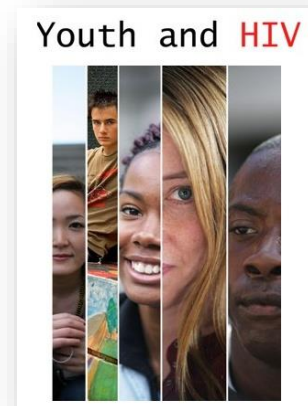# IAS 2021&
Pediatric HIV Workshop
Selected PMTCT,
Pediatric, Adolescent,
and Maternal/Adult
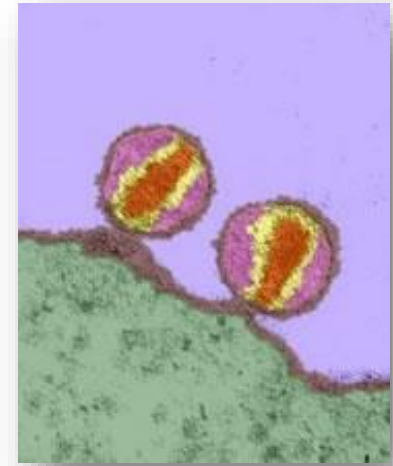## Abstracts

Lynne M. Mofenson MD
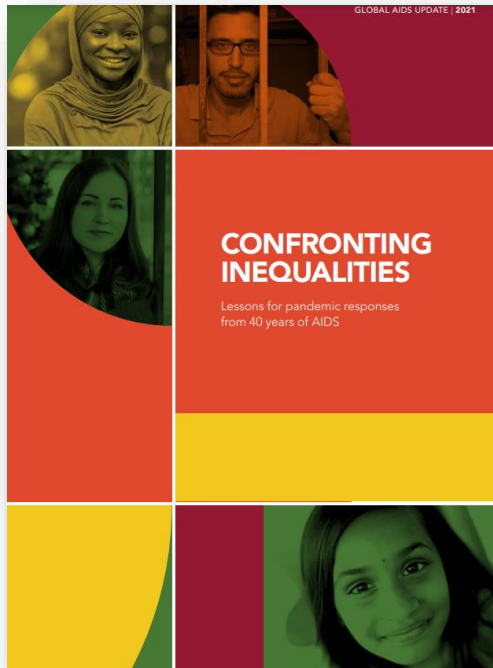
7/29/21

Update on Epidemiology

of Pediatric HIV

2021

INVITED SPEAKER

MARY MAHY, ScD, MHSc

UNAIDS, Switzerland

GLOBAL AIDS UPDATE | 2021

CONFRONTING INEQUALITIES

Lessons for pandemic responses from 40 years of AIDS

UNAIDS

INTERNATIONAL WORKSHOP ON HIV PEDIATRICS

VIRTUAL WORKSHOP 16 - 17 JULY

2021

ART Coverage in Pregnant Women Was 85% in 2020 – But Progress Has Stalled
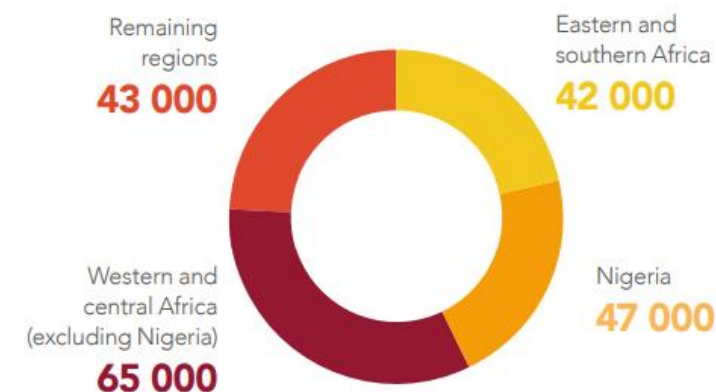
Maternal ART and New Infections in Children Globally, 2010-2020
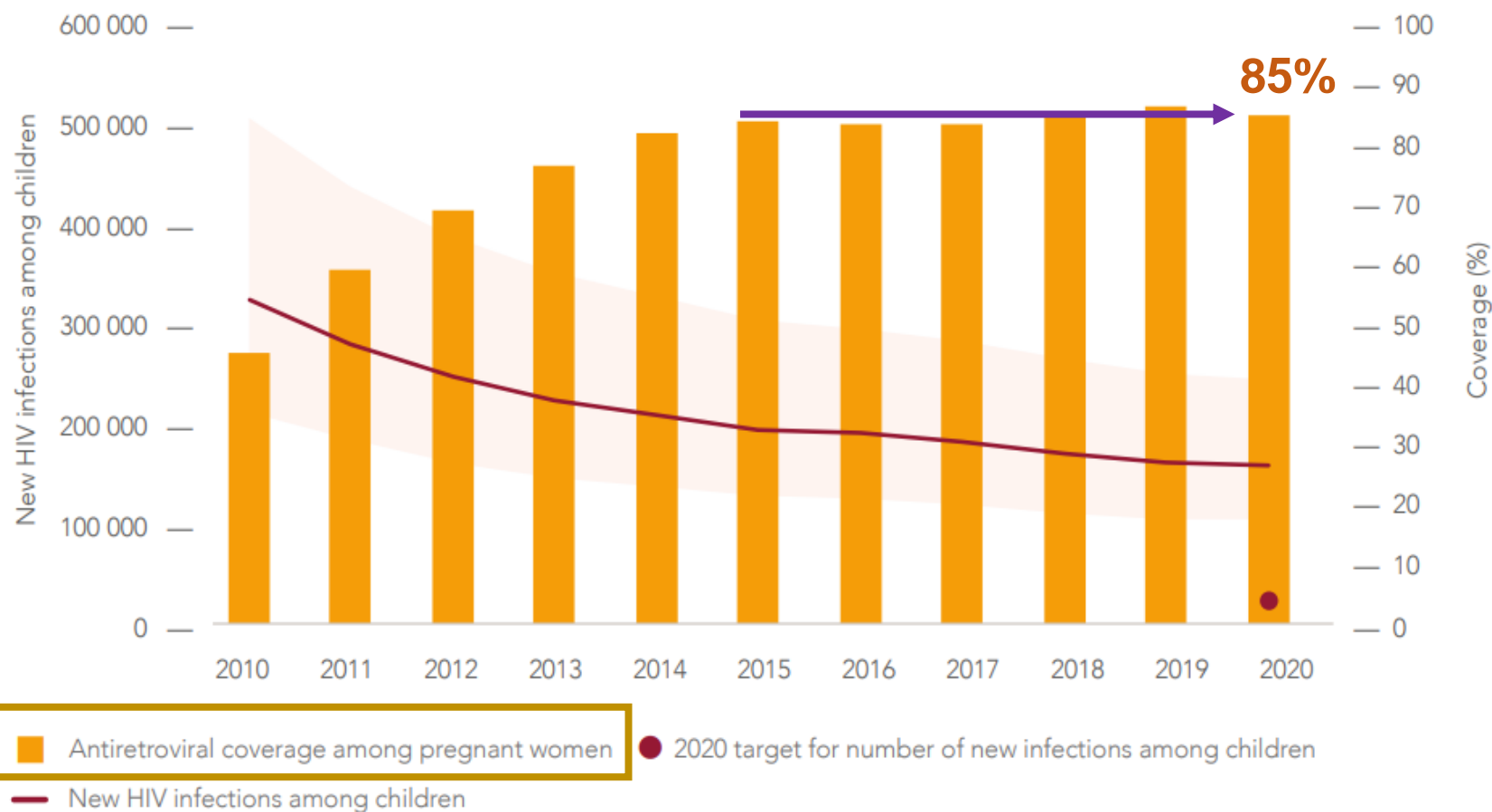
→ **85% of pregnant women with HIV received ART** in 2020 – but **little expansion since 2015**

→ 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 _not_ on ART by region, 2020

Remaining regions **43 000**

Eastern and southern Africa **42 000**

Western and central Africa (excluding Nigeria) **65 000**

Nigeria **47 000**

85%

Antiretroviral coverage among pregnant women

2020 target for number of new infections among children

New HIV infections among children

Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).
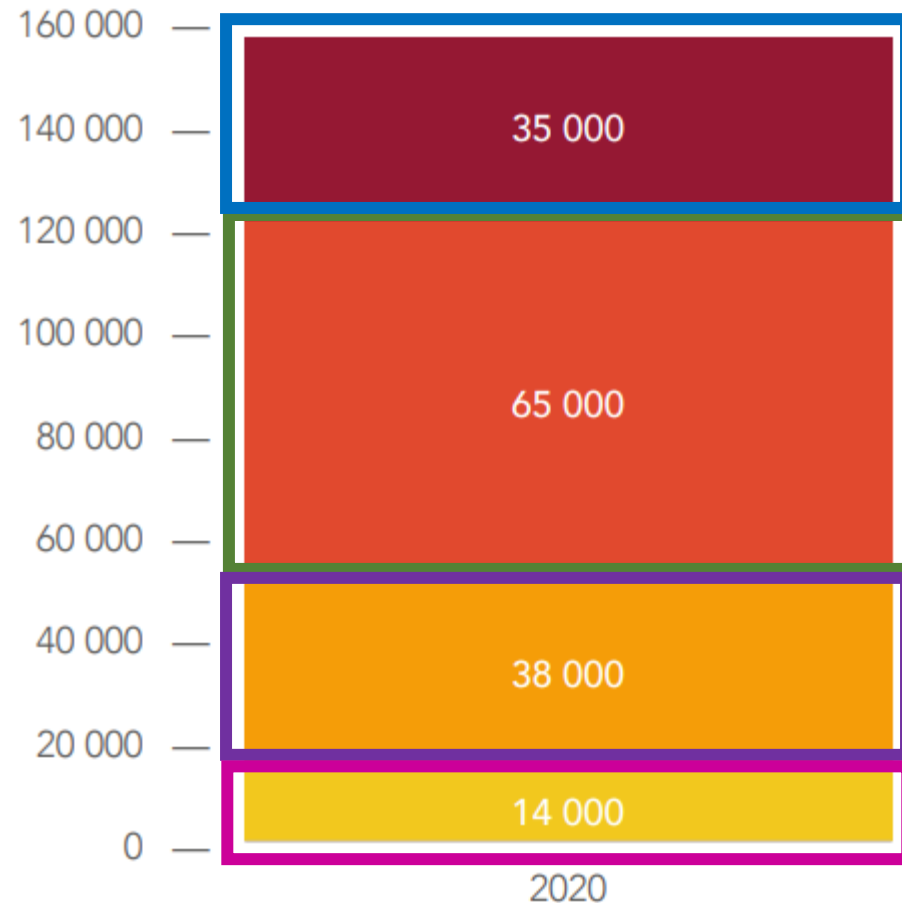
There Has Been a 53% Decline New Pediatric Infections Since 2010 – But Progress Has Also Stalled

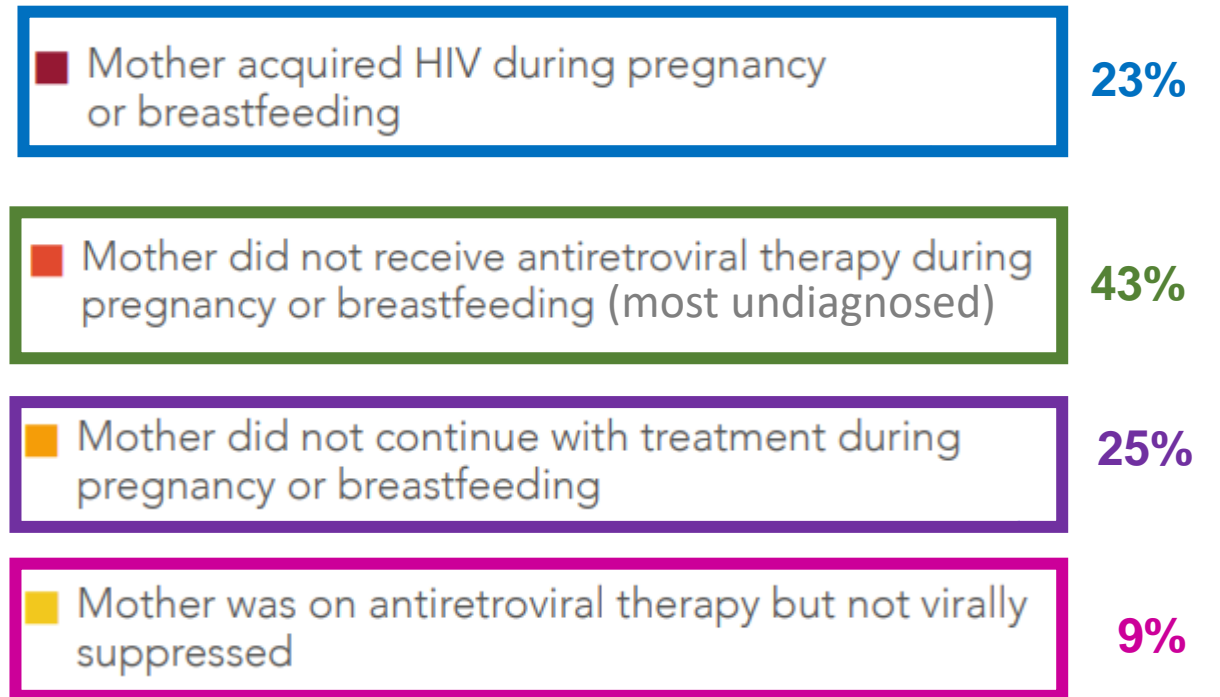Maternal ART and **New Infections in Children** Globally, 2010-2020
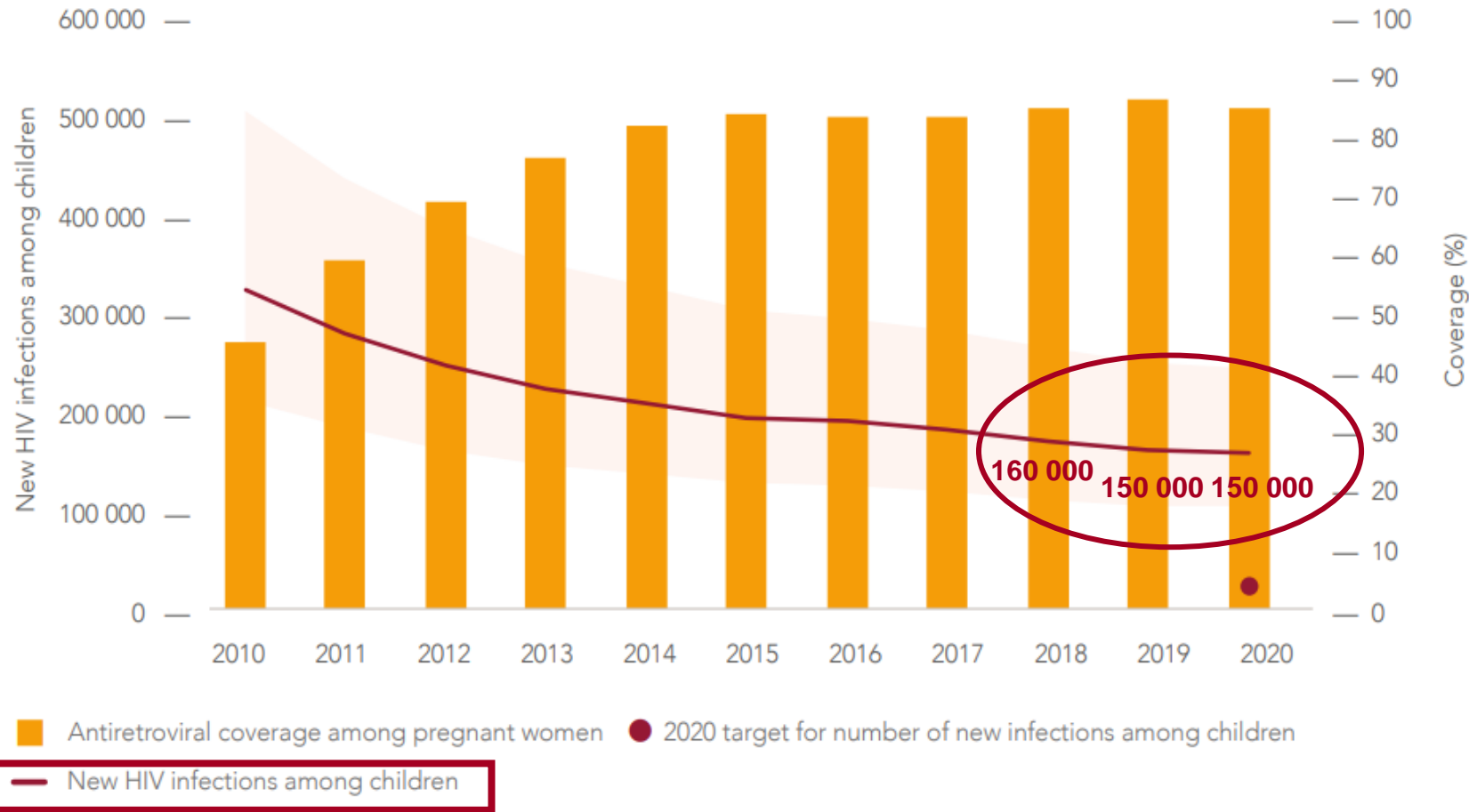
→150,000 new pediatric HIV infections estimated in 2020

→Minimal change in new infections between 2018 and 2020

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

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

Causes of New Child Infections Globally 2020

Primary gaps in PMTCT:

160 000
140 000 — 35 000
120 000
100 000
80 000 — 65 000
60 000
40 000 — 38 000
20 000
0 — 14 000

