

# *Research needs and potential for EDCTP supported projects on PMTCT and paediatric HIV care*

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***PMTCT***

# *What has been acquired from PMTCT research*

- **Prevention of de perinatal HIV transmission:**

- ✓ Early initiation of prophylaxis during pregnancy;
- ✓ Combination ART are more effective than monoprophyllactic regimens;
- ✓ Some drugs are more efficacious, some may be hazardous (Efavirenz and neurological defects)\* ;
- ✓ The target of elimination (MTCT < 5%) seems achievable, if no breastfeeding.

- **Prevention of postnatal (breastfeeding) HIV transmission:**

- ✓ No prophylactic trial covering the whole duration of breastfeeding exposure (= 12 months);
- ✓ Important residual transmission (3,6% at 6 months in the Kesho Bora trial);
- ✓ Concerns about adherence ;
- ✓ The target of elimination seems out of reach.

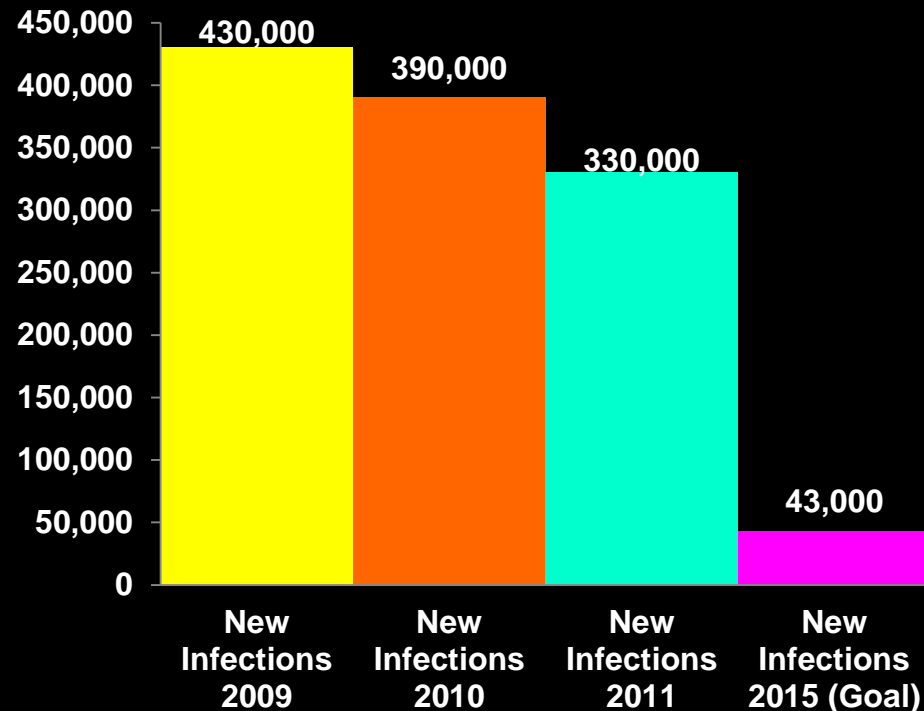
## *Objectives of the UN Agencies for 2015*

