GLOBAL PAEDIATRIC HIV CONTROL

WHERE WE'VE BEEN, WHERE WE'RE AT, WHERE WE'RE GOING

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OUTLINE

Where we've been

- Early impact of global HIV epidemic on children
- Development of paediatric HIV prevention and treatment strategies

Where we're at

- Assess current global situation
- Bask in some glories, acknowledge shortcomings

Where we're going

- Breaking down barriers
- Key areas for development
- End HIV/AIDS epidemic by 2030

EARLY IMPACT

HIV MTCT up to 40%

- In utero, intrapartum, breastfeeding

Rapid disease progression

- 50% die by 2 years
- Median time to AIDS for remainder ~ 7 years

For those exposed but not infected

- Poor growth and development
- Increased mortality
- Loss of caregivers

YEAR 2000

1.4 million children living with HIV

- 600,000 new infections annually
- 1500/day (>90%) occur in sub-saharan Africa

500,000 AIDS-related deaths per year (aged < 15 years)

- 20% of AIDS deaths in children (cf. 4% living with HIV)

Few countries had PMTCT or ART programs

HIV prevalence up to 25% in expectant mothers in sub-Saharan Africa

> 95% paediatric infections acquired via vertical transmission

YEAR 2000

Millennium development goals

- Reduce by 2/3 the under-five mortality rate

- Reduce by 3/4 the maternity mortality ratio
- Universal access to reproductive health

- Have halted and begun to reverse spread of HIV/AIDS
- Achieve (by 2010) universal access to treatment for HIV/AIDS

DEVELOPMENTS

Prevention of MTCT

- Maternal ART
- Caesarean section (vaginal delivery if HIV VL undetectable)
- Neonatal ART
- Exclusive formula (or AFASS) feeding

DEVELOPMENTS

Diagnostics

- ELISA (1984), Western Blot (1987), PCR (1996)
- Viral genotypic resistance profile
  - Only available in regional or national reference laboratories
  - Conserve effectiveness of first-line therapies
  - Guide second-line ARV selection
- Pharmacogenomics
- Cell-based tropism

DEVELOPMENTS

Point of care diagnostic technologies

- Rapid diagnostic test (RDT) kits
  - Immunochromatographic-lateral flow devices
  - Concerns about false-positive rates in certain settings
  - Need for quality assurance and alternative diagnostic strategies
  - Developed for non-blood samples (saliva, urine)
    - Self-testing programs
      - Need to ensure linkage to HIV care
- CD4 count
  - Variable performance
  - Limited (but positive) evidence for impact on therapeutic outcomes
    - Reduce loss-to-follow-up before ART initiation
    - Increase proportion of ART-eligible patients

DEVELOPMENTS

Access to antenatal diagnosis

- Scale up of PMTCT-specific health care services
- Opportunity to engage women in health care
- Facilitates timely initiation of ARVs
    - For PMTCT and maternal health

Early infant diagnosis (EID)

- RNA/DNA PCR, p24 antigen assays
    - Dried blood spot
        - Heat stable, non-infectious, easily transportable
    - Point-of-care technologies in development
        - None in practice
- Allows early initiation of ART

DEVELOPMENTS

Therapeutics

- Antenatal access through PMTCT services
- Drug development
- Refining regimens
  - Evolving ARV regimens for pregnant women
  - First WHO paediatric HIV guidelines in 2006
  - Paediatric clinical trials
    - Incentives and/or penalties from regulatory agencies
- Paediatric formulations
  - Liquids, granules, sprinkles, FDCs

DEVELOPMENTS

Maternal ART

- **Option A:** AZT throughout MTCT risk period
  - Lifelong if CD4 ≤ 350 or WHO stage 3/4

- **Option B:** cART throughout MTCT risk period
  - Lifelong if CD4 ≤ 350 or WHO stage 3/4

- **Option B+:** lifelong cART
  - Irrespective of CD4 count or clinical status

DEVELOPMENTS

Paediatric treatment strategies

- Initially deferred until immunological/clinical deterioration
  - Drug toxicities
  - Development of resistance
  - Limited treatment options

- New focus on early initiation of HAART
  - Maximal suppression of HIV replication
  - Preservation / better recovery of immunity
  - Better clinical outcomes
  - Normal growth and development
  - Expanding therapeutic options with improved tolerability
  - Treatment as prevention

