IAS 2021&
Pediatric HIV Workshop
Selected PMTCT, Pediatric, Adolescent, and Maternal/Adult Abstracts





Lynne M. Mofenson MD

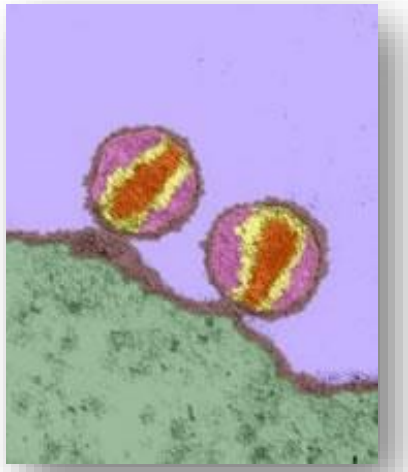
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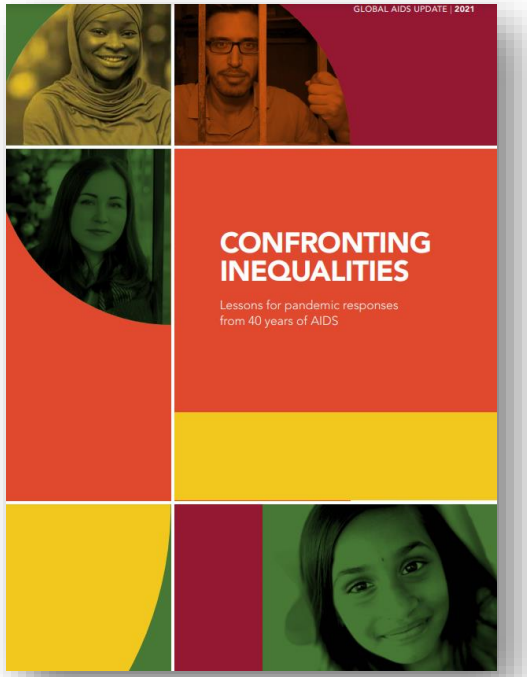






Update on Epidemiology of Pediatric HIV 2021





UNAIDS

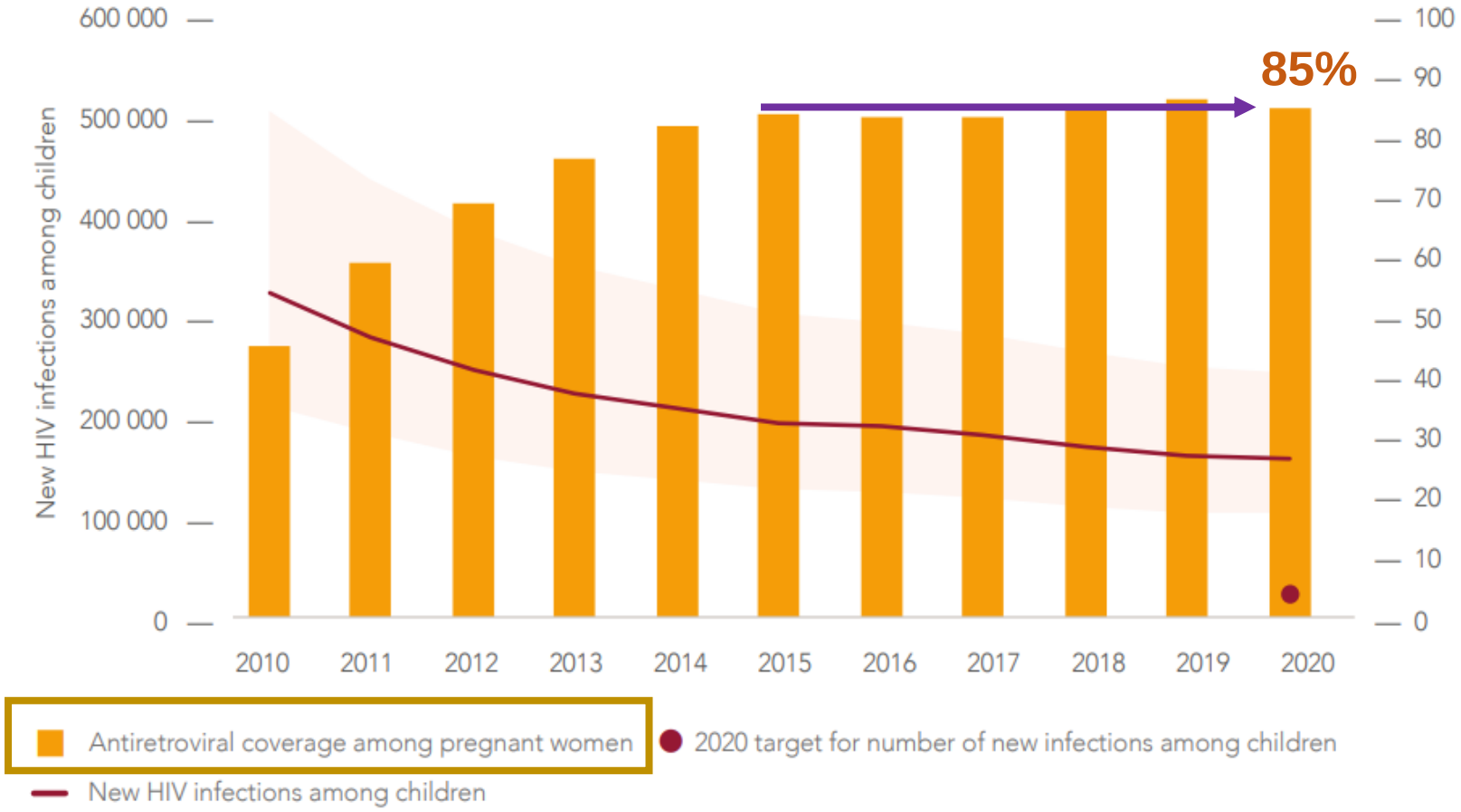
INTERNATIONAL WORKSHOP ON HIV PEDIATRICS
VIRTUAL WORKSHOP
16 - 17 JULY
2021



INVITED SPEAKER
MARY MAHY, ScD, MHSc
UNAIDS, Switzerland

ART Coverage in Pregnant Women Was 85% in 2020 – But Progress Has Stalled

Maternal ART and New Infections in Children Globally, 2010-2020

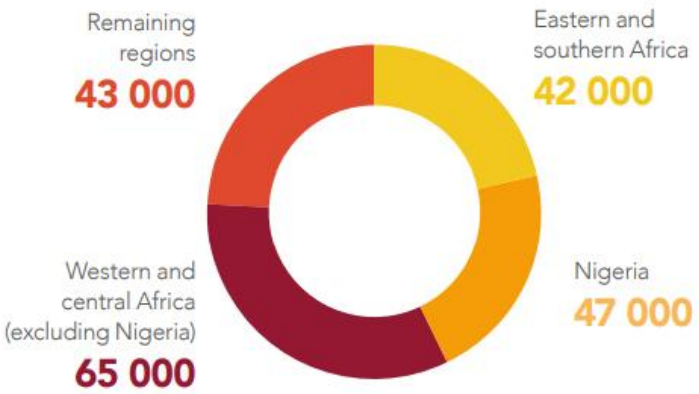


Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).

→ 85% of pregnant women with HIV received ART in 2020 – but **little expansion since 2015**

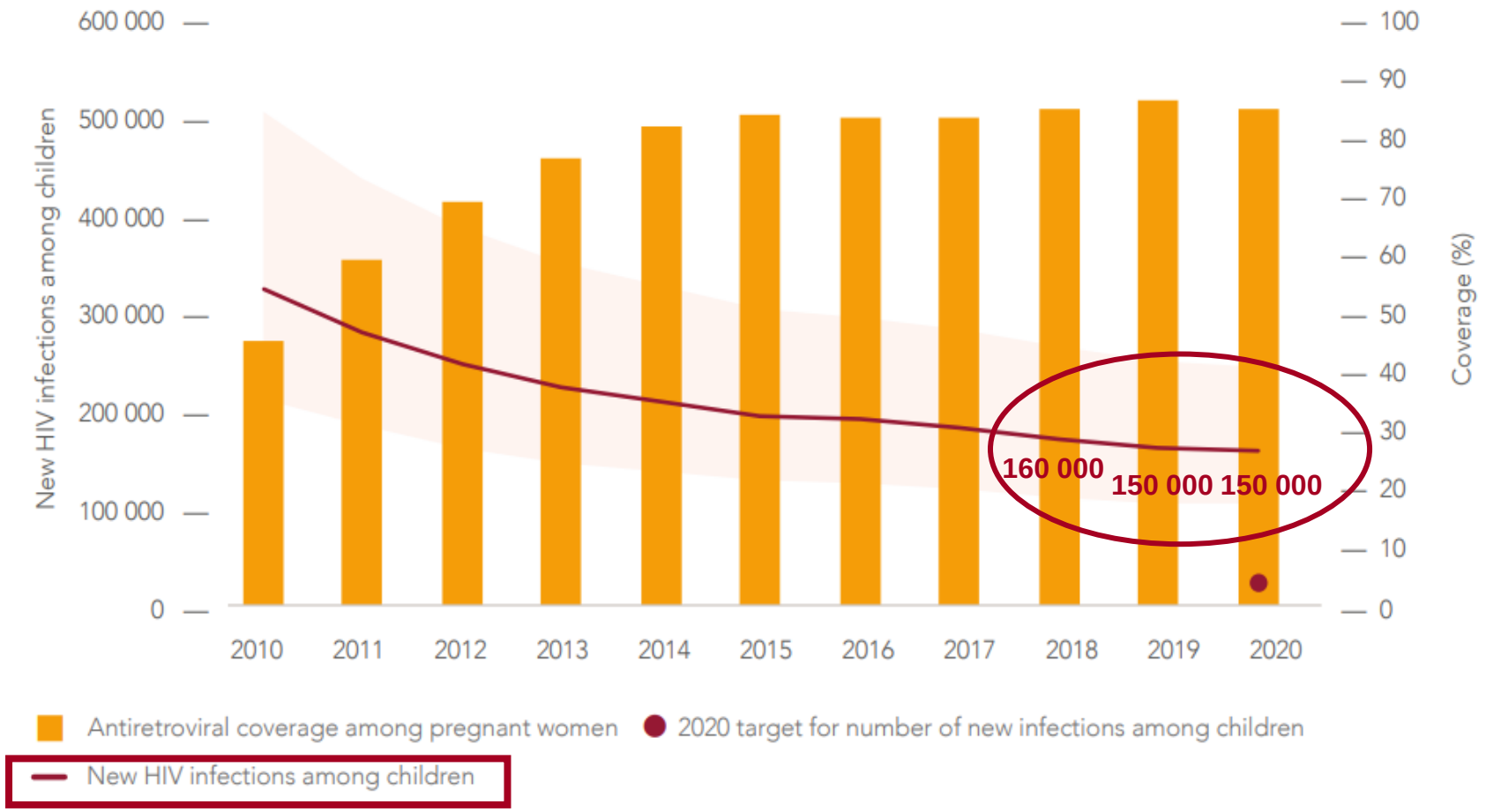
→ Regional differences: almost 25% of women not on ART are in Nigeria and further 33% in West or Central Africa

Distribution pregnant women with HIV <u>not</u> on ART by region, 2020



There Has Been a 53% Decline New Pediatric Infections Since 2010 – But Progress Has Also Stalled

Maternal ART and **New Infections in Children** Globally, 2010-2020



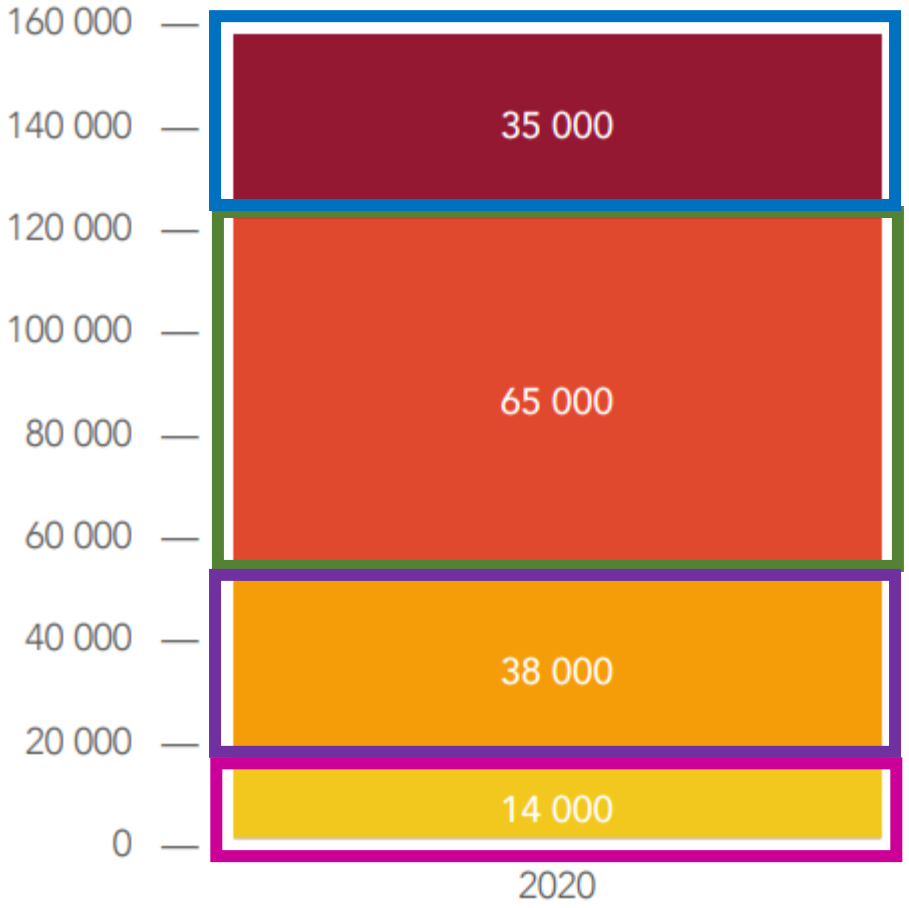
Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).

→ 150,000 new pediatric HIV infections estimated in 2020

→ Minimal change in new infections between 2018 and 2020

→ Significantly missed our target of 20,000 new infections by 2020

Causes of New Child Infections Globally 2020



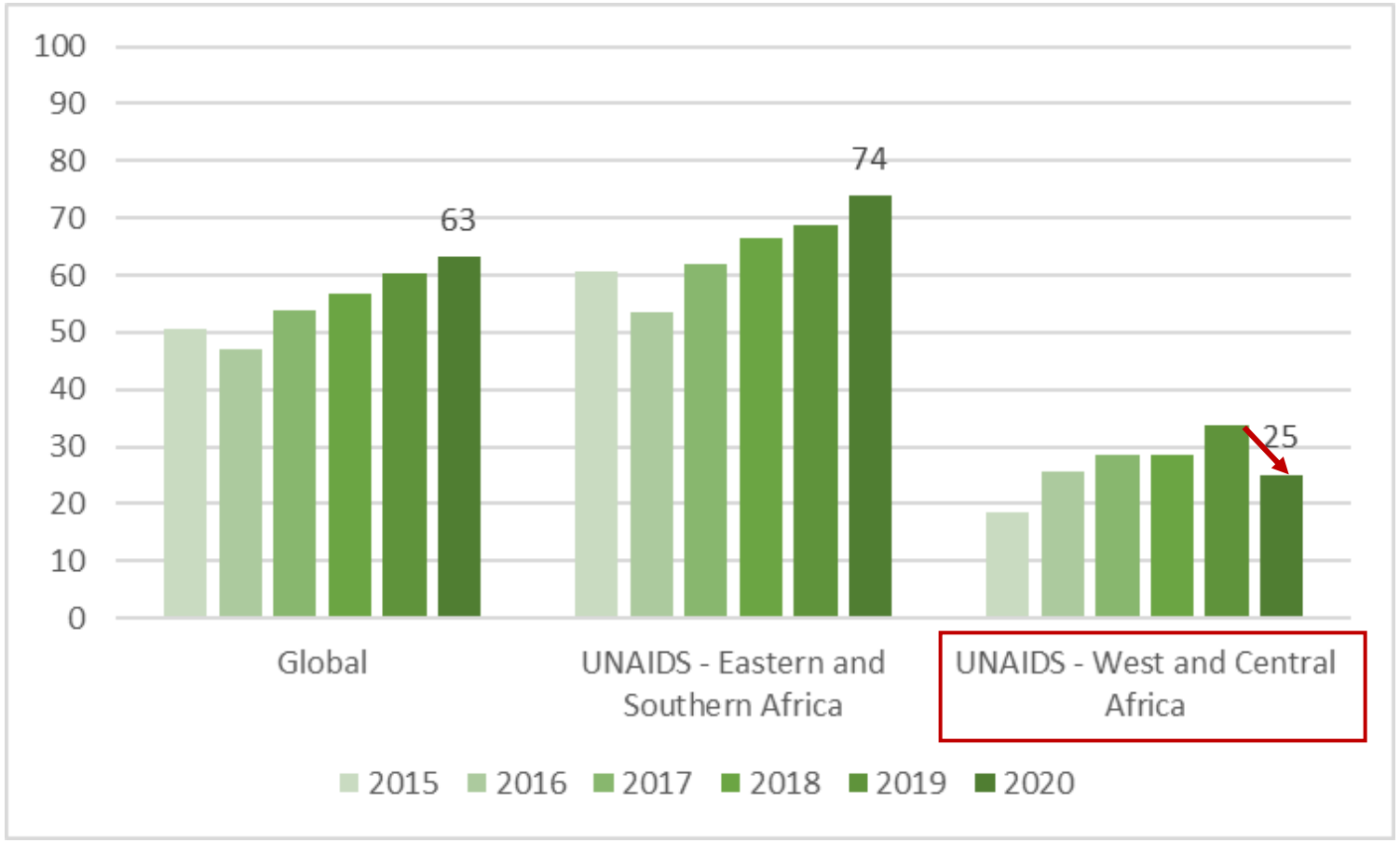
Primary gaps in PMTCT:

- Mother acquired HIV during pregnancy or breastfeeding — **23%**
- Mother did not receive antiretroviral therapy during pregnancy or breastfeeding (most undiagnosed) — **43%**
- Mother did not continue with treatment during pregnancy or breastfeeding — **25%**
- Mother was on antiretroviral therapy but not virally suppressed — **9%**

Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).

Early Infant Diagnosis Only 63% Globally, and is Particularly Low in West and Central Africa

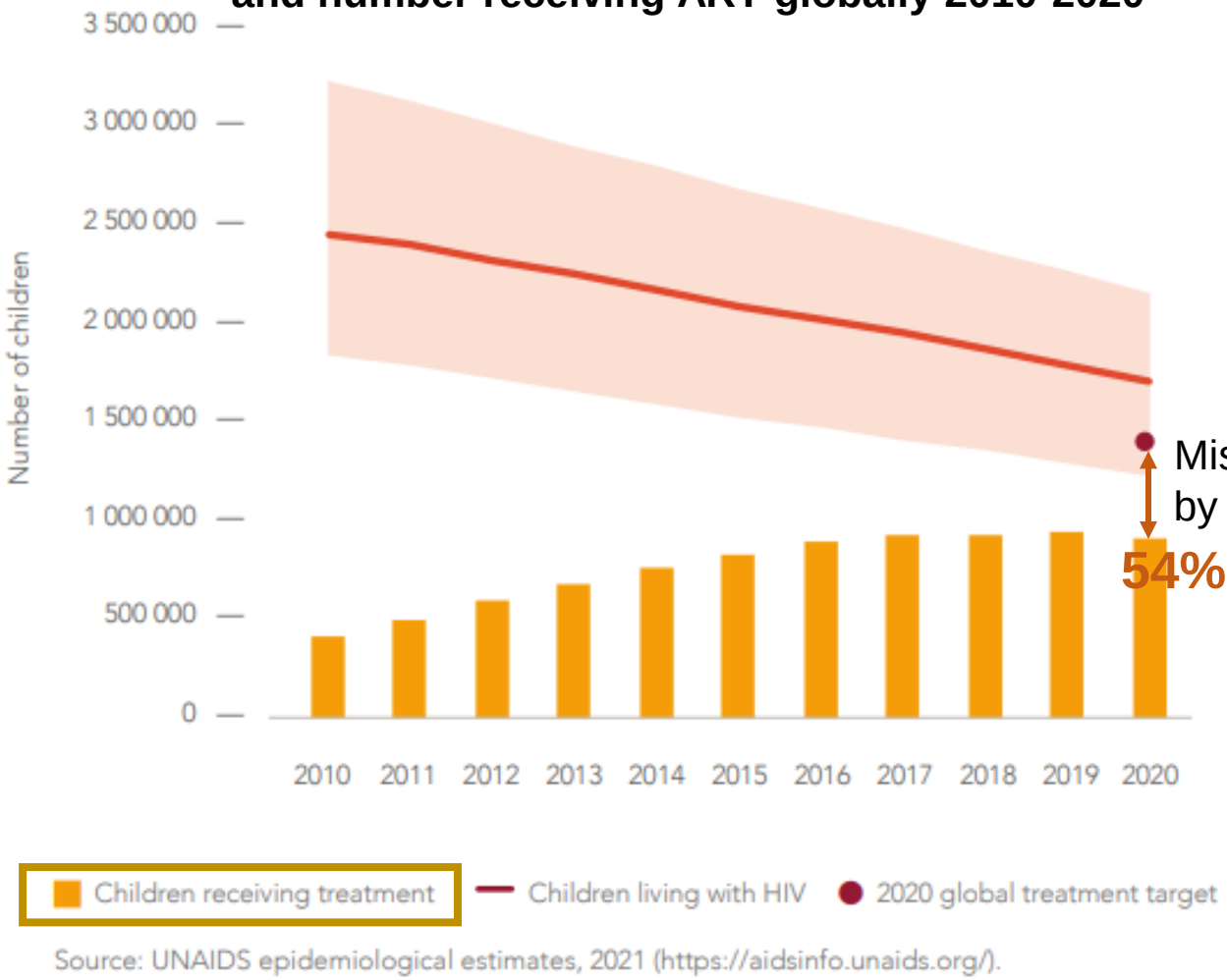
Percent of HIV-Exposed Children with PCR Test 8 Weeks, Global and by Region, 2015-2020



→ EID in West and Central Africa only 25% - and actually **decreased** between 2019 and 2020 (while increased in Eastern and Southern Africa over same time span)

Decrease in Number of Children with HIV Receiving ART in 2020

Number of children (0-14 years) living with HIV and number receiving ART globally 2010-2020



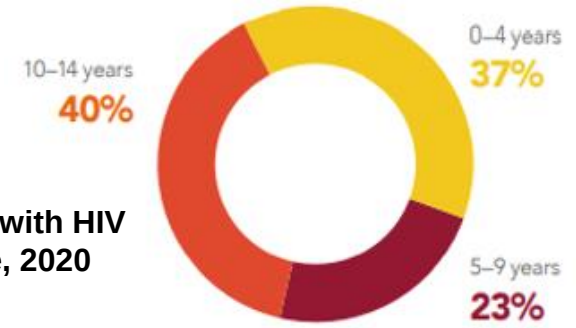
Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).

Despite decline in number of children with HIV since 2010, ART coverage remains low at only 54%

→ The number of children on ART actually **declined** in 2020

→ Almost 2/3 of the 800,000 children with HIV not receiving ART were aged ≥5 years

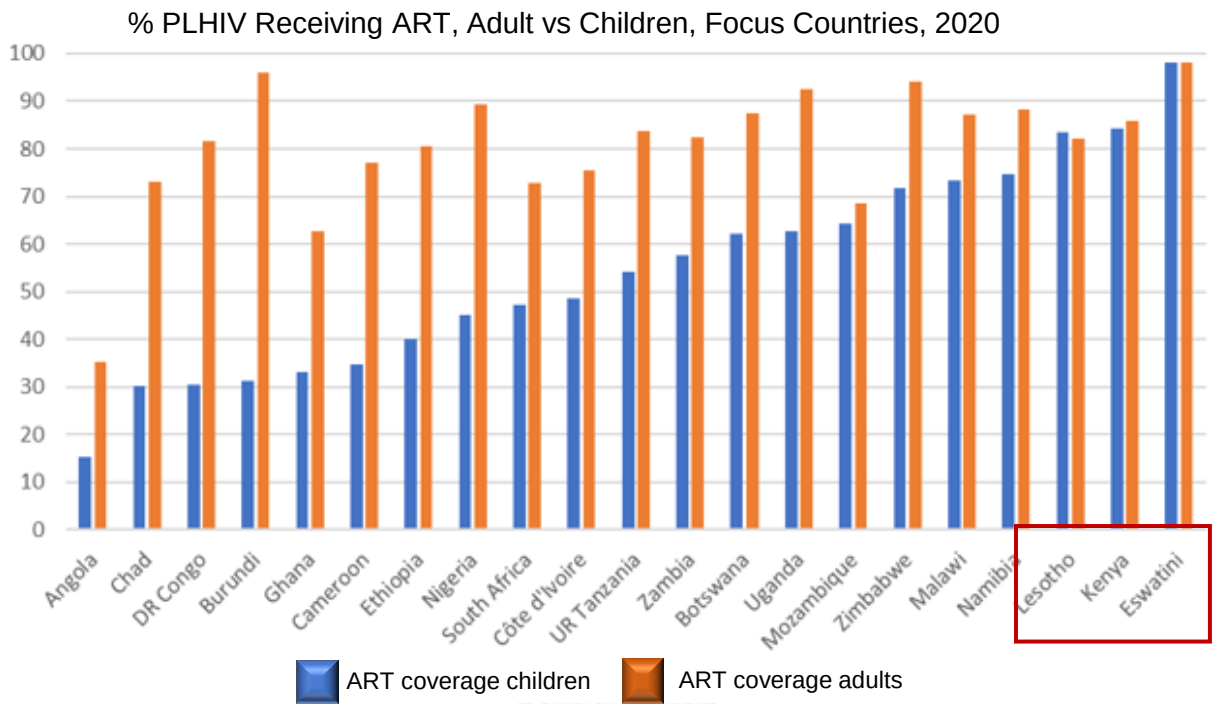
Distribution children with HIV not on ART by age, 2020



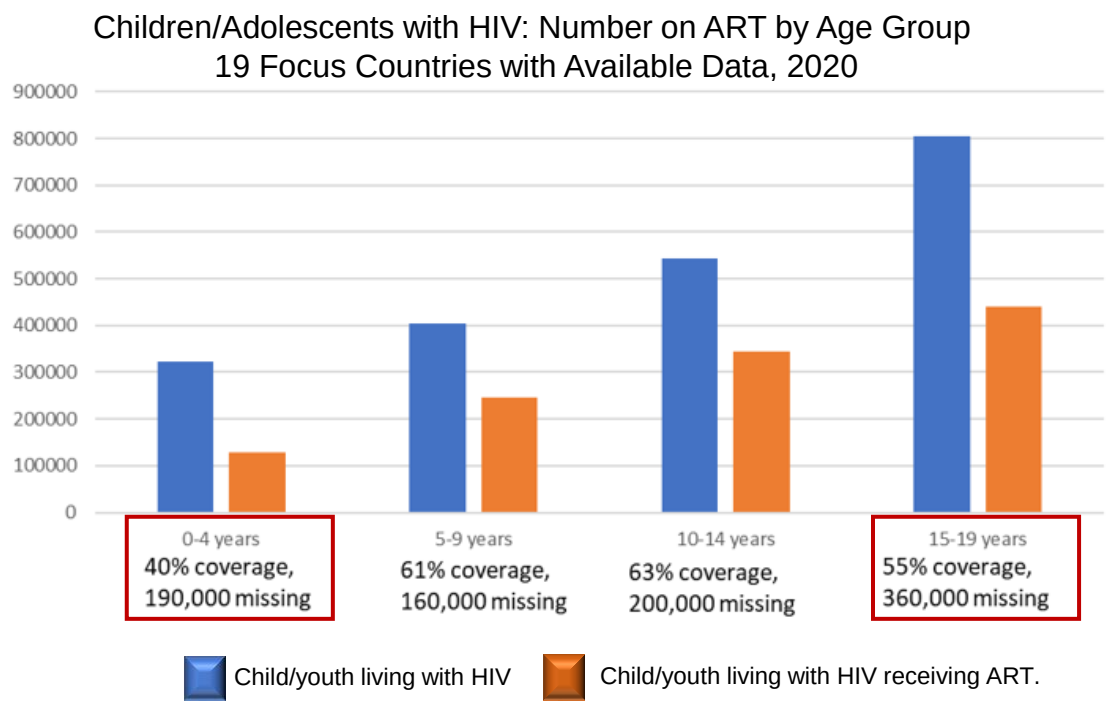
Lower ART Coverage in Children and Adolescents vs Adults

- In 2020, ART coverage in children 0-14 years was 54% [37–69%], significantly lower than 74% [57–90%] ART coverage in adults.

→ In almost all countries, pediatric ART coverage is significantly lower than in adults



→ Proportionately, ART coverage lowest in children 0-4 and adolescents 15-19 years

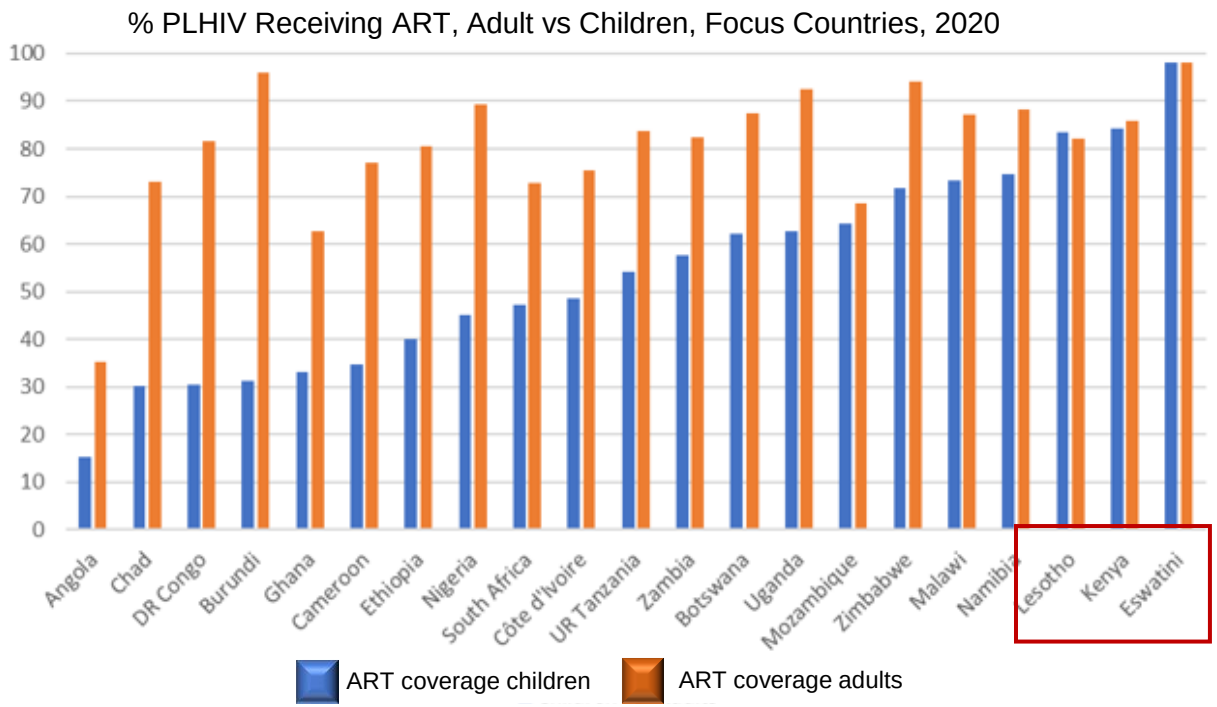


Source: Special analysis of UNAIDS 2021 epidemiological estimates.

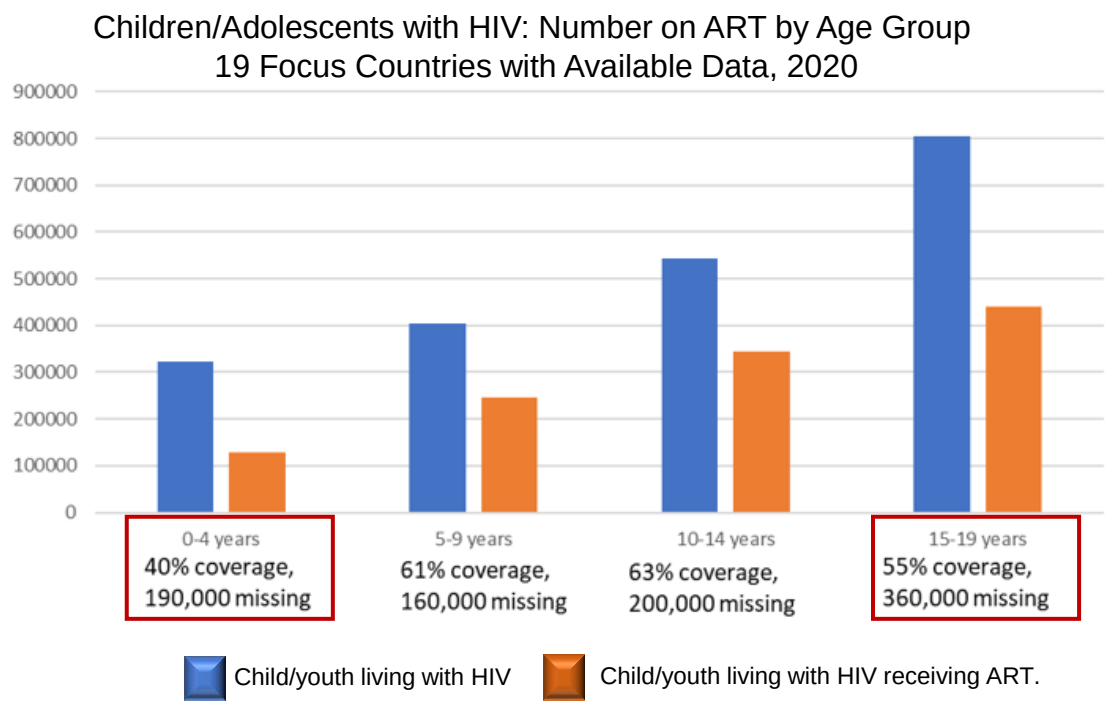
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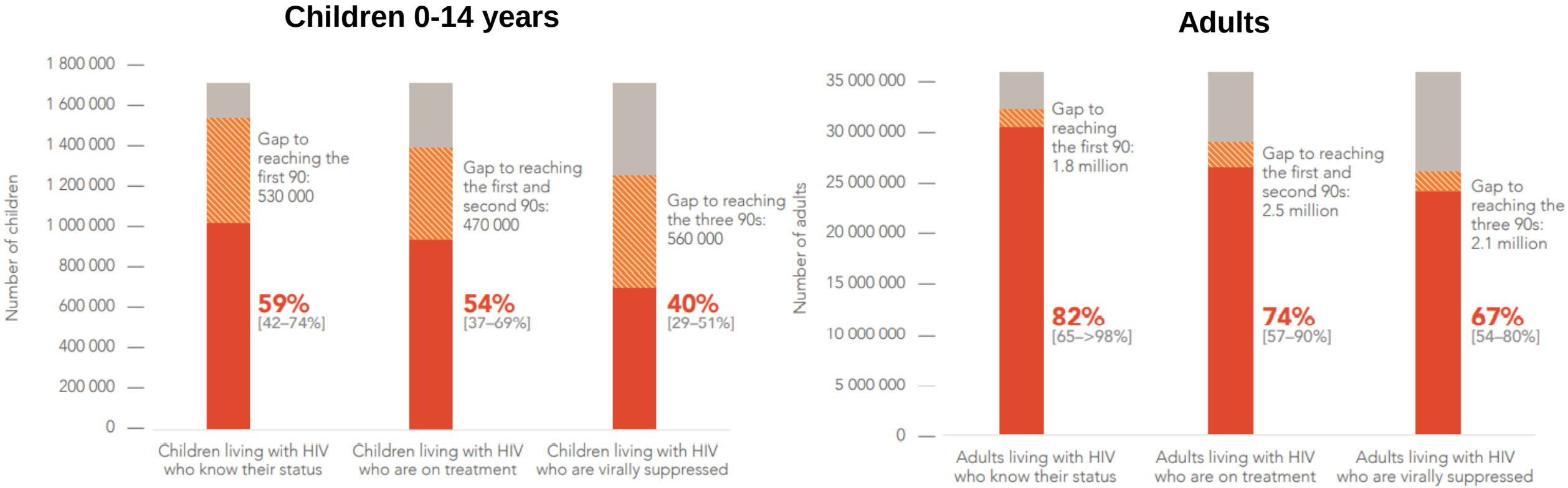


→ Proportionately, ART coverage lowest in children 0-4 and adolescents 15-19 years



Source: Special analysis of UNAIDS 2021 epidemiological estimates.

Gap in Reaching 90-90-90
Children vs Adults, 2020

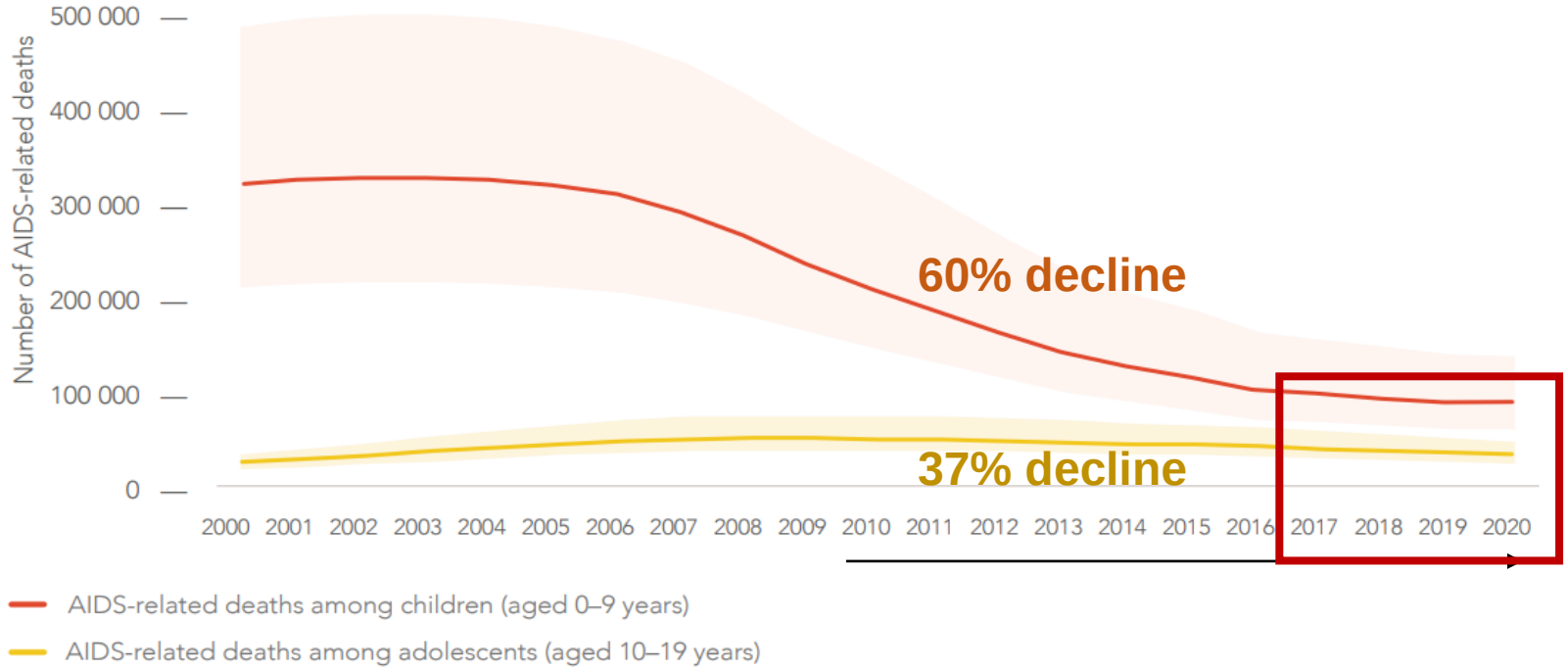


→ Only 40% [29–51%] of <u>all children</u> with HIV were virally suppressed in 2020.