2020

- ■ 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%**

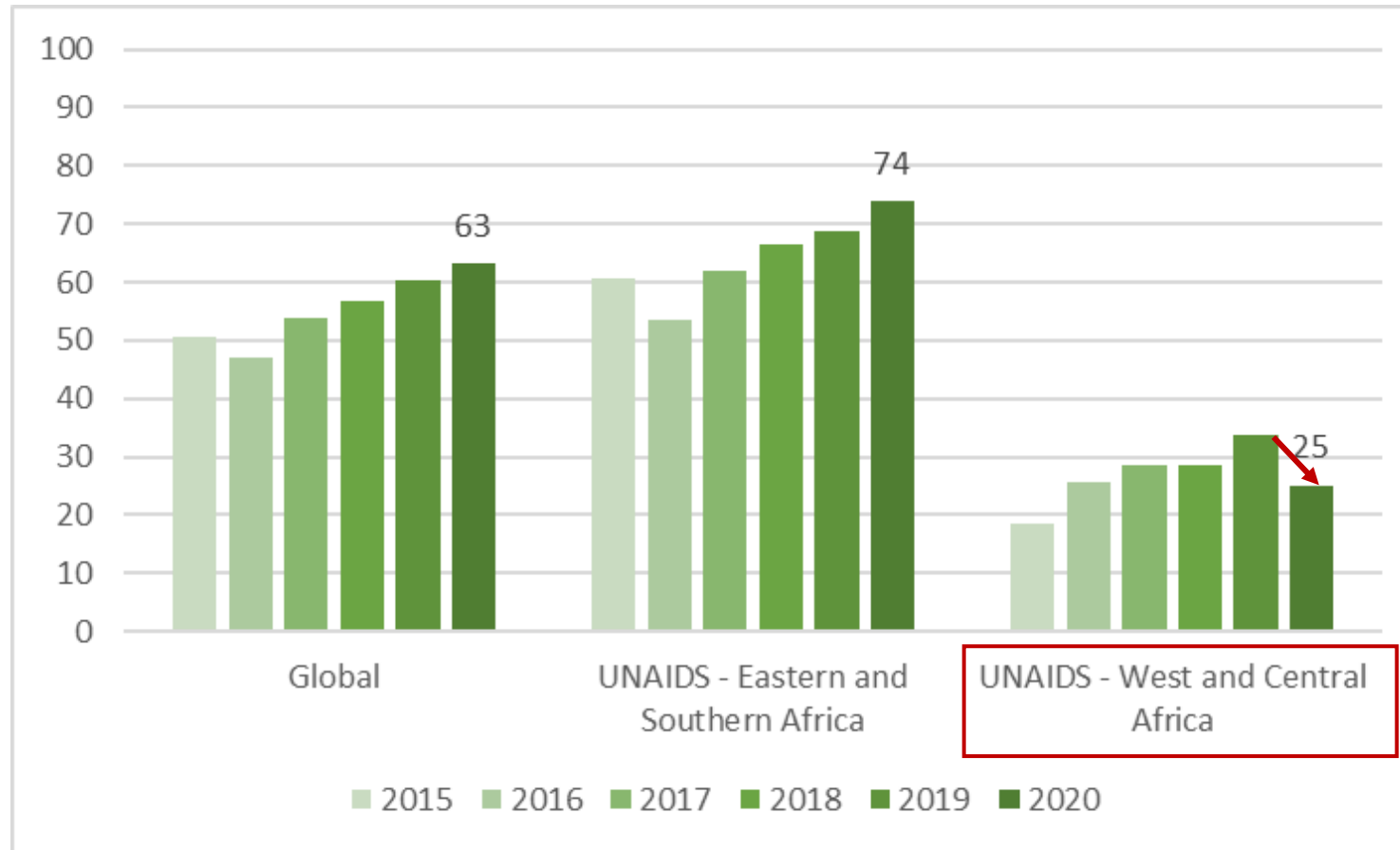Source: UNAIDS epidemiological estimates, 2021
(https://aidsinfo.unaids.org/).

# 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

Missed target by 800,000 in 2020

54%
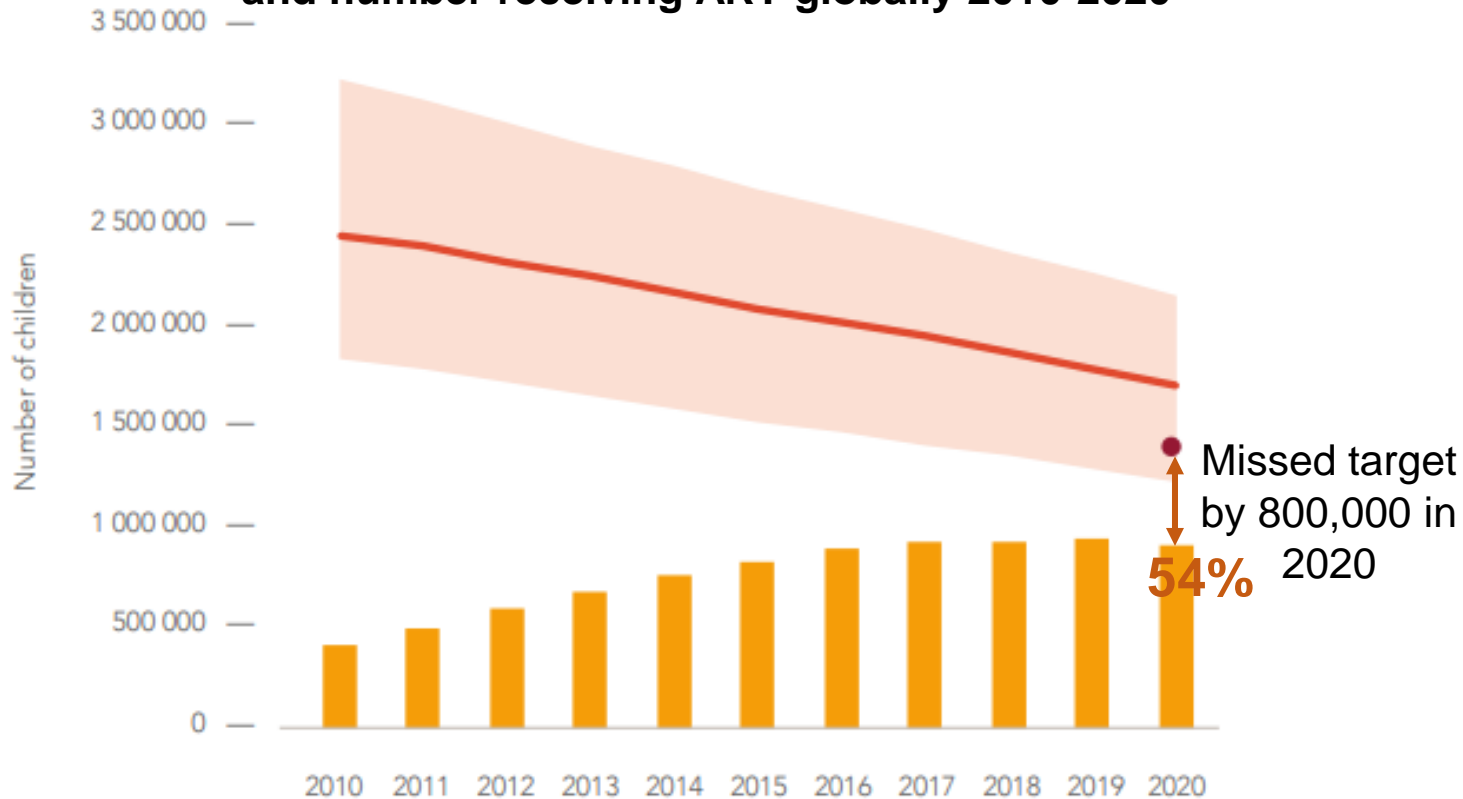
Children receiving treatment — Children living with HIV ● 2020 global treatment target

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

10–14 years **40%**

0–4 years **37%**

5–9 years **23%**

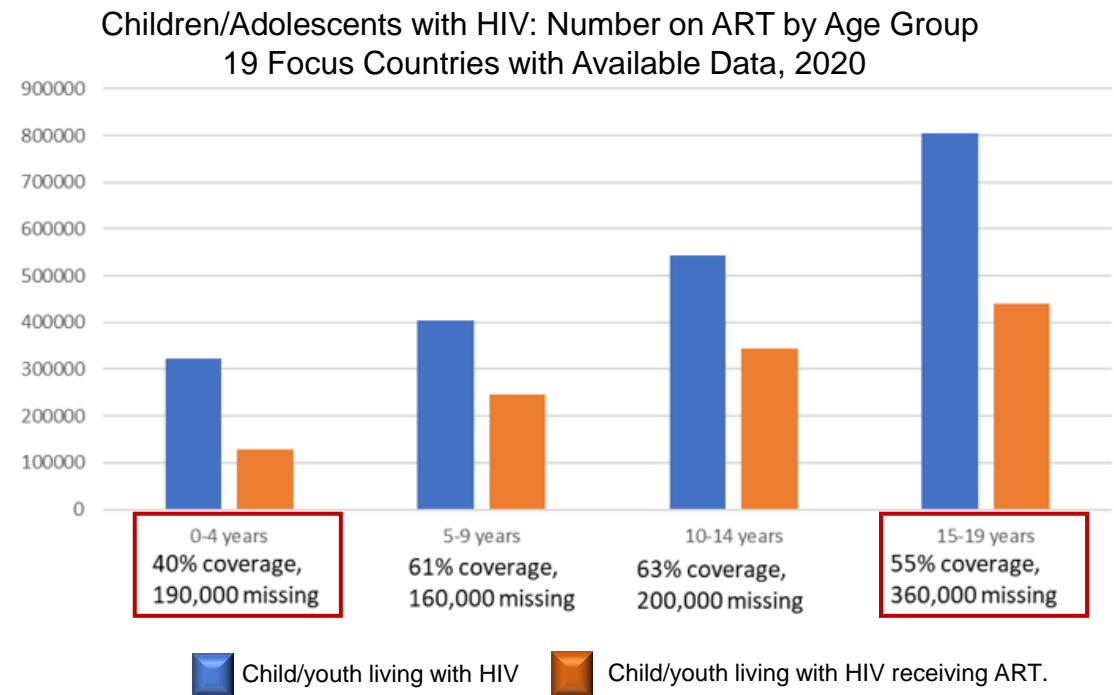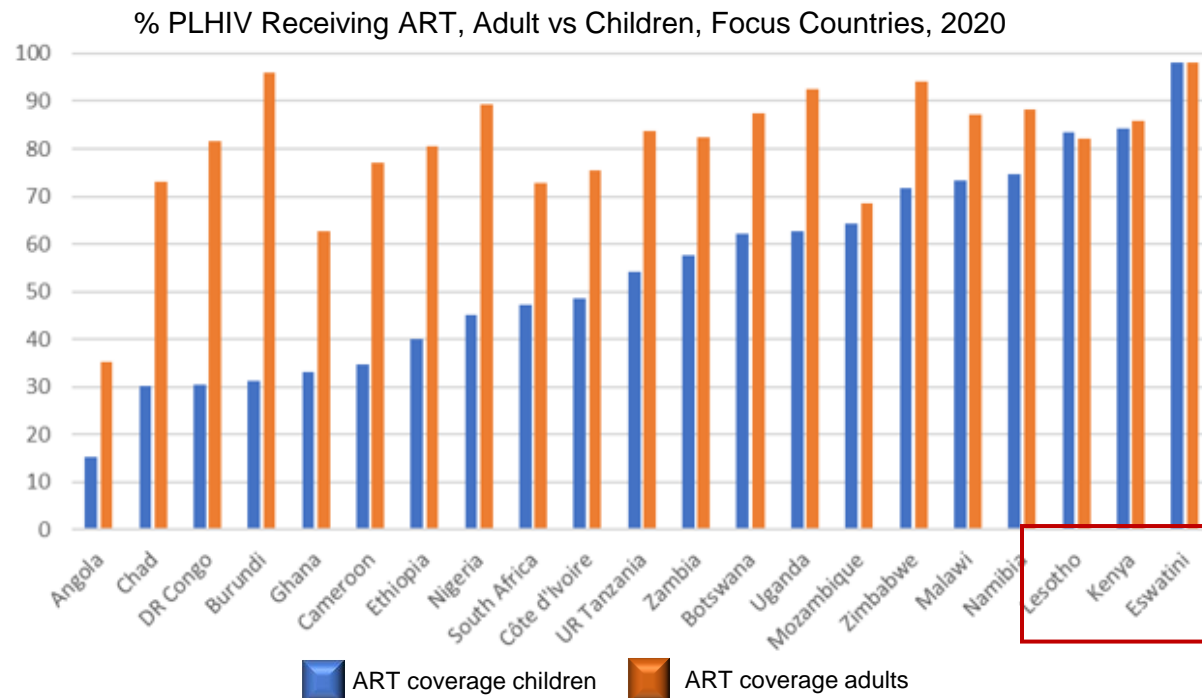**Distribution children with HIV not on ART by age, 2020**
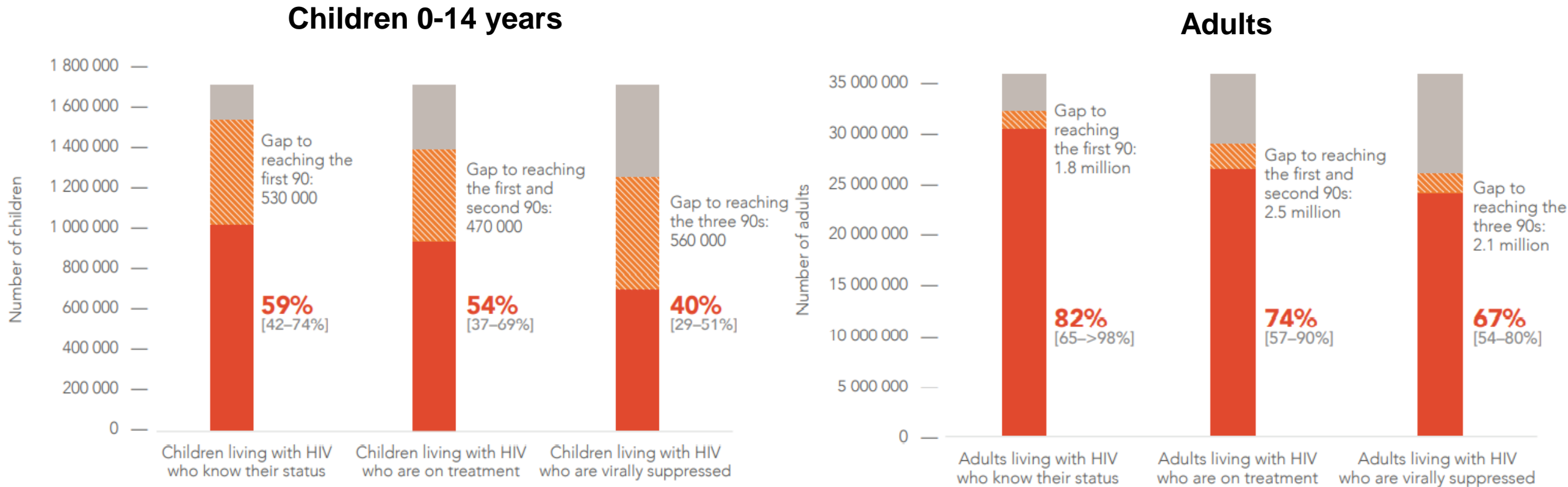
Lower ART Coverage in Children and Adolescents vs Adults

- 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

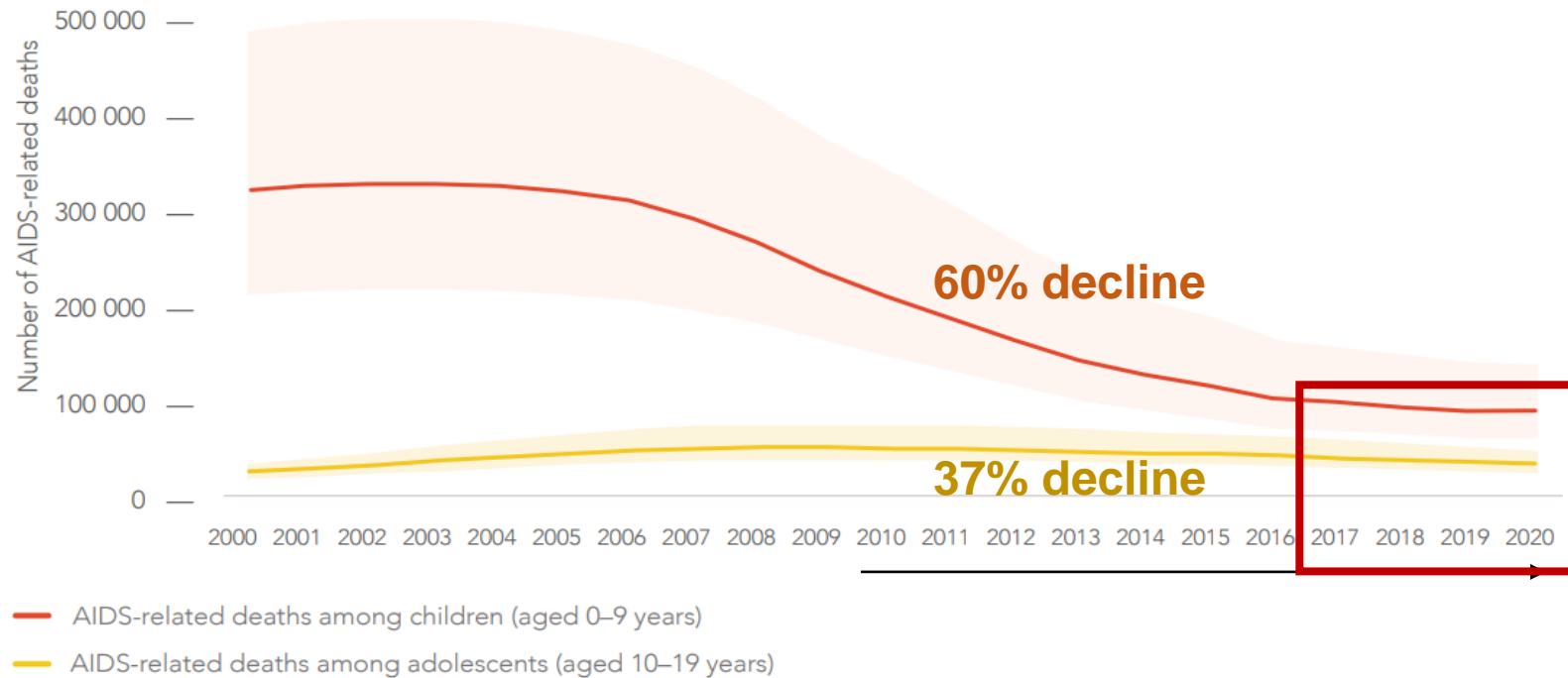→ Proportionately, ART coverage lowest in children 0-4 and adolescents 15-19 years

% PLHIV Receiving ART, Adult vs Children, Focus Countries, 2020

ART coverage children   ART coverage adults

Children/Adolescents with HIV: Number on ART by Age Group
19 Focus Countries with Available Data, 2020

0-4 years
40% coverage,
190,000 missing

5-9 years
61% coverage,
160,000 missing

10-14 years
63% coverage,
200,000 missing

15-19 years
55% coverage,
360,000 missing

Child/youth living with HIV   Child/youth living with HIV receiving ART.