ART THROUGHOUT CHILDHOOD

Recommended first-line ART (not in the context of HBV or TB co-infection)

		< 1 year	1–3 years	3–6 years	6–12 years	> 12 years
Preferred	Third agent	LPV/r NVP	LPV/r NVP	LPV/r EFV	ATV/r EFV	ATV/r DRV/r EFV
	Backbone	ABC*/3TC (+ ZDV if NVP)†	ABC*/3TC (+ ZDV if NVP and CNS involvement or high VL)‡	ABC*/3TC	ABC*/3TC	TDF/FTC§ ABC*/3TC (if VL < 10^5 copies/mL)
Alternative	Third agent	–	–	NVP DRV/r	NVP LPV/r DRV/r	NVP LPV/r RAL** DTG
	Backbone	ZDV¶/3TC	ZDV¶/3TC	ZDV¶/3TC TDF/3TC (FTC)	ZDV¶/3TC TDF/3TC (FTC)	ABC*/3TC

Source: PENTA guidelines for treatment of paediatric HIV-1 infection 2015: optimising health in preparation for adult life

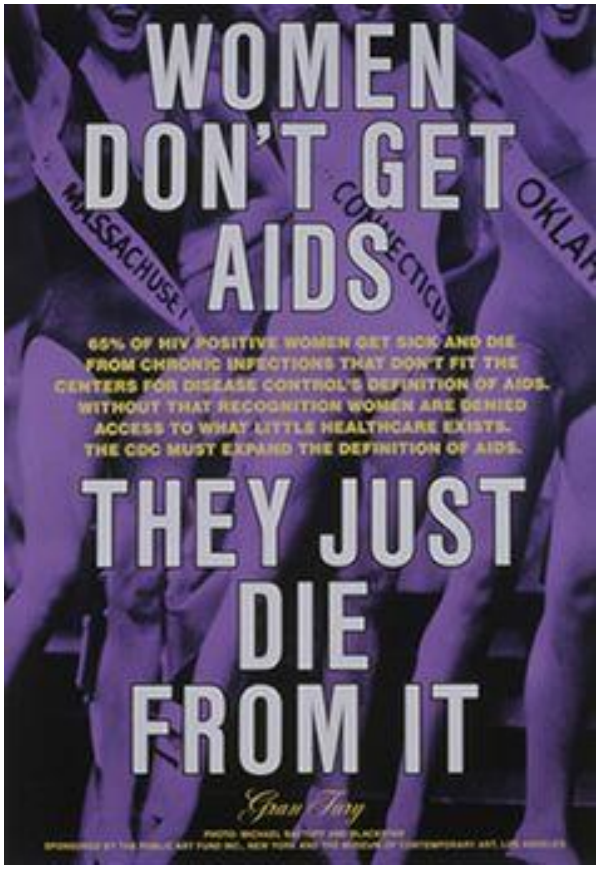
DEVELOPMENTS

De-stigmatising HIV/AIDS

- Overcoming barriers to accessing HIV care
- Legal recourse to protect infected individuals