→ If focus specifically on suppression in children or adults with known HIV <u>on ART</u>, still major gap, with 75% suppression vs 91% suppression for adults on ART

Source: UNAIDS special analysis, 2021.

Between 2010 and 2020, Lower Reduction in AIDS-Related Deaths in Adolescents Than in Children with HIV



→ Reductions in AIDS-related deaths steepest among children aged 0 to 9 years (a 60% decline since 2010), but among adolescents aged 10–19 years, progress is slower, with AIDS-related deaths declining just 37% over the same period.

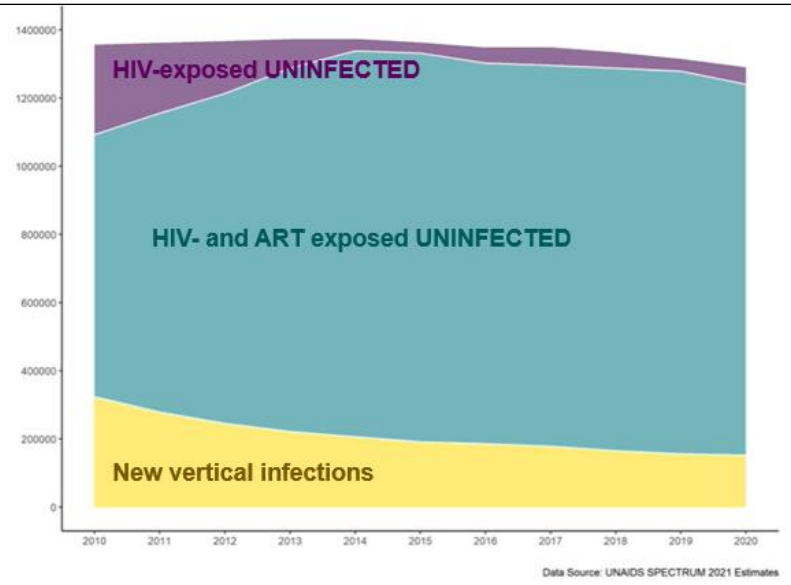
→ **Little improvement in mortality since 2017**, regardless of age.

Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).

HIV-Free Survival

Optimizing Outcomes for HIV-Exposed Uninfected and Infected Children

Penazzato M et al. IAS Virtual Abs Workshpop 07 – 7th Workshop on HEU



In 2020:

- Worldwide, 1.7 million children were living with HIV; 530,000 **a third of these**, are aged ≤5 years
- **5.4 million children aged ≤5 years are HIV-exposed and uninfected** &1.3 million births/year to HIV+ women, most of whom will be uninfected.
- In Botswana, Eswatini, Lesotho and South Africa, **more than one in five children are HIV-exposed and uninfected.**

HIV-free survival is not enough!



2025 HIV/AIDS Targets: Next Generation of Global AIDS Response Goals

Goals Focused on Pregnant/BF Women and Children

IAS Virtual Session SA-14

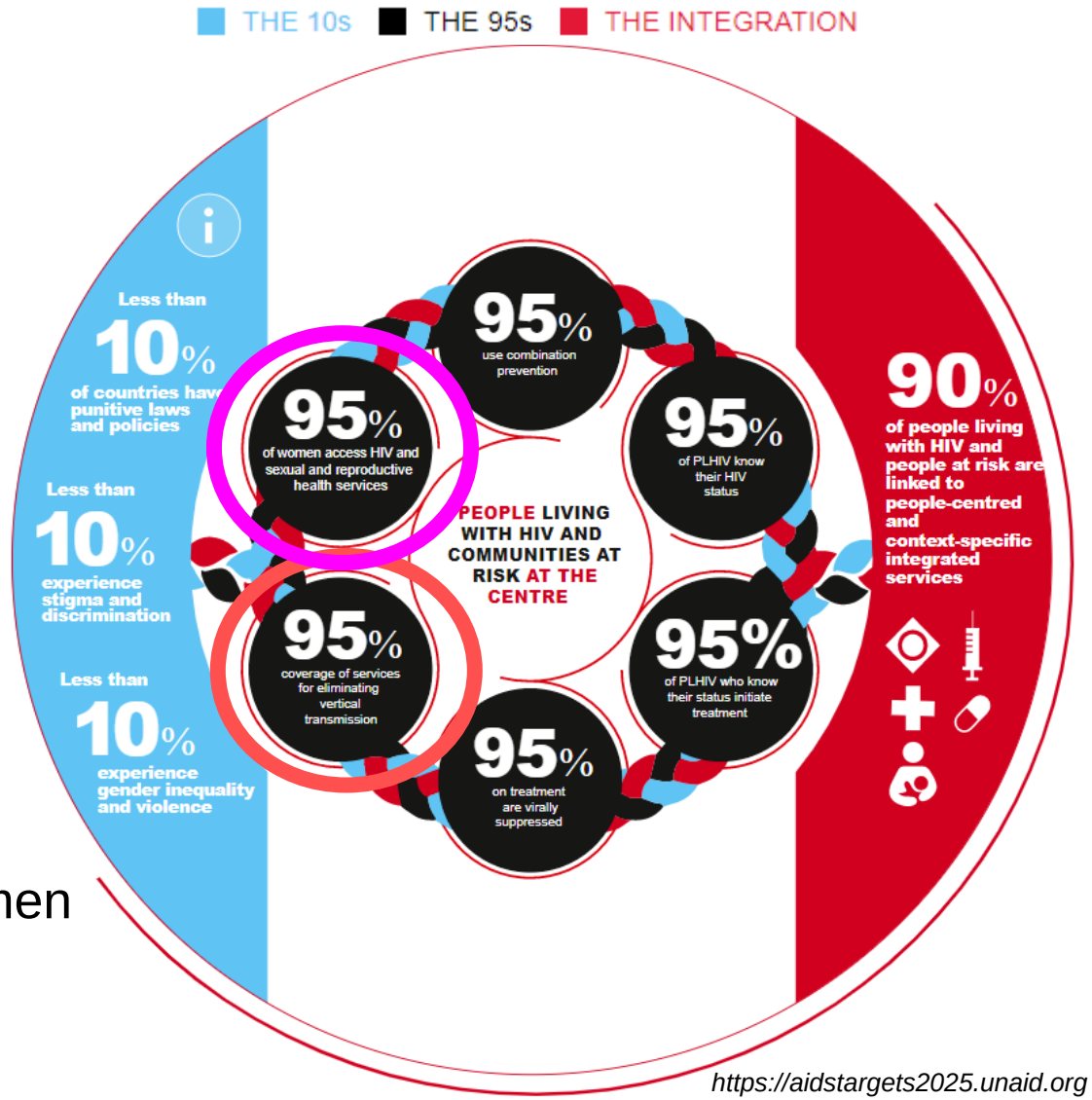
Move from 90-90-90 to **95-95-95**:

- HIV knowledge
- HIV+ on ART
- HIV+ on ART have suppression

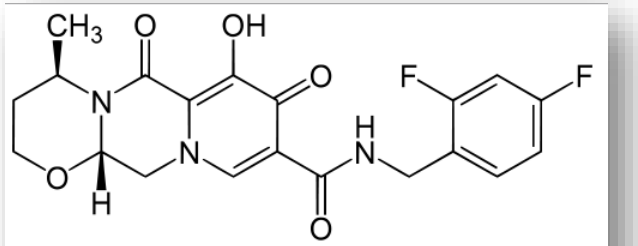
Including pregnant and BF women and children

New targets for **SRH** **and** **vertical transmission**

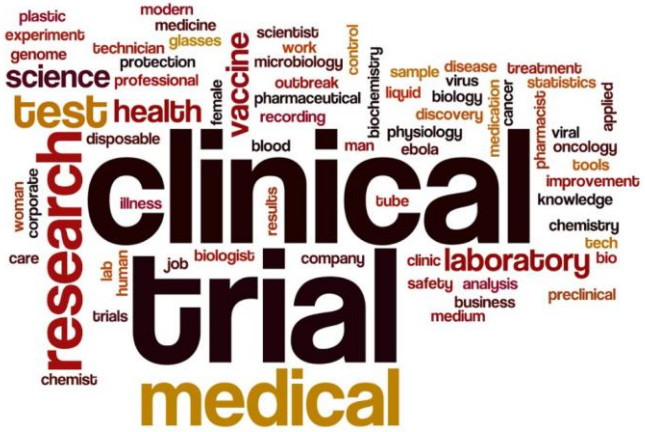
- 95% coverage services to eliminate MTCT
- 95% of pregnant women tested for HIV, syphilis and HBV at least once in pregnancy and in high burden settings 95% HIV-negative re-test 3rd trimester/PP
- 100% HIV+ pregnant/BF women on ART, with 90% on ART **before** current pregnancy
- 95% VL testing q6-12 mos for breastfeeding HIV+ women
- 95% HEI infants EID by 2 mos
- 95% HEI infant tested at cessation BF



https://aidstargets2025.unaid.org



DTG in Children
New Clinical Trial Data



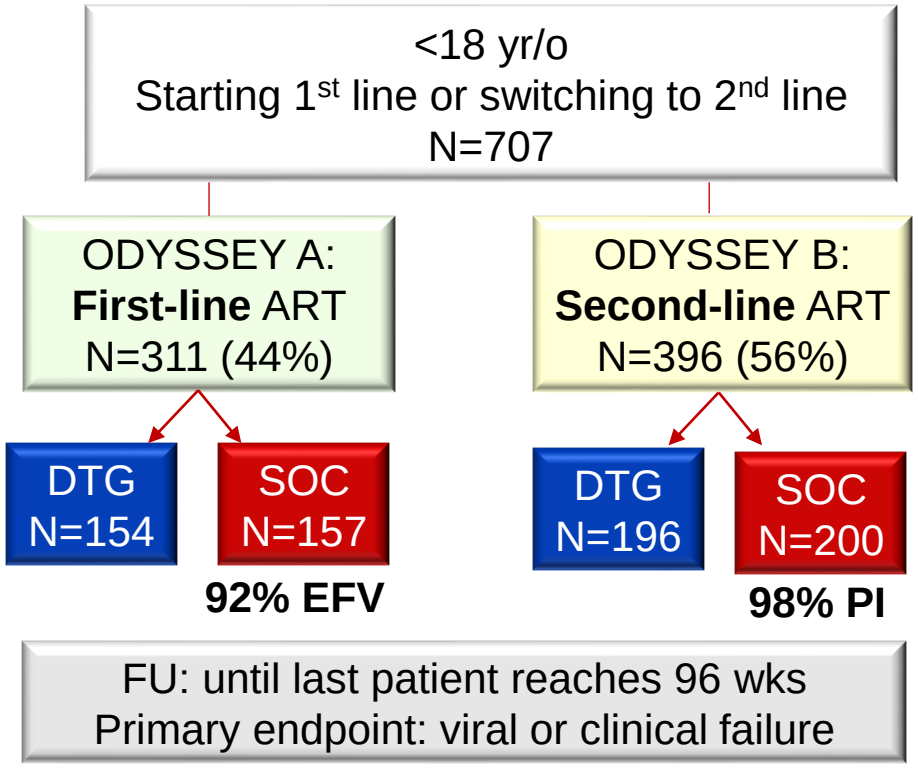


DTG-Based ART Shown Superior to SOC in **Older Children ≥14 kg** Living with HIV: ODYSSEY

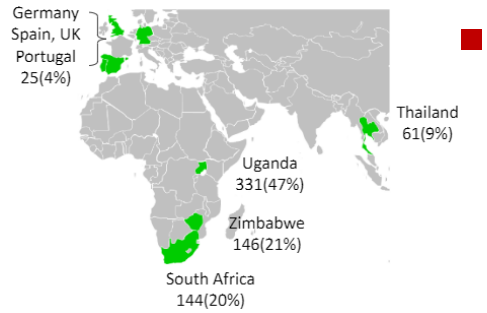
Turkova A et al. CROI March 2021 Abs 174

Older children:

Turkova et al. CROI 2021, Abs 174



- Enrolled Sept 2016-June 2018
- 96 wk FU completed April 2020



- RCT non-inferiority trial DTG vs SOC in children (median age 12 yr, wt 31 kg) starting 1st (ODYSSEY A) or 2nd (ODYSSEY B)-line ART in 8 countries

- Primary outcome: viral/clinical failure (new/recurrent WHO 3 or 4 event or death)

- Results:
  - Superior efficacy **DTG**: 8% (95% CI 3 to 14%) less failure by 96 weeks than **SOC** in older children

ODYSSEY Evaluation of DTG-Based ART vs SOC in **Young HIV+ Children <14 Kg**

Amuge P et al. International Pediatric HIV Workshop Abs 124 /IAS Virtual Abs. PEBLB18 July 2021

- Enrolled children in 3 weight bands for intensive PK in DTG arm; not specifically powered for efficacy
- 85 children enrolled (n=23, 3-<6kg; n=40, 6-<10kg; n=22, 10-<14 kg)
  - Median baseline age (IQR): 1.4 years (0.6, 2.0)
  - 72 children (85%) started 1st line, 13 (15%) 2nd line
  - SOC ART was LPV/r in 74%
- Follow-up:
  - Median FU (IQR): 120 weeks (97, 132)
  - Only 5 (6%) LTFU

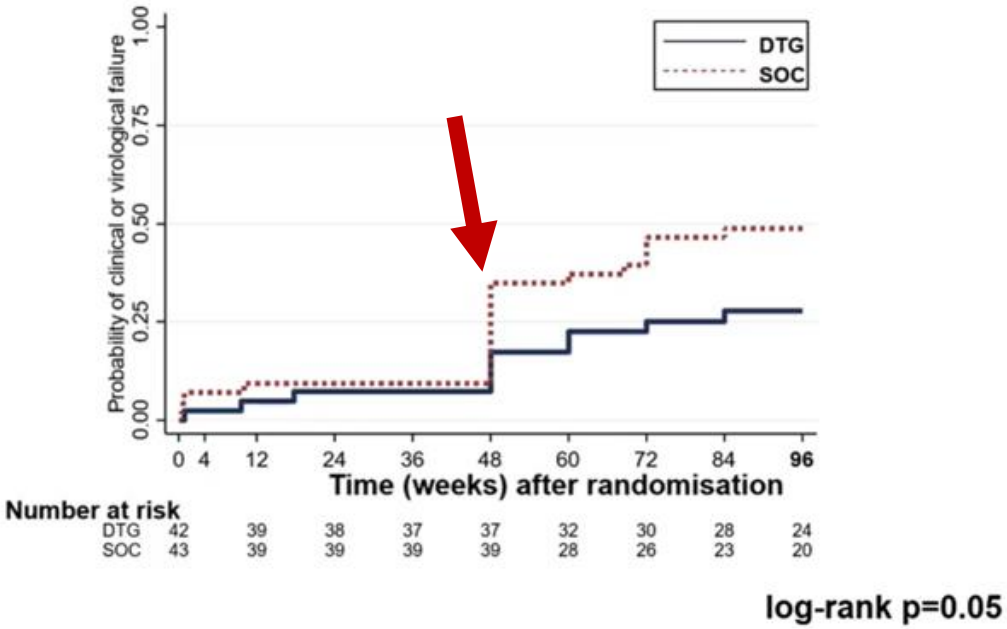
Viral or Clinical Failure by 96 Weeks is Lower in DTG vs SOC Arm in Young HIV+ Children <14 kg

Amuge P et al. International Pediatric HIV Workshop Abs 124 /IAS Virtual Abs. PEBLB18 July 2021

Endpoint	DTG N=42	SOC N=43	Total N=85
Primary endpoint (viral or clinical failure)	**11 (26%)**	**21 (49%)**	32 (38%)
Confirmed VL >400 c/mL >36 weeks	**8 (19%)**	**16 (37%)**	24 (28%)
WHO 4 event	1 (2%)	1 (2%)	2 (2%)
Death	2 (5%)	4 (9%)	6 (7%)

→Difference between arms driven by virologic, as opposed to clinical, endpoints

Time to viral or clinical failure

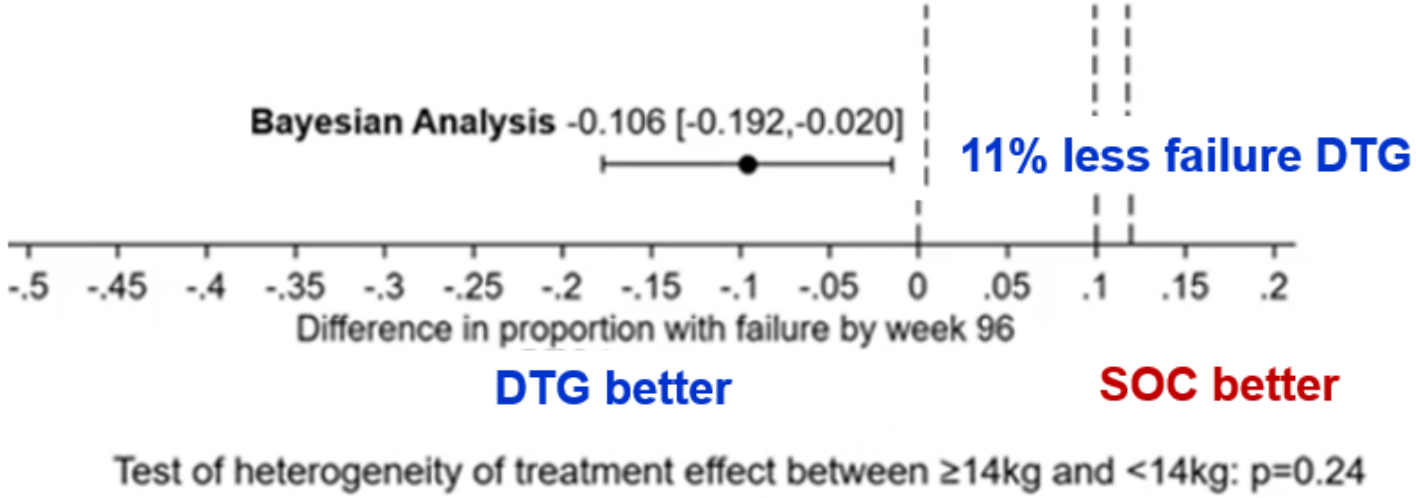


→Differences between arms only first emerge after one year (48 weeks) on ART

Viral or Clinical Failure by 96 Weeks Lower with DTG vs SOC in Pooled Analysis

Amuge P et al. International Pediatric HIV Workshop Abs 124 /IAS Virtual Abs. PEBLB18 July 2021

Difference in Proportion with Viral/Clinical Failure DTG vs SOC



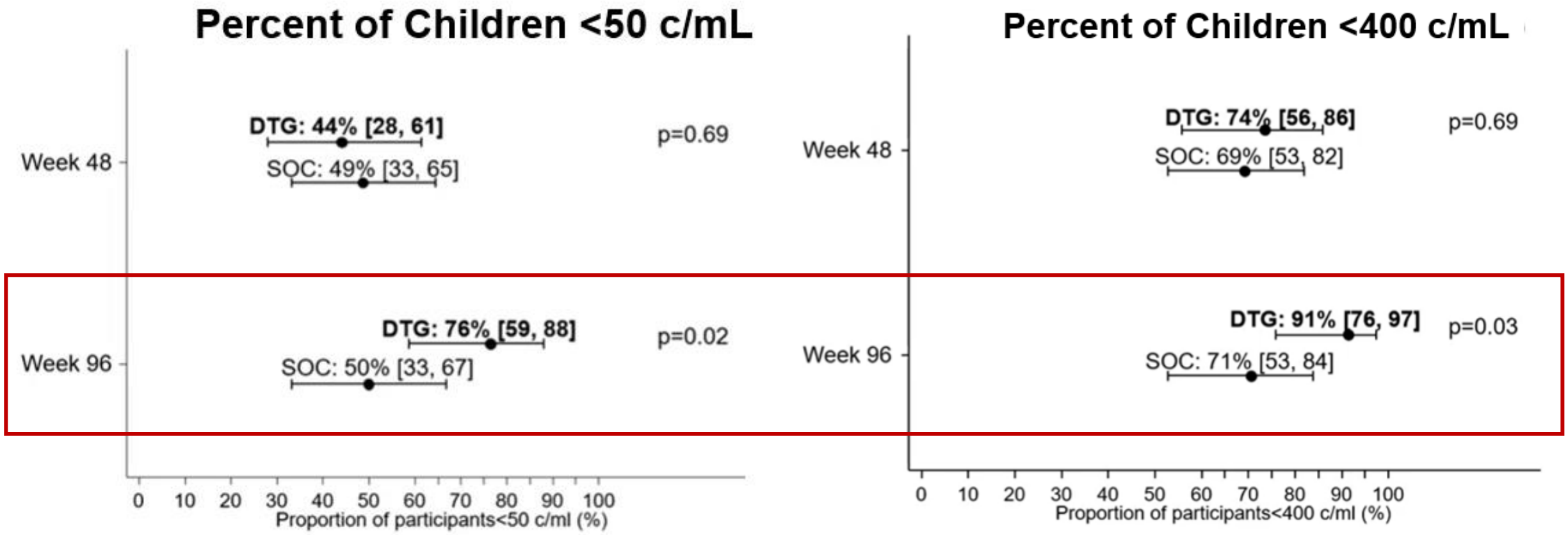
Test of heterogeneity of treatment effect between ≥14kg and <14kg: p=0.24

Primary Efficacy Analysis *Bayesian analysis*:

- Pooled the <14 kg trial data in 85 children with the ≥14 kg trial data from 707 children, with 78% weighting of data from children ≥14 kg (based on clinical opinion)

VL<50 or <400 c/mL at 96 Weeks (but not 48 Weeks)
Better with DTG vs SOC in Young HIV+ Children <14 kg

Amuge P et al. International Pediatric HIV Workshop Abs 124 /IAS Virtual Abs. PEBLB18 July 2021



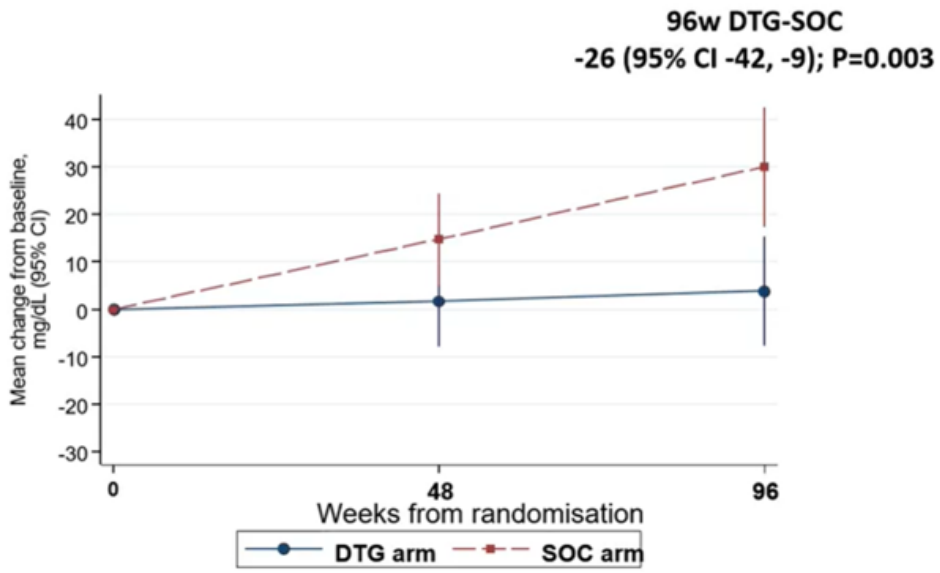
No Difference in Adverse Events Between DTG vs SOC in Young HIV+ Children <14 kg

Amuge P et al. International Pediatric HIV Workshop Abs 124 /IAS Virtual Abs. PEBLB18 July 2021

Adverse Event	DTG N=42	SOC N=43	P value
Serious adverse event	15 (11%)	19 (11%)	0.92
Grade 3 or above	36 (19%)	34 (21%)	0.79
ART modifying event	0 (0%)	2 (2%)	0.31

- Similar rates of AE and SAE between arms
- Most Grade ≥3 events infections or hematologic
- 2 ART modifying events in SOC only
- 6 deaths (2 DTG, 4 SOC)

Change Total Cholesterol from Baseline



- Increase total cholesterol over time in SOC (most on LPV/r) but not DTG arms.

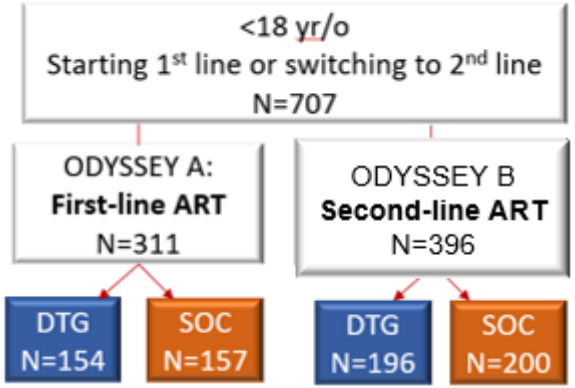
Summary: DTG Superior to SOC in Young Children as Well as Older Children Living with HIV

Amuge P et al. International Pediatric HIV Workshop Abs 124 /IAS Virtual Abs. PEBLB18 July 2021

- DTG was superior to SOC in young children <14 kg based on viral or clinical failure.
- At 96 weeks, higher proportion of children in DTG vs SOC arm were suppressed to <50 or <400 c/mL.
- Adverse events were similar with DTG and SOC, with no safety concerns for DTG; total cholesterol lower in DTG than SOC at 96 weeks.
- Few treatment changes, with all in SOC arm.
- **Provides strong support for WHO guidelines and roll-out DTG for younger children starting 1st or 2nd line ART.**
- Need to expedite procurement of dispersible DTG for young children!

Viral Failure and Genotypic Resistance in Children in the ODYSSEY Trial

Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021



(Original study older children)

- Viral failure defined as:
  - <1 log drop VL at week 24 and ART switch for treatment failure
  - Confirmed VL ≥400 c/mL any time after week 36

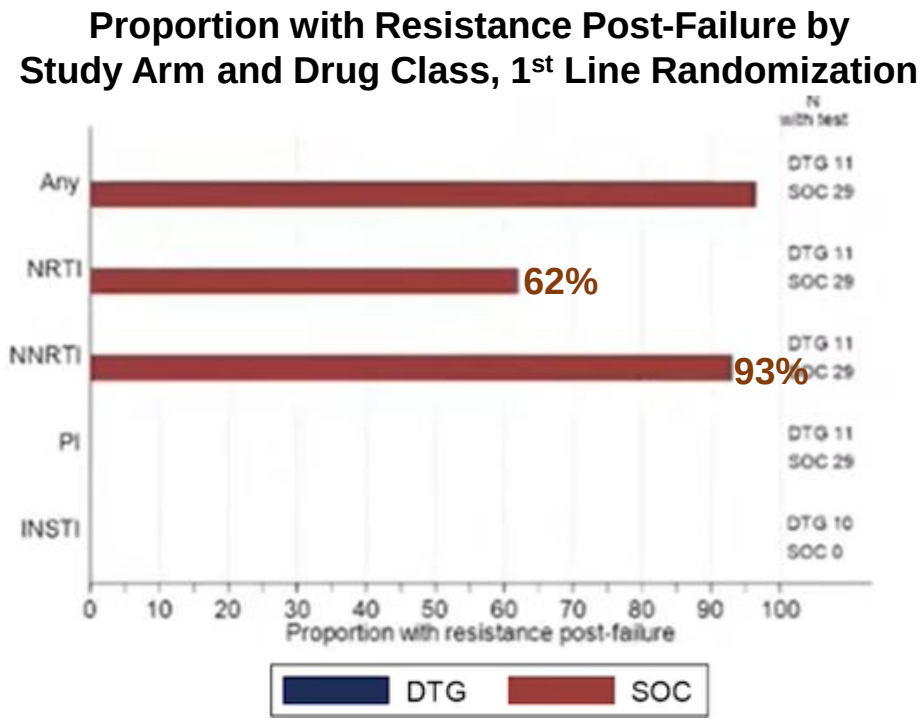
	Viral Failure by Study Arm	
	DTG	SOC
ODYSSEY A: first line	11 (7%)	30 (19%)
ODYSSEY B: second-line	31 (16%)	40 (20%)

- Patients with viral failure were tested for resistance with closest sample with VL >1,000 after failure (and prior to ART change if occurred); earlier baseline samples sequenced if major resistance mutation identified to determine the incidence of **new** mutations during study.

Viral Failure and Genotypic Resistance in Children Randomized to 1st Line ART, ODYSSEY

Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021

- Odyssey A (1st line): Major resistance mutations post-failure of 1st line ART



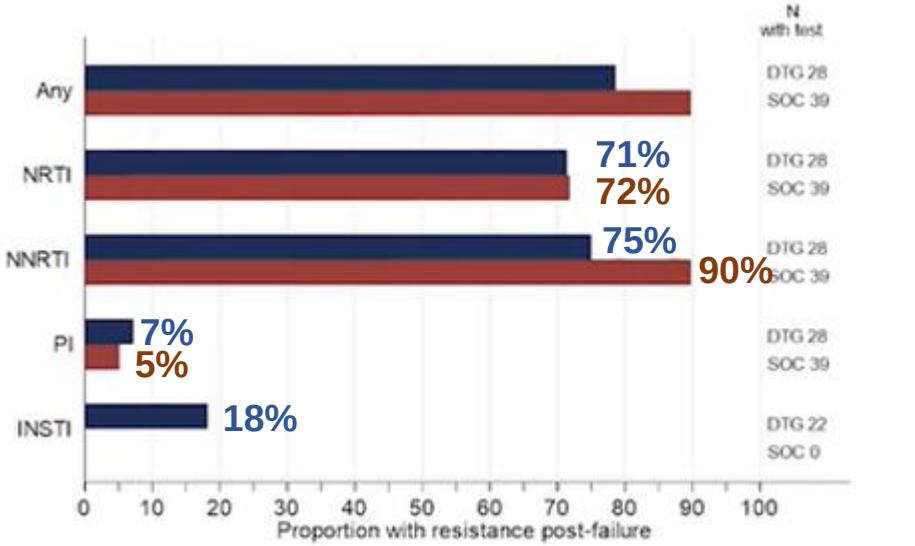
- **No resistance mutations with failure of DTG 1st line ART.**
- In **SOC 1st line ART** (100% NNRTI-based), for those with viral failure, 93% had NNRTI, 62% NRTI resistance; no PI resistance observed.

Viral Failure and Genotypic Resistance in Children Randomized to 2nd Line ART, ODYSSEY

Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021

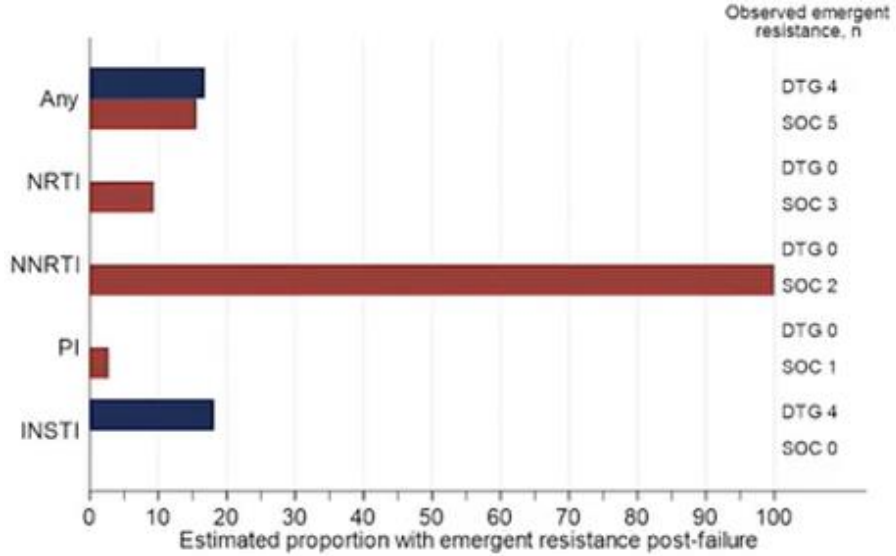
- Odyssey B (2nd line) (SOC 92% PI, 8% NNRTI anchor drug): Major resistance mutations post-failure of 2nd line ART

Proportion with Resistance Post-Failure by Study Arm and Drug Class, 2nd Line Randomization





Proportion with New Resistance Post-Failure by Study Arm and Drug Class, 2nd Line Randomization

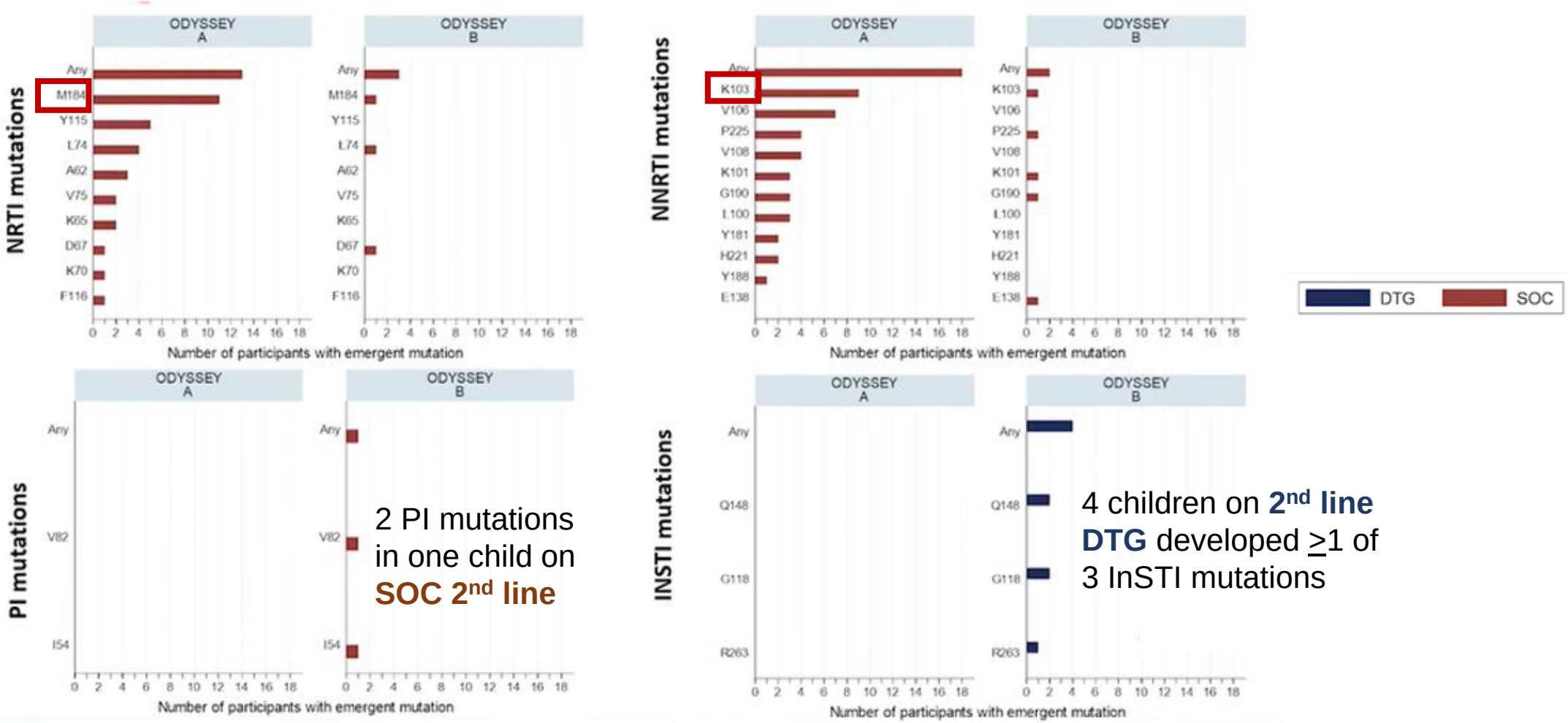


- Resistance with viral failure on **2nd line** similar **DTG** vs **SOC** in NRTI, NNRTI and PI class.
- New resistance (those with baseline data) to NRTI, NNRTI and PI only seen in **SOC arm**.
- In **DTG arm**, 4/22 (18%) had new 2nd line InSTI resistance (3/4 on AZT/3TC backbone).

New Genotypic Resistance Mutations by Class and Type in Children in the ODYSSEY Trial

Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021

Emergent New Resistance Mutations by Drug Class and Arm



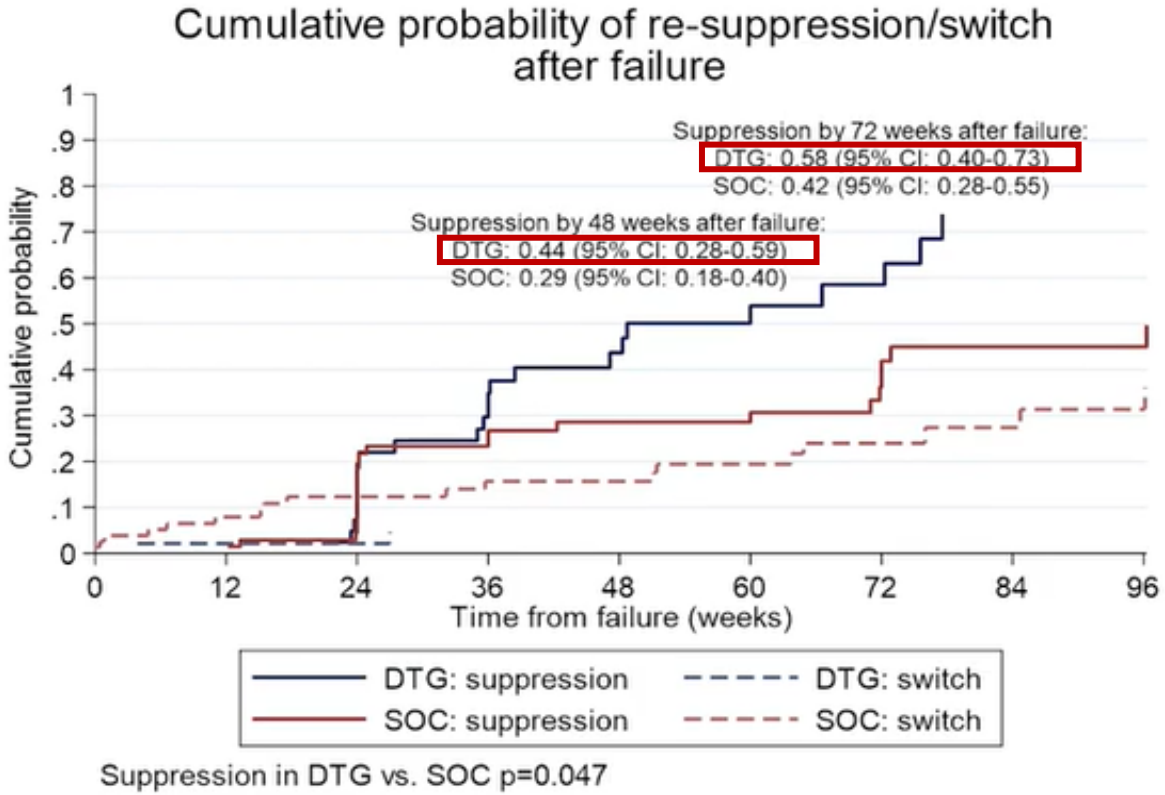
2 PI mutations in one child on **SOC 2nd line**

4 children on **2nd line DTG** developed ≥1 of 3 InSTI mutations

Time to Re-Suppression or ART Switch Post-Failure in Children in the ODYSSEY Trial

Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021

- Time to re-suppression [solid line] (2 consecutive VL <200 c/mL) or ART switch [dashed line] following viral failure (>400 c/mL)



**ART switch: switch in any drug due to treatment failure or switch in 3rd drug due to toxicity, pregnancy or protocol deviation (none in DTG arm)*

- ~15% of children in **SOC** with failure switched regimens by week 48, ~30% by week 96 (no switching with **DTG**).
- High proportion of children with viral failure resuppress after viral rebound even without ART switch; this was marginally better in **DTG** arm (44% vs 29% SOC resuppress by week 48, 58% vs 42% SOC by week 72).