Source: Special analysis of UNAIDS 2021 epidemiological estimates.

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

Children 0-14 years

Number of children

1 800 000
1 600 000
1 400 000
1 200 000
1 000 000
800 000
600 000
400 000
200 000
0

Gap to reaching the first 90: 530 000

59% [42–74%]

Gap to reaching the first and second 90s: 470 000

54% [37–69%]

Gap to reaching the three 90s: 560 000

40% [29–51%]

Children living with HIV who know their status | Children living with HIV who are on treatment | Children living with HIV who are virally suppressed

Adults

Number of adults

35 000 000
30 000 000
25 000 000
20 000 000
15 000 000
10 000 000
5 000 000
0

Gap to reaching the first 90: 1.8 million

82% [65–>98%]

Gap to reaching the first and second 90s: 2.5 million

74% [57–90%]

Gap to reaching the three 90s: 2.1 million

67% [54–80%]

Adults living with HIV who know their status | Adults living with HIV who are on treatment | Adults living with HIV who are virally suppressed

→ 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

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

60% decline

37% decline

- AIDS-related deaths among children (aged 0–9 years)
- AIDS-related deaths among adolescents (aged 10–19 years)

→ 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.

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

Goals Focused on Pregnant/BF Women and Children

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

Dolutegravir

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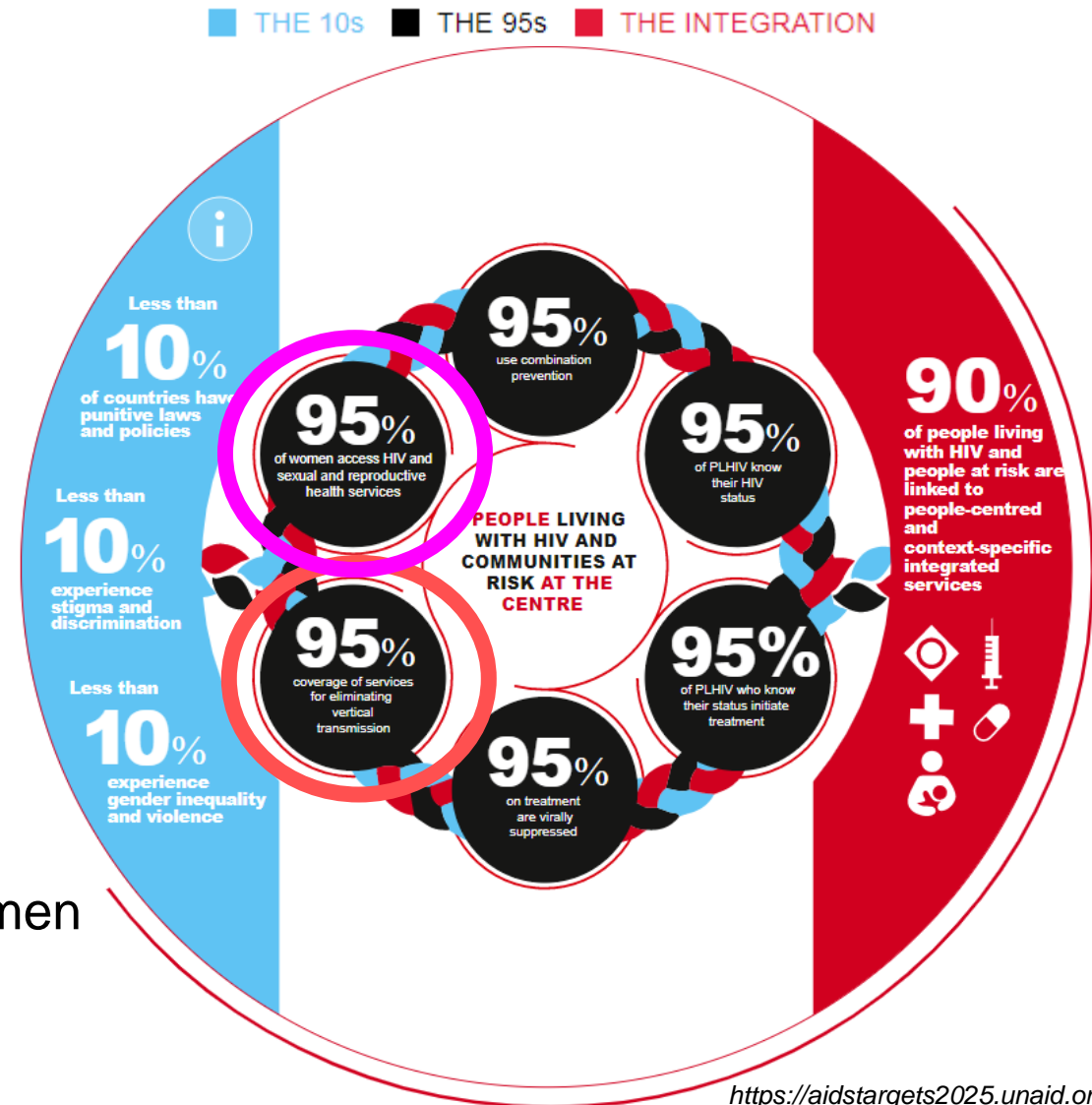
DTG-Based ART Shown Superior to SOC in **Older Children ≥14 kg** Living with HIV: ODYSSEY

Turkova A et al. CROI March 2021 Abs 174

Older children:

Turkova et al. CROI 2021, Abs 174
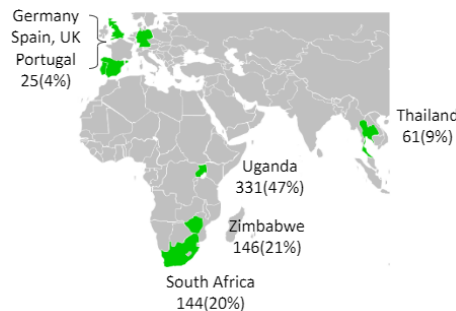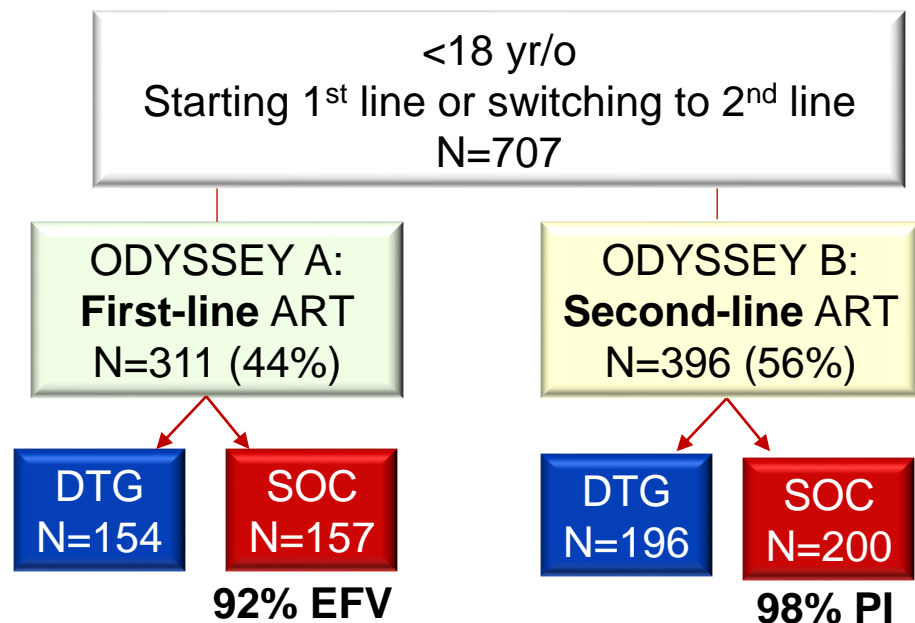
- RCT non-inferiority trial DTG vs SOC in children (median age 12 yr, wt 31 kg) **starting 1st** (ODYSSEY A) **or 2nd** (ODYSSEY B)-line ART in 8 countries

- 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

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

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 Lower with DTG vs SOC in Pooled Analysis

Difference in Proportion with Viral/Clinical Failure DTG vs SOC

Bayesian Analysis -0.106 [-0.192,-0.020]

11% less failure DTG

Difference in proportion with failure by week 96

DTG better **SOC better**

-.5 -.45 -.4 -.35 -.3 -.25 -.2 -.15 -.1 -.05 0 .05 .1 .15 .2
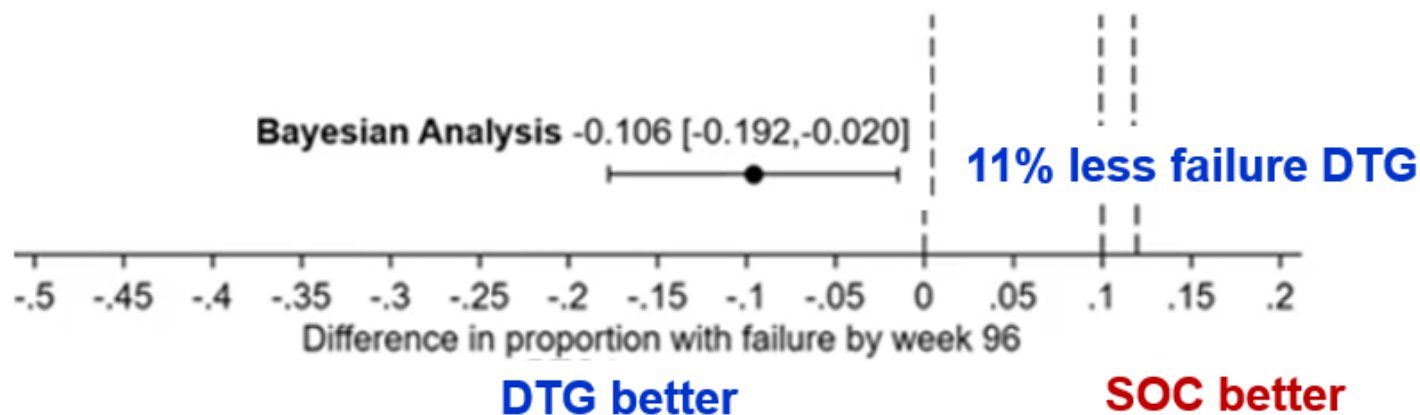
Test of heterogeneity of treatment effect between ≥14kg and <14kg: p=0.24

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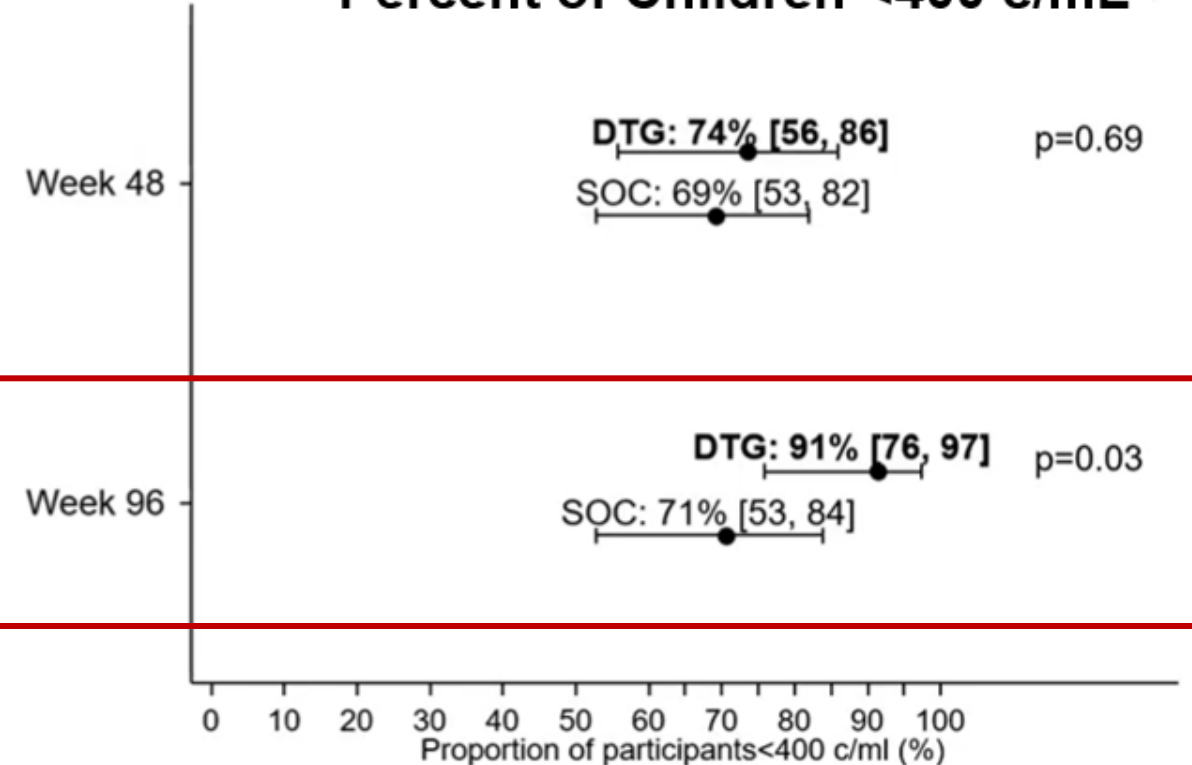
VL<50 or <400 c/mL at 96 Weeks (but not 48 Weeks) Better with DTG vs SOC in Young HIV+ Children <14 kg

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


Percent of Children <50 c/mL

Week 48 — DTG: 44% [28, 61] / SOC: 49% [33, 65] — p=0.69

Week 96 — DTG: 76% [59, 88] / SOC: 50% [33, 67] — p=0.02

Proportion of participants<50 c/ml (%)
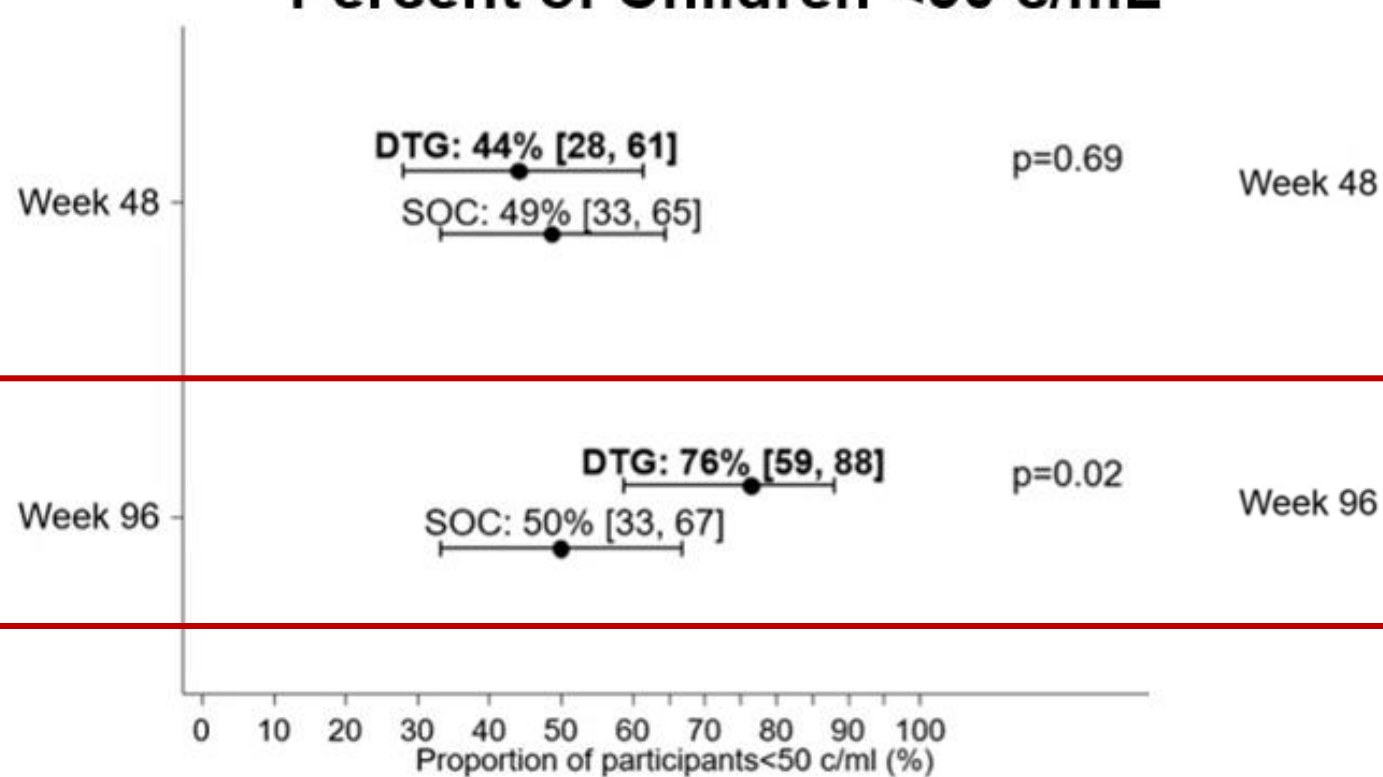
Percent of Children <400 c/mL