Rights of women and children

- Empowering women
- Mother/child focused health care facilities



GLORIES

Prevention of HIV MTCT

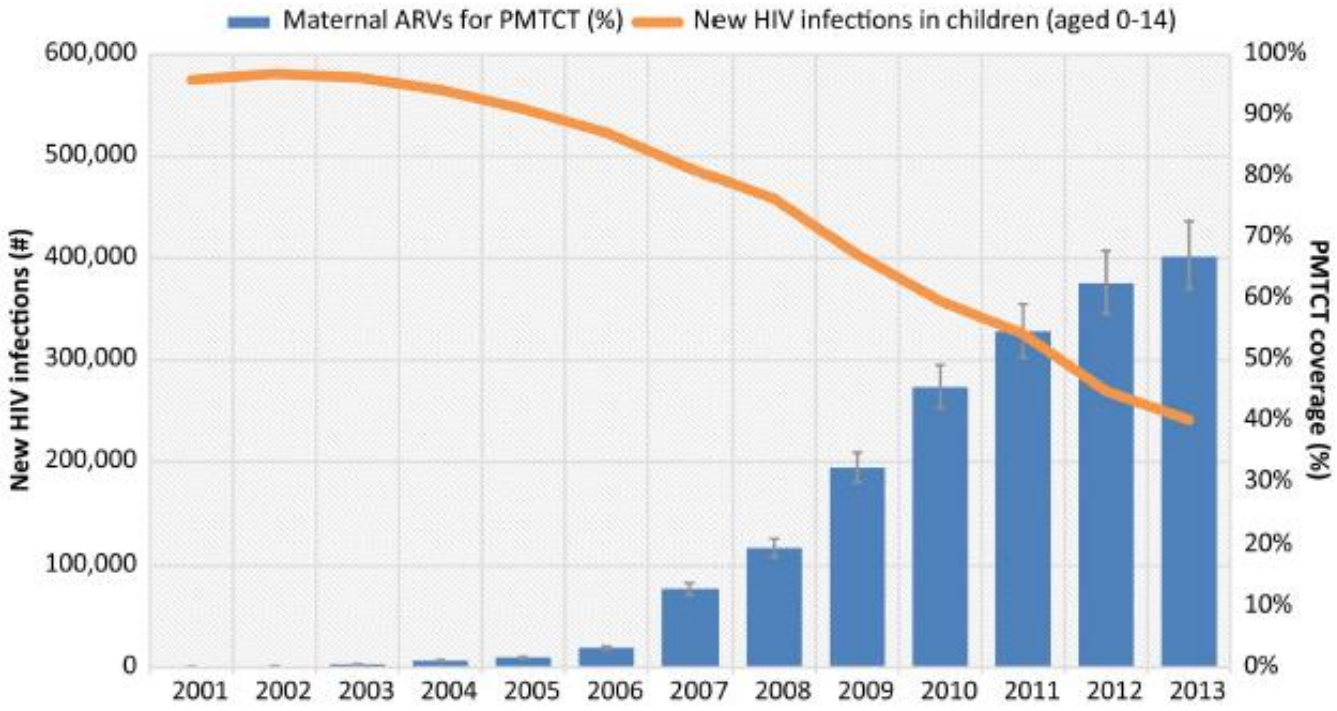
- Comprehensive strategies reduce MTCT < 0.5%
- ~2/3 of women have access to PMTCT programs (2012)
- 58% decline in new childhood infections (2001-2012) due to PMTCT

Anti-retroviral therapy

- 760,000 children receiving ART
- 40% decline in AIDS-related mortality (2005-2013)

PROGRESS

New HIV infections (aged 0-14) and coverage of maternal ART for PMTCT in low- and middle-income countries, 2001-2013



Source: UNAIDS 2014 HIV and AIDS estimates, August 2014

SHORTCOMINGS

3.3 million children living with HIV

- 240,000 new infections in 2013

~25% receive ART

- Limited available ART options

500 die each day of HIV/AIDS-related causes

22 priority countries account for 90% of new infections

SHORTCOMINGS

Access to antenatal diagnosis

- 54% of pregnant women in low- and middle-income countries did not receive a HIV test in 2013