Summary: Viral Failure and Genotypic Resistance in Children in the ODESSEY Trial

Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021

- DTG had high genetic resistance barrier in children.
- In children failing 1st line DTG ART, there was **no** post-failure resistance to any drug class.
- Among those on 2nd line DTG ART, there was no new NRTI/NNRTI/PI resistance, but 4 children developed new InSTI resistance.
- A high proportion of children resuppress after viral rebound without ART switch – with higher rates re-supppression in DTG arm.
- However, **none** of the children with **InSTI resistance** had resuppressed by end of trial.
- Supports use of DTG for both 1st and 2nd line ART - but **ongoing adherence support is needed, especially if child is on 2nd line DTG**.

Neuropsychiatric and Sleep Disturbances DTG vs SOC in the ODYSSEY Trial

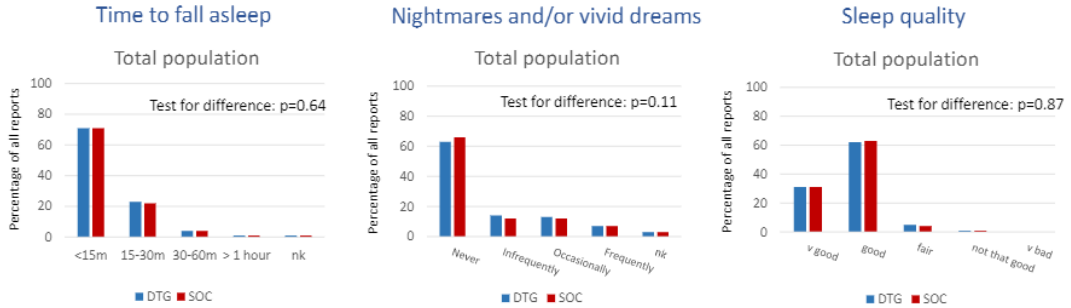
Violari A. International Pediatric HIV Workshop Abs 66/ Turkova A IAS Virtual Abs OAB505 July 2021

- Evaluated neuropsychiatric grade ≥3 adverse events or SAE; mood and sleep questionnaires completed wk 0, 4, 12, 24 and q24 wks.

	DTG	SOC	Total	P-value
	N=350	N=357	N=707	
All neuropsychiatric adverse events, N [N participants]	**18 [15]**	**13 [8]**	**31 [23]**	**0.125***
Serious Adverse Events	7 [5]	6 [5]	13 [10	
ART-modifying AEs$^{\Psi}$	2 [2]	2 [2]	4 [4]	
Hazard Ratio for time to first NPAE§ (95% CI)	1.87 (0.79, 4.41)	1 (ref)		**0.154**

	DTG	SOC	Total	P-value
	N=350	N=357	N=707	
Neurological AEs, N [N participants]	**6 [6]**	**6 [5]**	**12 [11]**	**0.736***
Epilepsy, convulsions	4 [4]	4 [4]		
Dizziness	0 [0]	2 [1]		
Headache, hypertension	1 [1]	0 [0]		
Dystonia	1 [1]	0 [0]		
Serious Adverse Events	**4 [3]**	**4 [3]**		
ART-modifying AEs$^{\Psi}$	**0 [0]**	**1 [1]**		
Hazard Ratio for time to first NPAE§ (95% CI)	1.18 (0.36, 3.87)	1 (ref)		**0.784**
	N=350	N=357	N=707	
Psychiatric AEs, N [N participants]	**12 [10]**	**7 [4]**	**19 [14]**	**0.097***
Suicidal ideation/behaviour	8 [8$^{\chi}$]	7 [4]		
Depression	2 [2$^{\chi}$]	0 0		
Insomnia	1 [1$^{\pi}$]	0 0		
Psychosis	1 [1$^{\pi}$]	0 0		
Serious Adverse Events	**3 [2]**	**2 [1]**		
ART-modifying AEs$^{\Psi}$	**2 [2]**	**1 [1]**		
Hazard Ratio for time to first PAE§ (95% CI)	**2.48 (0.78, 7.90)**	**1(ref)**		**0.125**

- AE infrequent; no difference neuropsych, neurologic AE; non-significantly more *psychiatric AE* in DTG

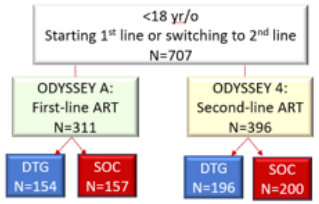


- No significant difference DTG vs SOC sleep data

N Reports, N [N participants]	TOTAL						
	DTG		SOC		Total		P-value*
Self-harm	8	[8]	1	[1]	9	[9]	0.038
Life not worth living	20	[17]	5	[5]	25	[22]	0.009
Suicidal thoughts	13	[13]	0	[0]	13	[13]	<0.001
Life not worth living or suicidal thoughts combined	27	[23]	5	[5]	32	[28]	0.001

* Comparison between participants ever reporting (carer or participant or both)

- No difference "low mood" or anxiety, but more participants/ carers report symptoms of self-harm, "life was not worth living" or suicidal thoughts in DTG arm. Most transient, none required ART change.



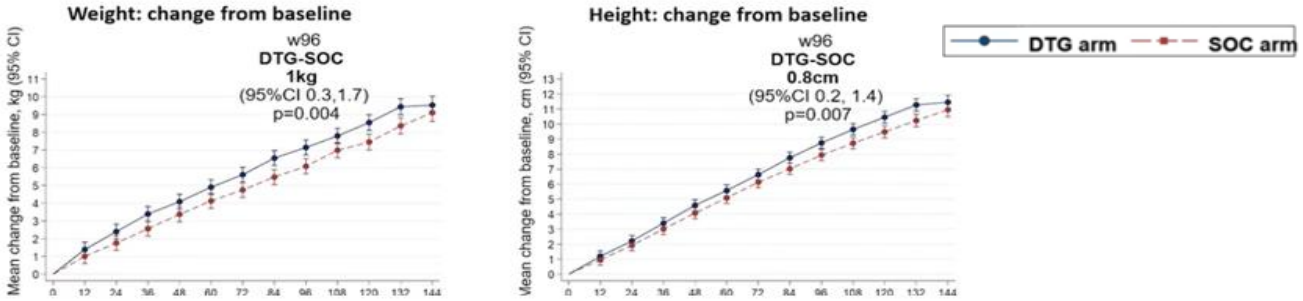
(Original study older children)

Weight Gain and Change in BMI in Children on DTG vs SOC in the ODYSSEY Trial

Mujuru H et al. International Pediatric HIV Workshop Abs 7/IAS Virtual Abs PEB202 July 2021

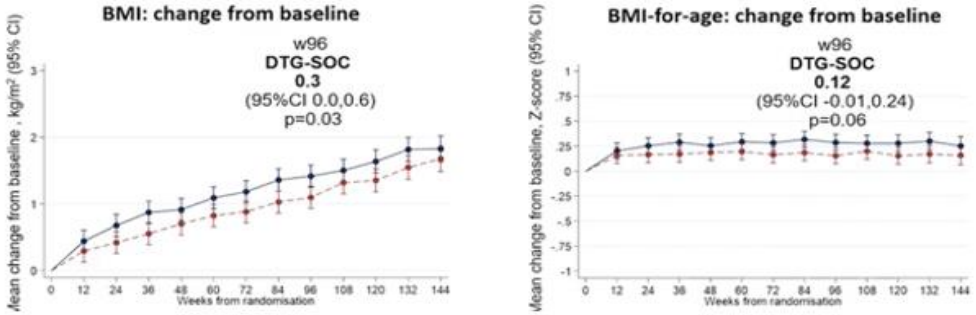
- At baseline only 5% overweight, 1% obese
- SOC arm anchor drugs: 1st line (A): 92% EFV-based; 2nd line (B): 72% LPV/r, 25% ATV/r; NRTI backbone overall: 65% ABC/3TC, 23% TDF/XTC, 11% AZT/3TC

Change from Baseline in Weight and Height DTG vs SOC



- Small additional gains from baseline in height and weight in DTG vs SOC
- At 96 weeks, mean added gain in DTG vs SOC in weight was 1 kg and height 0.8 cm
- The differences occurred early and stabilized

Change from Baseline in BMI and BMI-for-Age DTG vs SOC



- Small additional gains from baseline in BMI and BMI-for-age in DTG vs SOC
- At 96 weeks, mean additional gain in BMI in DTG vs SOC was 0.3
- The differences occurred early and gap between arms did not increase with time

- Differences were similar by 1st vs 2nd line, sex, age, and NRTI backbone (non-TDF vs TDF).
- 25 (4%) were newly overweight/obese at 96 weeks: 14 (4%) **DTG**, 11 (3%) **SOC**, **p=0.55**.

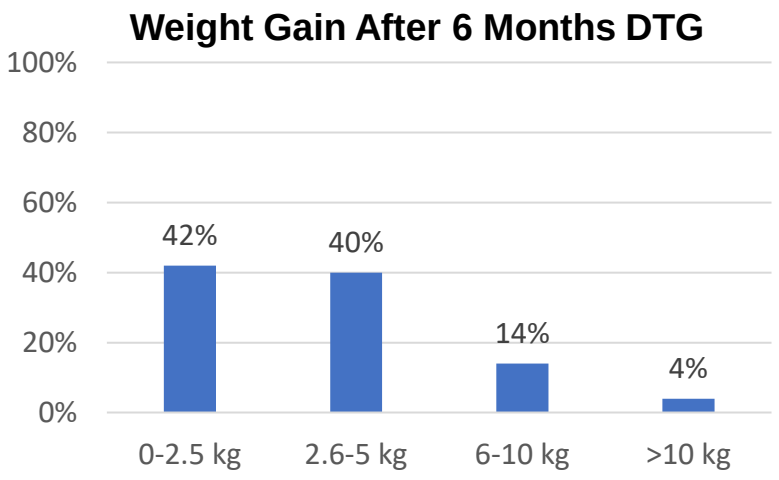
→ Children grew better after starting DTG vs SOC; differences between arms in weight, height and BMI were small and stabilized; few became newly overweight/obese either arm.

→ **DTG-based ART was not associated with excessive weight gain in children.**

Impact of DTG on Weight Gain in Adolescents at Baylor Mwanza-Tanzania

Masunga E et al. International Pediatric HIV Workshop Abs 8/IAS Virtual July 2021

- Retrospective study of 229 adolescents aged 10-19 years on DTG ART for >6 months (91% switched from other ART regimen); 96% had VL <1,000.
- Compared weight before (DTG switch visit) and after (visit after six months DTG).
- At baseline, 98% had normal BMI for age and 1.7% were overweight.
- After 6 mos DTG, 90% of youth gained weight, although only 18% gained >6 kg.



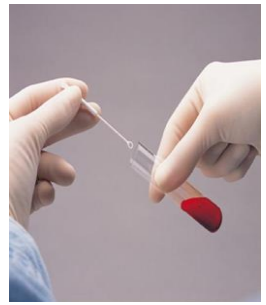
- The percent of youth overweight increased from 1.7% (4/229) before DTG to 8.7% 20/229) after being on DTG for 6 months (16 overweight, 4 obese).

→ In contrast to the ODYSSEY RCT, in this study, there was an increase in % of overweight/obese adolescents after 6 months on DTG.



Photo credit: Paul Jeffrey, World Council of Churches

ART Optimization, DTG Transition and VL Implementation Data

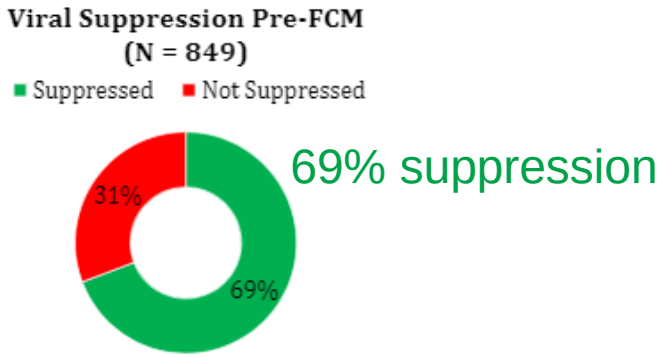




Impact Family-Centered Care on Viral Suppression in Children in Migori, Kenya

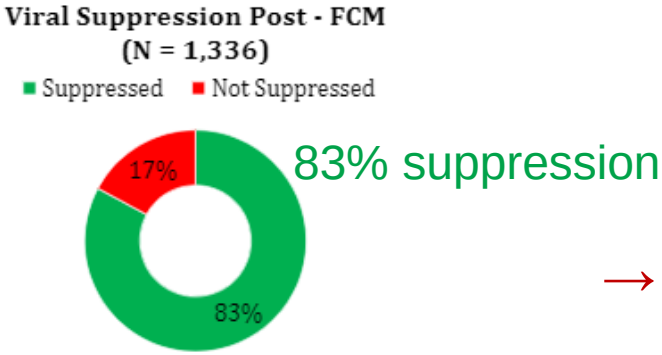
Ogiti D et al. IAS Virtual July 2021 Abs PED392

- Pre (Sep 2016-Dec 2017, n=849) and Post- (Dec 2018-Sep 2020, n=1336) evaluation of viral suppression in children 2-9 years before and after family-centered care model intervention (family/caregiver literacy sessions, peer educators, psychosocial support groups, ART optimization, and link to OVC support programs) implemented at 8 sites.



69% suppression

Characteristic	n	Sup-pressed	% Sup-pressed
Age groups (yrs)			
2 - 6	374	233	62
6 - 9	475	355	75
Sex			
Female	489	339	69
Male	360	249	69
ART Regimen			
EFV Based	212	159	75
NVP Based	360	239	66
PI Based	268	185	69
Other	9	5	56



83% suppression

	N	Sup-pressed	% Sup-pressed
Age Category (yrs)			
2 - 6	591	473	80
6 - 9	745	634	85
Sex			
Female	753	641	85
Male	583	466	80
ART Regimen			
DTG Based	94	84	89
EFV Based	646	542	84
NVP Based	68	54	79
PI Based	502	403	80
Other	25	23	92

→ After adjusting for age and sex, children in the post-FCM period were 2-fold more likely to be virally suppressed compared to those in the pre-FCM period (aOR 2.2, 95% CI 1.7-2.7)

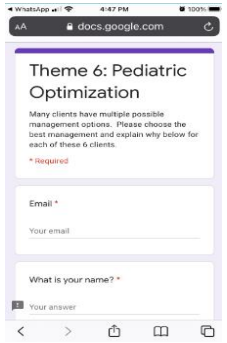
Virtual Pediatric Optimization Toolkit (V-POT) and Family ART Days Support Pediatric ART Optimization in Malawi during COVID-19

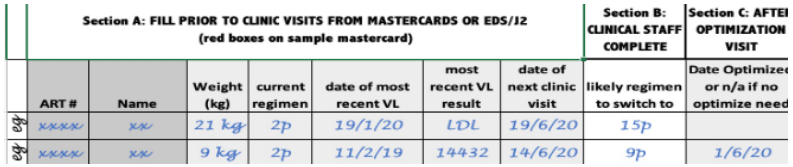
Cox C et al. International Pediatric HIV Workshop Abs 115/IAS Virtual Abs PED516 July 2021

- To facilitate transition to optimized pediatric ART despite COVID-19 restrictions at 120 health facilities in Malawi, Ap-Dec 2020.
  - Established **family ART days** to facilitate phone consult by clinician mentors and encourage guardian peer-peer support.
  - Created **V-POT** for clinical and lay staff via email and WhatsApp using voice notes, video and Google form quizzes (examples below).

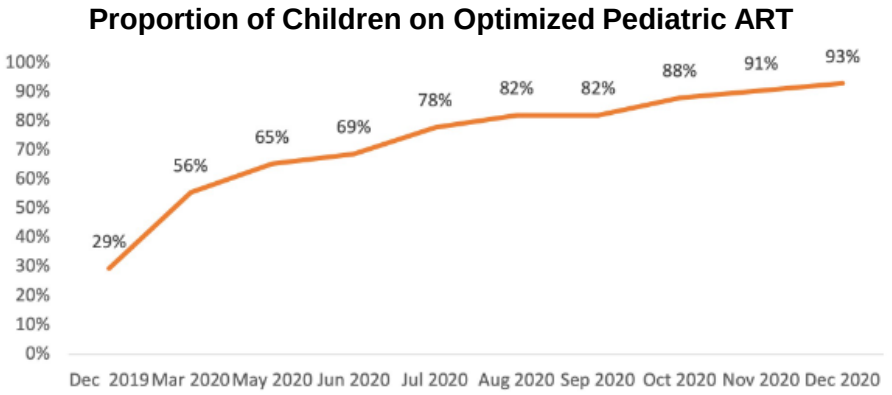








	Section A: FILL PRIOR TO CLINIC VISITS FROM MASTERCARDS OR EDS/J2 (red boxes on sample mastercard)							Section B: CLINICAL STAFF COMPLETE	Section C: AFTEI OPTIMIZATION VISIT
	ART #	Name	Weight (kg)	current regimen	date of most recent VL	most recent VL result	date of next clinic visit	likely regimen to switch to	Date Optimize or n/a if no optimize need
eg	xxxx	xx	21 kg	2p	19/1/20	LDL	19/6/20	15p	
eg	xxxx	xx	9 kg	2p	11/2/19	14432	14/6/20	9p	1/6/20



Educational video on LPV/r granules administration

- Offloading need to disrupt busy staff during clinic hr
- Accurate and consistent messaging
- Allow repeat viewing by guardians/clinic staff

Case-based self-study for clinical mentors

- Orienting and reinforcing recommended optimization strategies by reviewing common questions and challenging cases

Decision-making tool to guide ART transition

- Facility-based providers record child's data and experienced clinician mentors provide clinical action guidance by phone

→ Children on optimized ART regimens ↑ from 29% in Dec 2019 to 93% by Dec 2020

→ V-POT and family ART days easily implemented at scale to facilitate identification and consultation on complex cases for pediatric regimen optimization

Rapid-VL Study: Optimizing VL Monitoring and Outcomes for High-Risk Populations, Uganda

Vivek J et al. IAS Virtual July 2021 Abs OALD01LB3

- Pre-post-cluster randomized trial looking at 'differences in differences' analysis

Non-high-risk adults and 4 **high risk** groups:
- **Pregnant/breastfeeding women**
- **Children/adolescents**
- Viremic patients
- Patients overdue for VL (>1 yr)

2017-2018 Pre-intervention phase
(retrospective)
N=1200
20 clinics, n=60/clinic

2018-2020 Intervention phase
(prospective)
N=1200
20 clinics, n=60/clinic

10 clinics: RAPID-VL intervention

10 clinics: SOC

Primary outcomes:
- Results to patient turn-around time
- Guideline adherent VL ordering

Secondary outcome:
- HIV viral suppression (<400 c/mL)

RAPID-VL: 3 component intervention

1. Viral load flow sheet tool

Today's Date	ART Start Date	Last Viral Load			Today's Visit				
		Date Drawn	Result (circle one or enter value)	Date Given to Patient	ART Status (circle one)	Adherence (circle one)	VL Counseling Done? (circle Y or N)	Ordering VL Today? (circle Y or N)	Type of Test: (circle one)
			<40 c/mL <1000 c/mL Result invalid No prior VL Result Value: _____		Pre-ART ART <6mo. ART >6mo.	Off ART Incomplete Good	Y N	Y N	Routine DBS Rapid POC Both

\+ **2. Cepheid Xpert VL in Hub**



- Hub-spoke model
- 2 hubs & 10 clinics in 2 geographic regions
- Specimen transport daily by motorcycle
- Result by phone to clinician

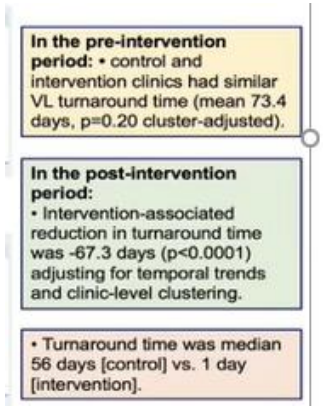
\+ **3. VL Counseling Script**

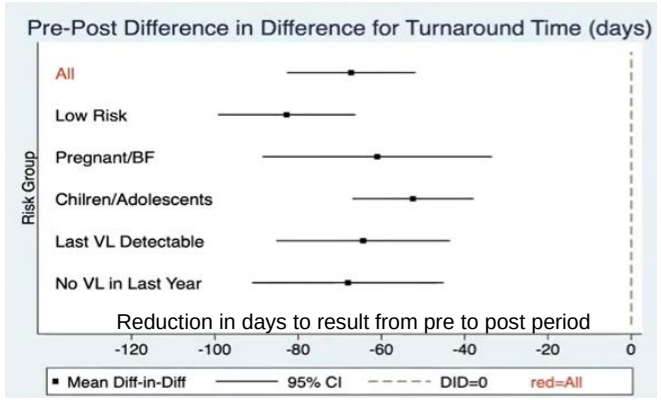
New patient	Established patient
VL Undetectable	VL Detectable

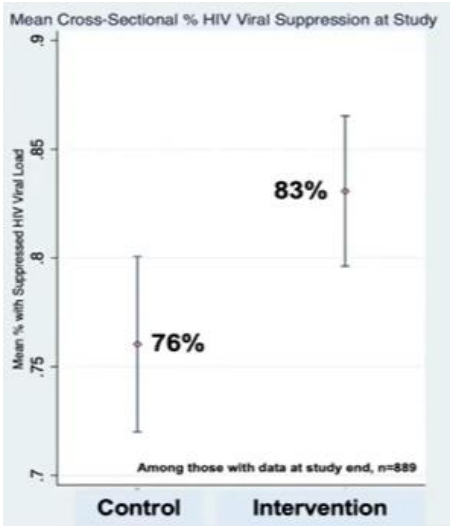
Rapid-VL Study: Optimizing VL Monitoring and Outcomes for High-Risk Populations, Uganda

Vivek J et al. IAS Virtual July 2021 Abs OALD01LB3

- Substantial **reduction in VL result turnaround time** to patients in RAPID-VL clinics pre-post compared to control clinics pre-post in **all subgroups**
- RAPID-VL had significantly **improved VL ordering** (+10.4%, p=0.01), including in pregnant/BF women, last VL detectable, VL overdue
- RAPID-VL **improved viral suppression** including in children (but not pregnant/BF women - who had high suppression to begin with)





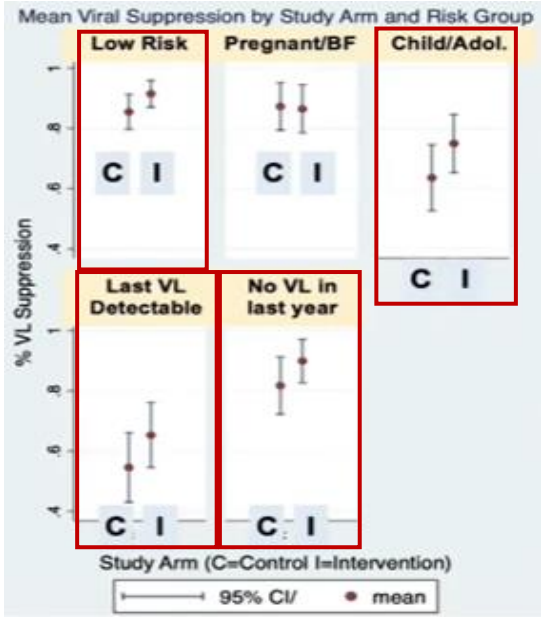


Overall mean VL suppression one year after intervention start among measured persons:

Control clinics: **76%**
Intervention clinics: **83%**
Difference: **+7%**, p=0.03 (cluster-adjusted)

Suggestion of improvement in VL suppression in subgroups:
- Non high-risk persons
- Children/adolescents
- Persons with last VL detectable
- Persons with VL overdue

VL suppression appeared similar in:
- Pregnant/breastfeeding women

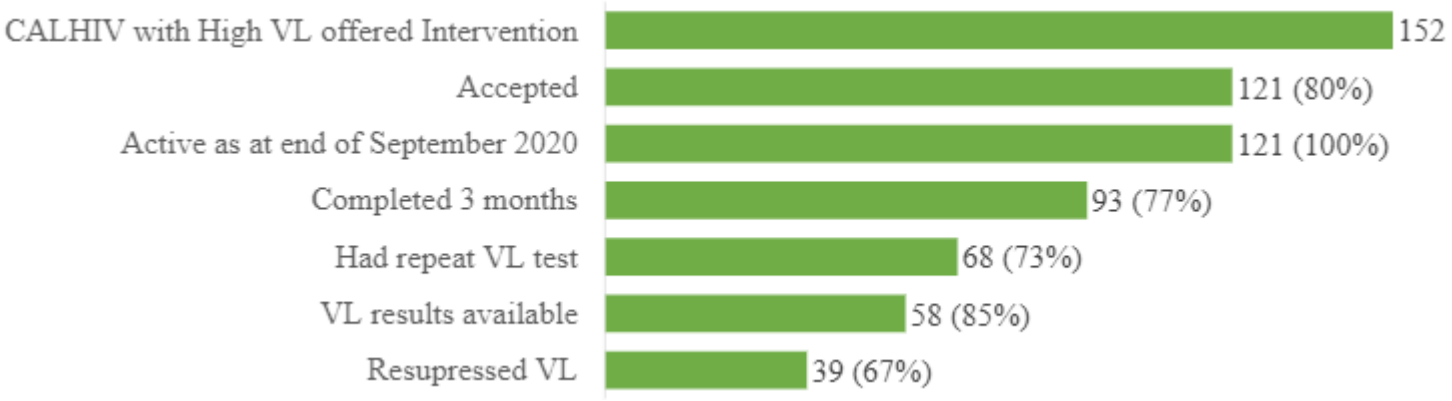


Virtual Enhanced Counseling and Viral Suppression During COVID-19 Pandemic, Kenya

Wangusi R et al. IAS Virtual July 2021 Abs Late Breaker PEV213

- For children with high viral load during COVID-19, implemented phone-based virtual enhanced adherence counseling (VEAC) and daily ART intake reminders at 18 facilities; evaluated 3 mo VL.
  - SOP and training of HCW with provision of phones;
  - Written consent from caregivers;
  - Phone alarms aligned for clients and case managers to the time of taking medication and case-manager conducted daily calls to confirm drug intake.
  - Adherence counselors called caregivers 2 weekly for VEAC.

Retention and Viral Load Resuppression Among Children Provided Daily ART Reminder and VEAC, May-Sept 2020



→ High acceptability of intervention

→ Excellent retention in program

→ Viral re-suppression in 67% within 3 months

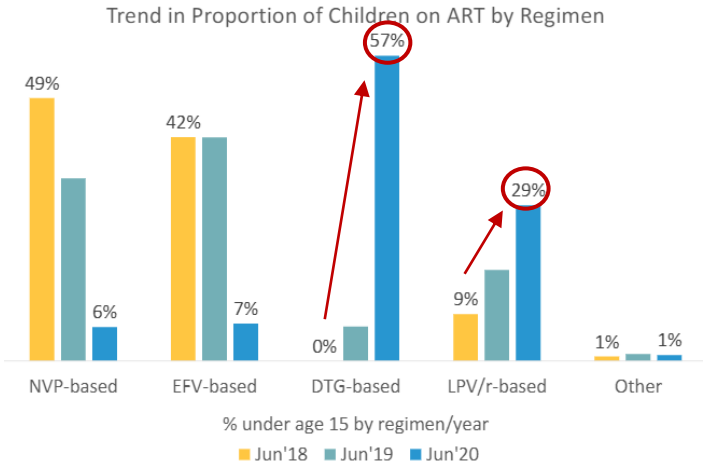
→ Consideration of scale-up of program for children with viral failure

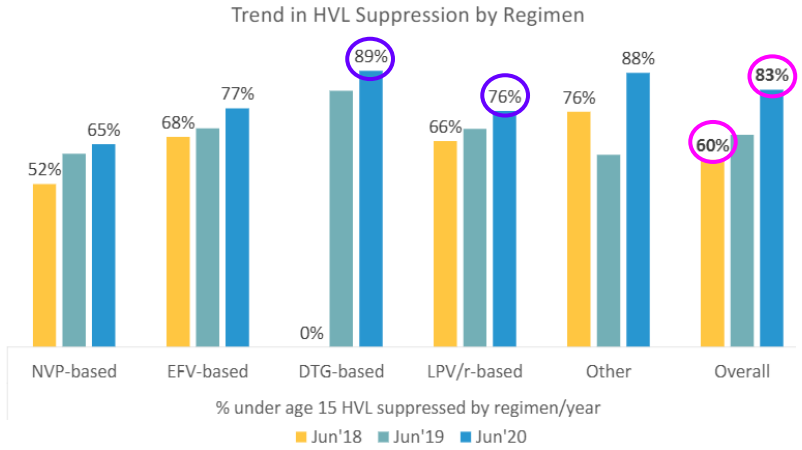
Elizabeth Glaser Pediatric AIDS Foundation
Fighting for an AIDS-free generation

Impact of Pediatric ART Optimization 2018-2020 on Viral Suppression in Tanzania

van de Ven Ret al. IAS Virtual Ab PEB210 July 2021

- Retrospective cross-sectional review program data from 325 facilities in 5 regions in Tanzania to assess transition to optimal ART regimens (LPV/r <20 kg, DTG ≥20 kg) & viral suppression in children 0-14 yr.





→ Within 2 years (June 2018-June 2020) children on optimal regimen ↑ from **9%** to **86%**

→ Viral suppression ↑ over same period from **60%** to **83%**.

→ Children on LPV/r as optimal regimen lower suppression **76%** vs DTG **89%**; **may see added benefit once DTG becomes available for young children instead of LPV/r**.



Viral Suppression in Children and Adolescents on DTG, Zimbabwe

Kouamou V et al. International Pediatric HIV Workshop Abs 56

- 390 children/youth enrolled in a community-based ART (CBART) trial in rural Zimbabwe enrolled 2018-2019; **184 had switched to TLD as of July 2020** (median age 15 years, IQR 11-19 years).
- Prior to switch, 63% (n=115) were receiving 1st line NNRTI (83% on TLE, 17% ABC/3TC/EFV or NVP); and 38% (n=69) were on 2nd line PI ART (81% ATV/r) primarily with ABC/3TC (only 6% receiving TDF).
- Prior to TLD switch, **76%** (139/184) had **VL <1,000**.
- After median duration 6.9 mos (IQR 5-9.1) on TLD, **95% (174) had VL <1,000**.
- Of the 10 patients with VL ≥1,000 on TLD, 9/10 had VL >1,000 on *prior* regimen.
- Being on prior **PI-based ART regimen** more likely to fail compared to prior 1st line NNRTI ART (10.1% vs 2.6%, p=0.042).

→Suggests need for **enhanced VL monitoring and adherence counseling in children with prior ART failure** (esp. 2nd line PI ART) who are switched to TLD.

DTG Transition in Mozambique

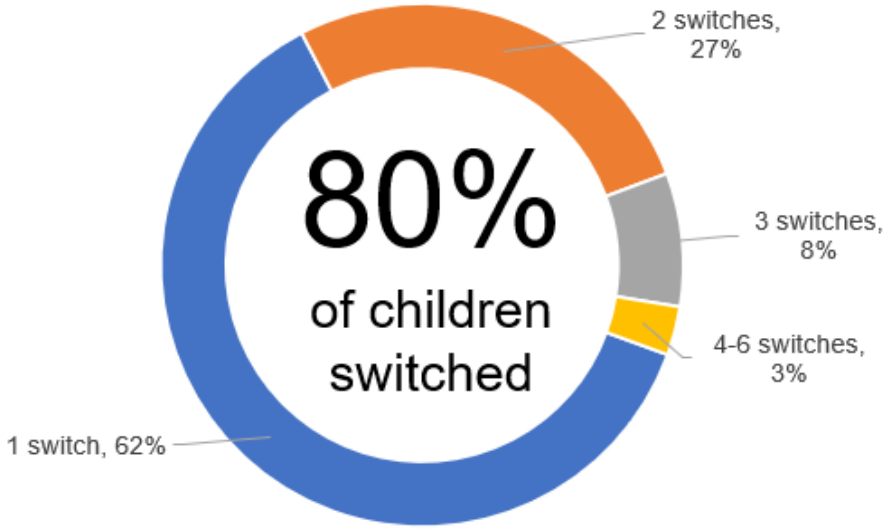
Gill M et al. International Pediatric HIV Workshop Abs 26/IAS Virtual Ab PED639 July 2021



- Evaluation of **ART optimization** in 3,107 HIV-positive pediatric clients ≥5 yrs (proxy for weight ≥20 kg) on ART at 16 facilities in 2 provinces, Mozambique.
- Clinical record abstraction from children/adolescents receiving HIV services the start of new Mozambique ART guideline implementation (rollout of DTG 50 mg tablets for children ≥20 kg) in September 2019 to August 2020.
- Data collected in 'rounds' to allow for ongoing data cleaning and analysis
  - First round: Sept 2019 – Feb 2020 (completed) – evaluate **switching**
  - Second round: Mar 2020-Oct 2020 (completed) – evaluate **VL response**
  - Third round: Nov 2020 – Aug 2021 (planned)

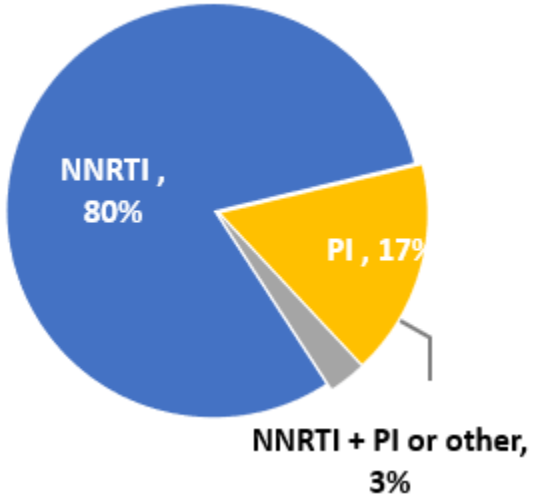
Pediatric ART Regimen Switching

Gill M et al. International Pediatric HIV Workshop Abs 26/IAS Virtual Ab PED639 July 2021



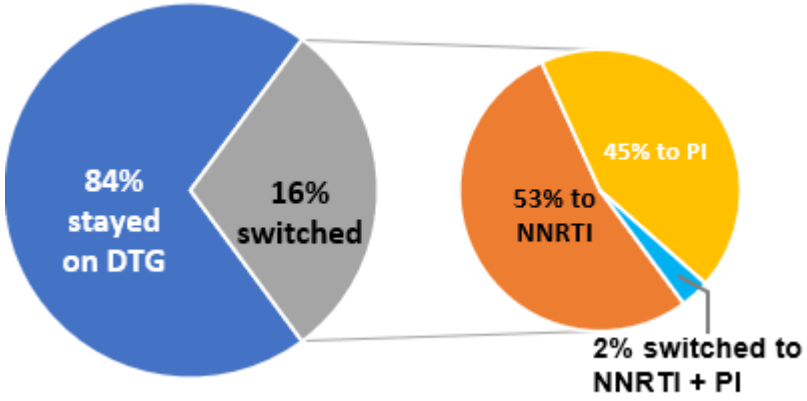
Of those who switched, **81%** (2,009/2,488) switched to a DTG-based regimen within 6 mos

Regimens prior to switch to DTG



However, **16%** (319/2,009) of children switched to DTG **then** switched to other regimens within 6 mos

Regimens switched to after DTG



→ At last visit, 74% (2,311/3,107) of children were on DTG (includes 1,904 who *switched* to DTG and 407 who were on DTG for the *full* 6-month follow-up period)

Reasons for Switching From DTG to Other ARV

Gill M et al. International Pediatric HIV Workshop Abs 26/IAS Virtual Ab PED639 July 2021



- At least 5 out of 16 sites reported **stock-outs** of DTG 50mg tablets.
  - Some site stock-outs reflected broader stock shortages at provincial or national level.
- 48/319 (15%) children who switched to DTG and then switched to other regimens had recorded weights of < 20 kg at ≥ 1 visits within the 6 months.
  - Providers may have course-corrected for DTG ineligibility.
  - 19/319 (6%) children did not have any weight data available.

1st - 2nd Round Analysis – Viral Load

Gill M et al. International Pediatric HIV Workshop Abs 26/IAS Virtual Ab PED639 July 2021



- **1,121 children were on continuous DTG for ≥3 months** (median 11.0 months).
- Of these children, 1,085 had VL results available after ≥3 months on DTG (median 7.3 months after DTG start), with 998 having both pre- and post-DTG viral load available.

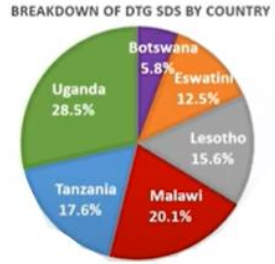
998 children with VL pre-DTG and post-DTG ≥ 3 mos

VL Result N (%)	VL Pre-DTG	VL Post DTG ≥ 3mos
Undetectable VL <50	414 **(41.9)**	698 **(70.7)**
Suppressed VL 50-<1000	89 (9.0)	85 (8.6)
Unsuppressed VL ≥1000	485 (49.1)	205 (20.7)

Outcomes of Single-Drug Substitutions in Children Switched to DTG ART, 6 Countries Africa

BIPAI Baylor International Pediatric AIDS Initiative at Texas Children's Hospital

Bacha J et al. International Pediatric HIV Workshop Abs 25/IAS Virtual Abs OALB0504 July 2021



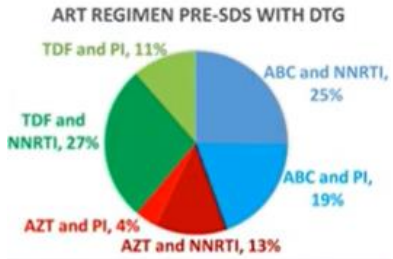
- Retrospective review from 7 Baylor sites in 6 countries in 2,655 children 0-19 years enrolled in care and switched to DTG ART **without modifying NRTI backbone** from Jan17-Dec 20; **most children (96%) were suppressed** at time of switch.

→Those suppressed at baseline remained suppressed after switch

Cohort of CALHIV with DTG SDS	Viral Suppression Rate (VL<1000cp/mL)		P-value
	Pre-DTG switch	Post-DTG switch	
With pre- and/or post-DTG VL (n=2660)	**95.1%**(2496/2625)	**94.0%** (2016/2145)	0.09
With both pre- and post-DTG VLs (n=2120)	**95.9%** (2032/2120)	**95.0%** (2014/2120)	0.19
TLE→TLD cohort (N=694)	**96.2%** (657/683)	**95.0%** (555/584)	0.30
TDF-3TC-PIr→TLD cohort (N=298)	**90.3%** (269/298)	**88.0%** (182/207)	0.43
ABC/NNRTI→ABC/DTG cohort (N=669)	**92.5%** (347/375)	**95.7%** (538/562)	**0.04**
ABC/PI→ABC/DTG cohort (N=513)	**93.8%** (473/504)	**91.3%** (348/381)	0.16

→83% of the 88 children <u>not</u> suppressed at baseline became suppressed after switch

Cohort of CALHIV (N, % previously unsuppressed pre-DTG)	Viral Suppression after SDS with DTG (among those with post-DTG VLs)
All CALHIV with DTG SDS (n=129, 4.9%)	83.0% (73/88)
TLE→TLD cohort (n=26, 3.8%)	90.5% (19/21)
TDF-3TC-PIr→TLD cohort (n=29, 9.7%)	72.7% (8/11)
ABC/3TC/NNRTI→ABC/3TC/DTG cohort (n=28, 7.5%)	89.5% (17/19)
ABC/3TC/PI→ABC/3TC/DTG cohort (n=31, 6.2%)	79.2% (19/24)



→Switch of only 3rd anchor drug was effective option for achieving viral suppression.

