Paediatric HIV infection: antiretroviral treatment, management and long-term care

Di Gibb

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PENTA 20

Outline

- Epidemiology of Paediatric HIV
- HIV diagnosis
- Natural History of Paediatric HIV and Clinical presentations
- Antiretroviral Therapy
  - When to start
  - What to start and updates in 2025/2026
- Other treatments/managment:
  - Prophylaxis for opportunistic infections and late disease presentation
- Adolescents
  - Models of care and transition to adult care
- Life course data is needed

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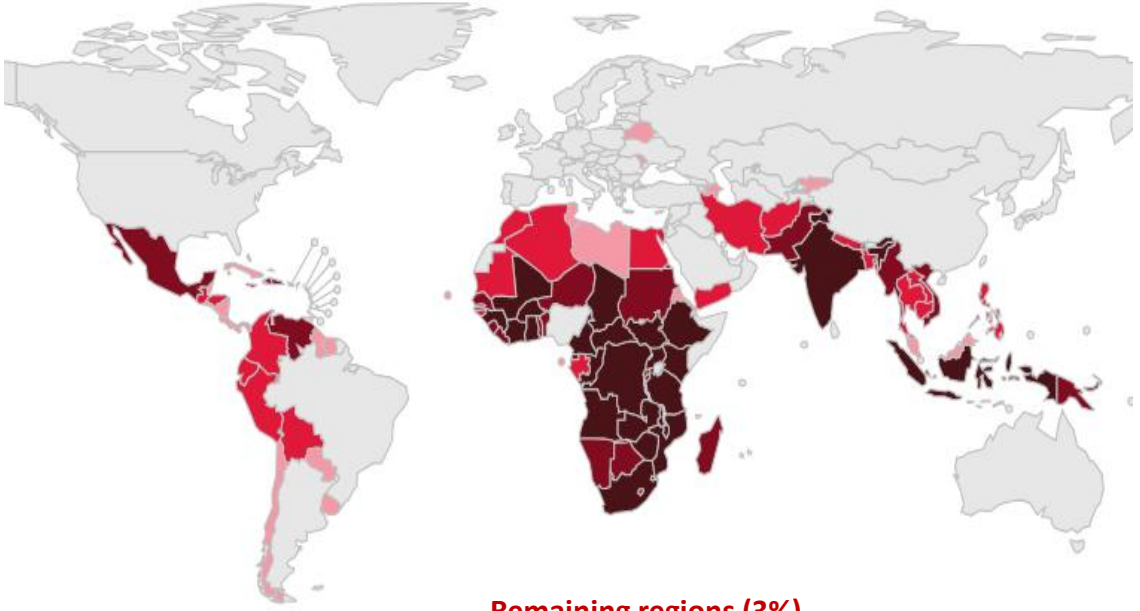
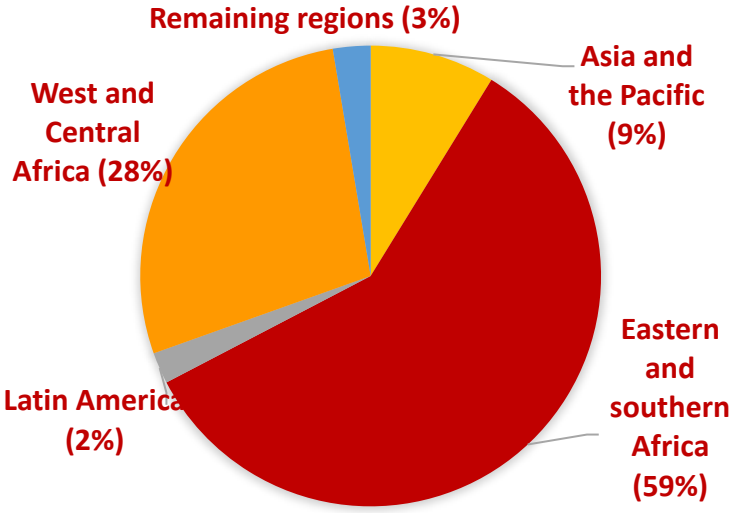
2024: 2.4 million children and adolescents aged 0-19 living with HIV

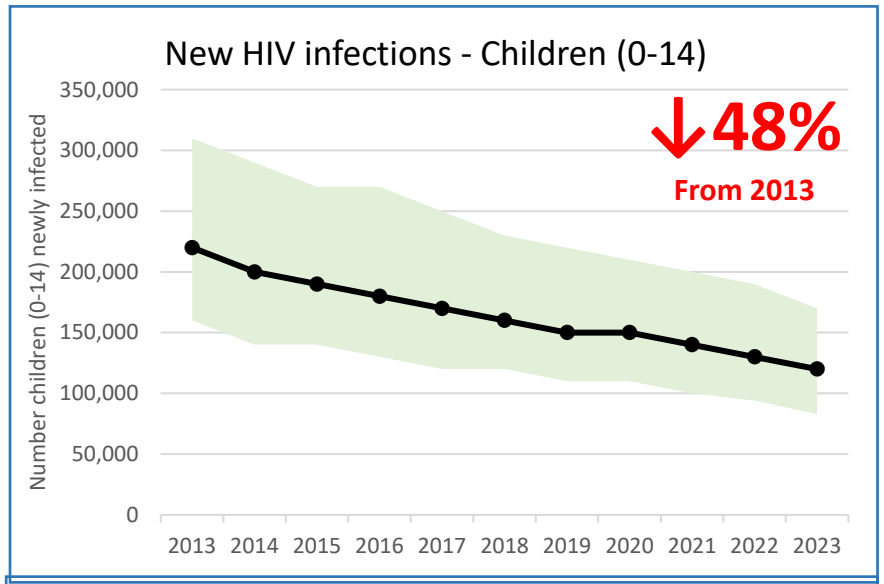
- Among the 1.4 million children 0-14 years:
- Most (86%) live in the Global South
- Estimated numbers of children and adolescents with HIV in ASIA and Pacific:
  - approximately 120,000 to 130,000 children aged 0–14 years are living with HIV (9% of the global total).
  - Around 10,000 children in the region **newly acquired HIV in 2024**
  - significant burdens in Indonesia, India, Papua New Guinea, Fiji
  - **Estimated children in China are low in '24/25: ? Total numbers in low 1000's?**
    (UNICEF estimated 7,000 in 2007)

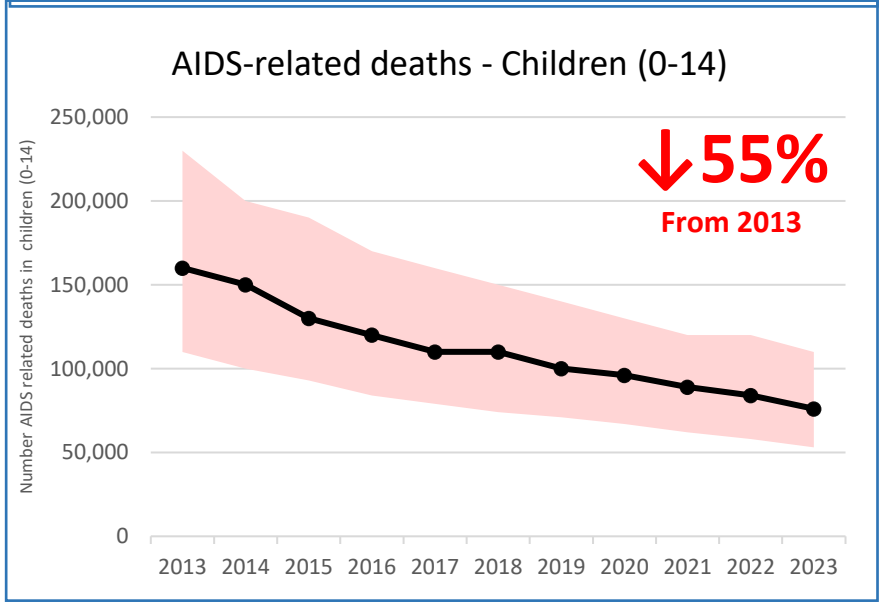




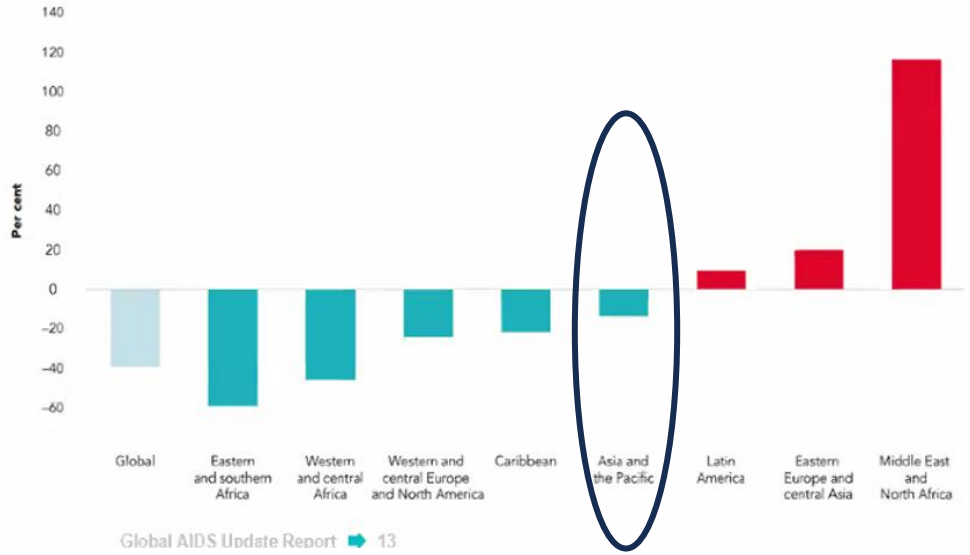
UNAIDS epidemiological estimates, 2025 (https://aidsinfo.unaids.org/ ; https://www.unicef.org/hiv)

Considerable progress over the past decade

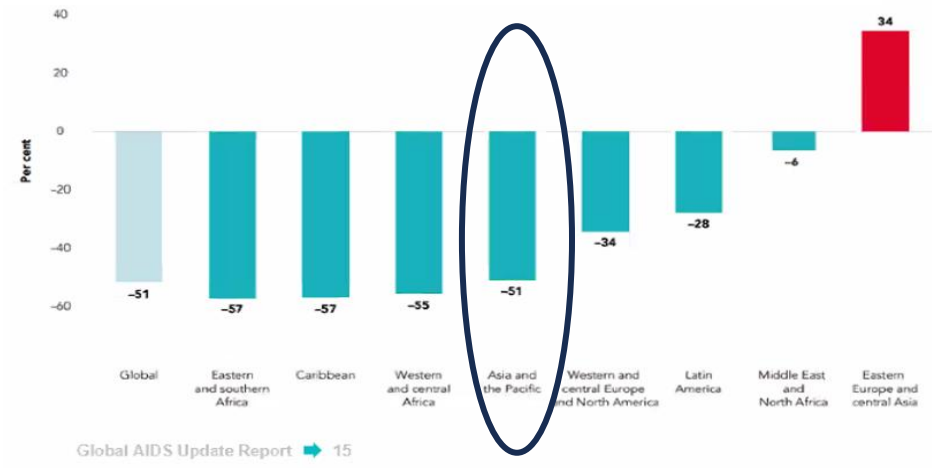




Change in new HIV infections between 2013 and 2023, by region

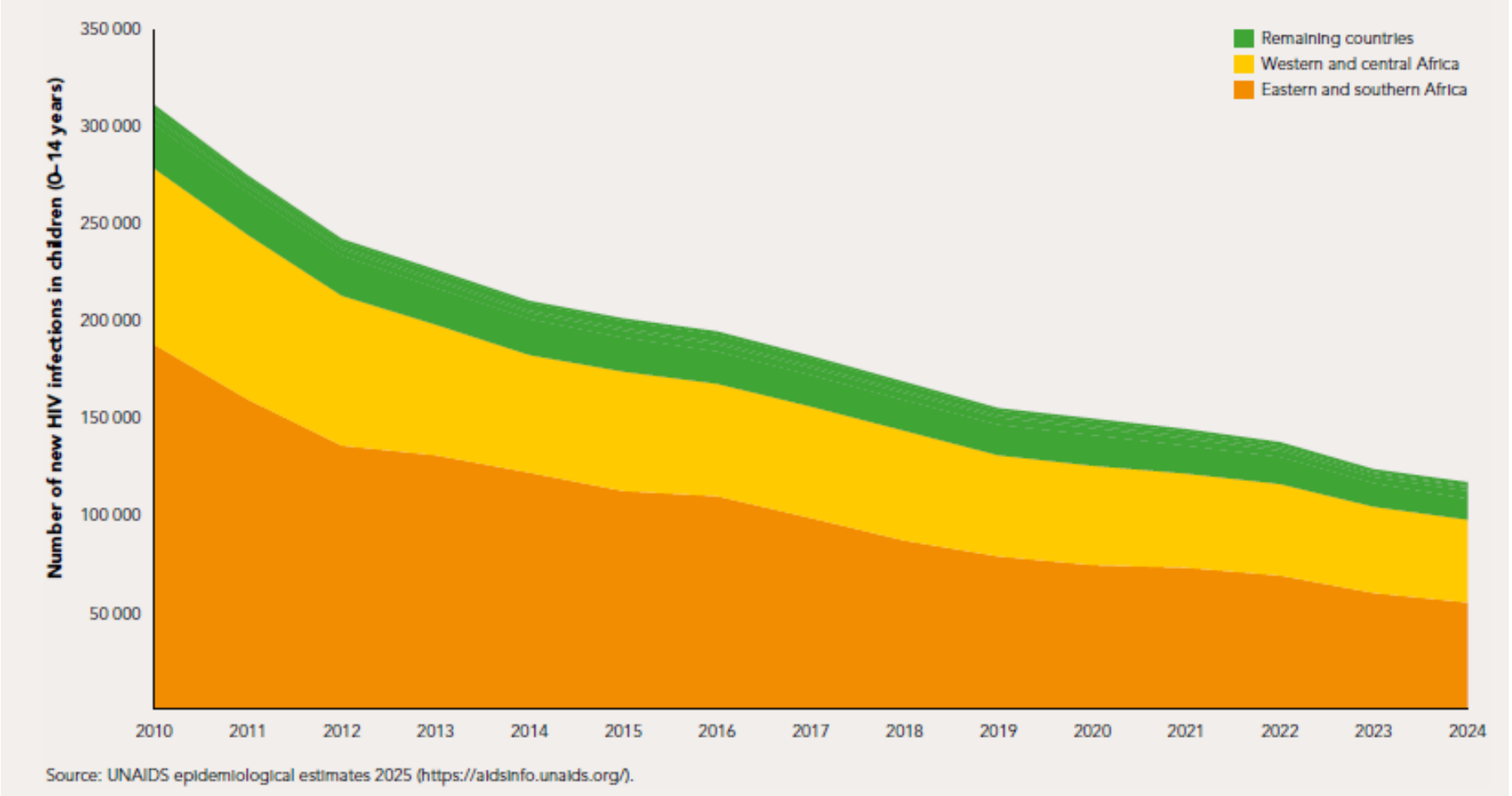


Change in AIDS-related deaths between 2013 and 2023, by region



Source: UNAIDS epidemiological estimates, 2024 (https://aidsinfo.unaids.org/)

Steepest decline in HIV infections in children has been in Eastern and southern Africa



UNAIDS Global AIDS Update, 2025

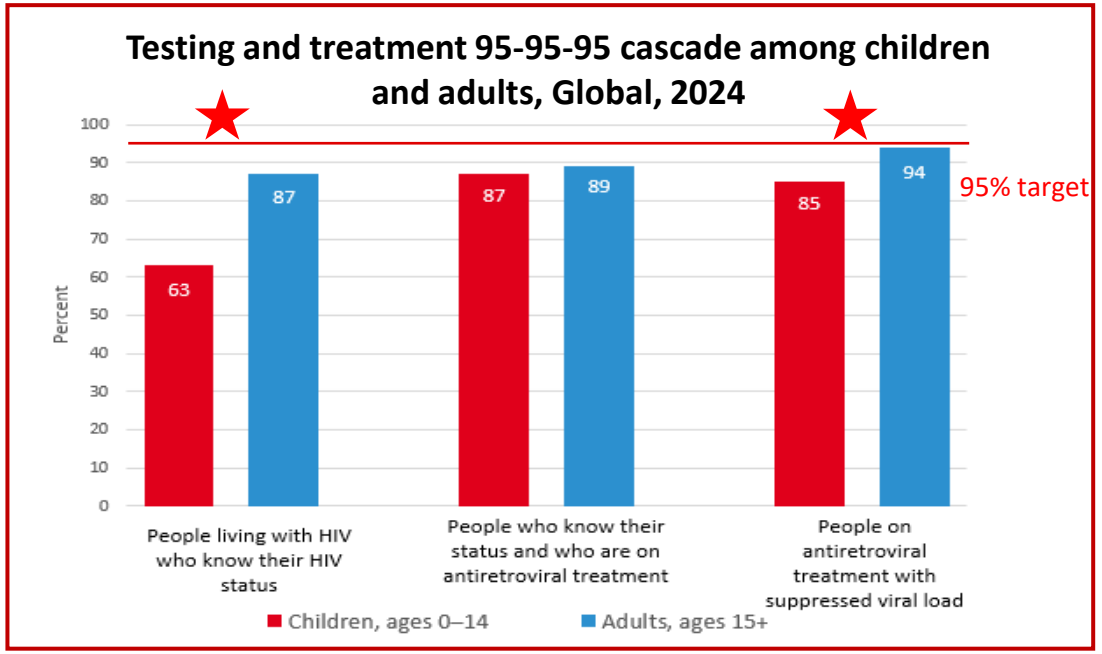
95-95-95 UNAIDS targets

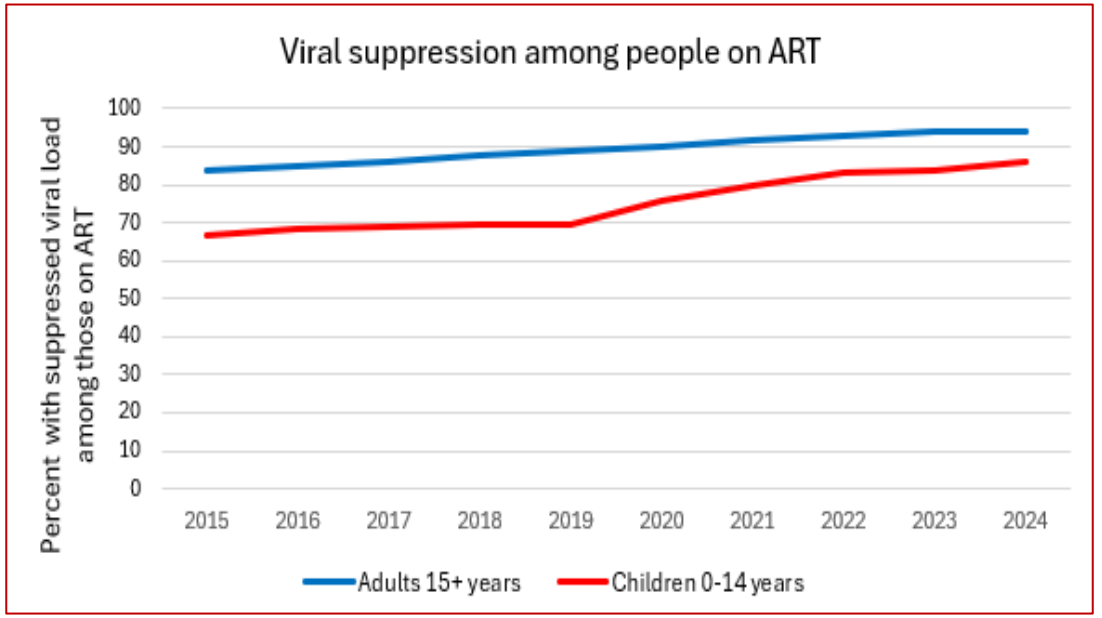
- **First 95: HIV status is known for 95%**
  - 63% children vs 87% adults **(gap 24%)**
  - >1/3 children not diagnosed
  - (and cannot be started on ART)

- **Second 95: 95% of those diagnosed receive ART**
  - 87% children vs 89% adults (gap 2%)

- **Third 95: viral suppression <1000 c/mL for 95% of those treated**
  - 85% children vs 94% adults **(gap 9%)**

➢ **New effective and safe child-friendly ARVs are essential to improve outcomes**

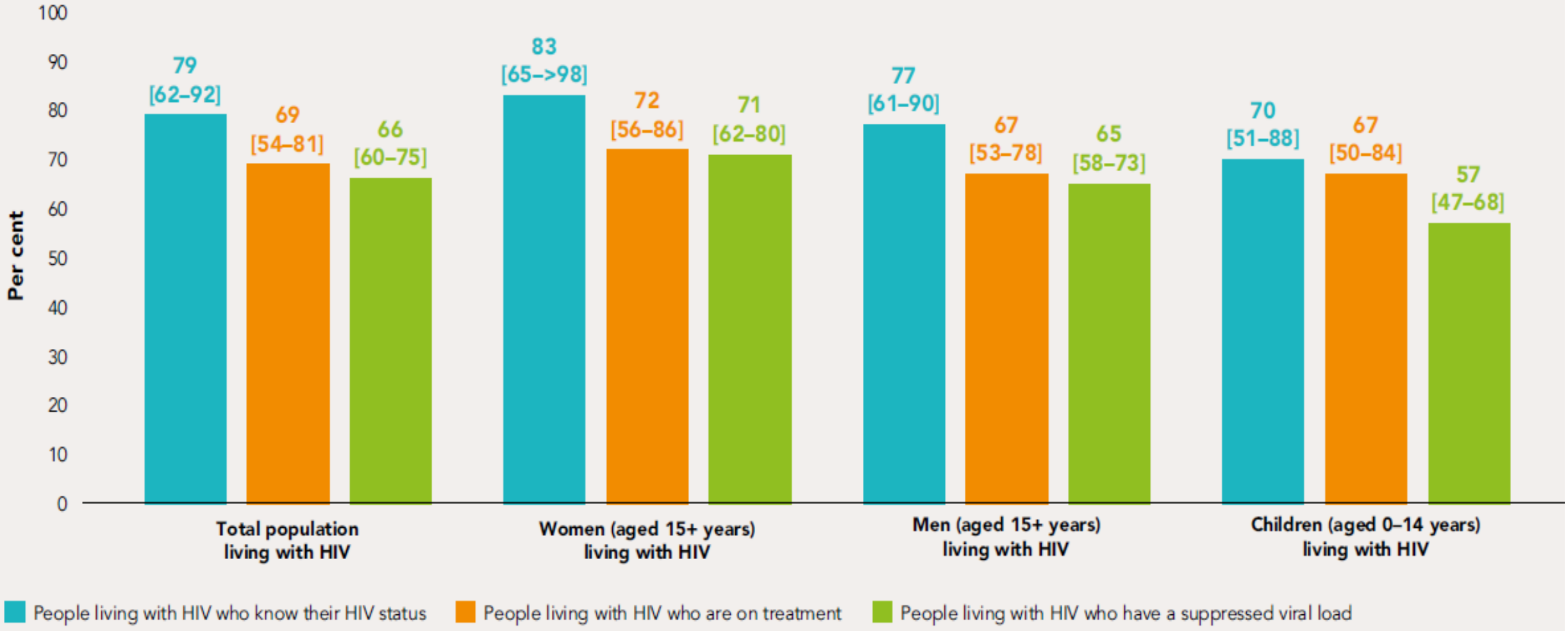




Source: UNAIDS epidemiological estimates, 2025 (https://aidsinfo.unaids.org/)

HIV testing and treatment cascade, by age and sex, Asia and the Pacific, 2024

Figure 10.3. HIV testing and treatment cascade, by age and sex, Asia and the Pacific, 2024



Source: UNAIDS epidemiological estimates 2025 (https://aidsinfo.unaids.org/).