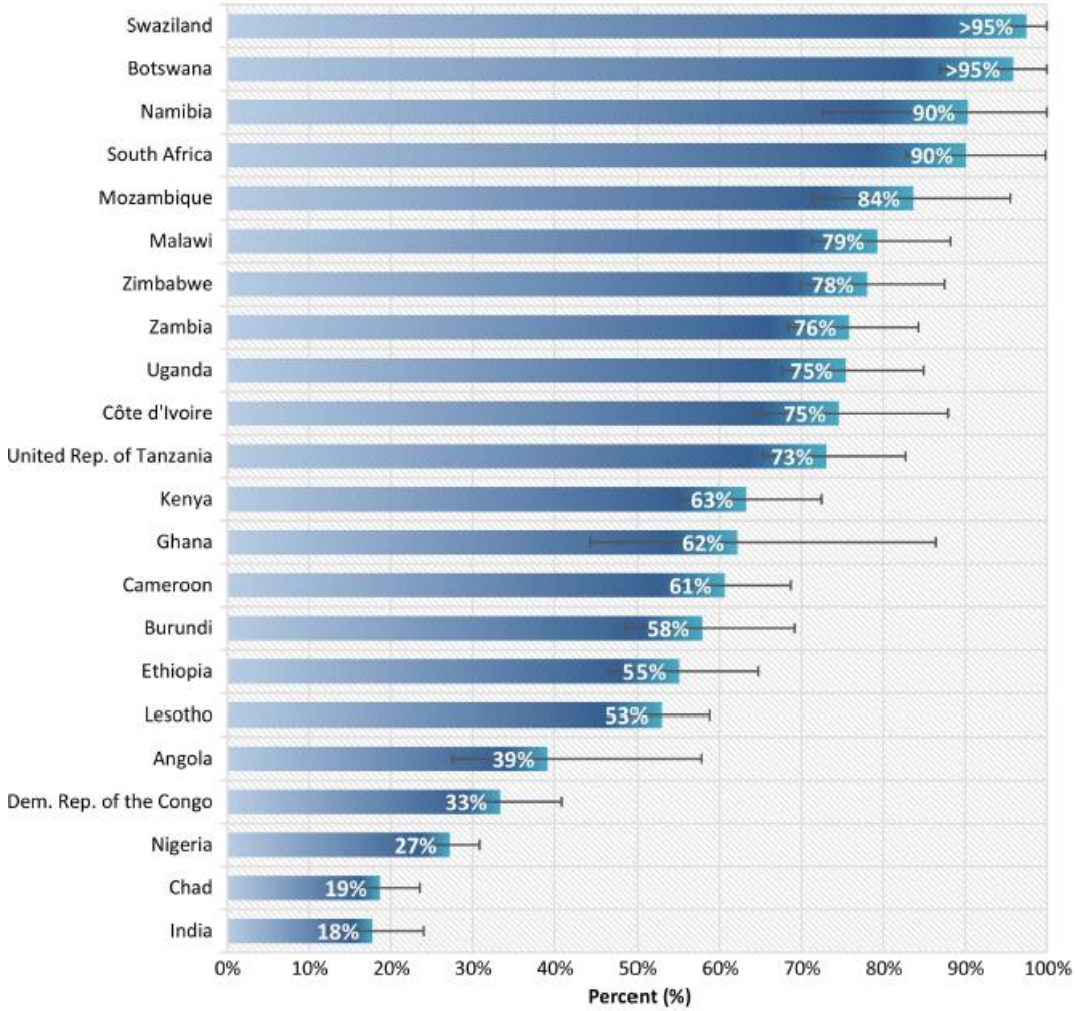
Early infant diagnosis

- 44% of all HIV-exposed infants tested < 2 months of age
  - 6 priority countries have EID coverage > 50%
  - 5 priority countries have EID coverage < 6%
- Variable infrastructure between decentralised management programs and centralised laboratory services

HIV not a focus outside of PMTCT settings

- Nutritional services, TB clinics, children of parents in HIV clinics, hospitalised adolescents, immunisation clinics

