Paediatric Transition

Dr. Edmund Wilkins

Head of the HIV Clinical Trials Unit

North Manchester General Hospital

GreenShoots FOUNDATION

“Support needing populations through medical assistance and the transfer of knowledge to local medical practitioners.”

Our vision for the

Medical Assistance & Medical Education (MAME) Programs

GreenShoots FOUNDATION

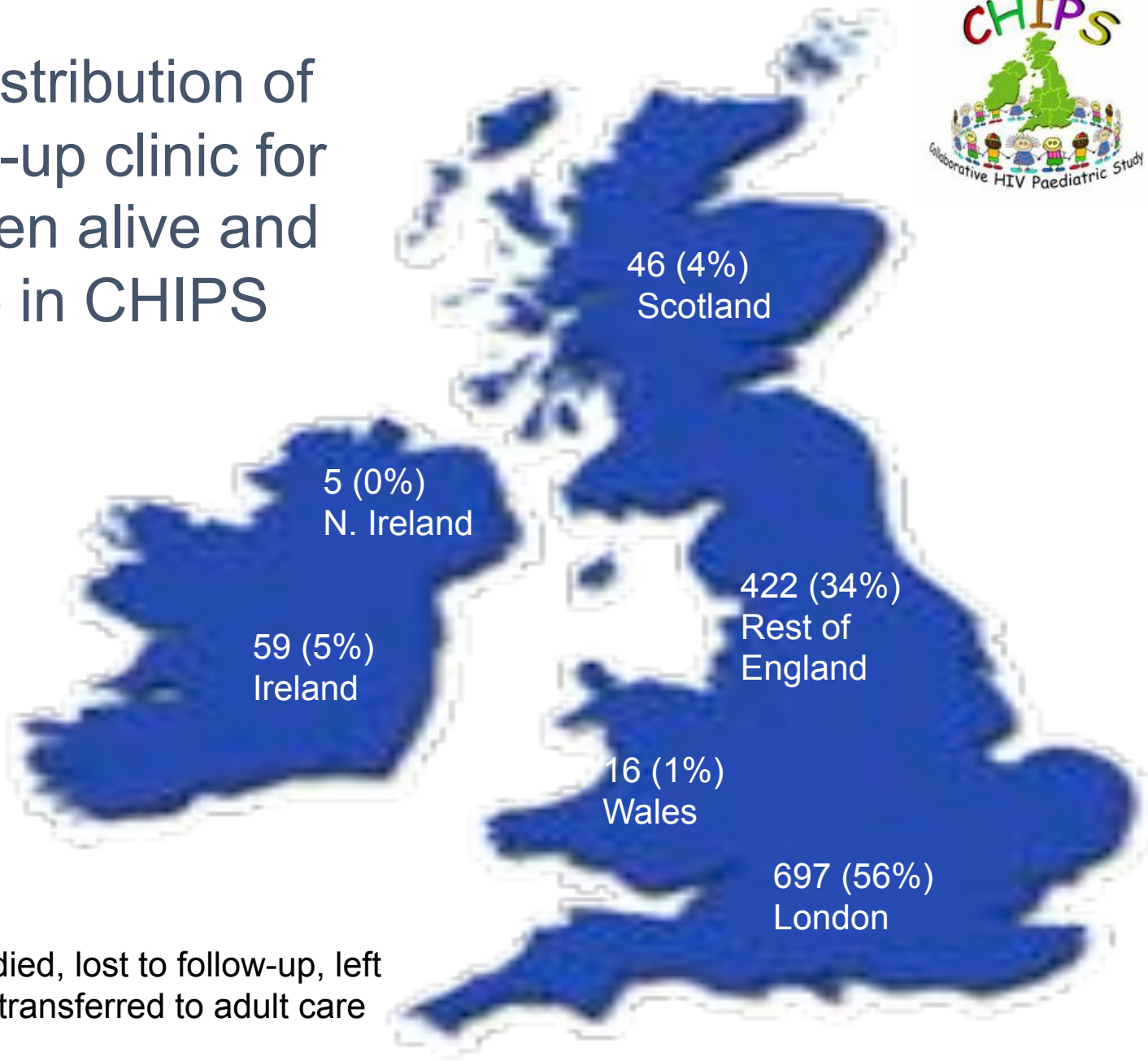
Times have changed

- Prolonged survival now expectation
- Children with vertically acquired HIV infection may well have near normal life expectancy

Plan

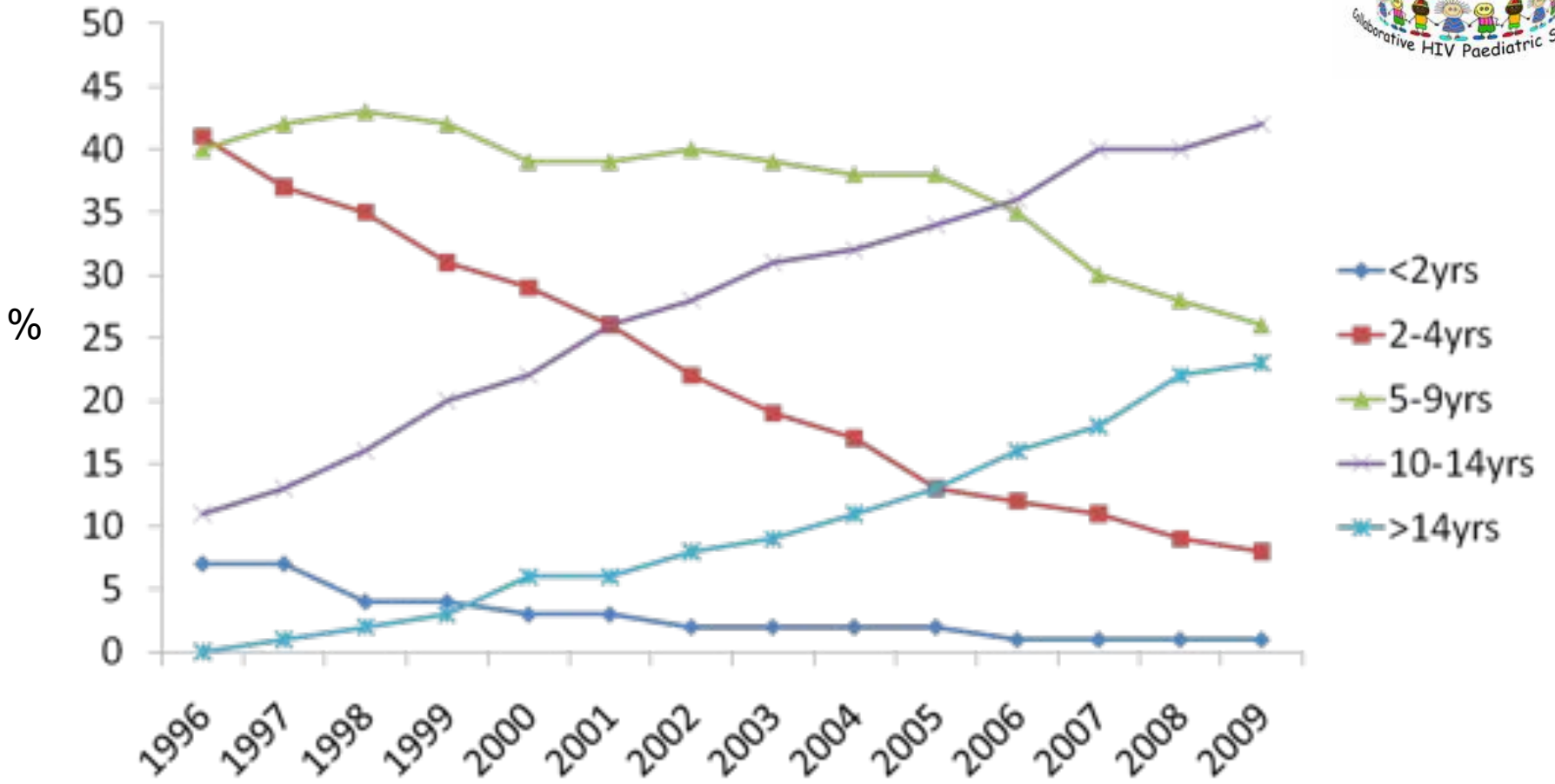
- Introduction
  - UK
  - Global
- Presentation
- Treatment and guidelines
  - When to start
  - What to start
- Transition of care

Regional distribution of main follow-up clinic for 1245 children alive and followed up in CHIPS



Children who have died, lost to follow-up, left the UK & Ireland or transferred to adult care are excluded