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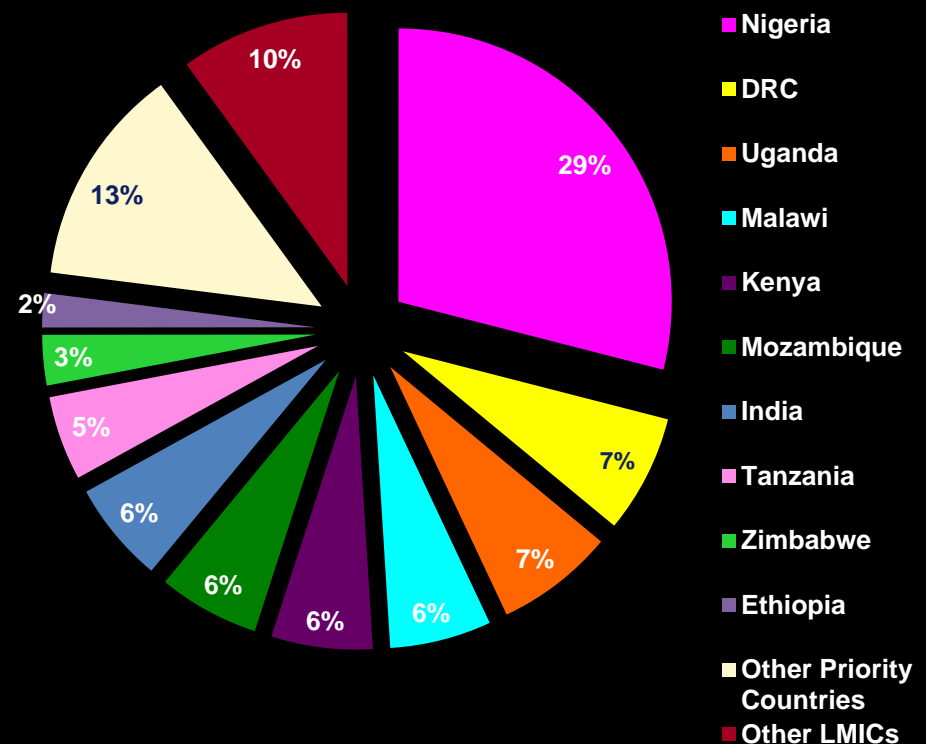
- Reduction of the MTCT rate  $< 5\%$  (definition of « elimination »)
- 90% reduction of new paediatric infections (430.000 en 2009, 43.000 en 2015?)
- 50% reduction of HIV-related maternal mortality

# Reduce the Number of New HIV Infections among children by 90% by 2015

Estimated new Paediatric Infections in Low and Middle Income Countries (LMICs)



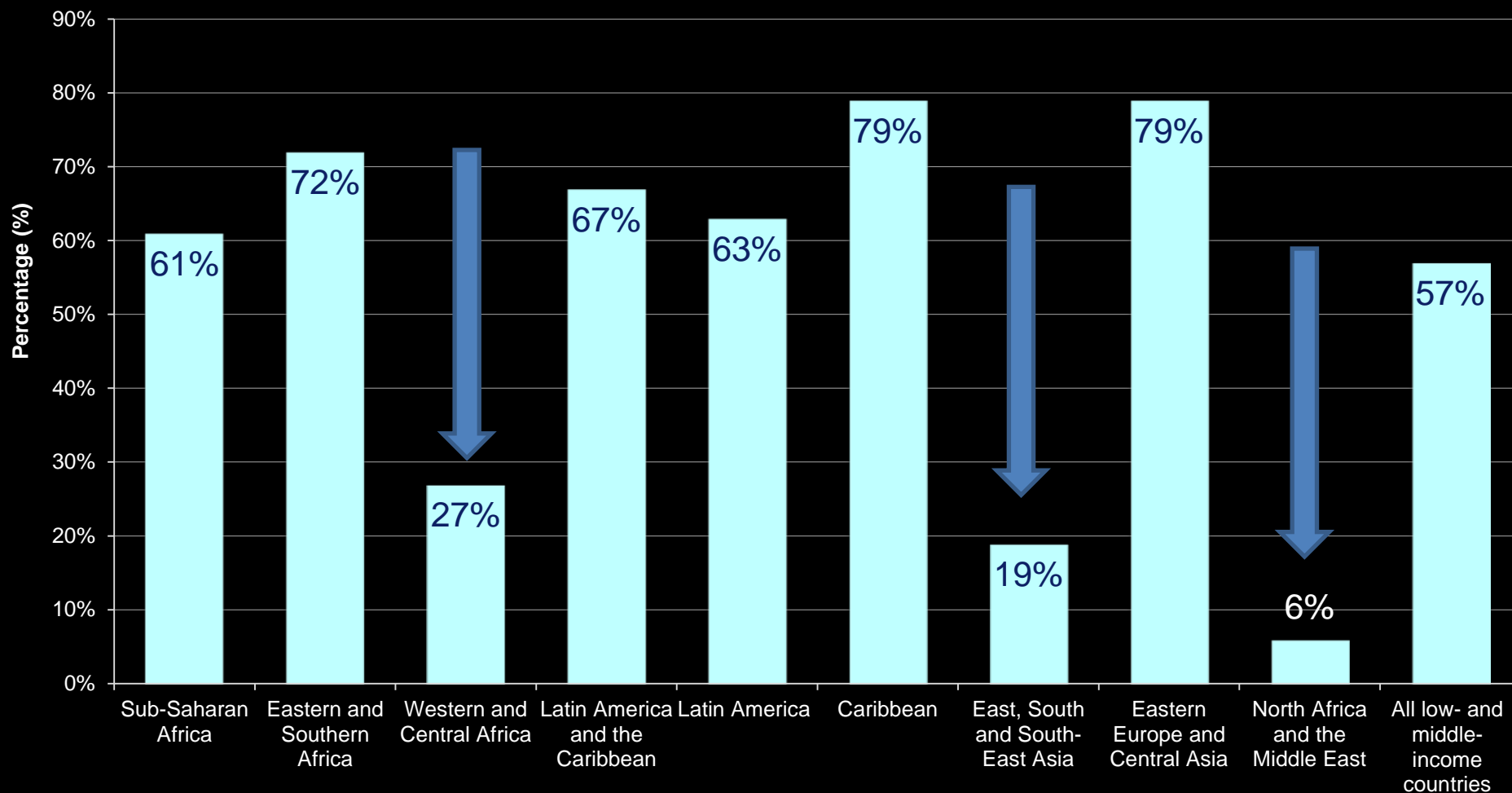
Country Contribution to 390,000 Paediatric HIV Infections in LMICs in 2010