→Those who were suppressed generally maintained suppression.

→Most of those who were not suppressed (although few in number) remained suppressed despite single drug substitution.

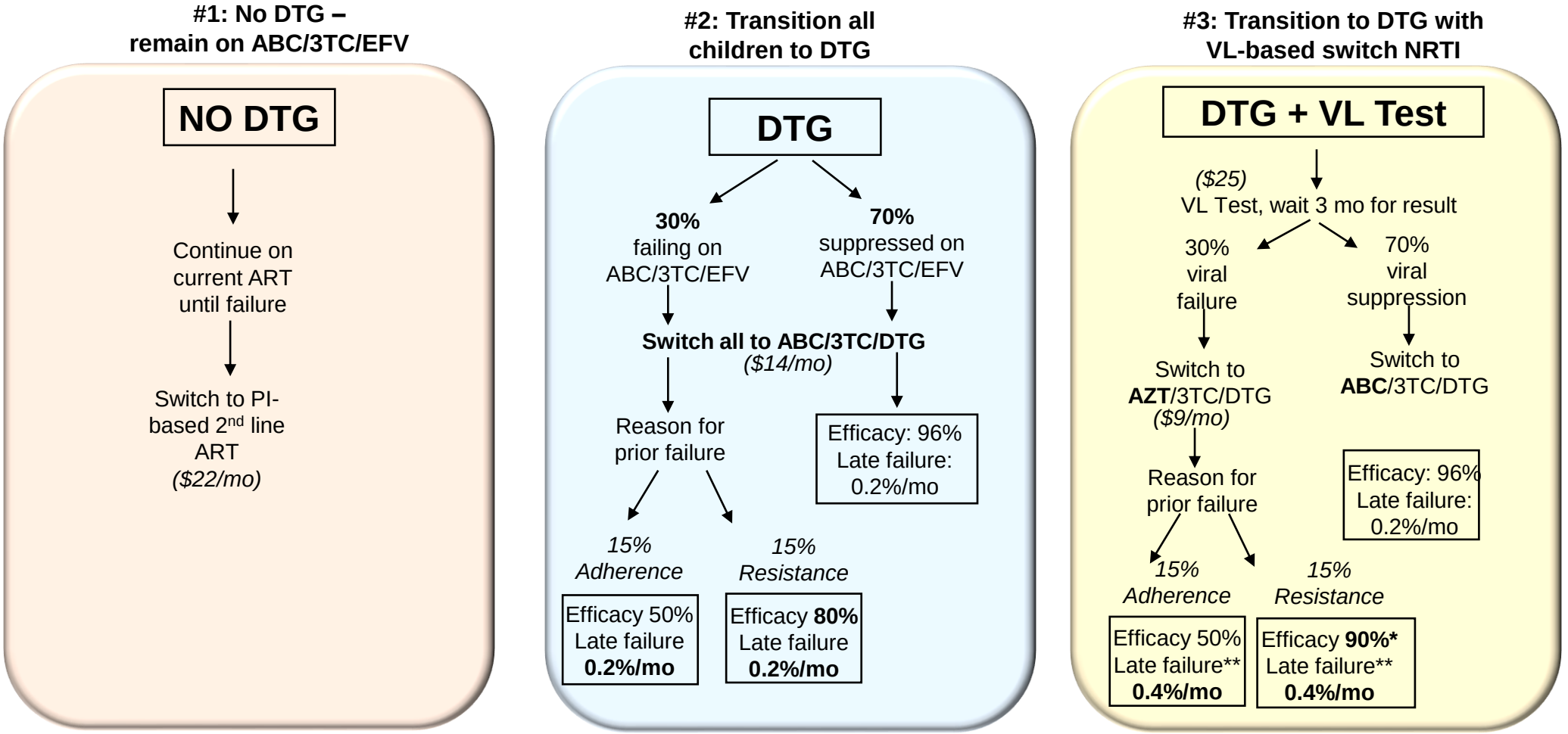
→Supports programmatic switch to DTG in settings without pre-switch VL testing.

MASSACHUSETTS GENERAL HOSPITAL
MEDICAL PRACTICE EVALUATION CENTER

Impact and Cost-Effectiveness of VL Testing to Inform Transition to DTG ART in ART-Experienced Children, South Africa – CEPAC Model

Brenner IR et al. International Pediatric HIV Workshop Abs 6

- Modeled cohort of HIV+ children aged 8 years on ABC/3TC/EFV and 3 strategies:



** efficacy better when resistance because here you change NRTI*

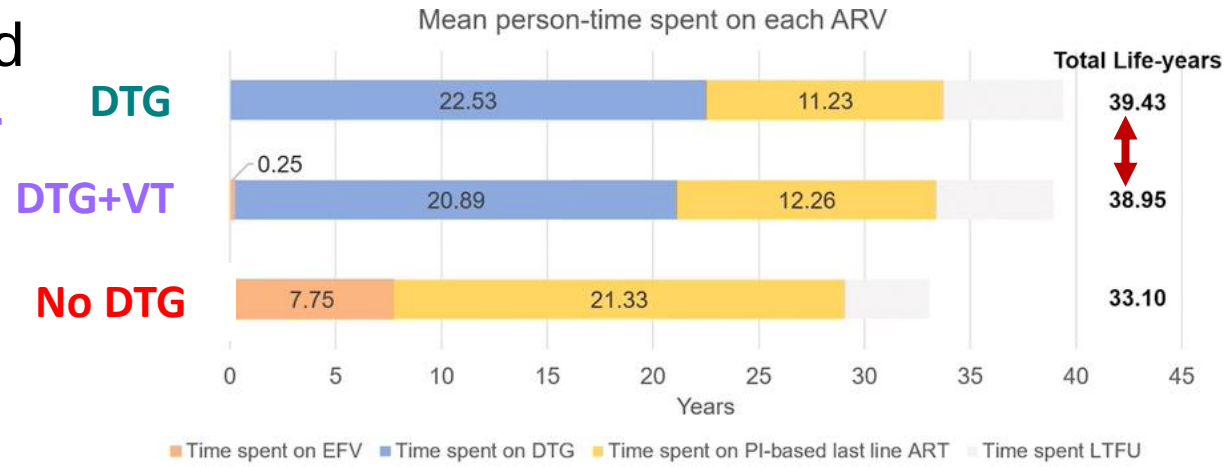
*** late failure higher with twice daily AZT*

Efficacy: probability of viral suppression at 24 weeks; Late failure: Monthly probability of viral failure after 24 weeks

Impact and Cost-Effectiveness of VL Testing to Inform Transition to DTG ART in ART-Experienced Children, South Africa – CEPAC Model

Brenner IR et al. International Pediatric HIV Workshop Abs 6

- Clinical outcomes: Both DTG strategies had better life expectancy than **no DTG**; **DTG + VL testing** had lower life expectancy than switch to **DTG without VL testing**, *mostly due to assumed lower efficacy of bid AZT switch associated with VL testing strategy.*



- Cost: Both DTG strategies had cost-savings compared to **no DTG**. **DTG without VL** testing gave more life-years at slightly higher cost than **DTG with VL testing**, resulting in preferred strategy, with incremental cost-effectiveness ratio of $850/life-year saved, below the threshold of $3000 for S Africa.

Lifetime projections

Strategy	LY (undiscounted)	Costs, $ (discounted)	ICER* ($/LYS)
No DTG	33.10	12,000	Most expensive, least effective
DTG+VT	38.95	11,260	-
DTG	39.43	11,340	850

Cost-effectiveness threshold: $3,000/LYS

Impact and Cost-Effectiveness of VL Testing to Inform Transition to DTG ART in ART-Experienced Children, South Africa – CEPAC Model

Brenner IR et al. International Pediatric HIV Workshop Abs 6

- Transition to DTG will improve outcomes and save money regardless of use of VL testing to select NRTIs.
- Results related to DTG + VL testing depend on 1*) the effectiveness of AZT compared to ABC (limited data)* and 2) *delay in time to return of VL results*.
  - Sensitivity analysis:
    - If AZT was **at least as clinically effective** as ABC, **then *DTG + VL testing preferred***
    - If time to receive VL result was **<1 month** (e.g., POC testing or strengthen lab system), **then *DTG + VL testing preferred***
- If VL testing is used to guide transition, use of POC or other strategies to improve VL return time should be implemented.
- Long-term data on efficacy of DTG in combination with different NRTIs should be collected as DTG roll-out in children occurs.





Photo credit: Paul Jeffrey, World Council of Churches

Pediatric ART
New ARV Drug Formulation/ Regimens in Children





PK and Safety of Dispersible and Whole Tablet FDC ABC/3TC/DTG in Children ≥14 kg: IMPAACT 2019

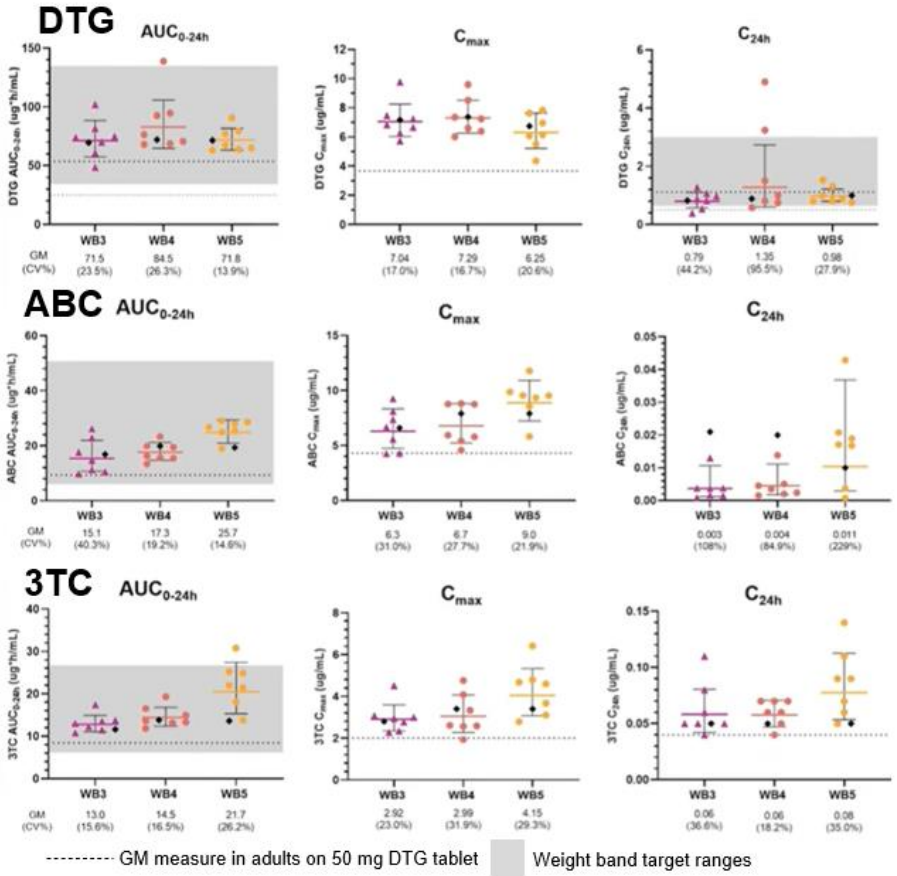
Brooks K et al. International Pediatric HIV Workshop Abs 3/IAS Virtual PEBLB15 July 2021

- Phase I/II dose confirmation study of FDC ABC/3TC/DTG dispersible tablet; enrolled children age <12 years, ART-naïve or ART-experienced with VL <200 on stable non-NNRTI regimen for >6 mos in 5 WHO weight bands (results for bands 3-5 [14-≥25 kg]).

WB1 (6 to <10 kg)	ABC 180mg/DTG 15mg/3TC 90mg •3 DT dispersed in 15 mL water	
WB2 (10 to <14kg)	ABC 240mg/DTG 20mg/3TC 120mg •4 DT dispersed in 20 mL water	
WB3 (14 to <20 kg)	ABC 300mg/DTG 25mg/3TC 150mg •5 DT dispersed in 20 mL water	N=7
WB4 (20 to <25kg)	ABC 360mg/DTG 30mg/3TC 180mg •6 DT dispersed in 20 mL water	N=7
WB5 (≥25 kg)	ABC 600mg/DTG 50mg/3TC 300mg •1 IR tablet swallowed whole	N=7

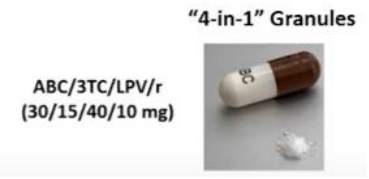
Safety

- No Grade >3 AE
- No dc study drug
- No AE needed intervention



→PK targets were met for dispersible release ABC/3TC/DTG in children >14 kg; dispersible tablets were well tolerated

→Long-term data through week 48 and PK/safety data on children **<14 kg** are forthcoming



PK, Safety, and Acceptability of Single-Dose ABC/3TC/LPV/r (4-in-1) Fixed-Dose Granule Formulation in Newborns: PETITE Study

Cressey T et al. International Pediatric HIV Workshop Abs 5/IAS Virtual Abs PEBLB16 July 2021

- Phase 1/2 study of 4-in-1 formulation in neonates

Cohort 1A: (n=8)
- HIV-exposed neonate (pending HIV status)
- On SOC ARV prophylaxis
- **>14 days of age**
- BW ≥**2500** to ≤4000 g



Single dose 4-in-1 & PK Sampling

≥14 and <21 d life

Cohort 1B(n=8)
- HIV-exposed neonate (pending HIV status)
- On SOC ARV prophylaxis
- **≥3 and <14 days of age**
- BW ≥**2000** to ≤4000 g



Single dose 4-in-1 & PK Sampling

≥3 and <14 d life



Single dose 4-in-1 & PK Sampling

10-14 d afterward

Acceptability

Administration 4-in-1 to neonates



4-in-1 was found easy to swallow

Capsule opened and suspended in milk and given by syringe or cup

Safety

All Adverse Events reported were **not related** to study drug

No deaths of life-threatening events occurred: **16 participants had 35 AEs**

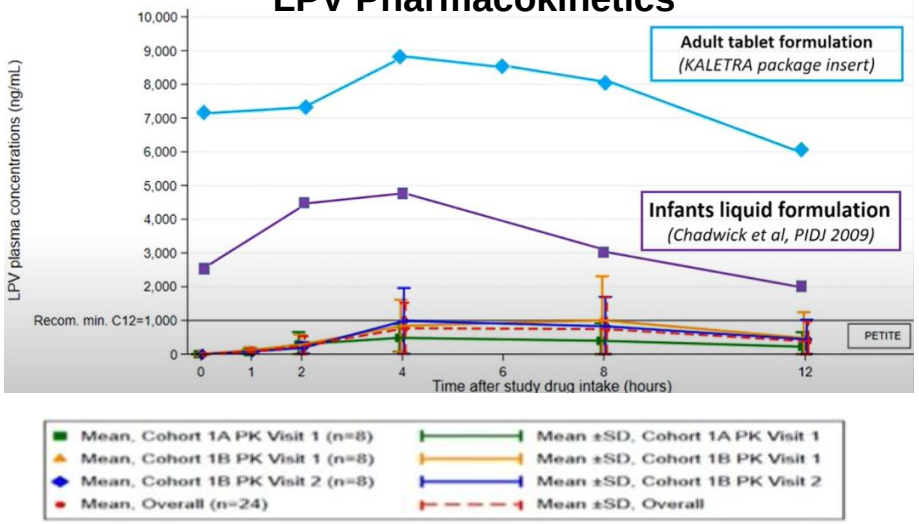
Severity	Participants with at least one AE	Number of AEs
Grade 1 (Mild)	15 (83%)	27 (77%)
Grade 2 (Moderate)	7 (39%)	7 (20%)
Grade 3 (Severe)	1 (6%)	1 (3%)
Total	16 (89%)	35 (100%)

Only 1 SAE with a participant requiring hospitalization

Severe adverse event	Relatedness	Outcome
RSV pneumonia	Not Related	Recovered/ resolved

ECG findings: All HRs, QT intervals and QTcF calculations were within normal limits for neonates

LPV Pharmacokinetics



ABC/3TC Pharmacokinetics

- ABC and 3TC plasma concentrations were as expected (slightly higher than older children)

→**Very low LPV/r levels of concern** (rtv BLQ in 4/120 (3%) samples)

→Protocol amendment will evaluate separate LPV/r granules (40/10 mg) and ABC/3TC dispersible tablet

Once-Daily NNRTI-Sparing ART Regimen DRV/r + InSTI is Non-Inferior to SOC in Virally-Suppressed Children – PENTA-17

Compagnucci A et al. International Pediatric HIV Workshop Abs 1/IAS Virtual Abs PEB201 July 2021

- PENTA-17 SMILE trial: phase 2/3 multicenter, open-label non-inferiority trial

318 HIV+ children aged 6-18 years
- On 3 drug PI/r or NNRTI ART ≥6 mos
- VL <50 c/mL for ≥12 mos
- No evidence resistance to DRV or InSTI

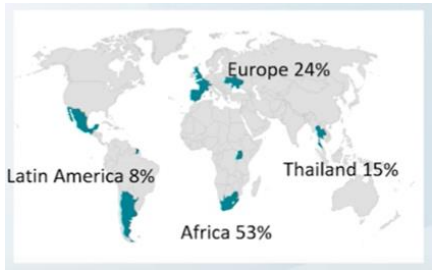
NNRTI-Sparing DRV/r + InSTI N=158

Standard Triple ART N=160

FU weeks 4, 12, 24, 36, 48 and every 12-16 weeks thereafter

PRIMARY ENDPOINT: Viral failure at 48 weeks
(non-inferiority margin 10%)

- Enrolled 318 children from 31 sites in 11 countries



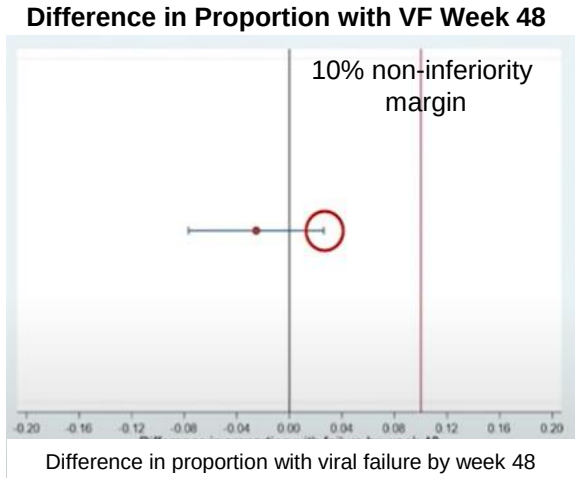
- Median age 14.7 years
- Median CD4 count 782
- Median cumulative ART exposure 11 years
- ART prior to randomization
  - NNRTI 59%, PI 41%
  - ABC/3TC 36%, AZT/3TC 33%, TDF/FTC 18%

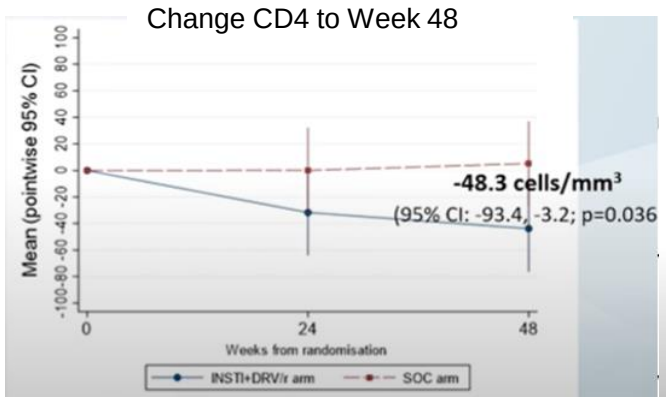
Once-Daily NNRTI-Sparing ART Regimen DRV/r + InSTI is Non-Inferior to SOC in Virally-Suppressed Children – PENTA-17

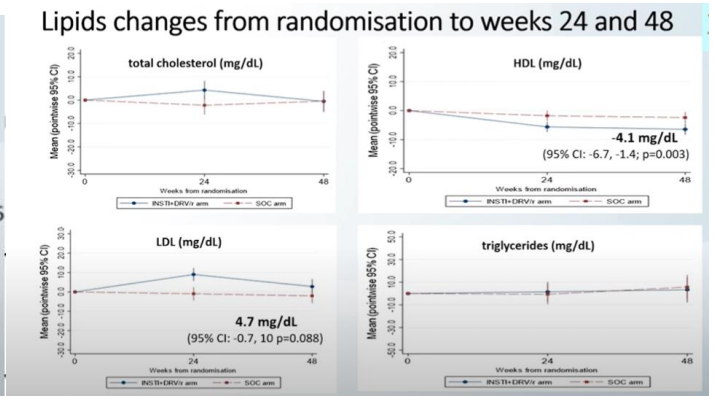
Compagnucci A et al. International Pediatric HIV Workshop Abs 1/IAS Virtual Abs PEB201 July 2021

	InSTI+DRV/r n=158	SOC n=160
Failure (RNA ≥50 c/mL)	8	12
Probability failure (95% CI)	5% (1.7, 8.4)	7.6% (3.5, 11.7)
Difference (InSTI+DRV/r – SOC)	-2.5% (-7.7, +2.6); **p value 0.335**	

- Non-inferior viral response with InSTI+DRV/r
- No new clinical events and no deaths
- No difference AE; no InSTI or PI resistance in failures



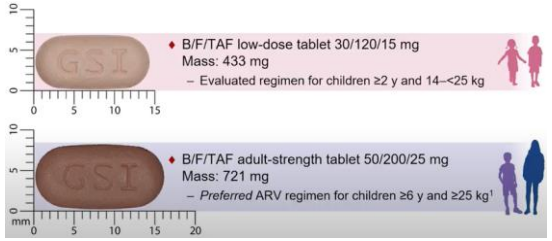




InSTI+DRV/r SOC

- Slight difference in CD4 count (slight loss with InSTI+DRV/r) and lipids (lower HDL, higher LDL)

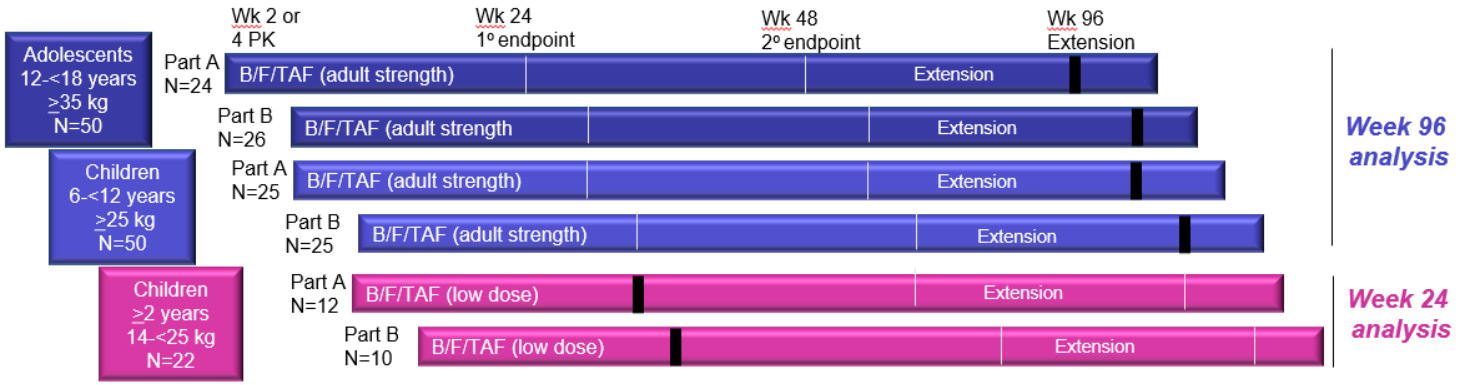
→ In virologically suppressed children without PI/InSTI resistance, switching to NNRTI-sparing regimen InSTI+DRV/r was **non-inferior** virologically and clinically

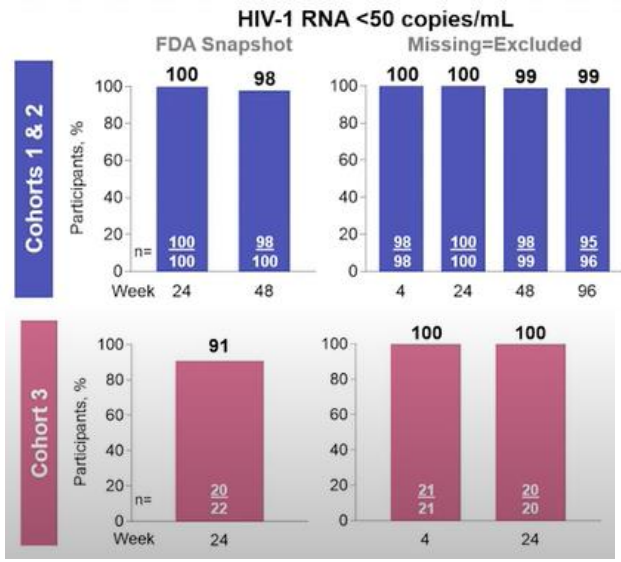


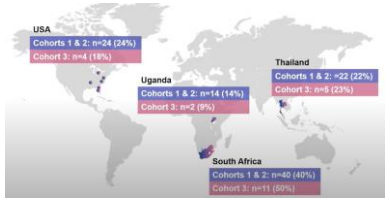
Long-Term Safety and Efficacy of Bictegravir/FTC/TAF in Virally Suppressed Adolescents and Children

Natukunda E et al. International Pediatric HIV Workshop Abs 2

- Phase 2/3 open-label switch to B/F/TAF 50/200/25 mg (lower dose 30/120/15 mg in children ≥2 years & 14-<25 kg) in children on stable ART with RNA <50 c/mL for ≥6 mos, CD4 ≥200 and eGFR ≥90mL/min/L; part A was PK to confirm dose; Part B complete cohort and start enrollment into next younger cohort.







No treatment emergent resistance observed

	Age 6-<18 yr N=100	Age ≥2 yr & 14-25 kg N=22
Median exposure drug (IQR)	151.4 wk (126, 154)	54.9 wk (29, 66)
AE related to study drug	13 (13%)	3 (14%)
Grade ≥3 AE	5 (5%)	0
SAE	5 (5%)	0
AE with drug dc*	1 (1%)	0
Death	0	0

*One pt dc drug around week 20 due to grade 2 insomnia and anxiety cohort 2

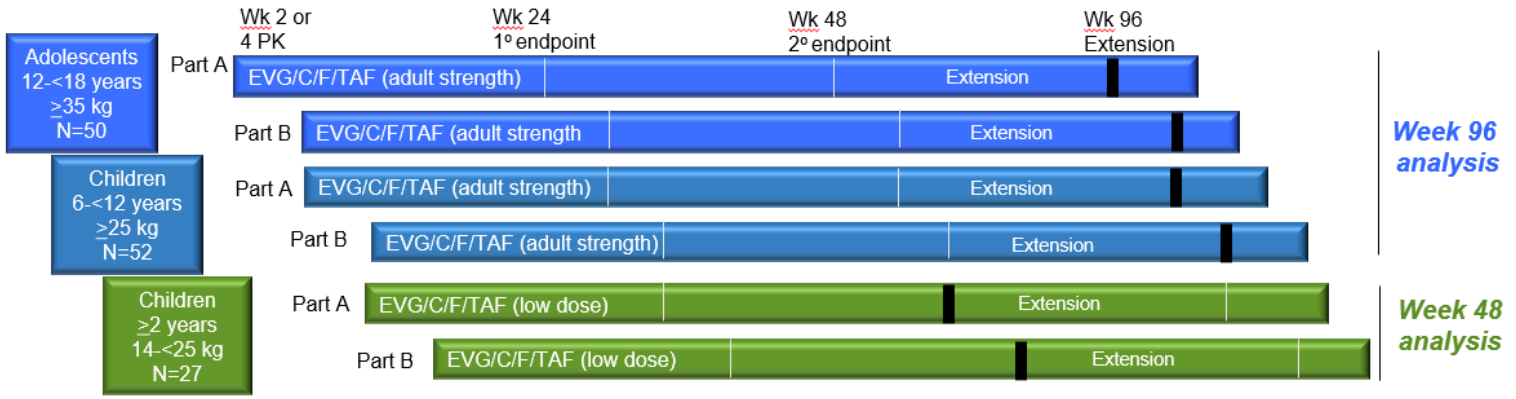
→In virologically suppressed children and adolescents through 96 weeks and young children through 24 weeks FU, B/F/TAF maintained viral suppression with no resistance; both formulations well tolerated even in young cohort.

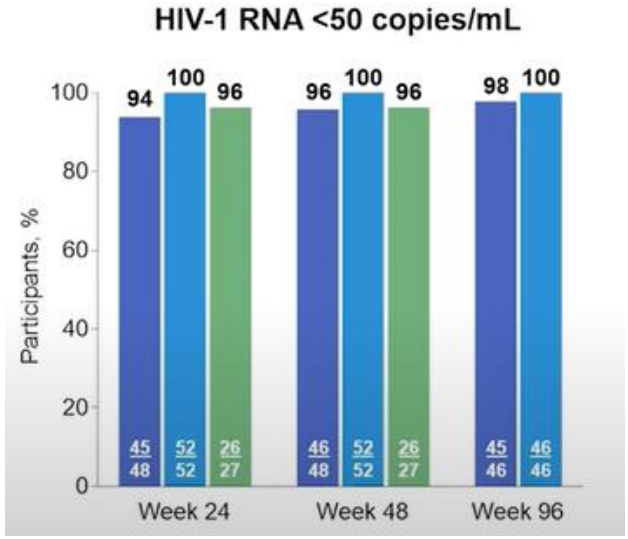
→Formulation for children <2 years planned.

Long-Term Safety and Efficacy Elvitegravir/Cobicistat/FTC/TAF in Virally Suppressed Adolescents and Children

Anugulruengkitt S et al. International Pediatric HIV Workshop Abs 4

- Phase 2/3 open-label switch to EVG/COBI/TAF in children on stable ART with RNA <50 c/mL for ≥6 mos, CD4 ≥100 (>400 youngest cohort) and normal eGFR; part A was PK to confirm dose; Part B complete cohort and start enrollment into next younger cohort.





None of children met criteria for resistance testing

	12-<18 yr; ≥35 kg N=50	6-<12 yr, ≥25 kg N=52	>2 yr; 14-<25 kg N=27
AE related to study drug	22 (44%)	14 (27%)	4 (15%)
Grade ≥3 AE	7 (14%)	2 (4%)	0
SAE*	9 (18%)	4 (8%)	1 (4%)
AE with drug dc	0	0	0
Death	1 (2%)	0	0

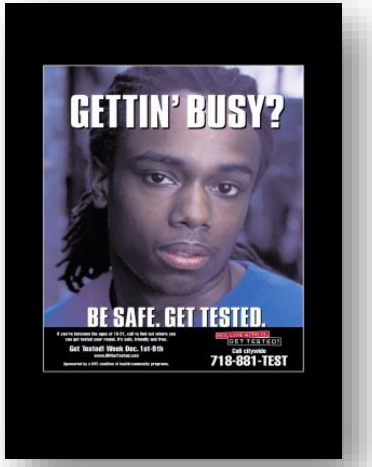
Most AE mild-moderate severity and none led to study drug dc
*Only 1 SAE thought possibly related to study drug (grade 2 autoimmune uveitis)

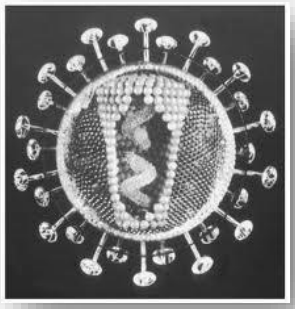
→In virologically suppressed children and adolescents through 96 weeks and young children through 48 weeks FU, EVG/COBI/F/TAF maintained viral suppression with no resistance; acceptable bone and renal safety profile; both formulations well tolerated.





Adolescents and HIV

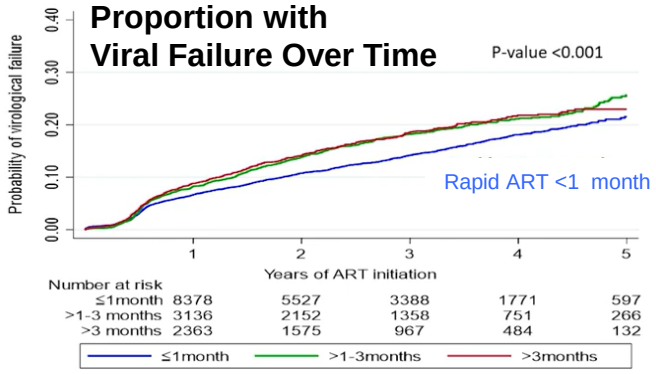


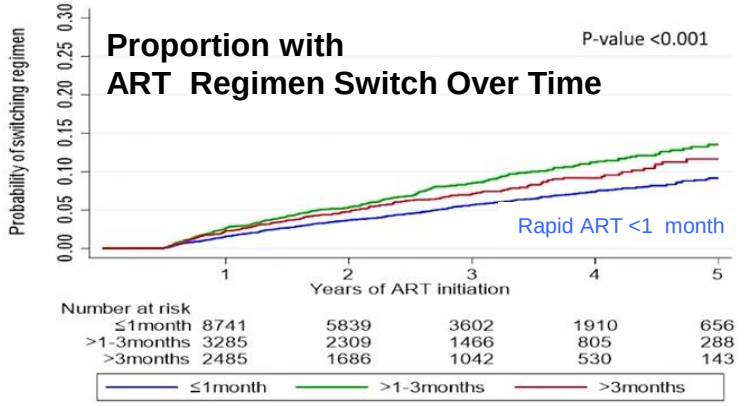


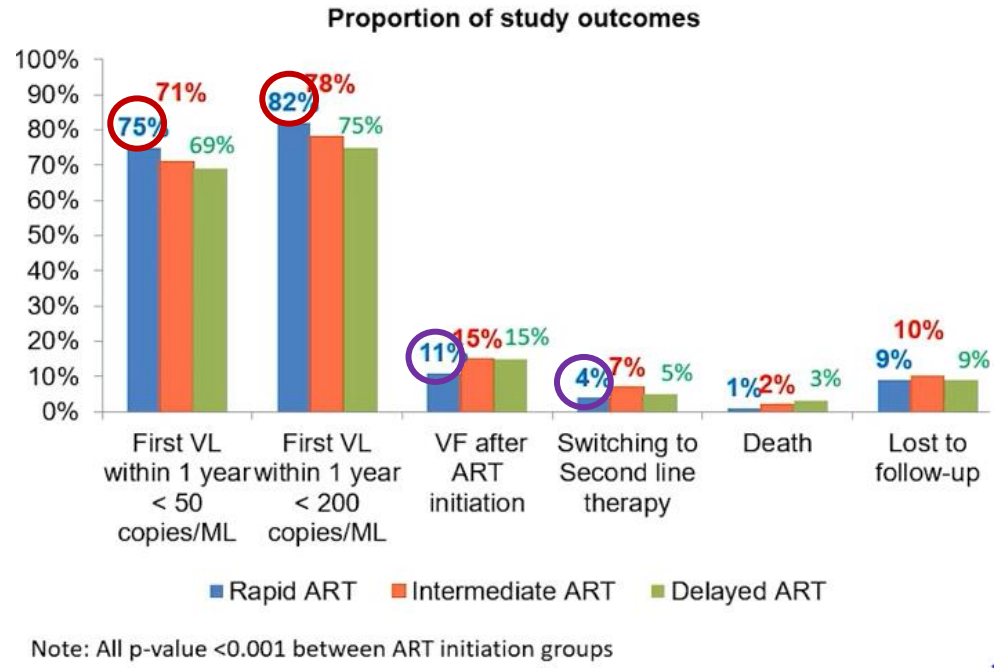
Rapid ART Initiation in Adolescents in Thailand Associated with Improved Clinical Outcome

Teeraananchai S et al. International Pediatric HIV Workshop Abs 31

- Thailand national ARV database and National Death Registry data to assess treatment outcome among 19,825 HIV+ youth aged 15-24 years initiating NNRTI-based ART (89% EFV-based) from 2014-May 2019 with FU data to May 2020
- Classified youth into 3 categories based on timing ART start post diagnosis:
  - Rapid – <1 month (n=12,216)
  - Intermediate – 1-3 months (n=4,275)
  - Delayed –>3 months (n=3,337)







Note: All p-value <0.001 between ART initiation groups

→Higher suppression

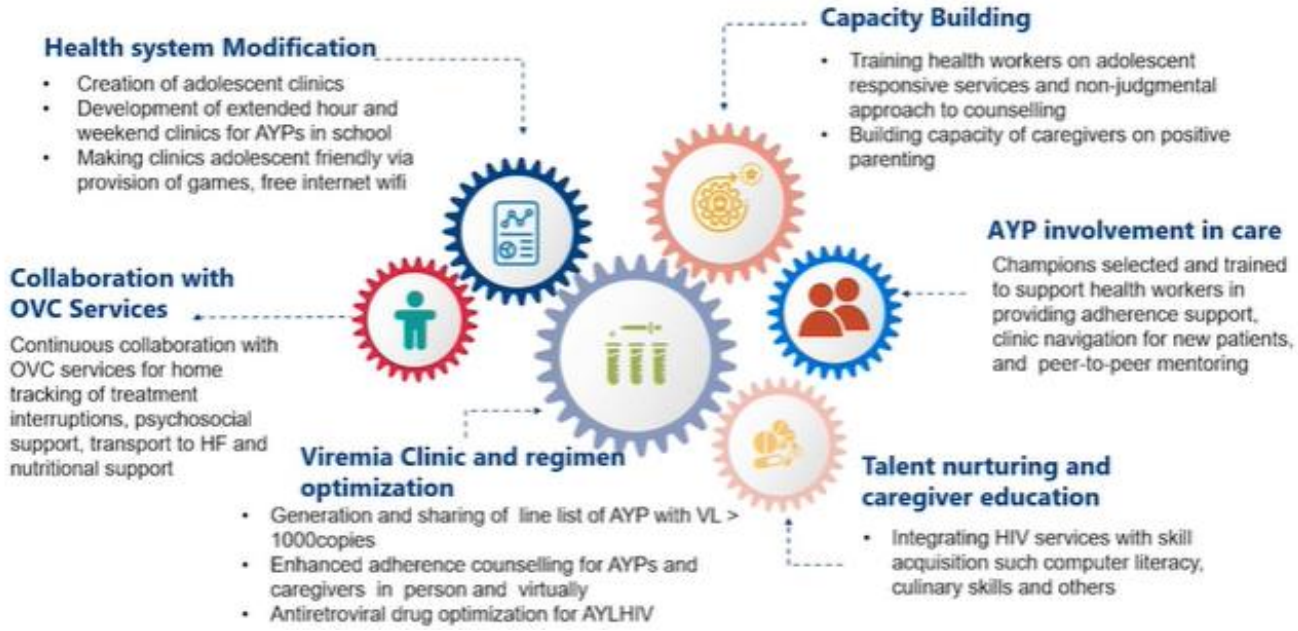
→Lower failure and switching

→No difference death, LTFU

Optimizing ART and Viral Suppression Nigerian Adolescents Reaching Impact, Saturation, and Epidemic Control (RISE)

Emerenini F et al. International Pediatric HIV Workshop Abs 32/IAS Virtual Abs OAD0505 July 2021

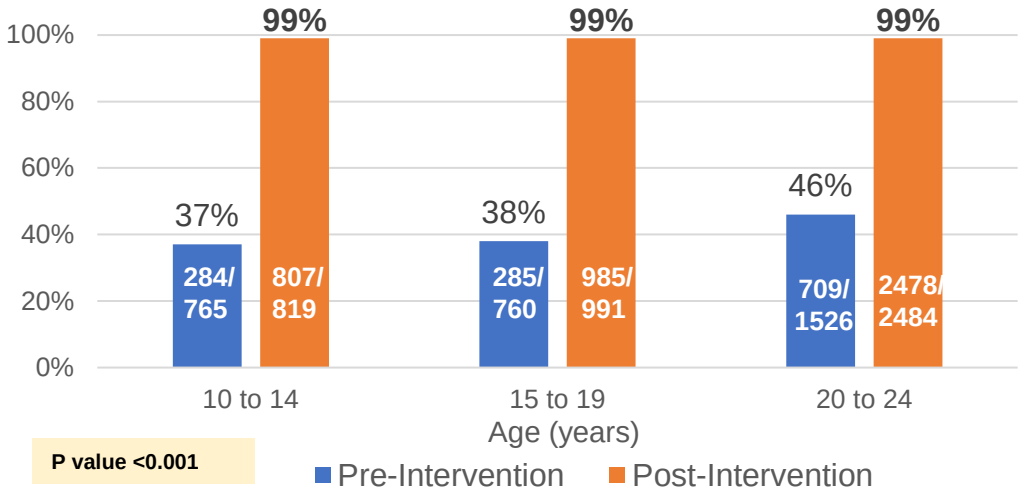
- Implementation of integrated multi-disciplinary intervention for 4,617 adolescents/youth 10-24 years in 103 facilities in 4 states in Nigeria; compared regimen optimization, VL testing and suppression 6 mos **pre-intervention** (Oct 2019-Mar 2020) and 6 mos **post-intervention** (Ap-Sept 2020) chart review.
- Intervention: **adolescent-based case management**; **peer-peer support** and **behavioral interventions** to identify and address age-specific barriers to adherence; **add-on such as free Wi-Fi and games** to improve adherence to clinic and appointments; **capacity building HCW and caregiver**.