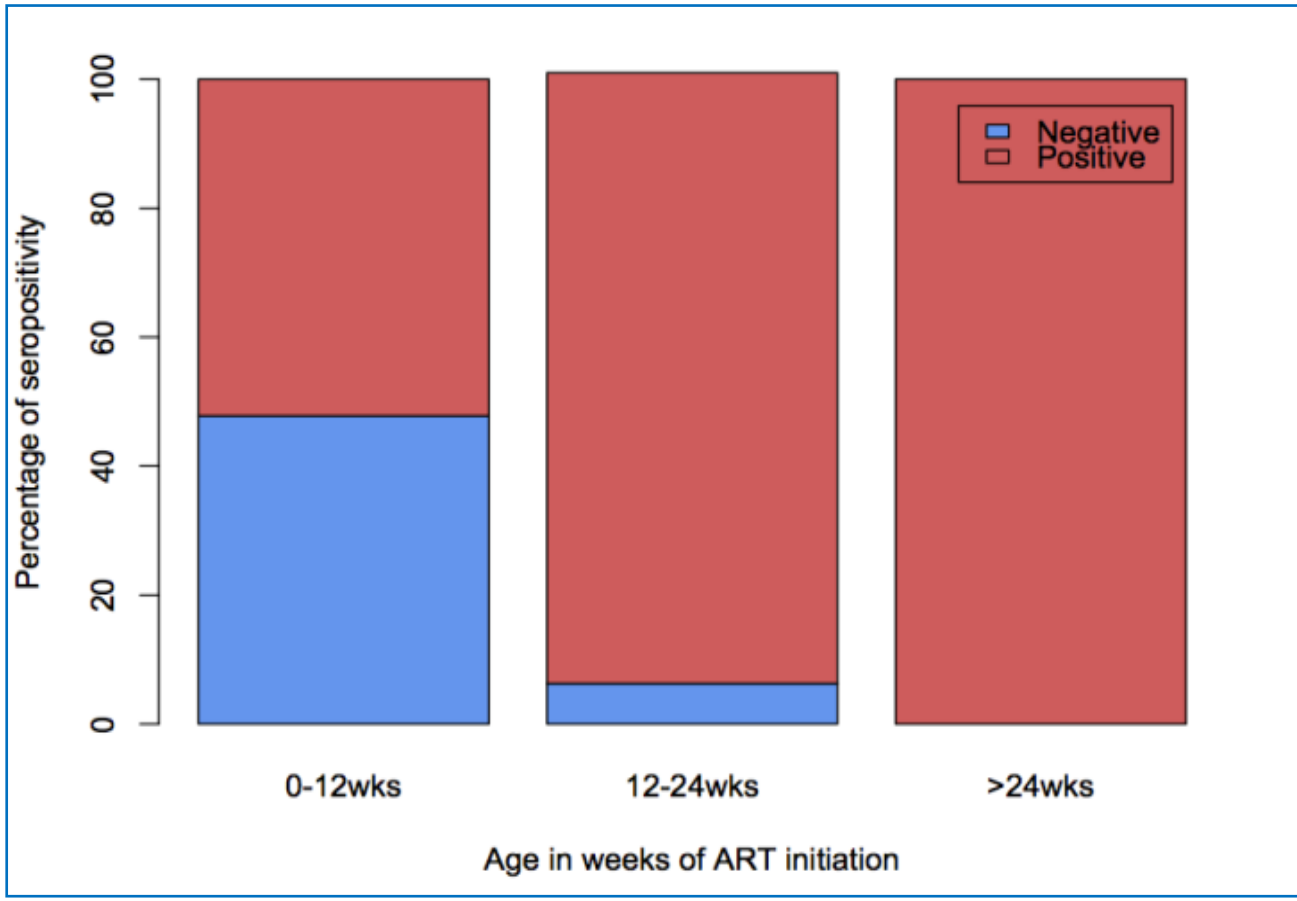
Age	Diagnostic test of choice for HIV infection in Children		If HIV-infected - establish level of HIV disease progression
	Serology	**Genomic Amplification**	**Viral Parameters**
> 18 mths	***HIV antibody***	***HIV viral load (RNA)***	**HIV viral load CD4 count Baseline HIV resistance**
< 18 mths	**HIV antibody + category C/ stage 4 condition in an infant makes an HIV diagnosis highly likely**	***HIV DNA PCR or HIV viral load (RNA)***	**HIV viral load CD4 count Baseline HIV resistance**

A positive HIV result should always be confirmed by another test

Also important:
Lack of HIV antibody in early treated infants

- **Early ART prevents HIV antibody production:**
  - in 50% infants starting ART <3 months
    - No correlation with DNA PCR reservoir

HIV antibody cannot be used to confirm HIV status in children started on early ART; They are NOT CURED!



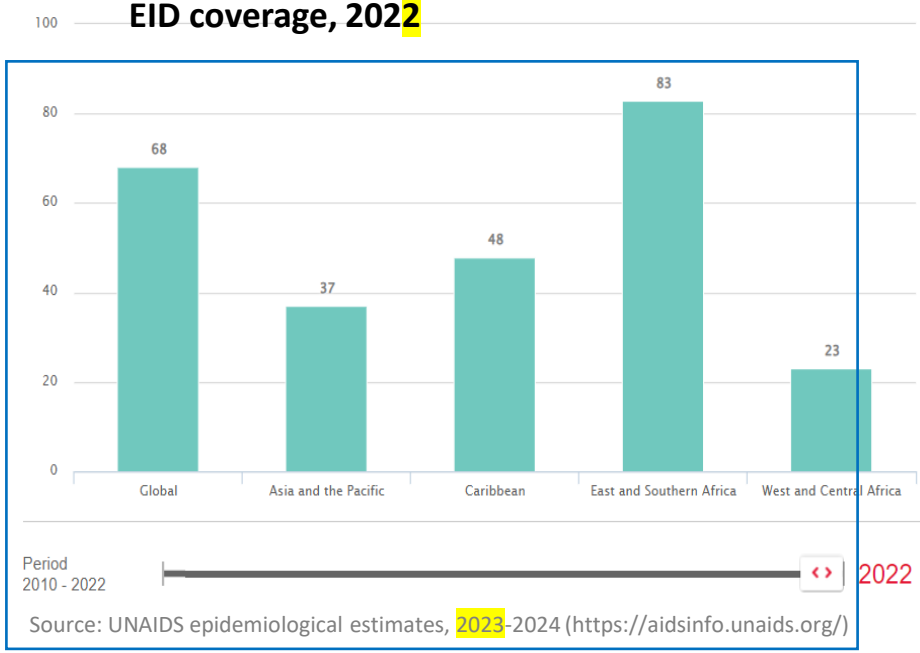
H. Payneet al Lancet Infectious Diseases 2015

Finding missing children: early infant diagnosis (EID)

- ✓**EID is now available in nearly all high-prevalence countries**
- ✓Increasingly Point-of-care
- ❑However, the EID coverage is very variable between regions and countries

EID = testing before age of 2 month

EID coverage, 2022



Source: UNAIDS epidemiological estimates, 2023-2024 (https://aidsinfo.unaids.org/)

*Bianchi et al. Lancet HIV 2019; Jani et al. LIFE study. Pre-print 2024

**CHAI. HIV Market report 2023

EID limitations

- ❑ Where ART in pregnancy is high, EID has low yield of positive samples***
- ❑ EID will not pick up:
  - Infants, whose mothers not engaged in care
    - Adolescent and young mothers are overrepresented in this group^
  - Infants who acquire HIV during breastfeeding
  - Older undiagnosed children
    - ❖ Most undiagnosed children are aged >2 years (63% are aged 5-14)$^{\theta}$

***PEPFAR Panorama Spotlight Datasets 2024

^Tassembedo et al. AIDS 2024

$^{\theta}$Gross et al PIDJ 2023

Possible solutions / ways forward:

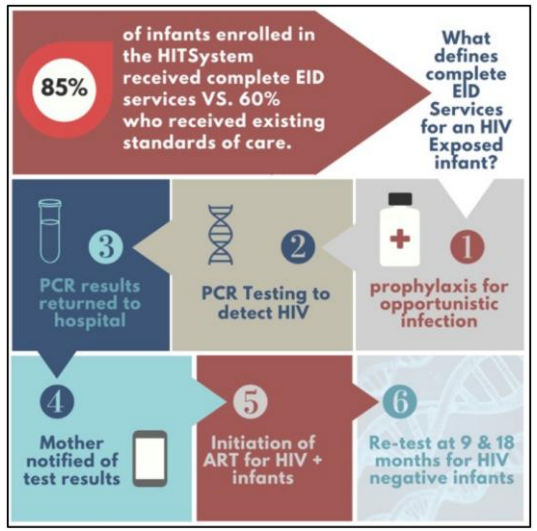
- ❖ Community POC-EID may help to engage “hard-to-reach” populations#
- ❖ testing infants throughout and at end of breastfeeding
- ❖ test older children

#Tembo et al. Global health: Science and Practice 2022

Innovative approaches to HIV testing

Digital Health

- Algorithm-based alerts for EID providers and lab staff and text appointment reminders
- ✓ Earlier EID testing and ART initiation
- ✓ Higher re-testing at the end of breast feeding
- ✓ Cost-effective



- ✓ Implemented at 300 facilities in Kenya, Malawi, Tanzania, Nigeria

XXX, Finocchario-Kessler et al. Lancet Global Health 2023

Oral mucosal POC HIV tests

- ✓ **Rapid**
- ✓ **No bloods**
- ✓ **High acceptability**
- ✓ **Low tech**
- ✓ **Cost-saving**
- ✓ **Feasible**

Caregiver-assisted tests

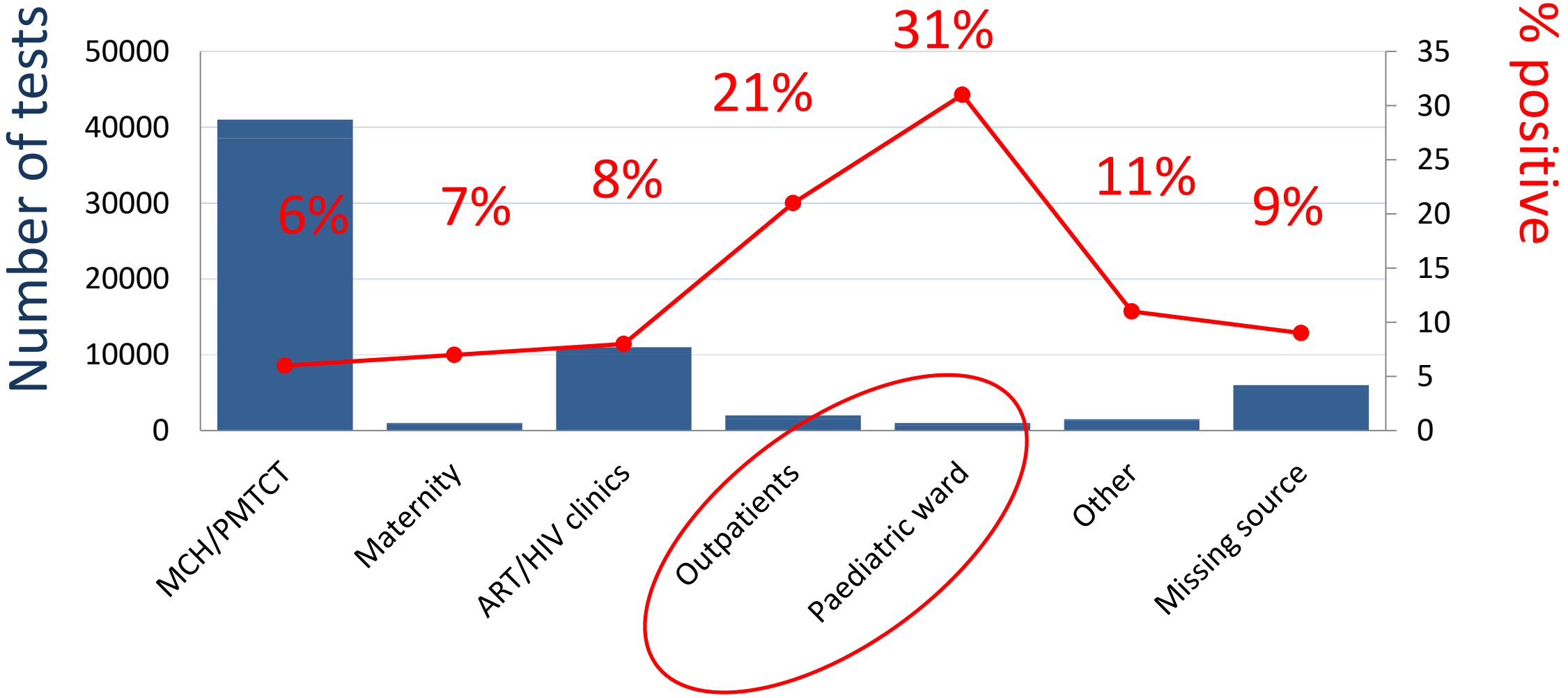
Stecker et al. FASTER. HIV Ped Workshop 2022

Community-based self-tests

UNICEF. Adolescent HIV prevention. 2024

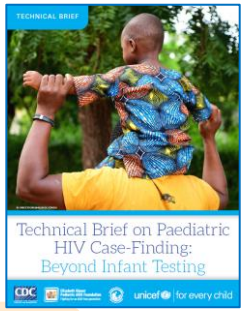
Chikwari et al. JAIDS 2019; Stecker et al. HIV Pediatrics Workshop 2022; Wilson et al. AIDS Behav 2022; Choko et al. PLoS Med 2015; Tonen-Wolyec et al. Med Mal Infect 2020; Hector PLoS One 2018

Early Infant Diagnosis Test Results by Entry point: Kenya 2014



NASCOP, MOH Kenya, 2014

Catch-up testing needed to reach children with HIV who are not yet diagnosed



Sick child clinic:

TB

Malnutrition

In/Outpatients

Family index case

All family members of HIV+ cases

Well-child clinics

Test mothers ± child

(consider unintended consequences)

School or community-based screening

Adolescent health services

(legal age of consent issues)

TARGET KEY GROUPS (higher yield) ⟷ **POPULATION LEVEL (lower yield)**

Cost effectiveness varies by setting: prevalence (population-level strategies for high HIV prevalence settings), CLHIV age distribution, maternal ART, EID and post-natal prophylaxis coverage → **need more implementation data**

Dunning et al. JIAS 2021; Stanic et al. Open Forum ID 2022; McCann et al. JIAS 2022; Kinyaga et al. JIAS 2018; Chikwari et al. Lancet HIV 2021; Dunlop et al. PIDJ 2023; Gross et al PIDJ 2023

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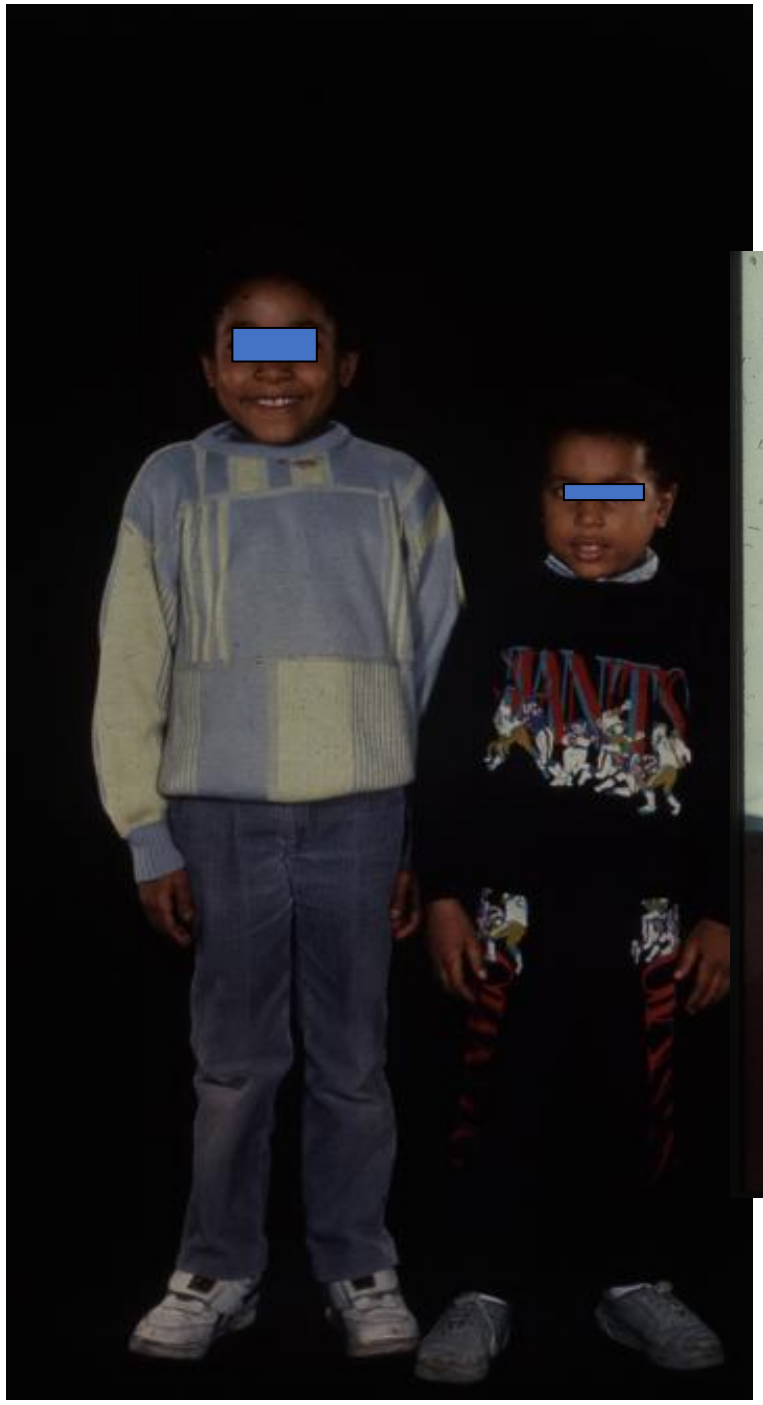
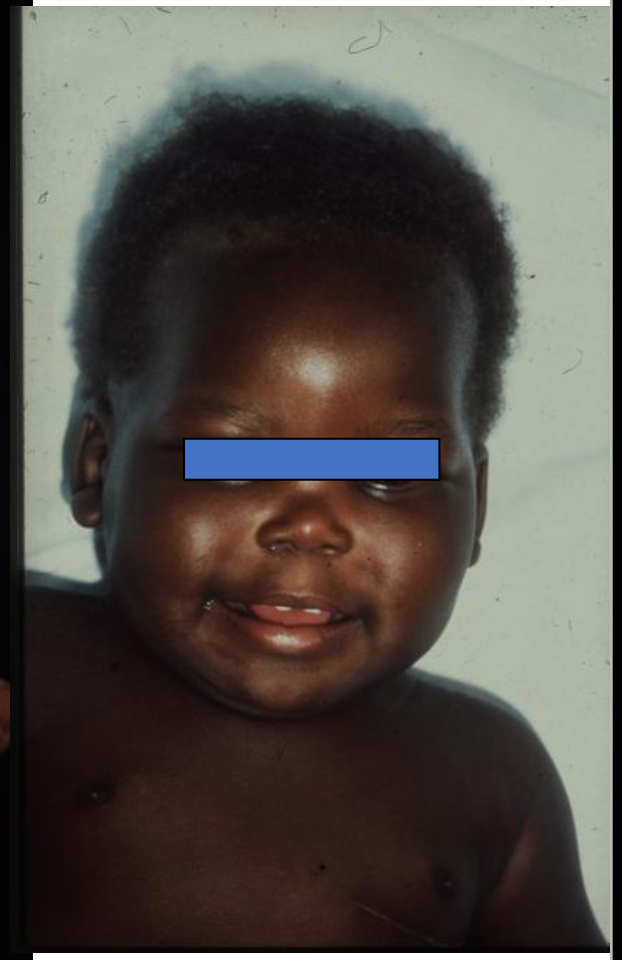
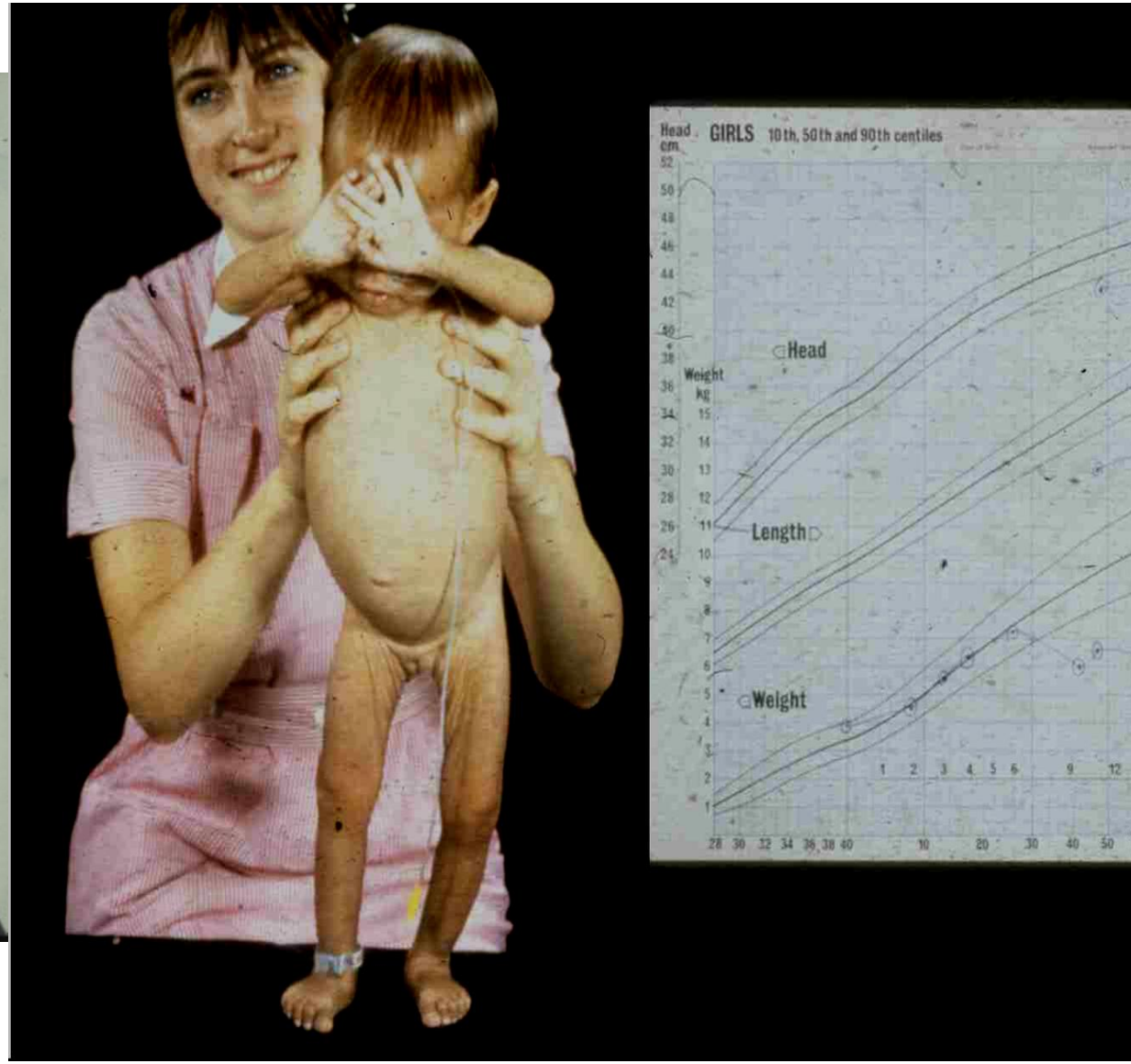
First kids with HIV at Great Ormond Street Childrens Hospital, London - late 1980s…