Age distribution* of children in follow-up by year, 1996-2009



are slowly transfers

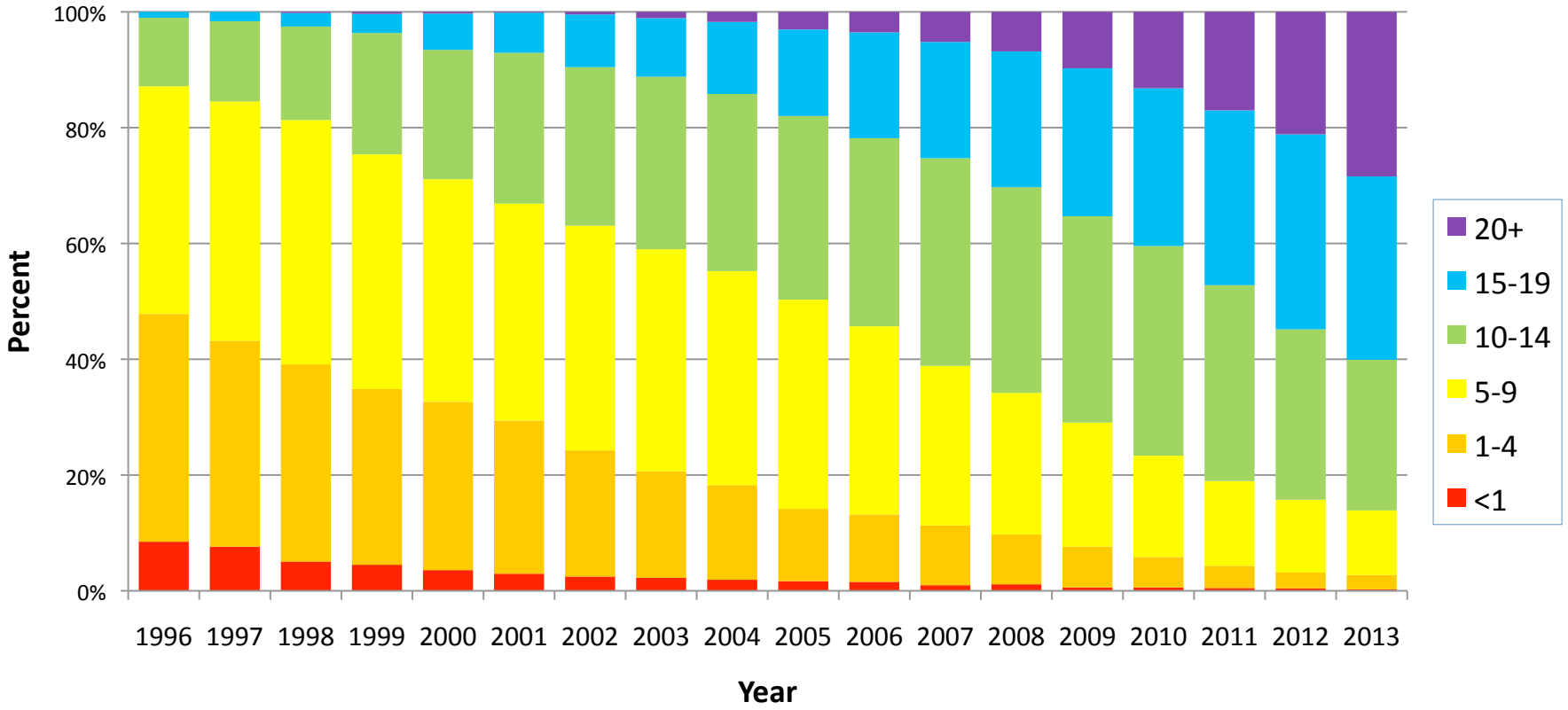
PAEDIATRICIAN TRANSITIONAL ADULT

National Study of HIV in Pregnancy and Childhood

NSHPC

Age of UK/Irish paediatric cohort by year of follow-up, 1996-2013

CHIPS Collaborative HIV Paediatric Study



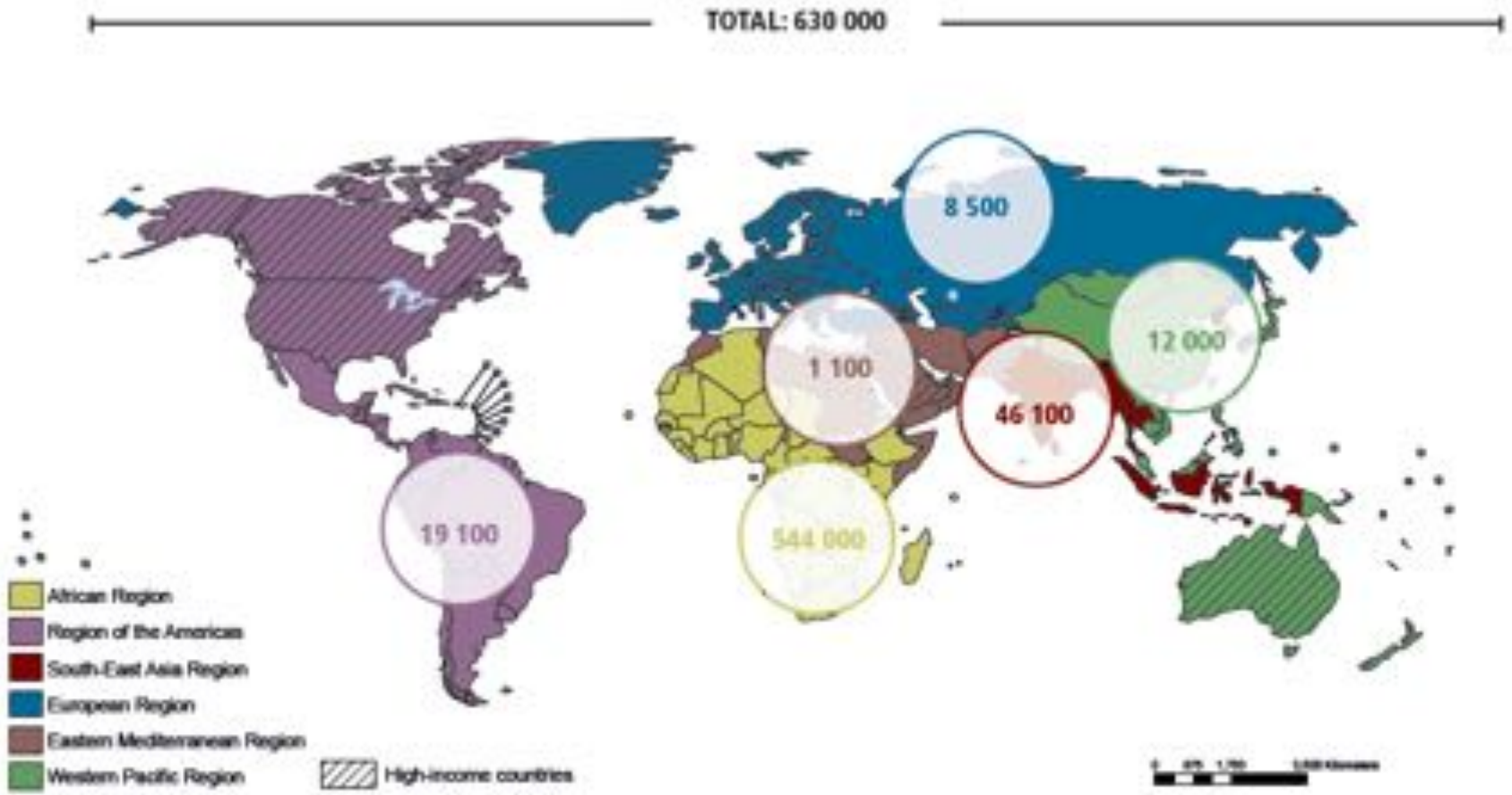
N	389	514	671	891	1150	1357	1509	1607	1645								
		433	577	779	1027	1251	1444	1569	1646	1541							

Note: Data are for all children and young people alive who were ever in follow-up from 1996 onwards, including children who have since transferred to adult care; those who subsequently died or were lost to follow-up are excluded from the year of death or loss to follow-up. All paediatric infections are included, regardless of mode of acquisition (94% perinatal). CHIPS includes all diagnosed HIV-infected children known to be living in the UK/Ireland, of whom ~55% were born abroad. Data for 2013 are incomplete as subject to reporting delay.

Global summary of HIV epidemic 2013

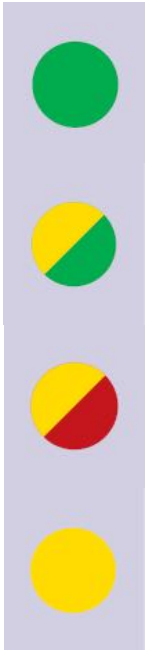
Number of people living with HIV in 2013	**Total**	35.0 million	[33.1 million – 37.2 million]
	Adults	31.8 million	[30.1 million – 33.7 million]
	Women	16.0 million	[15.2 million – 16.9 million]
	Children (<15 years)	3.2 million	[2.9 million – 3.5 million]
People newly infected with HIV in 2013	**Total**	2.1 million	[1.9 million – 2.4 million]
	Adults	1.9 million	[1.7 million – 2.1 million]
	Children (<15 years)	240 000	[210 000 – 280 000]
AIDS deaths in 2013	**Total**	1.5 million	[1.4 million – 1.7 million]
	Adults	1.3 million	[1.2 million – 1.5 million]
	Children (<15 years)	190 000	[170 000 – 220 000]

Children receiving ART 2013

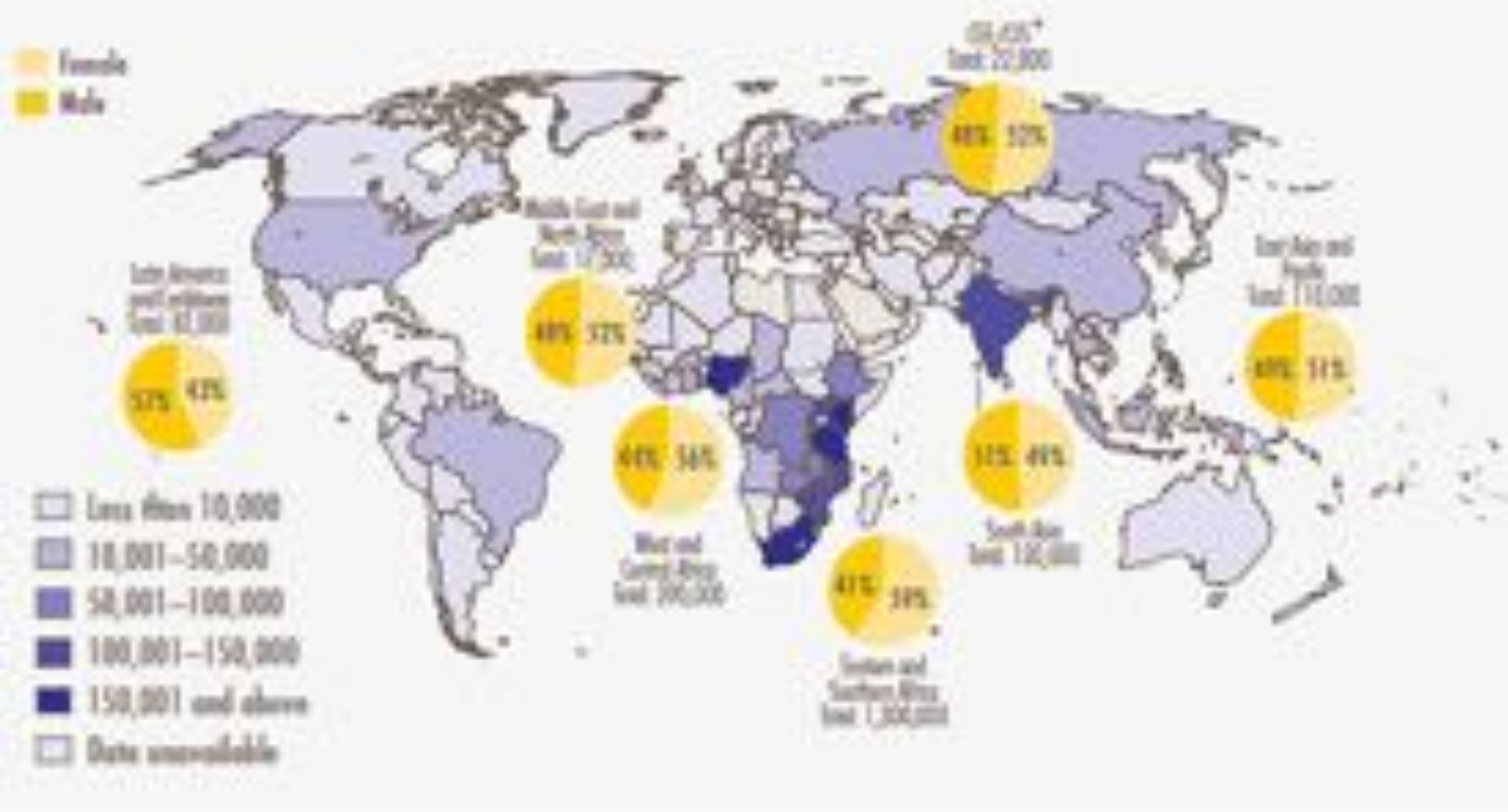


Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

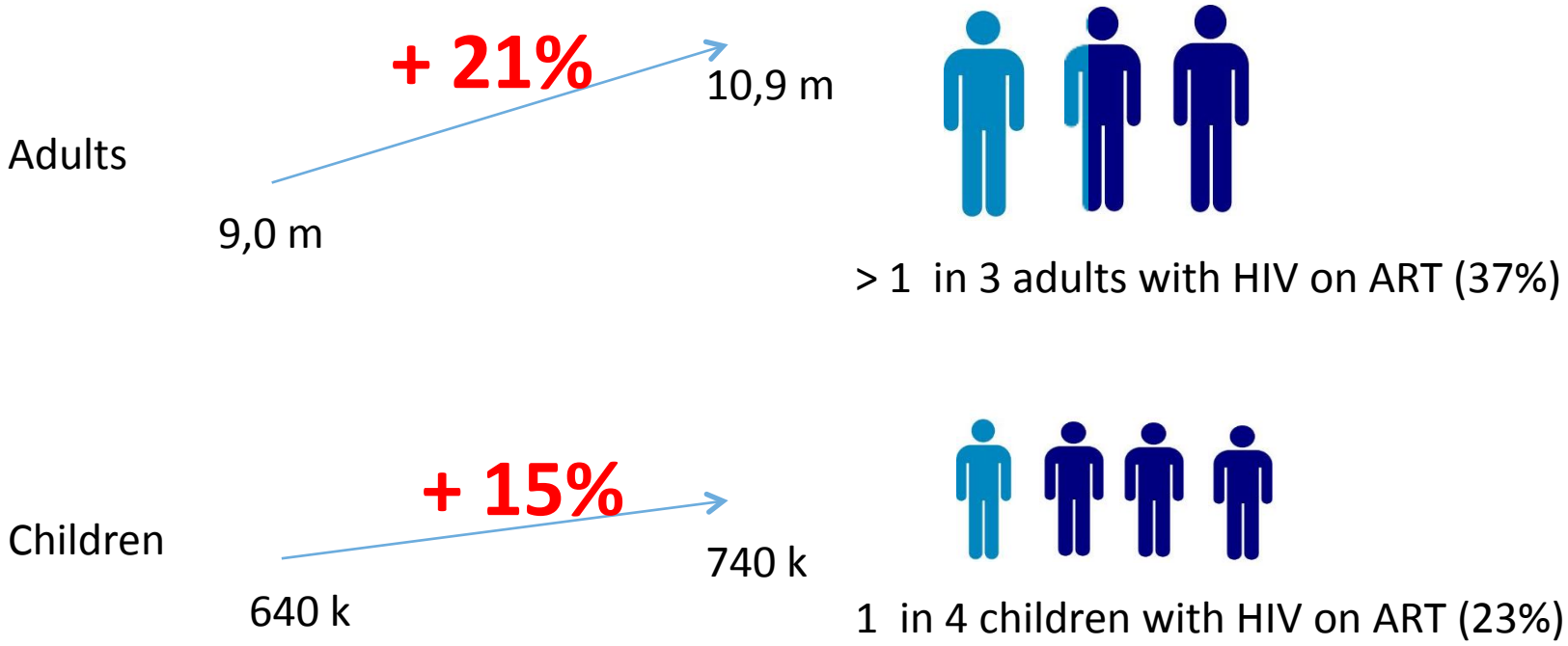
Gauging recent progress in the global HIV response

2013		2009-2013
1.5 million HIV related deaths [1.4 – 1.7 million]		▼ 25%
320 000 TB-related deaths in PLWHA* [300 000 – 340 000]		▼ 36%**
2.1 million HIV infections [1.9 – 2.5 million]		▼ 15%
240 000 HIV infections in children [210 000 – 280 000]		▼ 40%

Adolescents living with HIV – male/female 2012

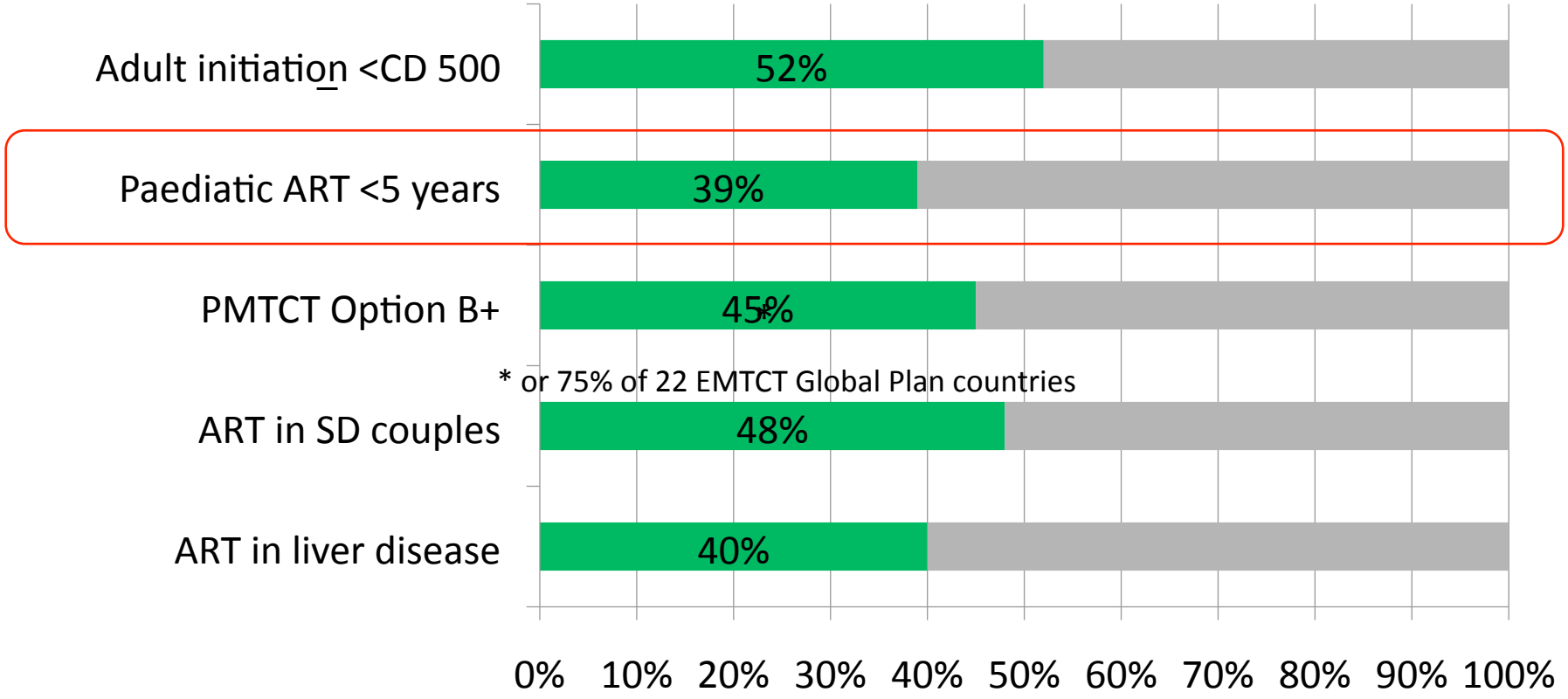


The gap between access to ART for children and adults continues to widen



Source: 2014 Global AIDS Response Progress Monitoring (WHO/UNICEF/UNAIDS) and UNAIDS/WHO/UNICEF estimates