Week 48 — DTG: 74% [56, 86] / SOC: 69% [53, 82] — p=0.69

Week 96 — DTG: 91% [76, 97] / SOC: 71% [53, 84] — p=0.03

Proportion of participants<400 c/ml (%)

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

Change Total Cholesterol from Baseline

96w DTG-SOC
-26 (95% CI -42, -9); P=0.003

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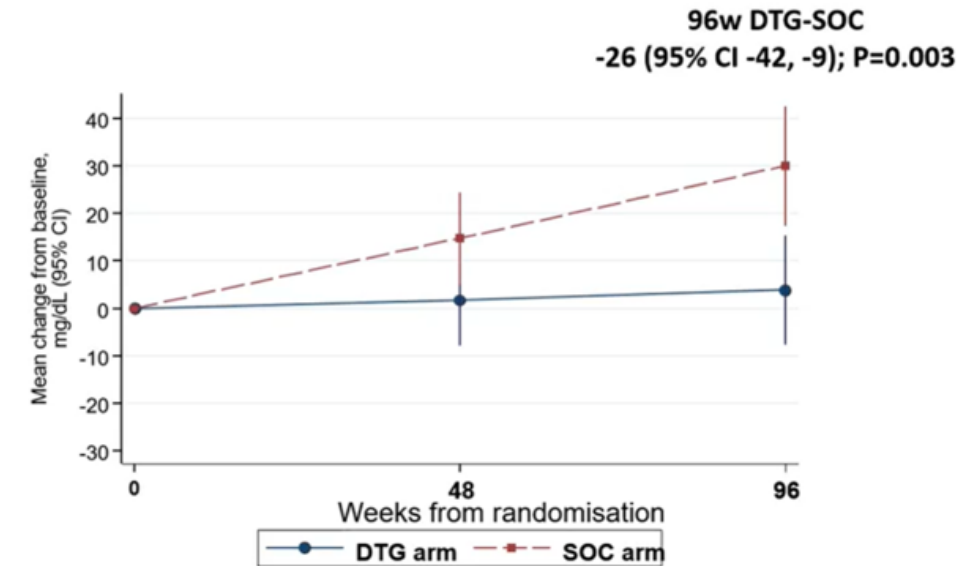
- Increase total cholesterol over time in SOC (most on LPV/r) but not DTG arms.

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

<18 yr/o
Starting 1st line or switching to 2nd line
N=707

ODYSSEY A:
First-line ART
N=311

ODYSSEY B
Second-line ART
N=396

DTG N=154   SOC N=157   DTG N=196   SOC N=200

(Original study older children)

- Viral failure defined as:
  - <1 log drop VL at week 24 and ART switch for treatment failure
  - Confirmed VL $\geq$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.
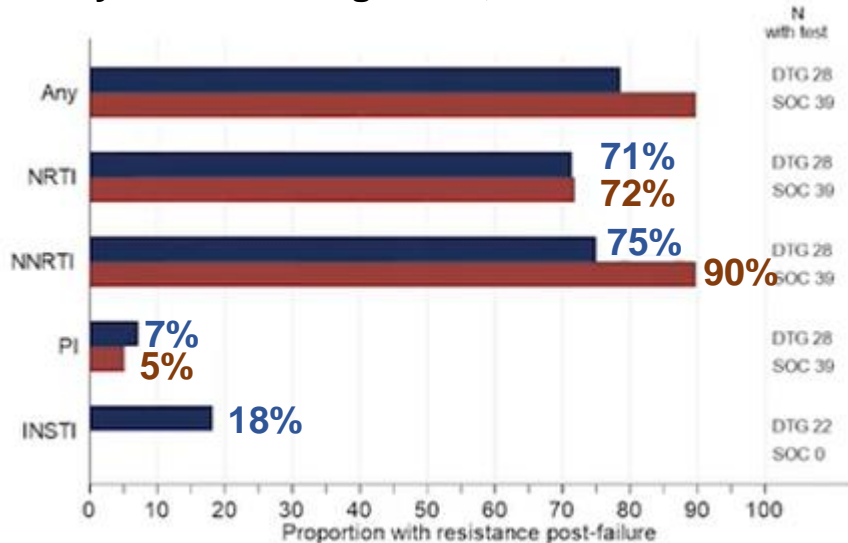
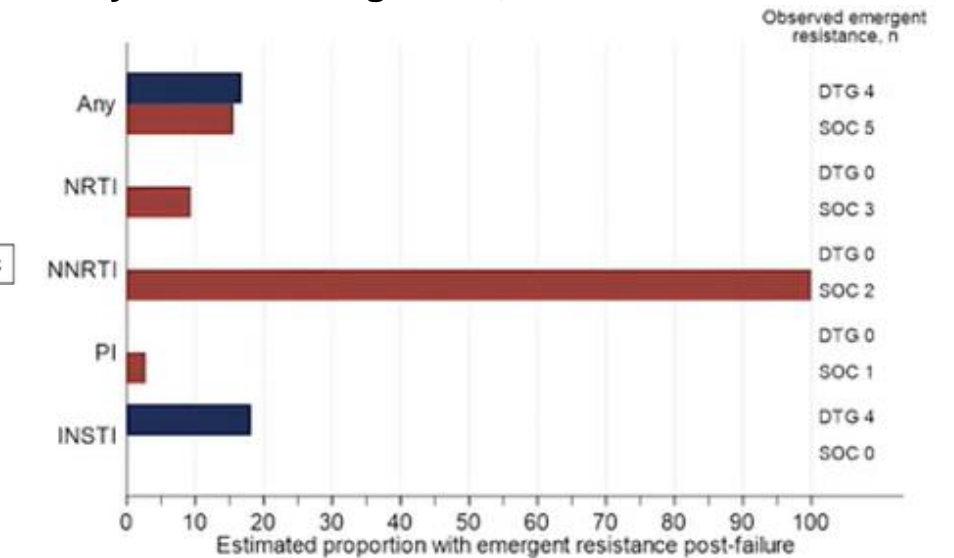# Viral Failure and Genotypic Resistance in Children Randomized to **1st Line ART**, ODYSSEY

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

Proportion with Resistance Post-Failure by Study Arm and Drug Class, 1st Line Randomization
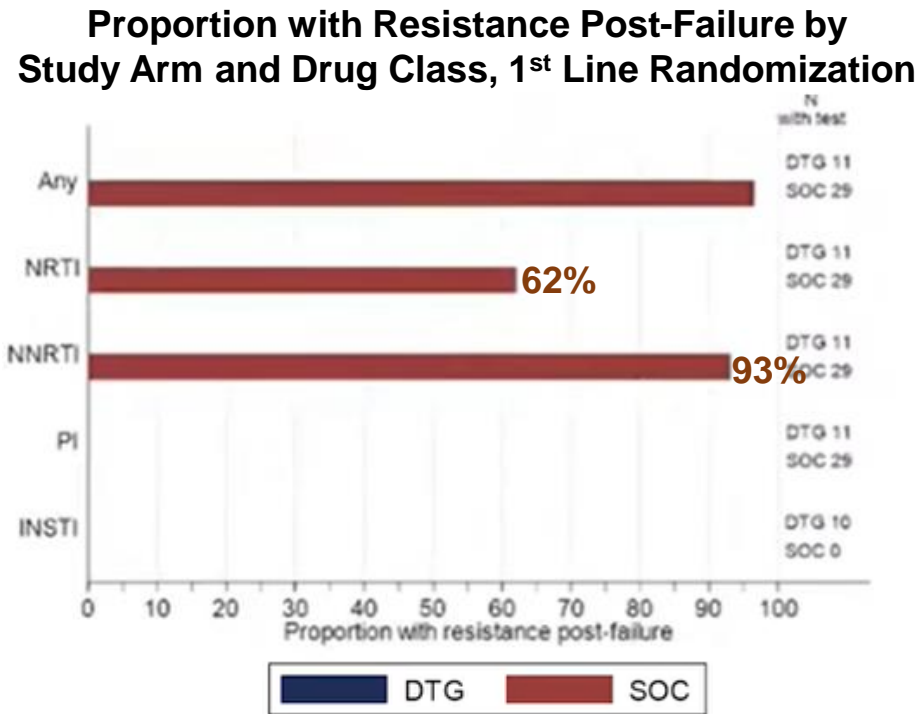
- **No resistance mutations with failure of DTG 1st line ART**.

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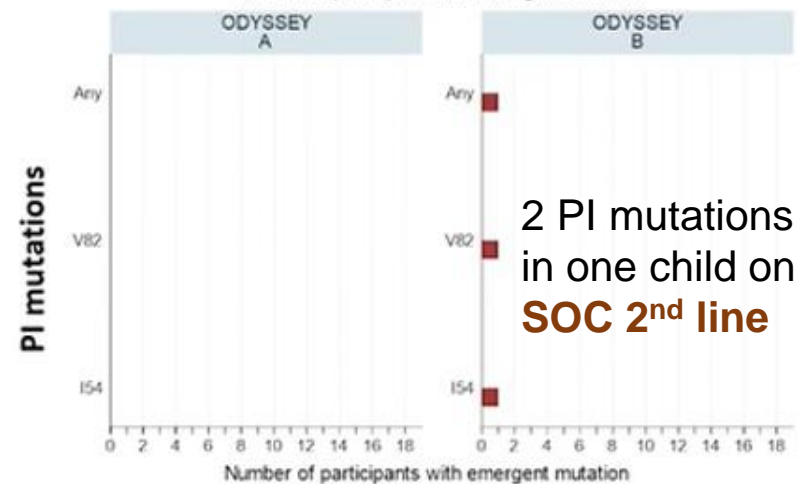
New Genotypic Resistance Mutations by Class and Type in Children in the ODYSSEY Trial

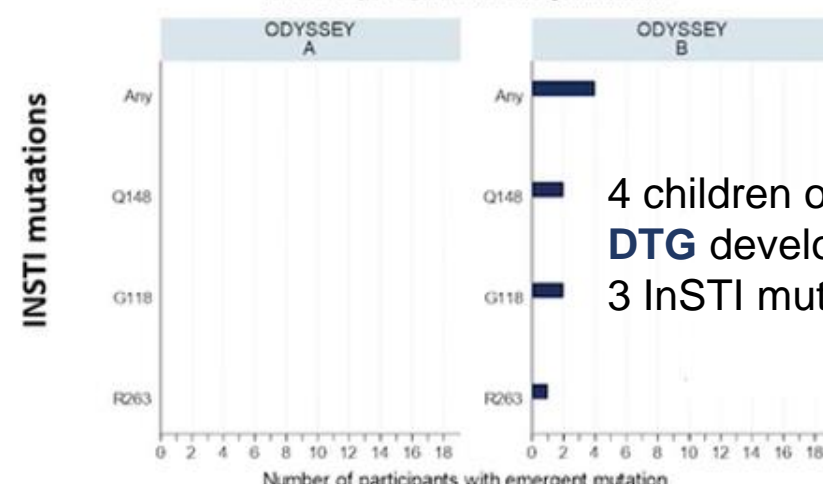*Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021*

Emergent New Resistance Mutations by Drug Class and Arm
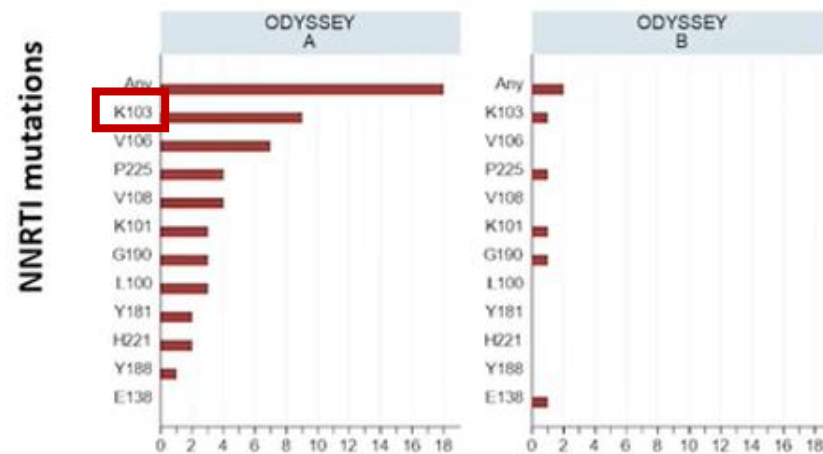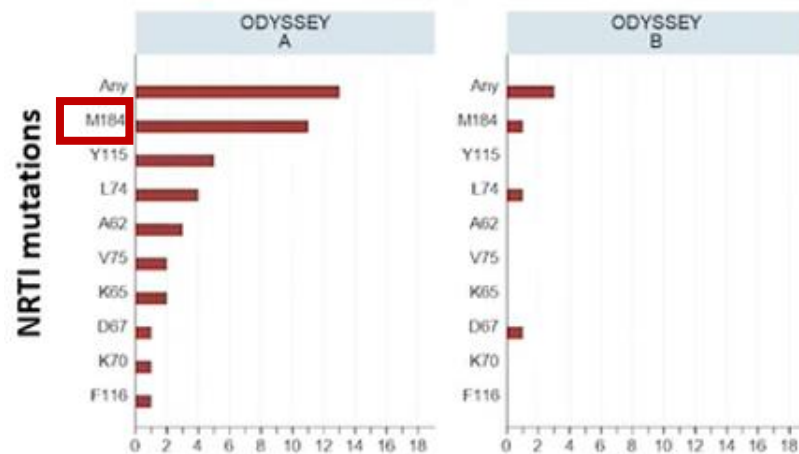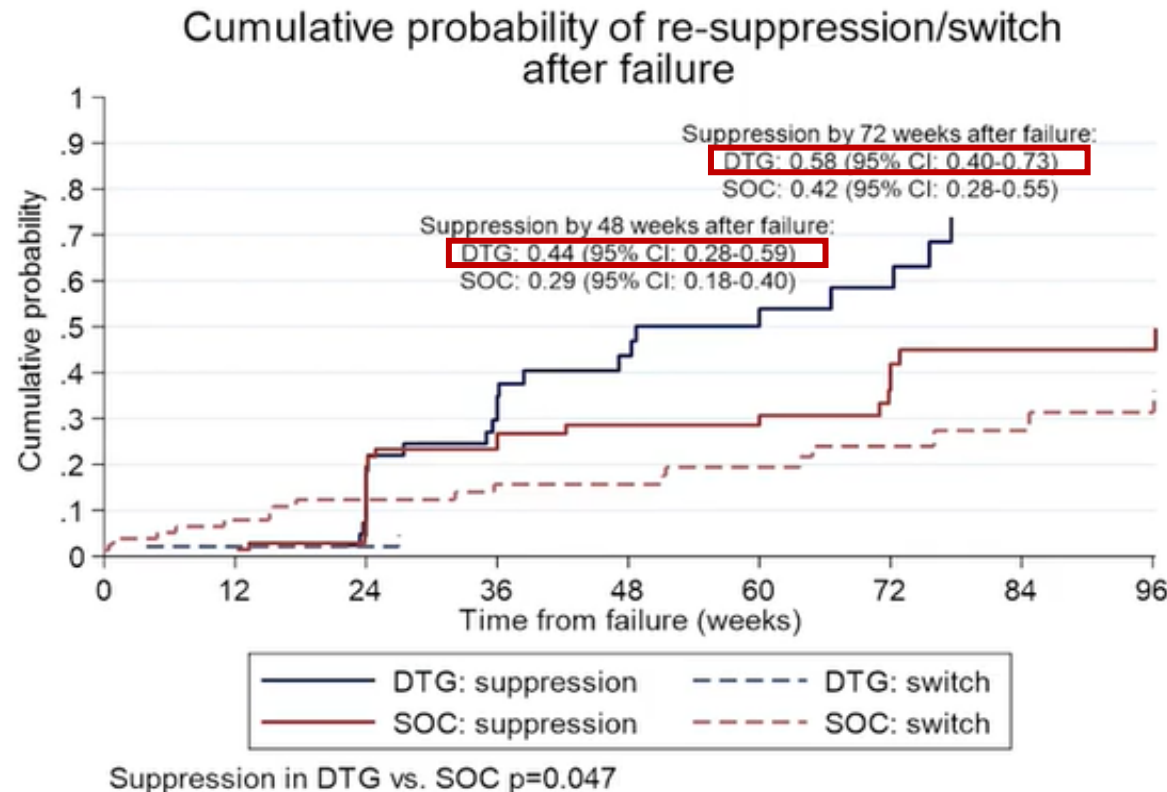