Infants with HIV can become sick very rapidly

Respiratory disease

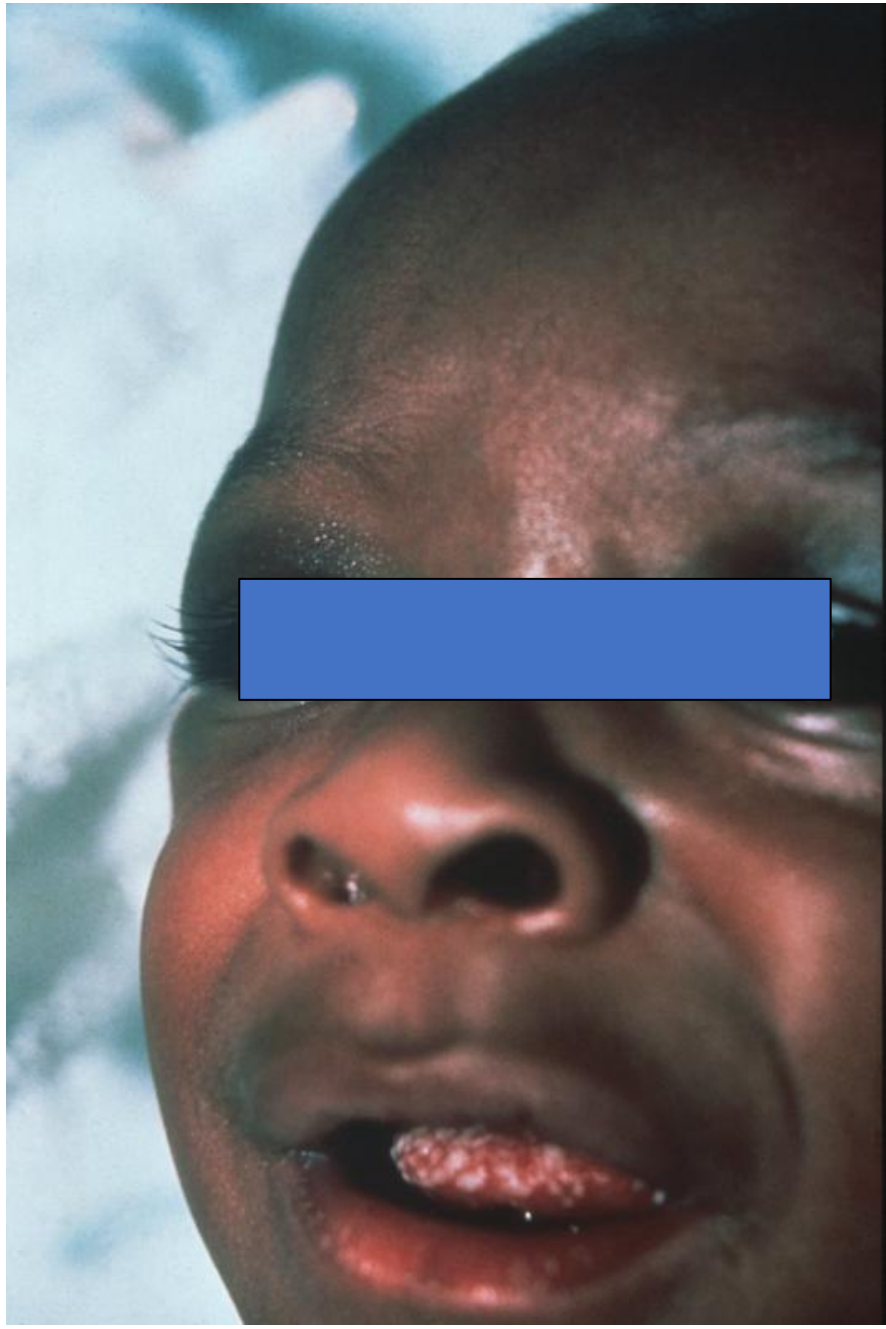
Encephalopathy

GI symptoms & wasting

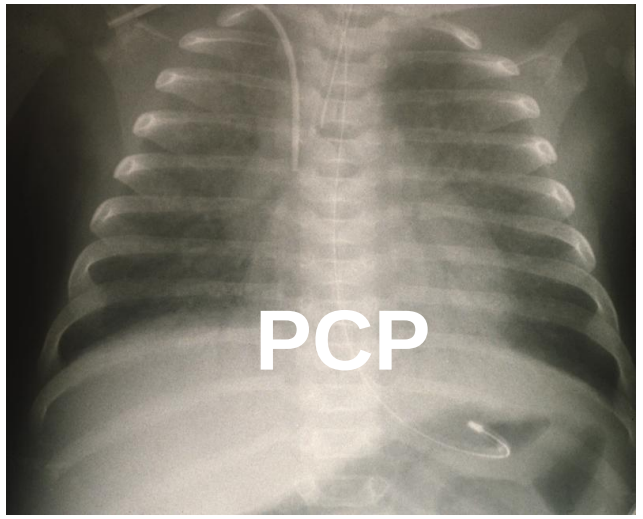
Recurrent URTI's

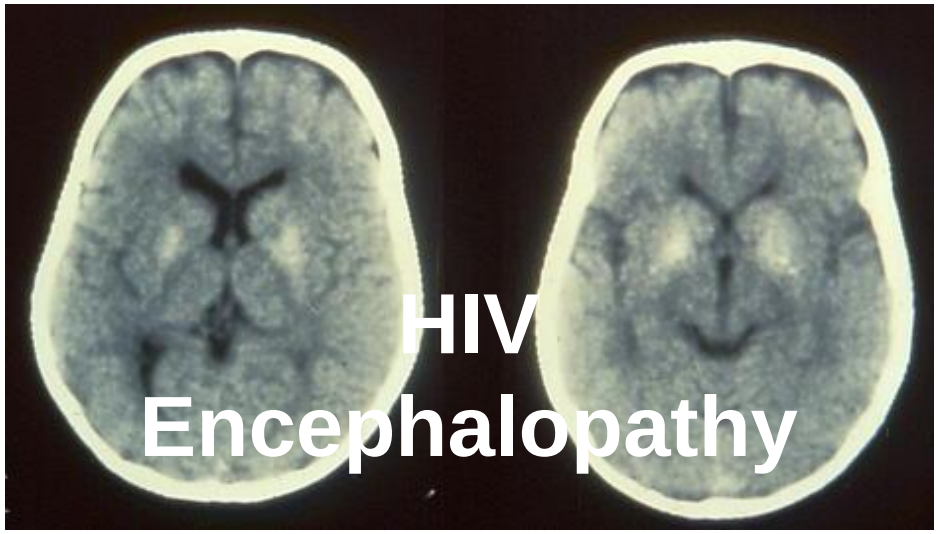
Recurrent oral thrush

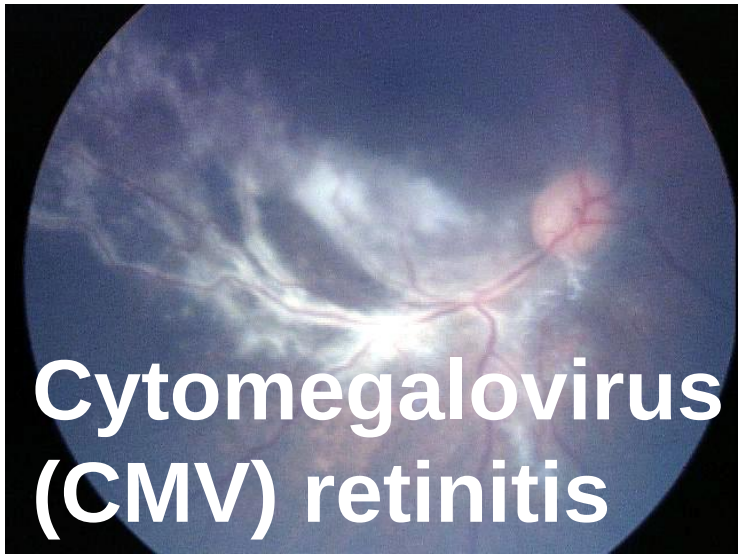
Hepato-splenomegally / lymphadenopathy

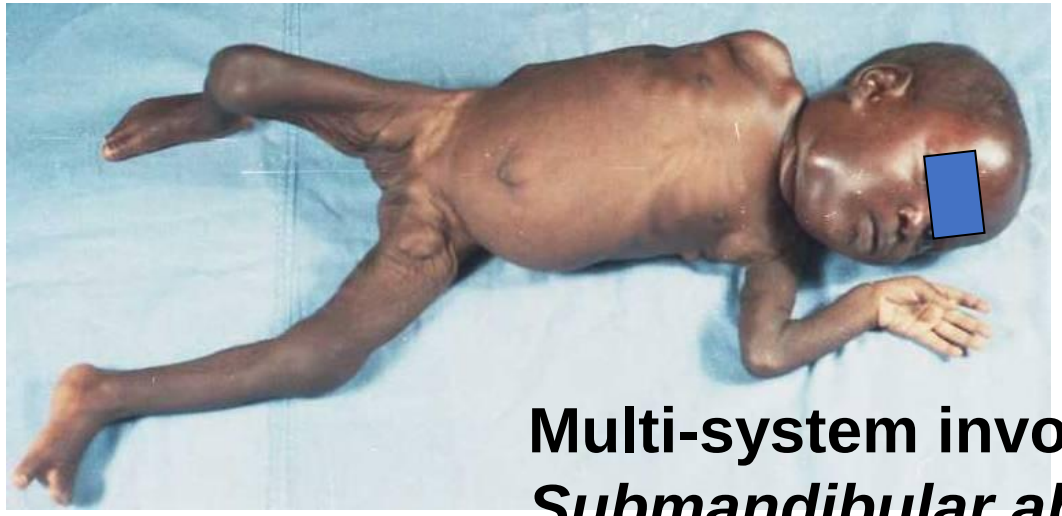


Infants presenting with severe HIV - AIDS









Multi-system involvement:
Submandibular abscess
Severe wasting
Developmental delay

OBSERVER SUNDAY 21 APRIL 1991

Child Aids crisis leads to first family clinic

Annabel Ferriman
Health Correspondent

BRITAIN's first family Aids clinic is to open next month at Great Ormond Street Children's Hospital in London to deal with the growing Aids crisis.

Doctors at the hospital are facing the problem of whole families discovering they are

Archives of Disease in Childhood 1997;77:478–482

ORIGINAL ARTICLES

A family clinic—optimising care for HIV infected children and their families

Diana M Gibb, Janet Masters, Delane Shingadia, Sue Trickett, Nigel Klein, Candy Duggan, Vas Novelli, Danielle Mercey

Abstract
A family clinic providing specialist paedi-

In London, detection of HIV infection in previously undiagnosed pregnant women is only around 10%,[3] and an infected child is fre-

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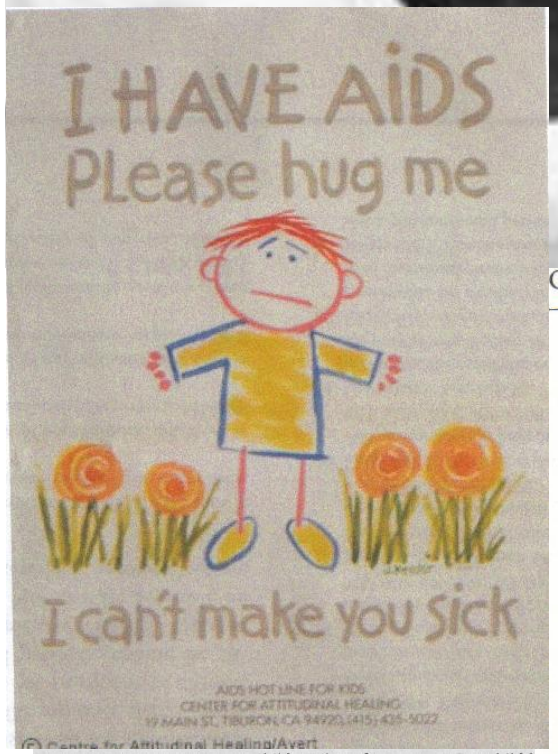

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Could this child have HIV?