Uptake of 2013 WHO guidelines increases eligibility for treatment

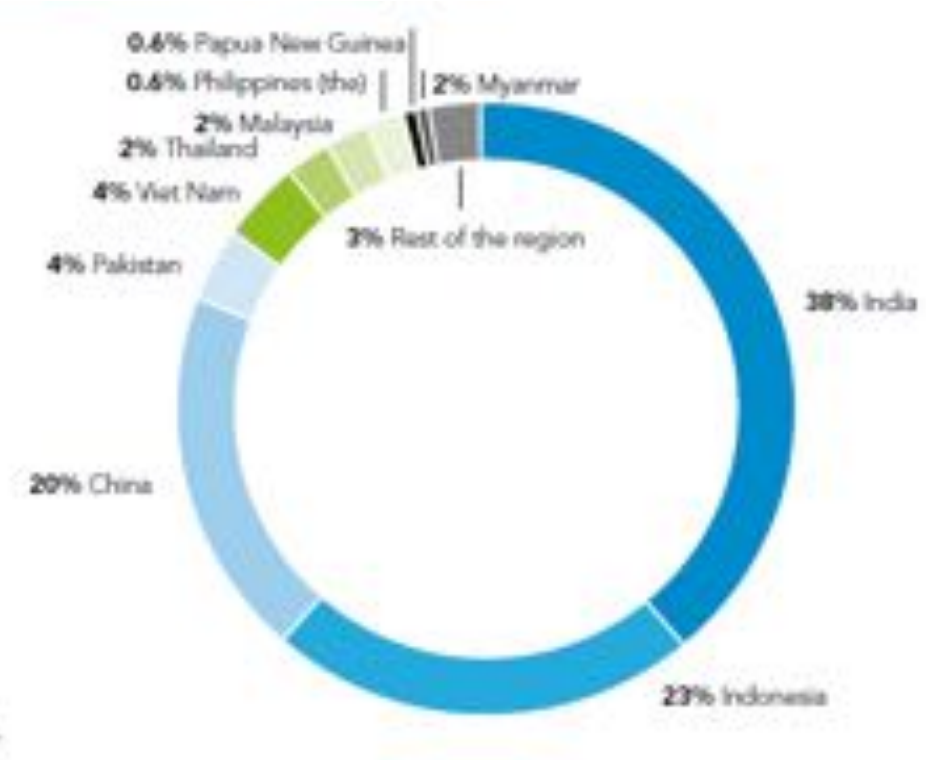


Percentage of 58 WHO HIV Focal Countries with confirmed adoption of select WHO 2013 ARV recommendations, June 2014

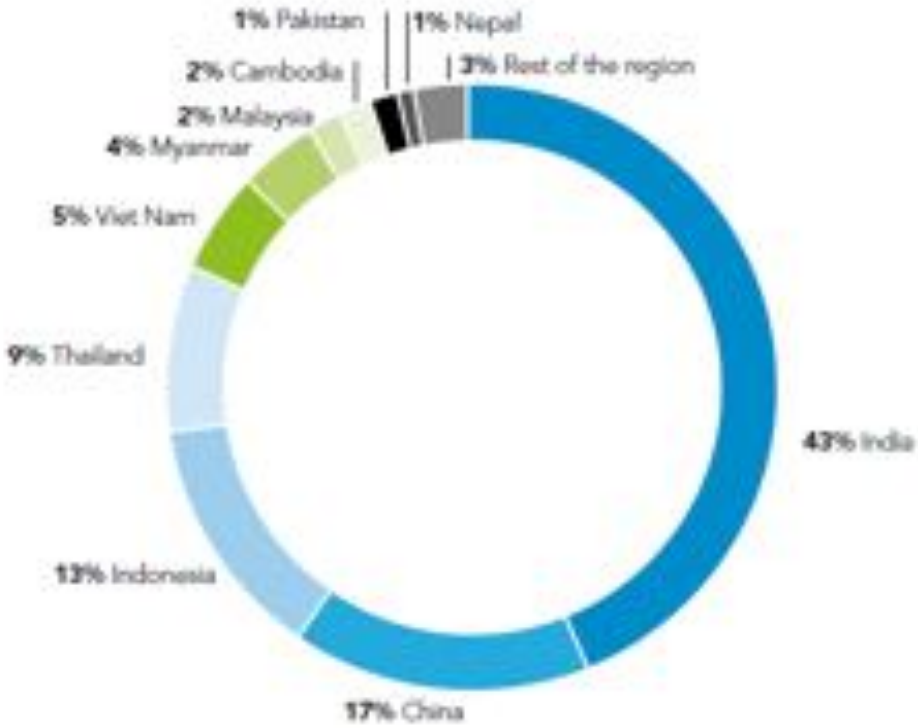
Source: WHO HIV Country Intelligence Database, June 2014

Incidence and prevalence HIV 2013
SE Asia

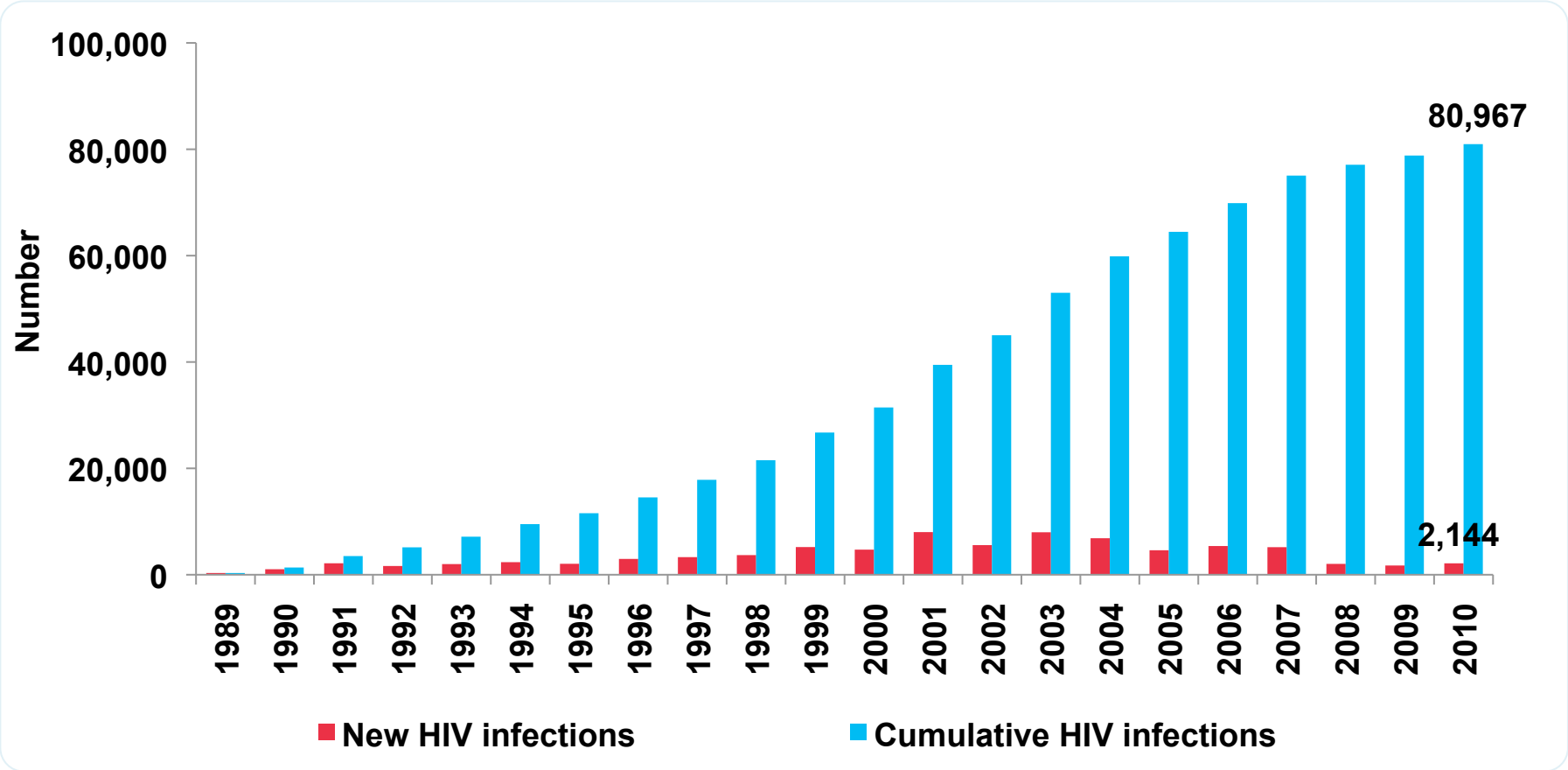
Incidence



Prevalence

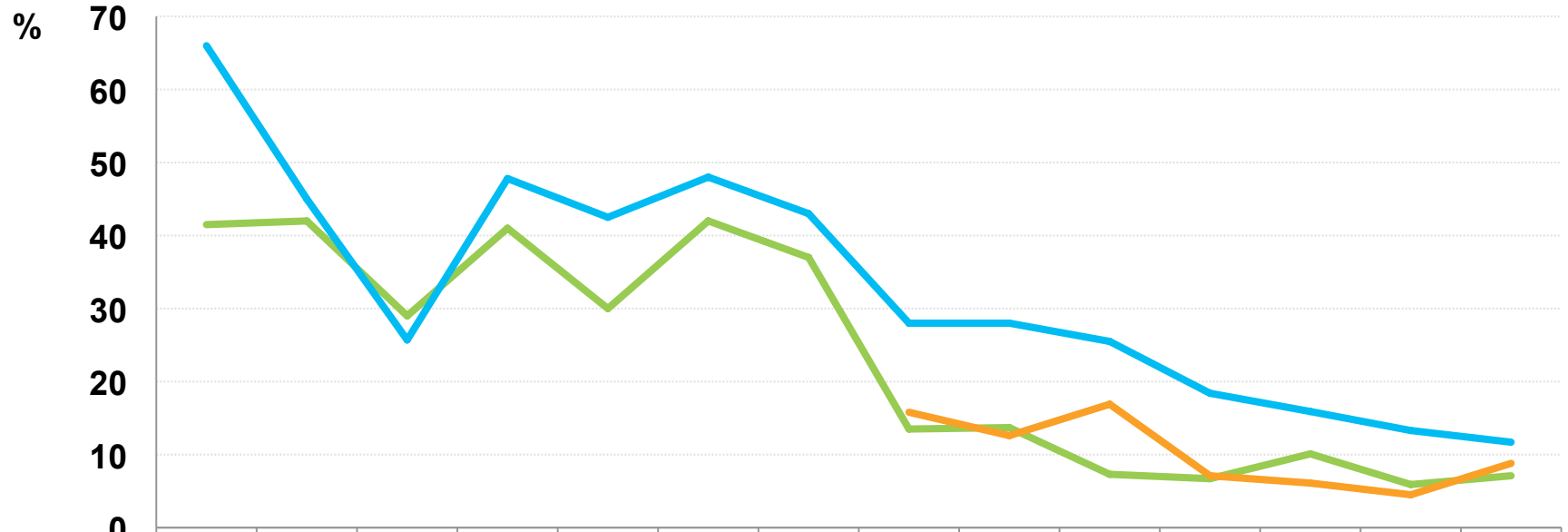


Myanmar: annual cumulative and new HIV cases, 1989-2010



Source: Prepared by www.aidsdatahub.org based on National AIDS Programme Myanmar. (2011). Progress Report 2010: National Strategic Plan for HIV/AIDS in Myanmar.

Myanmar: HIV prevalence among young key populations (15-24), 2000-2013



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
FSW	41.5	42	29	41	30	42	37	13.5	13.7	7.3	6.7	10.1	5.9	7.1
PWID	66	45	25.7	47.8	42.5	48	43	28	28	25.5	18.4	15.9	13.3	11.7
MSM								15.8	12.6	16.9	7.1	6.1	4.5	8.8

Source: Prepared by www.aidsdatahub.org based on National AIDS Programme, Myanmar (2014). HIV Sentinel Sero-surveillance Survey Report, 2013.

