Diarrhoea**

- Usually chronic > 1month
- Result into hypovolemic shock, electrolyte disorders esp. hyponatremia, hypokalemia
- IV fluid rescuscitation is key
- Aetiology;

CD4 Count	Types of Germs
Any CD4 count	*Salmonella, Campylobacter,* Tuberculosis, *C. difficile, Giardia, Entamoeba, Strongyloides*
<200 cells/mm^3	Cryptosporidium
<150 cells/mm^3	Histoplasma
<100 cells/mm^3	Isospora, Microsporidia
<50 cells/mm^3	MAC, CMV

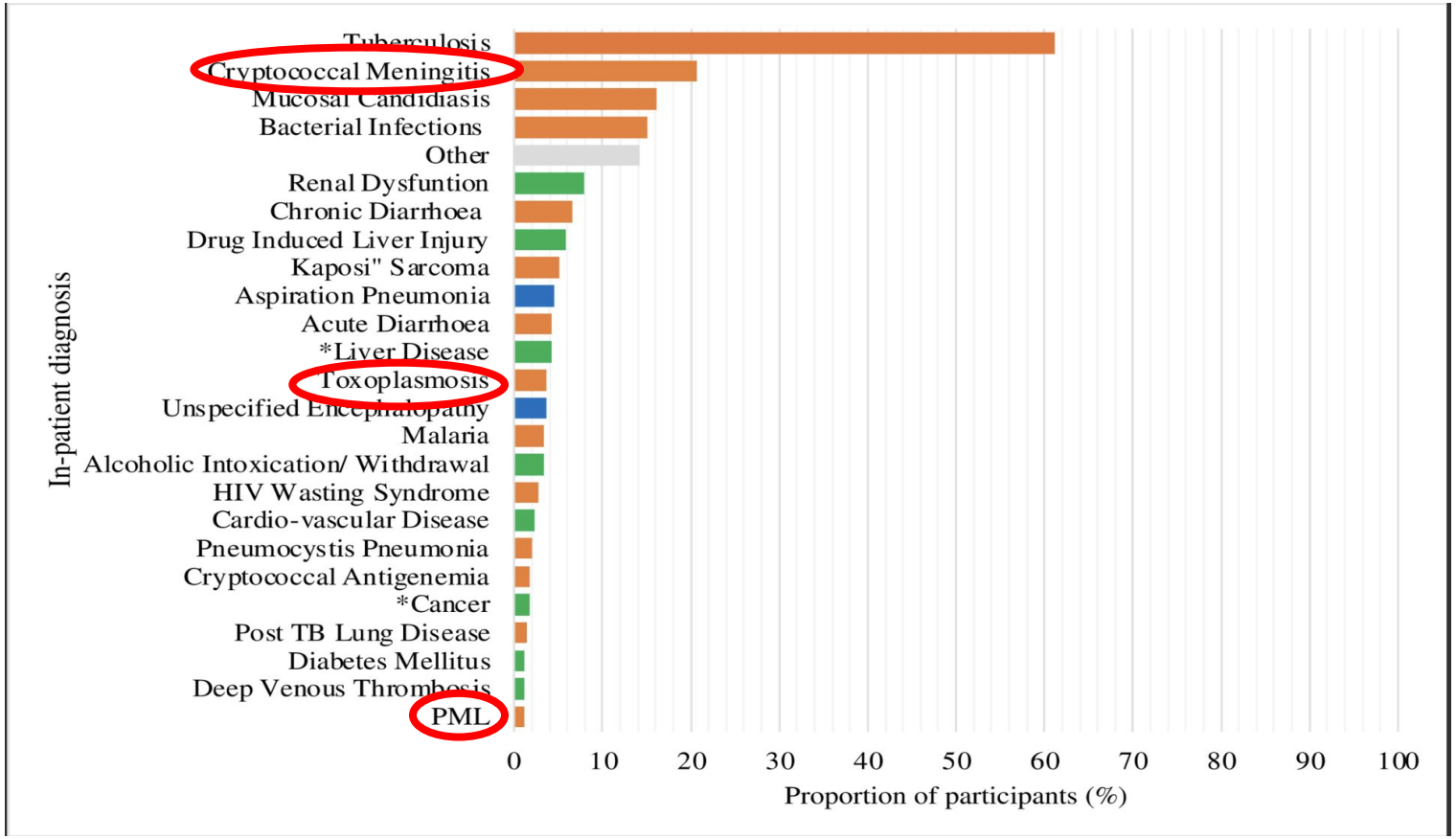
4. **Neurological HIV emergencies**

- Contribute ~25% of ***AIDS related deaths***

- Presentation; headache, seizures, altered mental status, focal neurologic deficits