ENT

Dentist

Haematology

Family Dr

Pulmonology

NICU

PICU

Dermatology

Neurology

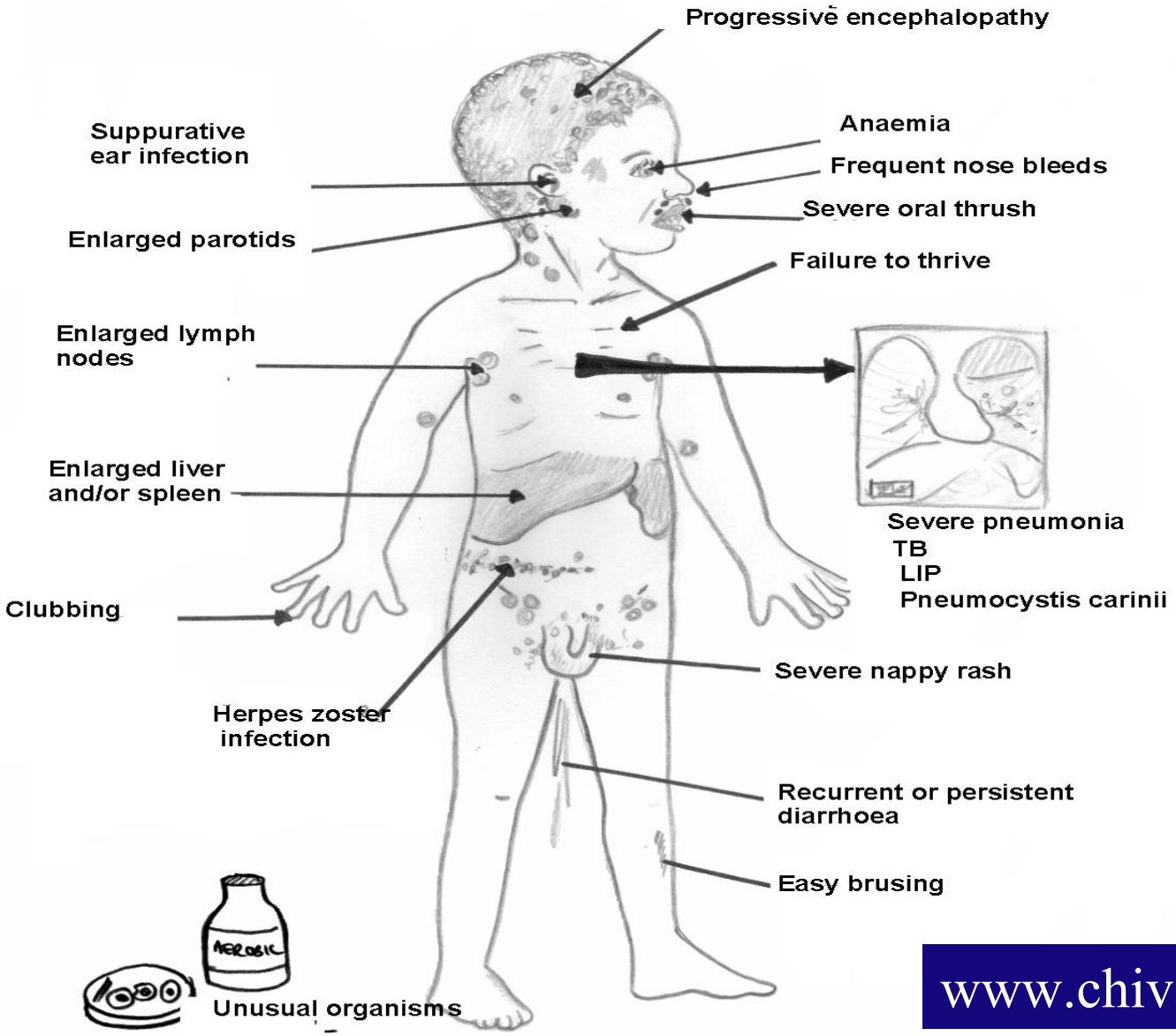
Immunology

Social Services

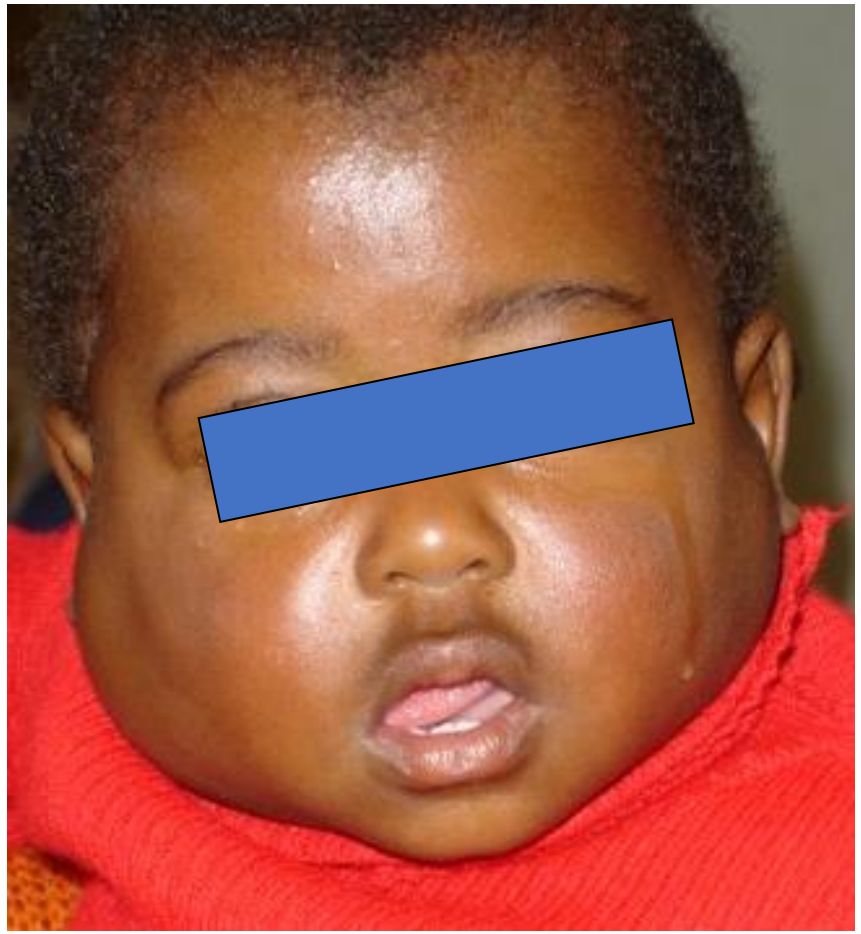
Oncology

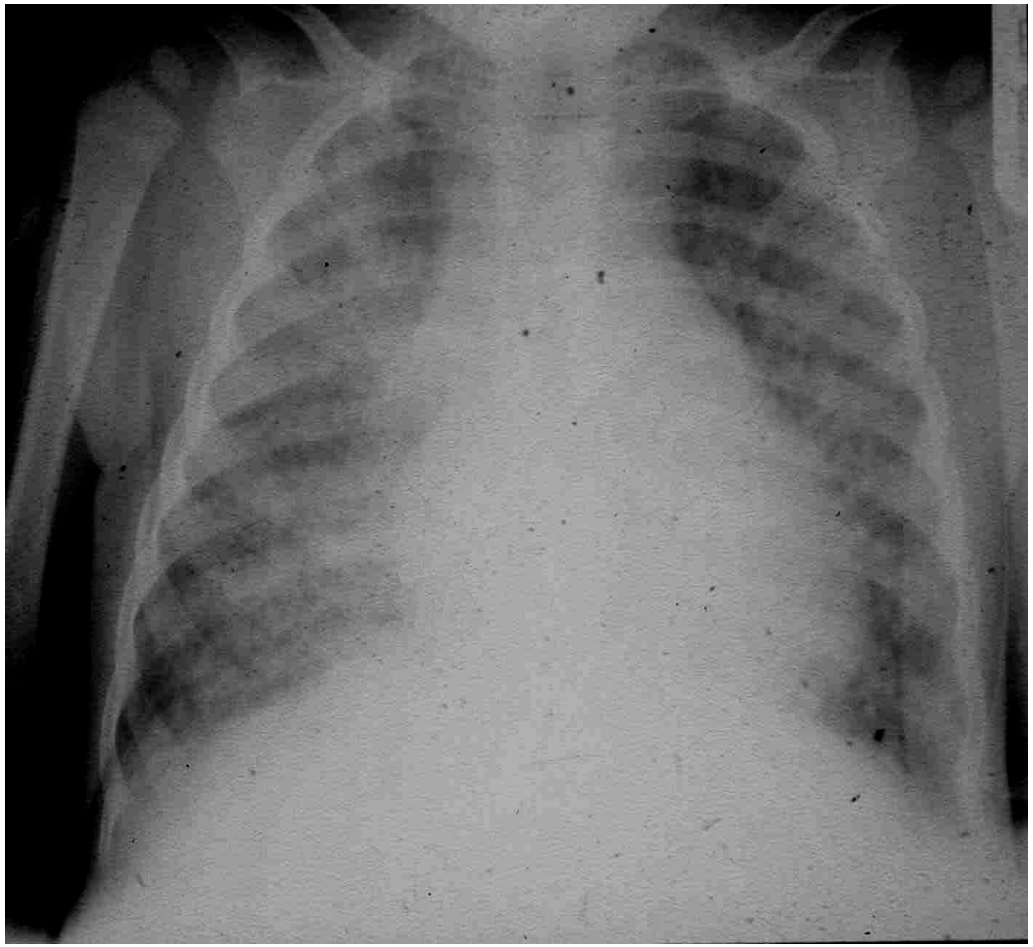
Gastroenterology

Clinical Features of HIV Infection

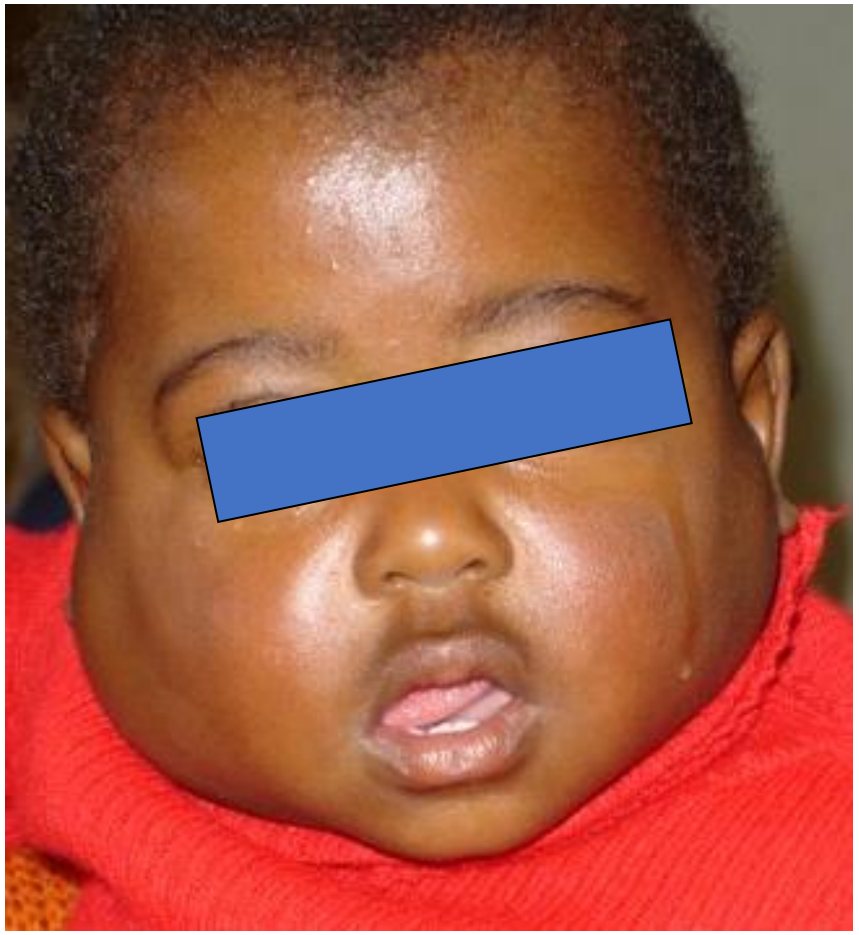


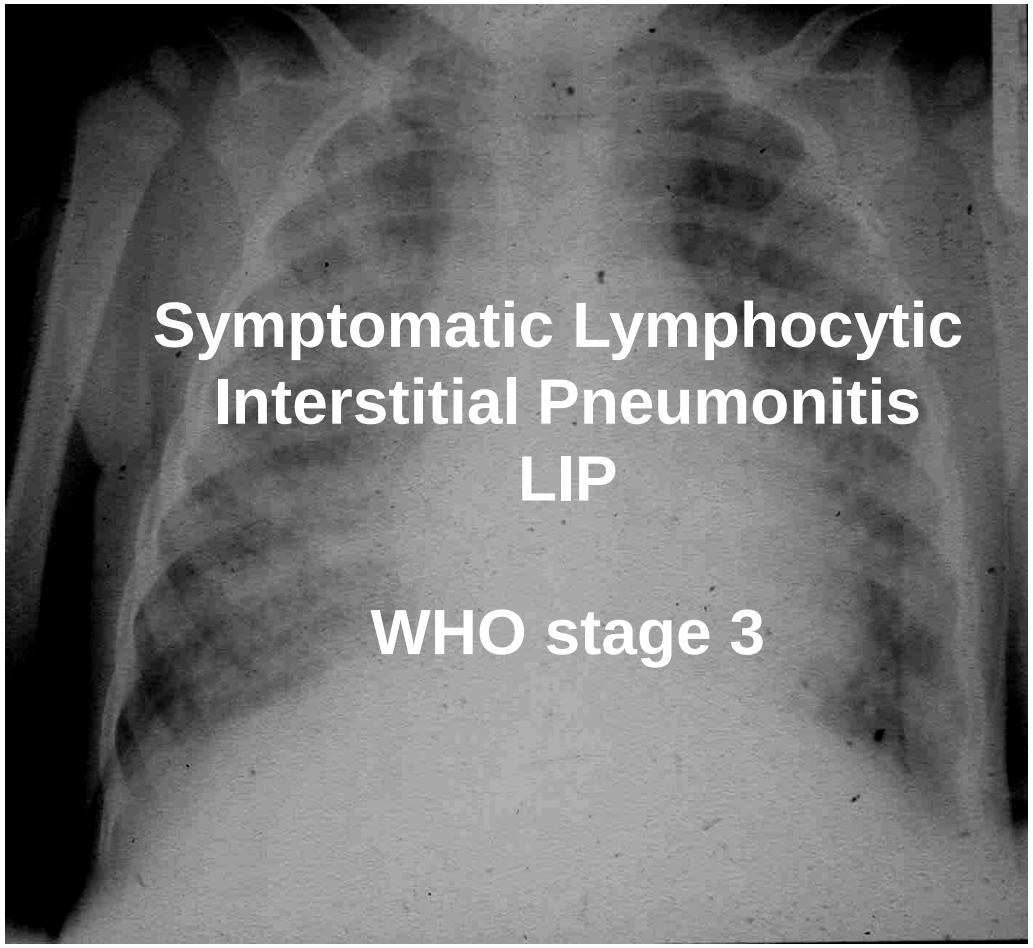
www.chiva-africa.org





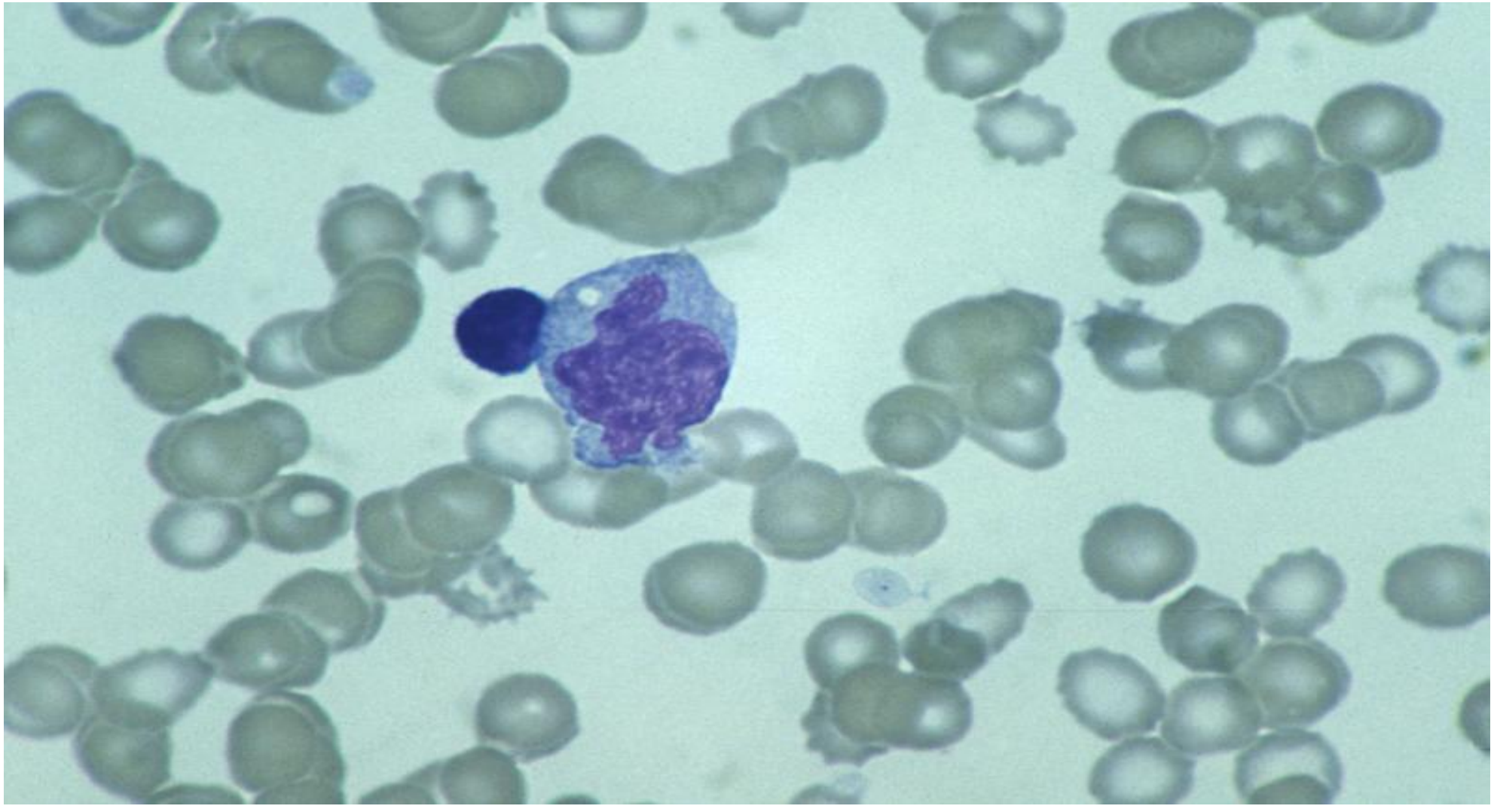
This 15 month old child with HIV has a chronic cough & poor growth. He has had BCG, his grandmother was treated last year for TB.
What do you think he has?





Parotitis & Lymphoid interstitial pneumonitis (LIP)
Associated with better survival in pre HAART era
Usually good CD4 count with high HIV viral load
Possible interaction between HIV and EBV

A 4 year old child with a fever and cough presents to hospital,
He has generalised lymphadenopathy & hepatosplenomegally
This is his blood film – what's your differential diagnosis?



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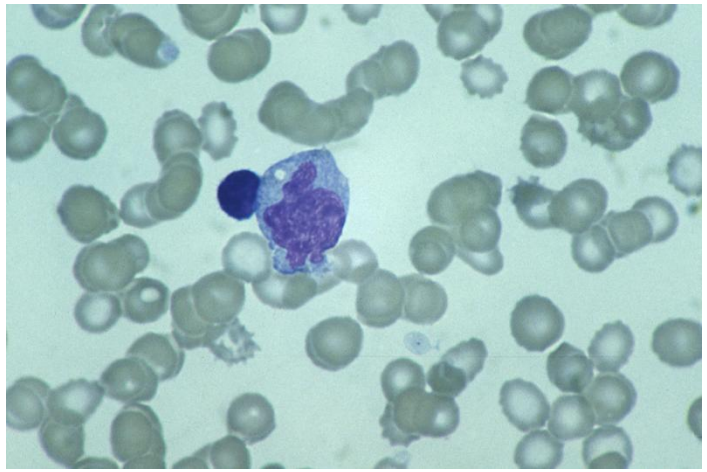
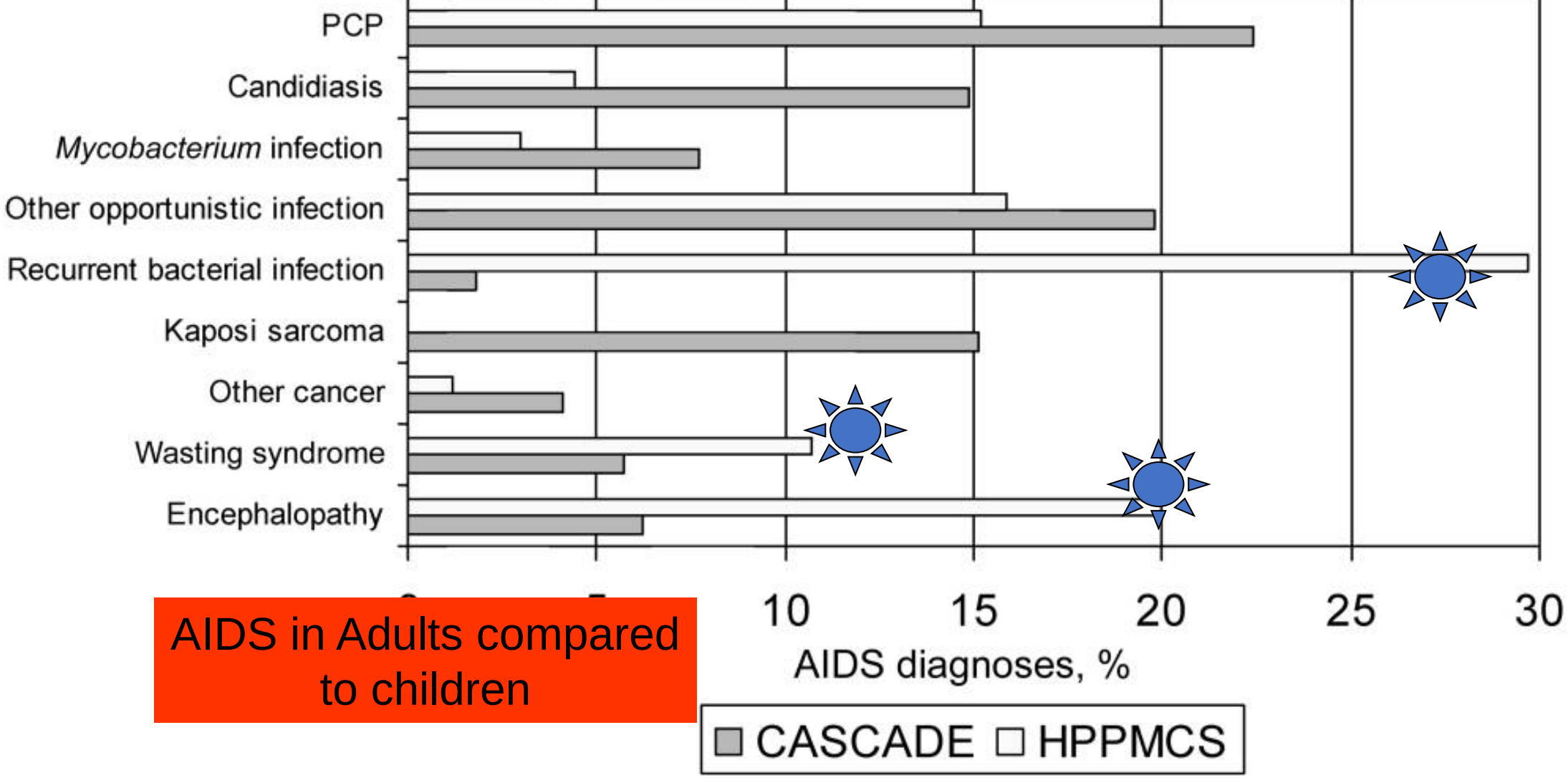


Thrombocytopaenia:

Sepsis
Malignancy
Idiopathic thrombocytopenia
HIV

All children with persistent thrombocytopenia should have an HIV test:
↓↓ platelets occurs in up to 10% of children with HIV
May be the presenting condition
Not correlated with immunological status



AIDS in Adults compared to children

CASCADE - Current CD4 Cell Count and the Short-Term Risk of AIDS and Death before the Availability of Effective Antiretroviral Therapy in HIV-Infected Children (n = 3244) and Adults (n = 3497).

Dunn et al The Journal of Infectious Diseases 2008; 197:398–404

First HIV presentation in children / Young People over 10 years of age

May have mild symptoms during childhood that we fail to recognise as HIV infection

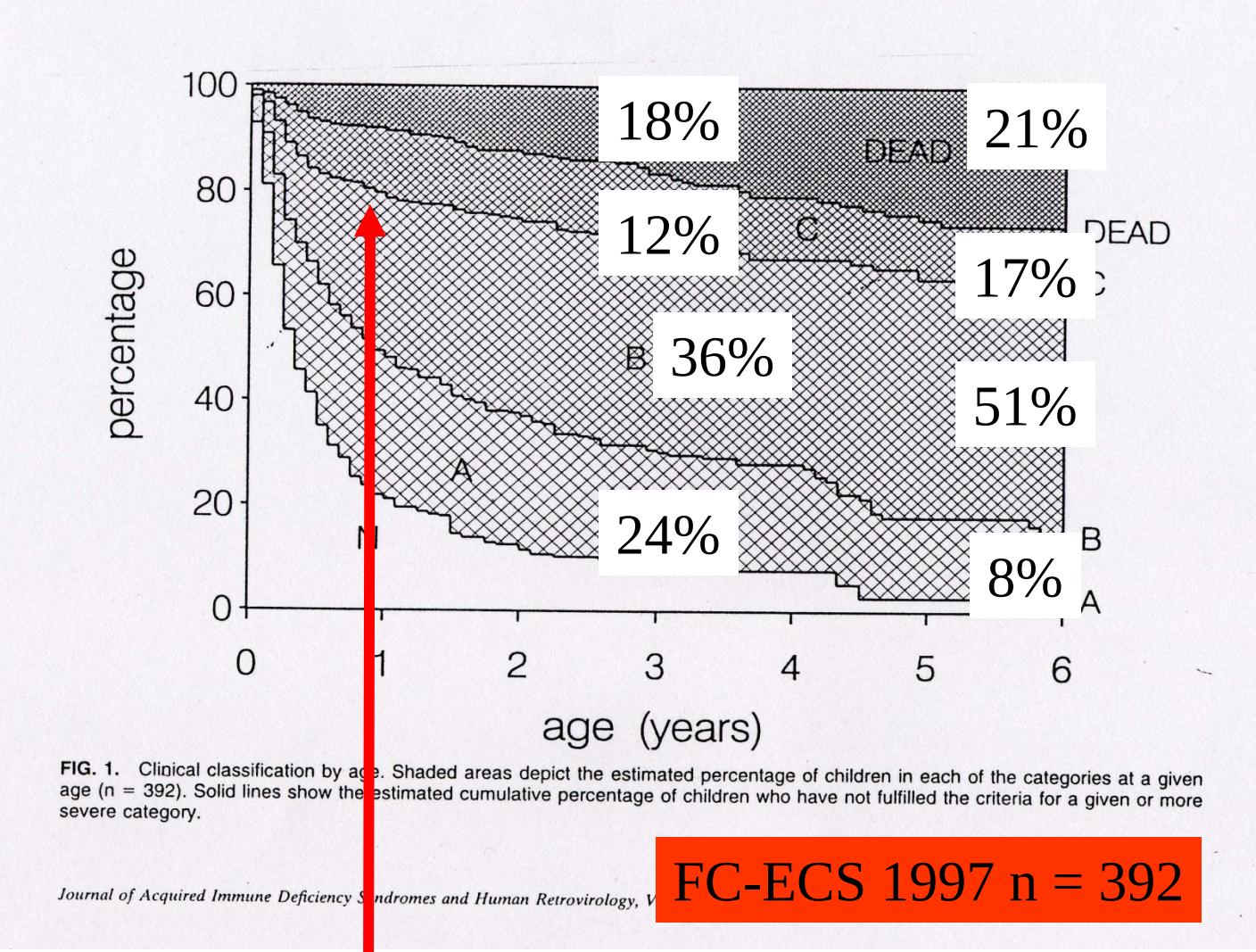
May present for first time in 2nd decade of life

‘Don’t Forget the Children’

Guidance for the HIV testing of children with HIV-positive parents

*When any family member is diagnosed with HIV then **ALL** other members should be offered the test, what ever their age, & whether they have symptoms or not*

Resource rich settings - 20% of infants progress rapidly



Symptom Category & Survival before ART

European Collaborative Study 1999

dead / C
20% by 1 year

48% by 10yrs

5% annual progression to death / C

HIV in African Children

Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis

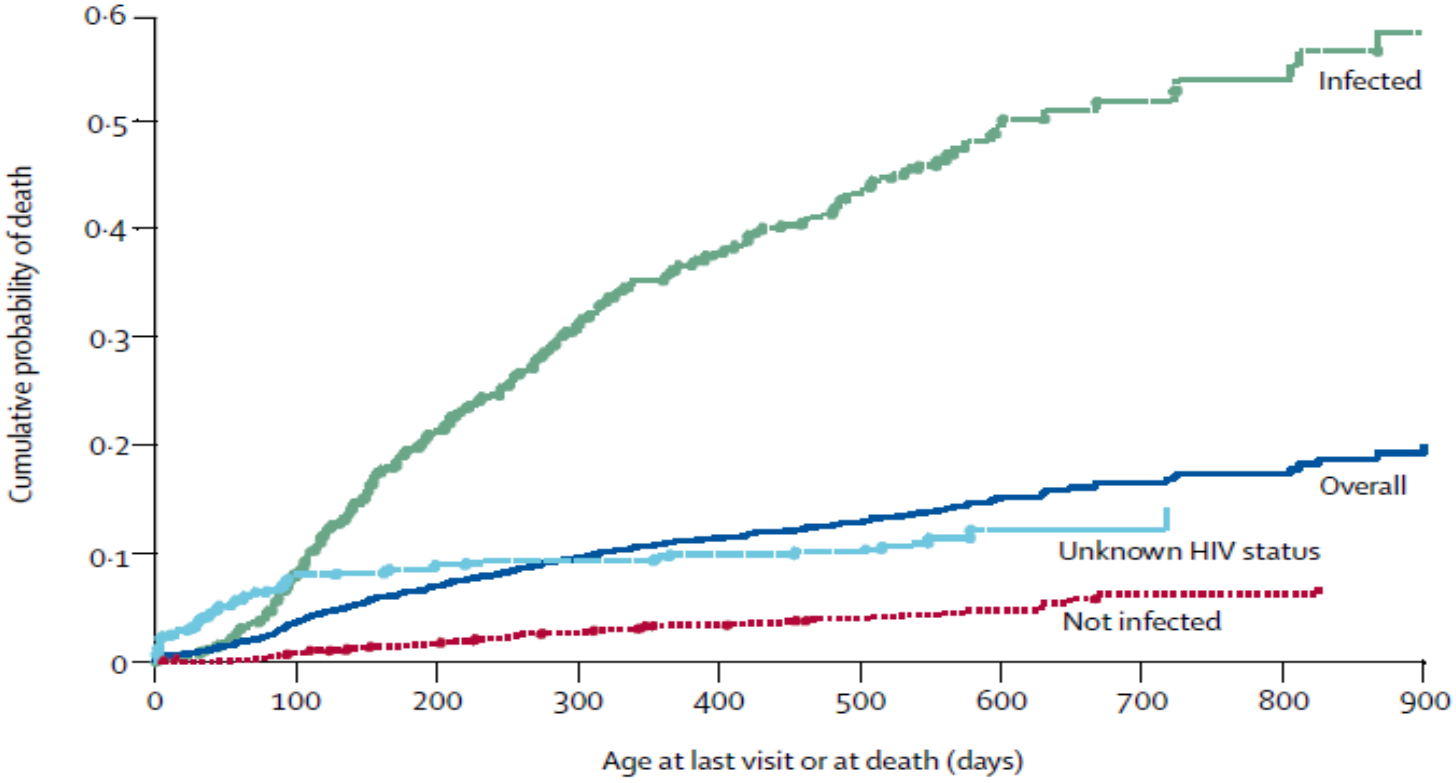
*Marie-Louise Newell, Hoosen Coovadia, Marjo Cortina-Borja, Nigel Rollins, Philippe Gaillard, Francois Dabis, for the Ghent International AIDS Society (IAS) working group on HIV infection in women and children**

Summary

Background HIV contributes substantially to child mortality, but factors underlying these deaths are inadequately described. With individual data from seven randomised mother-to-child transmission (MTCT) intervention trials, we estimate mortality in African children born to HIV-infected mothers and analyse selected risk factors.

Methods Early HIV infection was defined as a positive HIV-PCR test before 4 weeks of age; and late infection by a negative PCR test at or after 4 weeks of age, followed by a positive test. Mortality rate was expressed per 1000 child-years. We investigated the effect of maternal health, infant HIV infection, feeding practices, and age at acquisition of infection on mortality assessed with Cox proportional hazards models, and allowed for random effects for trials grouped geographically.

