

## Reaching the Third 90: Implementing High Quality VL Monitoring at Scale

# Reaching the third 90 for infants, children and adolescents: preparing for a steep climb

Stephen Arpadi, MD, MS

Professor of Pediatrics and Epidemiology

ICAP

Columbia University

Ezulwini, Swaziland

June 27-30, 2016



# WHO Consolidated Guidelines on the use of antiretroviral for treating and preventing HIV infection

- **“preferentially offering viral load testing to HIV-infected infants and children** for whom CD4-based criteria are particularly poor and in light of the limited drug options available for lifelong treatment; in additions, infants exposed to maternal ART and/or postnatal prophylaxis have high risk of acquiring and selecting HIV drug resistance and, as a result, are at higher risk of early treatment failure early, especially if treated with NNRTI-based regimens;
- **“giving consideration to more frequent viral load testing in adolescents** who are at the highest risk for HIV drug resistance and for whom monitoring of adherence might be particularly challenging in settings where viral load monitoring is widely available; “

# Starting the cascade-will young children have access to VL monitoring?

- Often overlooked - low capacity for blood sampling from small children
- Limited HR with skills in pediatric blood sampling
  - Inadequate/no training
  - Restricted scope of practice
- Assess and strengthen capacity for venipuncture and DBS from finger stick suitable for quantitative VL testing



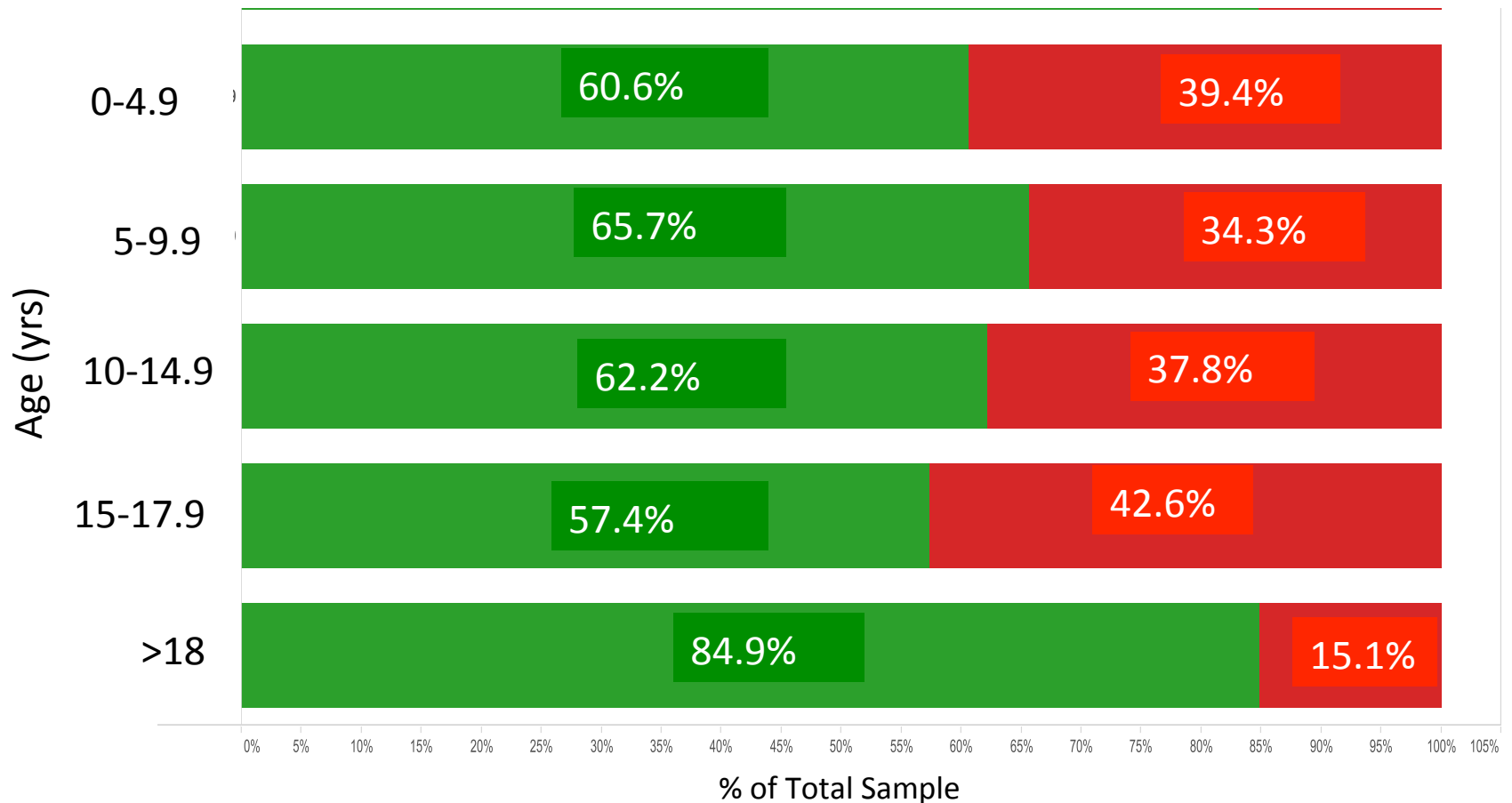
# What should we expect from routine VL testing in infant, children and adolescents?