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Differences between Adults and Children

- OI in children often reflects primary infection rather than reactivation
- Different disease manifestations
- OI occurs at a time when infant's immune system is immature
- Early symptomatic disease is invariably an indication for treatment
- Some conditions much commoner in children than adults
- Classical features of infection may not be present

Difficulty of Diagnosing OI in Children

- Inability to describe symptoms
- Antibody-based tests confounded by maternal transfer of antibody
- Samples often difficult to obtain without invasive procedures

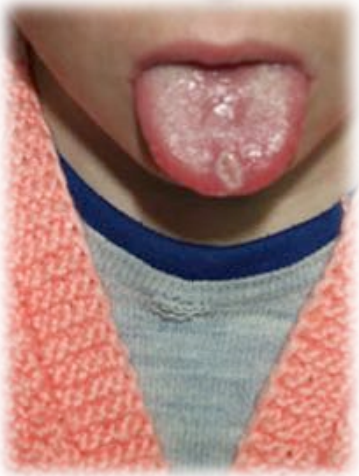
Frequency of OI among HIV-Infected Children ***in the pre-ART era***

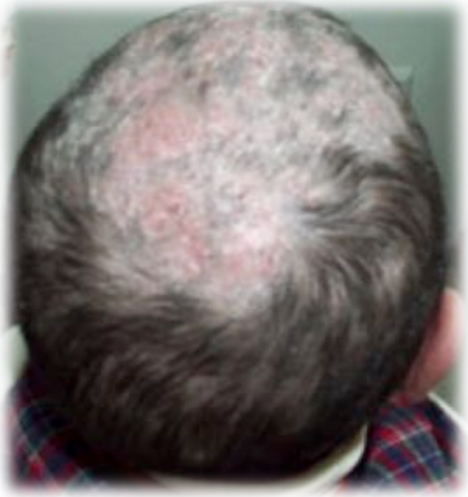
- Pre-HAART era, most common OIs occurring at >1 events/100 child years
  - Serious bacterial infections (bacteremia and pneumonia), herpes zoster, *Pneumocystis jiroveci* (*carinii*) pneumonia, candidiasis, *Mycobacterium avium* complex
- Pre-HAART era, most common OIs occurring at <1 events/100 child years
  - Cytomegalovirus, toxoplasmosis, cryptosporidiosis, TB, systemic fungal infections

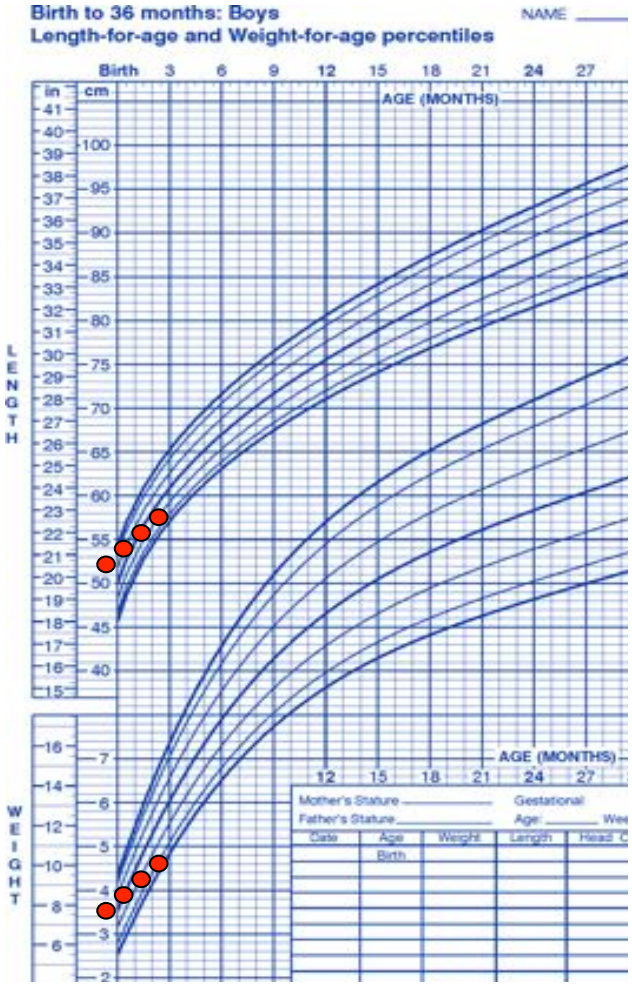
Changes in Frequency of OI among HIV-Infected Children

Infection	Pre-HAART Rate per 100 Child Years	Post-HAART Rate per 100 Child Years
Bacterial pneumonia	11.1	2.2
Herpes zoster	2.9	1.1
Disseminated Mycobacterium avium	1.8	0.14
Pneumocystis jiroveci	1.3	0.09

Common presentations in children

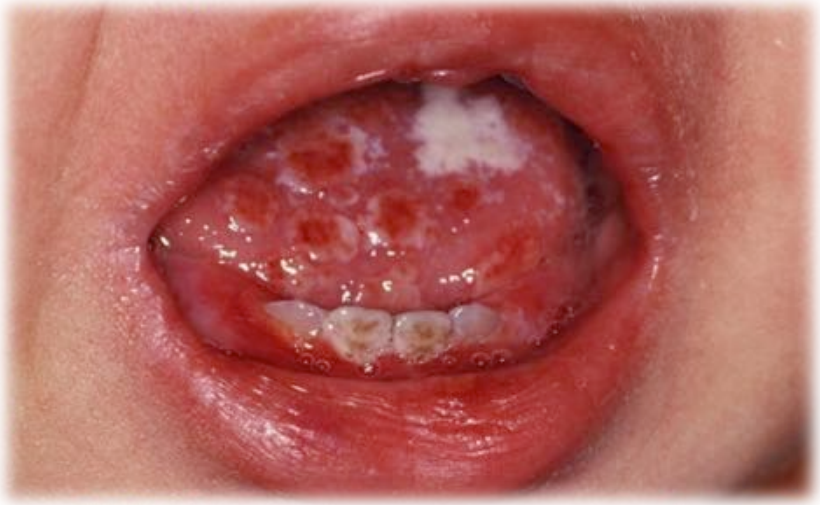


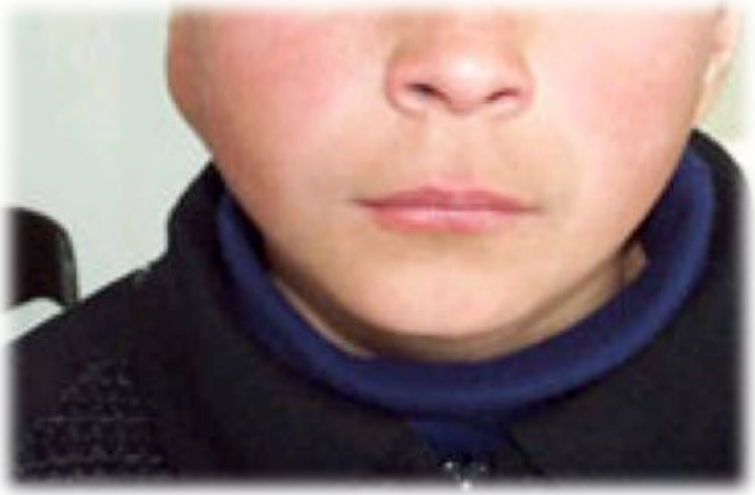


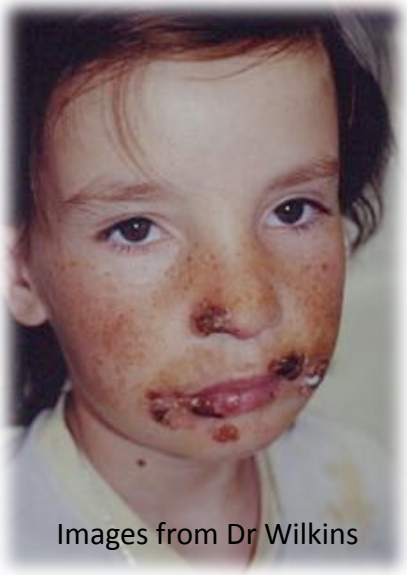


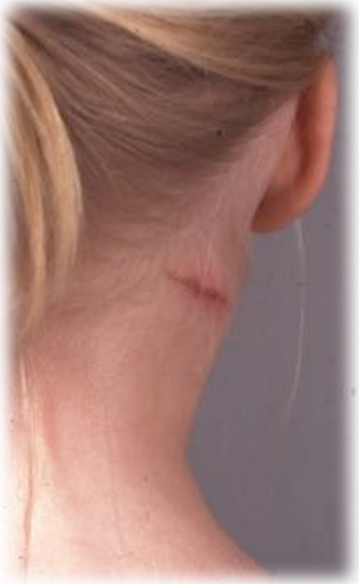
Images from Dr Wilkins & Dr Siranthana

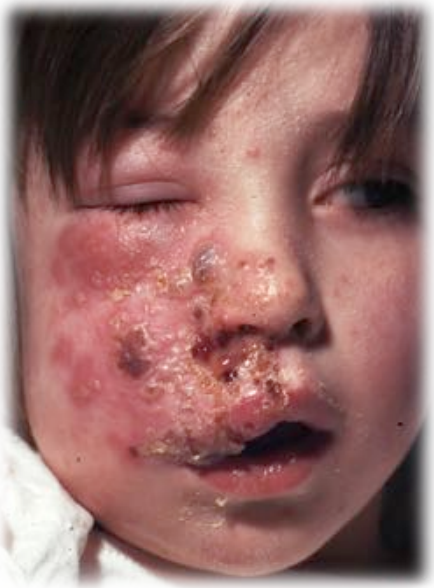
Common presentations in children

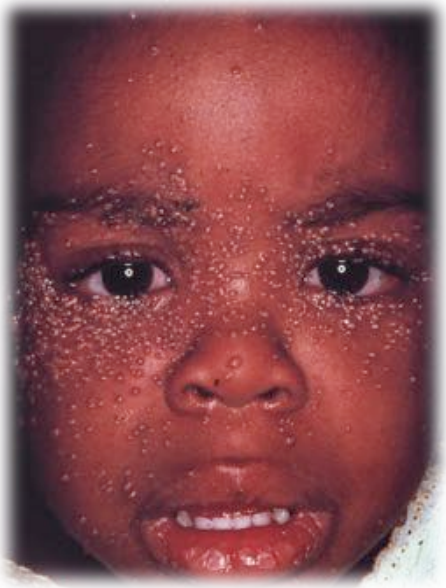












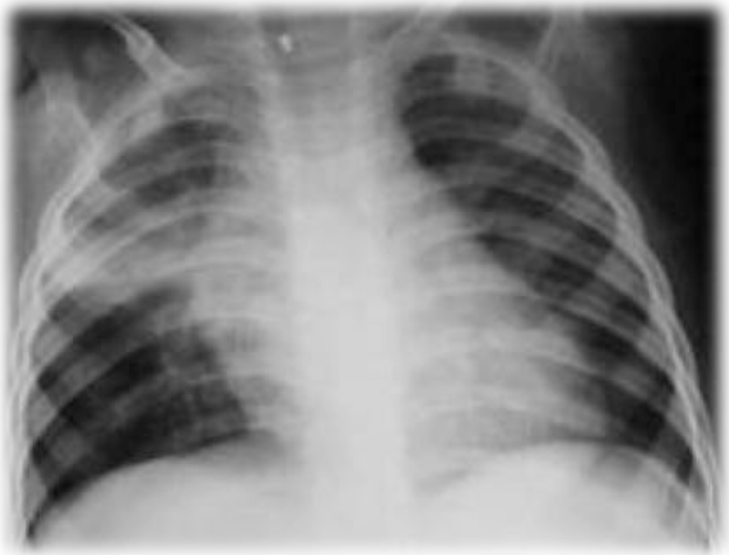
Images from Dr Wilkins

Presentations in children

- Failure to thrive
- Development delay (especially neurological)
- Fall off on growth centiles
- Delayed puberty
- Recurrent ENT infections
- Severe/unusual viral infections
  - Cutaneous (HPV, Molluscum, HS, HZ)
  - Systemic (RSV, VZV, measles, adenovirus)
- Disseminated BCG

Bacterial pneumonia

- Most common infection in pre-HAART era (15/100 child years)
- Because of difficulties in obtaining appropriate diagnostic specimens, bacterial pneumonia is often a presumptive diagnosis in a child with fever, pulmonary symptoms, and an abnormal CXR



Images from Dr Siranthana

Serious Recurrent Bacterial Infections:

- Bacteria isolated include:
  - *Streptococcus pneumoniae*,
  - *Haemophilus influenzae* type B,
  - *Staphylococcus aureus*,
  - Gram –ve (*E. coli*, *Pseudomonas*, non-typhoid *Salmonella)*
- *S pneumoniae* accounts for >50% of bacteremia
- Increased rate of bacteraemia
- Gram-negative bacteremia more common in children with advanced disease

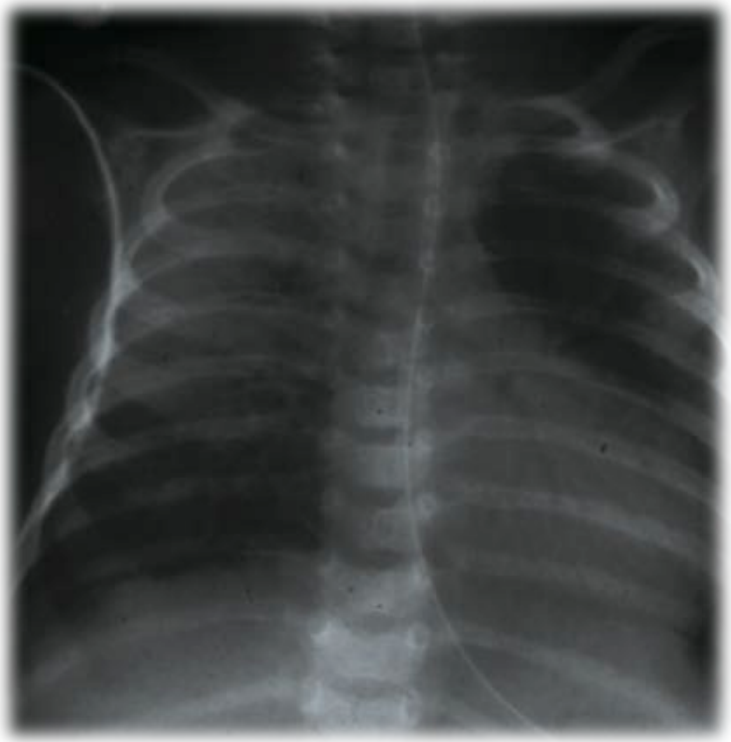
Pneumocystis jiroveci (*carinii*): Epidemiology