2 PI mutations in one child on **SOC 2nd line**

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

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

Cumulative probability of re-suppression/switch after failure

Suppression by 72 weeks after failure:
DTG: 0.58 (95% CI: 0.40-0.73)
SOC: 0.42 (95% CI: 0.28-0.55)

Suppression by 48 weeks after failure:
DTG: 0.44 (95% CI: 0.28-0.59)
SOC: 0.29 (95% CI: 0.18-0.40)

DTG: suppression — — — DTG: switch
SOC: suppression — — — SOC: switch

Suppression in DTG vs. SOC p=0.047

*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 <u>without</u> 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
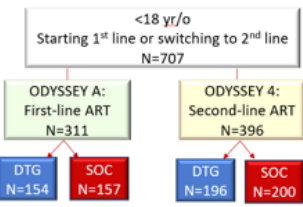
Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021

- 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.**

# Weight Gain and Change 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

(Original study older children)

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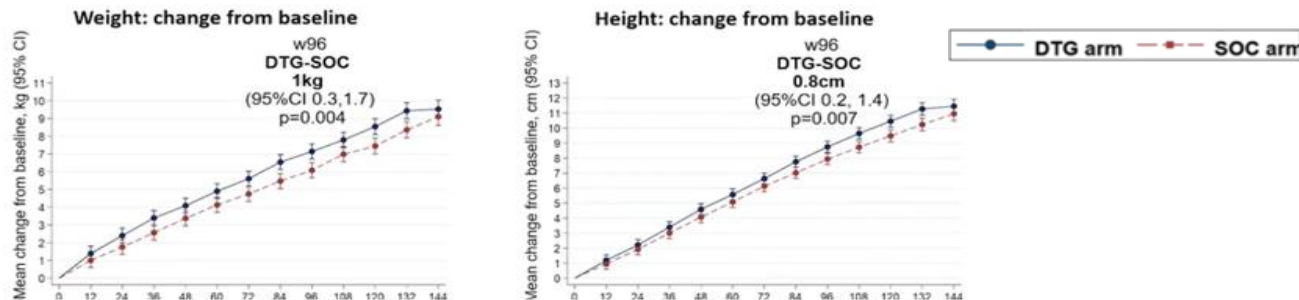
**Change from Baseline in BMI and BMI-for-Age DTG vs SOC**
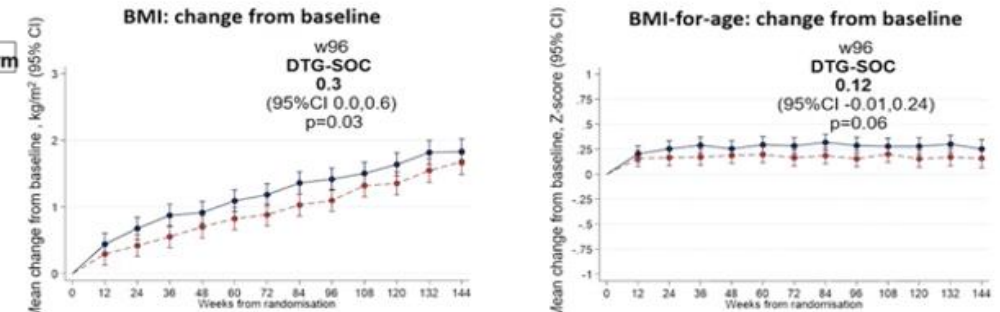
- Small additional gains from baseline in height and weight in **DTG** vs **SOC**
- At 96 weeks, mean added gain in **DTG** vs **SOC** in weight was 1 kg and height 0.8 cm
- The differences occurred early and stabilized

- 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.

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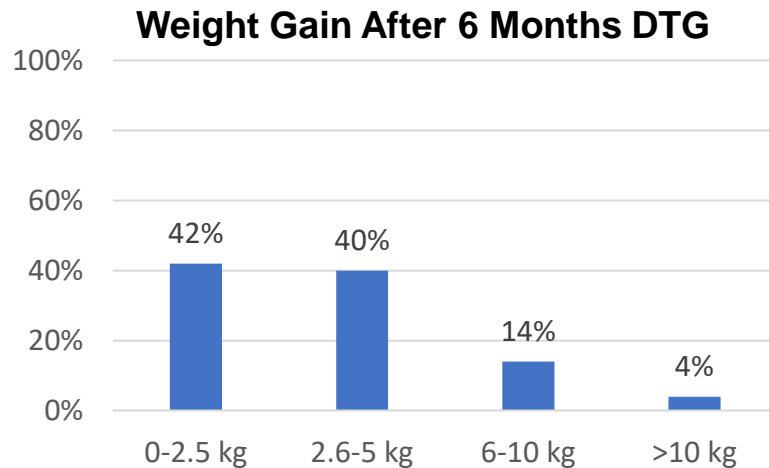
- The percent of youth overweight increased from 1.7% (4/229) before DTG to 8.7% 20/229) after being on DTG for 6 months (16 overweight, 4 obese).

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

# 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.

Viral Suppression Pre-FCM (N = 849)
- Suppressed
- Not Suppressed

69% suppression

31%
69%
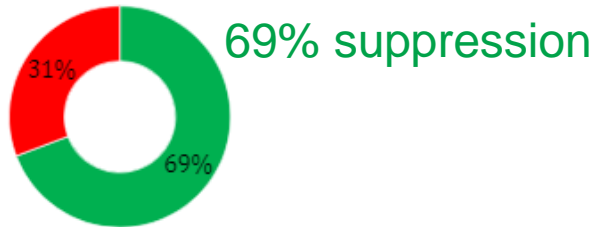
Characteristic	n	Sup-pressed	% Sup-pressed
Age groups (yrs)			
2 - 6	374	233	62
6 - 9	475	355	75
Sex			
Female	489	339	69
Male	360	249	69
ART Regimen			
EFV Based	212	159	75
NVP Based	360	239	66
PI Based	268	185	69
Other	9	5	56

Viral Suppression Post - FCM (N = 1,336)
- Suppressed
- Not Suppressed

83% suppression

17%
83%
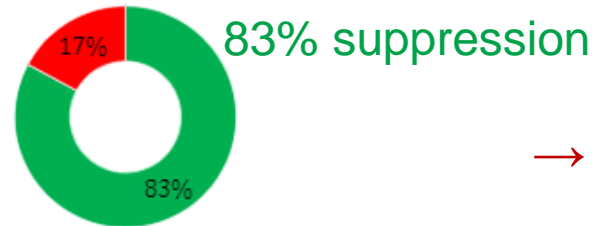
	N	Sup-pressed	% Sup-pressed
Age Category (yrs)			
2 - 6	591	473	80
6 - 9	745	634	85
Sex			
Female	753	641	85
Male	583	466	80
ART Regimen			
DTG Based	94	84	89
EFV Based	646	542	84
NVP Based	68	54	79
PI Based	502	403	80
Other	25	23	92

→ 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).

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

Proportion of Children on Optimized Pediatric ART

- 29% — Dec 2019
- 56% — Mar 2020
- 65% — May 2020
- 69% — Jun 2020
- 78% — Jul 2020
- 82% — Aug 2020
- 82% — Sep 2020
- 88% — Oct 2020
- 91% — Nov 2020
- 93% — Dec 2020

→ 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

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
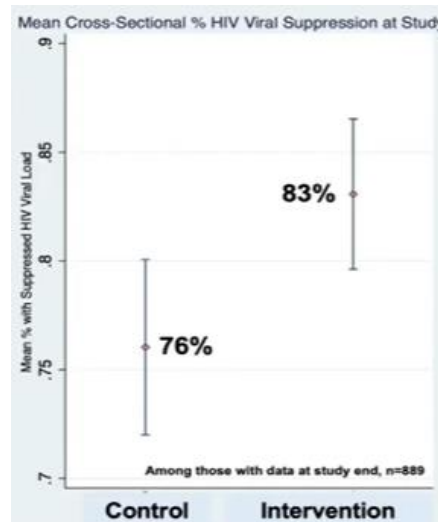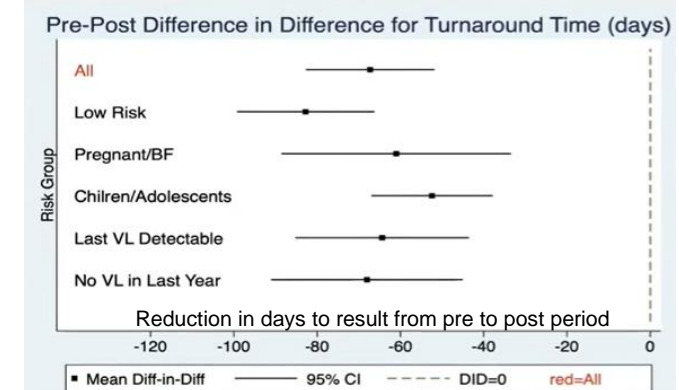
Vivek J et al. IAS Virtual July 2021 Abs OALD01LB3

- 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)

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
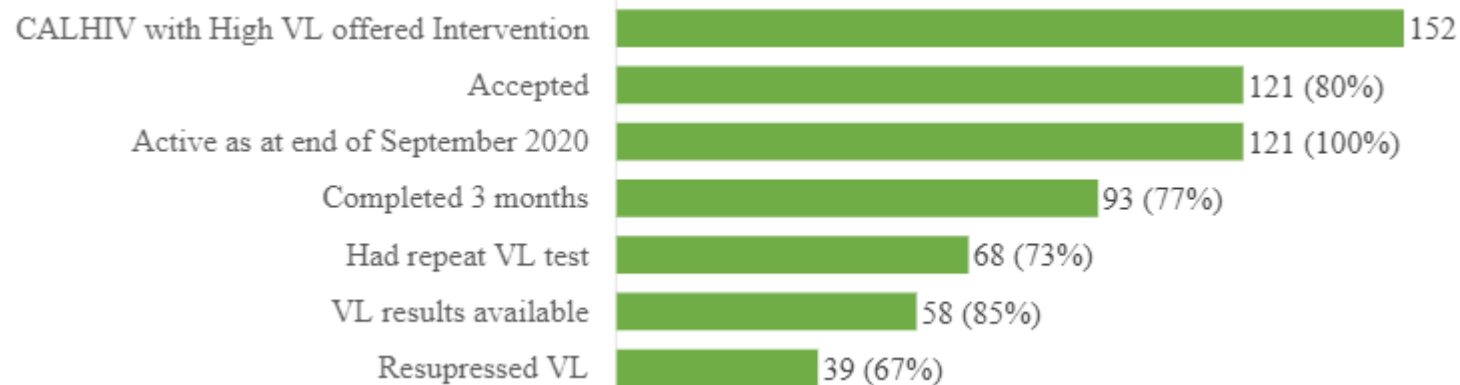

CALHIV with High VL offered Intervention	152
Accepted	121 (80%)
Active as at end of September 2020	121 (100%)
Completed 3 months	93 (77%)
Had repeat VL test	68 (73%)
VL results available	58 (85%)
Resupressed VL	39 (67%)

→ 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

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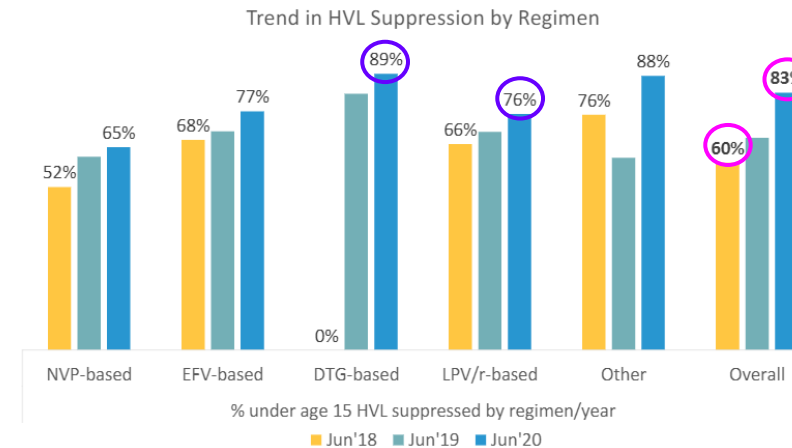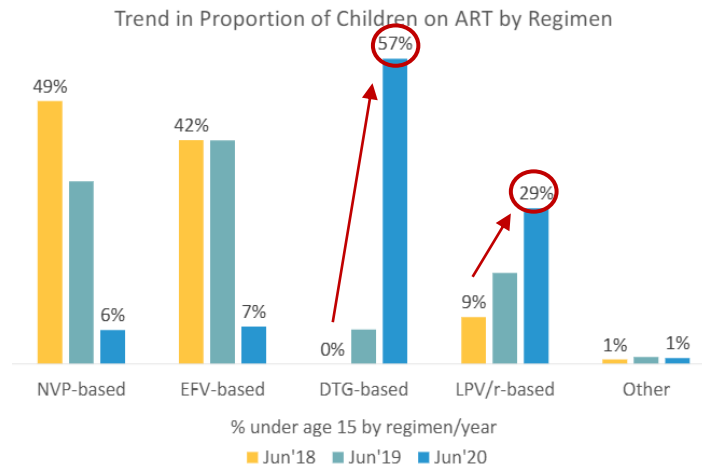
→ Within 2 years (June 2018-June 2020) children on optimal regimen ↑ from **9%** to **86%**

→ 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**.

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

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

Regimens prior to switch to DTG

Regimens switched to after DTG

80% of children switched

2 switches, 27%

3 switches, 8%

4-6 switches, 3%

1 switch, 62%

NNRTI, 80%

PI, 17%

NNRTI + PI or other, 3%

84% stayed on DTG

16% switched

53% to NNRTI

45% to PI

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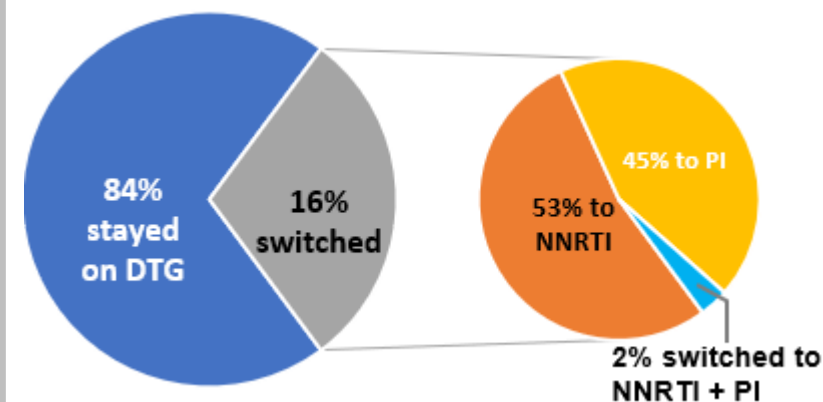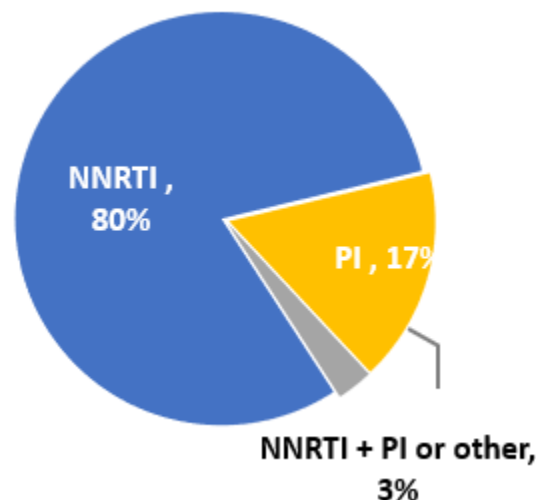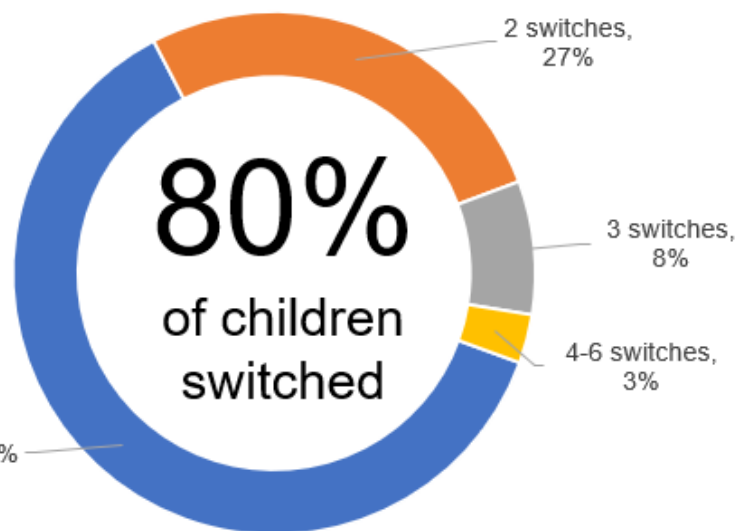
→At last visit, 74% (2,311/3,107) of children were on DTG (includes 1,904 who *switched* to DTG and 407 who were on DTG for the *full* 6-month follow-up period)