Source: 1. UNAIDS. Together we will end AIDS. 2012

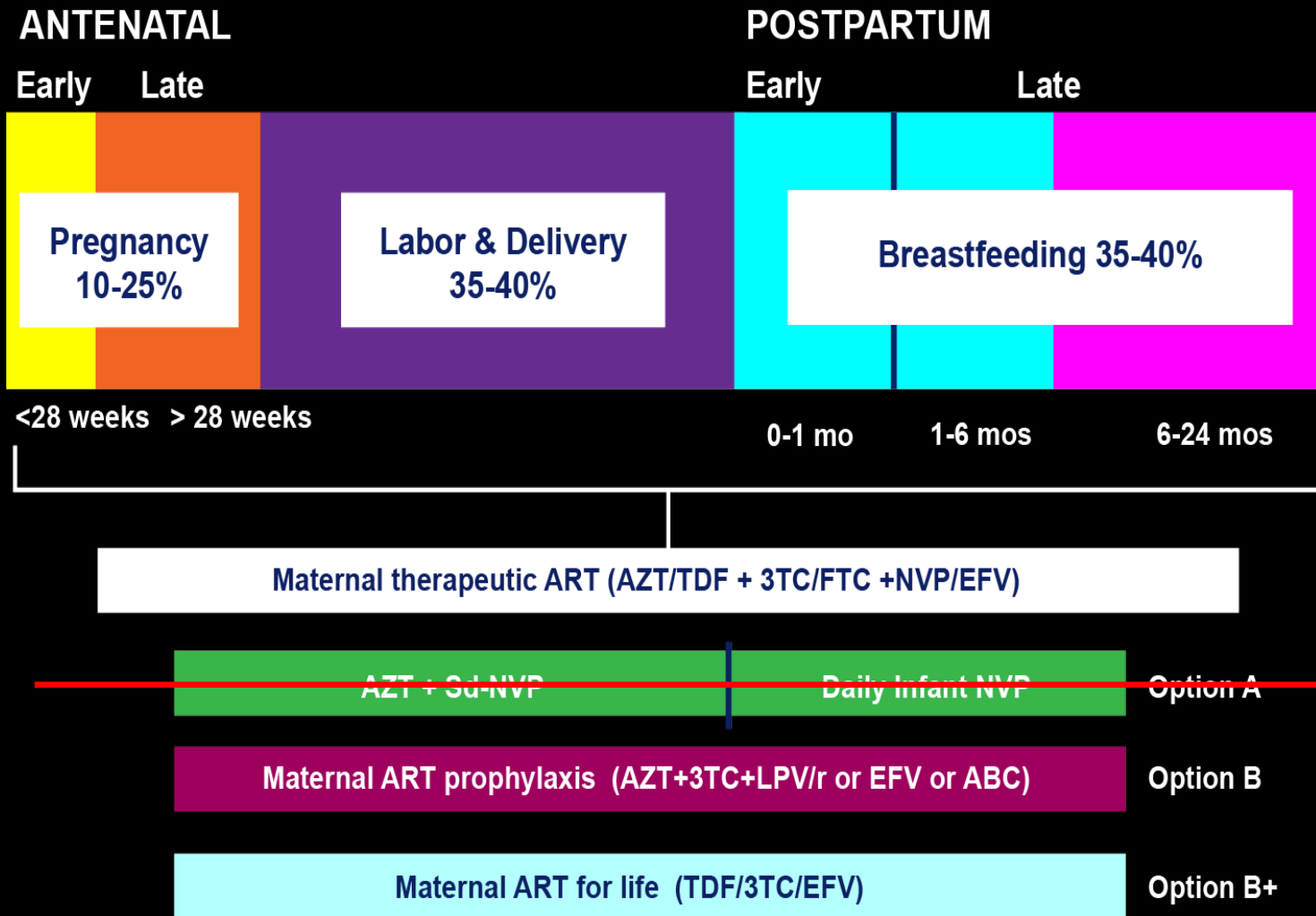
2. HIV/AIDS Response – Epidemic Update and Health Sector Progress Towards Universal Access 2011