- Are AIDS defining

- Meningitis most common Neurologic complication



https://doi.org/10.1371/journal.pgph.0002457

- Etiology of meningitis in Adults

Hospital	Country	Sample Size	HIV infected	Meningitis Prevalence			
				Bacterial / Pyogenic	Tuberculosis	Cryptococcal	Aseptic / Viral Meningitis
Mulago and Mbarara[1]	Uganda	416	98%	4%	8%	**59%**	29%
GF Jooste [2]	South Africa	1,737	96%	19%	13%	**30%**	38%
Queen Elizabeth Central [3]	Malawi	263	77%	20%	17%	**43%**	20%
Harare Central & Parirenyatwa [4]	Zimbabwe	200	90%	16%	12%	**45%**	28%
Pooled Average		2616	93%	9.3% (8.2-10.5%)	12.7% (11-14%)	**37% (35-39%)**	41% (40-43%)

[1] Durski K et al. *JAIDS* 2013; 63(3);e101-e108.
[2] Jarvis JN, et al. *BMC Infect Dis.* 2010; 10: 67.

CNS INFECTIONS IN HIV

@RAV7KS

Most CNS opportunistic infections result from reactivation of latent pathogens, including PML, toxoplasmic encephalitis, and primary CNS lymphoma

(IRIS) might unmask previously unsuspected CNS opportunistic infections when cART is started

Toxoplasmic encephalitis:

CD4<200

Suspect in movement disorders

Fever, headache, altered mental status, and focal neurologic complaints or seizures

-IMAGE:

- MRI: ring enhancing
  Frontal, basal ganglia, parietal
- Toxoplasma gondii PCR nearly 100% specific and 50-80% sensitive
- Size lesions < 4cm
- + mass effect/Edema

Tuberculous meningitis

Variable, but <200

- IMAGE:
- Hemorrhage, tuberculomas, or abscesses
- <50% show basilar enhancement on CT
- Hydrocephalus possible

PML

CD4 <100

Demyelinating disease caused by the JC virus

AMS, motor deficits (hemiparesis or monoparesis), limb ataxia, gait ataxia, and visual symptoms such as hemianopia and diplopia

- IMAGE:periventricular areas and the subcortical white matter.
- JC-virus PCR sensitivity variable at 50-90%, but specificity 90-100%

Herpes simplex virus

CD4 Variable

Fever, headache, neck stiffness, vomiting, disorientation, memory loss, dysphasia, depression, confusion, personality change, seizures, visual hallucinations and photophobia

IMAGE:

- Enhancement- Inferomedial temporal lobes brainstem, cerebellum, diencephalon, and Periventricular regions; associated intracranial hemorrhage
- CSF PCR sensitivity 100%, specificity 99·6%

Primary CNS lymphoma

CD4 <100

Confusion, lethargy, memory loss, hemiparesis, aphasia, and/or seizures

IMAGE:

Enhancement:

- multifocal lesions
- Periventricular, frontal, cerebellum, temporal
- Generally >3 cm diameter
- EBV analysis has a sensitivity of 80-90%, and a specificity approaching 100% for primary CNS lymphoma
- + mass effect/Edema

Cytomegalovirus encephalitis

CD4 <50

Delirium, confusion, and focal neurologic abnormalities, rapidly progressive encephalopathy.

IMAGE:

- Enhancement: Periventricular
- PCR >90% sensitive and specific and <25% culture positive

Cryptococcal meningitis

CD4 <50

Headache, vomiting, visual changes, hearing loss, palsy of the abducens nerve, and impaired consciousness

IMAGE:

- leptomeningeal enhancement, especially in patients with IRIS
- Frequently "punched-out" cystic lesions
- CSF: CSF cryptococcal antigen sensitivity 92% and specificity 83%;sensitivity of serum CrAg testing is comparable to CSF testing

PRINCIPLES OF HIV-ASSOCIATED CNS OPPORTUNISTIC INFECTIONS

- CNS opportunistic infections typically occur when the CD4-cell count is less than 200 cells per µL
- Diagnosis should be based on clinical presentation, temporal evolution, CSF, and radiographic features
- Multiple infections are present in 15% of cases and some infections might be revealed only after combination antiretroviral therapy is started
- Combination antiretroviral therapy should be started, modified, or continued with appropriate antimicrobial therapy
- Antimicrobial treatment is generally required until immune recovery (CD4-cell count more than 200 cells per µL) is achieved with antiretroviral therapy