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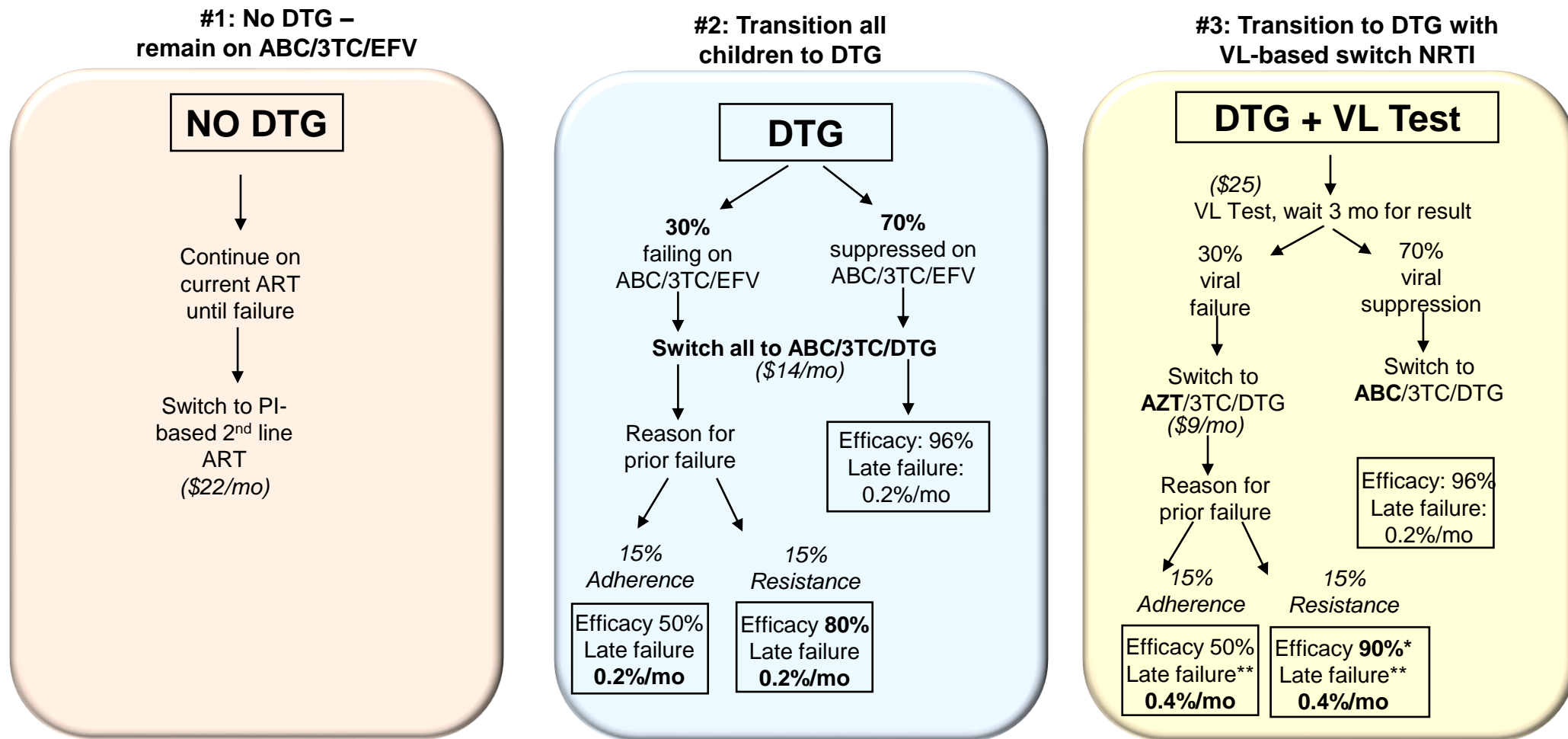
VL Result N (%)	VL Pre-DTG	VL Post DTG ≥ 3mos
Undetectable VL <50	414 **(41.9)**	698 **(70.7)**
Suppressed VL 50-<1000	89 (9.0)	85 (8.6)
Unsuppressed VL ≥1000	485 (49.1)	205 (20.7)

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:

#1: No DTG – remain on ABC/3TC/EFV

NO DTG

Continue on current ART until failure

Switch to PI-based 2nd line ART
($22/mo)

#2: Transition all children to DTG

DTG

30% failing on ABC/3TC/EFV → **Switch all to ABC/3TC/DTG** *($14/mo)* → Reason for prior failure

70% suppressed on ABC/3TC/EFV →
Efficacy: 96%
Late failure: 0.2%/mo

15% Adherence
Efficacy 50%
Late failure **0.2%/mo**

15% Resistance
Efficacy **80%**
Late failure **0.2%/mo**

#3: Transition to DTG with VL-based switch NRTI

DTG + VL Test

($25) VL Test, wait 3 mo for result

30% viral failure → Switch to **AZT**/3TC/DTG *($9/mo)* → Reason for prior failure

70% viral suppression → Switch to **ABC**/3TC/DTG
Efficacy: 96%
Late failure: 0.2%/mo

15% Adherence
Efficacy 50%
Late failure** **0.4%/mo**

15% Resistance
Efficacy **90%***
Late failure** **0.4%/mo**

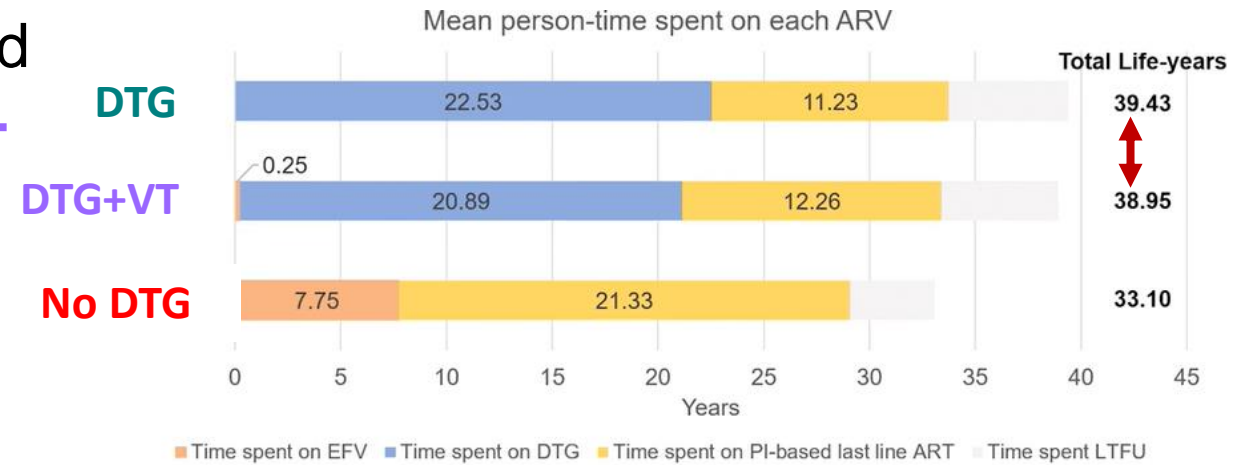** efficacy better when resistance because here you change NRTI*

** 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

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

Mean person-time spent on each ARV

	Total Life-years
DTG	39.43
DTG+VT	38.95
No DTG	33.10

■ Time spent on EFV ■ Time spent on DTG ■ Time spent on PI-based last line ART ■ Time spent LTFU

- Cost: <u>Both</u> 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.
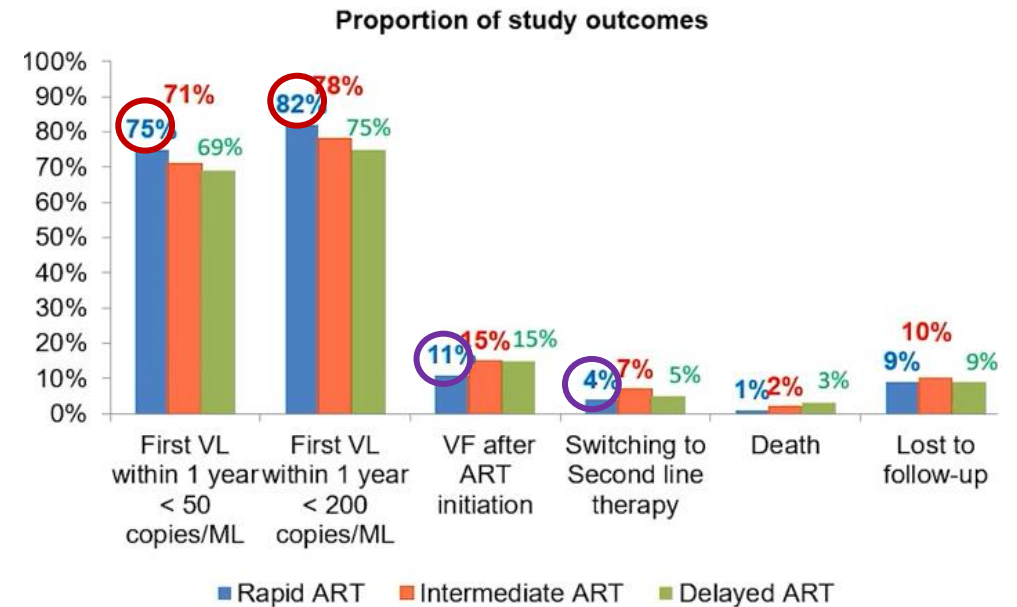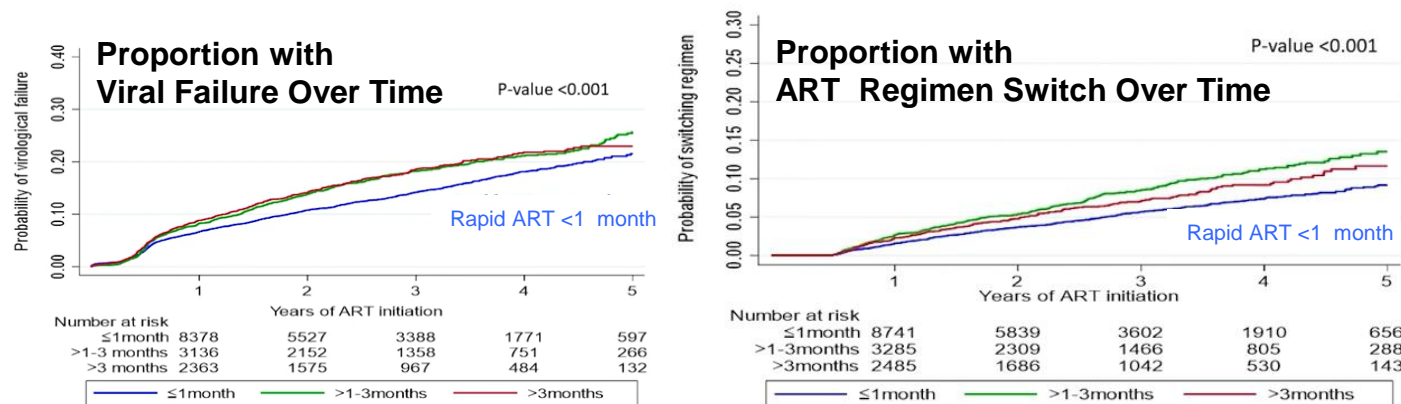
Adolescents and HIV
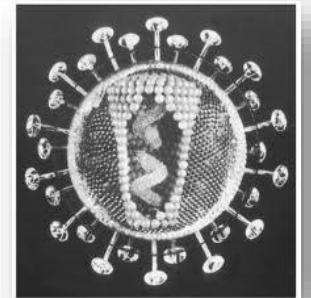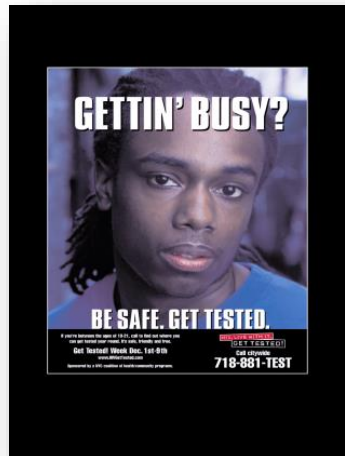
Rapid ART Initiation in Adolescents in Thailand Associated with Improved Clinical Outcome

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)

Proportion of study outcomes

Rapid ART | Intermediate ART | Delayed ART

	First VL within 1 year < 50 copies/ML	First VL within 1 year < 200 copies/ML	VF after ART initiation	Switching to Second line therapy	Death	Lost to follow-up
Rapid ART	75%	82%	11%	4%	1%	9%
Intermediate ART	71%	78%	15%	7%	2%	10%
Delayed ART	69%	75%	15%	5%	3%	9%

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

→Higher suppression
→Lower failure and switching
→No difference death, LTFU

Proportion with Viral Failure Over Time   P-value <0.001

Probability of virological failure

Years of ART initiation

Rapid ART <1 month

Number at risk
≤1month 8378   5527   3388   1771   597
>1-3 months 3136   2152   1358   751   266
>3 months 2363   1575   967   484   132

≤1month | >1-3months | >3months

Proportion with ART Regimen Switch Over Time   P-value <0.001

Probability of switching regimen

Years of ART initiation

Rapid ART <1 month

Number at risk
≤1month 8741   5839   3602   1910   656
>1-3months 3285   2309   1466   805   288
>3months 2485   1686   1042   530   143

≤1month | >1-3months | >3months

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

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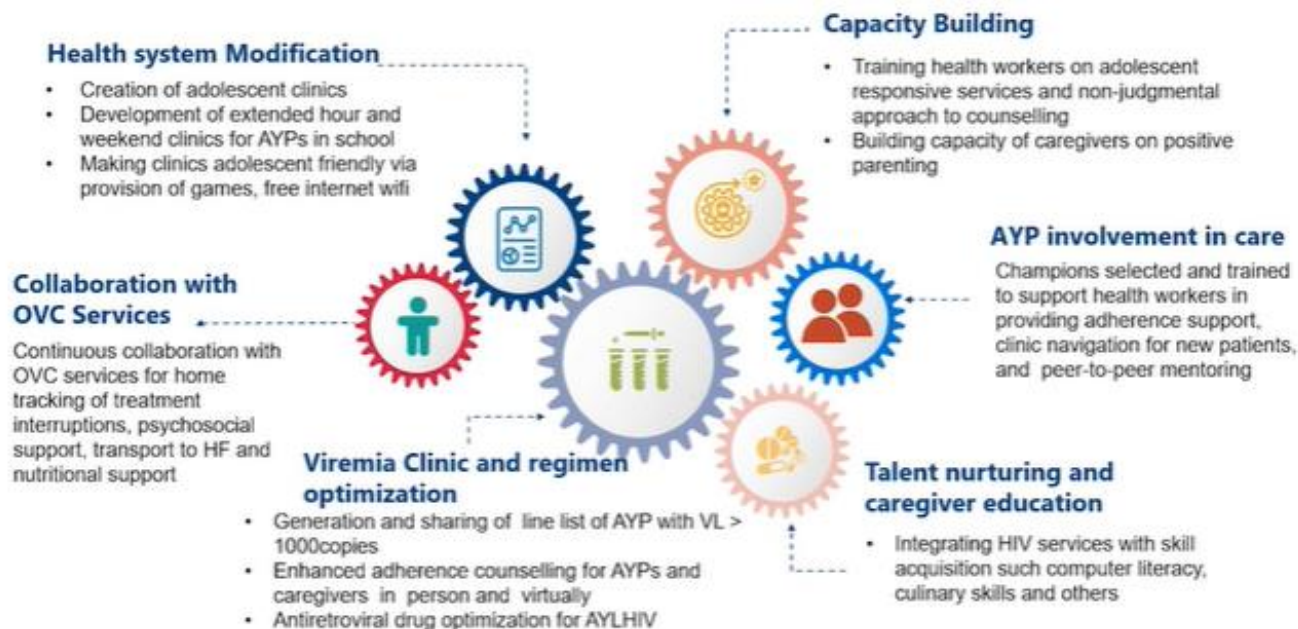
Optimizing ART and Viral Suppression Nigerian Adolescents Reaching Impact, Saturation, and Epidemic Control (RISE)

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

Percentage Receiving Optimal Regimen by Age

P value <0.001

■ Pre-Intervention ■ Post-Intervention
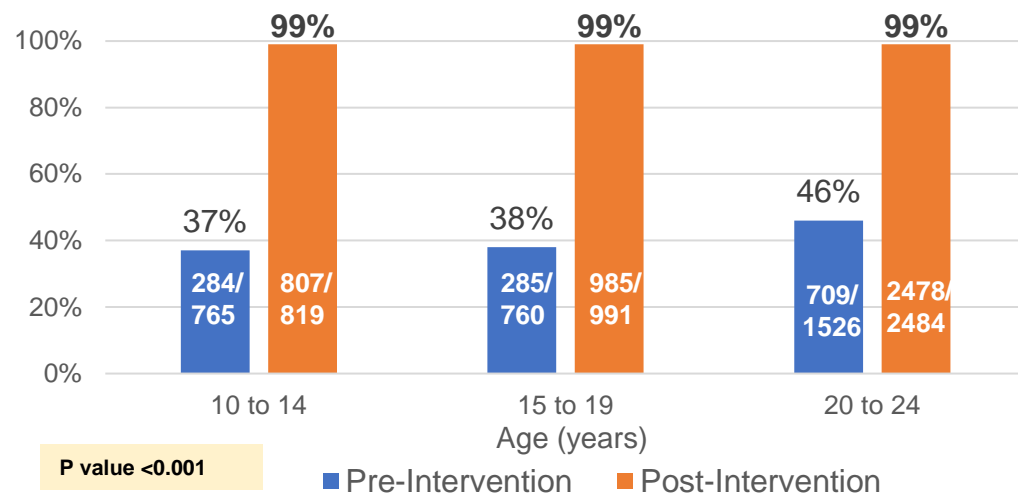
Percentage with VL Result of Those Eligible for VL Check