# Coverage of antiretroviral medicine for preventing mother-to-child transmission: most effective regimens, low- and middle-income countries, by region, 2011



Source: UNAIDS. Together we will end AIDS 2012

# WHO guidelines for PMTCT and infant feeding (June 2013)



... but research on breastfeeding transmission should continue!

# *Option A, B or B+? A critical analysis*

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- Alarming inflation in the number of WHO-UNICEF PMTCT recommendations ( '90s: n=1, 2000s: n=4, 2011-2013: n=2);
- Current WHO PMTCT recommendations are not evidence-based;
- Push for option B+ is based on mathematical models, best guess estimates on feasibility but NOT on measured efficacy or efficiency.



# Option B ou B+ ?

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- **Suboptimal efficacy on postnatal transmission** in the Kesho Bora trial: in mothers with  $> 350 \text{ CD4}/\mu\text{l}$ , 6-month efficacy = 29% (NS)\*;
- **Suboptimal adherence**: in a metanalysis of more than 20,000 pregnant women, adherence of 53% at 12 months post partum\*\*;
- **Extremely high rate of resistance in infants who get HIV-infected despite maternal prophylaxis\*\*\***

\* Kesho Bora Study Group, Lancet Infect Dis, 2011

\*\* Nachega et al, AIDS 2012

\*\*\* Zeh, PlosMed 2011; Fogel, Clin Infect Dis 2011; Lidström, CROI 2010

# *Option A ?*

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- **Until now, unknown efficacy** if infant PreP is extended during the whole duration of exposure (12 months breastfeeding recommended by WHO);
- **Adherence and tolerance** uncompletely explored;
- Results of the **ANRS 12274-PROMISE-PEP** trial

# ***PMTCT: Scientific/programmatic questions?***

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- What is the community effect of rolling out option B/B+? Acceptability? Adherence? Protection of future pregnancies? Reduction of breastfeeding transmission events?
- How to operationalize the access to prevention and therapy within national programs (coverage, acceptability, adherence, retention, ...)?;
- How to optimise recommended PMTCT regimens in order to cover breastfeeding? Combine B/B+ and A?;
- Infant PreP: a place for extra-long acting ARV drugs (rilpivirine-LA, GSK 744, others)?;
- What is the role of co-infections (herpesviruses, MTB, others...) in MTCT?
- How to take into account acute maternal infections (2<sup>+</sup>-fold risk of transmission) in PMTCT?;
- Is there a place for alternative strategies in PMTCT? Passive immunoprophylaxis (NIH45-46<sup>G54W</sup> based cocktails)? Vaccine? Control of co-infections?