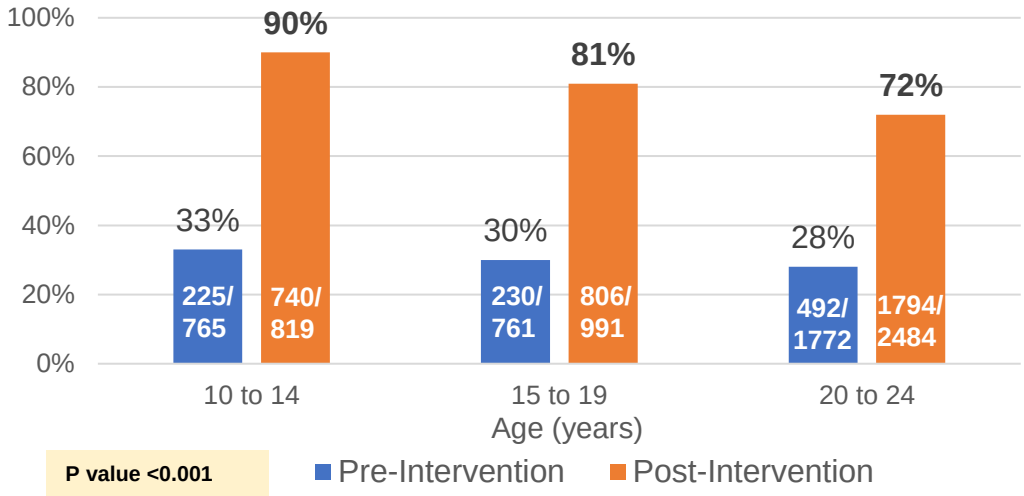
Optimizing ART and Viral Suppression Nigerian Adolescents Reaching Impact, Saturation, and Epidemic Control (RISE)

Emerenini F et al. International Pediatric HIV Workshop Abs 32/IAS Virtual Abs OAD0505 July 2021

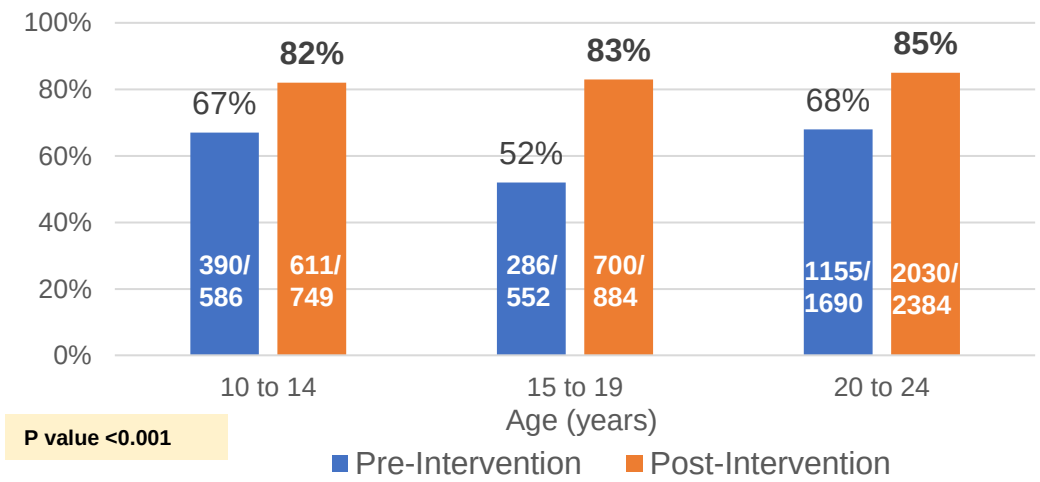
Percentage Receiving Optimal Regimen by Age



Percentage with VL Result of Those Eligible for VL Check



Percentage with Viral Suppression of Those Tested



→Adolescent-specific programming and capacity; involvement of adolescents in their care resulting in improvement in commitment to self-care; and caregiver involvement in health care improved health outcomes among AYP.

Development of a Transition Readiness Score for Adolescent with Perinatal HIV Transitioning to Adult Care

Zanoni B et al. International Pediatric HIV Workshop Abs 36/IAS Virtual Abs PEB223 July 2021

- 199 adolescents >12 years (median age 13) with perinatal HIV on last visit to pediatric clinic prior to transition to adult clinic in South Africa administered questionnaire and evaluated associations with viral suppression (RNA <200 c/mL) one year after transition to adult clinic:
  - Youth behavioral risk survey
  - Adolescent social support scale
  - Rosenbeg self-esteem scale
  - HIV adolescent readiness for transition scale (HARTS)

Factors Associated with Viral Suppression 1 Year Post Transition

Covariate	AOR	95% CI	P-value	
First-line ART	13.9	4.2 – 46.4	<0.001	Positive correlation
Disclosed HIV Status	2.8	1.2 – 6.2	0.015	
HARTS score (per unit score)	1.6	1.2 – 2.2	0.004	
Alcohol use	0.3	0.1 – 0.7	0.004	Negative correlation
Age at ART initiation (years)	0.8	0.7 – 0.9	0.004	
Female	0.4	0.2 – 0.9	0.018	

Transition Readiness Scoring

Variable	Categories	Beta	Reference Value (W)	Beta (W-Wref)	Points = Beta(W-Wref)/$B_{constant}$*-1
Regimen line	Second line*	2.63	0=ref	0	0
	First line		1	2.63	5
Disclosed	No*	1.01	0=ref	0	0
	Yes		1	1.01	2
HARTS Score	2-20*	0.05	11	0	0
	21-30		25.5	0.73	1
	31-39		35	1.20	2
	40-56		48	1.85	4
Alcohol use	No*	-1.23	0=ref	0	0
	Yes		1	-1.23	-2
Age at ART initiation	0-5*	-0.21	2.5	0	0
	6-8		7	-0.95	-2
	9-15		12	-2.0	-4
Sex	Male*	-0.91	0=ref	0	0
	Female		1	-0.91	-2
Range					-8 to 11

Transition readiness	Sensitivity	Specificity	Positive PV	Negative PV
Low (≤2) vs intermediate-high (>2)	**96.4%**	27.7%	50.0%	**91.2%**
High (≥5) vs intermediate-high (<5)	56.0%	**86.6%**	**75.8%**	72.4%

- **High readiness (≥5):** likely ready to transition to adult care
- **Intermediate readiness (3-4):** may benefit from additional time in ped clinic and additional interventions/resources before transition
- **Low readiness (≤2):** should have additional time in ped clinic; should receive additional interventions/resources prior to transition

Adherence to the Dapivirine Ring and Oral PrEP Among Adolescent Girls/Young Women – Interim REACH

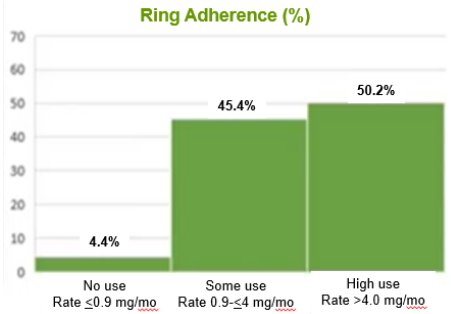
Nair G et al. IAS Virtual July 2021 Abs OALC01LB01

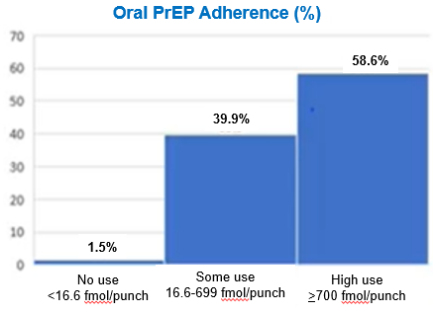
- Randomized open-label crossover study DPV ring vs oral PrEP in 247 HIV-negative adolescent girls aged 16-21 years(mean age 18.2 years) in S Africa, Uganda and Zimbabwe to evaluate safety, adherence, acceptability and preference



- Safety: 54% ≥1 AE, no difference DPV ring vs oral PrEP; no AE-related product holds, discontinuations or product-related SAE

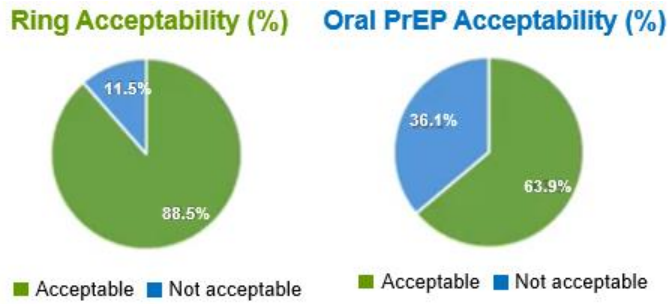
Adherence





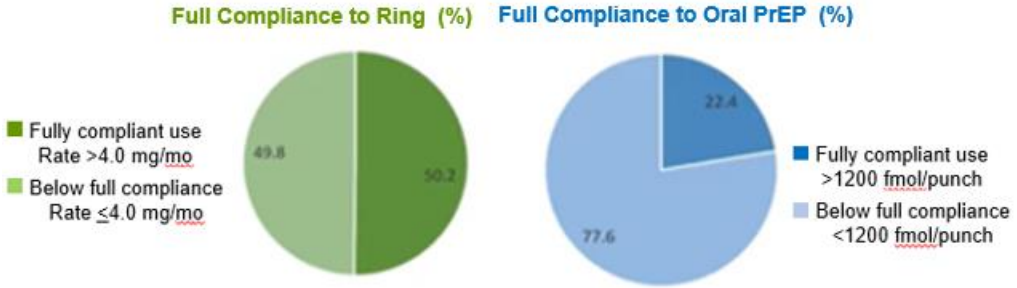
→ >50% highly adherent over 12 mos

Acceptability



→ More ring pt felt ring acceptable vs oral

Compliance

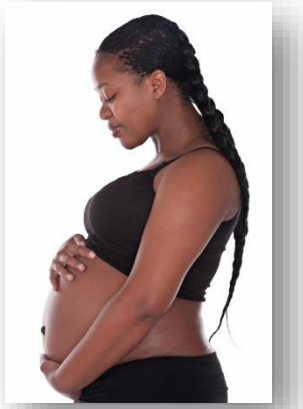


→ More ring pt fully compliant (leaves ring full mo) vs oral PrEP (6+ doses/wk ,>1200 fmol/punch)

→ Adherence to ring and oral PrEP as higher than anticipated among African AGYW

→ Both well tolerated and highly acceptable

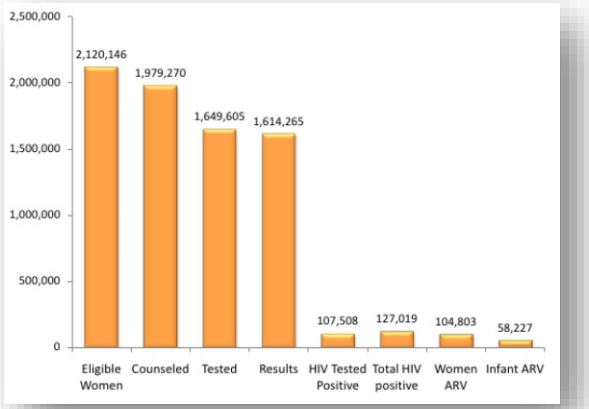
→ Adherence to both can be achieved with tailored adherence support







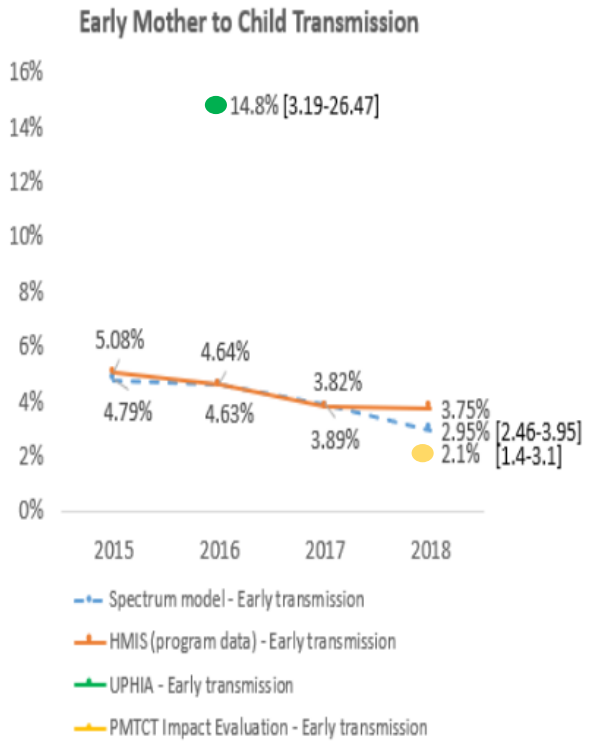

PMTCT Cascade and ARV in Pregnancy

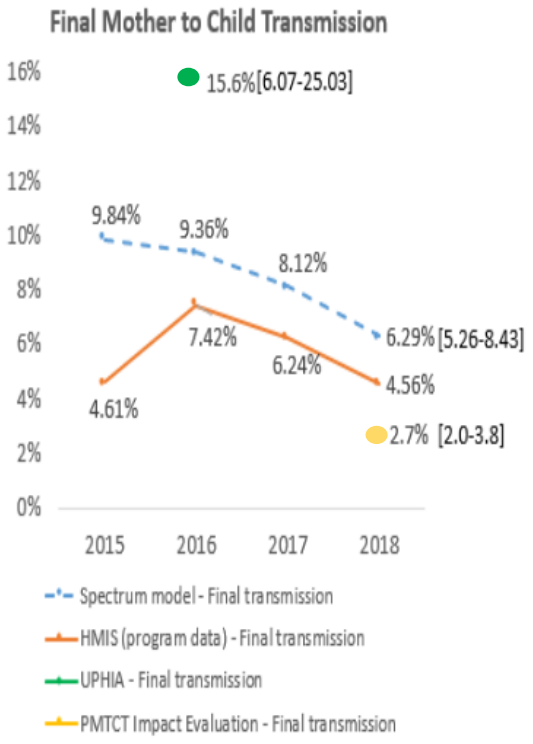


Importance of Surveys to Complement Program Data in Informing MTCT Estimates – Uganda

Nabitaka L et al. IAS Virtual Abs PEC348 July 2021

- Triangulated early (1st EID) and final (end of 18 mos) MTCT rates from:
  - MTCT data routinely reported to Uganda's Health Management Information System (HMIS 2015-2018)
  - Uganda's Population-based HIV Impact Assessment (UPHIA, Aug 2016-Mar 2017)
  - National PMTCT Impact Evaluation (PMTCT IE, Sept 2017-Jul 2019) (prospective FU 11,564 infants at 206 sites over 18 mos)
  - Annual Spectrum modeled estimates





→All data show marked ↓ in MTCT over time, although early & especially final MTCT rates differed by method.

→UPHIA demonstrated the strength of population-based surveys in capturing **higher MTCT among HIV+ women not accessing care**, and therefore <u>not represented</u> in program data.

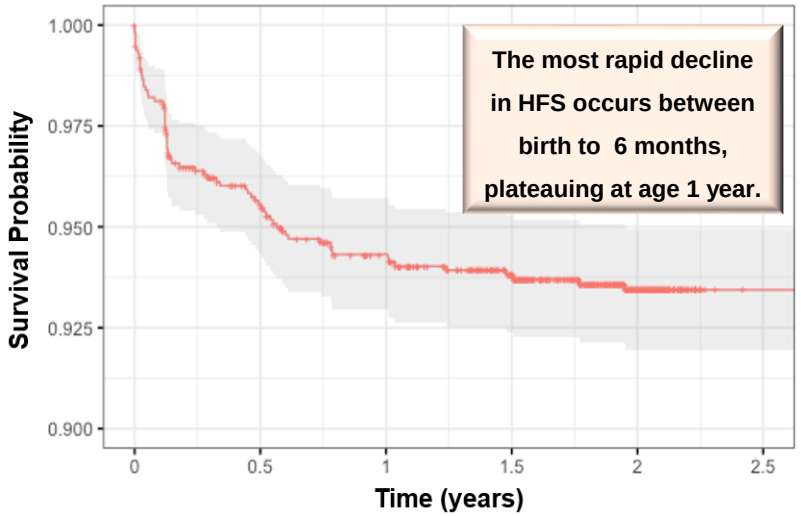
→Facility-based PMTCT IE demonstrated reassuring low MTCT among mother-infant pairs accessing care, even at lower-level facilities that do not offer comprehensive PMTCT services.

Determinants of HIV-Free Survival in Era of Universal ART: Pooled Data from PEA-WIL and IMPROVE Cohorts, Lesotho

Tiam A et al. International Pediatric HIV Workshop Abs 22/IAS Virtual Abs PEB223 July 2021

- Assessed factors associated with HIV-free survival, pooling data from two Lesotho cohort studies (PEA-WIL and IMPROVE) enrolling HIV+ pregnant women attending ANC in the universal ART era with follow-up 12-24 mos PP.

	PEA-WIL Study	IMPROVE Study
Aim	Evaluated the effectiveness of PMTCT program and assessed progress toward elimination of MTCT	Evaluated the effect of a multidisciplinary, integrated management team intervention on PMTCT service uptake and outcomes.
Sites	13 facilities in Thata-Tseka, Butha-Buthe, and Mohale's Hoek districts	6 facilities in Maseru District
Design	Prospective observational cohort	Prospective cluster-randomized trial
Participants	HIV-positive pregnant women and their infants followed for 24 months postpartum	HIV-positive pregnant women and their infants followed for 12-24 months postpartum
Data Collection	June 2014 – September 2018	July 2016 – July 2019



MTCT, Death and HIV-Free Survival by Study and Overall

Outcome	PEA-WIL (2014-2018)	IMPROVE (2016 -2019)	Combined Cohort
Number of exposed children	652	570	1222
Number infected 24 months	17/607, 2.8%	10/507, 2.0%	27/1114, **2.4%**
Number of deaths	57, 8.7%	59, 10.4%	116, **9.5%**
Deaths minus stillbirths	38, 6.0%	33, 6.1%	71, **6.1%**
HIV-free survival: # alive and HIV free, % [95% CI]	582, 91.8% [89.4 – 93.8]	499, 92.4% [89.8 – 94.5]	1081, **92.1% [90.4 – 93.6]**

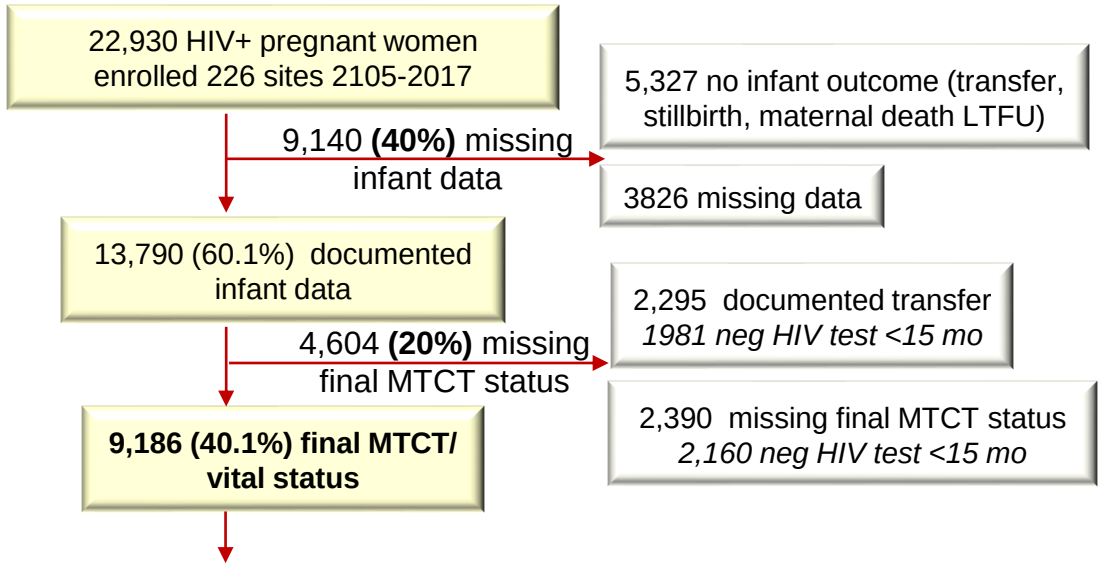
Factors Associated with HIV-Free Survival

Characteristic		N	Alive & HIV-free	Adjusted OR	p-value
Age group	15 – 24 years	306	274 (89.5)	1	
	25 – 48 years	809	772 (95.4)	**2.41 [1.36 – 4.26]**	0.002
Gestational age	**Term (≥37 wks)**	1055	994 (94.2)	**3.69 [1.61 – 8.42]**	0.002
	Preterm (<37 wks)	59	50 (84.7)	1	
Breastfeeding ≥ 6 mos	**Yes**	343	333 (97.1)	**2.42 [1.19 – 4.92]**	0.014
	No	740	682 (92.2)	1	
Disclosed HIV status to partner	**Yes**	852	814 (95.5)	**1.99 [1.04 – 3.81]**	0.037
	No	214	191 (89.3)	1	

HIV-Free Survival in Era of Universal ART: Data from Tanzania

Lyatuu GW et al. IAS Virtual Abs PEC345 July 2021

- Prospective study pregnant HIV women starting Option B+ 2015-2017 in 226 clinics in Tanzania; 9,186 had documented final MTCT and vital status; 47% of women were on ART preconception.



- 159 (1.7%) infants HIV+ (18 mos)
- 300 (3.3%) infants died
- **18-month HIV-free survival 95%**

Factors Associated with Odds of HIV-Free Survival

	Univariable, N = 7483		Multivariable Complete case, N = 7483	
Characteristic‡	Crude odds ratio	p-value	adjusted odds ratio	p-value
Patient characteristics				
Age at start of PMTCT care		0.91		0.77
<20 years	1.02 (0.53, 1.99)		0.95 (0.49, 1.86)	
20-29 years	0.95 (0.76, 1.18)		0.91 (0·72, 1.14)	
30-39 years	1 [referent]		1 [referent]	
40+ years	1.11 (0.70, 1.78)		1·12 (0.70, 1.80)	
Gestational age, weeks§		<0.0001*		0.0002*
<13 (first trimester)	1 [referent]		1 [referent]	
13-27 (second trimester)	1.59 (1.15, 2.19)		1.52 (1.10, 2.09)	
≥28 (third trimester)	2.18 (1.50, 3.17)		2.10 (1.44, 3.06)	
Advanced HIV disease versus none	1.00 (0.78, 1.27)	0.99	1.37 (1.03, 1.80)	0.028
When ART was started		0.0001		0.0001
Before PMTCT enrolment	0.63 (0.50, 0.80)		0.58 (0.44, 0.76)	
At PMTCT enrolment	1 [referent]		1 [referent]	
31+ days after enrolment	9.69 (0.81, 116.25)		6.73 (0.55, 82.35)	
NNRT Inhibitor ART backbone versus Protease Inhibitor	1.24 (0.44, 3.51)	0.69	1.56 (0·54, 4·48)	0.41
Female versus male infants	1.12 (0.91, 1.39)	0.28	1.13 (0.92, 1.40)	0.25
Health facility attributes				
PMTCT clients' volume		<0.0001*		0.0002*
1-10 women per year	1 [referent]		1 [referent]	
11-100 women per year	0.56 (0.37, 0.86)		0.61 (0.40, 0.94)	
101-515 women per year	0.31 (0.19, 0.50)		0.36 (0.22, 0.59)	
Couple HIV testing rate of 50%+ at first ANC visit versus <50%	1.56 (0.96, 2.54)	0.076	1.33 (0.85, 2.06)	0.21

Time enter ANC

HIV disease

Timing ART Start

Clinic volume

Use of HIV POC Viral Load Testing to Identify Infants at High Risk of MTCT in Primary Care Clinics Mozambique

Meggi B et al. International Pediatric HIV Workshop Abs 20

- Part of ongoing study at 14 facilities Mozambique evaluating POC VL vs conventional VL at birth in mother at birth.
- Viral load at birth significantly correlated with MTCT by age 12 weeks.
- Looked at factors associated with **lack of suppression at birth** to identify characteristics that may be associated with increased risk MTCT.

Factors Associated with Viral Suppression at Delivery

	Viral load count					Wald Chi-square	
	Suppressed, n=2096	%	Not suppressed, n=1089	%	Total, n=3105	OR p-value	p-value
Mother's age							
18 - 24y	427	58%	314	42%	741	ref.	
25 - 29y	709	66%	362	34%	1071	1,164 0,0297	
30- 34y	572	73%	209	27%	781	1,499 0,0000	0,0000
35y+	387	76%	122	24%	509	1,673 0,0000	
Education level							
Post secondary school	108	76%	34	24%	142	ref.	
Secondary school	897	69%	411	31%	1308	0,690 0,0187	
Primary school	841	67%	412	33%	1253	0,619 0,0036	0,0000
None	250	62%	152	38%	402	0,467 0,0000	
ANC visits							
3 visits	434	69%	197	31%	631	ref.	
2 visits	1329	69%	605	31%	1934	0,972 0,8680	
1 visit	275	61%	174	39%	449	0,737 0,1391	0,2221
None	58	64%	33	36%	91	1,106 0,8724	
HIV disclosure							
No	118	53%	103	47%	221	ref.	
Yes	1978	69%	906	31%	2884	1,725 0,0004	0,0004
Time since HIV diagnosis							
1y or more	647	76%	207	24%	854	ref.	
Less than 1y	642	52%	581	48%	1223	0,367 0,0000	0,0000

Age

Education

Disclosure

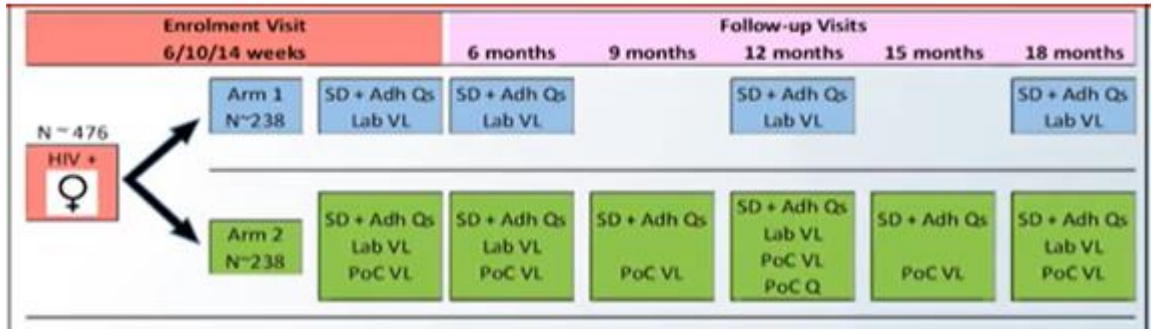
Time HIV dx

→Risk factors for <u>lack</u> of maternal viral suppression at birth were younger age 18-24 years; lower education level; lack of HIV disclosure; and more recent HIV diagnosis.

More Frequent VL Testing with POC Tests Has No Impact on Suppression in Postpartum HIV+ Women, RCT S Africa

Fairlie L et al. International Pediatric HIV Workshop Abs 19/IAS Virtual Abs OALB0402 July 2021

- Non-blinded RCT comparing POC VL testing q 3 mo to SOC lab-based VL testing q 6 mo in HIV+ postpartum women on 1st line ART; evaluated viral suppression at 6, 12,18 mo.



VL <1000 (p=0.898)	SOC	POC
Baseline	188/200 **(94.0%)**	178/201 **(88.6%)**
6-months	125/130 (96.2%)	124/136 (91.2%)
12-months	127/135 (94.1%)	131/143 (91.6%)
18 months	128/136 **(94.1%)**	115/122 **(94.3%)**

VL <200 (p=0.701)	SOC	POC
Baseline	179/200 **(89.5%)**	174/201 **(86.6%)**
6-months	121/130 (93.1%)	116/136 (85.3%)
12-months	115/135 (85.2%)	118/143 (82.5%)
18 months	116/136 **(85.3%)**	104/122 **(85.3%)**

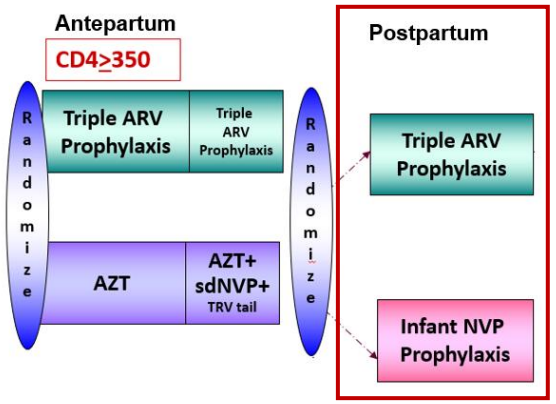
- No significant differences at baseline btn arms
- Preconception ART 57%
- At enrollment, 88% <200, 91% <1,000 c/mL
- **36% LTFU**

→ No significant differences in viral suppression between q6 month SOC vs q3 month POC VL testing.

→ **Caveats**: 36% LTFU in the study; viral suppression rates in both groups very high, so ability to detect a difference with this sample size may be limited.

Association Self-Reported Adherence with Viral Suppression in Postpartum Component PROMISE

N Nevrekar et al. IAS Virtual July 2021 Abs PEB175



- Self-reported adherence to maternal ART (mART) and infant NVP (iNVP) in the postpartum component of PROMISE compared and association of viral suppression with self-reported adherence to ART in mART arm examined.

→ Self-reported adherence to study drug was **lower** in the mART arm compared to the iNVP arm.

	mART	iNVP	P value
No missed doses within **4 weeks** of all study visits	65.8%	83.3%	<0.001
No missed doses within **2 weeks** of all study visits	70.9%	85.2%	<0.001

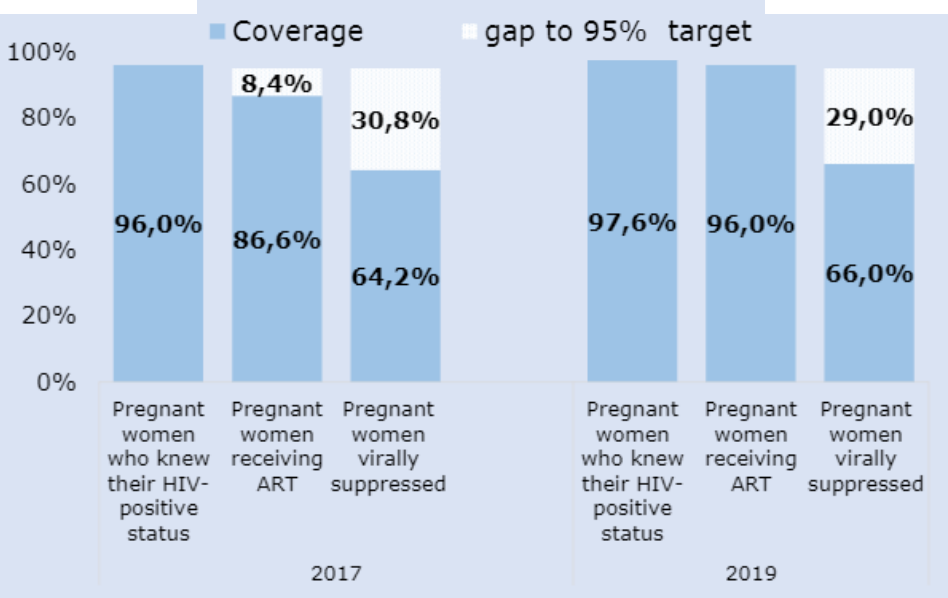
→Maternal self-report of adherence in mART arm was associated with VL: report of missing 1 day of ART in the 3 days prior to study visit was associated with **58% higher risk of VL >400 c/mL** (HR 1.58, 95% CI 1.3-1.9) and **66% higher risk of VL >1000 c/mL** (HR 1.66, 95% CI 1.4-2.0)

Progress Toward 95-95-95 Targets Among Pregnant Women in S. Africa 2017 and 2019 National Antenatal HIV Sentinel Surveys

Woldesenbet S et al. IAS Virtual Abs PED536 July 2021

- National cross-sectional ANC sentinel surveys conducted 2017 (10,065 women) & 2019 (11,321 women) in South Africa.

→ In 2019 met first two 95-95 targets (knowledge status and HIV+ on ART), but 3rd viral suppression target remains a challenge; 34% of <u>all</u> pregnant HIV+ women not suppressed in 2019.



Factors Associated with Viral Suppression (<50 c/mL)

	Sample distribution n=17 820 *	Percent virally suppressed (95% CI†) 2017	Percent virally suppressed (95% CI) 2019	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age group (in years)					
15–24	3 800 (22.3)	56.1 (54.2–58.0)	56.4 (54.6–58.2)	0.6 (0.6–0.7)	0.7 (0.6–0.8)
25–49	12 754 (77.7)	66.8 (65.7–68.0)	68.2 (67.2–69.1)	Ref	Ref
Province					
Eastern Cape	2 705 (11.6)	62.1 (59.1–65.0)	63.6 (61.6–65.4)	0.7 (0.7–0.8)	0.7 (0.6–0.8)
Free State	1 570 (4.7)	72.6 (69.8–75.1)	63.4 (60.8–66.0)	0.9 (0.8–1.0)	0.8 (0.7–0.9)
Gauteng	2 441 (25.7)	70.6 (68.6–72.5)	69.1 (67.2–70.9)	Ref	Ref
KwaZulu-Natal	5 986 (30.1)	64.1 (62.3–65.8)	77.3 (75.9–78.6)	1.0 (0.9–1.1)	1.0 (0.9–1.1)
Limpopo	839 (6.3)	33.9 (30.2–37.9)	43.4 (39.6–47.2)	0.3 (0.2–0.4)	0.2 (0.1–0.3)
Mpumalanga	1 702 (8.8)	64.1(61.4–66.7)	50.4 (47.4–53.5)	0.6 (0.5–0.7)	0.6 (0.5–0.6)
North West	1 082 (4.0)	40.0 (35.9–44.3)	47.8 (43.8–51.7)	0.4 (0.3–0.5)	0.7 (0.6–0.9)
Northern Cape	486 (2.5)	69.7 (64.2–74.7)	50.3 (44.8–55.8)	0.8 (0.6–0.9)	0.3 (0.2–0.4)
Western Cape	1 009 (6.3)	70.5 (67.5–73.3)	69.7 (66.4–72.9)	1.0 (0.9–1.1)	1.0 (0.8–1.1)
Timing of ART ‡ initiation					
Before pregnancy	12 290 (69.8)	69.4 (68.3–70.5)	73.3 (72.3–74.2)	Ref	Ref
During pregnancy	5 145 (30.2)	53.6 (51.9–55.2)	48.8 (47.3–50.4)	0.4 (0.3-0.5)	0.5 (0.4–0.6)

Age

Province of ANC care

Timing ART Start

Factors Associated with Recent HIV Infection in Pregnant Women in Lilongwe Malawi, Case-Control Study

UNC PROJECT Lilongwe, Malawi

Huffstetler HE et al. IAS Virtual Abs PEC246 July 2021

- Baseline HIV testing with validated algorithm for recency (Limiting Antigen Avidity EIA [OD ≤1.5] and quantitative VL [>1,000]) offered to 416 HIV-negative women enrolled in behavioral intervention trial in Malawi.
- 44 women (10.6%) were found to have recent HIV infection (cases). Women with recent HIV were compared to 350 HIV-negative women presenting in same setting.