- Recent data from national VL monitoring programs, prior observational cohorts, systematic reviews and meta-analyses indicate:
  - Rates of VS are lower for infants, children and adolescents compared to adults
- VS rates do not appear to have changed substantially as a result of changes in ART (i.e. replacement of D4T with abacavir; PI-based regimens for 1<sup>st</sup> line for all < 5 years)

# Viral load suppression by age

## Kenya national VL monitoring 2015

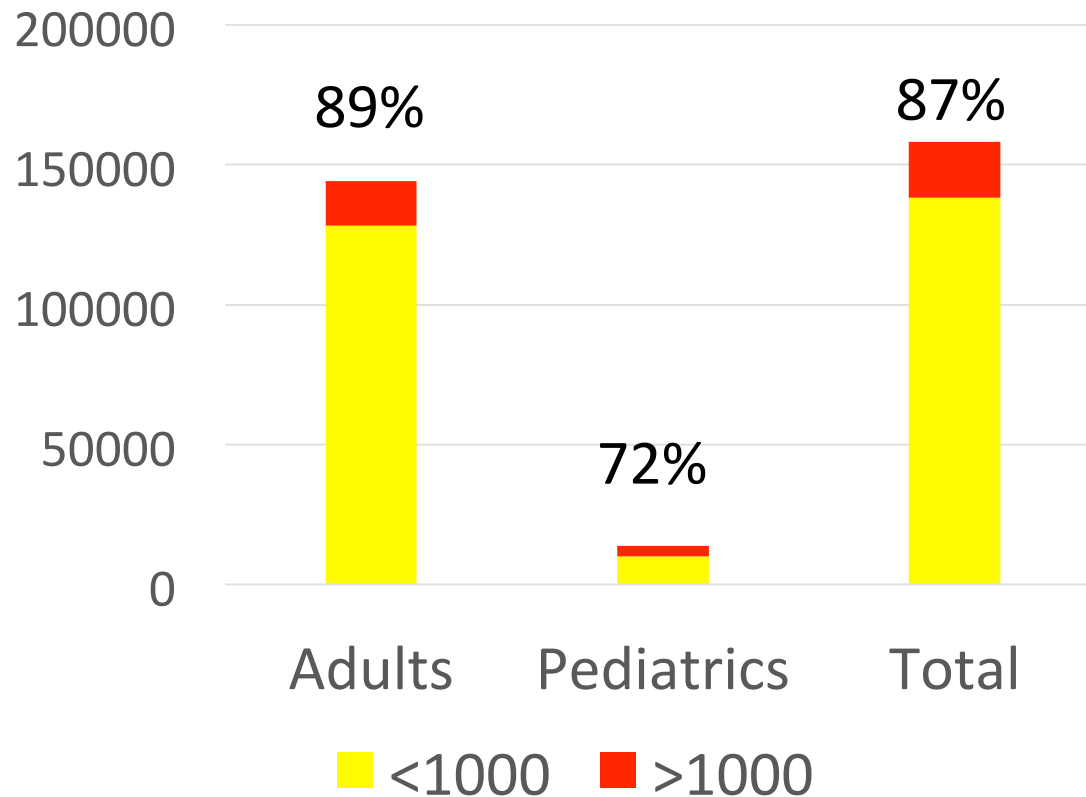
**Viral Load Suppression lower in those < 18**