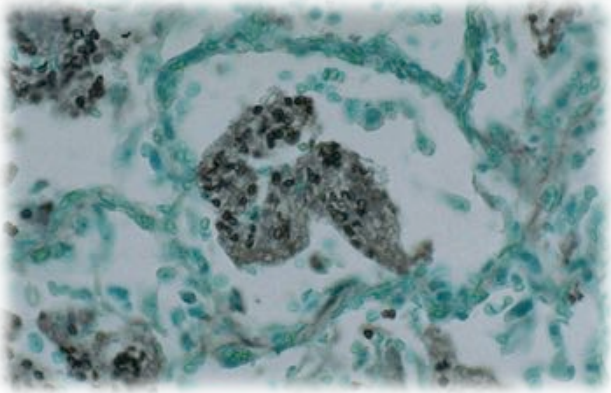
- Most common AIDS indicator disease in children
- Incidence highest in first year of life, peaking at 3-6 months
- Accounted for 57% of AIDS-defining illnesses in infants age <1 year pre-ART
- CD4 T-cell count not a good indicator of risk in infants <1 year old
- Infection now unusual owing to routine prophylaxis with TMP-SMX

Pneumocystis jiroveci (*carinii*):

Clinical Manifestations

- Fever, tachypnea, cough, dyspnea, poor feeding, weight loss
- Extra-pulmonary locations: spleen, liver, colon, pancreas, ear, eye, GI tract, bone marrow, heart, kidney, lymph nodes, CNS





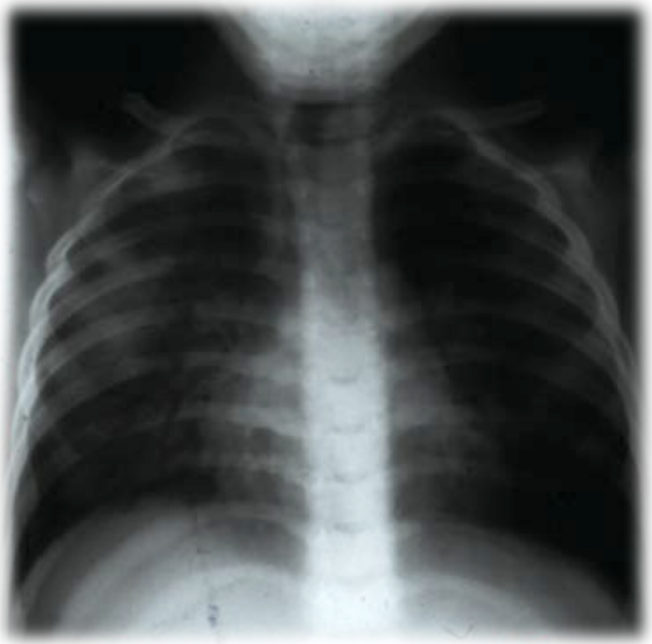
Images from Dr Wilkins

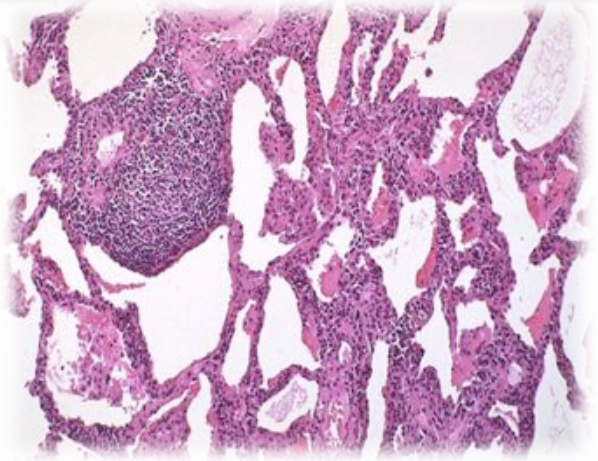
Pneumocystis jiroveci (*carinii*): Prevention

- Chemoprophylaxis with TMP-SMX recommended as follows, based on CD4 counts and patient age:
  - 6 years: CD4 count <200 cells/µL or CD4 percentage <15%
  - 1 to 5 years: CD4 count <500 cells/µL or CD4 percentage <15%
  - All HIV-infected infants <12 months of age regardless of CD4 count or percentage

Lymphocytic interstitial pneumonitis

- 40% of children
- EBV co-factor
- Disease asymptomatic or mild
- CXR shows diffuse reticulo-nodular changes
- Occasionally symptoms:
  - Chronic onset
  - Cough, SOB, low grade fever
- Diagnosis by TBB
- Treatment not indicated





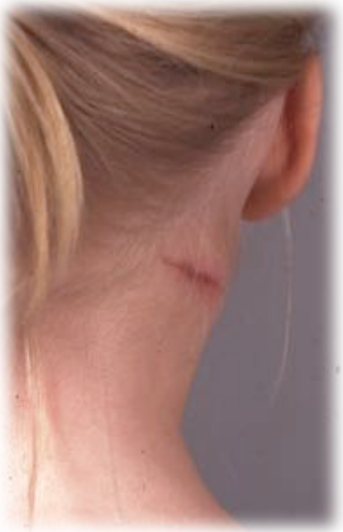
Images from Dr Wilkins

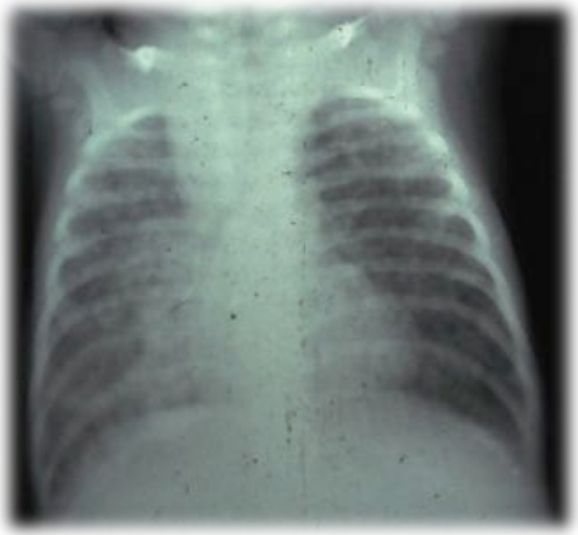
Tuberculosis in HIV

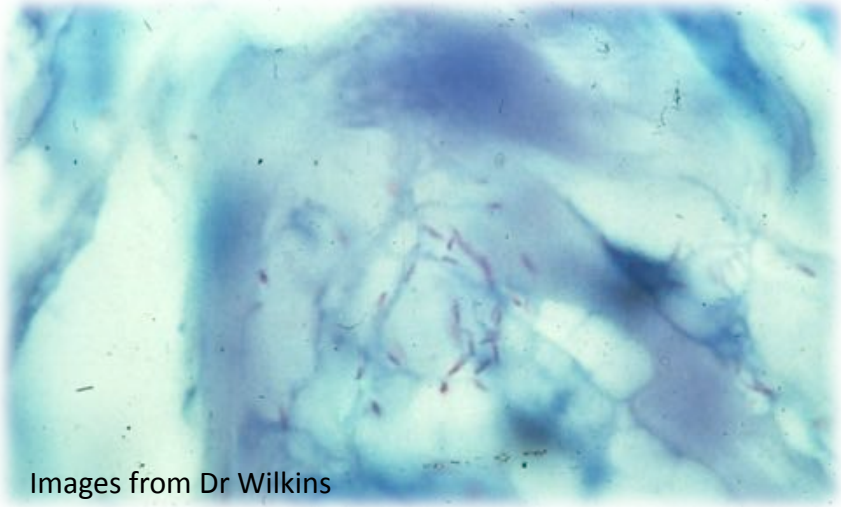
More likely:

- Infection after exposure
  - 10-20% vs 5-10%
- Progressive primary disease after infection
  - 30% vs 5-10%
- Reactivation of latent infection
  - 5-10% annual vs 5-10% lifetime
- Reinfection with new strain
  - 50:50 vs 90:10
- Reduced smear-positive rates in pulmonary TB (40%)
- Less cavitation and atypical chest x-ray appearance with lower CD4 count
- Increased disseminated disease and extra-pulmonary infection with lower CD4
  - > 60% vs <20%
- Greater risk of adverse drug reactions

TB







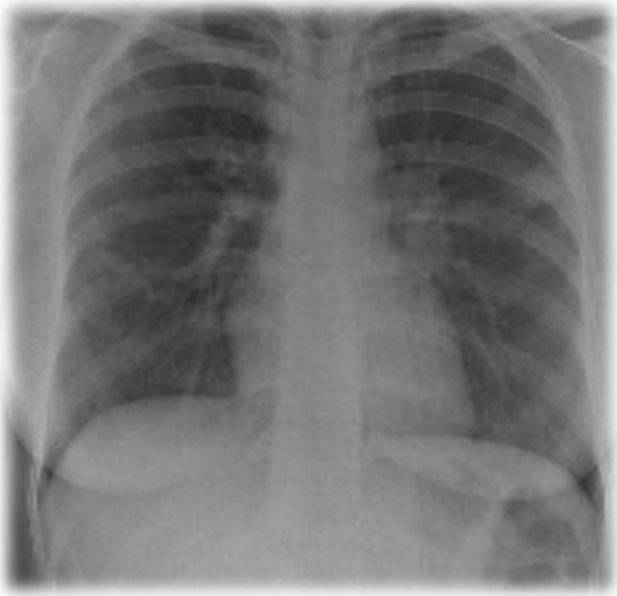
Images from Dr Wilkins

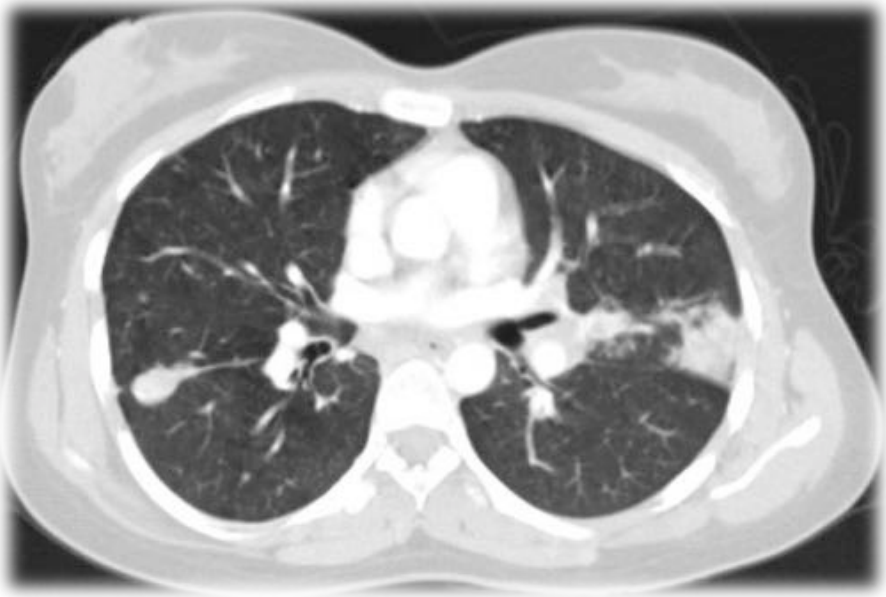
Features of primary TB

Disease

- Lymphadenopathy
  - Collapse
  - Consolidation
  - Obstructive emphysema
  - Cavitation
- Pleural effusion
- Endobronchial
- Miliary
- Meningitis
- Pericarditis

MDRTB/XDRTB



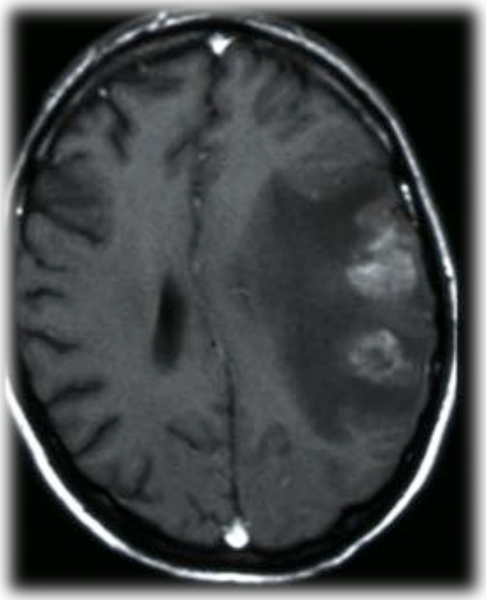


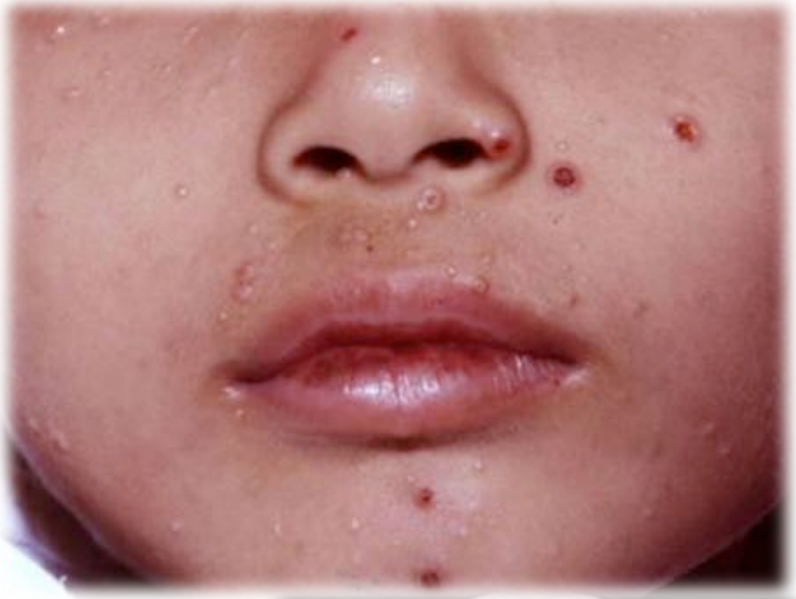
	CYC	CLA	RIF	INH	PZA	EMB	MOX	PRO	LIN	PAS	AMI
S/R	NA	S	R	R	S	R	S	R	S	NA	S