Final Adjusted Model for Risk Recent HIV Infection

	HIV- (N=349)		Recent (N=44)		Unadjusted			Adjusted		
	N	%	N	%	OR	95% CI	p-value	OR	95% CI	p-value
Female characteristics										
Syphilis status										
Negative	342	(98.0)	39	(88.6)	1.			1.		
Positive	7	(2.0)	5	(11.4)	6.26	1.90-20.68	0.003	5.57	1.43-21.76	0.014
Primary male partner characteristics										
Partner HIV status										
HIV negative	257	(73.6)	18	(40.9)	1.			1.		
HIV positive	7	(2.0)	5	(11.4)	10.20	2.94-35.35	<0.001	7.84	2.12-28.88	0.002
Status unknown	85	(24.4)	21	(47.7)	3.53	1.79-6.93	<0.001	4.46	2.16-9.20	<0.001
Couple characteristics										
Participant and primary partner are married										
Married	338	(96.8)	38	(86.4)	1.			1.		
Not married	11	(3.2)	6	(13.6)	4.85	1.70-13.86	0.003	4.04	1.24-13.08	0.020
Overnight travel outside home (past 6 mo.)										
No participant and partner travel	169	(48.8)	11	(25.0)	1.			1.		
Any participant or partner travel	177	(51.2)	33	(75.0)	2.86	1.41-5.88	0.004	3.09	1.43-6.67	0.004

Factors Associated with Recent Infection

→Positive syphilis rapid test

→Partner HIV+ or HIV status unknown

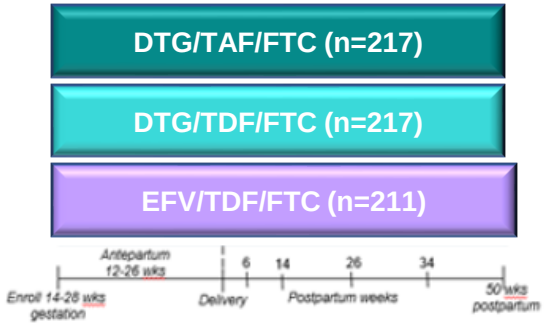
→Unmarried

→Overnight travel past 6 months



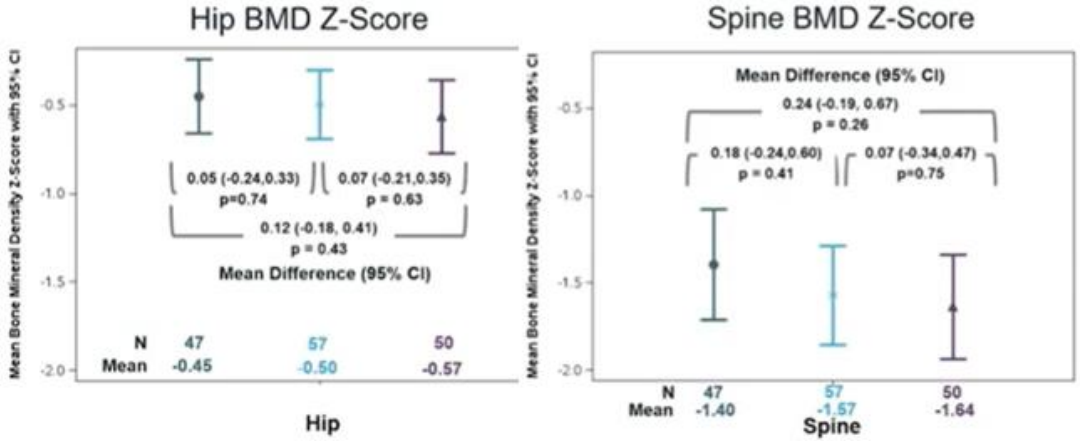

BMD in PP Mother on DTG/TDF/FTC, DTG/TAF/FTC or EFV/TDF/3TC and Their Infants – IMPAACT 2010 Trial

Mbengeranwa T et al. International Pediatric HIV Workshop Abs 12

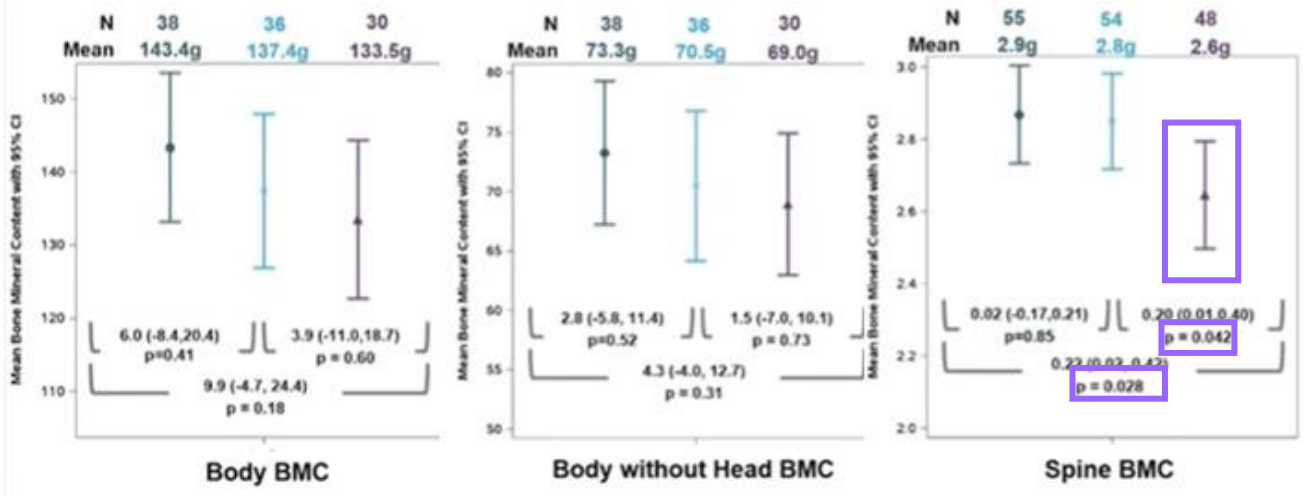


- **Perinatal RCT:** DTG (with TAF or TDF) superior virologic efficacy vs EFV
- DXA evaluation of BMC at week 50 postpartum in 154 **mothers** (median duration ART 66 wk, median duration BF 44 wk) and age 26 weeks in 165 **infants** (median age 5.8 mo); central reading done

Mother: No significant difference BMD z-scores between treatment arms; lowest in EFV/TDF/3TC arm



Infant: No significant difference BMD z-scores between treatment arms for whole body; but significantly lower **spine** BMC in EFV/TDF/3TC arm

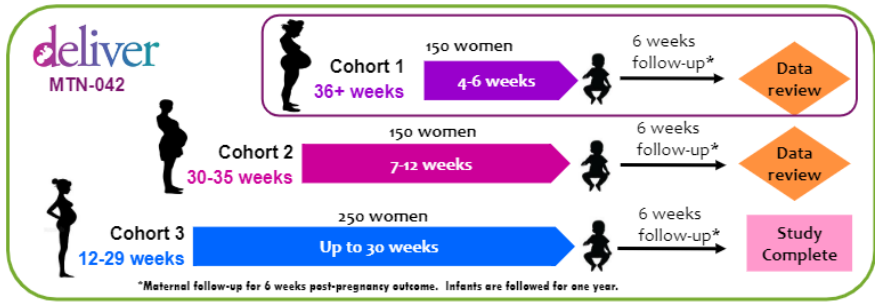


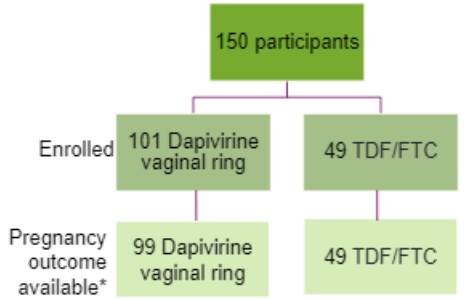
DTG/TAF/FTC DTG/TDF/FTC EFV/TDF/FTC

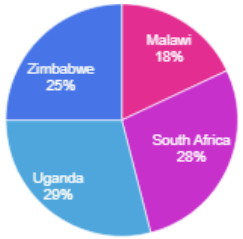
Safety of Dapivirine Ring in Late Pregnancy

Makanani B et al. IAS Virtual July 2021 Abs PECLB26

- Pregnant women randomized 2:1 to monthly dapivirine ring or daily TDF/FTC starting at 36-37 wk gestation – interim analysis.







	Dapivirine n=99 n (%)	TDF/FTC n=49 n (%)	Overall N=148 N (%)
Stillbirth	0 (0)	1 (2)	1 (1)
Live birth	99 (100)	48 (98)	147 (99)
Full term birth	98 (99)	46 (96)	144 (98)
Preterm birth	1 (1)	2 (4)	3 (2)

	Dapivirine n=99 n (%)	TDF/FTC n=49 n (%)
Any hypertensive disorder of pregnancy[3]	3 (3)	4 (8)
Gestational hypertension	3 (3)	2 (4)
Pre-eclampsia without severe features	0 (0)	1 (2)
Pre-eclampsia with severe features	0 (0)	1 (2)
Eclampsia	0 (0)	0 (0)
Hemorrhage		
Peripartum/Antepartum hemorrhage	0 (0)	1 (2)
Postpartum hemorrhage	2 (2)	1 (2)

Severe Adverse Events (SAEs)

Maternal SAEs

- Of the SAEs/grade ≥3 AEs reported, only one AE (grade III nausea) was deemed related to study product use in the TDF/FTC arm

Infant SAEs

- There were no infant SAEs/grade ≥3 AEs related to study product
- At the time of this report, there was one neonatal death following delivery in the TDF/FTC arm

→Adverse pregnancy outcomes and complications were uncommon when the DVR and TDF/FTC were used in late pregnancy and were generally similar to rates observed in the communities where the study is being conducted.

No Association Between Prenatal PrEP Exposure and Adverse Growth Outcomes in Kenyan Infants

Gomez L et al. IAS Virtual July 2021 Abs PEC353

- The PrEP Implementation for Mothers in Antenatal Care (PrIMA) Study cluster RCT of PrEP counseling strategies for women attending antenatal care in 20 facilities in Western Kenya; evaluated relationship between prenatal PrEP exposure and infant growth outcomes.

Table 1. Enrollment characteristics of participants

	N (%) or Median (IQR)		
	PrEP Unexposed (n=3,437)	PrEP Exposed (n=549)	p-value
Age (years)	24 (21, 28)	25 (21, 30)	<0.001
Partner living with HIV	1%	19%	<0.001
Partner HIV status unknown	30%	42%	0.01
Gestational age (weeks)	24 (20, 30)	24 (19, 28)	0.01
Positive Syphilis Test Results	1%	2%	<0.001
Transactional sex	2%	3%	<0.001
STI diagnosis	2%	5%	<0.001
Intimate partner violence	6%	14%	<0.001

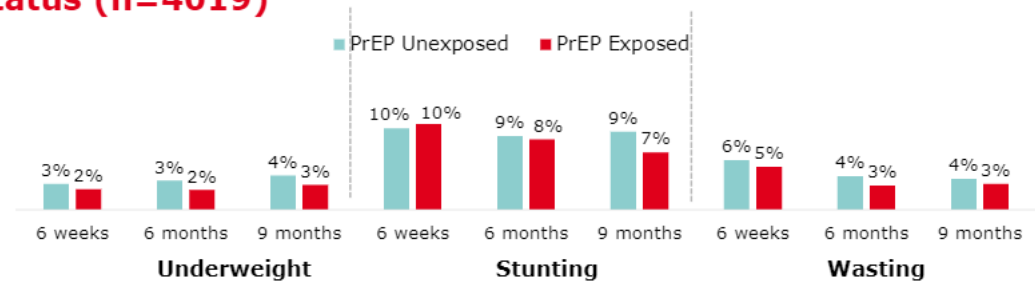
- 3,986 mother-infant pairs analyzed (90% of total PrIMA participants)
- 13.8% used PrEP at any time during pregnancy
- Median gestational age at PrEP initiation: 27 weeks (IQR 22, 31)
- Median duration of PrEP use during pregnancy: 12 weeks (IQR 7, 17)
- Key differences between PrEP exposed/unexposed (Table 1)

Table 2: Infant growth at 6-weeks, 6-months and 9-months by prenatal PrEP exposure (n=4019)

	Median (IQR)		Adjusted Coeff (95% CI)*	P-value
	PrEP Unexposed (n=3471)	PrEP Exposed (n=548)		
Weight (kg) 6-week	5.0 (4.5, 5.4)	5.0 (4.5, 5.4)	0.03 (-0.06, 0.11)	0.52
6-month	7.7 (7.0, 8.5)	7.8 (7.2, 8.7)	0.22 (0.08, 0.36)	0.004
9-month	8.6 (7.9, 9.6)	8.6 (8.0, 9.5)	0.09 (-0.04, 0.21)	0.16
Length (cm) 6-week	55.0 (54.0, 57.0)	55.3 (54.0, 57.2)	-0.60 (-2.01, 0.81)	0.39
6-month	66.0 (64.0, 68.0)	66.0 (64.0, 69.0)	0.31 (-0.51, 1.13)	0.44
9-month	70.0 (68, 72)	70.5 (68.6, 72.0)	-0.02 (-1.32, 1.28)	0.97

*Adjusted for gestational age at birth, maternal syphilis, maternal age and partner HIV status

Figure 1: Infant growth outcomes by prenatal PrEP exposure status (n=4019)*



	Underweight			Stunting			Wasting		
Adj RR (95% CI)*	0.8 (0.4-1.5)	0.6 (0.4-1.4)	0.8 (0.4-1.9)	1.2 (0.8-1.7)	1.0 (0.7-1.4)	0.7 (0.4-1.5)	0.8 (0.5-1.4)	0.9 (0.4-1.7)	0.7 (0.3-1.5)
P-value	0.45	0.16	0.33	0.20	0.81	0.10	0.45	0.68	0.36

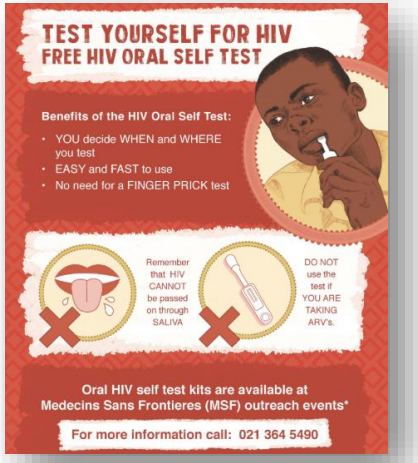
*Adjusted for gestational age at birth, maternal syphilis, maternal age and partner status

Results were similar when analyzed separately by trimester of PrEP initiation





HIV Testing and Case Finding





Prior HIV Diagnosis in Children with HIV from 6 Countries from Population HIV Incidence Assessments (PHIA)

Teasdale C et al. International Pediatric HIV Workshop Abs 29/IAS Virtual Abs PEC271 July 2021

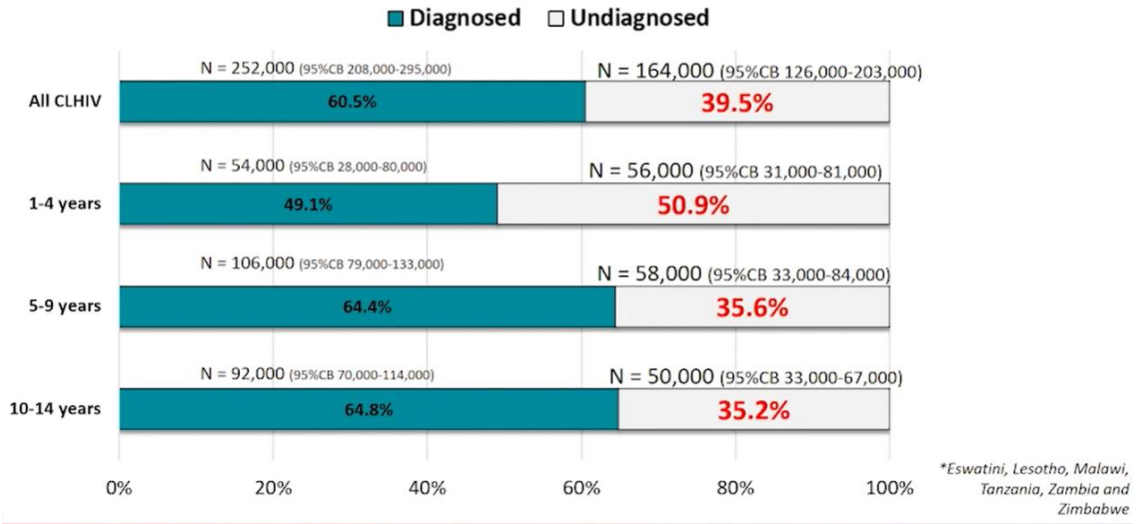


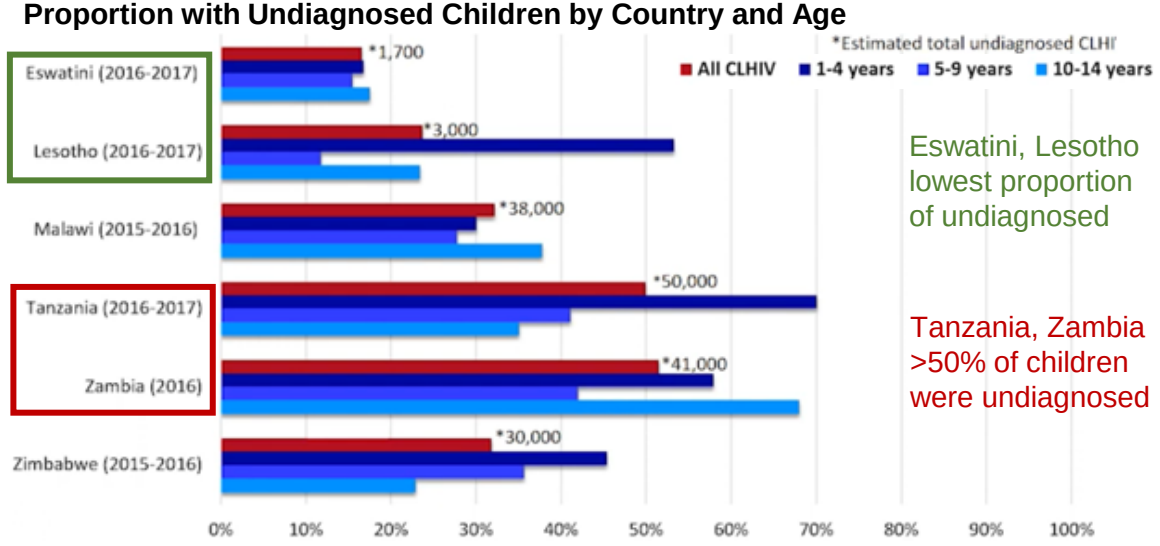
- Data from national household 2015-2017 surveys from 6 countries to estimate proportion of 521 HIV+ children aged 1-14 years with known diagnosed vs unknown undiagnosed status.

Definition Diagnosed vs Undiagnosed Status

Diagnosed	Undiagnosed
Reported as previously tested HIV+ OR ARVs detected **If child not reported as HIV+ but ARVs detected, considered diagnosed*	Reported previously tested HIV-negative, no previous HIV test, results not received AND No ARVs detected

- Of 521 CLHIV, 355, 61%, were known and 166, 40% were undiagnosed prior to PHIA, with the highest proportion of undiagnosed children aged 1-4 years; this varied by country.





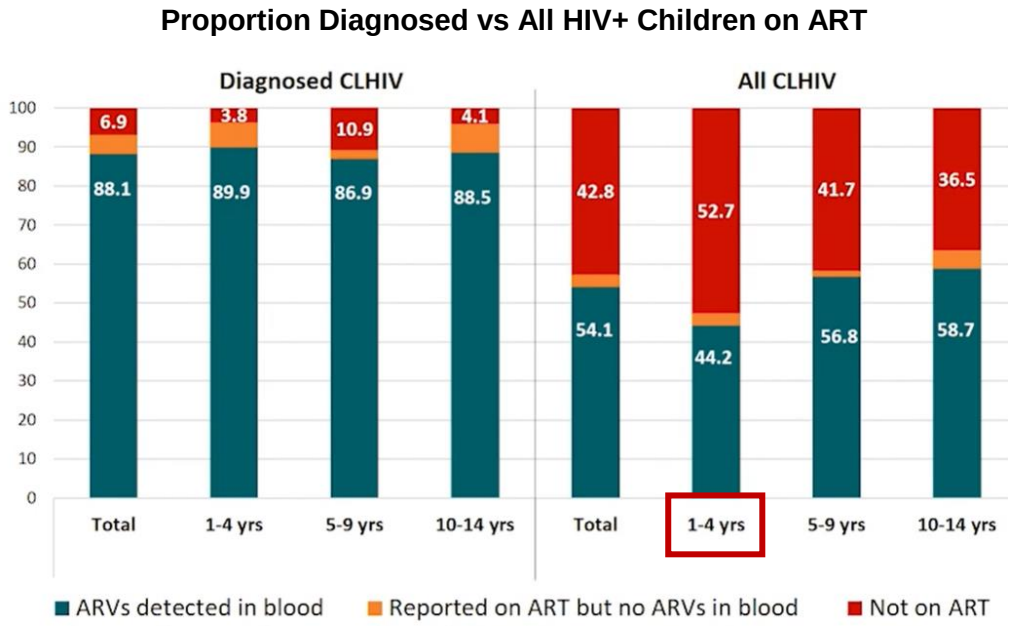
Eswatini, Lesotho lowest proportion of undiagnosed

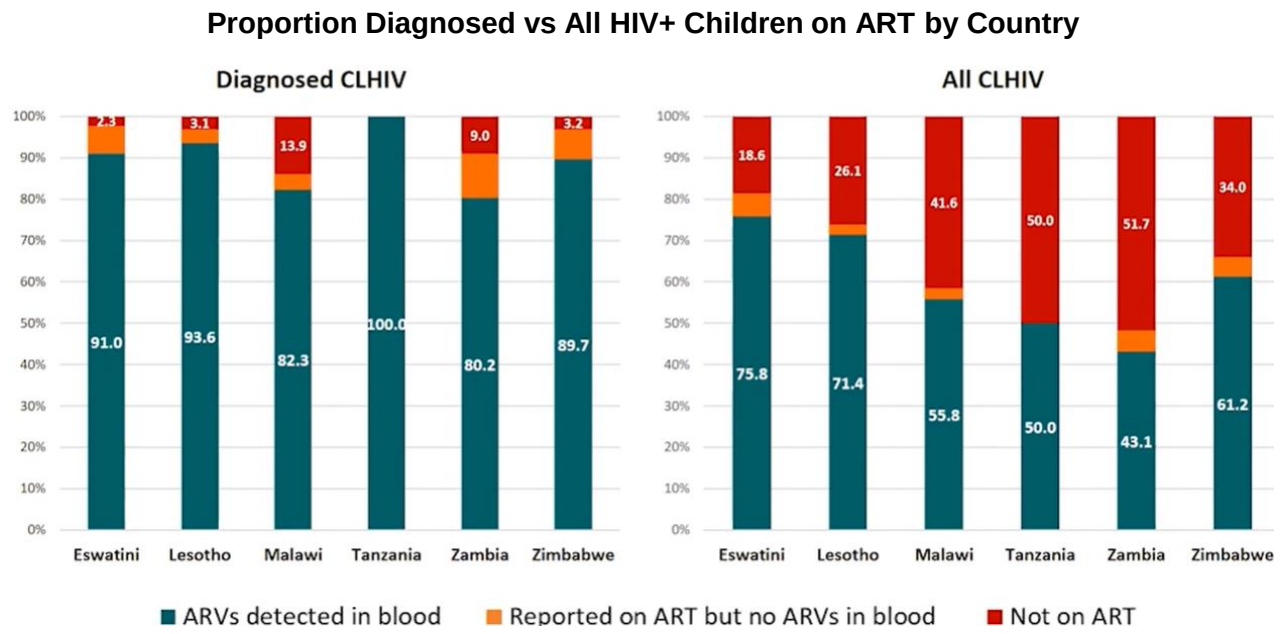
Tanzania, Zambia >50% of children were undiagnosed

Prior HIV Diagnosis in Children with HIV from 6 Countries from Population HIV Incidence Assessments (PHIA)

Teasdale C et al. International Pediatric HIV Workshop Abs 29/IAS Virtual Abs PEC271 July 2021

- Children with undiagnosed status more likely to have mother with unknown status or be diagnosed during the PHIA survey (55% undiagnosed vs 10% diagnosed).
- 88% of children with diagnosed HIV were receiving ART; however, when include undiagnosed children only 54% ART coverage, worse among 1-4 years, with variation by country.



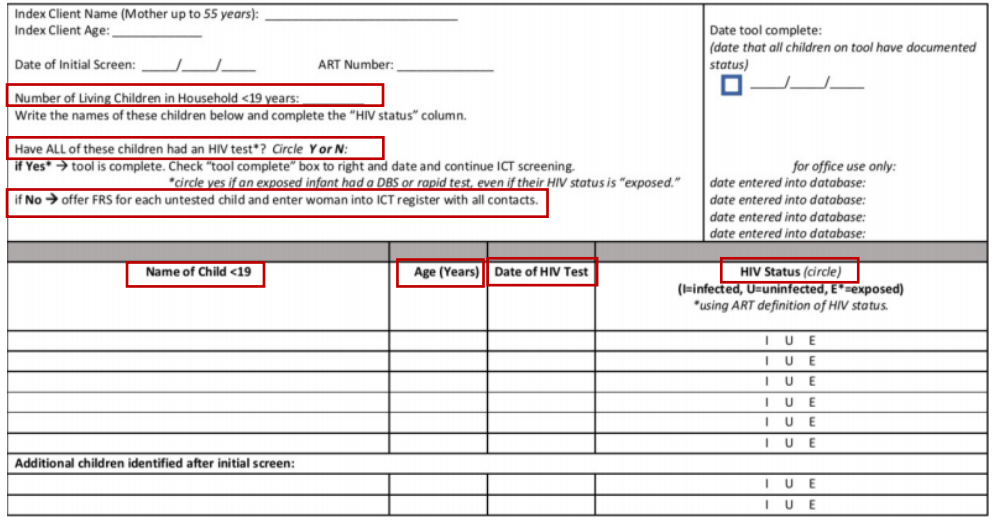


Impact of a Community Health Worker (CHW) Administered Index Case Screening Tool on Pediatric HIV Case Identification, Malawi

Simon KR et al. International Pediatric HIV Workshop Abs 89/IAS Virtual Abs OAD0403 July 2021

- Developed brief (<5 minute) CHW administered index case testing screening tool to document children's HIV status during mothers ART clinic visits in 118 facilities in Malawi Oct-Dec 2020
- Compared women screened, child HIV testing and results, HIV+ children identified comparing Oct-Dec 2019 to post-intervention Oct-Dec 2020.

Index Case Testing (ICT) Screening Tool



Index Client Name (Mother up to *55 years*): _____
Index Client Age: _____

Date of Initial Screen: ____/____/____ ART Number: _____

Number of Living Children in Household <19 years:
Write the names of these children below and complete the "HIV status" column.

Have ALL of these children had an HIV test*? *Circle* ***Y or N:***
if Yes* → tool is complete. Check "tool complete" box to right and date and continue ICT screening.
if No → offer FRS for each untested child and enter woman into ICT register with all contacts.
**circle yes if an exposed infant had a DBS or rapid test, even if their HIV status is "exposed."*

Date tool complete:
(date that all children on tool have documented status)
☐ ____/____/____

for office use only:
date entered into database:
date entered into database:
date entered into database:
date entered into database:

Name of Child <19	Age (Years)	Date of HIV Test	HIV Status *(circle)* (I=infected, U=uninfected, E*=exposed) *using ART definition of HIV status.
			I U E
			I U E
			I U E
			I U E
			I U E
			I U E
Additional children identified after initial screen:			
			I U E
			I U E

- Invited to bring untested children for test (CHW counsel, identify barriers, improve access testing)
- Tool reviewed with mother subsequent visits to update status of child

→**26%** of women screened had at least 1 untested child

→Of 60,944 children identified, **23%** were untested

→Using tool, **55%** of children 0-19 yr with unknown status were tested by mother's next ART visit; **5%** new HIV+ dx (range 4-12% by age, with highest yield 1-2 yr/o)

Impact ICT Screening Tool on Screening, Testing and Ped Case ID Pre- and Post-Tool Use

Outcome	Oct-Dec 2019 (pre-tool use)	Oct-Dec 2020 (during tool use)	Change
# women screened	12,350	18,342	**+49%**
# children tested	2,500	4,075	**+63%**
# children testing HIV+	78	123	**+58%**



Pediatric HIV Care and HIV-Exposed Uninfected Children

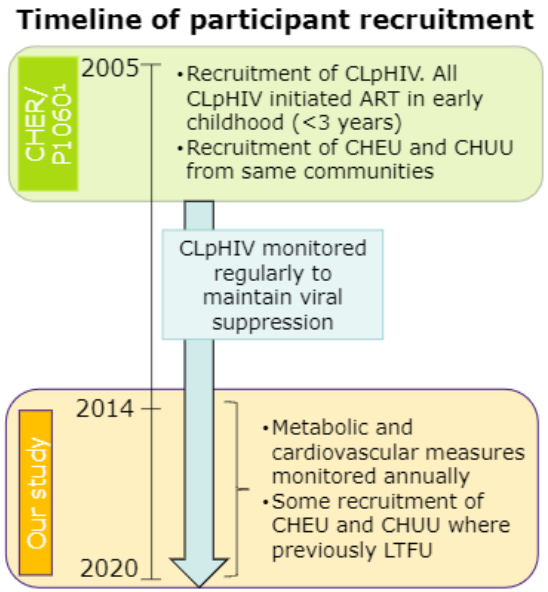


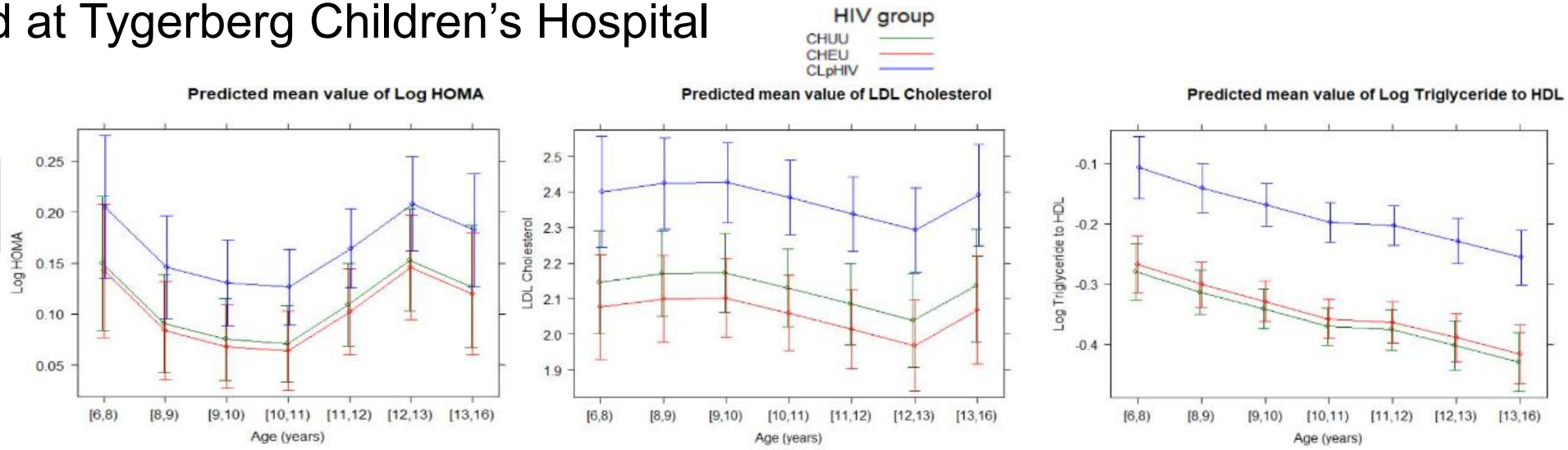
Photo credit: Paul Jeffrey, World Council of Churches

Insulin Resistance and Metabolic Syndrome in Children with Perinatal HIV Infection South Africa

Davies C et al. International Pediatric HIV Workshop Abs 9/ IAS Virtual Abs OAB0503 July 2021

- Longitudinal study 2014-2020 of 141 children with perinatal HIV and early ART (pHIV) (CHER, P1060), 169 HIV-exposed uninfected (HEU), and 175 HIV-unexposed (HUU) children followed at Tygerberg Children's Hospital





→Children perinatal HIV on early ART have persistently ↑ insulin resistance, triglyceride:HDL ratio, LDL cholesterol compared to HEU and HUU.

→Monitoring & preventive interventions for CV disease needed for children with perinatal HIV on ART.

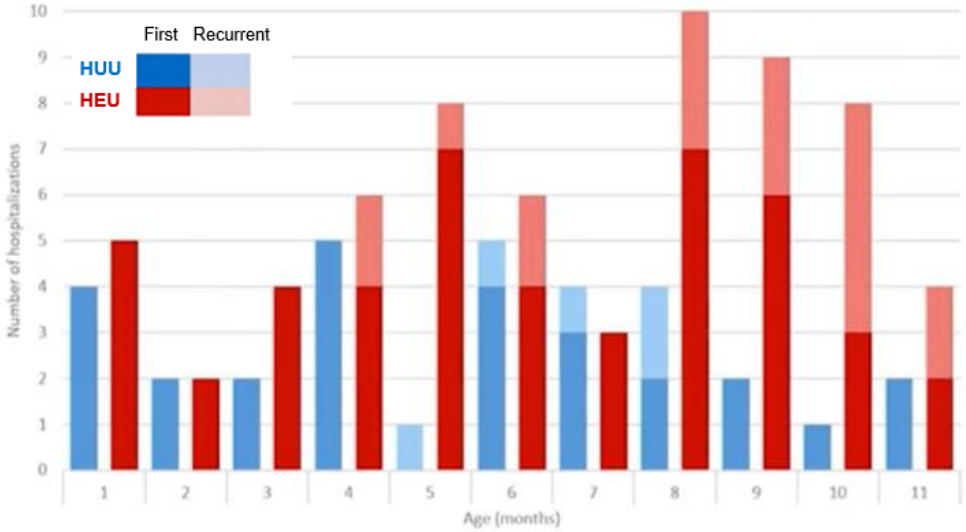
→No significant differences seen between HEU and HUU children.

Increased Infectious-Cause Hospitalizations in HIV-Exposed Uninfected Infants Compared to HIV-Unexposed Infants, S Africa

Anderson K et al. International Pediatric HIV Workshop Abs 23/IAS Virtual Abs PEB221 July 2021

- Prospective cohort of pregnant women with and without HIV from large antenatal clinic 2017-2018; included 458 HIV unexposed (HUU) and 455 HIV-exposed uninfected (HEU).

Number First and Recurrent Infection-Related Hospitalizations by Age and HIV-Exposure (HUU vs HEU)



Among infants hospitalized between 2-12 mos:

- 30% previously hospitalized as neonates
- 20% preterm
- 77% hospitalizations associated with infections
- 84% infectious causes respiratory tract

	HUU n=458	HEU n=455	P value
Post-neonatal hospitalization	32 (7%)	58 (13%)	0.004
Etiology: infectious	27 6%)	47 (10%)	0.014
Very severe infection	12 (3%)	27 (6%)	0.041

In models evaluating associations with infectious cause hospitalization in HEU between 2-12 months:

→**HIV exposure independently associated** with ~2 to 3-times higher risk of hospitalization

→Other independent associated factors:

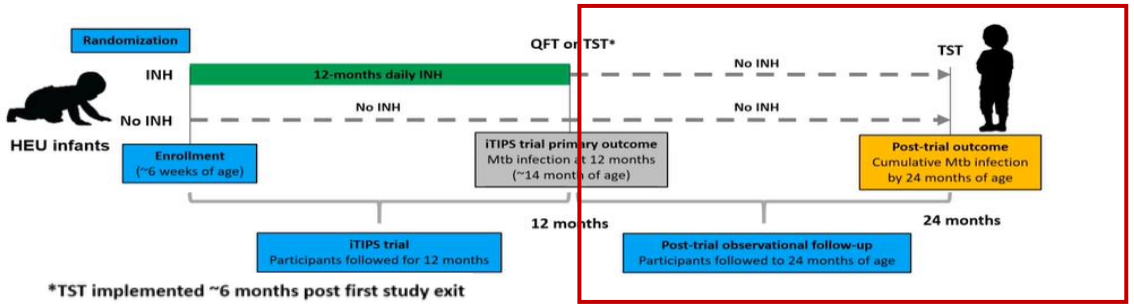
- Preterm birth
- Lower duration of breastfeeding

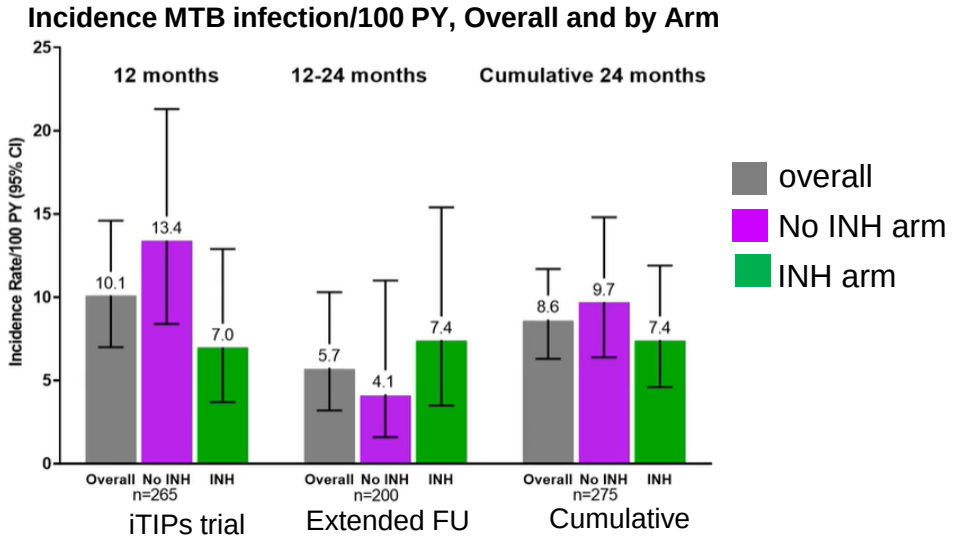
Infant Tuberculosis Prevention Study (iTIPS)

Extended Post-Trial Follow-Up: Factors Associated with TB Infection Age <2 Years

LaCourse SM et al. IAS Virtual Abs OAB0205 July 2021

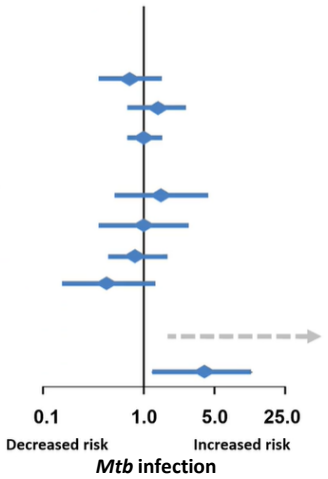
- iTIPS trial of INH prophylaxis in HIV-exposed uninfected infants *(LaCourse et al. BMJ Open 2020)* *Mtb* infection INH 7.0 vs No INH 13.4/100 PY, HR 0.53 (0.24,1.14), p=0.11.
- Follow-up to 24 months to look at factors associated with *Mtb* infection by age 2 years.





Correlates of 24-month cumulative Mtb infection

	RR (95% CI)	p
Infant Characteristics		
Study arm (INH)	0.8 (0.4-1.4)	0.38
Female	1.5 (0.8-2.7)	0.22
WAZ (kg)	1.0 (0.7-1.3)	0.79
Maternal Characteristics		
HIV viral load >1000	1.5 (0.5-4.4)	0.42
History of TB	1.0 (0.4-2.6)	0.99
Ever IPT	0.9 (0.5-1.7)	0.67
Current IPT	0.5 (0.2-1.3)	0.14
Household Characteristics		
No flush toilet	--	<0.001
No running water	3.9 (1.3-12.4)	0.02



→24-mo cumulative *Mtb* infection high in HEU (8.6%/yr)

→Prior receipt of INH prophylaxis did not ↓ incidence

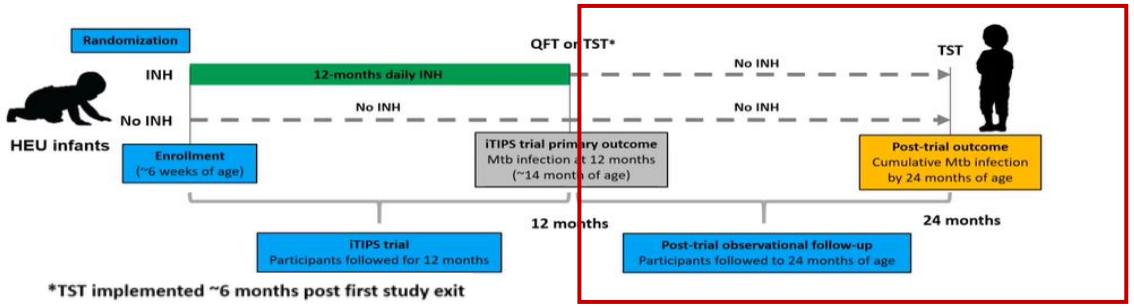
→Poor household conditions associated with infection

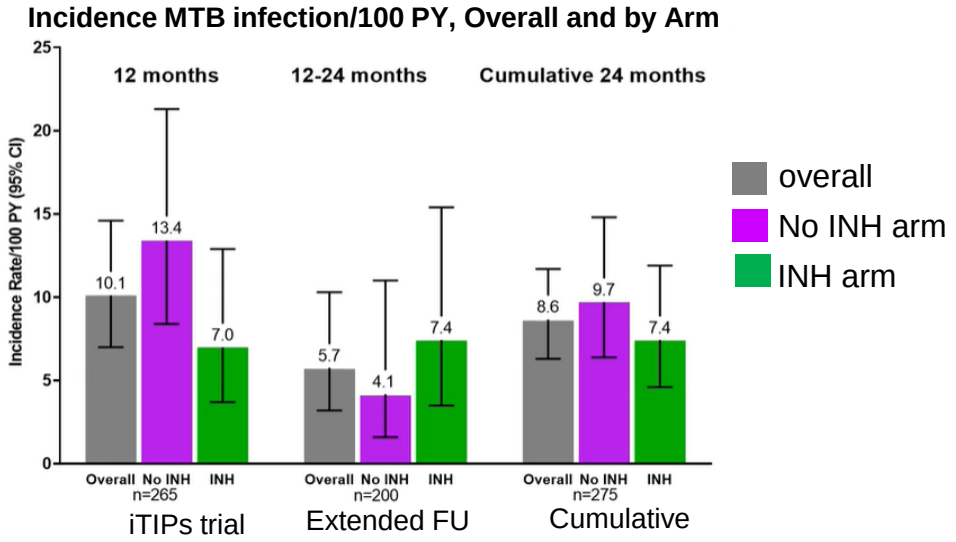
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LaCourse SM et al. IAS Virtual Abs OAB0205 July 2021

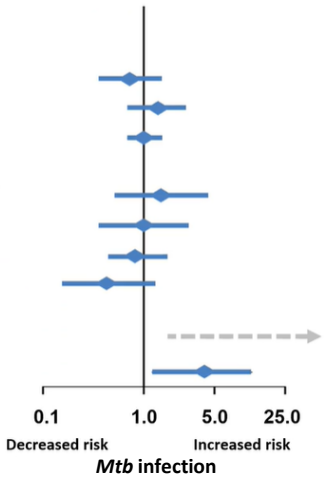
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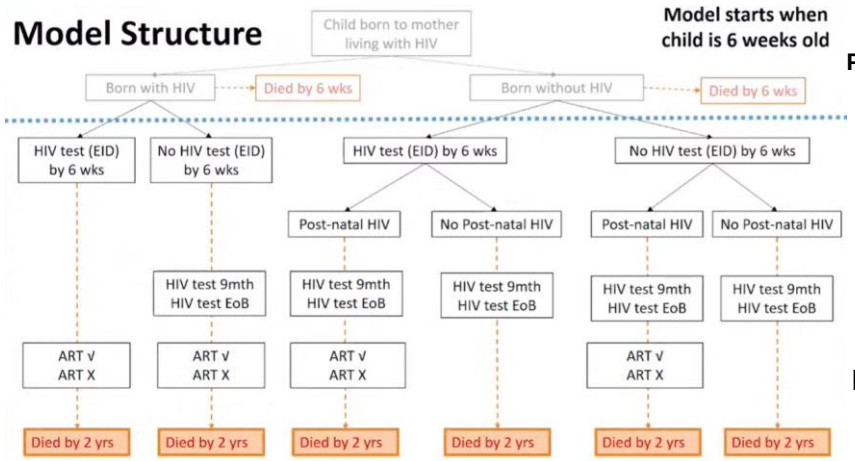
CTX Prophylaxis for HIV-Exposed Children – Modeling Impact of Different Strategies Up to Age 2 Years

Simon KR et al. International Pediatric HIV Workshop Abs 27

- Modeled 6 different strategies for CTX prophylaxis in 5 African countries: current rec (6 wk to end BF), 4 strategies with shorter durations, and 1 where only HIV+ children receive, with outcome death between 6 wk and 24 mos.