ANTENATAL ARV ACCESS

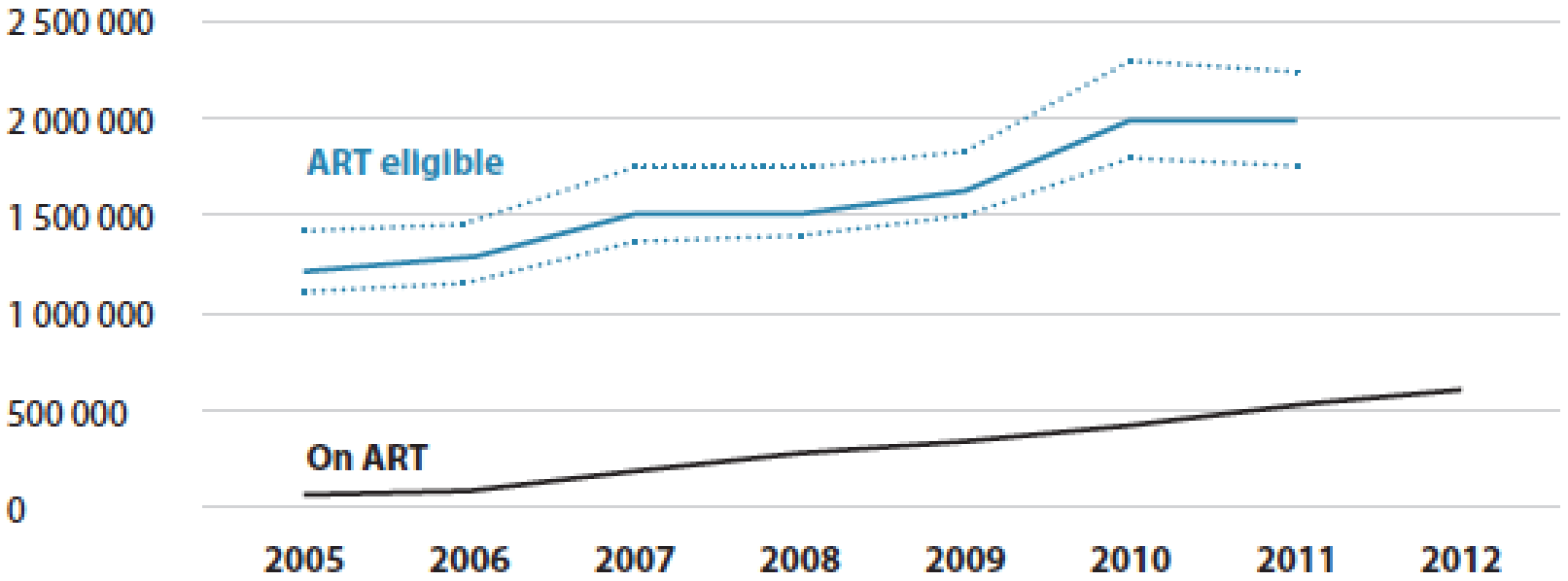


Percentage of HIV-infected pregnant women receiving most effective ARVs for PMTCT (2013).

Source: Joint United Nations Programme on HIV/AIDS, The Gap Report, Geneva, July 2014.

SHORTCOMINGS

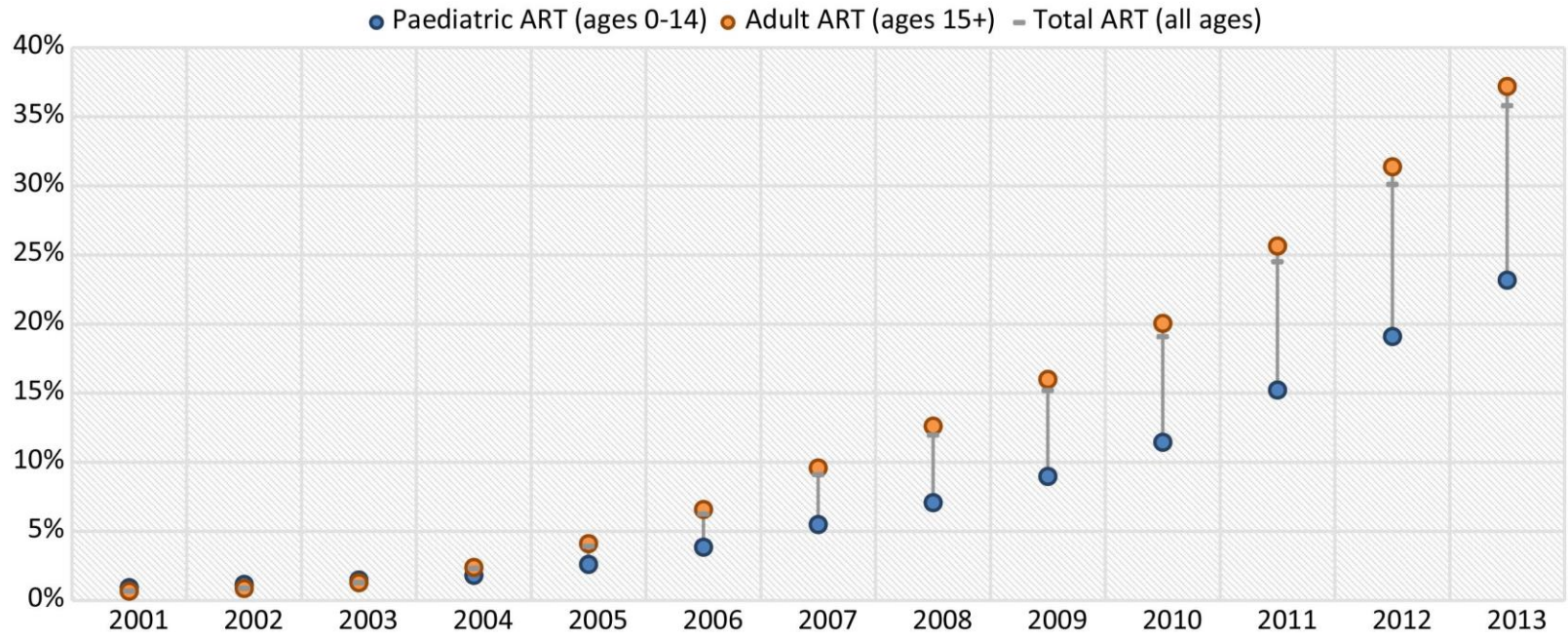
Treatment gap between children eligible and children receiving ART