Findings 378 (11%) of 3468 children died. By age 1 year, an estimated 35·2% infected and 4·9% uninfected children will have died; by 2 years of age, 52·5% and 7·6% will have died, respectively. Mortality varied by geographical region, and was associated with maternal death (adjusted odds ratio 2·27, 95% CI 1·62–3·19), CD4+ cell counts <200 per μL (1·91, 1·39–2·62), and infant HIV infection (8·16, 6·43–10·33). Mortality was not associated with either ever breastfeeding and never breastfeeding in either infected or uninfected children. In infected children



Children at risk	1 day	7 days	28 days	365 days	730 days
Overall	3330	3269	3212	2063	297
p (death)	0·002	0·006	0·008	0·110	0·174
Infected	693	691	681	299	54
p (death)	0·0015	0·003	0·008	0·352	0·525
Uninfected	2127	2114	2078	1364	211
p (death)	0·0005	0·003	0·006	0·049	0·076

Figure 1: **Estimated unadjusted overall mortality for infected and uninfected children**

Over half of HIV infected children in Africa die before their second birthday (2004)

Young Children differ from adults

Virology

High viral loads and for longer

Immunology

CD4 is high in young children and falls with age; CD4 percent less variable

Immature immune system at infection

Very active thymus once on antiretroviral therapy

Pharmacokinetics

Evolving metabolic pathways

Growth – frequent dose changes

Acceptability / tolerability

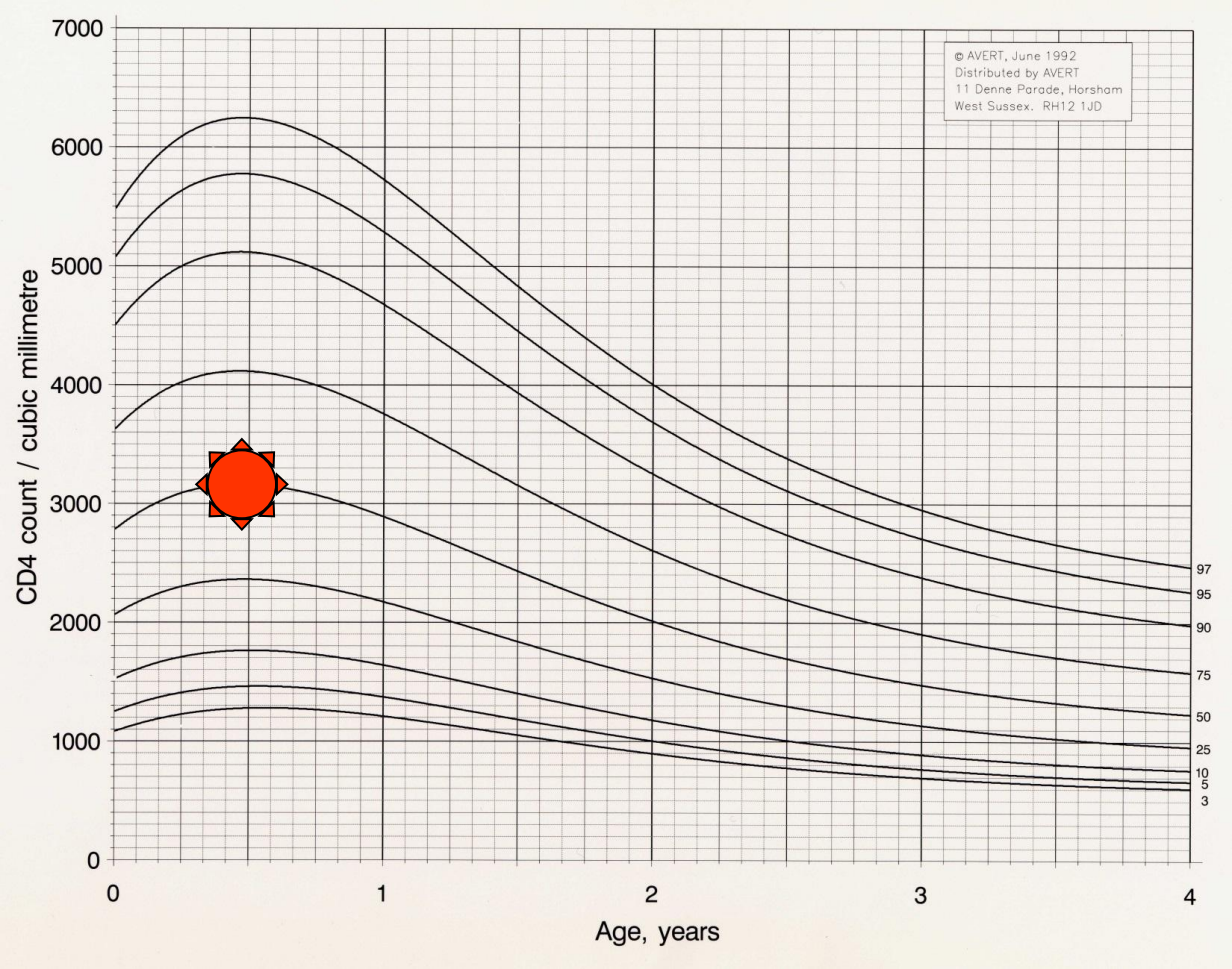
Need for appropriate formulations

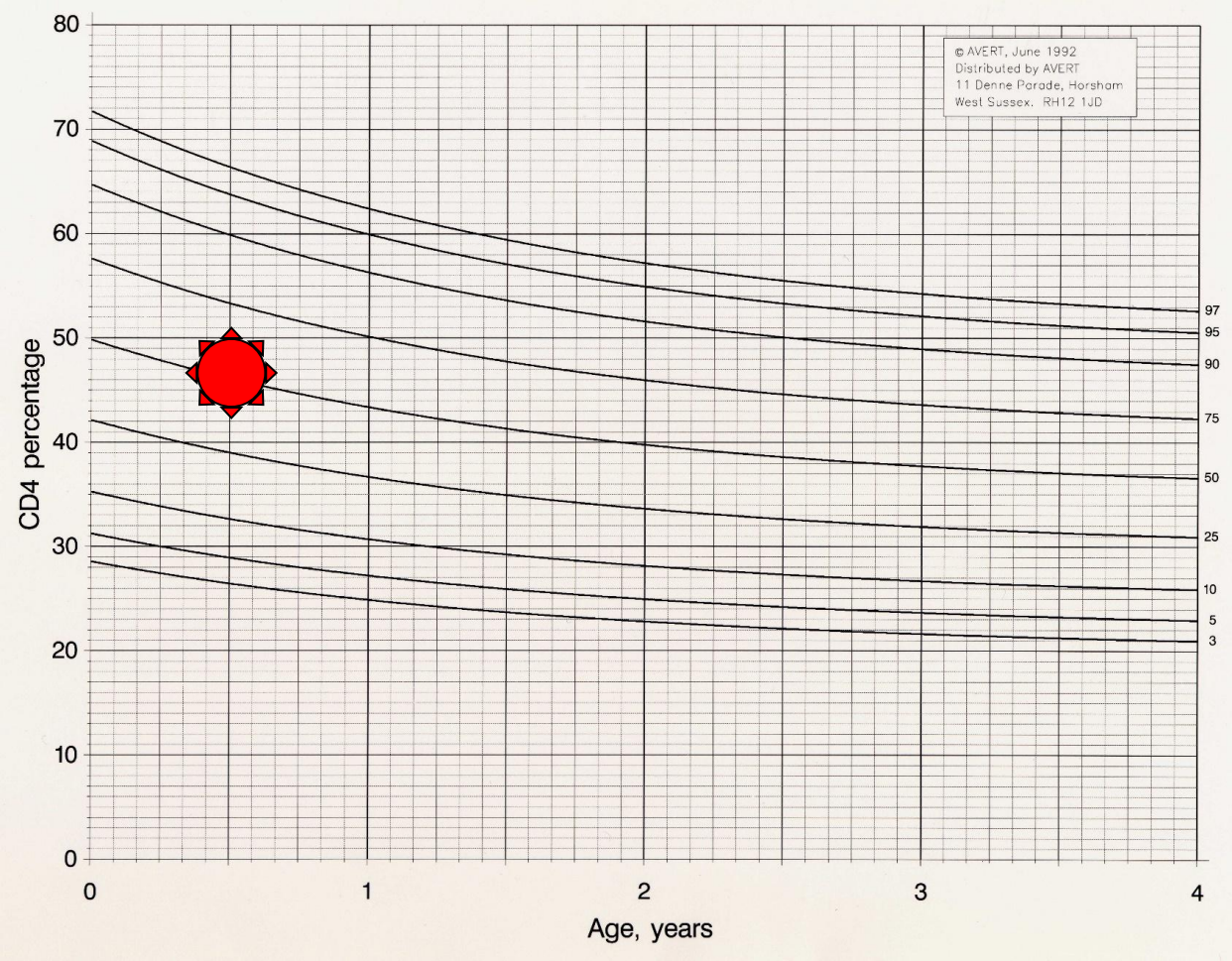
→ Different natural History and ART response in adults and children

→ Age is a key factor

Absolute CD4 count and percentage percentiles from 0-4 yrs of age.

ECS, Age related standards for T lymphocyte subsets based on **uninfected children** born to HIV-1 infected women. Pediatr Infect Dis J, 1992; 11: 1018-1026.





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Treatment During Primary Infection

South African CHER teams

Children with HIV and Early antiRetrovirals

CHER Trial

Will early ART for a limited time (1 or 2 years) following primary infection alter the natural history of HIV disease in resource limited settings?

All infants with HIV need to start ART immediately
RCT - early vs deferred ART in infants in South Africa, CHER Trial

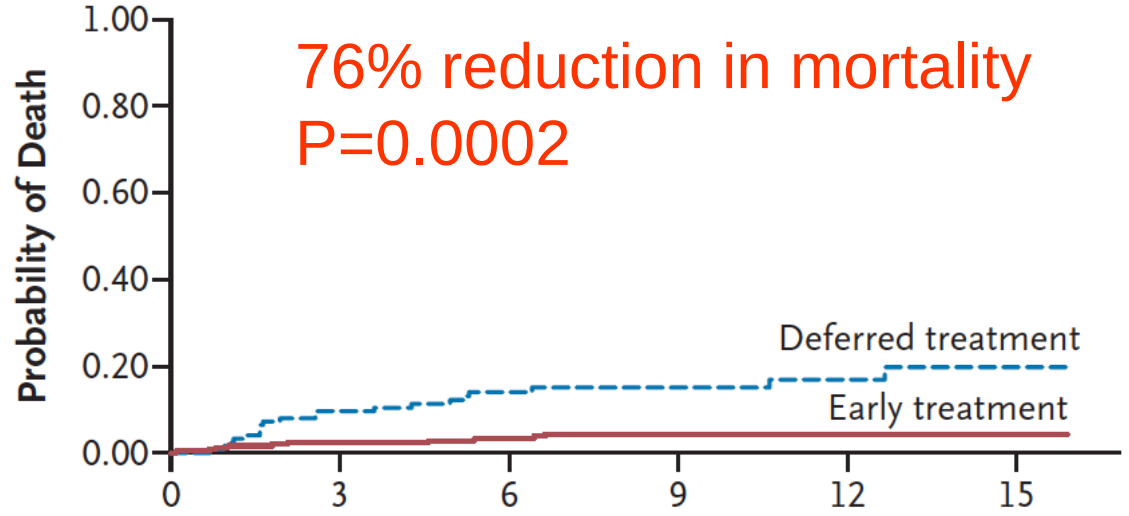
Mortality:

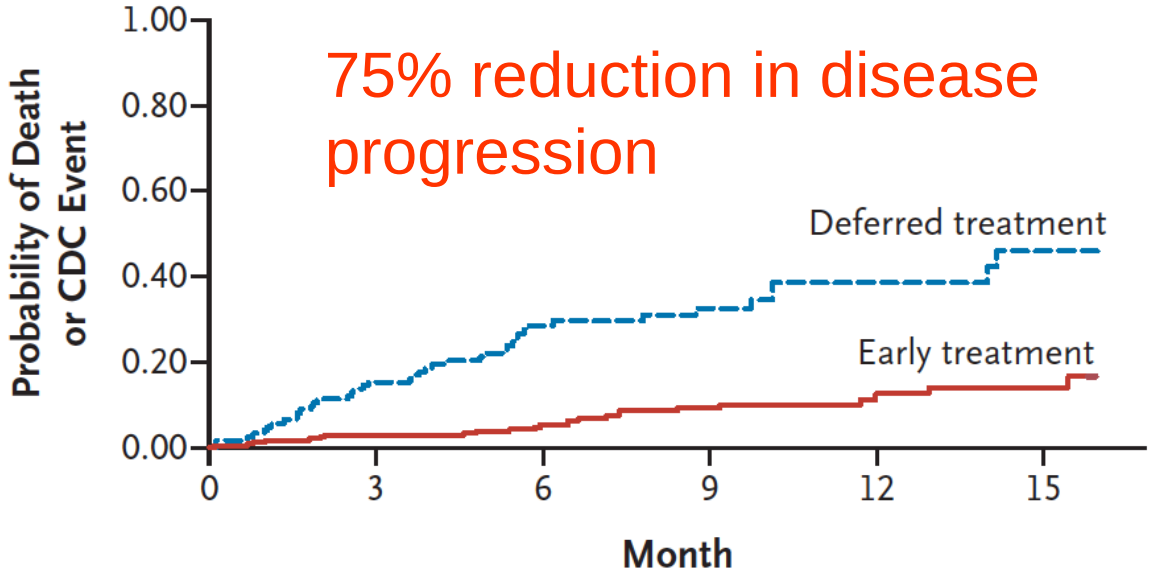
16% deferred ART

4% immediate ART

Most deaths were sudden, 40% occurred at home, and were not “AIDS-defining”

All infants with HIV should start ART as soon as possible



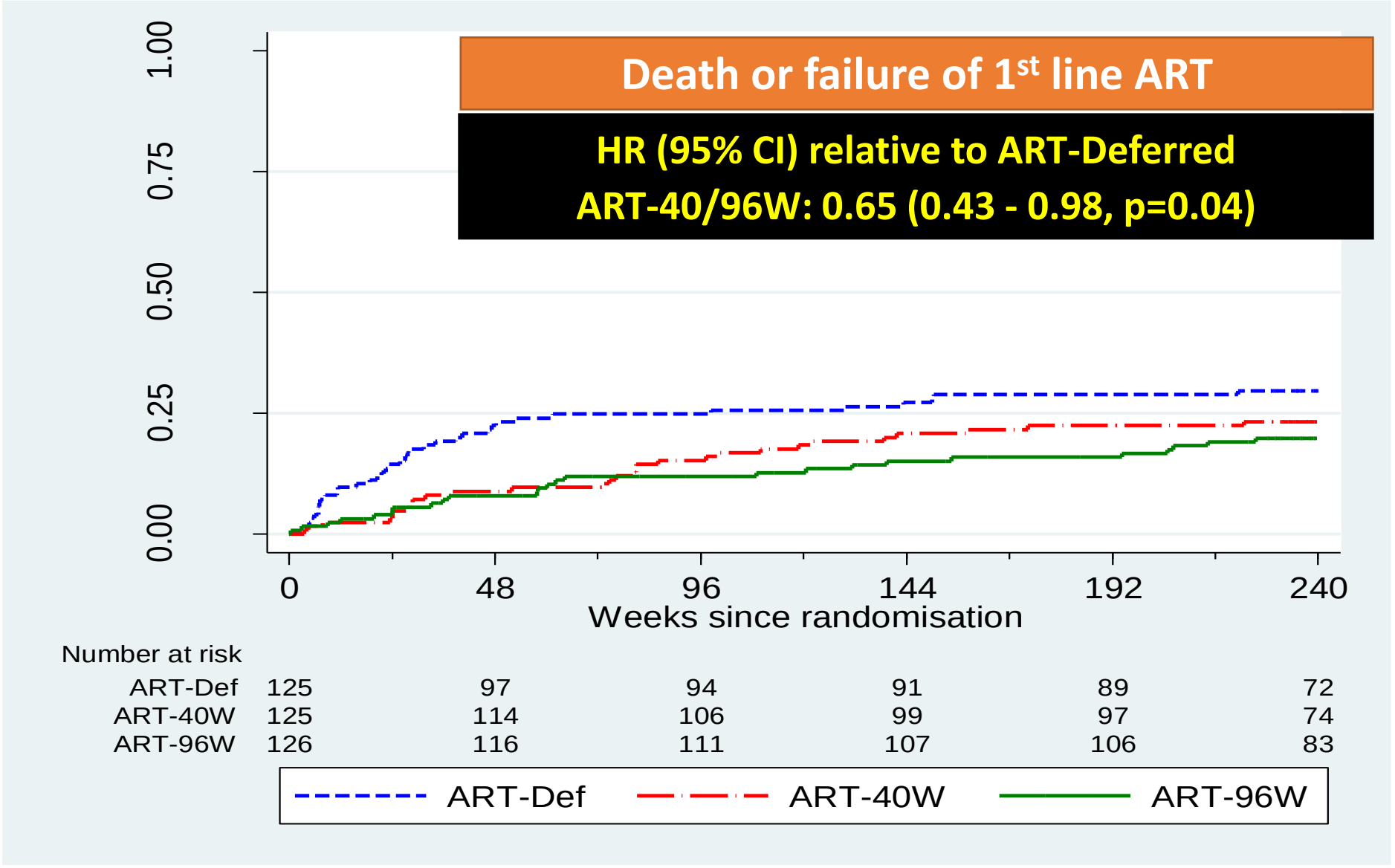


Violari et al., N Engl J Med 2008

CHER final 5-year results 2013

CIPRA-SA

Early Limited ART remained superior to delayed ART over 5 years of follow-up



CHER final 5-year results 2013

CIPRA-SA

Articles

Early time-limited antiretroviral therapy versus deferred therapy in South African infants infected with HIV: results from the children with HIV early antiretroviral (CHER) randomised trial

Mark F Cotton*, Avy Violari*, Kennedy Otwombe, Ravindre Panchia, Els Dobbels, Helena Rabie, Deirdre Josipovic, Afaaf Liberty, Erica Lazarus, Steve Innes, Anita Janse van Rensburg, Wilma Pelser, Handre Truter, Shabir A Madhi, Edward Handelsman, Patrick Jean-Philippe, James A McIntyre†, Diana M Gibb†, Abdel G Babiker†, on behalf of the CHER Study Team

Summary

Background Interim results from the children with HIV early antiretroviral (CHER) trial showed that early antiretroviral therapy (ART) was life-saving for infants infected with HIV. In view of the few treatment options and the potential toxicity associated with lifelong ART, in the CHER trial we compared early time-limited ART with deferred ART.

Methods CHER was an open-label randomised controlled trial of HIV-infected asymptomatic infants younger than 12 weeks in two South African trial sites with a percentage of CD4-positive T lymphocytes (CD4%) of 25% or higher. 377 infants were randomly allocated to one of three groups: deferred ART (ART-Def), immediate ART for 40 weeks (ART-40W), or immediate ART for 96 weeks (ART-96W), with subsequent treatment interruption. The randomisation schedule was stratified by clinical site with permuted blocks of random sizes to balance the numbers of infants allocated to each group. Criteria for ART initiation in the ART-Def group and re-initiation after interruption in the

Published Online August 22, 2013 http://dx.doi.org/10.1016/S0140-6736(13)61409-9

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(13)61717-1

*Contributed equally as first authors

†Contributed equally as senior authors

Children's Infectious Diseases

Early Limited ART remained superior to delayed ART over 5 years of follow-up

CHER team:

PENTA meeting in San Servolo, Venice. 2015

CHER has continued to lead the way in terms of looking for HIV CURE:

Potential for bNAbs Collaborations with PENTA & US colleagues in the EPPICAL project

The Hope for ART-free HIV Remission and Cure in Perinatal Infection

Present

Future

Life-long ART suppression

"Mississippi Baby" (2013)

Persaud D, Gay H, Luzuriaga et al. NEJM 2013;
Luzuriaga K, Gay H, Persaud D et al. NEJM 2015

27 months

"French Teenager" (2015)

Frange P et al. Lancet HIV 2016

12 years

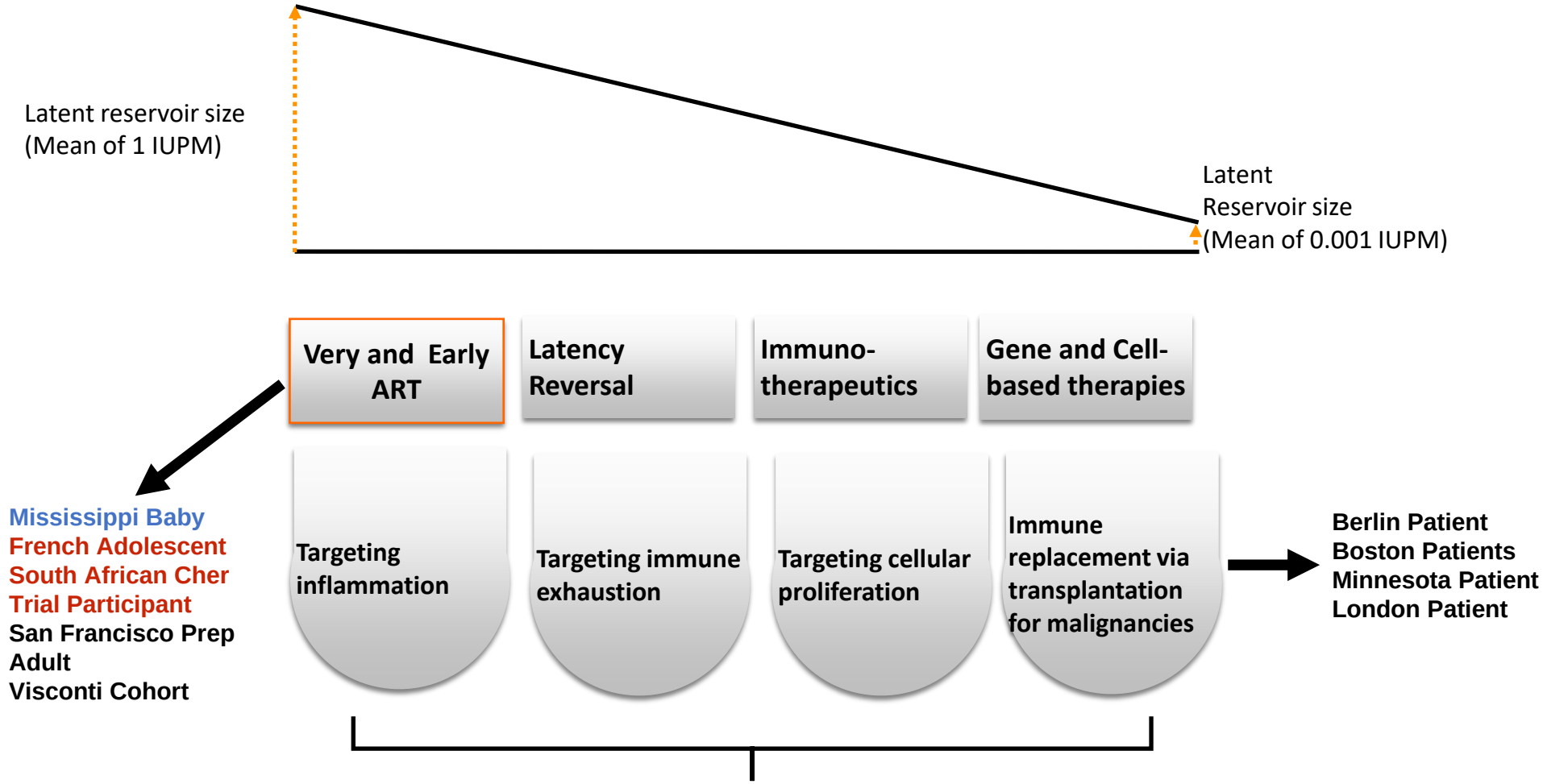
"South African Boy" (2017)

Violari A et al. Nature Communications 2019

18 years!

Duration of HIV Remission: off ART without detectable viremia

HIV Remission and Cure Therapeutics many clinical trials underway so far - expensive options.....



When to start?

As soon as possible!