CTX Prophylaxis Strategies (age 6 weeks to end of BF)

Strategy	Positive EID (6 wks)	No positive EID result (6 wks)	
		Prior to positive HIV test result	Once receive positive HIV test result
0: No CTX (Base case)	No CTX	No CTX	No CTX
1: CTX for all (current guidelines)	CTX	CTX until EoB	CTX
2: CTX for 3 mths	CTX	CTX until 3 months	Restart
3: CTX for 6 mths	CTX	CTX until 6 months	Restart
4: CTX for 9 mths	CTX	CTX until 9 months	Restart
5: CTX for 12 mths	CTX	CTX until 12 months	Restart
6: CTX once positive result	CTX	No CTX	CTX



Factor Associated with Risk Mortality

HIV test at 6 wks

Postnatal MTCT

HIV test at 9 mo

HIV+ started on ART

Primary Model assumptions 1

Parameter	Assumption	Source
HIV transmission (by end of breastfeeding)	South Africa: 4% Zimbabwe:8.2% Cote d'Ivoire: 13.3% Mozambique: 14% Uganda: 6%	UNAIDS Factsheets 2019; Dunning JIAS; Mahy AIDS 2017; Lain PLOS One 2020; Zimbabwe Ministry of Health
Early HIV test (by 6 wks)	South Africa: 83% Zimbabwe: 63% Cote d'Ivoire: 53% Mozambique: 71% Uganda: 56%	
Received 9-month/end of breastfeeding test if have early HIV test if no early HIV test	 50% 30%	Expert opinion
Death (6wks to 2 years): HIV exposed, uninfected HIV positive, no ART HIV positive, ART	 3.7% 53.6% 6.5%	Arikawa CID 2018 Evans CID 2021 (SHINE) Becquet PLOS One 2012 Cotton Lancet 2013 (CHER)
ART uptake	80%	JIAS Dunning

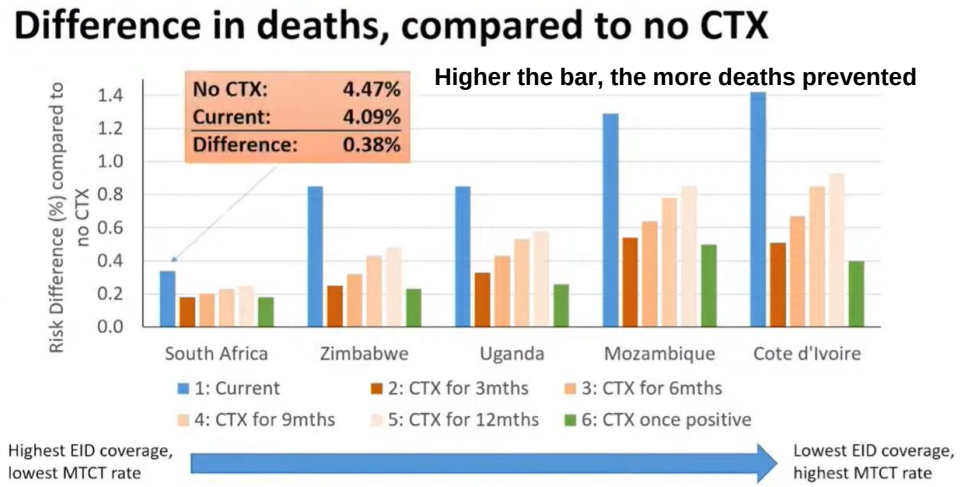
Primary Model assumptions 2

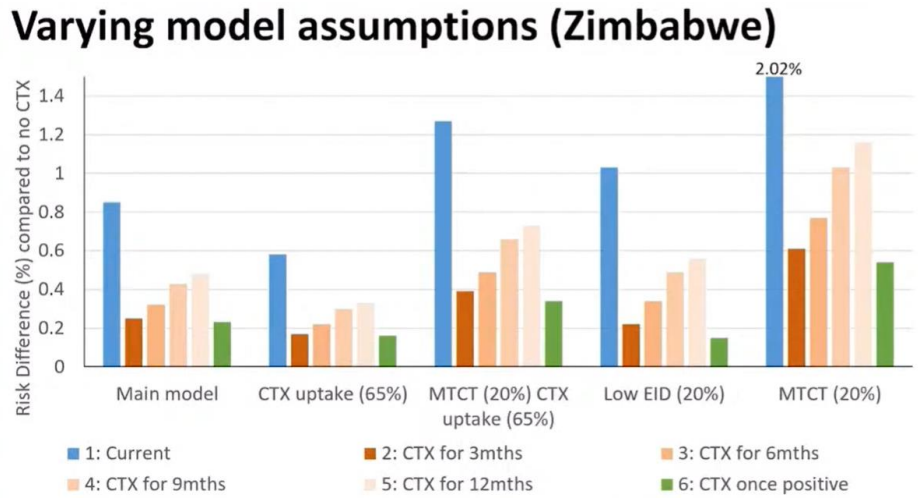
Parameter	Assumption	Source
CTX uptake	100%	Assumption
Relative risk for death: CTX vs no CTX Infants with HIV Infants without HIV	 0.57 1.00	CHAP NEJM 2013 Lockman Lancet GH 2017; Daniels Lancet GH 2019

CTX Prophylaxis for HIV-Exposed Children – Modeling Impact of Different Strategies Up to Age 2 Years

Smith C et al. International Pediatric HIV Workshop Abs 27

- Evaluated **risk difference in mortality** compared to no CTX.





→ In all countries, current strategy provides most benefit.

→ However, in countries with **high testing coverage** and **low MTCT**, the benefit is relatively small compared to the other strategies – so shorter duration of CTX or only provision to HIV+ might be considered.

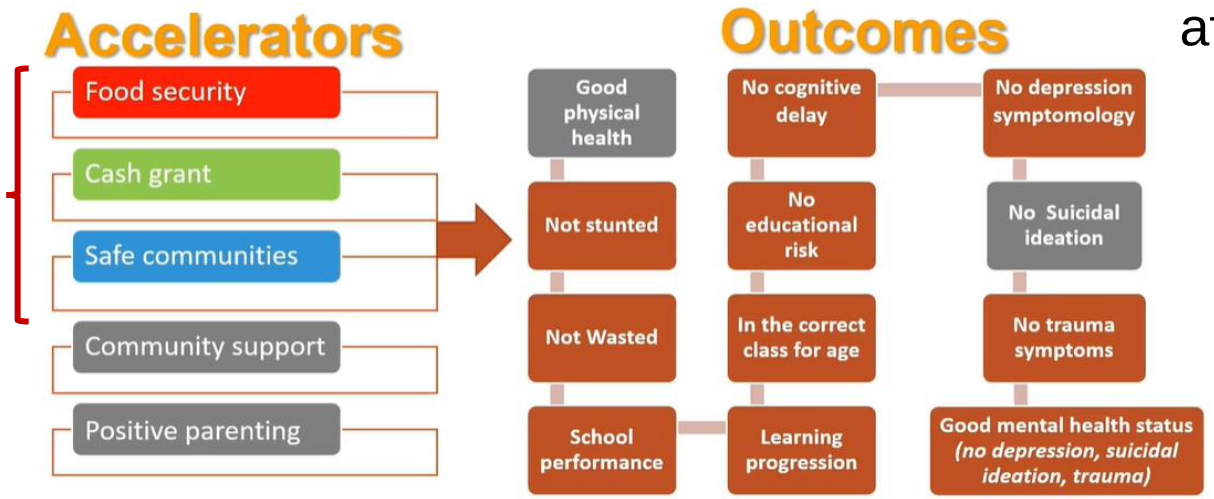
→ In countries with **low testing coverage** and **high MTCT**, considerably larger benefit for providing CTX for prolonged – due to the larger %children with undiagnosed HIV and not receiving CTX in the alternative strategies.

→ Varying model assumptions on CTX uptake, MTCT, and EID modify the risk difference compared to no CTX but do not change overall findings.

Combined Interventions to Accelerate Delivery on Outcomes for Young Children Affected by HIV in Southern Africa

Mebrahtu H et al. IAS Virtual Abs

- Used data from longitudinal study 2013-2015 HIV-affected children and their caregivers attending 28 community-based organization in S Africa and Malawi, retention 86.3%
  - Baseline 989 children aged 4-13 years and caregivers
  - Follow-up 854 children aged 5-15 years and their caregivers



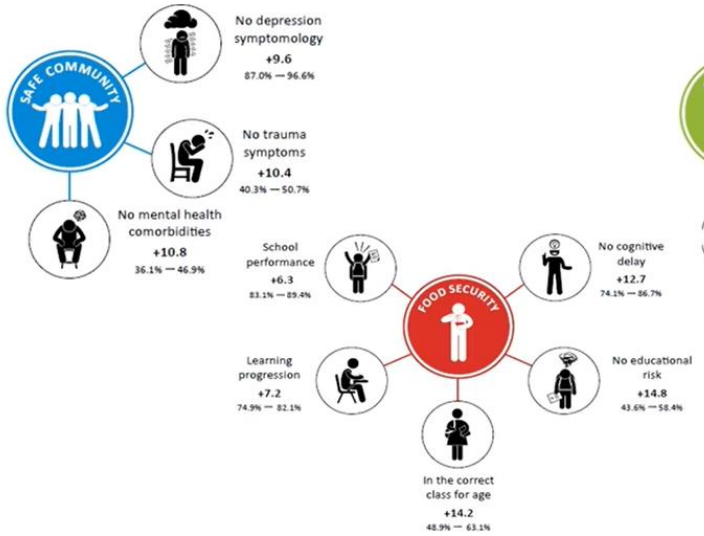
Accelerators community support and positive parenting were associated with mental health outcomes, however the other 3 accelerators had greater impact on several child outcomes.

- Accelerator: defined as a provision that positively affects child outcomes across ≥3 SDGs
  - 5 hypothesized accelerators investigated and **3 identified** – measured access baseline & FU; had to be present both baseline and FU to be viewed as present
  - 12 **child outcomes** measured at FU **and10 were associated** with accelerators.
  - Covariates – sociodemographic variables and selected baseline measures (child health status in past month and mental health outcomes).

Combined Interventions to Accelerate Delivery on Outcomes for Young Children Affected by HIV in Southern Africa

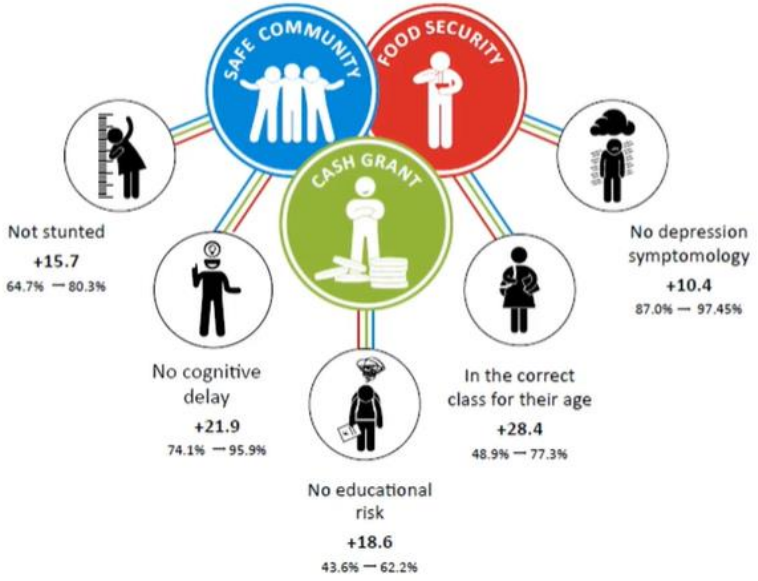
Mebrahtu H et al. IAS Virtual Abs

Adjusted probability and adjusted risk differences (RD, % points) of having SDG-aligned child outcomes with <u>single</u> accelerator provision

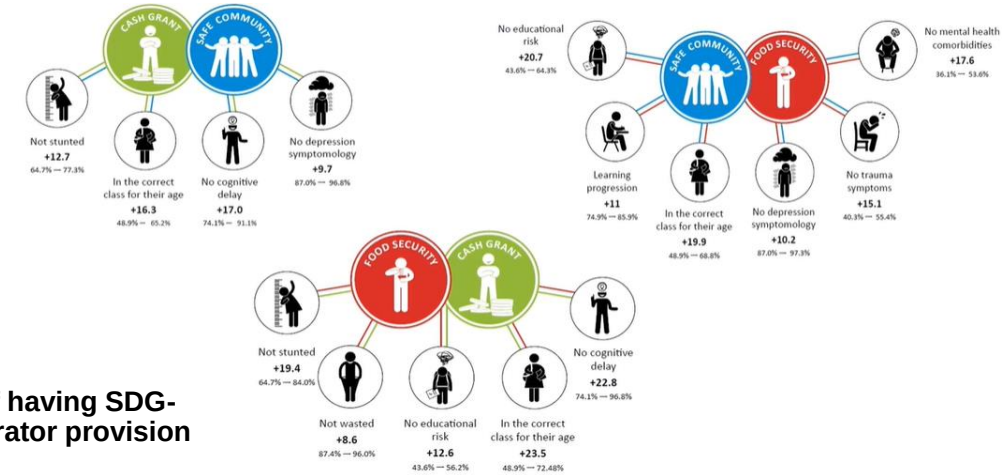


→Significant association of individual accelerator provision with decrease in adverse child and **increase in positive outcomes**

Adjusted probability and adjusted RD (% points) of having SDG-aligned child outcomes with <u>three combined</u> accelerator provision

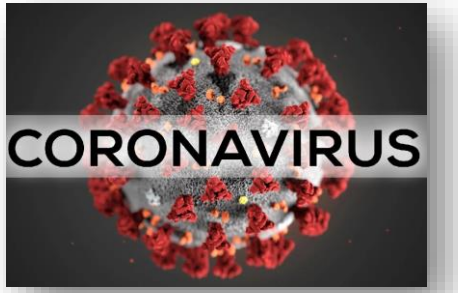


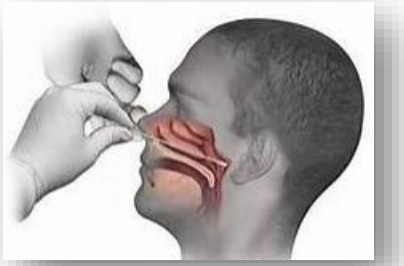
Adjusted probability and adjusted RD (% points) of having SDG-aligned child outcomes with <u>two combined</u> accelerator provision



→Additive value of having two accelerators provision with further improved child outcomes

→A combination delivery of these 3 accelerators results in highest probability of positive child outcomes and was superior to provision of individual components alone.





Effects of COVID-19-Related Mitigation Practices on Programs







Effect of COVID-19 Pandemic on HIV Services in Africa

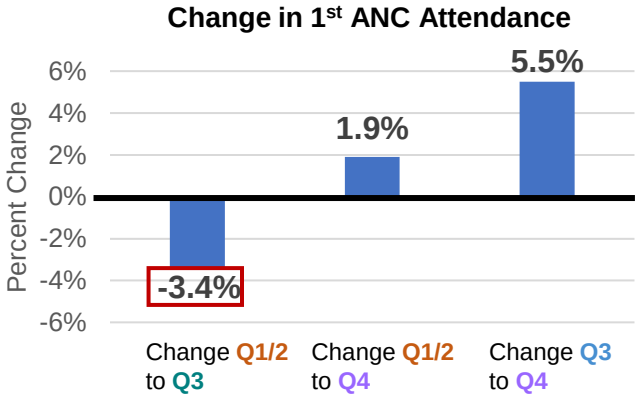
Pediatric HIV Workshop Vrazo A et al. Abs 14/IAS Virtual PEB189 July 2021

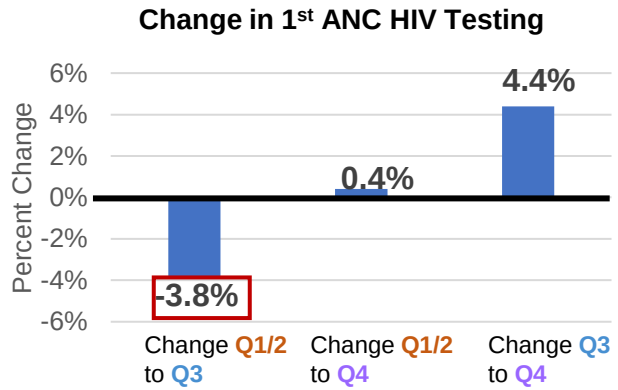
- 5 USAID/PEPFAR presentations (abstracts 14-17, 116) comparing services in pre-COVID to during COVID time-periods in 12-14 African countries.

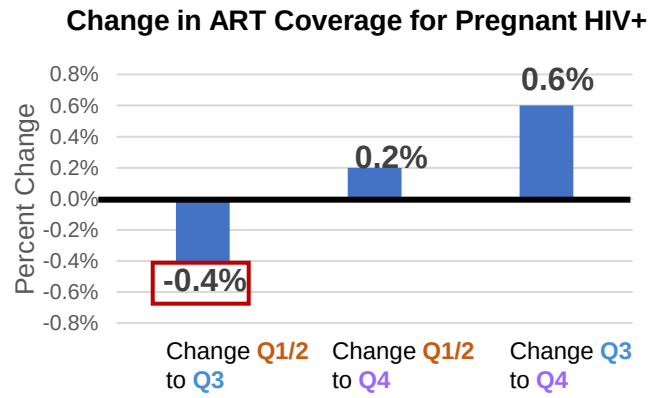
Pre-COVID-19 | **During COVID-19**

Q1: Oct 2018-Mar 2019 → Q2: Apr 2019-Sep 2019 → Q3: Oct 2019-Mar 2020 → Q4: Apr 2020-Sep 2020

- ***Services for pregnant/BF women before and during COVID-19***:
  - There were small initial early ↓ from **Q1/2** to **Q3** for ANC1 attendance, antenatal HIV testing and ART coverage for HIV+ but these reversed in **Q4.**







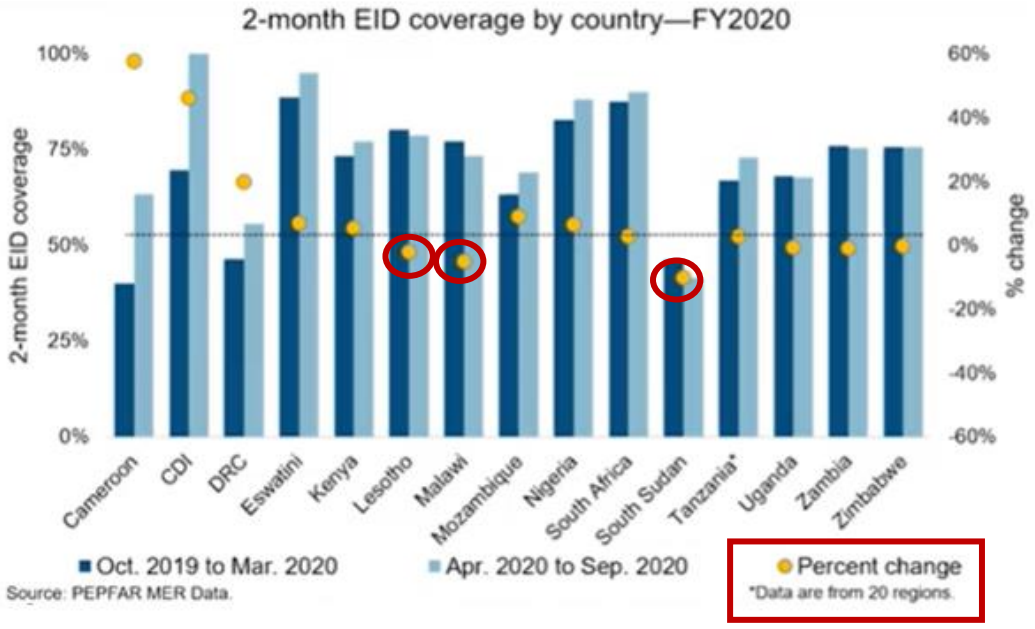
Effect of COVID-19 Pandemic on Pediatric HIV Services in Africa

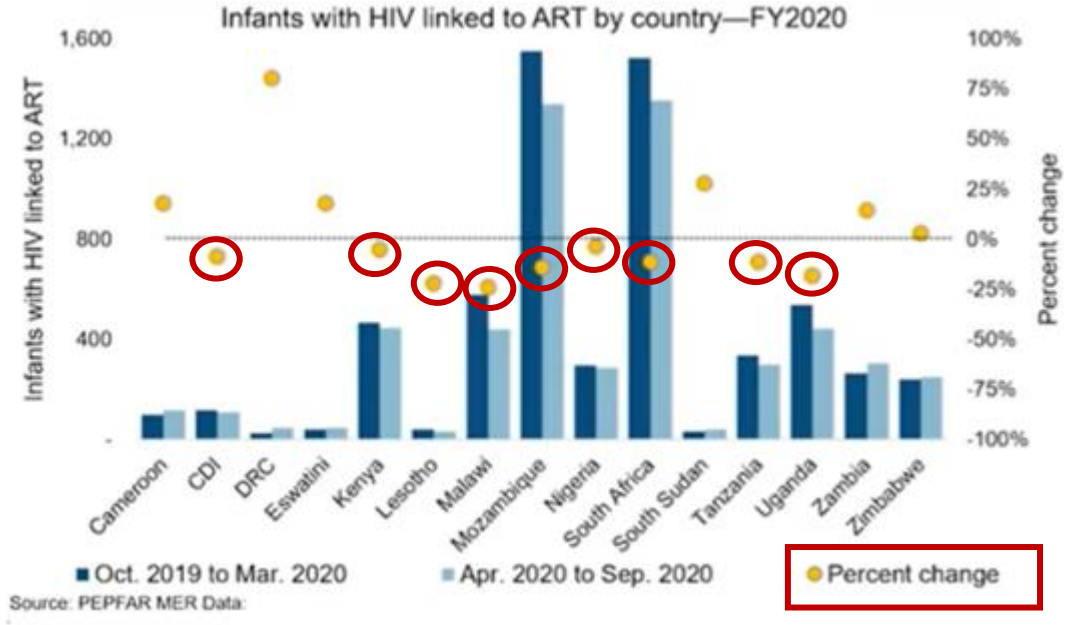
Pediatric HIV Workshop Abs 15 (Rabold E)

- ***Early infant diagnosis and linkage to care during COVID-19***:
  - EID testing volume and EID coverage were generally maintained, with ↓ in only 3 countries – but gains were less than prior year.
  - However, ↓ in HIV+ infants started on and linked to ART seen in 9 countries; overall, number linked to ART decreased by 9.8% in FY 2020.

During COVID-19

Q3: Oct 2019-Mar 2020 | Q4: Apr 2020-Sep 2020



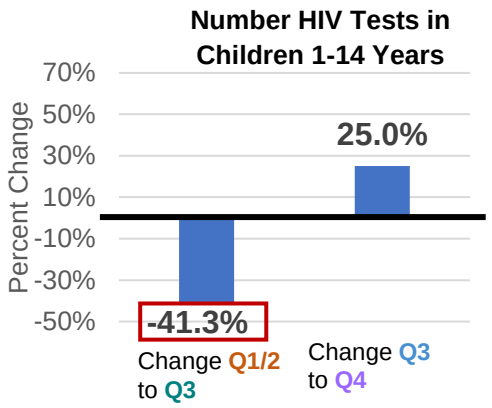


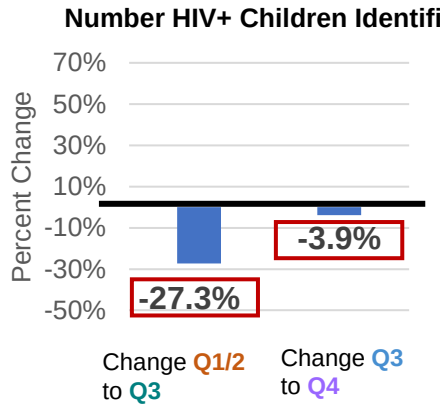
Effect of COVID-19 Pandemic on Pediatric HIV Services in Africa

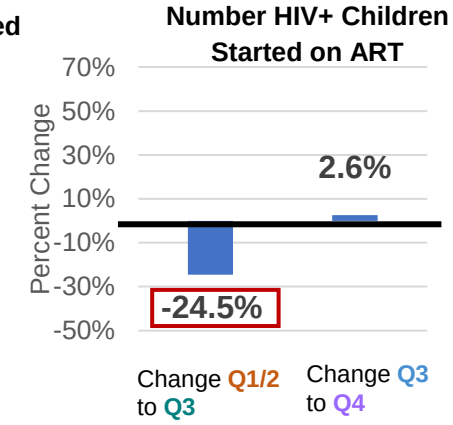
Pediatric HIV Workshop Abs 16 (Gleason M)

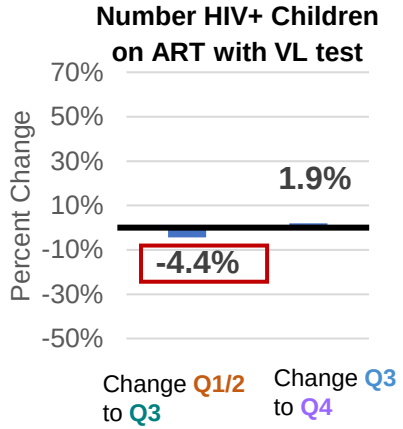
- ***Services children living with HIV:***
  - The number of children age 1-14 years receiving HIV test, started on ART, and who received VL ↓ in Q3, with some to minimal improvement in Q4.
  - The number of new HIV+ children aged 1-14 years identified ↓ significantly in <u>both</u> Q3 and Q4
  - Viral load suppression paradoxically increased during COVID-19 in both Q3 and Q4.

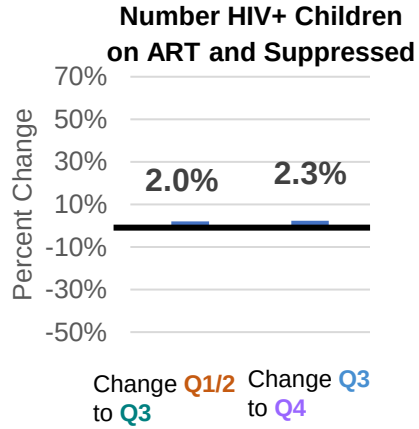








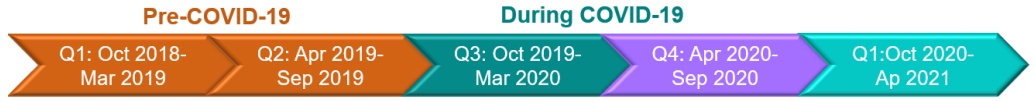




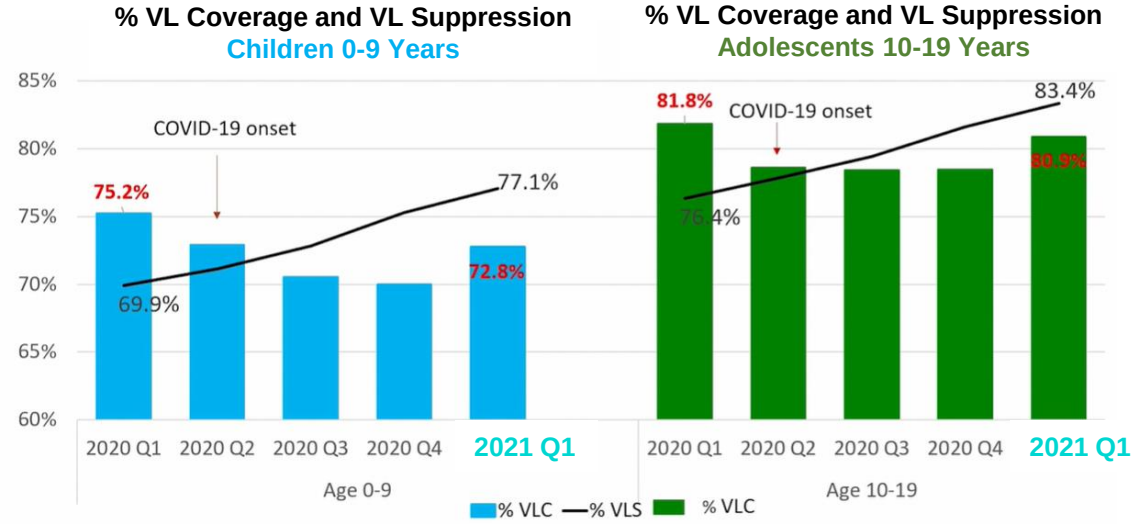
Effect of COVID-19 Pandemic on Pediatric VL Testing/Suppression in Africa

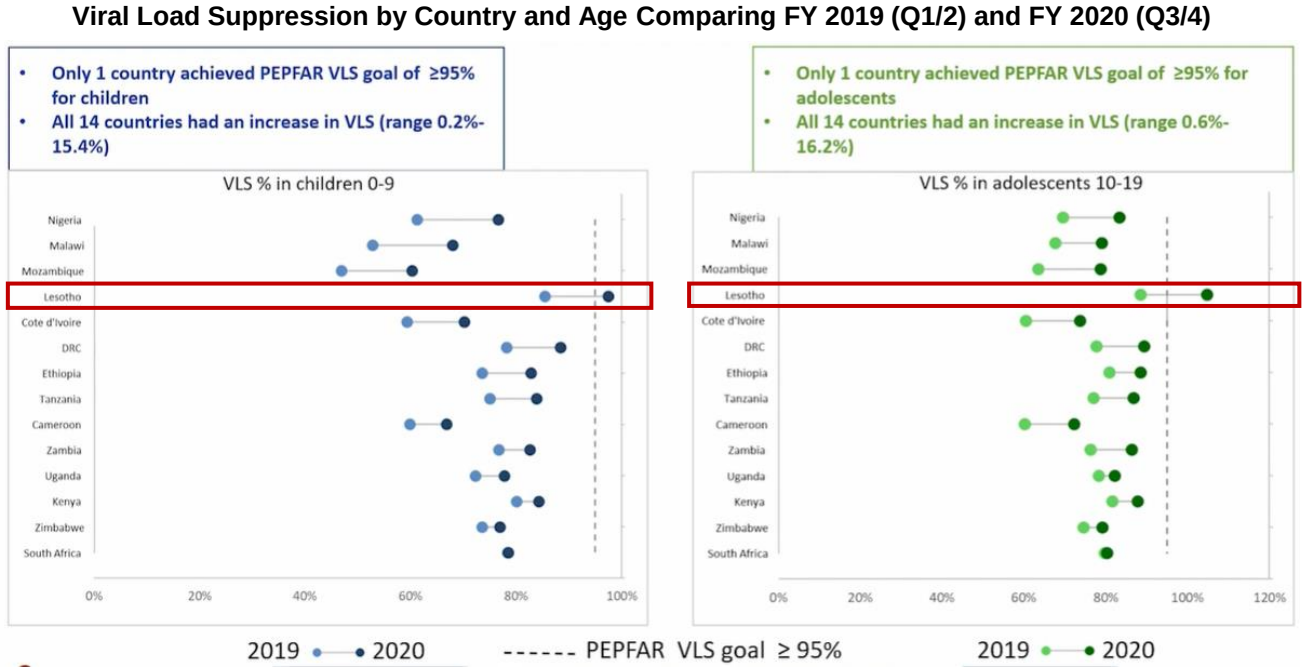
Pediatric HIV Workshop Abs 17 (Carpenter D)

- ***Viral load coverage and suppression by age:***



  - Viral load testing coverage decreased slightly in children and adolescents during COVID-19, rebounding slightly in Q1 2021.
  - Viral load suppression increased in both children and adolescents, with higher rates of suppression among adolescents – however, only one country achieved suppression goal of 95%.





Multi-Month ART Dispensing in Children During the COVID-19 Pandemic, 12 PEPFAR Focus Countries

Fernando N et al. Pediatric HIV Workshop Abs 116/IAS Virtual Abs PEB209 July 2021

- Evaluation of multi-month dispensing in children during COVID-19 in 12 countries

Table 1. MMD among <15y/o across 12 PEPFAR-supported countries, October 2019 - September 2020

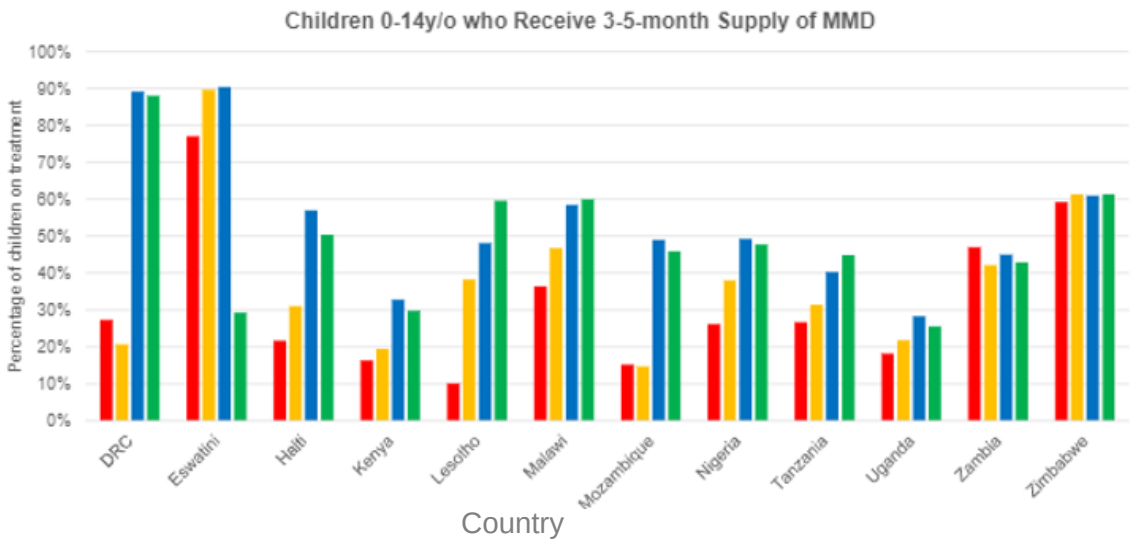
FY20 Quarters	CLHIV on Treatment[1]	<3MMD (%)	3-5MMD (%)	6MMD (%)
FY20Q1	176,516	108,210 (65.6%)	52,769 (32.0%)	3,919 (2.4%)
FY20Q2	181,123	109,186 (60.6%)	65,510 (36.4%)	5,453 (3.0%)
FY20Q1/Q2 (p<0.01)	178,820	108,698 (63.1%)	59,140 (34.2%)	4,686 (2.7%)
FY20Q3[2]	182,914	82,304 (46.3%) **	84,725 (47.6%) **	10,869 (6.1%) *
FY20Q4[3] (p<0.001)	185,357	7,944 (45.2%) **	80,673 (45.9%) *	15,774 (9.0%) **

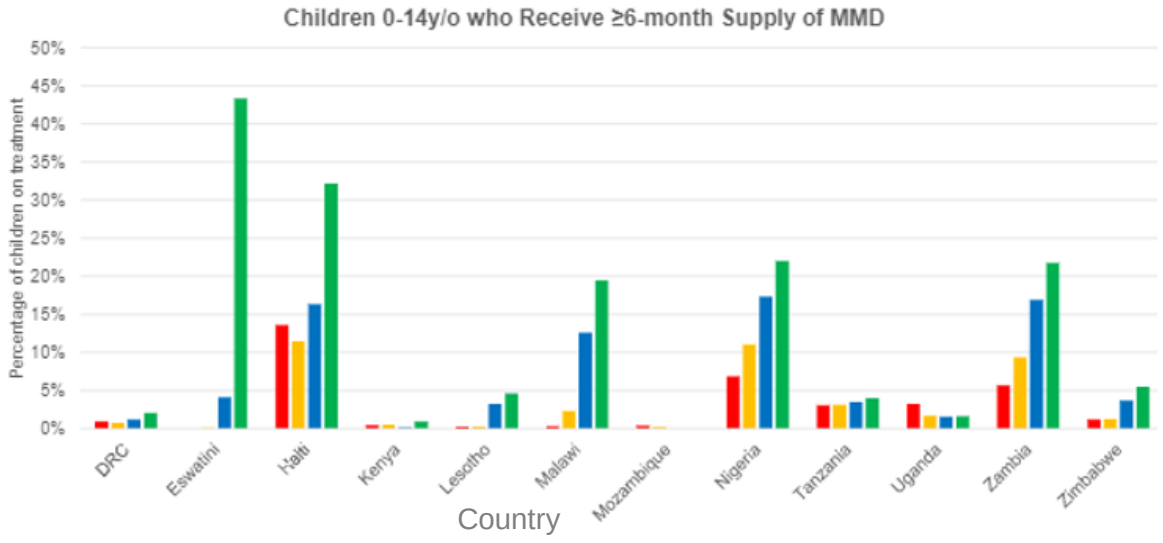
→ *Across all countries*, MMD uptake among CLHIV on ART increased significantly during the COVID-19 pandemic.