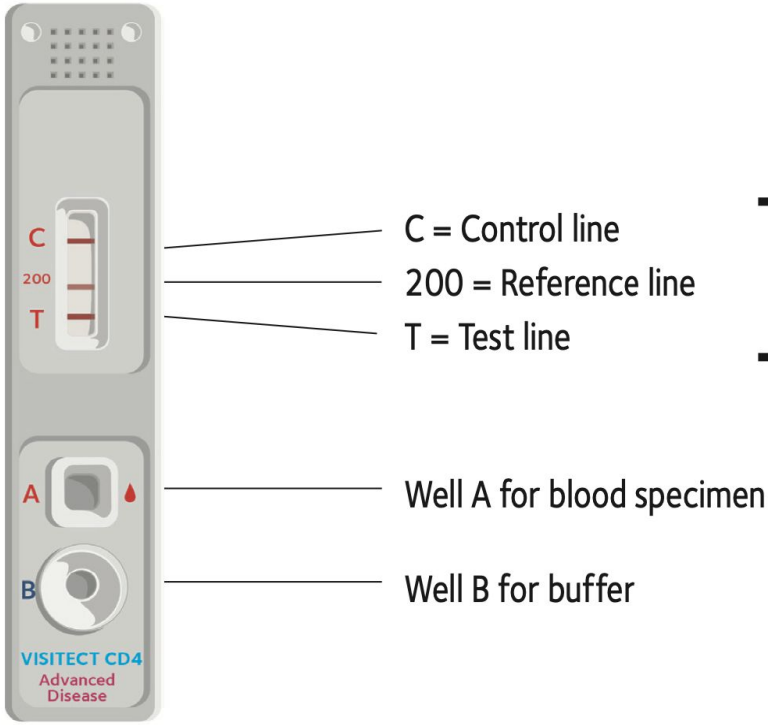
Others:

- CNS Syhpilis
- Aspergillosis
- Coccidiomycosis
- Histoplasmosis
- VZV
- HIV encephalopathy

https://doi.org/10.1016/S1474-4422(12)70098-4

Patient approach

- Cinical suspicion of CNS infection in the HIV setting
- CD_4 count?
- If <200, AHD screen (Crag LFA, Urine LAM)
- Is an LP safe? ~do LP
- Brain Imaging ~ CT/MRI