Higher risk of rapid progression and therefore more clinically urgent if:

Very low CD4
Very high VL
Advanced clinical stage
Under 1 year

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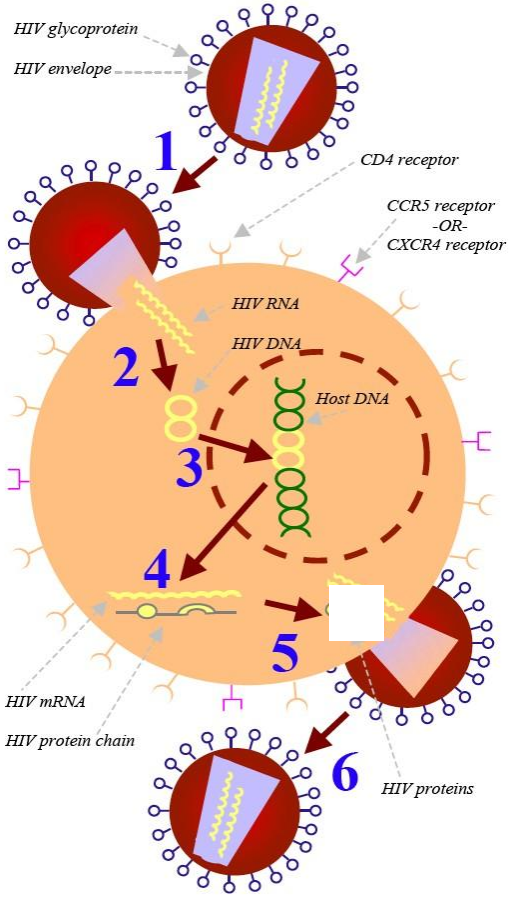
Classes of antiretrovirals



	Life cycle stage	Anti-retroviral blockers
1	Binding & Fusion	**CCR5 co-receptor inhibitor** (Maraviroc) **Fusion inhibitor** (Efuvirtide T20)
2	Reverse Transcription	**Nucleoside RT inhibitors NRTIs** (Abacavir, Tenofovir, TAF, Zidovudine) **None-Nucleoside RT inhibitors** **NNRTs** (Nevirapine, Efavirenz)
3	Integration	**Integrase Inhibitors** **INSTIs** (Dolutegravir)
5	Assembly	**Protease inhibitors** **PIs** (Darunavir / ritonavir)

New kids on the block:

Capsid inhibitors

Maturation inhibitors

Monoclonal antibodies

New kids on the block:

Long acting oral drugs

Long acting injectables

Long acting depots

2 NRTI (backbone) + 3rd agent (anchor drug)

Lamivudine (3TC) or **Emtricitabine (FTC)**

With

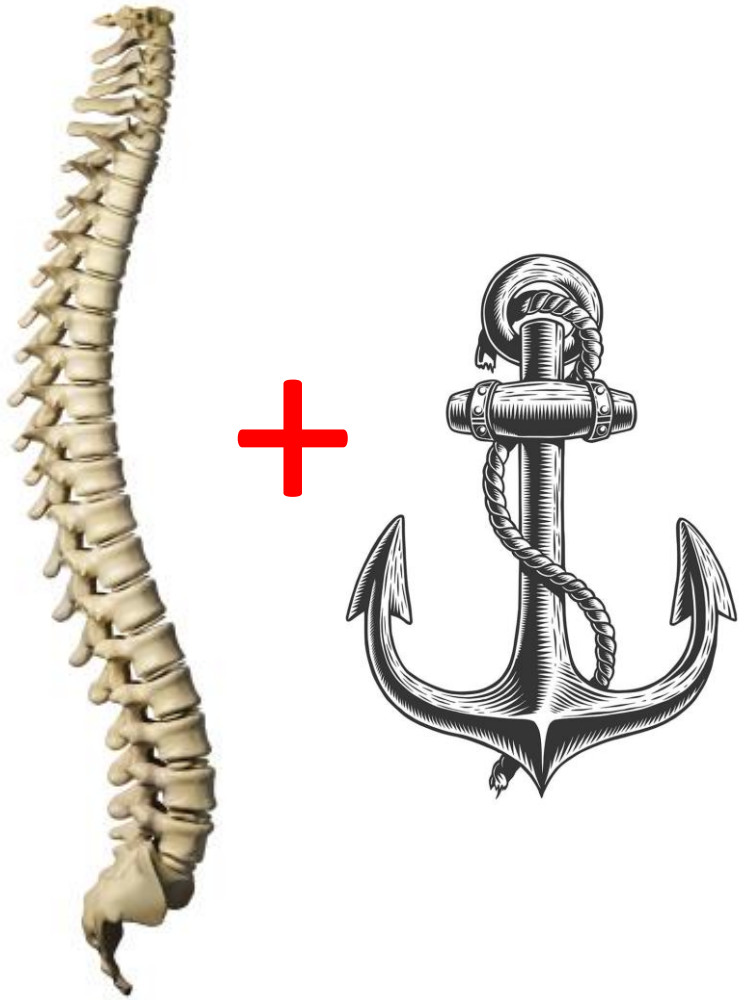
Abacavir (ABC)

or

Tenofovir (TDF/TAF)

or

Zidovudine (AZT/ZDV)



Integrase inhibitor (INSTI)

or

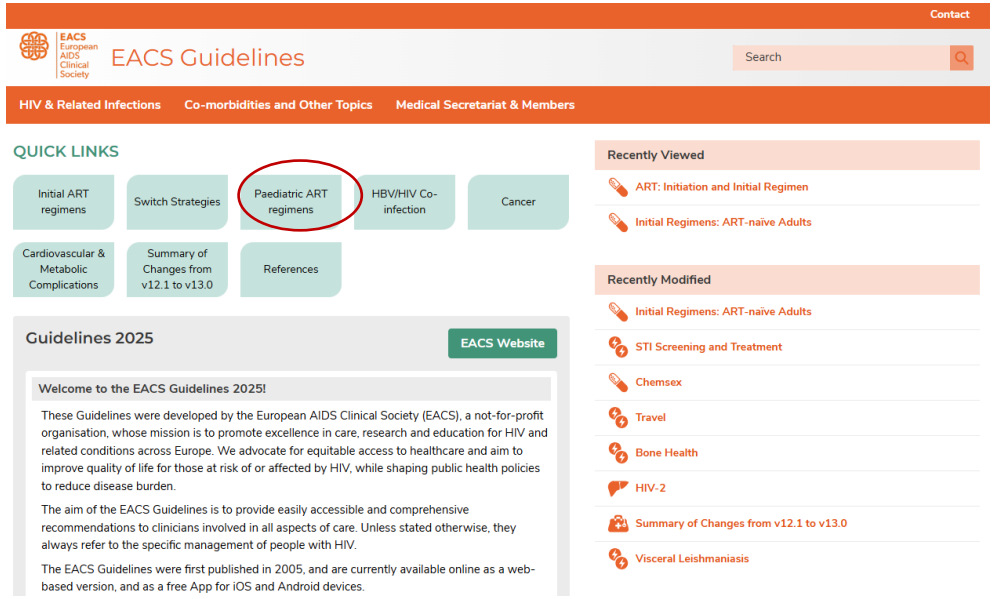
Protease inhibitor (PI)

or

Non-nucleoside reverse transcriptase inhibitor (NNRTI)

New ART guidelines released in 2025!

- The Guidelines 13.0 are now available (interactive website)!



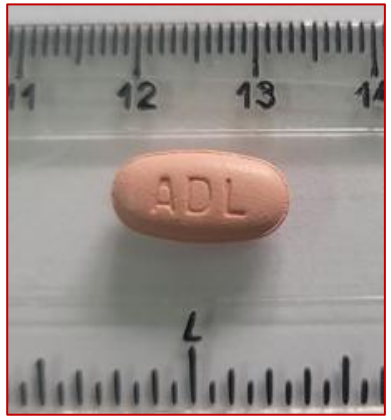
WHO. Overview of WHO recommendations on HIV and sexually transmitted infection testing, prevention, treatment, care and service delivery, July 2025; https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/guidelines/hiv-guidelines

EACS/Penta 2025 https://www.eacsociety.org/guidelines/eacs-guidelines/

Initial treatment options

WHO 2025 Preferred and alternative initial regimens*

Populations	Preferred initial regimen	Alternative initial regimen
Adults and adolescents	TDF(orTAF)+3TC(orFTC)+**DTG**	TDF+3TC+EFV400mg
Children	ABC + 3TC + **DTG**	**TAF**+3TC (or FTC)+**DTG** ABC+3TC + DRV/r (or ATV/r or LPV/r)
Neonates	ABC + 3TC + **DTG**	AZT + 3TC + NVP



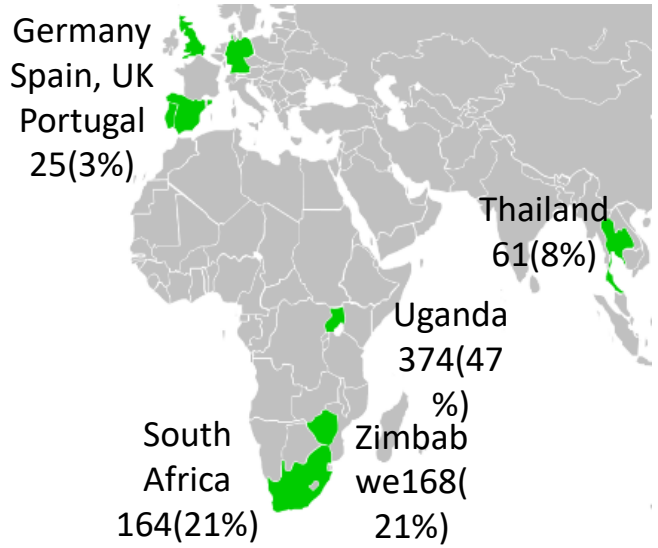
- **DTG/ABC/3TC (5/60/30mg)**
- **paediatric fixed-dose dispersible tablet**
- **Significant milestone - complete WHO- and EACS/Penta preferred ART regimen**
  - Recommended for children aged ≥4 weeks, 3 to <25 kg*
- **Roll-out increasing**

ABC = abacavir; DTG=dolutegravir; DRVb = darunavir+ritonavir or DRV+cobicistat
FTC=emtricitabine; TAF=tenofovir alafenamide; 3TC=lamivudine, XTC – 3TC or FTC

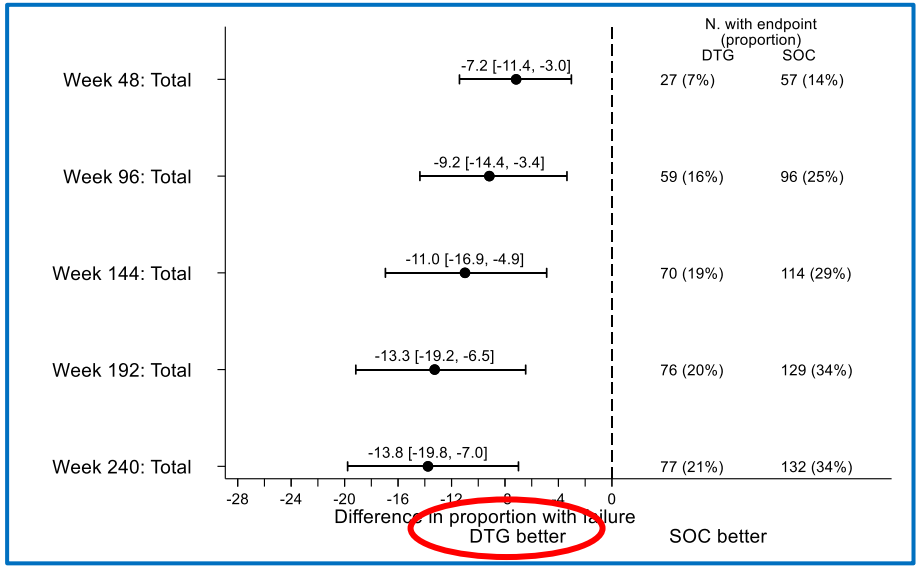
*WHO. Updated HIV guidelines 2025;
** EACS/Penta 2025 https://www.eacsociety.org/guidelines/eacs-guidelines/

ODYSSEY Trial

- ODYSSEY- a phase III 96-week non-inferiority RCT comparing Dolutegravir (DTG)-based ART vs standard-of-care, in children aged 4wks-17 years (N=792)
- Odyssey showed fewer treatment failures on DTG over 96 weeks (randomised phase) and 240 weeks (extended follow-up)
- Superiority of DTG was shown in all groups:
  - First-line ART (SOC mainly EFV)
  - Second-line ART (SOC mainly LPVr)
  - ≥14kg (median age 11)
  - <14kg (median age 1.4)
- Nested PK studies contributed to DTG dose evaluation
- Collaboration between **Penta** (ODYSSEY sponsor), **IMPAACT** (P1093 trial) and **ViiV Healthcare** ensured timely licensing approvals of DTG for children
- The trial results strengthened the **WHO recommendations** and helped to expedite global roll-out of paediatric DTG-based ART



Virological or clinical failure by follow-up week (intention-to-treat)



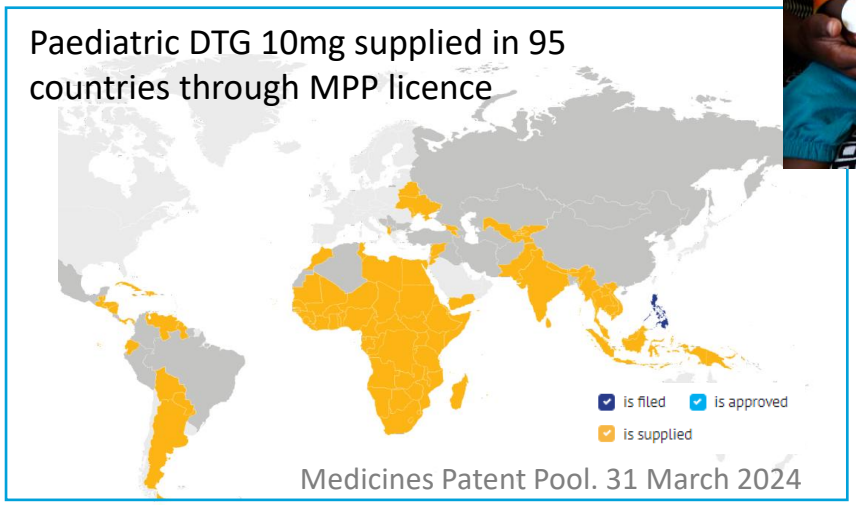
Penta

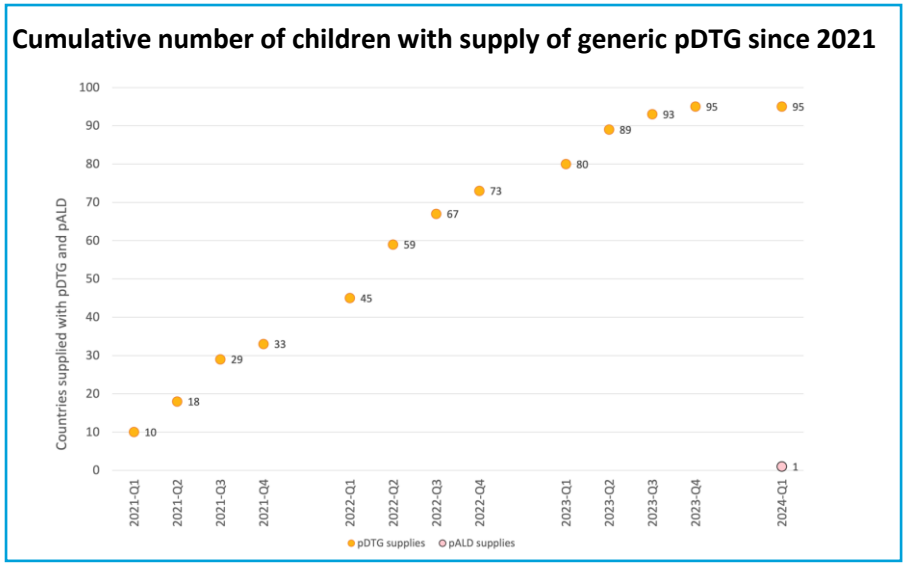
Turkova et al. NEJM 2021; Amuge et al. Lancet HIV 2022; Mujuru et al. CROI 2024
WHO Departmental Update 16 July 2021: https://www.who.int/news/item/16-07-2021-new-findings-from-the-odyssey-trial-confirm-superiority-of-dolutegravir-based-art-in-young-children

pDTG success story: coordinated efforts are paying off

- Innovative partnership: Unitaid, CHAI, ViiV, WHO and generics: Macleods, Mylan
- 👏 Generic pDTG was developed, approved and rolled out in record time!
  - Originator and generic drugs approved by US FDA in 2020
- 👏 Groundbreaking pricing agreement reduced the cost of ART by 75% for children in LMIC
  - Annual cost US$ ~27-45/child
- 👏 Rapid roll-out: 95 countries are procuring pDTG in which 99% of children with HIV reside^
- 👏 Improved viral suppression <400/<1000 c/mL following roll-out of DTG to ~90% (85-93% at ~1-4 years) in different settings*
- pALD: generic paediatric triple fixed-dose combination approved in 2023 - provides the complete WHO-preferred first-line treatment

https://www.clintonhealthaccess.org/our-programs/hiv-aids/





*Devendra et al. AIDS 2024; Gill et al. PIDJ 2023; Bacha et al. PIDJ 2023; Scott et al. AIDS 2024 OAB3803

^ Children living with HIV in the licensed territory covered by MPP-ViiV DTG Paed licence agreement and countries with no patent infringements

What about neonates?

New!

WHO 2025 Preferred and alternative initial regimens

Populations	Preferred initial regimen	Alternative initial regimen
Neonates	ABC + 3TC + **DTG**	AZT + 3TC + NVP

- **DTG and ABC/3TC dosing is established** and the dosing frequency of DTG and ABC/3TC can be aligned for neonates*^Ω

½ of 10mg scored DTG DT

¼ of 120/60mg double scored ABC/3TC DT

Neonatal ARV	Weeks 1 & 2	Weeks 3 & 4
DTG (5 mg)	every 48 hrs	every 24 hrs
ABC/3TC (30/15 mg)	every 48 hrs	every 24 hrs

5mg DTG DT

ABC (or ZDV) and 3TC syrups

ABC=abacavir; DTG=dolutegravir; BIC=bictegravir; FTC=emtricitabine; TAF=tenofovir alafenamide; 3TC=lamivudine; DT=dispersible tablet; ODF=oral dispersible film

*PETITE-DTG: Cressey et al 2025 JAIDS; Bekker et al. CROI 2025, Abs #122;
^IMPAACT 2023: Momper et al. CROI 2025, #1047
Ω PETITE-ABC/3TC-LPVr: Bekker et al. Lancet 2024; Panjasawatwong et al. CROI 2025, #1048
ψPETITE-DTG: Viljoen et al. CEOI 2025, Abs #1045

What are the options for children experiencing treatment failure on DTG?

DTG drug resistance is emerging:
4-20% in people unsuppressed on DTG*~

Vertical transmission of DTG-resistance virus does occur*

DRVr is the best PI and **TAF-NRTI backbone is** the best NRTI option for second-line ART in children**

Where are we with the formulations for children?

DRVr + TAF/FTC or recycle ABC/FTC

*WHO. HIV drug resistance: brief report 2024

~Rakhmanina N. International Workshop on Pediatrics and HIV 2024

**Musiime et al. NEJM 2025

Headlines for children and adolescents:

Recommendation 2025

Dolutegravir + lamivudine (DTG+3TC) can be used for treatment simplification in adults and adolescents, with undetectable HIV viral load on 3-drug ARV regimens and without active hepatitis B infection.

conditional recommendation, moderate certainty of evidence

Recommendation 2025

Long-acting injectable cabotegravir + rilpivirine (CAB+RPV) can be used as an alternative switching option in adults and adolescents who have an undetectable HIV viral load on oral ART and no active hepatitis B infection.

conditional recommendation, moderate certainty of evidence

HIV-infected children need the right drug formulations

American Academy of Pediatrics

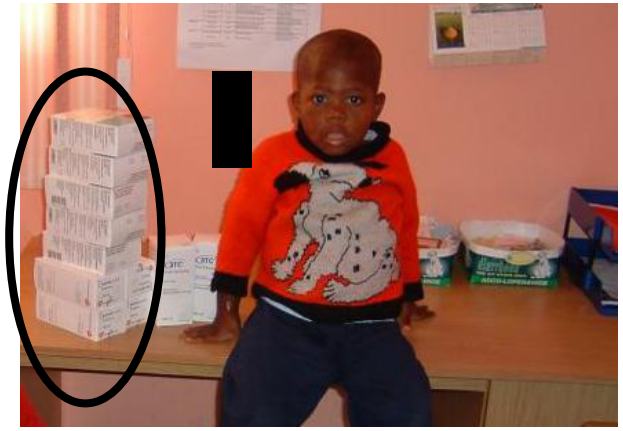
DEDICATED TO THE HEALTH OF ALL CHILDREN™

POLICY STATEMENT

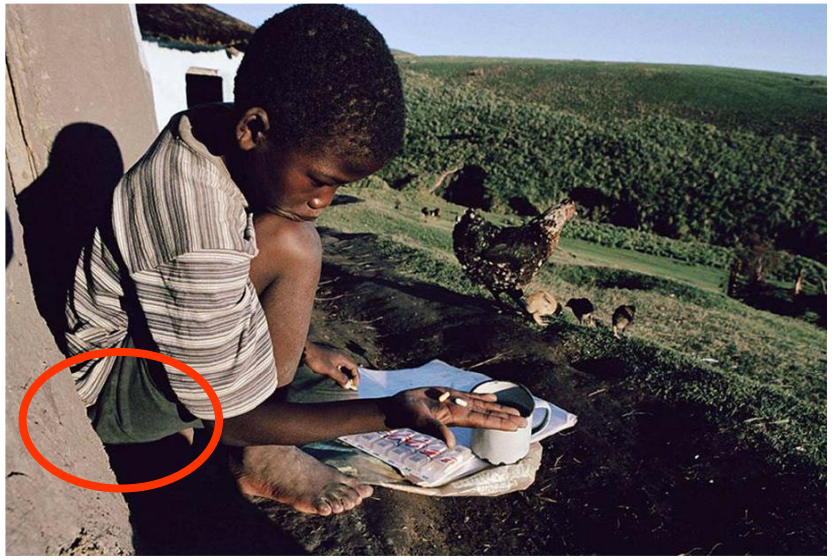
Increasing Antiretroviral Drug Access for Children With HIV Infection

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of All Children

Committee on Pediatric AIDS, Section on International Child Health



- **Lack of age and place-appropriate paediatric ARV formulations**



(18 November 2008)

The CHAPAS Trials

Trial	Focus
CHAPAS 1 (2005)- Zambia	Strategies for nevirapine initiation in children with HIV taking 'baby pills'
CHAPAS 2 (2009)-Uganda	PK of lopinavir/ritonavir syrup, sprinkles and tablets
CHAPAS- 3 (2010)- Zambia, Uganda	Toxicity and PK of 3 FDCs for ZDV, ABC & d4T for antiretroviral treatment
CHAPAS- 4 (2019) – Zambia, Uganda, Zimbabwe	Optimizing treatment for children failing 1st line antiretroviral therapy

Outstanding Research Team

The Outstanding Research Team prize was awarded to the **CHAPAS studies team** (Children with HIV in Africa – Pharmacokinetics and Acceptability of Simple antiretroviral regimens), a large research group that accomplished over more than a decade several crucial HIV paediatric and adolescent treatment trials.

Dr Mutsa Bwakura, Prof. Diana Gibb, Dr Cissy Kityo, Dr David Burger (in the back: Prof. Tanner and Dr Simão)

Chapas Clinical Tr…

MRC Clinical Trials Unit at UCL

https://vimeo.com/213630323

The CHAPAS Trials

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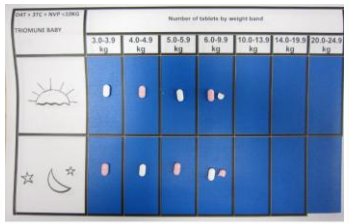
CHAPAS- 4 (2019) – Zambia, Uganda, Zimbabwe	Optimizing treatment f 1st line antiretroviral therapy

CHAPAS 5 is a new EDCTP funded platform trial in children and young people – several ways to simplify treatment – including injectables



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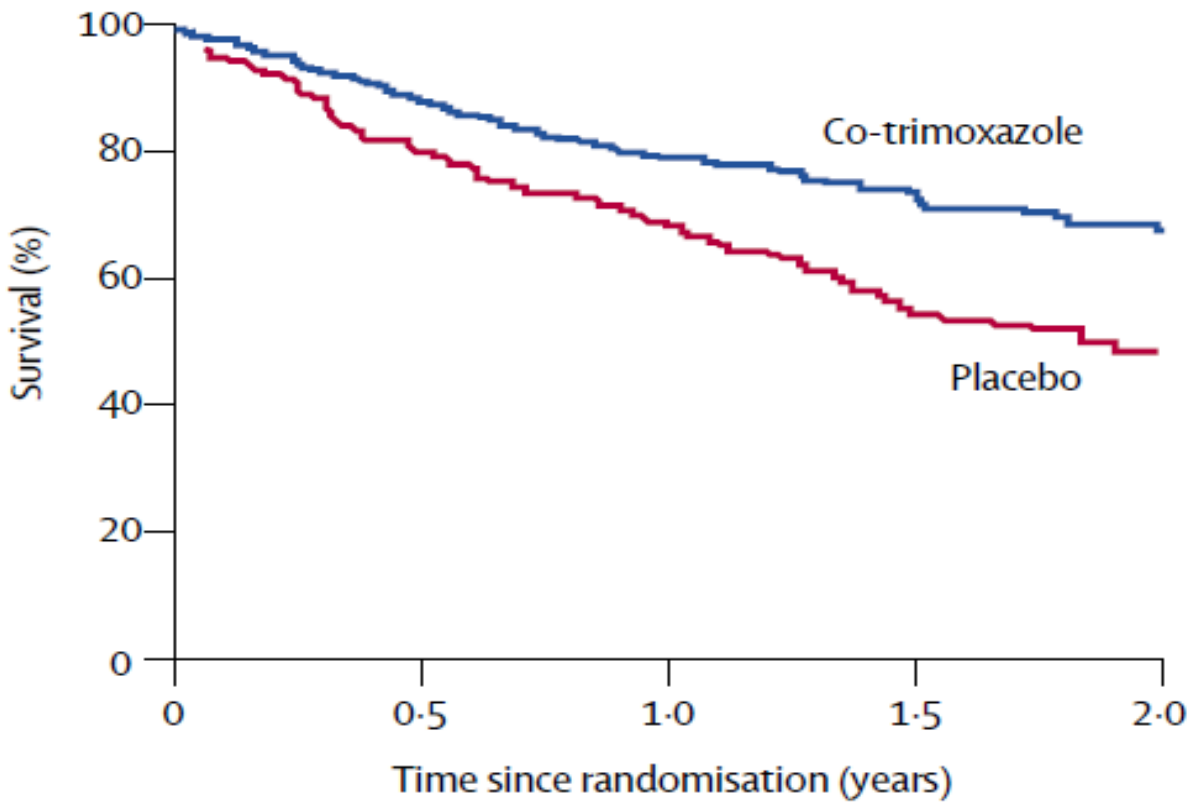
CHAP (Children with HIV Antibiotic Prophylaxis) trial

- 541 HIV-infected Zambian children (older than 12 months; average age 5 years), not on ART
  - Randomised to cotrimoxazole or matched placebo
- Trial stopped by the Independent Data Monitoring Committee in October 2003
- Substantial survival benefit from cotrimoxazole
  - Despite high levels of antibiotic resistance

45% reduction in Mortality



Number at risk					
Co-trimoxazole	265	232	177	106	47
Placebo	269	211	143	72	29

Lancet November 2004

The 3 by 5 Initiative
TREAT THREE MILLION PEOPLE LIVING WITH HIV/AIDS BY 2005

All WHO
This site only

3 by 5 home
About 3 by 5
Country support
Capacity building
Partnership
AIDS medicines and diagnostics service
Documents
Media centre

3 by 5 Initiative > Media centre

printable version

WHO, UNAIDS and UNICEF modify recommendations fc cotrimoxazole prophylaxis in children

Joint WHO/UNAIDS/UNICEF statement on use of cotrimoxazole as proph exposed and HIV infected children

Statement on use of cotrimoxazole prophylaxis

22 November 2004 -- WHO, UNAIDS and UNICEF, guided by recent evidence, have agreed to modify as an interim the current recommendations(1) for cotrimoxazole prophylaxis in children. This is based upon recent trial data from Zambia (2).