# VS in pediatrics and adults

## Namibia national VL monitoring 2015

(Adult N = 144,190; Peds N = 13,841)



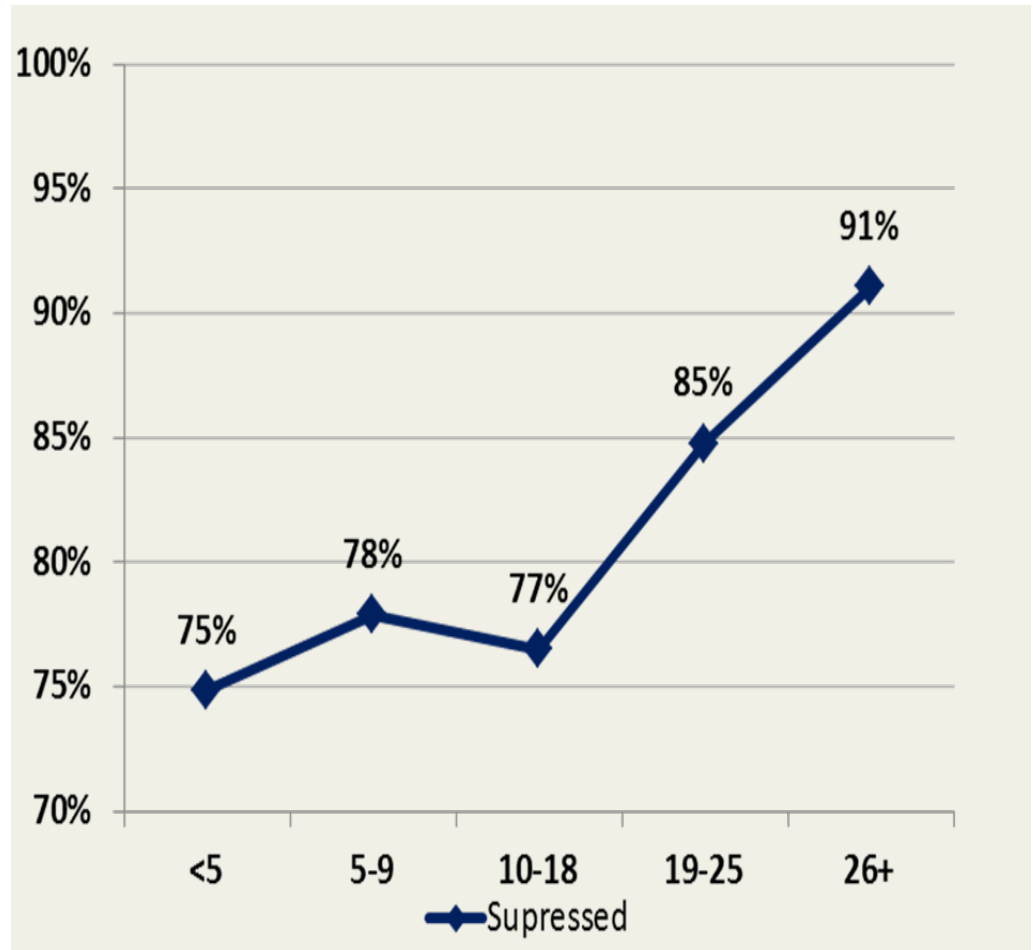
Source: Namibia COP outbreak  
May 2016

# VL Suppression – Uganda

## Uganda MOH - CPHL, September 2015

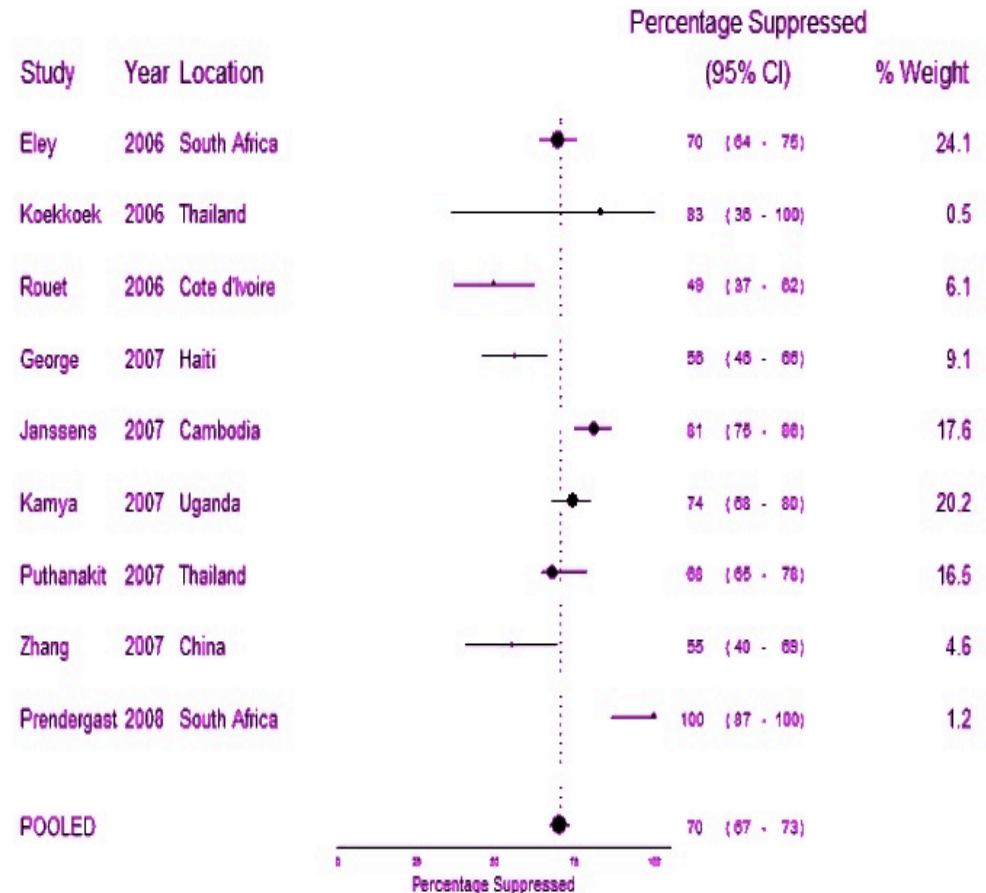
- Ugandan national VL program:
  - lower rates of VS in children and adolescents

Meeting Poster: Kiyaga et al



# Lower VS for children and adolescents on 1<sup>st</sup> line ART reported from multiple observational studies from LMIC

- Meta-analysis from 9 cohorts from Asia, Africa and Caribbean from 1997-2008,
- n= 1,457, ages, 0-15 y, >80% on NNRTI
- Pooled estimate VL <400 copies/mL after 12 m on ART:
  - 70% (CI: 67%–73%)



Ciaranello A *CID* 2009

Figure 2. Forest plot of viral suppression rates (proportion of children with HIV RNA <400 copies/ml) 12 months after ART initiation for treatment-naïve children in resource-limited settings



# VS low with currently recommended ART regimens

- Since 2010 several important revisions:
  - D4T replaced by ABC in 1<sup>st</sup> line ART (toxicity)
  - LPV/r replaced NNRTI in 1<sup>st</sup> line for children <5 (efficacy)
- 9,543 children, initiated either LPV/r or EFV with either d4T or ABC, 2004-2013,
- VS not improved with LPV/r +3TC +ABC

	LPV/r		NNRTI	
	ABC+3TC	D4T+3TC	ABC+3TC	D4T+3TC
	N (%)	N (%)	N (%)	N (%)
VL<400	158 (62%)	1437 (75%)	155 (77%)	2535 (84%)
VL<50	104 (41%)	985 (52%)	115 (57%)	1996 (66%)

IeDEA South Africa

Technau PIDJ 2014

# VS with ART is particularly challenging in infants

Viral suppression in ART naïve children starting treatment,  
Eastern Cape South Africa