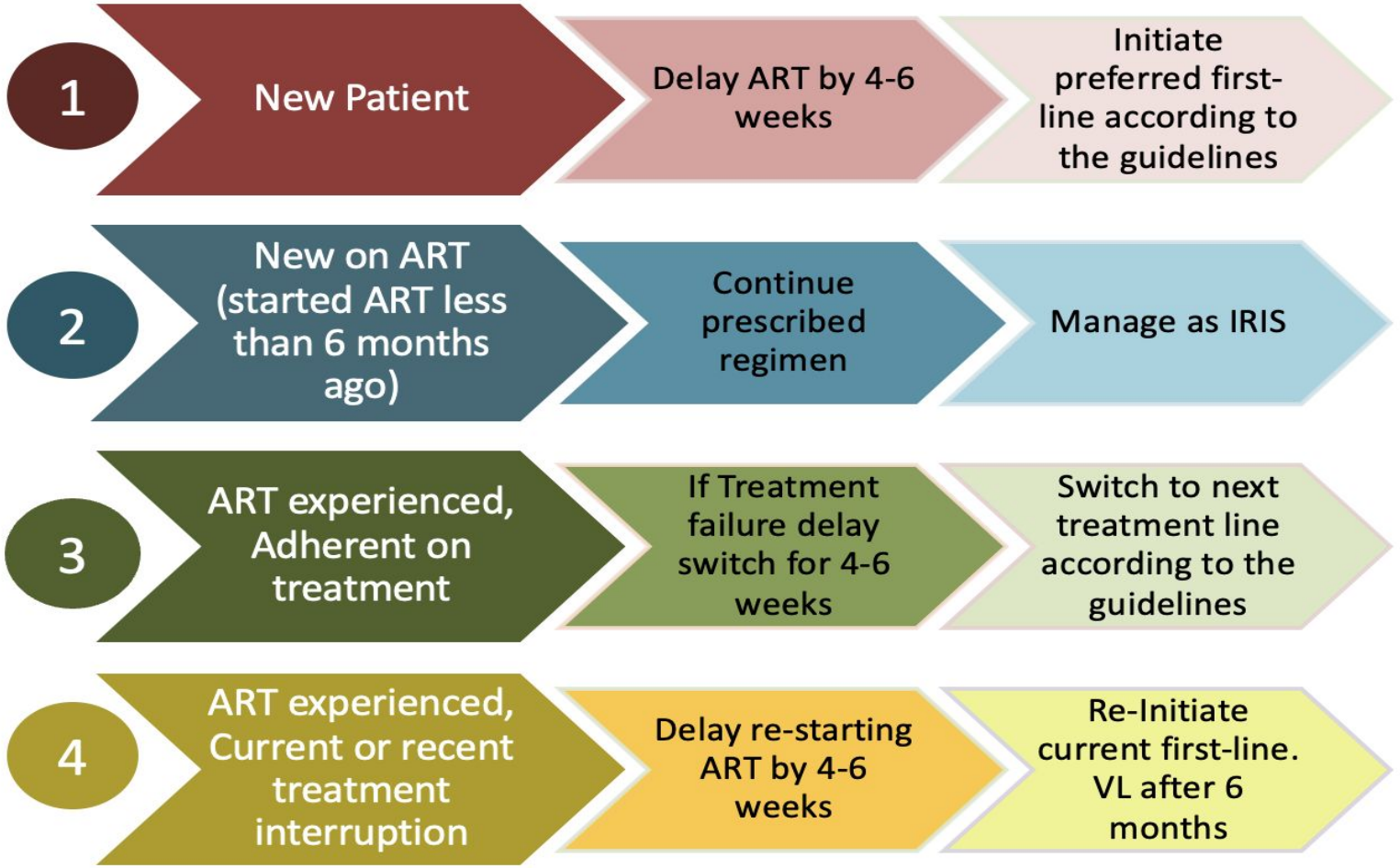
- Management of CM

Phase	Drug	Comments
Newly Diagnosed Patient		
Induction Phase (2 weeks)	**Recommended:** SINGLE high dose Amphotericin B liposomal (10mg/kg) AND Flucytosine (100mg/kg/day in four divided doses) + Fluconazole 1200mg/day for 14 days Or Amphotericin B deoxycholate (1mg/kg/day) + Flucytosine (100mg/kg/day in four divided doses) for 1 week, followed by 1 week of fluconazole (1200 mg/day for adults, 12 mg/kg/day for children and adolescents). Or Fluconazole (1200 mg daily for adults, 12 mg/kg/day for children and adolescents) + Flucytosine (100 mg/kg/day, divided into four doses per day for 14 days. Or Amphotericin B deoxycholate (1mg/kg/day) + high-dose Fluconazole 1200mg/day for 14 days	**Preventing Amphotericin toxicity:** To prevent nephrotoxicity and hypokalaemia, do the following: • Pre-hydration with 1L normal saline before starting the daily Amphotericin dose. • Monitor serum potassium and creatinine levels at initiation and at least twice weekly to detect changes in renal function. • Routine administration of 40 mEq/day of potassium chloride can decrease the incidence of Amphotericin-related hypokalemia. • Consider alternate day Amphotericin if creatinine is >3mg/dl.
	Alternative: Fluconazole 1200mg/day (or 6-12mg/kg/day in children)	
Consolidation phase (8 weeks)	Fluconazole 800mg/day (or 6-12mg/kg/day in children and adolescents)	Initiate ART 4–6 weeks after starting CM treatment and there is clinical response to antifungal therapy.
Maintenance Phase (18 months)	Fluconazole 200mg/day (or 6 mg/kg/day up to 200mg in children and adolescents)	Criteria to stop after a minimum of 18 months of maintenance phase: Adults: VL<1,000 copies/mm^3 & CD4 ≥ 200 or CD4 ≥200 (if viral load not available) after 12 and 18 months Children: If CD4>25% or viral suppressed
Note: For patients on rifampicin increase Fluconazole dose by 50%		