WHO/Michael Jensen 2004

These data and other new evidence will be reviewed in early 2005 by an expert committee convened to revise and update the recommendation cotrimoxazole fo children. Cotrimo remains importa increasing acces use can improve independently of treatment. Curre recommendation should be used t postpone the tim

Prophylactic dos with any sign or that should be o morbidity and m

Cotrimoxazo saving interve

Co-trimoxazole as prophylaxis against opportunistic infections in HIV-infected Zambian children (CHAP): a double-blind randomised placebo-controlled trial

C Chintu, G J Bhat, A S Walker, V Mulenga, F Sinyinza, K Lishimpi, L Farrelly, N Kaganson, A Zumla, S H Gillespie, A J Nunn, D M Gibb, on behalf of the CHAP trial team

Lancet 2004; 364: 1865–71

Medical Research Council Clinical Trials Unit, London, U (A S Walker PhD, L Farrelly BSc, N Kaganson MSc, Prof A J Nunn MSc, D M Gibb MD); University Teaching Hospital, Lusaka, Zambia (Prof C Chintu FRCP, Prof G J Bhat MD, V Mulenga M F Sinyinza MD, K Lishimpi MD); and Royal Free and University College Medical School, London, UK (Prof A Zumla FRC Prof S H Gillespie MD)

Correspondence to:
Dr D M Gibb,
Medical Research Council Clinic Trials Unit, 222 Euston Road, London NW1 2DA, UK
d.gibb@ctu.mrc.ac.uk

Cheap drug cuts child Aids deaths

A CHEAP and widely-available antibiotic could be used to cut Aids-related death in African children by more than 40 per cent, Government-backed scientists said today.

The findings were hailed as a breakthrough in medical science by the International Development Secretary Hilary Benn.

Scientists from the Medical Research Council conducted a trial in Zambia to see whether the drug, co-trimoxazole, could stop fatal infections linked to Aids.

A group of 541 children aged one to 14 infected with the Aids virus HIV were treated children had died, compared with more than 40 per cent of those receiving the dummy drug.

Using the antibiotic also reduced hospital admissions by 23 per cent.

The research, led by Dr Diana Gibb from the MRC's Clinical Trials Unit and funded by the Department for International Development, was reported today in The Lancet medical journal.

Affordable

Mr Benn said: "This is a breakthrough in medical research which can help to save children's lives all over the world.

signed and run by the MRC Clinical Trials Unit has shown how this widely available, affordable antibiotic drug can almost halve child deaths by warding off potentially fatal illnesses in children whose immune systems are weakened because of HIV."

Mr Benn on Wednesday attended a meeting of the Global Fund to Fight Aids, TB and Malaria in Tanzania.

Dr Gibb said: "Tackling HIV infection directly is just one approach to management.

"Reducing the secondary complications and infections, which can be just

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Growing global population of Youth with Perinatal HIV

One-third of the world's children with perinatal HIV infection are now adolescents

15-19 yrs: Only age group were HIV mortality continues to rise

Outcomes poorer at all stages of the cascade (diagnosis, retention, access to treatment, viral suppression)

(Slogrove JIAS 2017, Enane Curr Op HIV AIDS 2018)

Stress and HIV survival →

longer term consequences:

HIV / Drug effects or both?

Mental health / Brain function

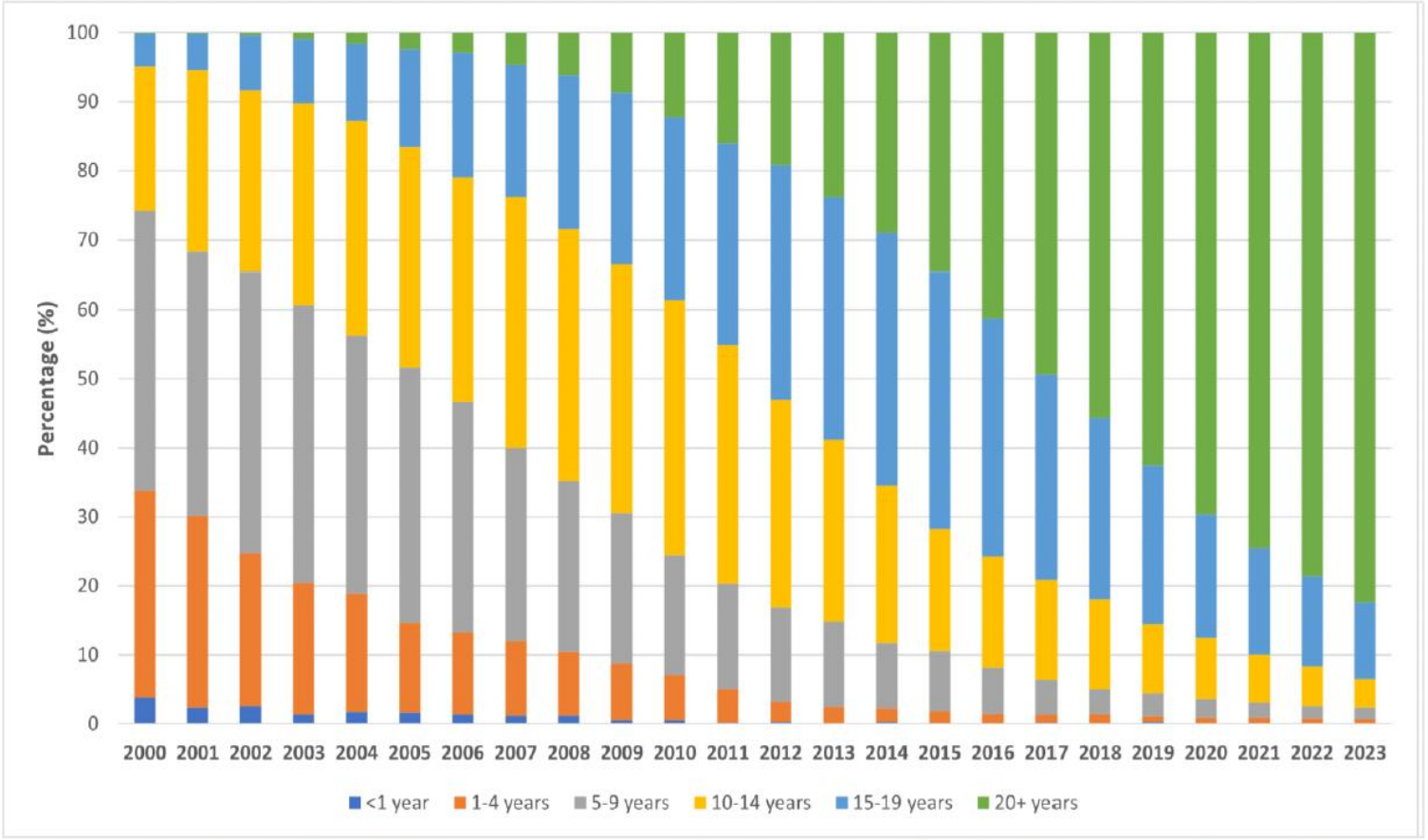
Growth / Metabolic

Cardiovascular / Renal /

Bones / Lungs

The next generation…..

Age distribution of people in England with HIV diagnosed in childhood (n=1,532), 2000-2023



Over **80%** of all children and young people with HIV in England are now over 20 years old

<15 years = 150

Data are for all children and young people who ever presented to medical services in the England, including children who have since transferred to adult care. CHARS does not collect outcome data (e.g. deaths or lost to follow-up) for those who have transferred to adult care. All paediatric patients are included, from date of first presentation to paediatric HIV services in the UK, regardless of mode of HIV acquisition. Those who died or moved abroad while in paediatric care are included up until the year of death or year they left the country. Data for 2022/23 are incomplete as subject to reporting delay.

CHARS
Children's HIV and AIDS Reporting System

Peters et al Chiva Conference 2024

Antiretrovirals alone can't treat HIV

To keep children and adolescents alive and enable them to reach their life potential:

- **Families and young people need support**
  - Nutrition, housing, education
  - Sharing HIV status
  - Adherence and retention in care
  - Dealing with mental health issues
  - Dealing with stigma
  - Sexual and reproductive health
  - U=U is insufficiently understood and not well communicated*

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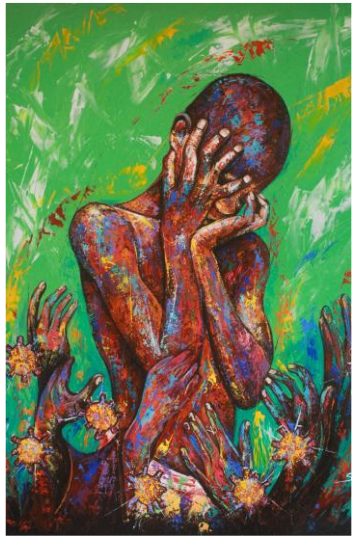
Key themes for successful interventions:

- Respectful, person-centred services
- Providers training
- Peer-support
- Community-based interventions
- Shift to integrated services in health systems
- Psychosocial support
- mHealth



Endurance by Senyonga Ismail, 2024

HIV Science as ART. Munich 2024

Adolescent HIV Models of Care, which place **peer- and psychosocial** support in its heart, show improved outcomes

- **Zvandiri**
- **Ariel Adherence Clubs**
- **Baylor Teen Club programme**
- **Operation Triple Zero**
- **REACH "Red Carpet Program" FANMI**
- **Project "YES"**

*Onoya et al. PLoS One 2023 WHO. Adolescent friendly health services for adolescents living with HIV: from theory to practice. 2019 Society for Adolescent Health and Medicine. J Adolesc Health 2023

Address Education about HIV Psychological & PEER Support

Stigma

Fear

Disclosure

Voices of young people

Voices of parents

www.chiva.org.uk

CHIVA

CHILDREN'S HIV ASSOCIATION

search

ABOUT | OUR WORK WITH YOUNG PEOPLE | INFORMATION FOR YOUNG PEOPLE | PARENTS AREA | SUPPORT CHIVA

LBEING OF CHILDREN AND YOUNG PEOPLE LIVING WITH HIV

Treatment as prevention!

Young people with HIV need to have Very good knowledge about HIV & Transmission U=U

Undetectable = Untransmittable

Ad

St

Fe

Dis

Voice people

Voices of parents

OUR NEWS

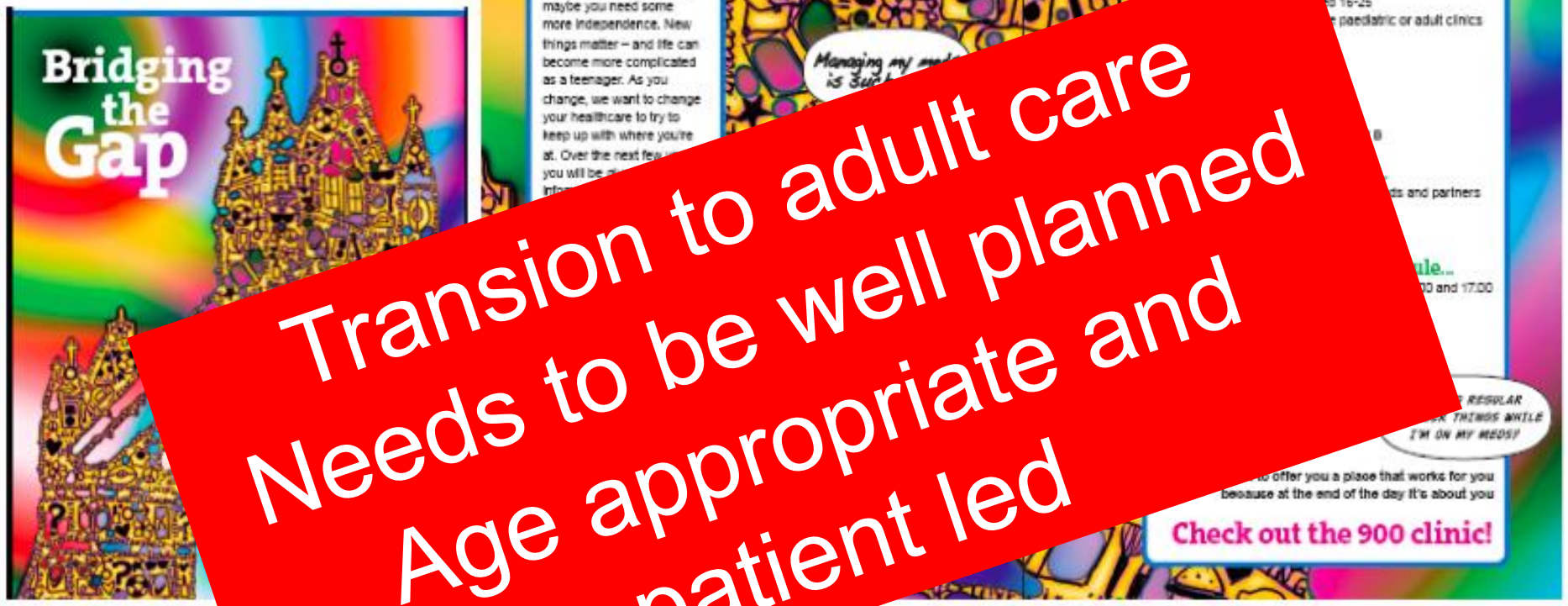
The ArcHIVe Podcast

You can now listen to the ArcHIVe Podcast, created by a group of young people who have grown up

Young People's Survey Report

Evaluation of The Impact of The National Lockdown on young

www.chiva.org.uk



Transion to adult care
Needs to be well planned
Age appropriate and
patient led

Making go tion to adult care is essential to keeping Young peo their health:

Family clinic with Adolescent care Young Adult care "900 Clinic"

Young people need to be well informed – (often reminded)

RESEARCH ARTICLE

Weekends-off efavirenz-based antiretroviral therapy in HIV-infected children, adolescents and young adults (BREATHER): Extended follow-up results of a randomised, open-label, non-inferiority trial

Anna Turkova[1,2]*, Cecilia L. Moore[1], Karina Butler[3], Alexandra Compagnucci[4], Yacine Saïdi[4], Victor Musiime[5,6], Annet Nanduudu[5], Elizabeth Kaudha[5], Tim R. Cressey[7,8,9], Suwalai Chalermpantmetagul[7], Karen Scott[1], Lynda Harper[1], Samuel Montero[1], Yoann Riault[4], Torsak Bunupuradah[10], Alla Volokha[11,12], Patricia M. Flynn[13], Rosa Bologna[14], Jose T. Ramos Amador[15], Steven B. Welch[16], Eleni Nastouli[17], Nigel Klein[18], Carlo Giaquinto[19], Deborah Ford[1☯], Abdel Babiker[1☯], Diana M. Gibb[1☯], on behalf of the BREATHER (PENTA 16) trial Group[¶]

PLOS ONE | https://doi.org/10.1371/journal.pone.0196239 April 23, 2018

- 199 patients (11 countries)
- **Short cycle ART with efavirenz is non-inferior to continuous for VL < 50 c/ml**
- Similar resistance, safety and inflammatory marker profiles in the two groups

- 144 week follow-up also published
- Results supportive of this strategy in adherence patients with regular monitoring

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BREATHER Trial (PENTA 16)

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- 144 week follow-up also published
- Results supportive of this strategy in adherent patients with regular monitoring

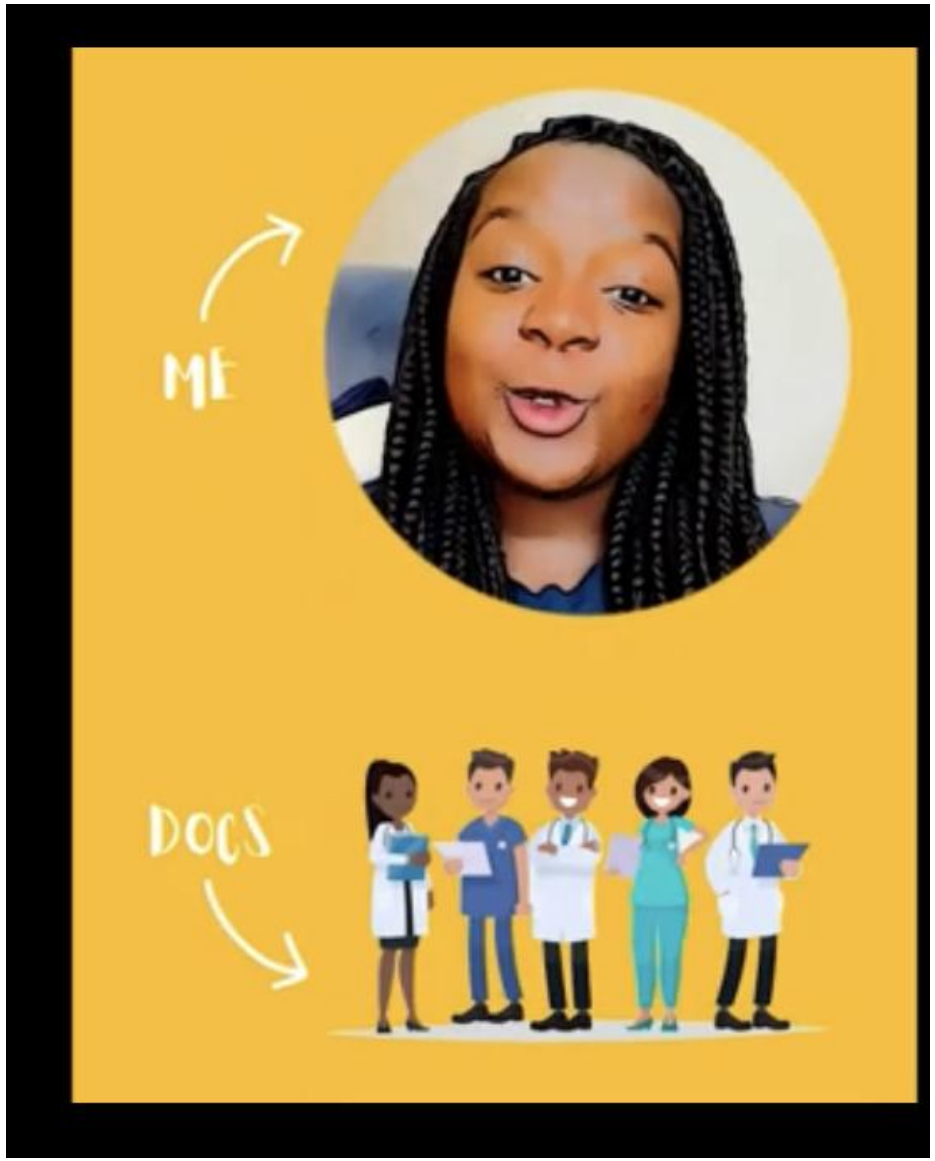
BREATHER PLUS:
Short cycle ART with weekends off is inferior to continuous ART in (adolescents 12-20 years) living with HIV receiving Tenofovir, lamivudine, Dolutegravir (TLD) in sub-Saharan Africa:

BREATHER Plus 96-week results, RWANDA AIDS conference 2025
Lancet HIV 2026

Youth Trial Board Videos on Odysseytrial.org

ODYSSEY trial findings videos

The **young people** involved in the ODYSSEY trial created **a three-part video series** to explain the trial's main findings. These videos were created in collaboration with influencers living with HIV.:



Outline

- Epidemiology of Paediatric HIV
- HIV diagnosis
- Natural History of Paediatric HIV and Clinical presentations
- Antiretroviral Therapy
  - When to start
  - What to start and updates in 2025/2026
- Other treatments/managment:
  - Prophylaxis for opportunistic infections and late disease presentation
- Adolescents
  - Models of care and transition to adult care
- **Life course data is needed**

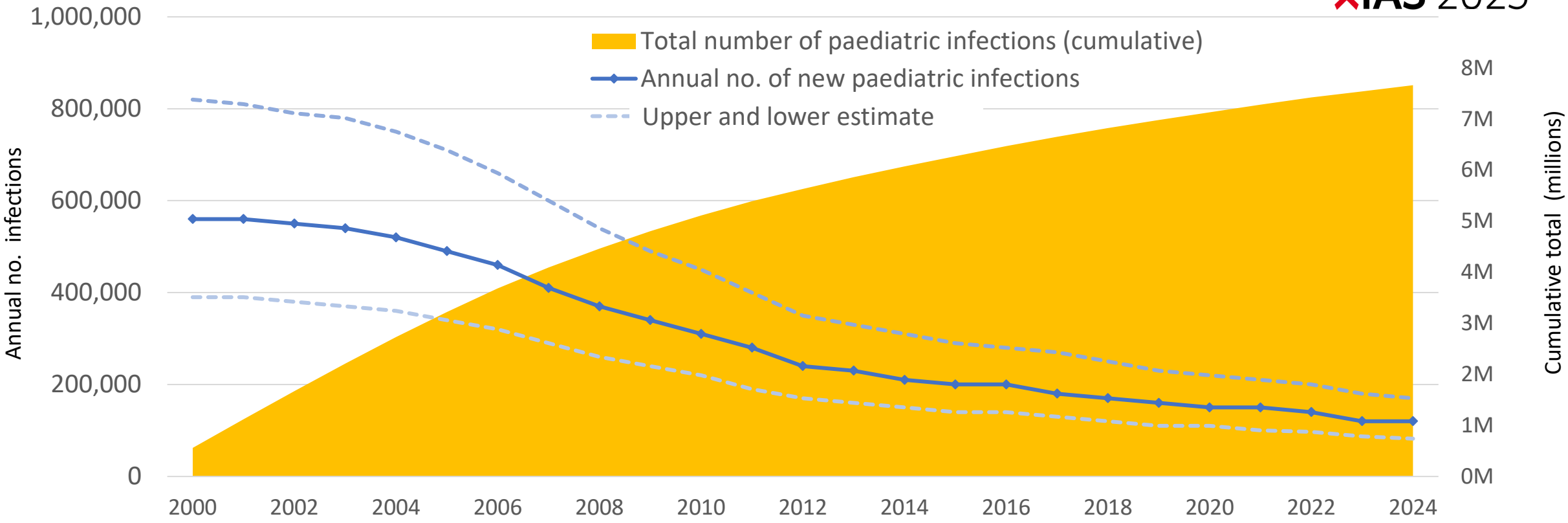
Intira Jeannie Collins, University College London, UK

Growing the paediatric response

Adults living with perinatally acquired HIV

Perinatal HIV: Global estimates

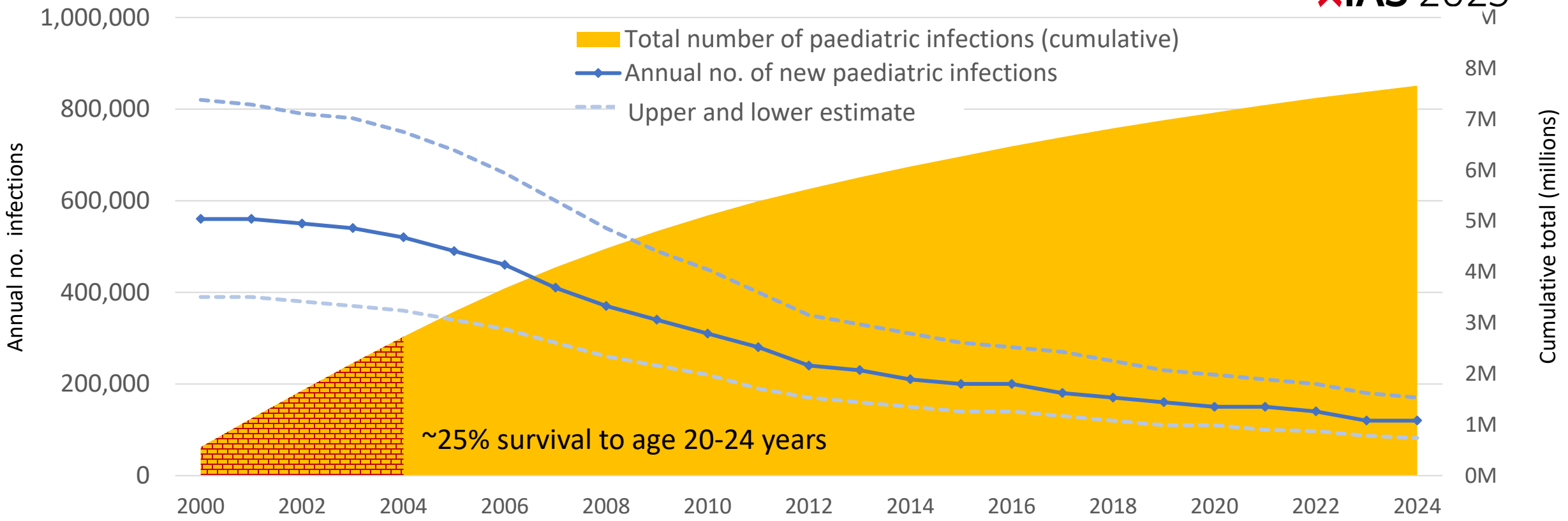
IAS 2025



- **Global success**: **77% reduction in annual number of new paediatric HIV infections since 2000:** from 530,000 in 2000 to 120,000 in 2024

- An estimated **cumulative total of 7.3 million children** with perinatally acquired HIV since 2000. The number surviving to adulthood is uncertain.