# ***Paediatric HIV care***

# The Children with HIV Early Antiretroviral Therapy (CHER) trial: Children Initiating Treatment Immediately have better chance of survival

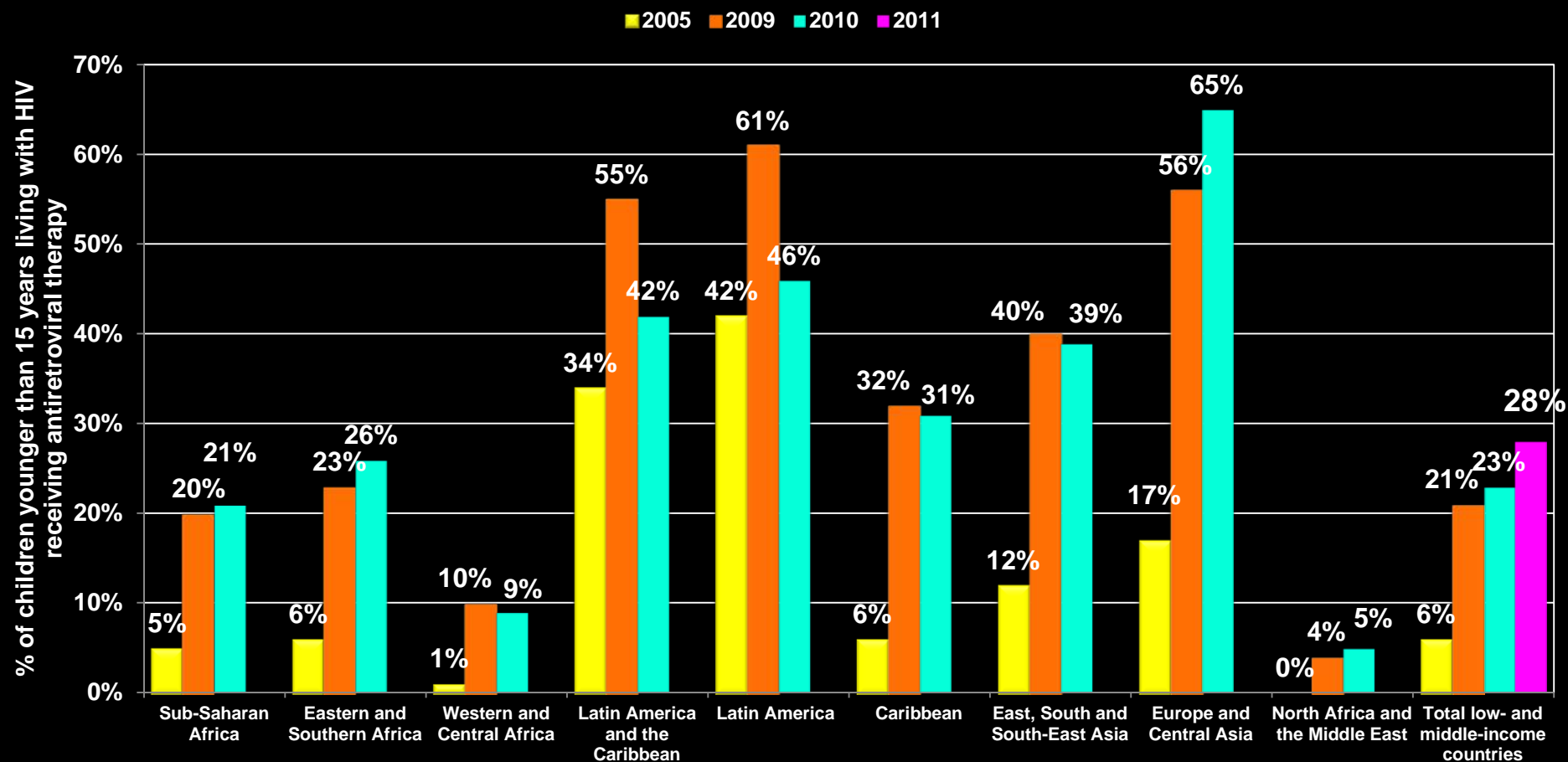


## PATIENTS AT RISK

	Month 0	Month 3	Month 6	Month 9	Month 12
Arm 1	125	104	72	44	22
Arm 2 & 3	252	213	145	99	52