## 12 month VS rates (95%CI)

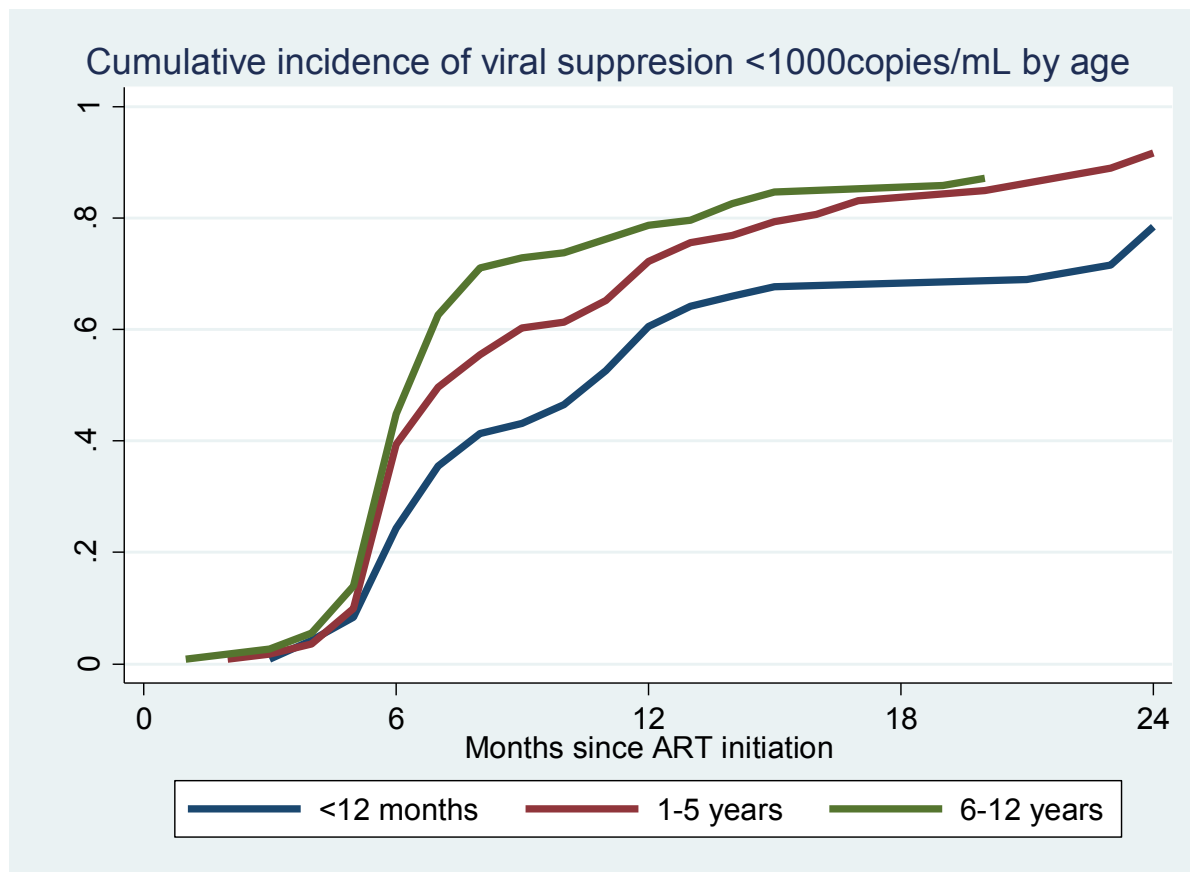
<12 months: 37.2%

(28.4-46.0)

1-5 years: 61.8% (51.6-70.4)

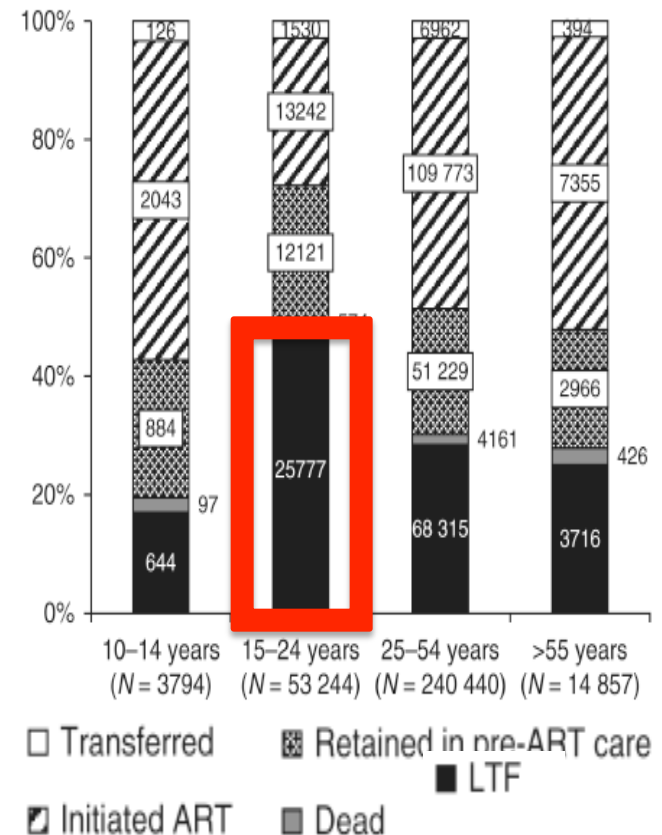
6-12 years: 71.3% (61.7-78.9)