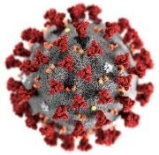
→ 3-5MMD ↑ from 34.2% Q1/Q2 to 45.9 to 47.6% Q3/Q4

→ 6MMD ↑ from 2.7% Q1/Q2 to 6.1% Q3 and 9.0% Q4 although coverage for 6MMD remains low

FY 20 Q1 FY 20 Q2 FY 20 Q3 FY 20 Q4







Effect of COVID-19 Pandemic on HIV Services in Africa

Conclusions from USAID Presentations

Pediatric HIV Workshop Abs 14 (Vrazo A), 15 (Rabold E), 16 (Gleason M), 17 (Carpenter D), 116 (Fernando)

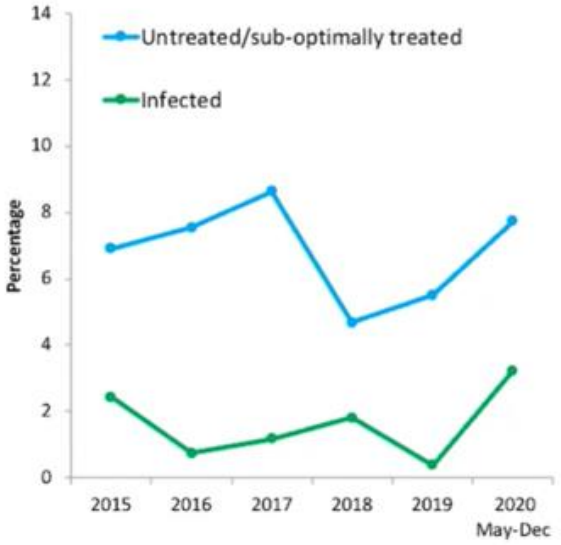
- Initial declines in services during COVID-19 pandemic improved as countries try to adapt services COVID-19 pandemic, showing resilience of country programs to implement and scale up strategies to improve outcomes for children and youth, such as MMD.
- However, of concern is decrease in identification of older infected children 1-14 years, linkage of newly identified HIV+ infants and children to treatment, and viral load coverage, all of which have decreased with only minimal improvement.
- The observed improvement in viral suppression may be biased as those children less likely to be adherent to ART may be more likely to lack VL testing, with testing limited to those more adherent to clinic and testing visits. Additionally, we still have a way to go to reach suppression of 90-95% in children and youth.

Impact of COVID-19 on Perinatal HIV Prevention in Canada: Canadian Perinatal HIV Surveillance Program

Singer J et al. Pediatric HIV Workshop Abs 13

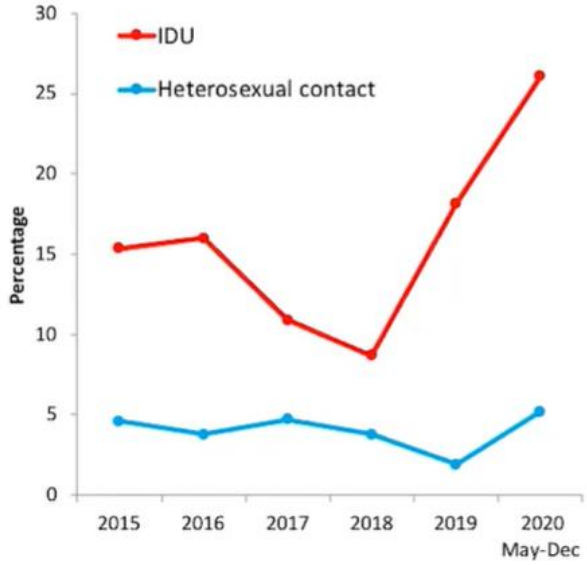
- Canadian National Perinatal HIV Surveillance Program compared rate of suboptimal care (no ART, <3 ARV drugs or <4 weeks of ART in the 4 weeks prior to birth) and vertical transmission from period 2015-2019 versus the period from May-Dec 2020.

Rate of no/suboptimal treatment increased along with rate of vertical transmission during COVID-19 to highest rate in over 5 years

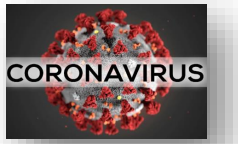


	2015-2019	2020 May-Dec
Untreated/ sub-optimally treated	86/1297 (6.6%)	12/155 (7.7%)
Infected	17/1297 (1.3%)	5/155 (3.2%)

Rate of no/suboptimal treatment was particularly elevated among drug using pregnant women

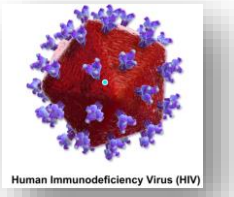


	2015-2019	2020 May-Dec
IDU	32/236 (13.6%)	6/23 (26.1%)
Heterosexual contact	30/803 (3.7%)	5/97 (5.2%)

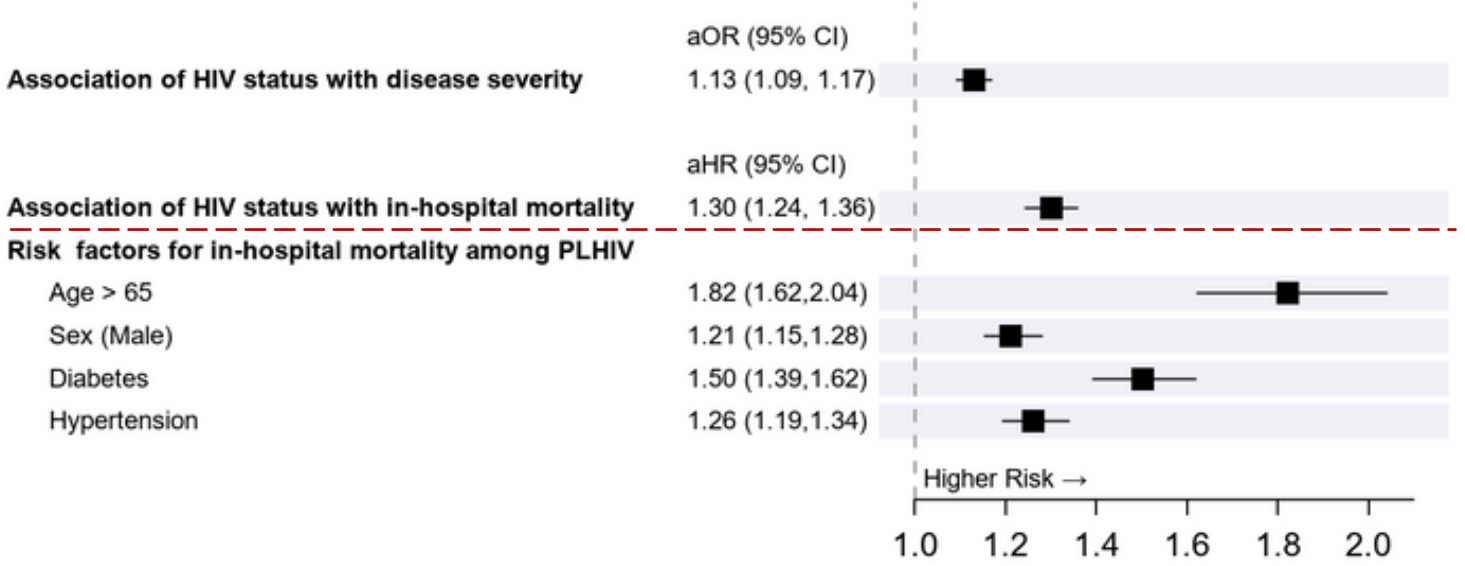


HIV Infection is Independently Associated with COVID-19 Disease Severity and In-Hospital Mortality in Adults

Bertagnolio S et al. IAS Virtual July 2021 Abs Late Breaker PEBLB20



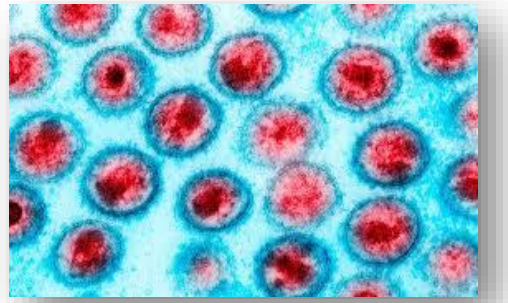
- Jan-Ap 2021 anonymized individual level data from 268,412 hospitalized adults with COVID-19 from 37 countries were reported to WHO.
- Outcomes of 15,522 PLHIV from 168,649 hospitalized patients were evaluated.
- 91.8% receiving ART; 36.2% had severe/critical illness, 23.1% died in-hospital.
- HIV was independently associated with severity of illness and in-hospital mortality.



World Health Organization

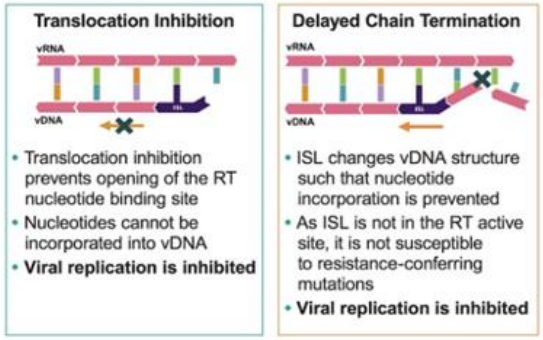


The Future:



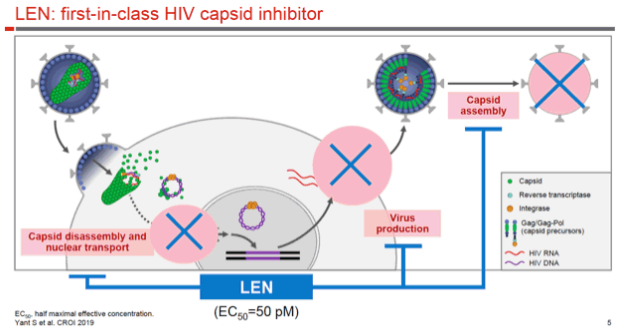
Long-Acting ART and PrEP Options

Islatravir





Lenacapavir



High Rates Drug Resistance (DR) in PrEP Failures Kenya, Zimbabwe, Eswatini, S Africa

Parikh U et al. IAS Virtual July 2021 Abs LB-02361

- Monitoring DR through national research protocols/demo projects for >104,000 persons on PrEP from Dec 2017-Jan 2021
- Reported on DR in 208 current PrEP users (118 specimens sequenced) identified as HIV+ after PrEP start [0.2% on PrEP]; pt mostly female (75%), young (52% 16-24 yrs), mostly AGYW or sero-different couples (65%); 58% were on PrEP >3 mos before seroconverting

Resistance **PrEP Adherence**

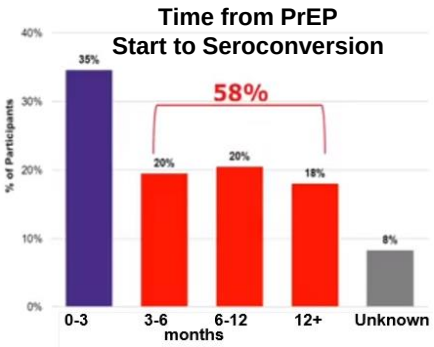
MUTATION PROFILE	# PARTICIPANTS	LOW <350 fmol/punch <2 doses/week	MODERATE 350-699 fmol/punch 2-3 doses/week	HIGH ≥700 fmol/punch 4-7 doses/week
No resistance mutations	65/118 (55%)	**34/41 (82%)**	1/41 (2%)	6/41 (15%)
Not associated with PrEP NNRTI DR only	26/118 (22%)	12/20 (60%)	1/20 (5%)	7/20 (35%)
PrEP-associated (K65R, K70E, M184IV)	**27/118 (23%)**	2/18 (11%)	2/18 (11%)	**14/18 (78%)**

→ 78% of pt with PrEP-related resistance had drug levels associated with high adherence, while 82% of those with no resistance had drug levels associated with low adherence

PrEP-Associated Resistance

PrEP mutations only (n=14)	PrEP & NNRTI mutations (n=13)
K65R, K70E, M184V	K65R, M184V + L100I, K103N
M184I/V *(13 cases)*	K65R, M184V + K101E, V106M, E138A, G190A
	K65R + K103N
	M184I/V + various NNRTIs *(10 cases)*

→ 50% of PrEP-related resistance cases had K65R and/or M184IV mutations only



→ Seroconversions on PrEP small (0.2%)

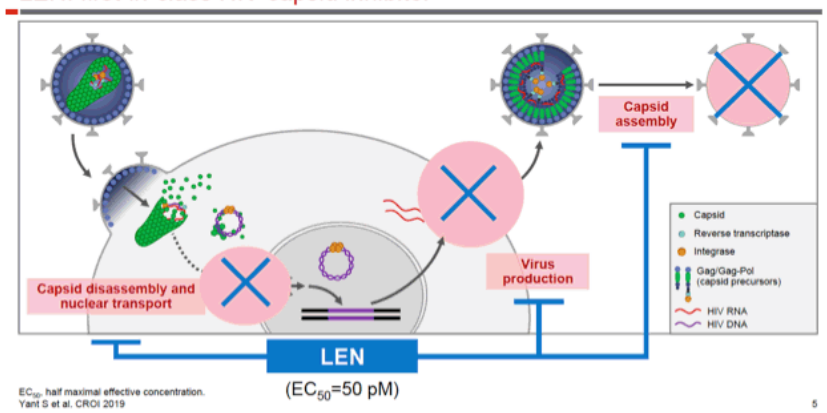
→ 23% had DR TDF/3TC, most having high adherence

→ 22% only NNRTI mutations = background transmitted DR

New Long-Acting Drugs for ART and PrEP – Studies in Adults

Lenacapavir

LEN: first-in-class HIV capsid inhibitor

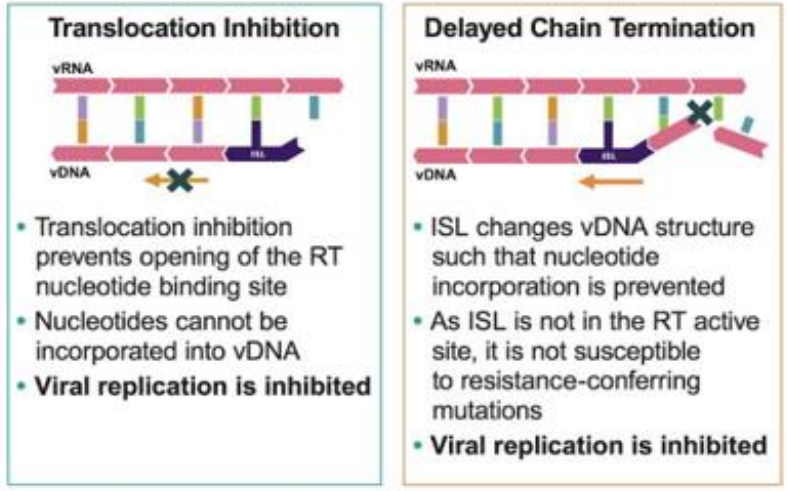


EC_{50}, half maximal effective concentration.
Yant S et al. CROI 2019

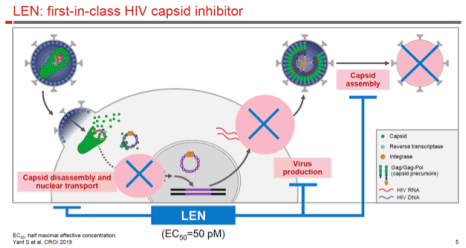
- LEN is given subcutaneously once every 6 months.
- LEN ART data from ART-experienced MDR HIV and ART-naïve patients presented
- **81%** suppression with OBR in ART-experienced at wk 26
- **94%** suppression with F/TAF in ART-naïve at wk 28 (similar to comparator B/F/TAF)
- PrEP studies in women and MSM/TGW planned

Islatravir

First-in-Class NRTTI with Multiple Mechanisms of Action



- ISL given orally once a month for PrEP, phase IIa study
- Well-tolerated, most AE mild and no drug-related SAE; lab ≥Grade 3 rare.
- ISL triphosphate in PBMC remained above the pre-specified PK threshold for HIV prevention through at least **8 weeks** after last dose.
- PrEP studies in women and MSM/TGW planned



Efficacy & Safety of Long-Acting Subcutaneous (SC) Lenacapavir (LEN) in **ART-Experienced Adults**

Monina J al. IAS Virtual July 2021 Abs OALX01LB02

- Enrolled adults with RNA ≥400 c/mL, resistance to ≥2 drugs and ≤2 fully active drug; median baseline log RNA 4.5 c/mL; 28% had RNA >75,000 c/mL at baseline

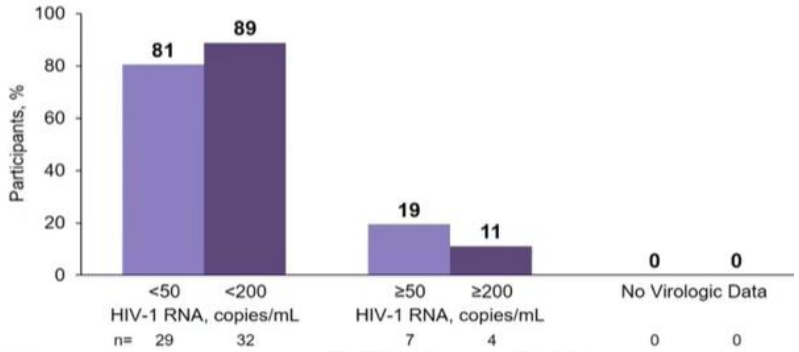


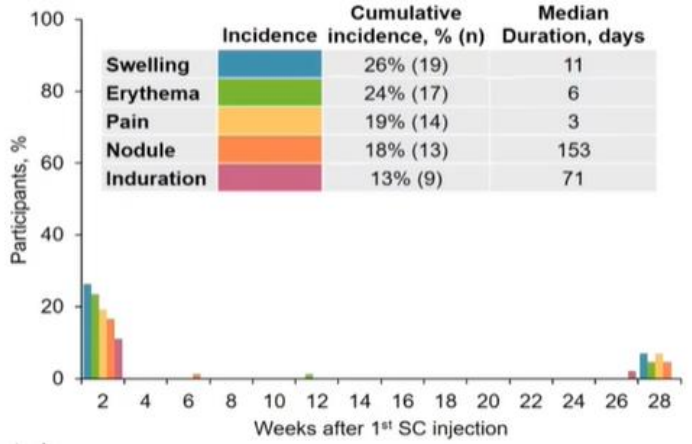
26-week data, all on SC LEN

n (%)	Randomized Cohort n=36
Participants meeting criteria for resistance testing	11 (31)
No emergent LEN resistance	7 (19)
Emergent LEN resistance	4 (11)
M66I	4
Q67H	1
K70N/R/S	1
N74D	1

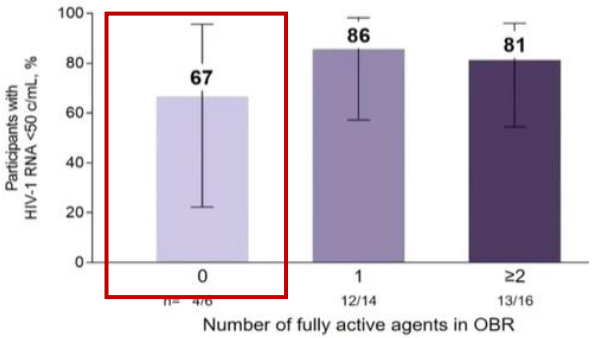
→ 4 with LEN resistance stayed on LEN; 3 resuppressed (2 without and 1 with OBR change), 1 with no fully active agent never suppressed.

26-week viral suppression





Suppression by # fully active drugs in OBR

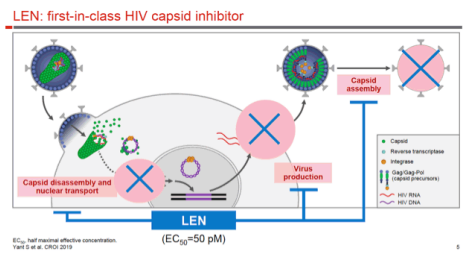


→ LEN+OBR led to high-rate viral suppression week 26 (81%)

→ Also increase CD4 (22% <50 baseline, none <50 week 26)

→ Well-tolerated, no AE leading to dc – all 36 pt received 2nd SC injection

→ Important agent for person with multi-drug resistance

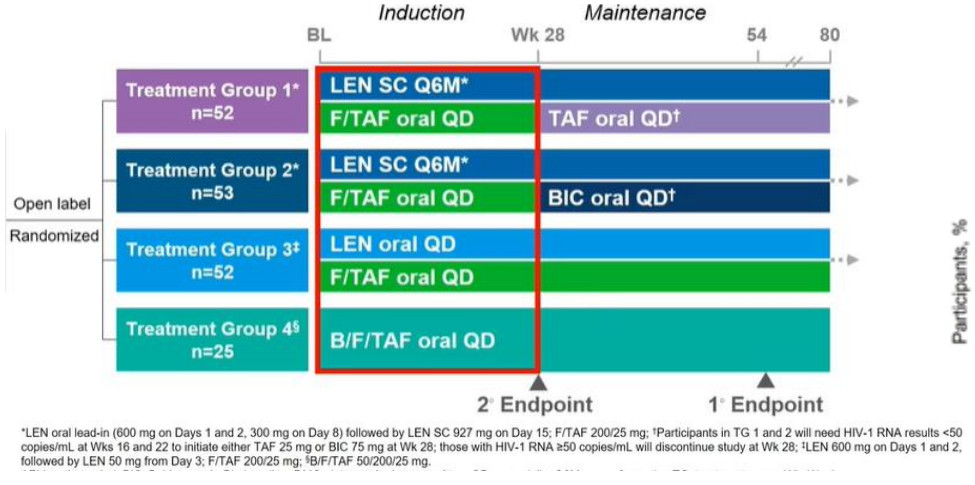


Efficacy & Safety of Long-Acting Subcutaneous Lenacapavir (LEN) in **ART-Naïve Adults**

Gupta S et al. IAS Virtual July 2021 Abs OALB0302

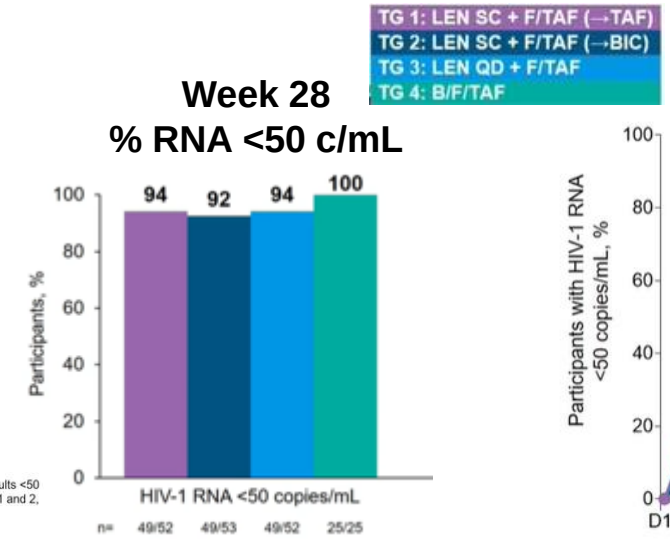
- Enrolled 182 ART-naïve adults with RNA ≥200 c/mL (15% >100,000), CD4≥200 to LEN SC q6mo plus F/TAF qd (with difference maintenance regimen after 28 wks) or LEN/F/TAF oral qd compared to BIC/F/TAF

28-week data

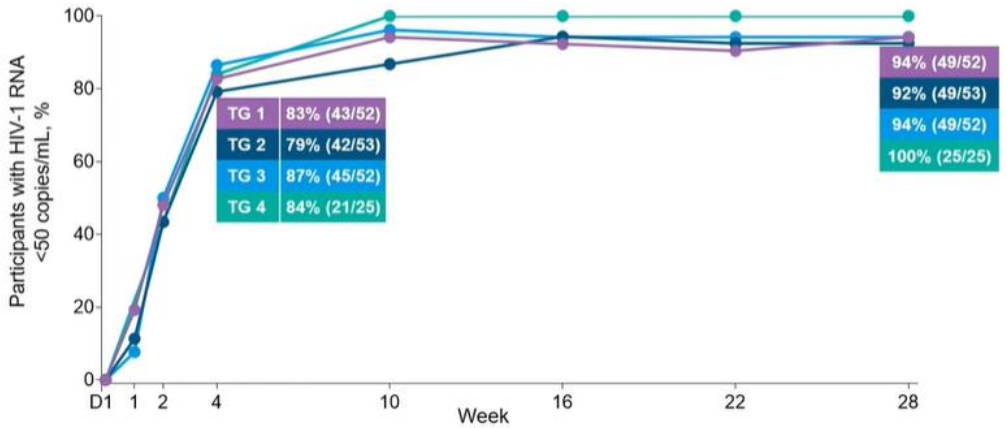


*LEN oral lead-in (600 mg on Days 1 and 2, 300 mg on Day 8) followed by LEN SC 927 mg on Day 15; F/TAF 200/25 mg; †Participants in TG 1 and 2 will need HIV-1 RNA results <50 copies/mL at Wks 16 and 22 to initiate either TAF 25 mg or BIC 75 mg at Wk 28; those with HIV-1 RNA ≥50 copies/mL will discontinue study at Wk 28; ‡LEN 600 mg on Days 1 and 2, followed by LEN 50 mg from Day 3; F/TAF 200/25 mg; §B/F/TAF 50/200/25 mg.

Week 28
% RNA <50 c/mL



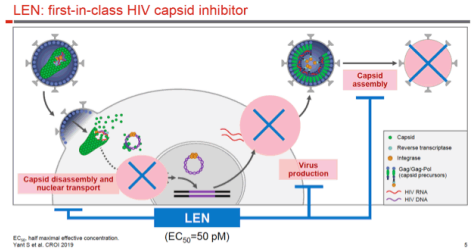
Proportion with RNA <50 c/mL over time



- Adverse events: no SAE or grade 4 AE related to study drug, no clinically relevant Grade ≥3 lab with no discontinuations for AE.
- 61% had no injection site reactions (ISR); 83% of IRS were Grade 1 and resolved in days; 1 Grade 3 ISR (nodule), no Grade 4.

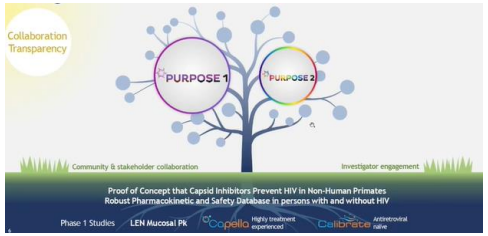
→ LEN SC or orally with F/TAF = safe, well-tolerated, with high suppression (94% <50 c/mL) at week 28

→ Continued study in ART-naïve, ART-experienced and for PrEP



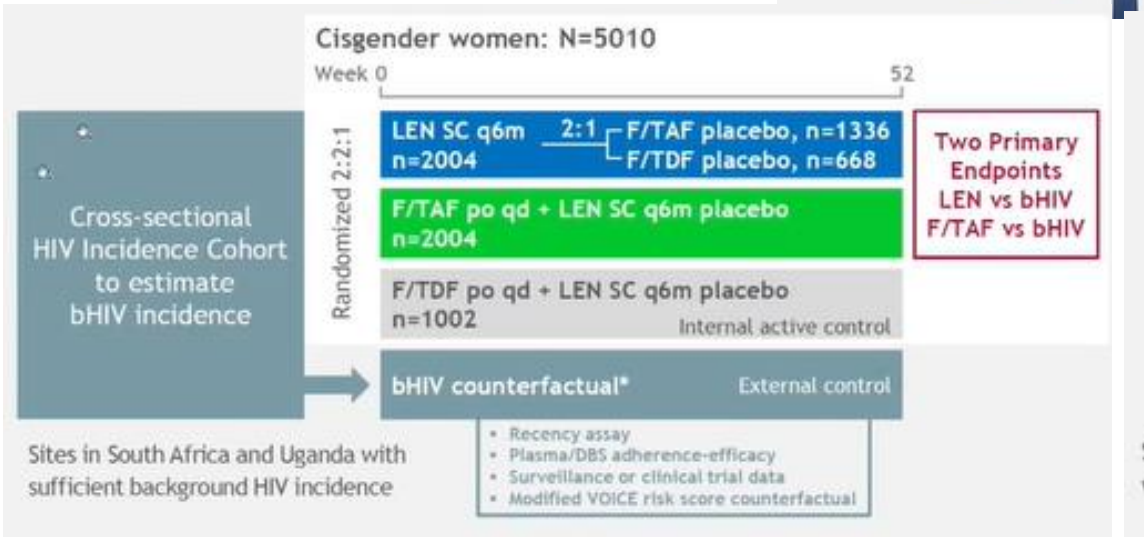
Lenacapavir (LEN) for PrEP Studies

Das M et al. IAS Virtual July 2021 Session SA15

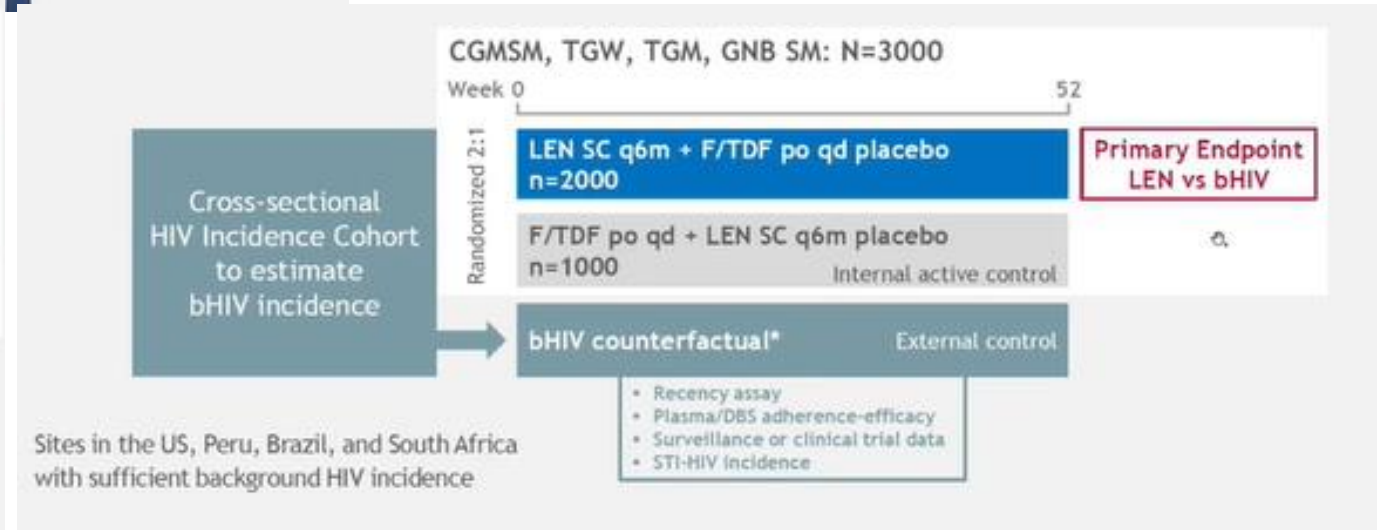




LEN for PrEP Cisgender Women



LEN for PrEP MSM/TGW

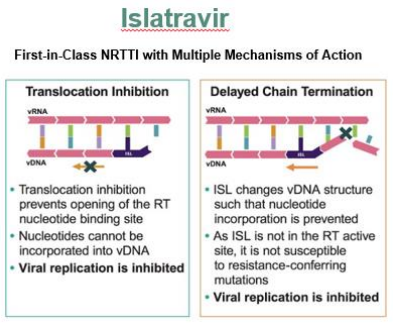


"Roots" – Underpinning Studies

Proof of concept capsid inhibitors prevent HIV in non-human primates

Robust PK and safety database in persons with and without HIV

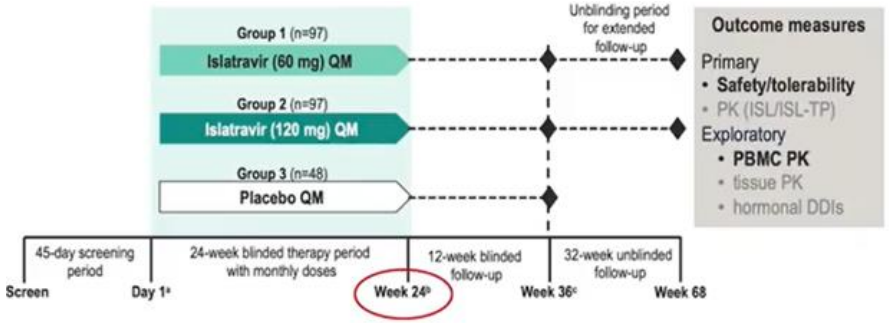
Phase I PK *LEN mucosal PK* *Highly ART-experienced* Capella *ART naive* Calibrate

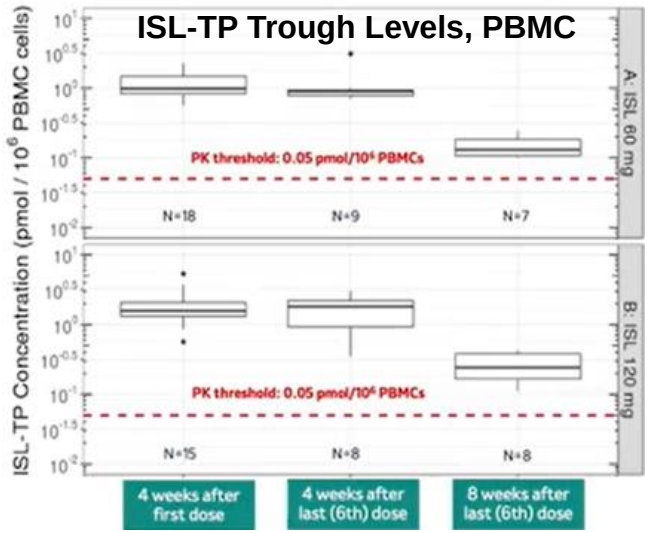


Safety and PK of Oral Islatravir (ISL) Once Monthly for PrEP – Phase IIA Safety-Dose Finding

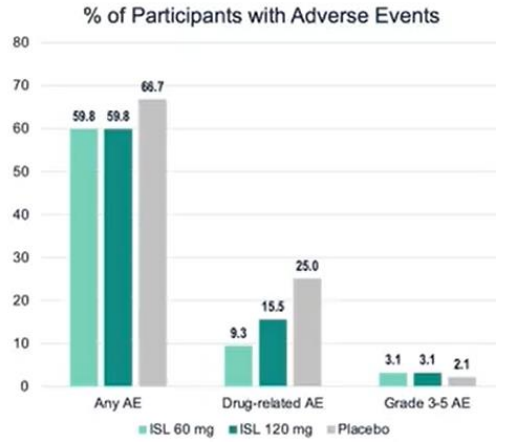
Hillier S et al. IAS Virtual July 2021 Abs OALCo1LB03

- Phase 2a placebo-controlled study of 2 doses of monthly oral ISL for PrEP in 242 low-risk adults, reporting on week 24 data





ISL-TP levels with 60 or 120 mg q month doses were all above prespecified PK threshold of 0.05 pmol/10^6 PBMC



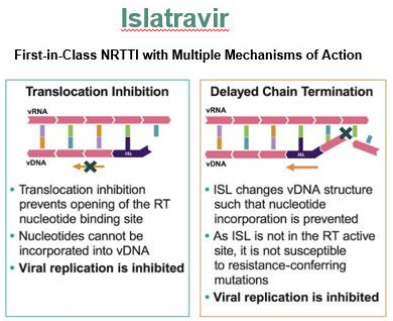
- Most AE mild (74%), similar to placebo arm, and did not lead to d/c study drug
- Rates drug-related AE <3% and no drug-related SAE

→ISL well-tolerated, most AE mild and no drug-related SAE; lab ≥Grade 3 rare.

→ISL triphosphate in PBMC remained above the pre-specified PK threshold for HIV prevention through at least 8 weeks after last dose.

→2 ongoing PrEP trials in MSM/TGW and cis-gender females

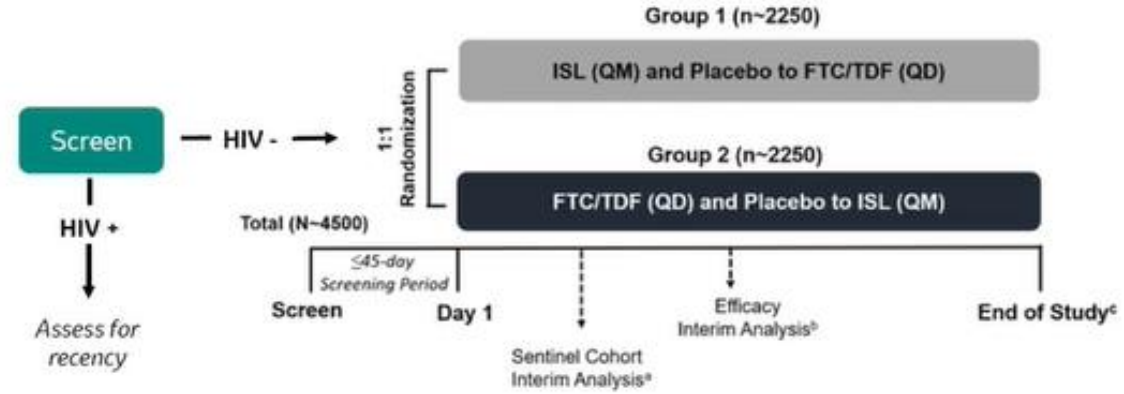
	Trial name (protocol number)	Population	Active comparator	ClinicalTrials.gov
Phase 3	IMPOWER-022	Cisgender women at high risk of HIV-1 infection	FTC/TDF	NCT04644029
	IMPOWER-024	Men and transgender women who have sex with men and are at high risk for HIV-1 infection	FTC/TDF or FTC/TAF	NCT04652700



Islatravir (ISL) Orally Once Monthly for PrEP
Phase III Studies

Robertson M et al. IAS Virtual July 2021 Session SA15

IMPOWER 022 Trial in Women: Study Schema



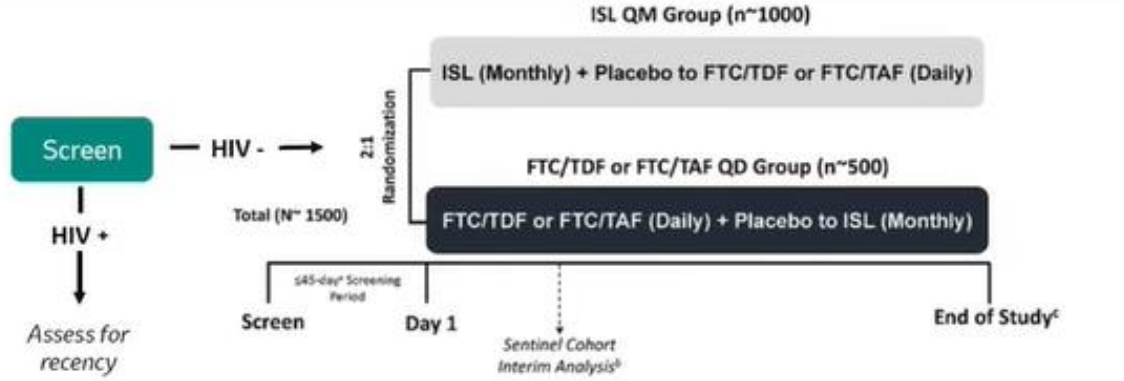
FTC/TDF= emtricitabine/tenofovir disoproxil (including brand TRUVADA and all generic versions); ISL=islatravir; QD=once daily; QM=once monthly

a Sentinel Cohort Interim Analysis (N=400) will be conducted 3 months after the last participant in the Sentinel Cohort has initiated study intervention.

b An efficacy Interim Analysis will be performed when 25 primary endpoint cases are observed.

c End of study includes the safety follow-up period of 42 days after the last dose of study intervention. End of Study will be determined based on estimated accrual of 40 primary endpoint cases. Participants will be enrolled over an approximately 12-month period with study intervention administered for approximately 1 year and up to 3 ye

IMPOWER 024 Trial in MSM and TGW: Study Schema



FTC/TDF= emtricitabine/tenofovir disoproxil (including brand TRUVADA and all generic versions); FTC/TAF = emtricitabine/tenofovir alafenamide (Descovy); ISL=islatravir (also known as MK-8591); N=number of participants in the study; n=number of participants in each intervention group; QD=once daily; QM=once monthly

[a] Screening period of up to 45 days is allowed, but participants are expected to enroll as soon as possible after eligibility is confirmed.

[b] Sentinel Cohort (first approximately 150 enrolled participants) interim analysis will be conducted 3 months after the last participant in the Sentinel Cohort has initiated study intervention.

[c] End of study includes the safety follow-up period of 42 days after the last dose of study intervention.



Thank You For Your Attention!









Questions?