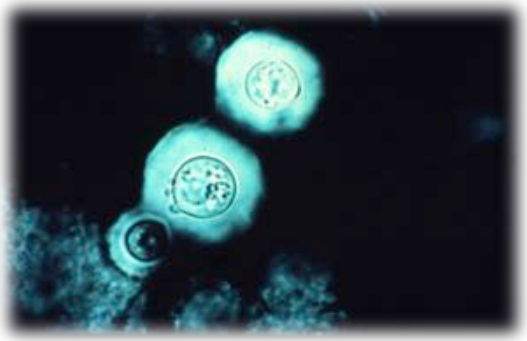
	RFB	STM	KAN	CAP	ETH	CIP	OFL	AZI
S/R	NA	R	S	R	S	R	S	R

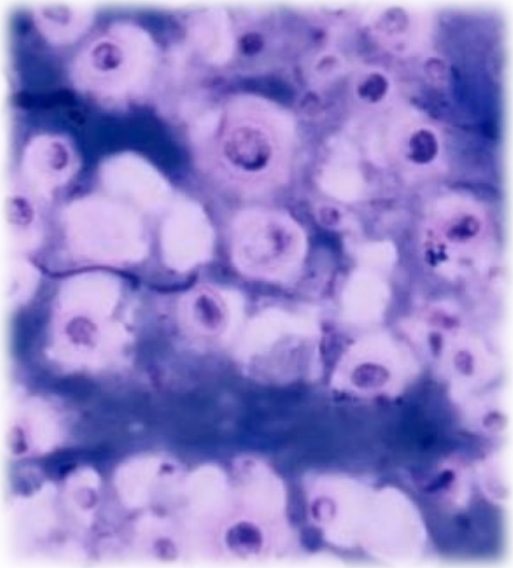
Images from Dr Wilkins

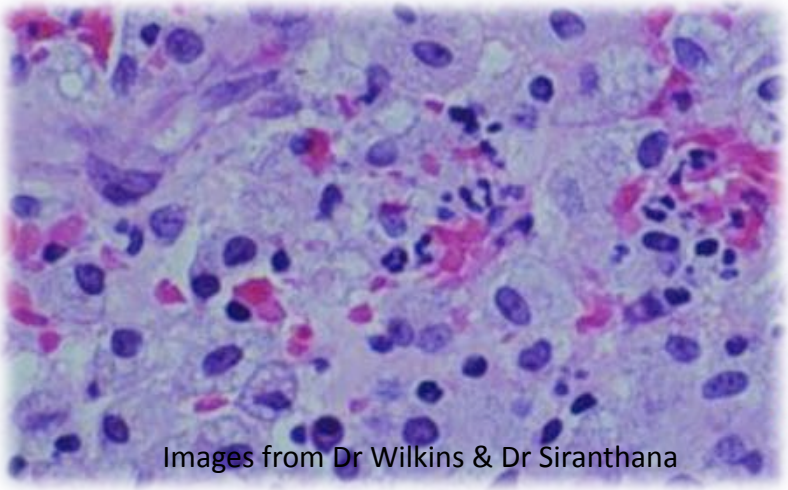
Other disseminated infections

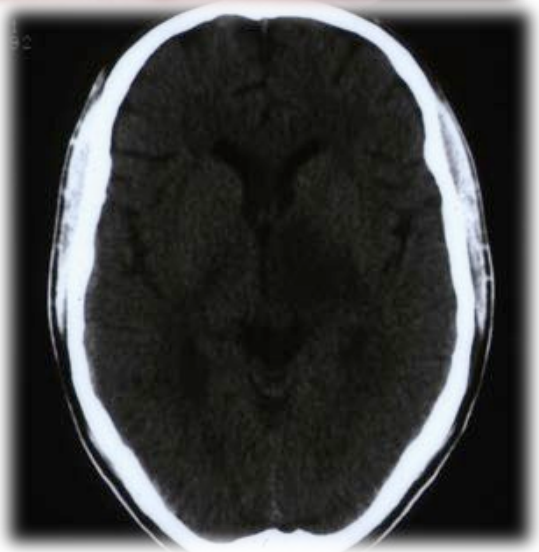












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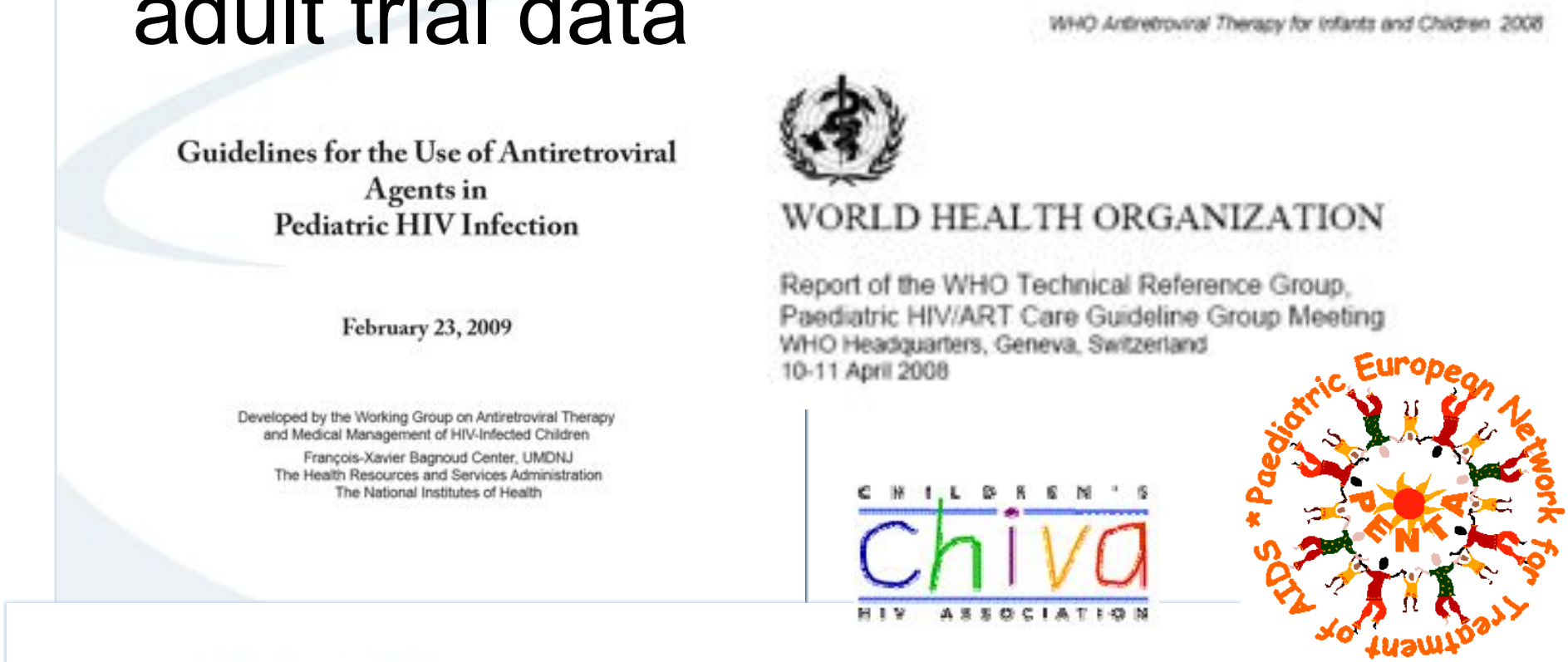
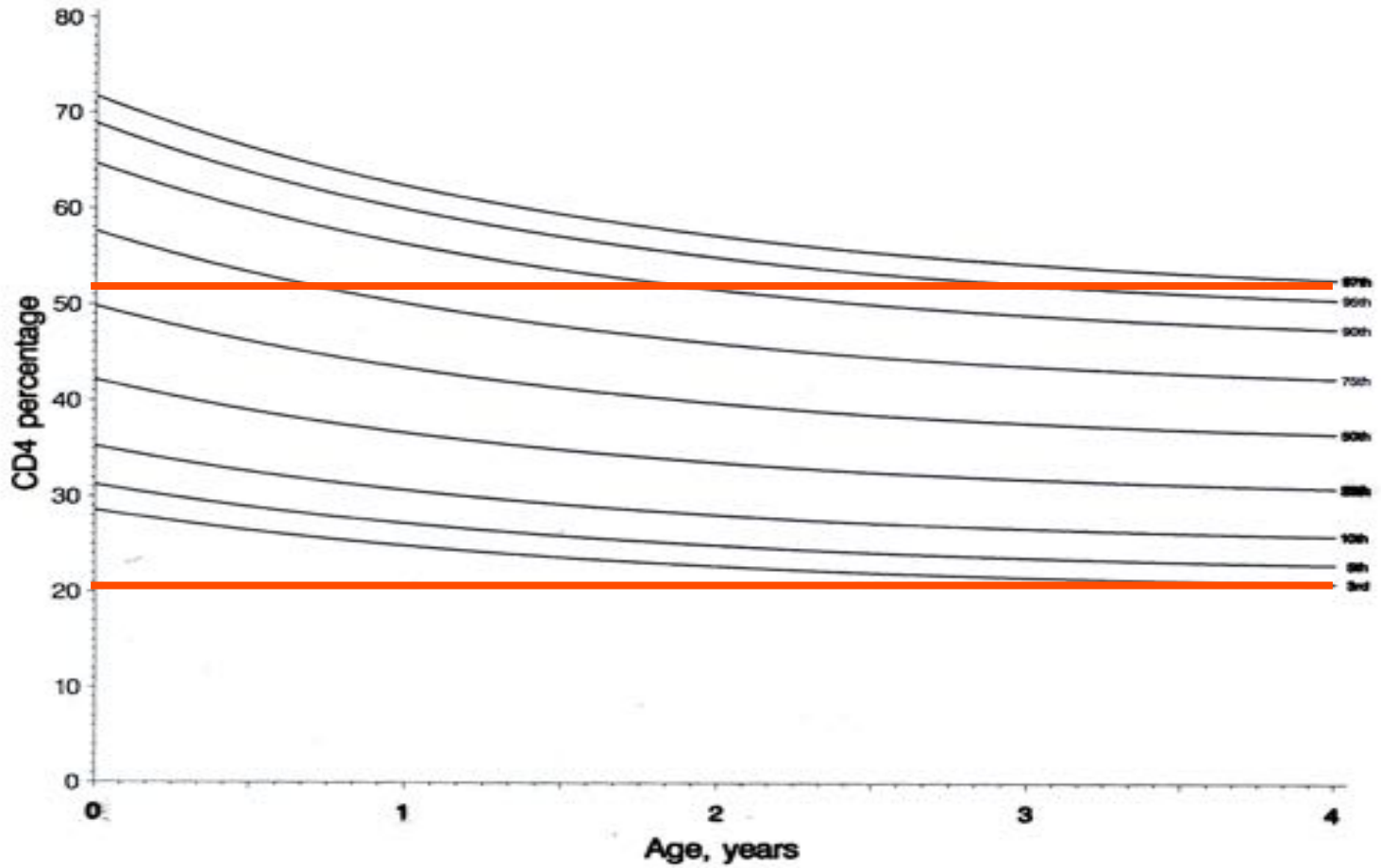
Treatment guidelines

Many guidelines still informed by adult trial data

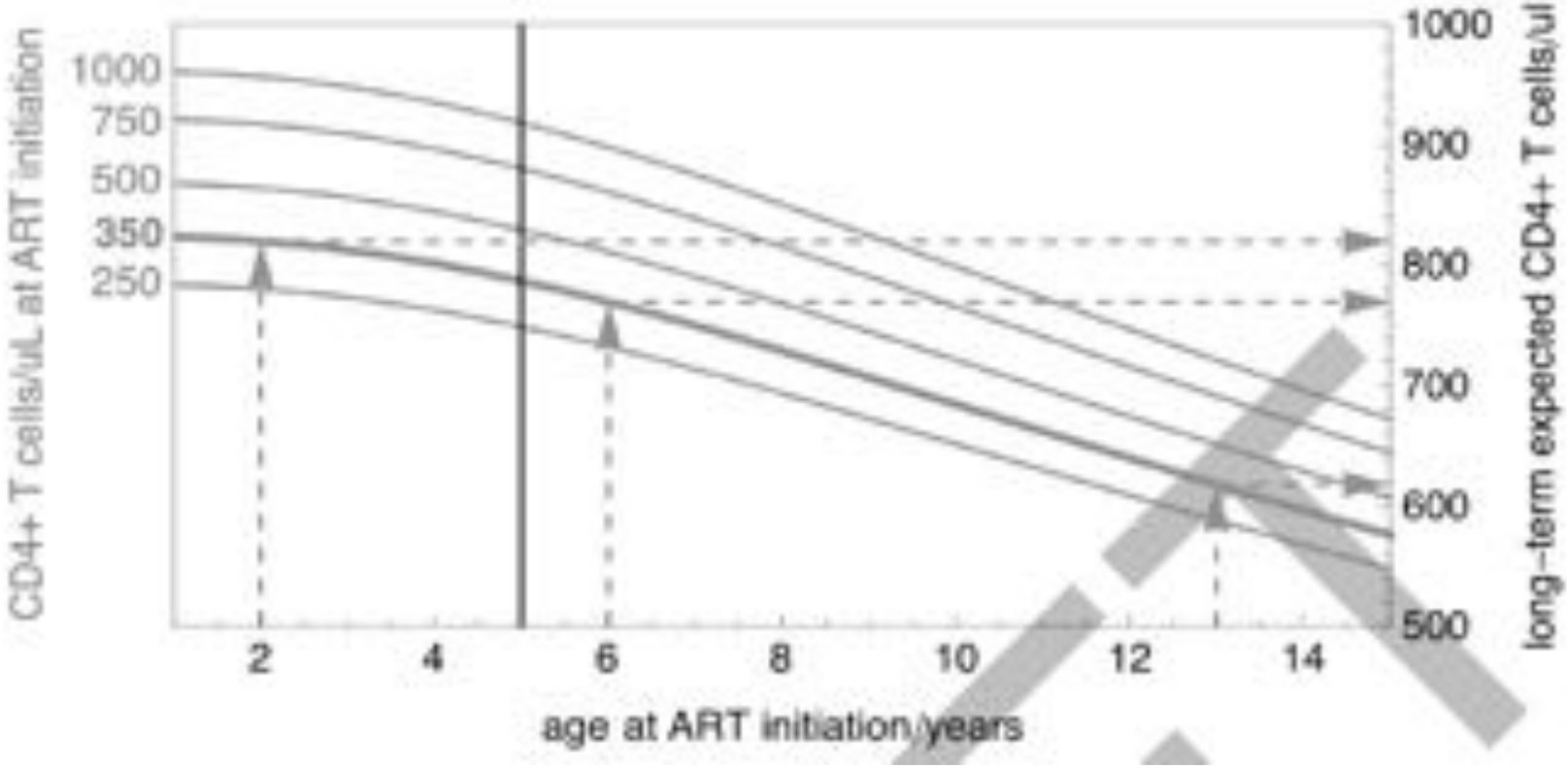


CD4% normal range by Age



ECS PIDJ 1992;11:1021

CD4 count after starting treatment



ART recommendations

- ART is recommended:
  - For all children under 1y of age
  - For all children with significant disease
  - Asymptomatic children >1y based on age-specific CD4 thresholds
  - For all children with hepatitis B/C co-infection
- ART should be considered:
  - In all children aged 1-3y
  - If the VL is >100,000 c/ml
  - If significant HIV-related symptoms
  - In sexually active adolescents as part of TASP