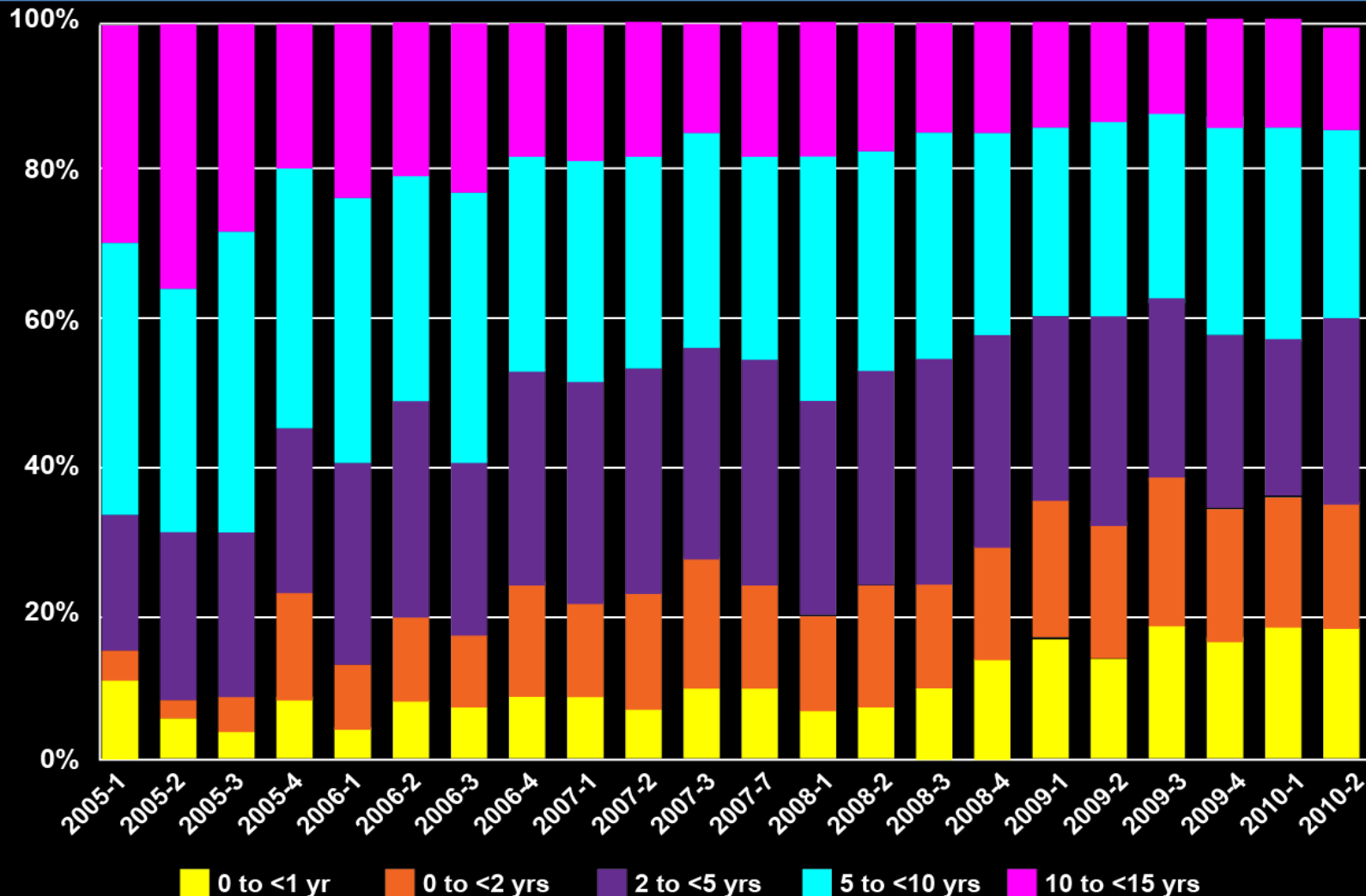
**76%  
REDUCTION  
IN THE RISK  
OF DEATH**