Compared to children <12 months, 1-5 year olds had 1.5 times more likely to have VS <1000 copies ( $p=0.007$ ) and 6-12 year olds had 1.7 higher hazards of VS<1000 copies ( $p<0.001$ )



# Adherence and viral suppression among adolescents with HIV

- Adolescents are the only age group without decline in AIDS-related deaths.
- Sub-optimal adherence and high treatment failure is major challenge during adolescence.
- Meta-analysis Pooled estimate for adherence from 8 African studies: 83.8 % (95%CI 78.8-88.7) Kim S-H, et al *AIDS* 2014
- Probably overestimate given large LTFU seen in this age group



Lamb M et al. *AIDS* 2015

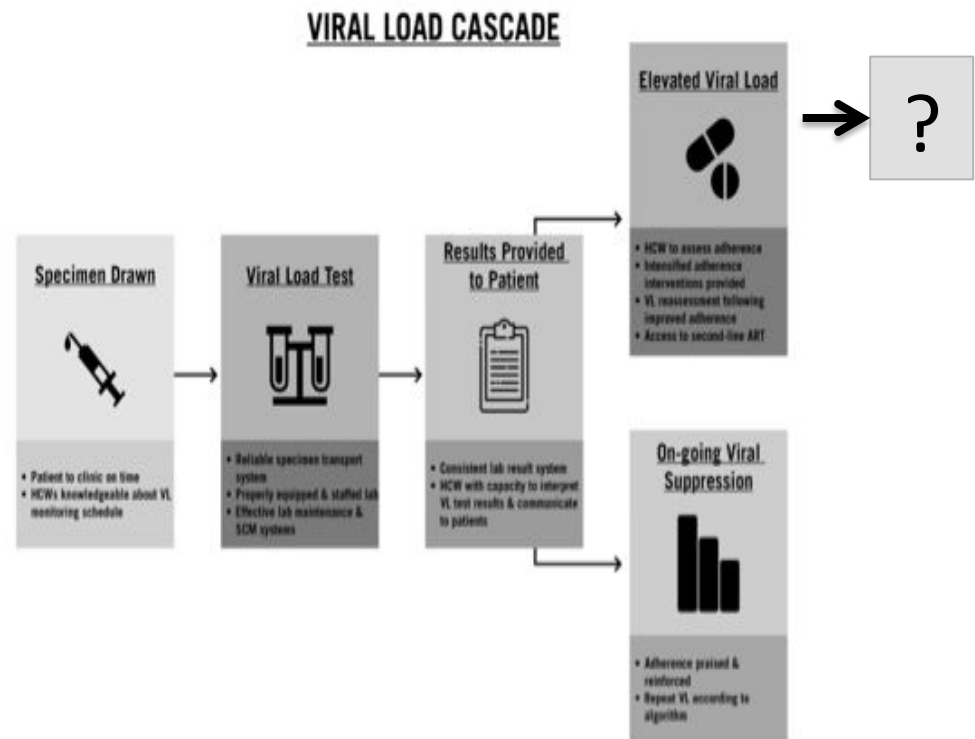
# Young adolescents highest risk for virologic failure

- 42, 427, >10 yrs, initiating 1<sup>st</sup> line ART in Guateng and Mpumalanga, >95% NNRTI
- Young adolescents (10-14 yrs) lowest VS at 12 months
- Young adolescents had highest failure rate, 3X compared adults.