P value <0.001

■ Pre-Intervention ■ Post-Intervention
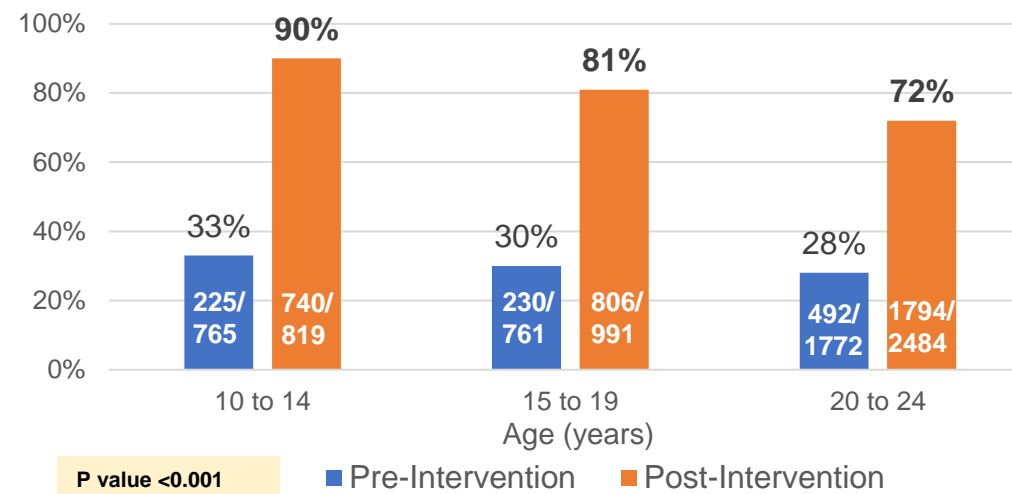
Percentage with Viral Suppression of Those Tested

P value <0.001

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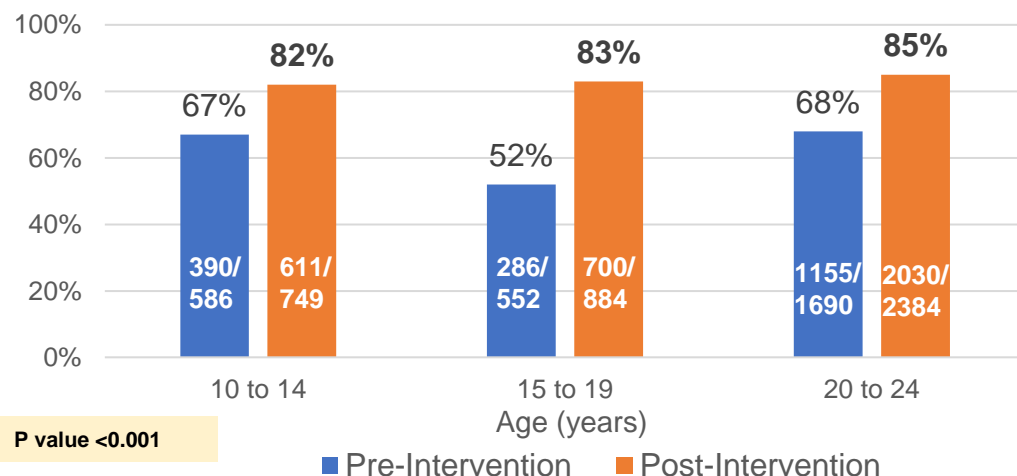
→Adolescent-specific programming and capacity; involvement of adolescents in their care resulting in improvement in commitment to self-care; and caregiver involvement in health care improved health outcomes among AYP.

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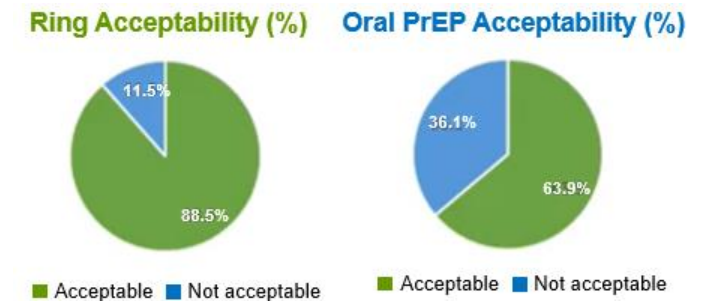
  - Safety: 54% >1 AE, no difference DPV ring vs oral PrEP; no AE-related product holds, discontinuations or product-related SAE

**Crossover Study Design**
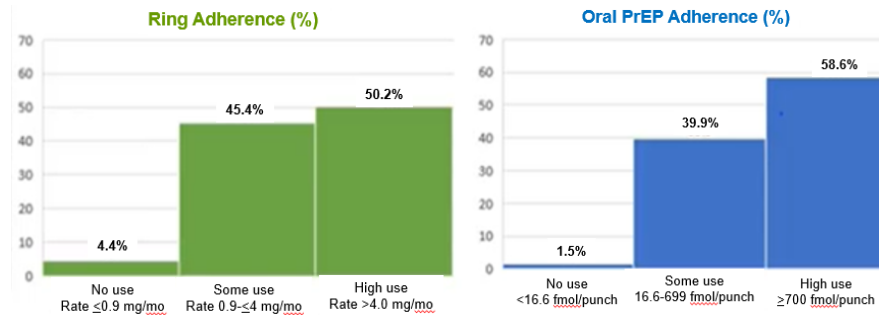
Adherence

Acceptability

Compliance

→ >50% highly adherent over 12 mos

→ More ring pt felt ring acceptable vs oral

→ 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
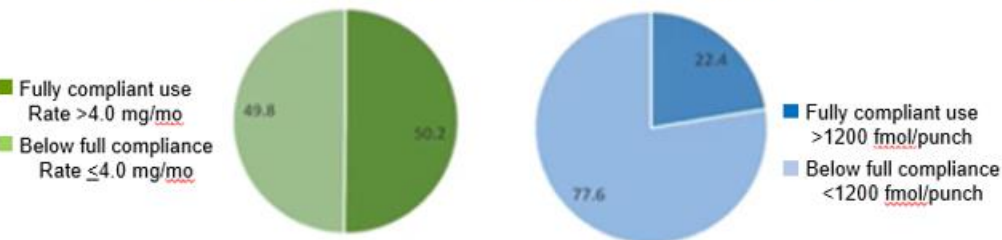
→ More ring pt fully compliant (leaves ring full mo) vs oral PrEP (6+ doses/wk ,>1200 fmol/punch)
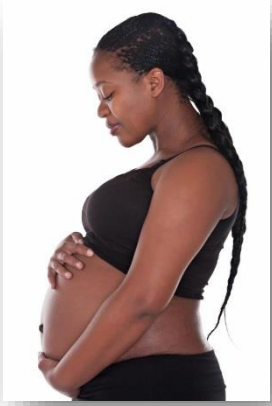
PMTCT Cascade
and ARV in Pregnancy
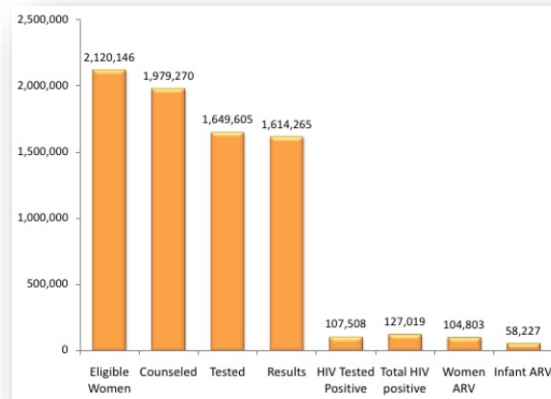
Importance of Surveys to Complement Program Data in Informing MTCT Estimates – Uganda

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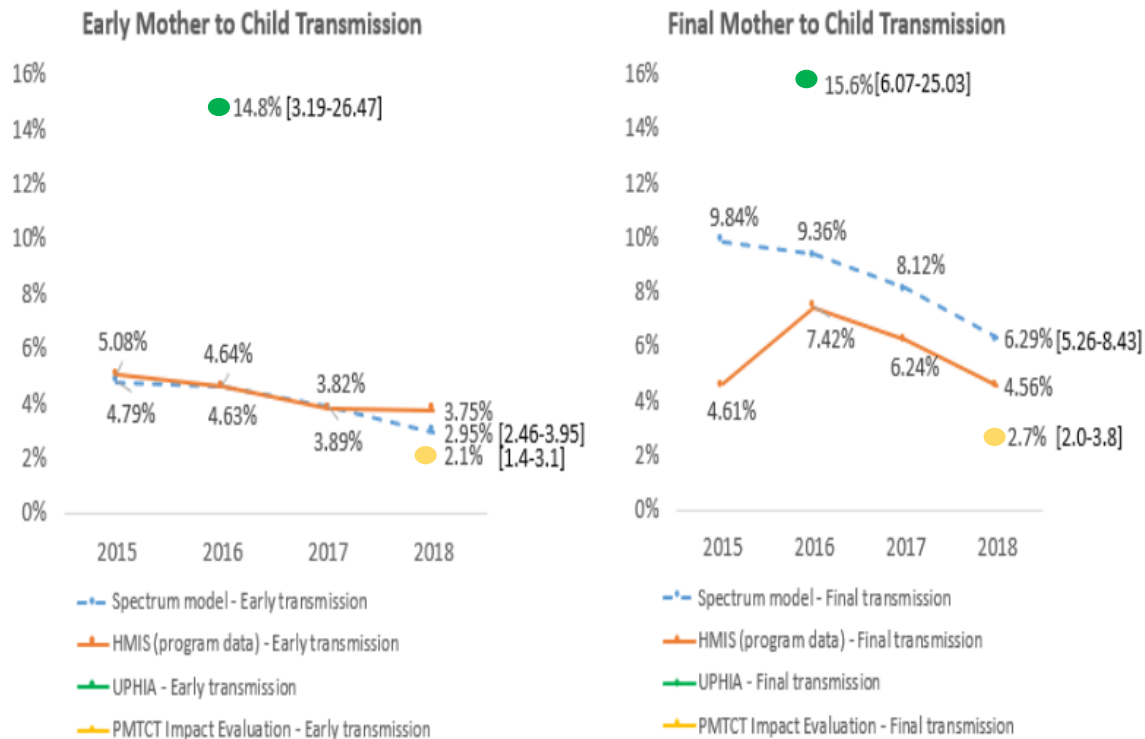
→ All data show marked ↓ in MTCT over time, although early & especially final MTCT rates differed by method.

→ 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

The most rapid decline in HFS occurs between birth to 6 months, plateauing at age 1 year.
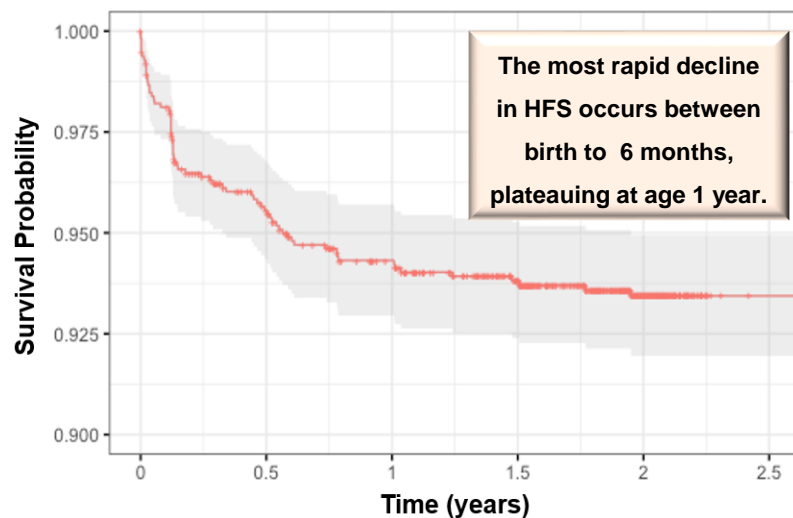
MTCT, Death and HIV-Free Survival by Study and Overall

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]**

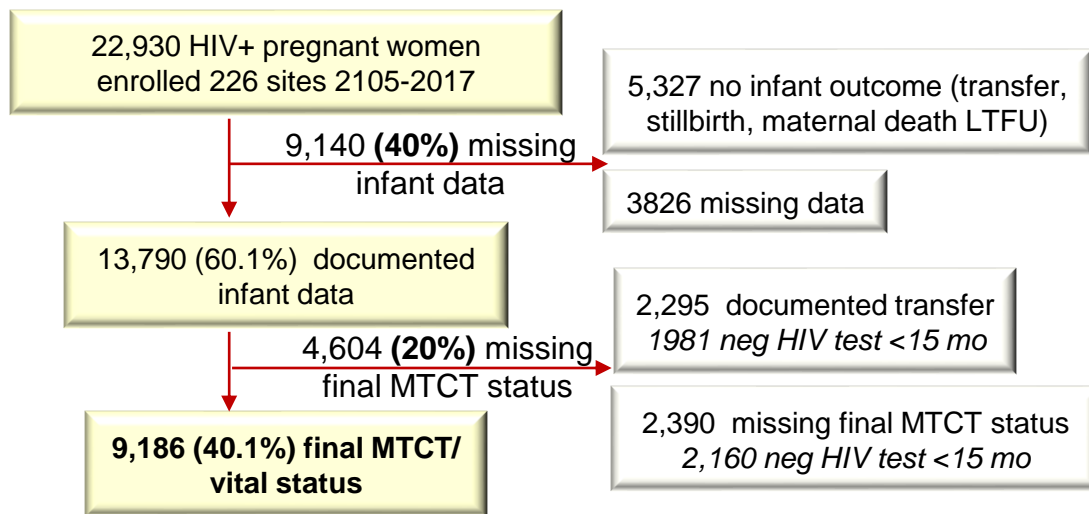**Factors Associated with HIV-Free Survival**

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.

Flowchart:

- 22,930 HIV+ pregnant women enrolled 226 sites 2105-2017
  - 9,140 **(40%)** missing infant data → 5,327 no infant outcome (transfer, stillbirth, maternal death LTFU); 3826 missing data
- 13,790 (60.1%) documented infant data
  - 4,604 **(20%)** missing final MTCT status → 2,295 documented transfer *1981 neg HIV test <15 mo*; 2,390 missing final MTCT status *2,160 neg HIV test <15 mo*
- 9,186 **(40.1%)** final MTCT/ vital status

- 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

Characteristic‡	Univariable, N = 7483 Crude odds ratio	p-value	Multivariable Complete case, N = 7483 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*	Time enter ANC
<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	HIV disease
When ART was started		0.0001		0.0001	Timing ART Start
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]		Clinic volume
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	

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

		Suppressed, n=2096	%	Viral load count Not suppressed, n=1009	%	Total, n=3105	OR	p-value	Wald Chi-square p-value
Age	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	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	
Disclosure	HIV disclosure								
	No	118	53%	103	47%	221	ref.		
	Yes	1978	69%	906	31%	2884	1,725	0,0004	0,0004
Time HIV dx	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

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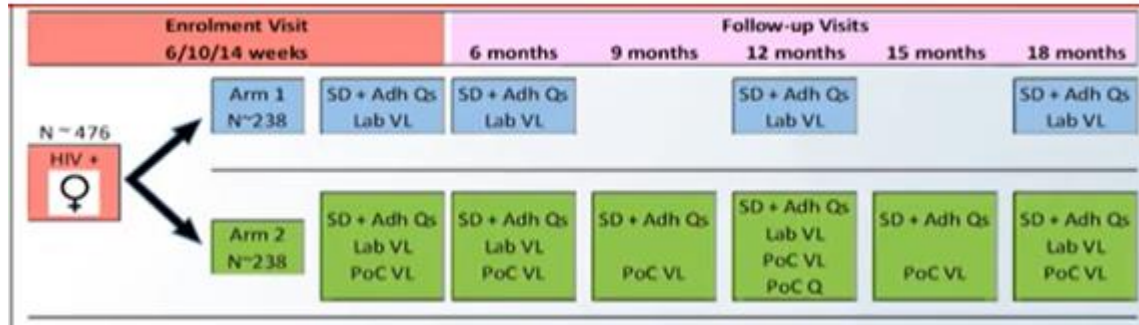
- No significant differences at baseline btn arms
- Preconception ART 57%
- At <u>enrollment</u>, 88% <200, 91% <1,000 c/mL
- **36% LTFU**

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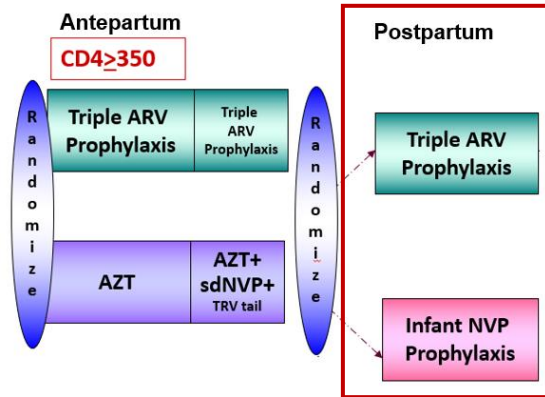
- Self-reported adherence to maternal ART (mART) and infant NVP (iNVP) in the postpartum component of PROMISE compared and association of viral suppression with self-reported adherence to ART in mART arm examined.