# Percentage of children living with HIV receiving antiretroviral therapy in low- and middle-income countries, 2005, 2009, 2010, and 2011



Source: WHO, UNAIDS and UNICEF. *Global HIV/AIDS Response: Epidemic Update and Health Sector Progress Towards Universal Access Progress Report 2011*

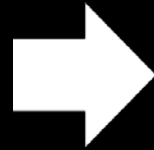
# Trends in pediatric age distribution at ART initiation (2005-2010)



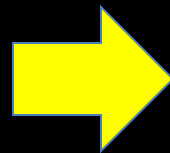
Source: McNairy M. et al. Retention of HIV+ Children on ART in ICAP-supported HIV Care and Treatment Programs. Paper # 959, 19th CROI, Seattle, USA 2012

# Paediatric Antiretrovirals: simplified dosing formats and analysing their adverse events

CHAPAS-1 trial  
PK sub-study 2007  
→ FDA licensing



CHAPAS-2  
LPV/r liquid vs tablets  
vs sprinkles PK study

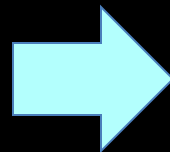


3TC/ZDV/N  
VP Baby



3TC/ABC Baby and  
Junior

CHAPAS-3  
Looking at specific  
toxicities in children



d4T vs  
AZT vs  
ABC

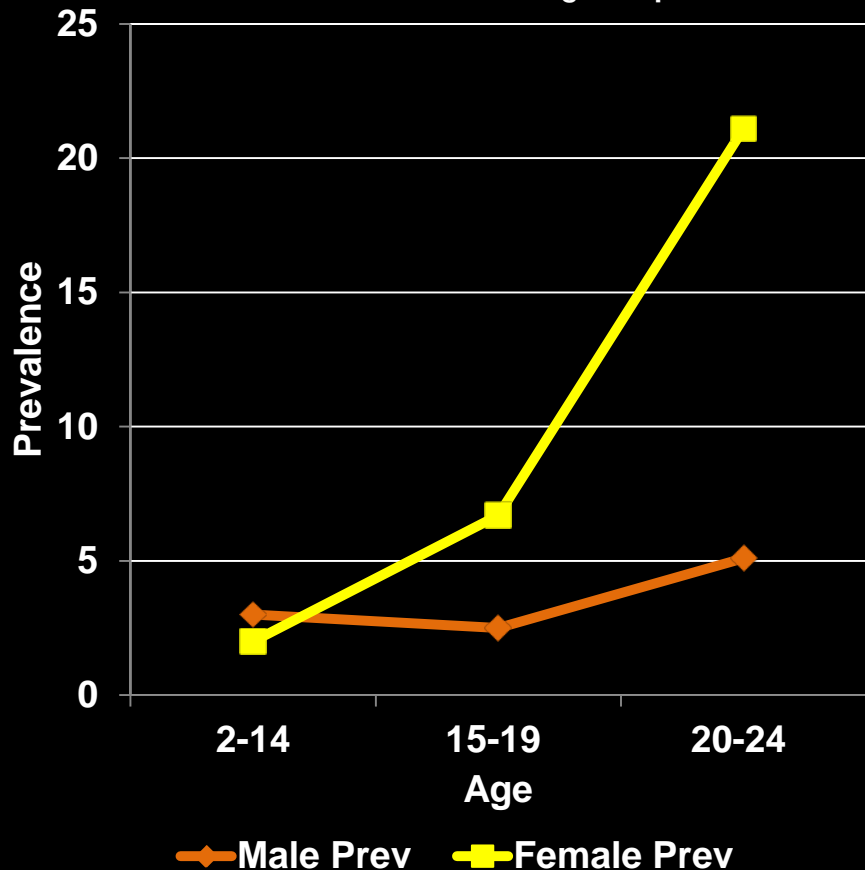


Efavirenz  
600mg  
2 x 300mg  
3 x 200mg

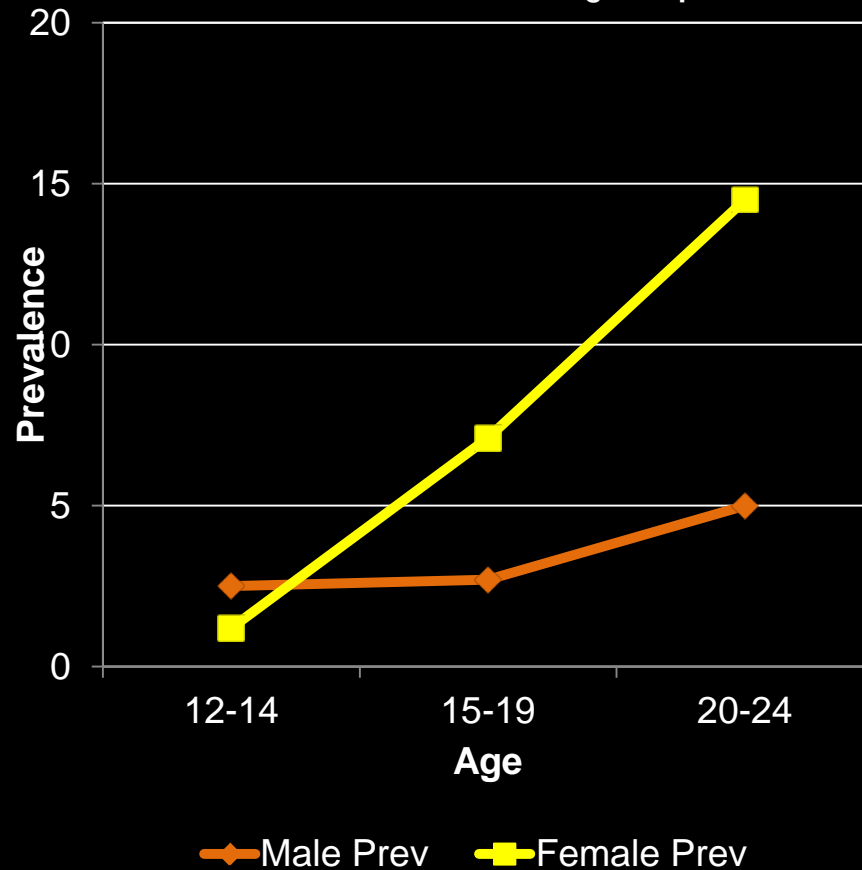


# Increasing HIV Prevalence in Adolescents

South Africa: HIV Prevalence Among Adolescents and Young People



Mozambique: HIV Prevalence Among Adolescents and Young People



Source: 1. National Institute of Health (INS), National Institute of Statistics (INE) and ICF Macro. 2010. National Enquiry on HIV/AIDS Prevalence, Behavior Risks and Information in Mozambique 2009. 2. Shisana O et al. South African national HIV prevalence, incidence, behaviour and communication survey 2008: A turning tide among teenagers?

# ***Paediatric HIV care: Scientific/programmatic questions?***

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- How to operationalize the access to prevention and therapy within national programs (coverage, acceptability, adherence, retention, ...)?;
- How to expand early infant diagnosis? New diagnostic tools and procedures?
- *How to simplify antiretroviral regimens? Extend the offer of paediatric drugs? Paediatric Single Tablet Regimens? Extra-long acting ARV drugs (rilpivirine-LA, GSK 744, others)?;*
- Second line paediatric ART. Which regimen? When to switch? How to ensure access?
- Adolescents with HIV: ensuring the continuum of care and prevention?;
- What is the optimal point of entry for an integrated (familial?) HIV/TB/other co-infections care & prevention program?
- Exposed Non Infected: morbidity and outcomes?