Comparison of current treatment guidelines

	WHO 2013	DHHS 2014	PENTA 2014
<1y	ALL	ALL	ALL
1-3y	ALL Prioritise: - 1-2y - WHO stage 3/4 - CD4 <750 <25%	CD4 <1000 <25% CDC Category B/C VL >1000 c/ml Consider: - ALL	CD4 <1000 <25% CDC Category B/C WHO stage 3/4 Consider: - ALL - VL >1000 c/ml

Comparison of current treatment guidelines

	WHO 2013	DHHS 2014	PENTA 2014
3-5y	ALL Prioritise: - WHO stage 3/4 - CD4 <750 <25%	CD4 <750 <25% CDC Category B/C VL >1000 c/ml Consider: - ALL	CD4 <750 <25% CDC Category B/C WHO stage 3/4 Consider - VL >1000 c/ml
>5y	CD4 <500 Prioritise: - WHO stage 3/4 - CD4 <350	CD4 <500 CDC Category B/C VL >1000 c/ml Consider: - ALL	CD4 <350 WHO stage 3/4 CDC Category B/C Consider: - ALL - CD4 <500 - VL >1000 c/ml

ART regimen

- For naïve children <1y:
  - NVP and LOP/r considered preferred options
    - Exception is for children exposed to NVP as part of failed MTCT
  - 4 drug regimen preferred over 3 (CHIVA)
  - NRTI backbone ABC, 3TC, AZT
- Alterations with age for 3rd drug:
  - NVP as preferred NNRTI for children <3y and EFV for children >3y
  - LOP/r as preferred boosted PI for children aged <6y, ATAZ/r for children >6y, and ATAZ/r or DAR/r for children >12y
  - RAL is as an option for children >12y

Recommended treatment PENTA

	<1y	1-3y	3-6y	6-12y	>12y
Backbone	ABC/3TC	ABC/3TC	ABC/3TC	ABC/3TC	TDF/FTC ABC/3TC
3rd agent	LPV/r NVP	LPV/r NVP	LPV/r NVP	ATZ/r EFV	ATZ/r DAR/r EFV
Alternative 3rd agent				NVP DAR/r LPV/r	NVP LPV/r RAL DTG

Plan

- Introduction
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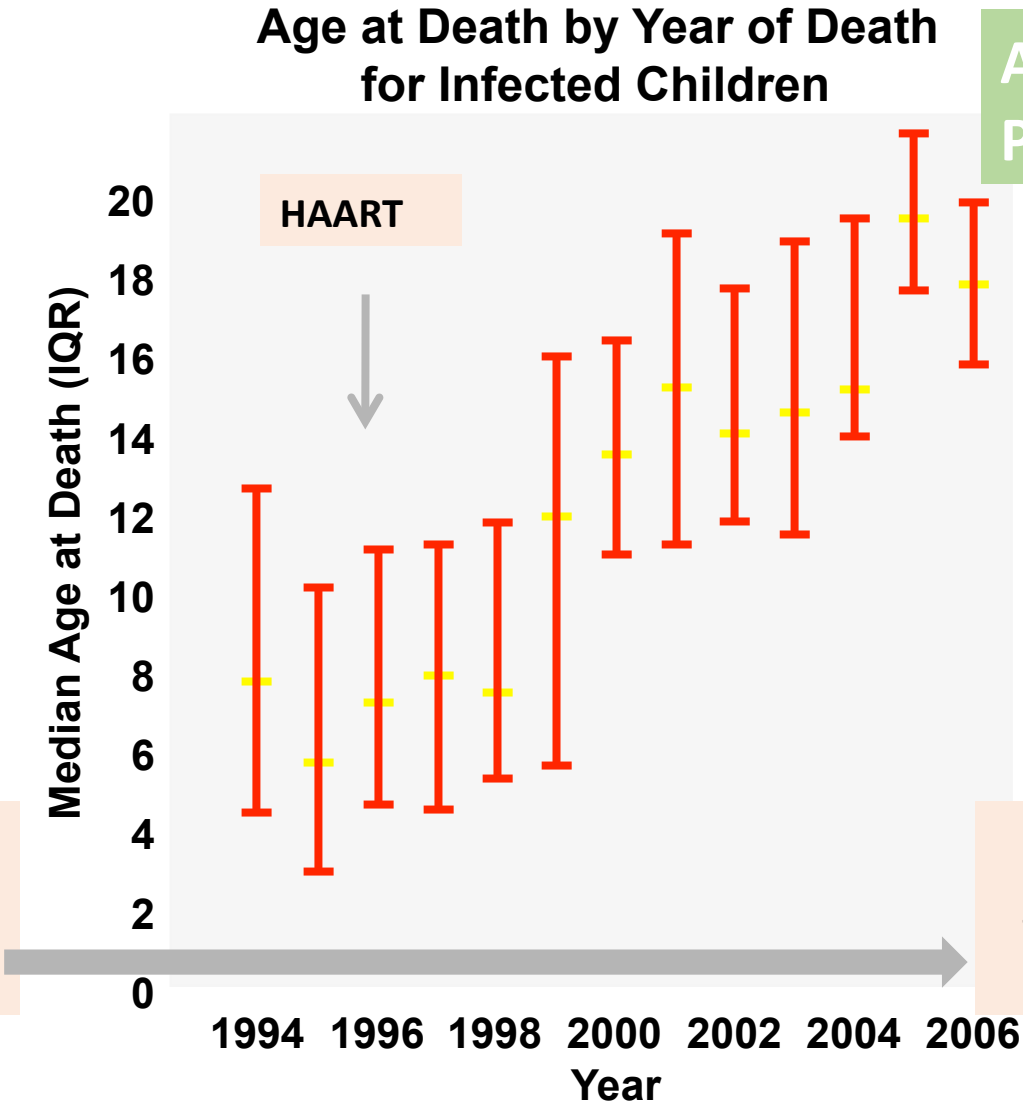
  - When to start
  - What to start
- Transition of care