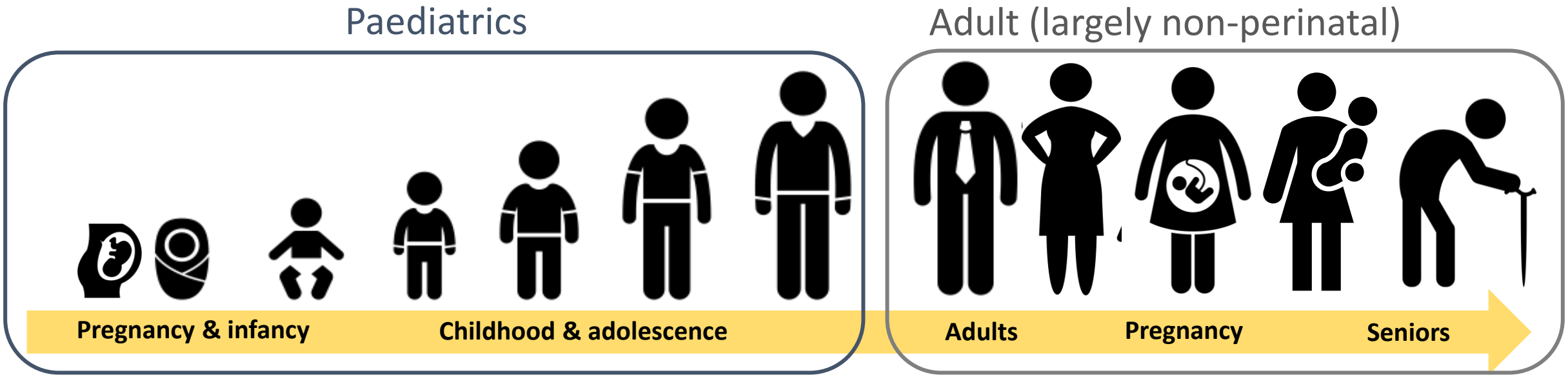
Adults living with perinatal HIV



- UNAIDS estimate **660,000 young adults (20–24y) living with perinatal HIV** globally in 2023 → **~25% survival** of those born 2000-2004[1]
- Scarce data on health outcomes and health care needs through adulthood. Rapidly growing and under-researched population

1. Sohn & Davies JIAIDS 2024

HIV Research: a siloed approach



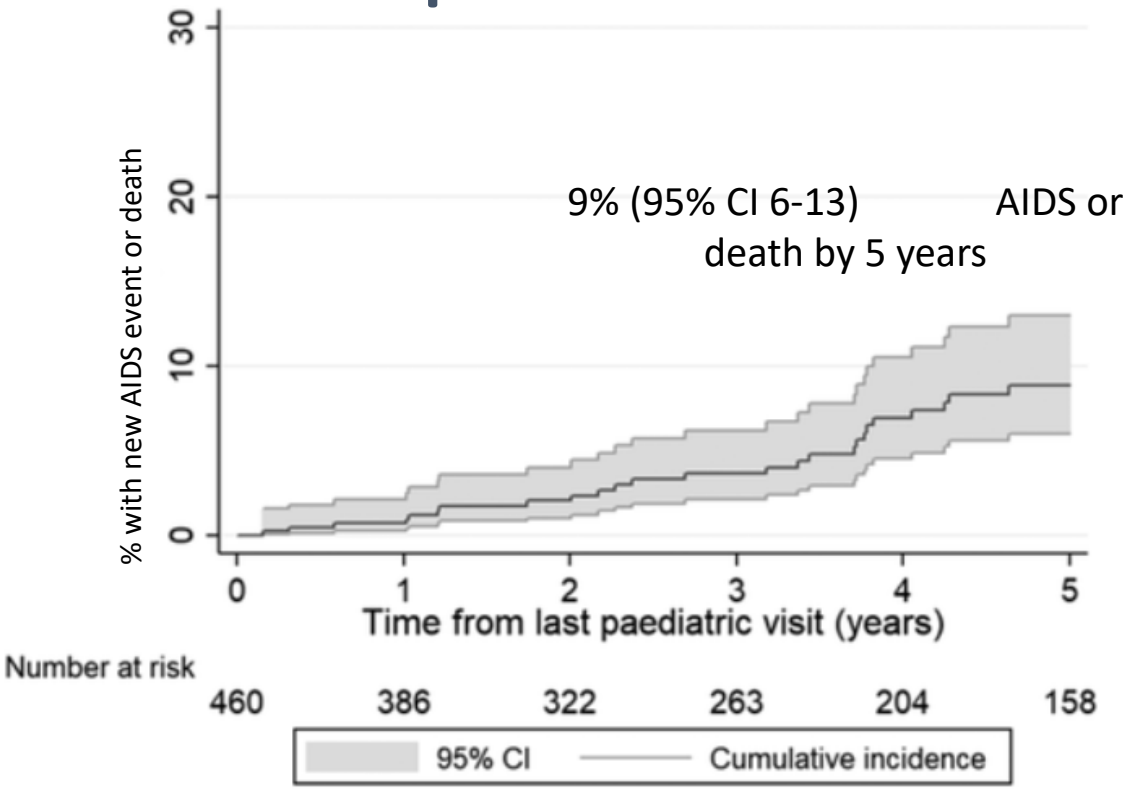
- HIV research is largely divided into paediatric versus adult populations
- Adults with perinatal HIV enter 'adult databases' when they transfer out of paediatric care but they are often excluded from analyses as a small and 'unique population'[1]
- **Unique & vulnerable population** especially in LMICs: high prevalence of orphanhood, poor growth and developmental disadvantage as they enter adulthood[2,3]

1. Trickey et al AIDS 2024; 2. Slogrove et al. PLoS Med 2018; 3. CIPHER J Int AIDS Soc 2022

Outcomes of young adults with perinatal HIV

Emerging data on outcomes after transfer to adult care or >age 18 years show higher risk of (mostly from high income settings):

- **Poorer retention, lower viral suppression**[1]
- **Increased risk of AIDS or death**[2,3,4] as compared to younger or older age groups
- Poorer outcomes often **associated with poorer clinical status in paediatric care**



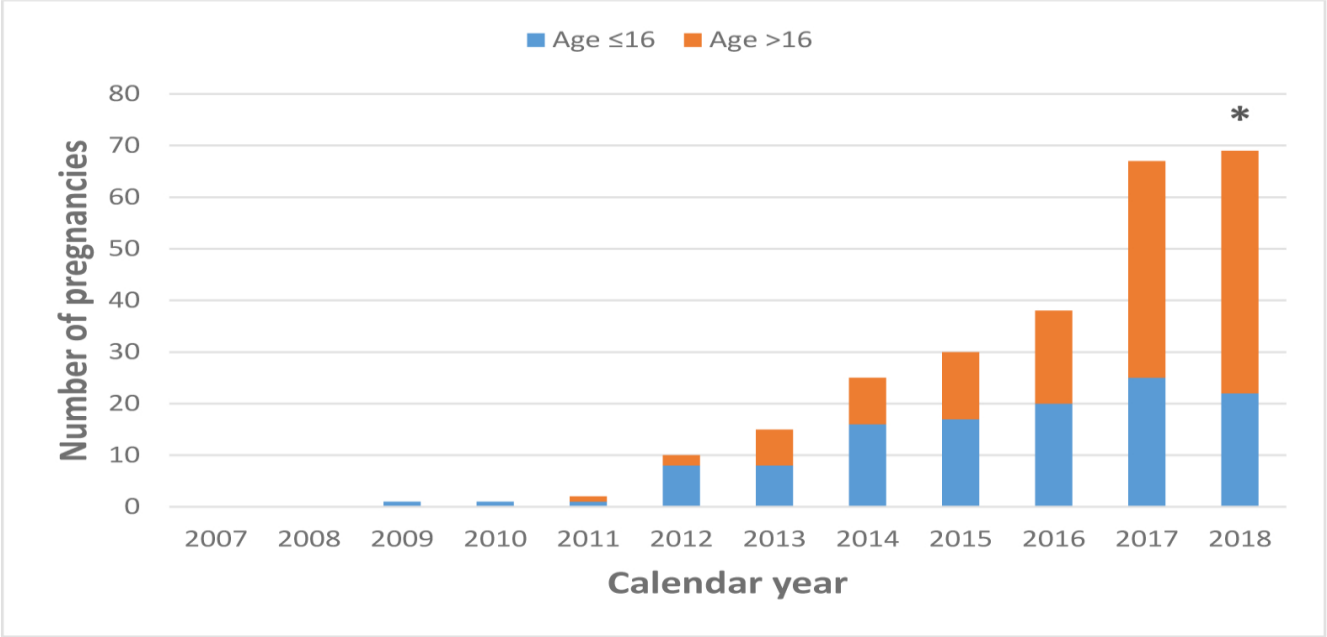
Asad et al. HIV Med 2021

- CD4 modelling study showed **steeper natural decline in CD4 by age 20 years** <u>despite suppressive ART</u>, if had **low nadir CD4 z-score in childhood**[5]

1. Tsondai et al. J Int AIDS Soc 2020; 2. Ounchanum et al. AIDS Care 20204; 3. Desmond et al, AIDS 2021; 4. Asad et al. HIV Med 2021. 5. *Castro et al. CID 2024*

Pregnancies in adults with perinatal HIV

South Africa study (2009-2018)[1]: **rise in pregnancies** in youth with perinatal HIV

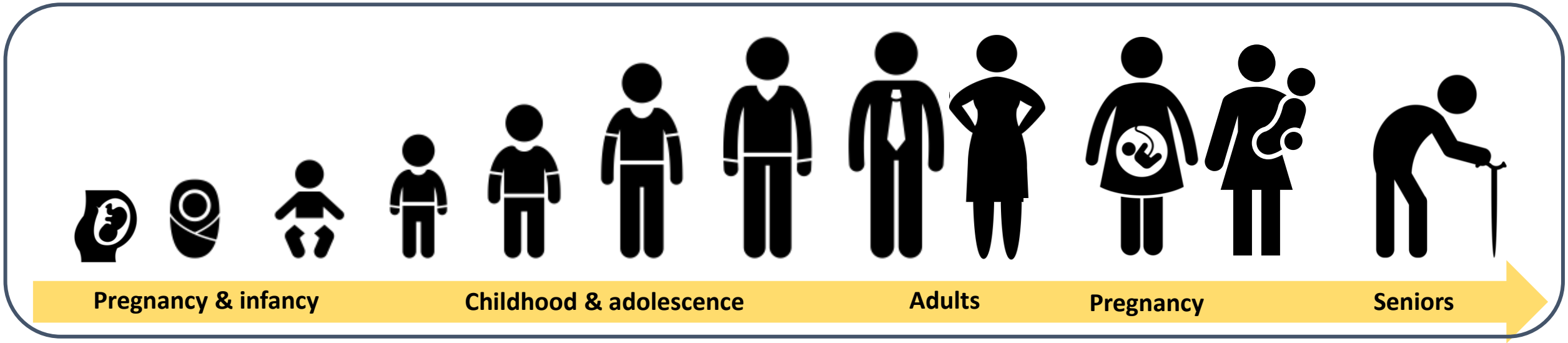


Of the pregnancies among youth/adults with perinatal HIV (n=258)

- 39% aged≤16 years
- 20% had CD4<200 cells
- 28% had VL >1000 c/ml at delivery
- 2.2% vertical transmission (23% infants unknown HIV status)

Anderson et al. South Afr. Med J. 2021

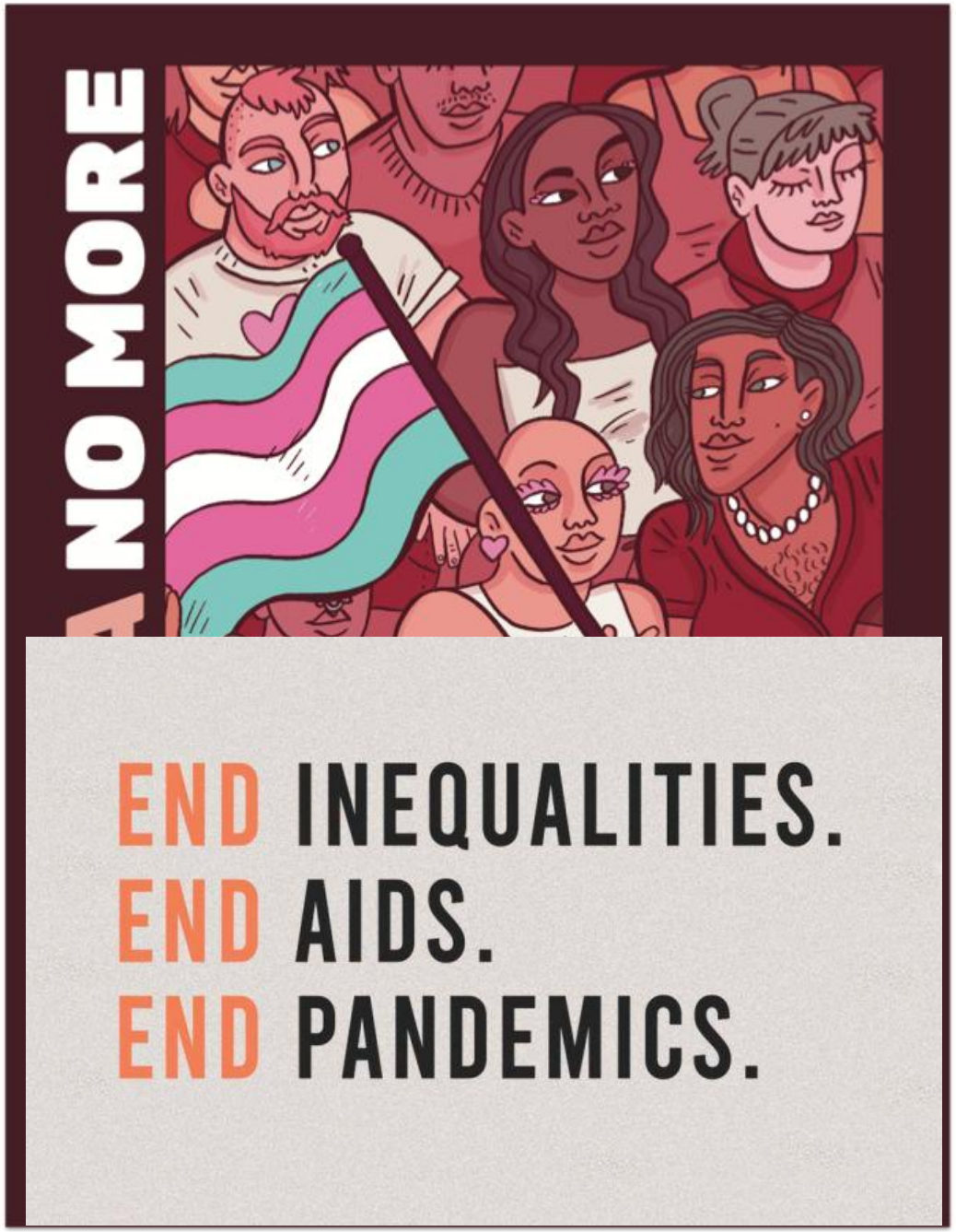
Need for a life course approach



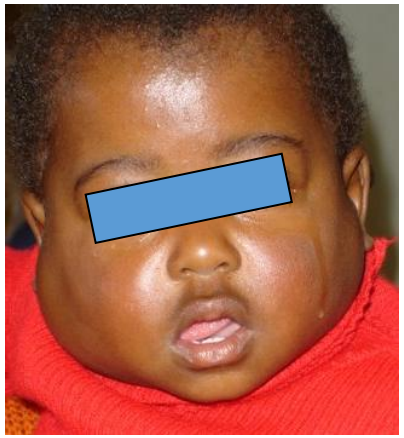
- Move beyond our silos to understand **how lifelong HIV and ARV exposure affects health across the lifespan, beyond HIV-specific outcomes**
- Opportunity to learn from **electronic medical records**
- Identify risk factors, risk time-periods→ **need studies to inform future care**
- Include **comparisons:** adults with non-perinatal HIV and non-HIV populations

HIV-exposed uninfected children are:

- **A Rapidly growing, under-researched population** of adult perinatal HIV survivors
- Evidence to date suggest **variable health outcomes**
- Urgent need to address **critical data gaps**, with **integrated** health data across the **lifespan; community partnerships essential**



Avac.org



Fewer children are now born with HIV, but Children & Young People with HIV need →

access to effective ART
timely access to new drugs
access to support
access to good information

Maximise future opportunities:

→ HIV suppression / elimination
→ prevent transmission
→ immune preservation
→ challenge the stigma of HIV

International paediatric virtual clinic

Dr Caroline Foster

PVC

Imperial College Healthcare NHS Trust

caroline.foster5@nhs.net
hermione.lyall@nhs.net
a.bamford@nhs.net

MDT:

Paeds ID
Adult HIV
Virology
Nurse specialists
Expert pharmacists

DART Trial Film

picturinghealth.org
And on u-tube

Christine in Northern Uganda
From the DART film
http://www.youtube.com/watch?v=MSyFmbiR-Hc

Penta is an international, independent, scientific collaboration devoted to advancing research on optimising the prevention and management of infections in pregnancy, infancy, childhood and adolescence

Our members are healthcare professionals, researchers, scientists and community workers from all over the world, who share a common vision to improving maternal and child health.

For more information:
info@penta-id.org
www.penta-id.org

Follow us:

Penta Foundation – Child Health Research

Penta ID

@pentafoundation.bsky.social

@penta_id

MRC Clinical Trials Unit at UCL Capacity Strengthening Hub

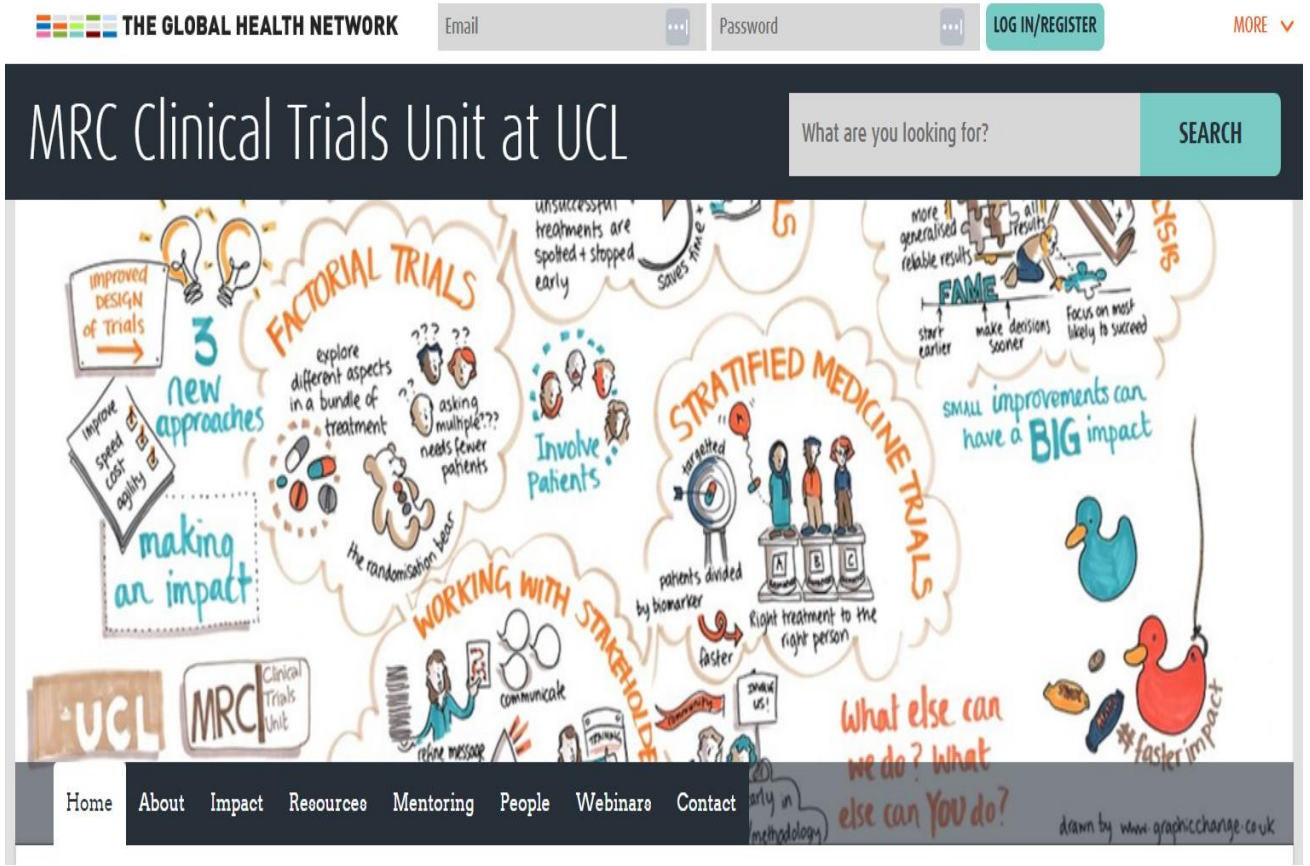
Aim to strengthen clinical trials capacity in LMICs
https://mrcctu.tghn.org/

What's on the hub?

Resources on:

- Trial design
- Trial conduct
- Analysis
- Knowledge transfer and exchange
- Observational studies
- Meta-analysis

Essential reading lists
Webinars



Resources

Essential reading lists

LMIC Mentoring scheme

Webinars

MRC Clinical Trials Unit

UCL

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

Thank You for Listening

Thankyou to:

- People living with perinatal HIV and their families
- Many colleagues at MRC CTU at UCL, Great Ormond Street NHS Trust, Imperial college and St Marys Hospital: in particular:
  - Anna Turkova, Alasdair Bamford, Jeannie Collins, Hermione Lyall, Caroline Foster, Claire Thorne