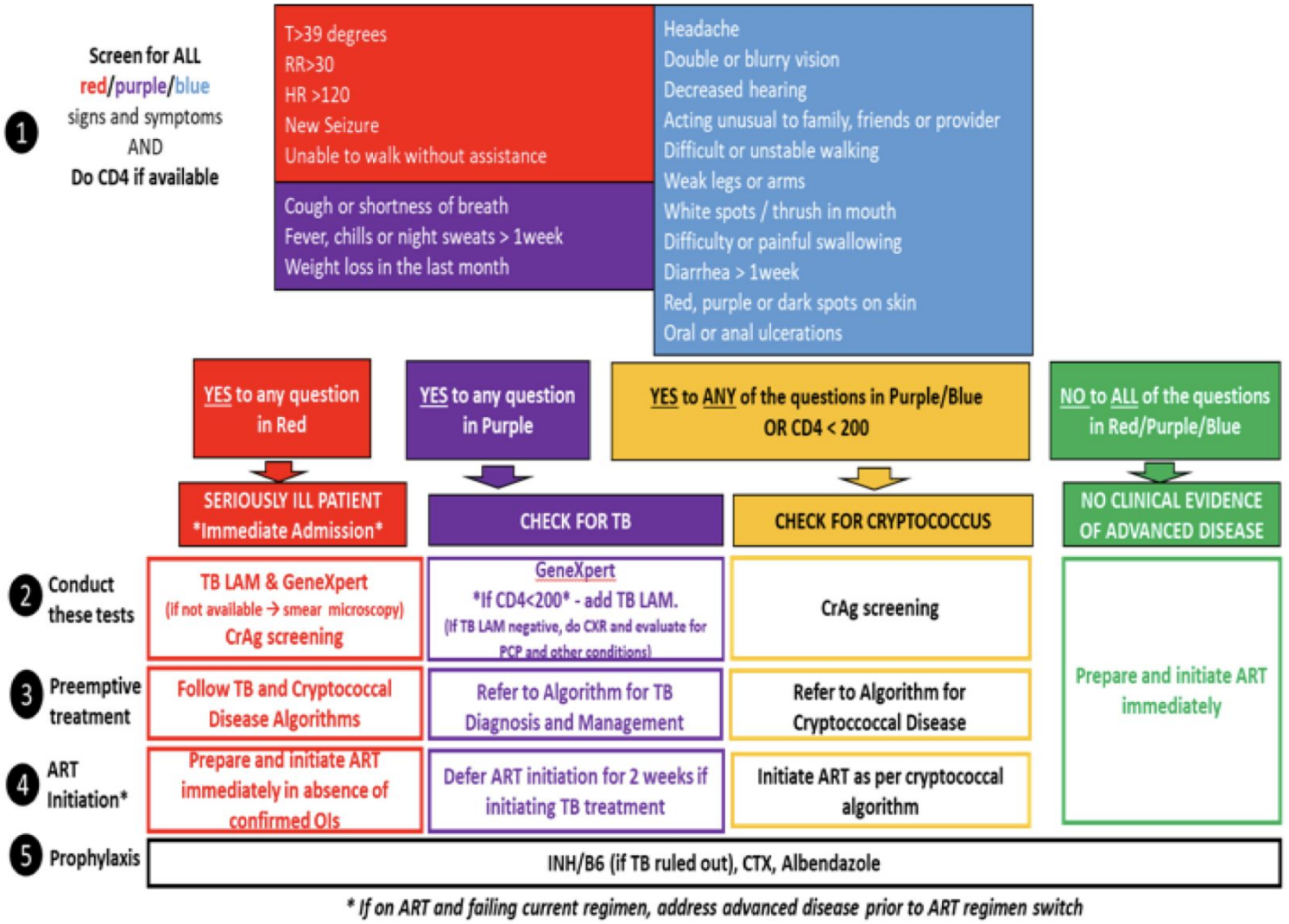
Justify Text

Phase	Drug	Comments
Managing Treatment Complications		
• K < 3.3 mmol/l: increase potassium supplementation to 40mmol iv or 2 Tbl three times daily and monitor daily • Creatinine >2-fold from baseline: increase pre-hydration to 1L 8-hourly. Consider temporary omission of an amphotericin dose and restart at 0.7mg/kg. If creatinine remains elevated discuss amphotericin-free regimen (Fluconazole 1200mg/day) with senior consultant. • Elevated liver enzymes: Fluconazole		
Relapse disease		
Presents with a recurrence of symptoms of Meningitis and have a positive cerebrospinal fluid culture following a prior confirmed diagnosis of Cryptococcal Meningitis • Evaluate for drug resistance: o Send CSF to microbiology reference laboratory at the College of Health Sciences, Makerere University for culture and sensitivity testing. • If there are no drug resistance results, re-initiate the induction therapy for two weeks and complete other phases of treatment • Other options for treatment are a combination of Flucytosine (100mg/kg/day in four divided doses) and Fluconazole 800-1200mg daily. For patients on rifampicin increase Fluconazole dose by 50%		
Adequate control of elevated CSF pressure		
• Control of increased intracranial pressure improves survival by 25% in persons with Cryptococcal Meningitis • All patients with a CSF Pressure >250mmH_2O will need a therapeutic LP the following day to reduce the CSF pressure to <200 mm. • In the absence of a manometer, one may use an IV giving set to create an improvised manometer measuring the height with a meter stick. • Removing 20-30mL of CSF (even in the absence of a manometer) may be adequate to decrease CSF pressure. Most patients will need 2-3LPs during the induction phase.		

- Management of ART



- How do you manage a new HIV patient



THANK YOU!