	Failure to suppress (>400 cps/mL) N (%)		Failure rate (100 person yrs)
	6 m	12 m	
Adults	2,314 (9.3)	1,147 (9.7)	2.1
Young adults (20-24)	100 (11.6)	57 (14.7)	2.6
Older adolescent (15-19)	28 (16.2)	10 (16.7)	3.8
Young adolescent (10-14)	24 (14.0)	24 (29.6)	6.3

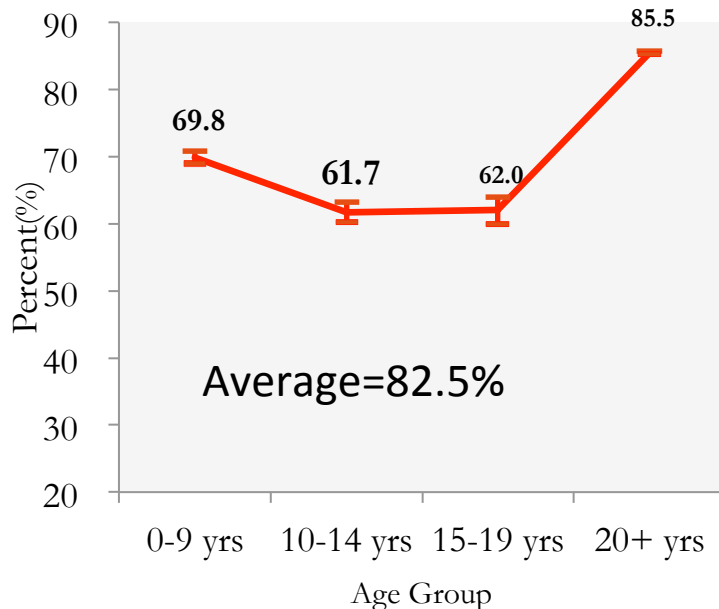
# VL triggered targeted adherence interventions can improve VS

- Meta-analysis with 6 studies  
8 countries Bonner K JAIDS 2013
- Assessed impact of routine RVLM
- Peer support, peer/adherence counselors, educational sessions, home visits.
- Pooled estimate 70.5% (95%CI 56.6-84.4%) suppressed repeat VL
- Shesilweni, Swazi Jopanputra JAIDS 2014
  - 61% of those who had EAC and repeat VL were <1000 (n=158)

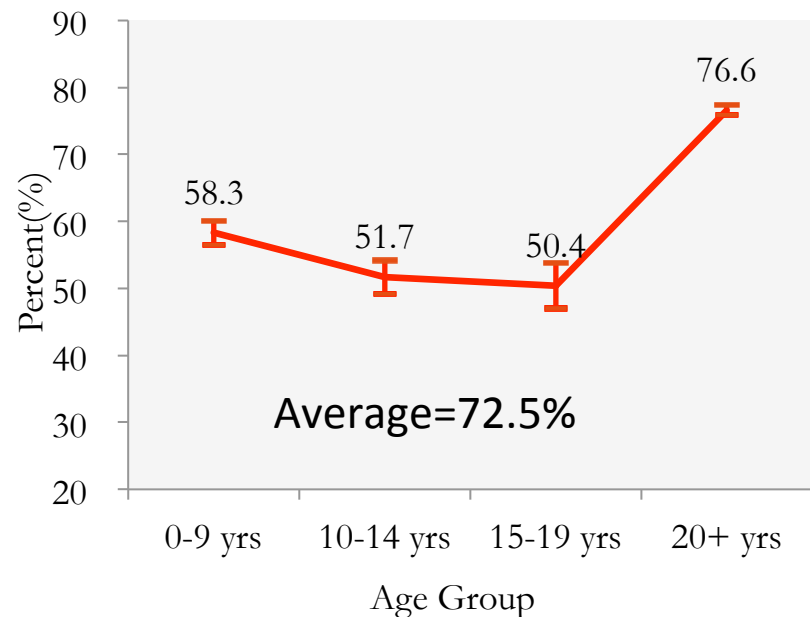


# Piloting routine VL monitoring with enhanced adherence intervention for VL>1000 in 5 counties: Kenya 2016

VS by age group – first test



VS by age group – after EAC



- VS lower initially and after EAC for children, especially adolescents

Odera, Mwangi, Syowai, and Hawkens  
ICAP in Kenya

# Effective interventions must address the adherence barriers that are unique to infants, children and adolescents

- ART Palatability- infants and children
- Disclosure- children, adolescents
- Peers & dating- adolescents
- Social, family, environmental, structural-all
- HCW need tools, training, mentoring in EAC