HIV prognosis in children is improving

3,553 children
Median f/u 5.3 yrs
298 deaths

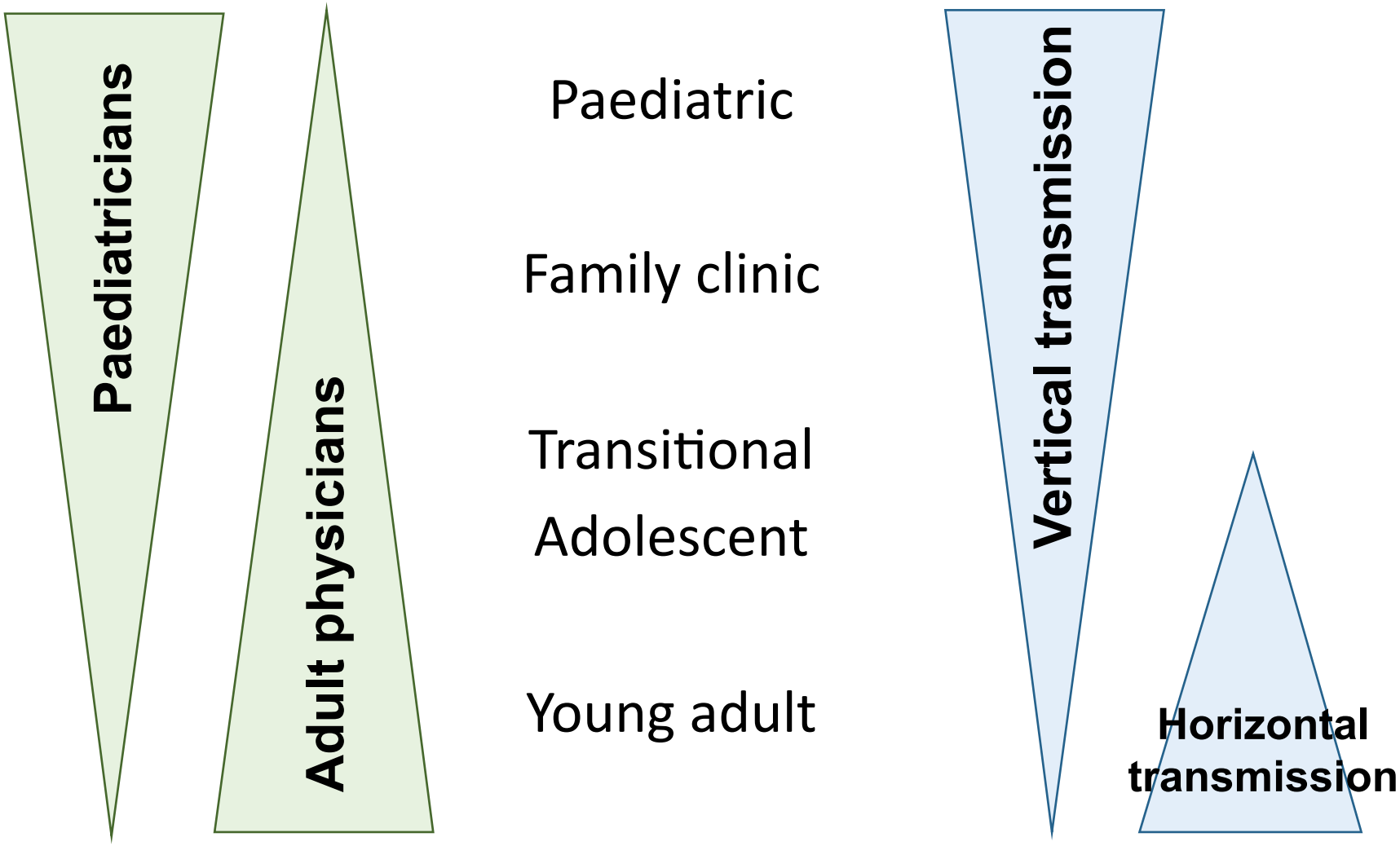


Age at death
PACTG 219

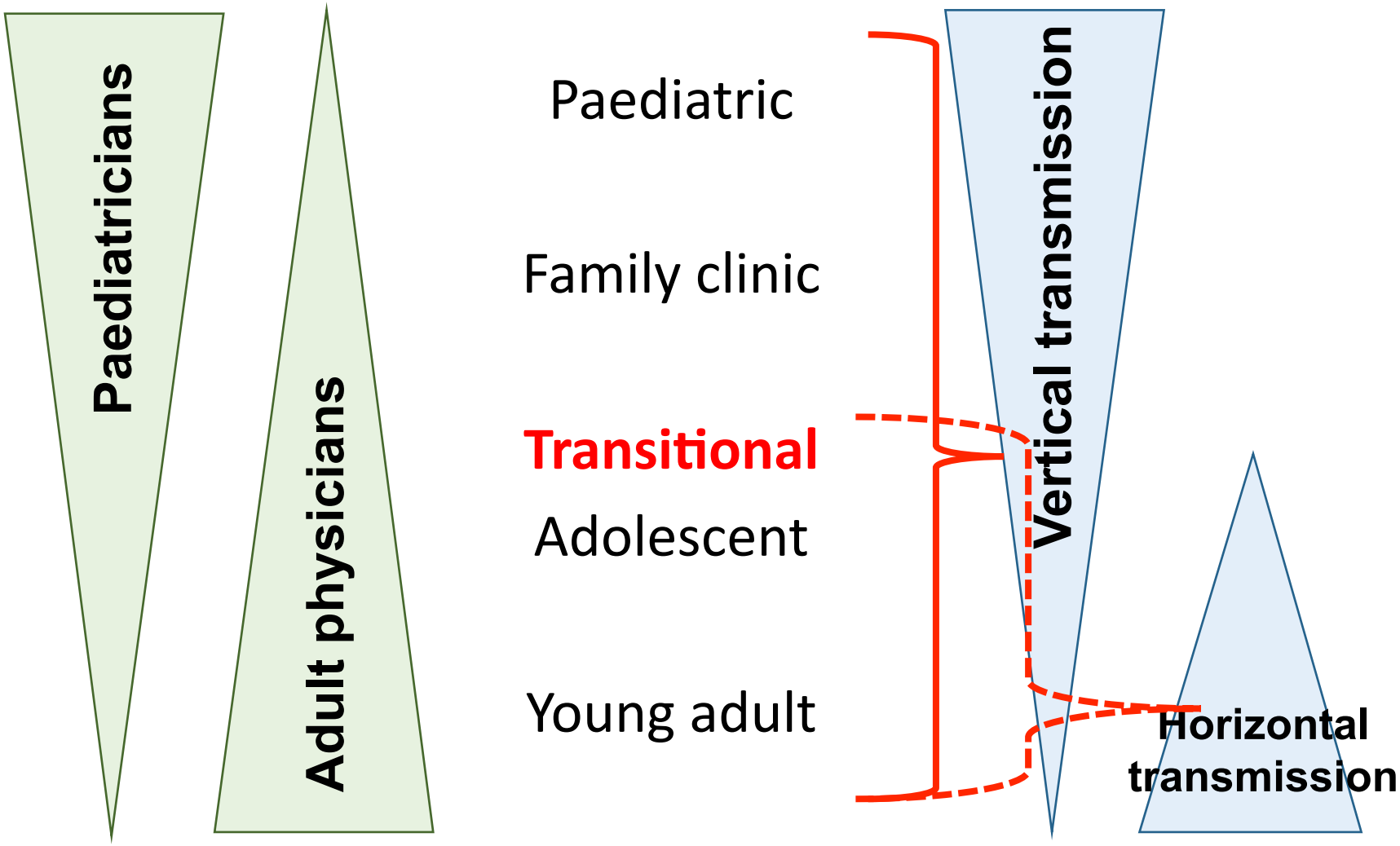
Mean age
at death 1994:
8.9 years

Mean age
at death 2006:
18.2 years

10yrs onwards



10yrs onwards



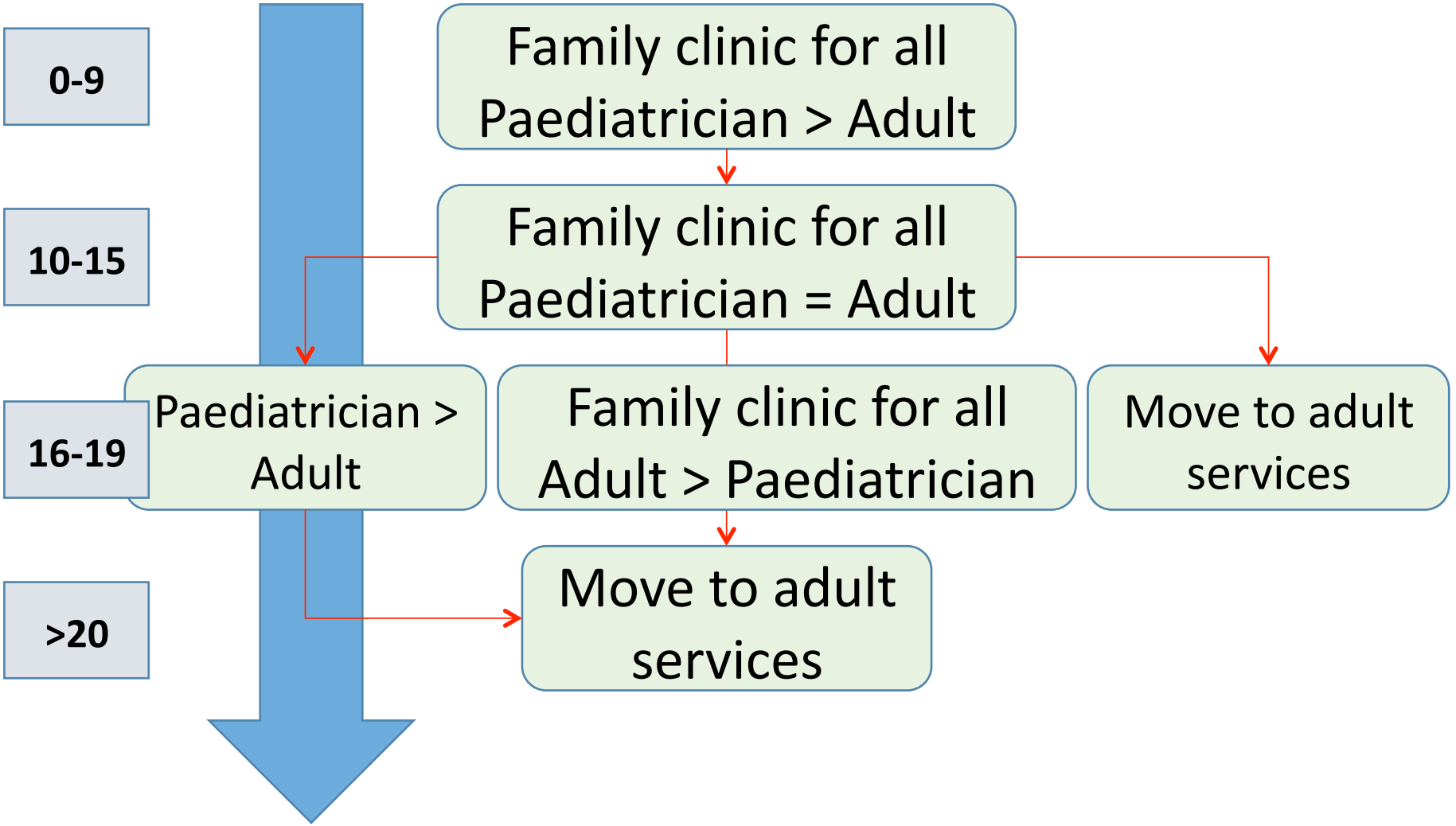
Of 1245 perinatally infected children in CHIPS (2010)

- 80% are of Black African origin
- 51% born outside the UK/Ireland
- 84% are on HAART (>10yrs)

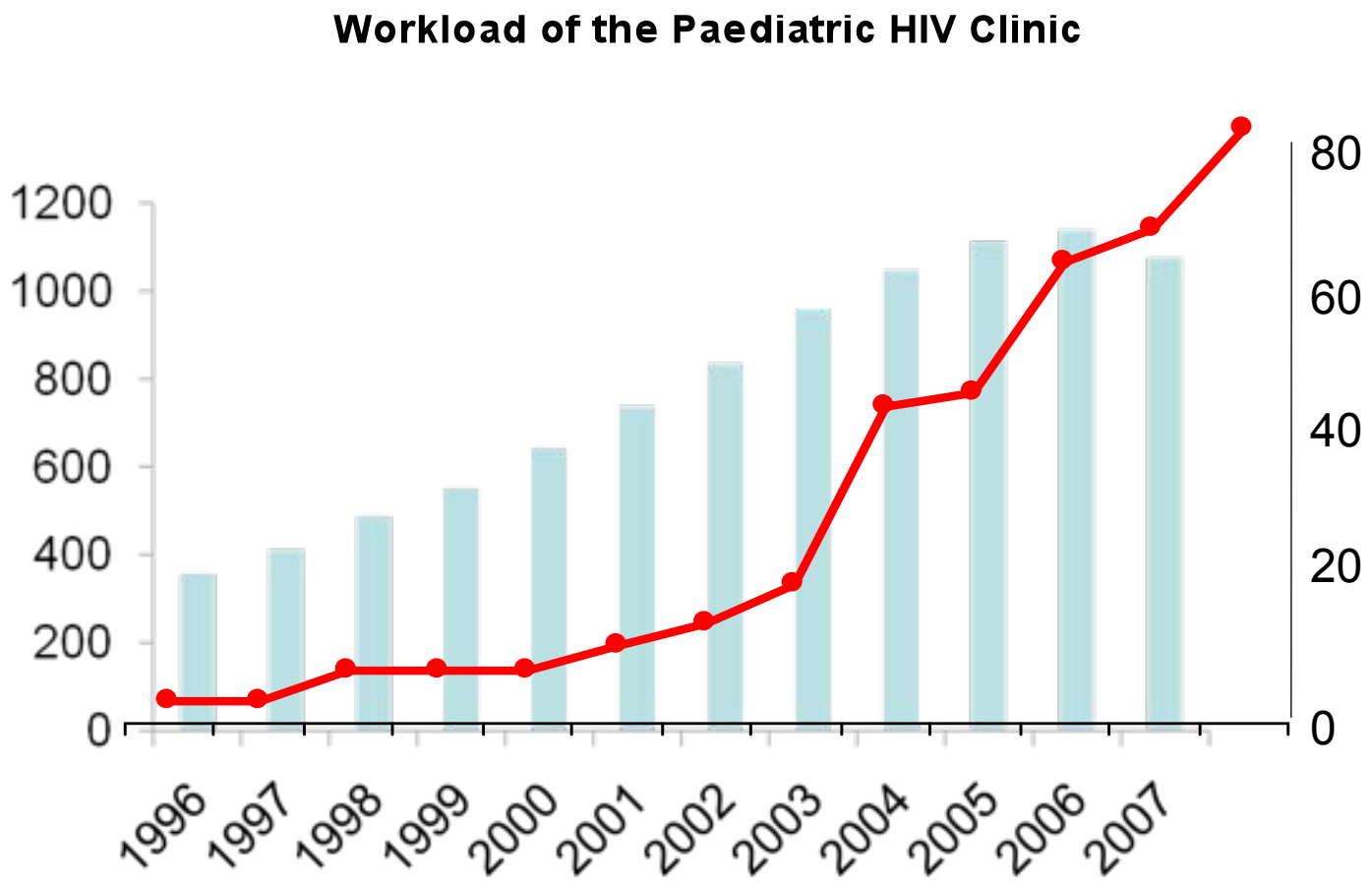
AT TRANSITION

- Median age of transfer = 17.0 yrs (15.2-20.7)
- Median duration of follow up pre-transfer = 10yrs (IQR 6.2-14.9)

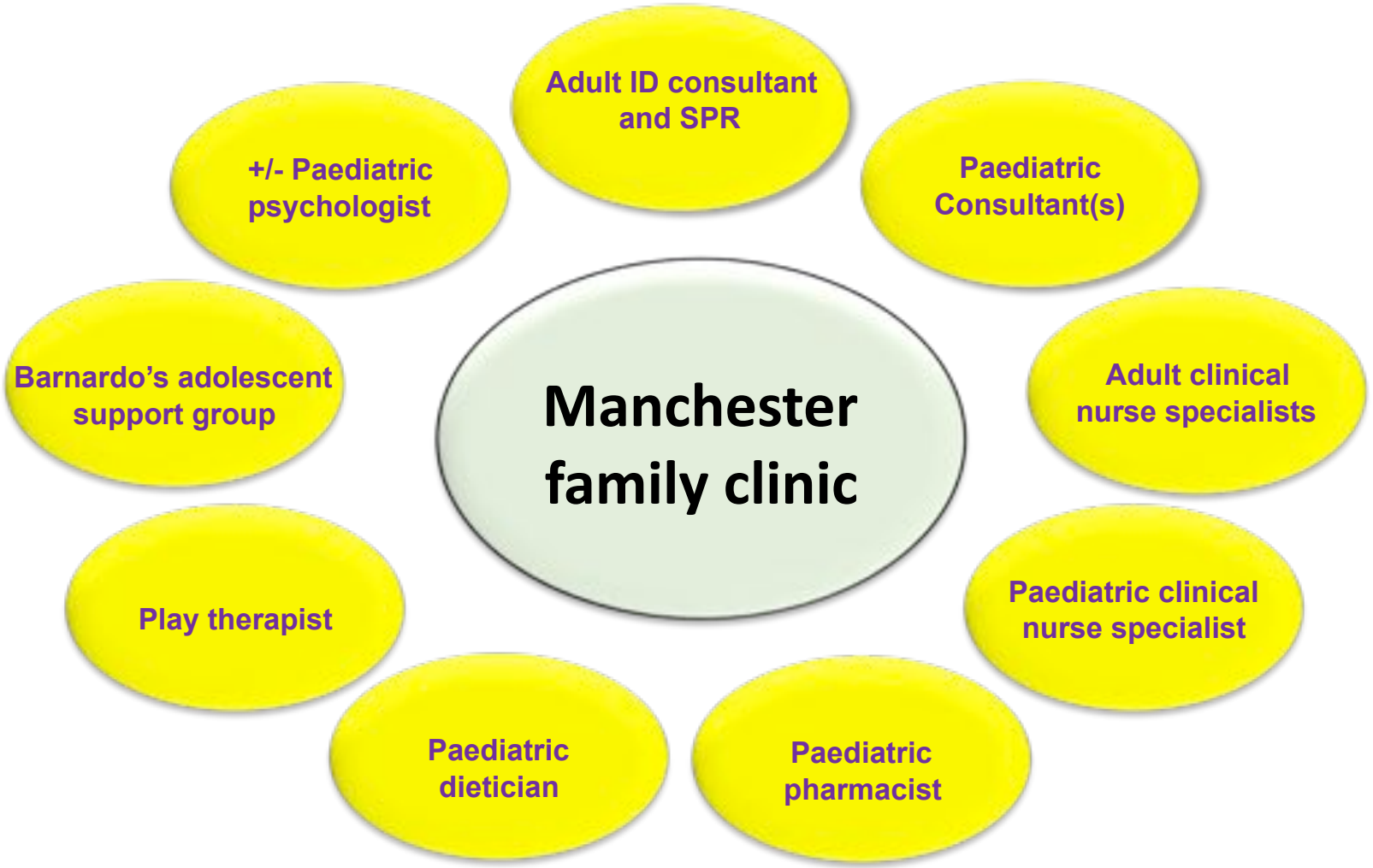
Manchester clinic



Numbers of children under care continues to increase



Weekly paediatric clinic



Separate testing clinic

Transitional vs Adolescent Service

- Transitional care is the planned movement of children with chronic health care problems from childrens' to adolescent services
- Aim to achieve the best outcome for their long-term health
- Adolescence is the time when health is often compromised eg renal transplant rejection, worsening diabetic control

Transitional care could offer

- Motivational interviewing
- Safer sex advice
- STI testing and screening
- Psychological and social support
- Drug abuse prevention and services
- Contracetion
- HPV and Hep B vaccination

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Thank you

For further information please contact :

Jean-Marc Debricon
CEO
jm@greenshootsfoundation.org
Mobile: +44 7595 600 766

Green Shoots Foundation
P.O. Box 63678
London, SW11 9BD
UK

UK charity number 1138412 US 501(c)(3) registered

General enquiries: info@greenshootsfoundation.org
Website: www.greenshootsfoundation.org

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