Source: 2013 UNAIDS Report on the Global AIDS Epidemic

SHORTCOMINGS

The treatment gap between paediatric and adult ART coverage (2014)
(low and middle income countries)



Source: UNAIDS 2014 HIV and AIDS estimates, August 2014

CASCADE OF CARE

- PMTCT
- Early infant diagnosis
- Provider-initiated testing and counselling
- Linkage to HIV care and treatment

TOWARD UNIVERSAL ACCESS

Decentralising HIV diagnosis and management

- Task-shifting to lower-level health facilities
- Integration into more accessible child health services
  - Tailored to national infrastructure, health budget, and HIV prevalence
- Affordable and feasible point-of-care diagnostic/monitoring technologies
  - With accessible reference laboratories
- Facilitate compliance and minimise loss to follow-up

TOWARD UNIVERSAL ACCESS

Paediatric HIV Treatment Initiative (PHTI)

- UNITAID + DNDi + MPP
  - Co-ordinate research and development for priority therapies
  - Sharing intellectual property
  - Assuring sustainability of paediatric HIV market

Co-ordination between PHTI and WHO

- Harmonise targeted ARV formulations with treatment guidelines
- For new ARVs and ARVs in the pipeline

PAEDIATRIC ARV PIPELINE

COMPOUND	FORMULATION(S) AND DOSE	STATUS/COMMENTS
NRTI		
TAF	Dose under investigation	Phase II/III FDC treatment-naïve adolescents
NNRTI		
ETR	Dispersible tablets	Approved 6-18yrs; Phase I/II age 2m– 6y
RPV	Paed tablets, granules	Phase II adolescents; Phase I/II planned for age 2-12yrs
PI + combinations		
ATV	Powder satchet, paed capsules	FDA approved >3m; Phase III/IIIb for aged 3m-6y
ATV/COBI	In development	Phase II/III treatment-experienced aged 3m-18y
DRV/COBI	In development	Phase II/III treatment-experienced aged 3m-18y
LPV/r	Pellets in capsules	Submitted to FDA
LPV/r/3TC/ABC or AZT	Granules	Formulation work ongoing
BOOSTER		
COBI	Paed tablets, dispersible tablets	Under development in FDC
INSTI + combinations		
RAL	Granules	FDA approved for >4w; Neonatal PK and safety study ongoing
EVG	Paed tablets, suspension	PK data completed for 12-18yrs; EVG/r study planned for all age groups
EVG/COBI/FTC/TDF (Stribild)	Paed tablets	Studies underway in treatment-naïve adolescents; 6-12yrs planned
EVG/COBI/FTC/TAF	Paed tablets	Studies underway in treatment-naïve adolescents; 6-12yrs planned
DTG	Granules, Paed tablets	Approved 12-18yrs; Phase I/II for age 6w-18y
DTG/ABC/3TC	Paed formulation in development	Studies ongoing to confirm DTG dosing
CCR5 receptor antagonist		
MVC	Suspension	Phase IV treatment experienced age 2-18yrs

Adapted from PENTA guidelines for treatment of paediatric HIV-1 infection 2015: optimising health in preparation for adult life

See www.pipelinereport.org for updates

ADOLESCENTS – KEY POPULATION

42% of new infections outside of childhood age group (2010)

Diverse demographic and socio-economic backgrounds

- Perinatal and behavioural acquisition

Treatment experienced and fatigued

- Toxicities, resistance, adherence issues, transmission risk

Difficulties engaging health care

Reproductive health and family planning

Transition issues

ENDING HIV/AIDS EPIDEMIC BY 2030

90-90-90 by 2020

- 90% know status (100% of all HIV-exposed newborns)
- 90% on treatment
- 90% undetectable viral load

HIV-free generation on the horizon!

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