## 10. Child doesn't want to take medication



## 9. Ways



Together we will find ways to make it easier to give child ARVs

## 3. Talking to your child about ARVs



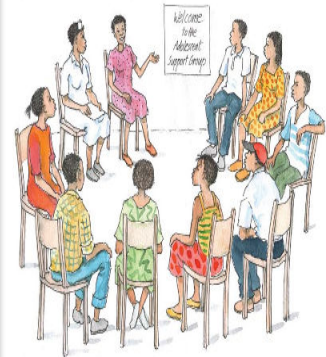
It is normal for your child to have questions about taking medications. Let's find some ways to talk about it.

## 6. What makes it difficult for you to take ARVs?



Together, we will discuss some reasons it is difficult to take your ARVs.

## Viral Load Monitoring and Enhanced Adherence Counseling Flipchart: Parent Version (Infants & Children)



## Viral Load Monitoring and Enhanced Adherence Counseling Flipchart: Adolescent & Young Adults



# Reaching the third 90 for infants, children, and adolescents: preparing for the steep climb

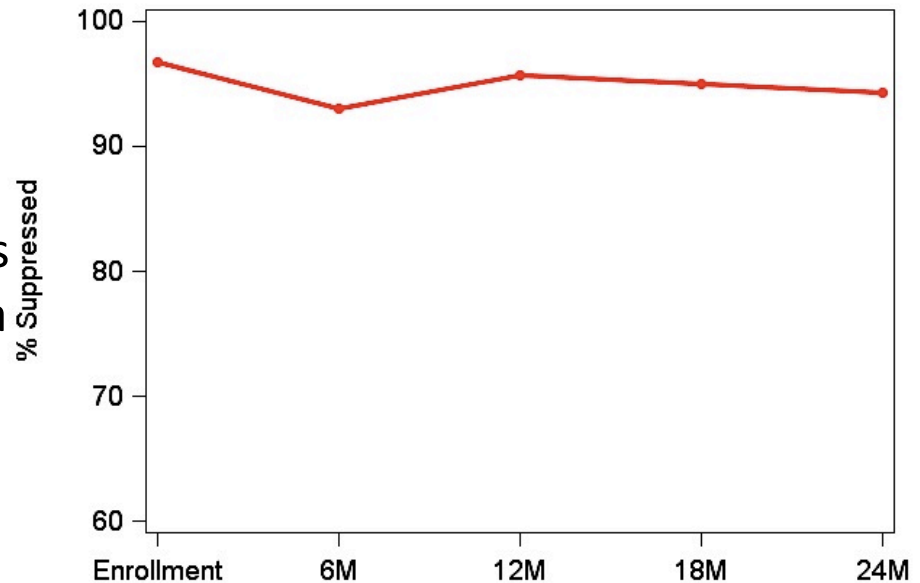
- For infants children and adolescents to fully benefit from RVLM all steps of the RVLM cascade must be made suitable
- Prepare HCW cadres and clinical settings for managing higher rates of non-suppression among their young patients
- Urgent need to expand capacity for VL triggered enhanced adherence interventions that address the specific needs of infants, children and adolescents adapted to local context
- Age disaggregated M&E and QI along the RVLM cascade
- It is important to establish whether more frequent VL monitoring for children and adolescents improves VS
- We must quickly learn and share successful and less successful practices





# Reaching the third 90: Sustained high levels of VS achievable throughout childhood with current ART

- Despite challenges achieving the third 90 for children is possible!
- Observational prospective cohort of > 500 HIV-infected children ages 6-9 yrs. from 2 sites in South Africa who started ART prior to age 2 years (mean 7 month)
- Time on ART 5.9 yrs, 70% on LPV/r
- VL monitoring every 6 months
- 95% VS (<1000 copies/mL) sustained over 2 years



N	523	476	511	497	493
% Suppressed	96.7	93.1	95.7	95	94.3

Shiau, Covaadia, Violari Arpadi, Kuhn  
Unpublished data