→ 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 all pregnant HIV+ women not suppressed in 2019.
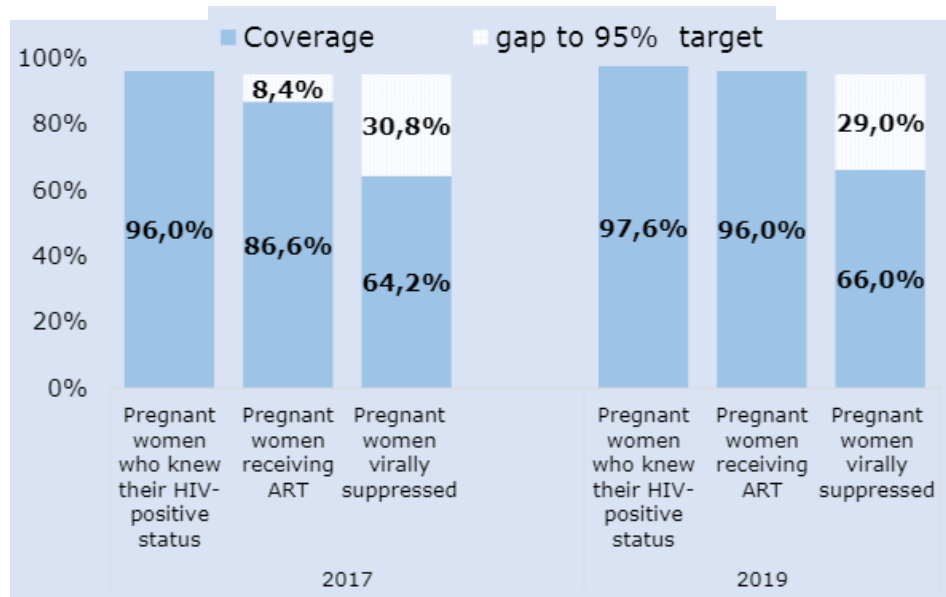
Factors Associated with Viral Suppression (<50 c/mL)

	Sample distribution n=17 820 *	Percent virally suppressed (95% CI[I]) 2017	Percent virally suppressed (95% CI) 2019	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
Age group (in years)						**Age**
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)	**Province of ANC care**
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						**Timing ART Start**
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)	

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

Huffstetler HE et al. IAS Virtual Abs PEC246 July 2021

UNC PROJECT
Lilongwe, Malawi

- Baseline HIV testing with validated algorithm for recency (Limiting Antigen Avidity EIA [OD $\leq$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

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.
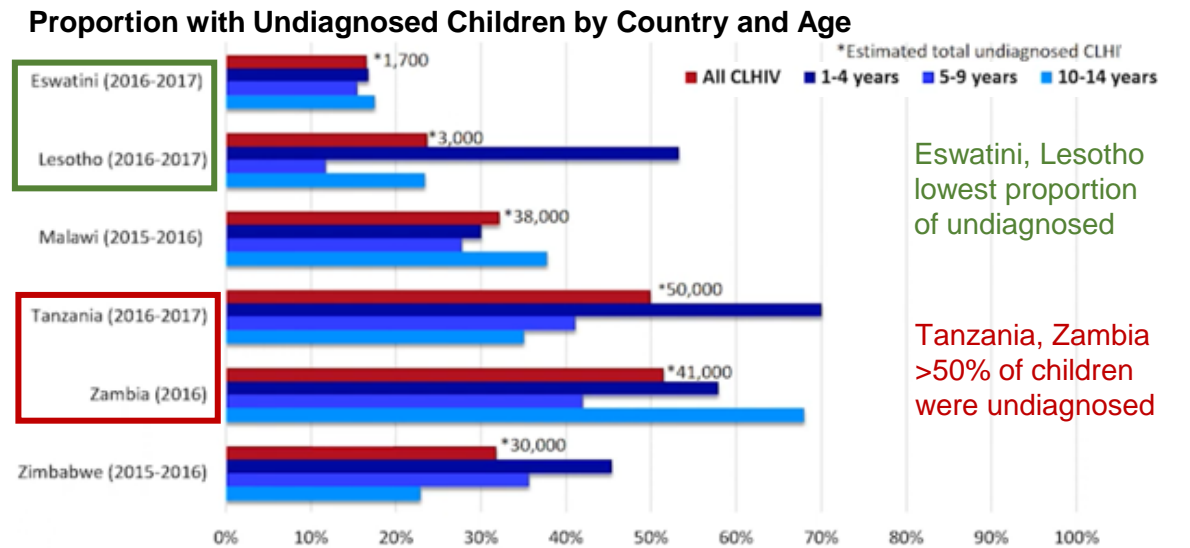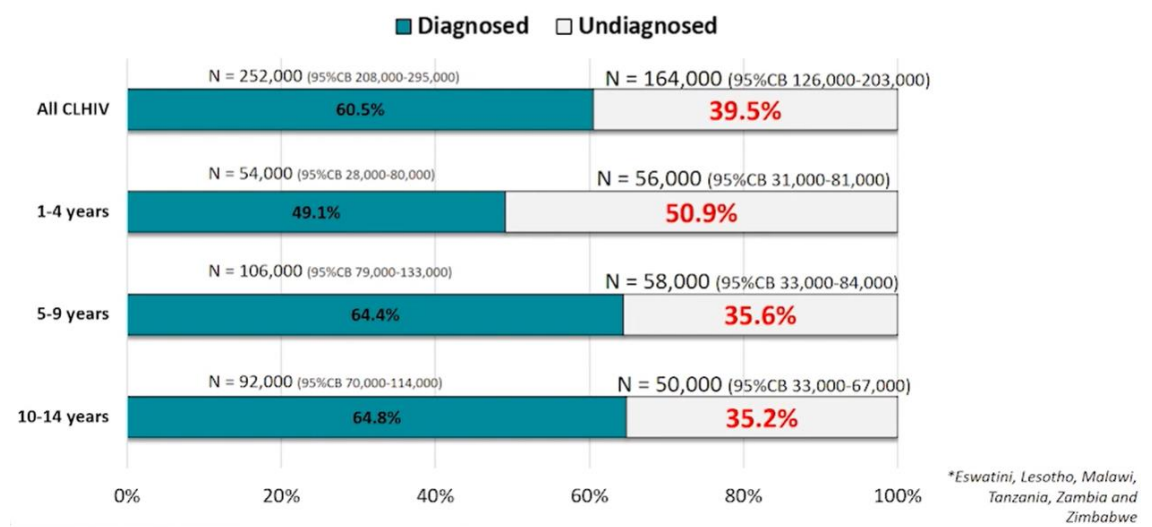
Eswatini, Lesotho lowest proportion of undiagnosed

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.

Proportion Diagnosed vs All HIV+ Children on ART

Proportion Diagnosed vs All HIV+ Children on ART by Country
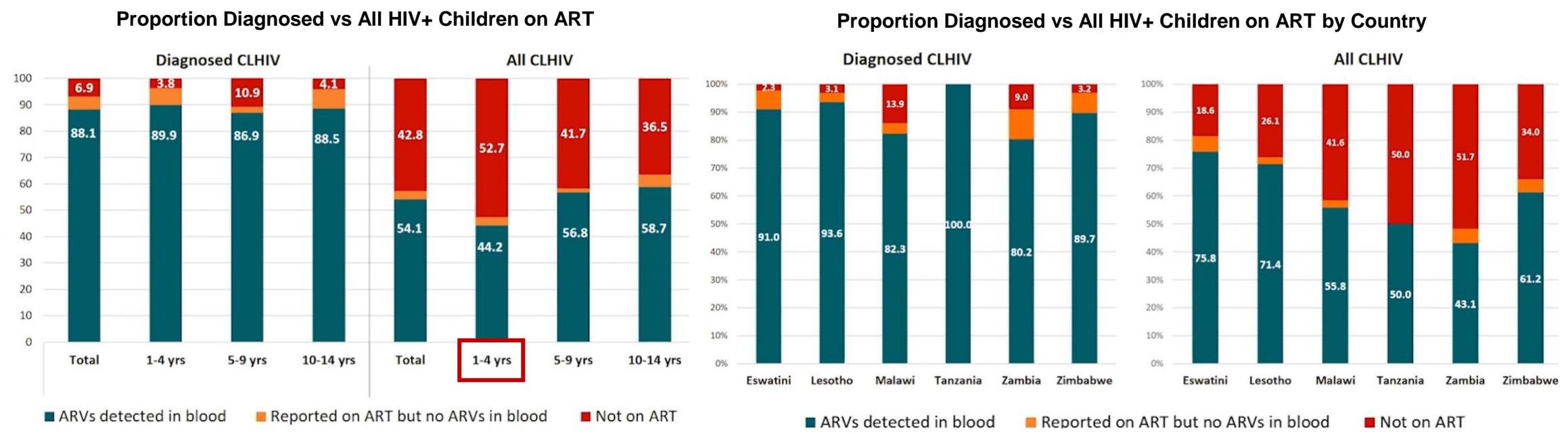
Impact of a Community Health Worker (CHW) Administered Index Case Screening Tool on Pediatric HIV Case Identification, Malawi

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

- 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

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.
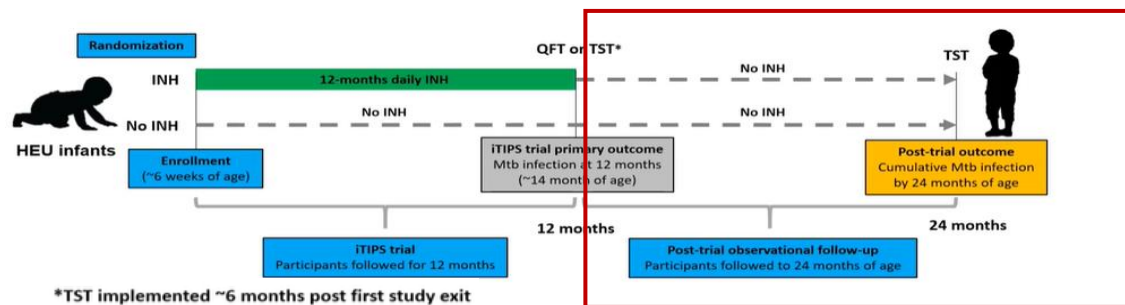
Correlates of 24-month cumulative Mtb infection

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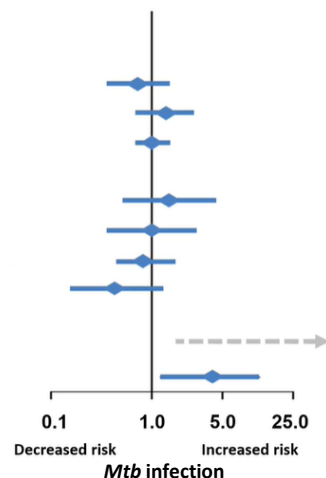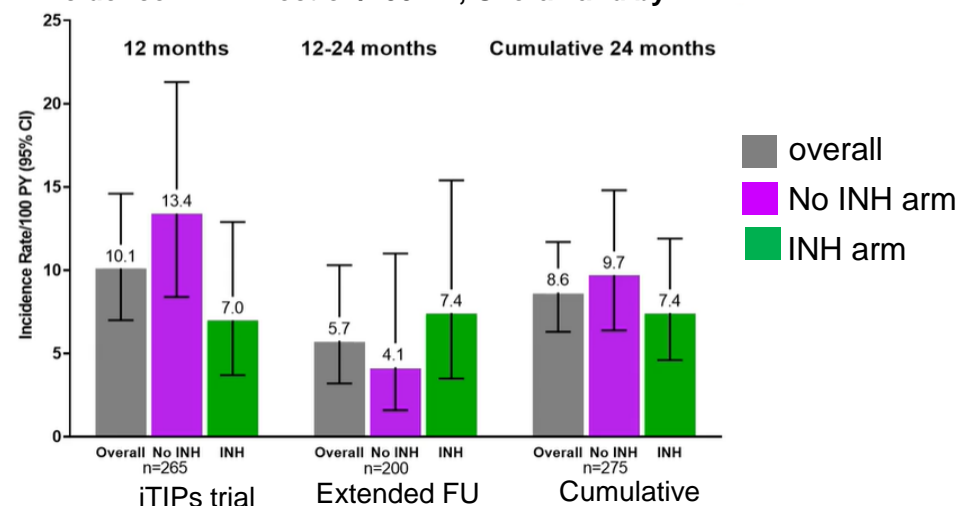
→24-mo cumulative *Mtb* infection high in HEU (8.6%/yr)

→Prior receipt of INH prophylaxis did not ↓ incidence

→Poor household conditions associated with infection

CTX Prophylaxis for HIV-Exposed Children – Modeling Impact of Different Strategies Up to Age 2 Years
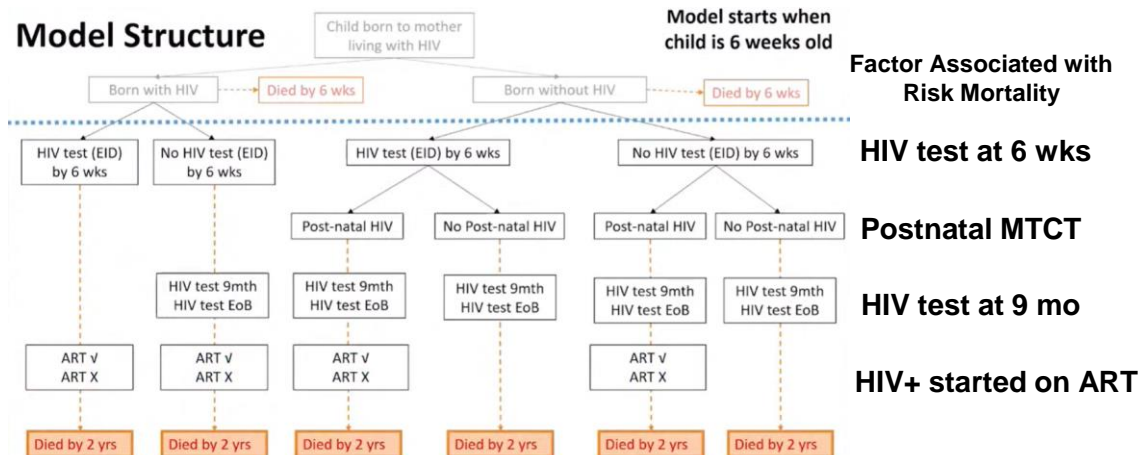
Simon KR et al. International Pediatric HIV Workshop Abs 27

- 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

Model Structure

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

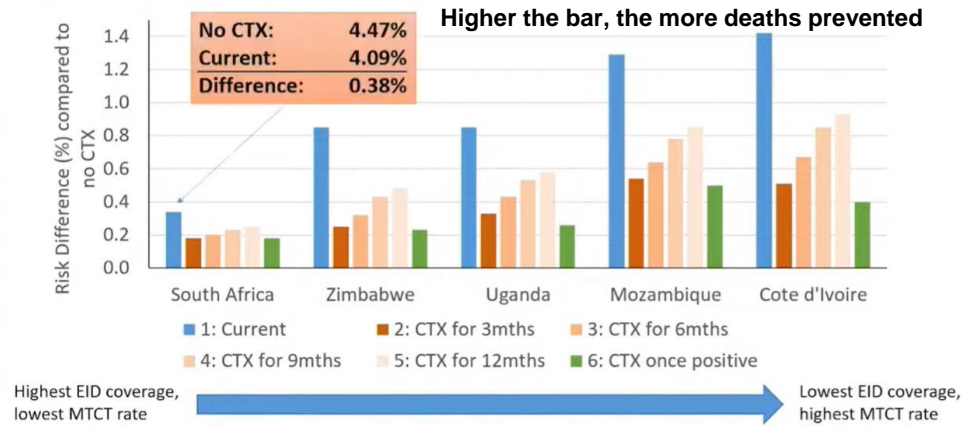| Parameter	Assumption	Source
HIV transmission (by end of breastfeeding)	South Africa: 4% Zimbabwe: 8.2% Cote d'Ivoire: 13.3% Mozambique: 14% Uganda: 6%	UNAIDS Factsheets 2019; Dunning JIAS; Mahy AIDS 2017; Lain PLOS One 2020; Zimbabwe Ministry of Health
Early HIV test (by 6 wks)	South Africa: 83% Zimbabwe: 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

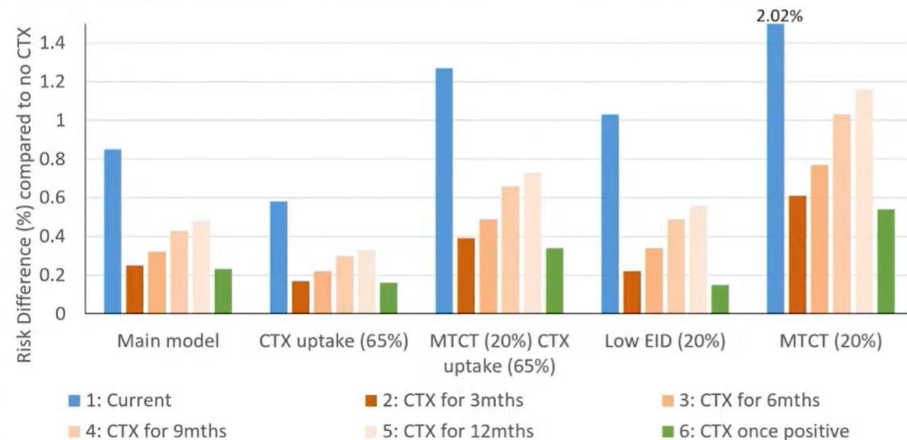*Smith C et al. International Pediatric HIV Workshop Abs 27*

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

Difference in deaths, compared to no CTX

No CTX:	4.47%
Current:	4.09%
Difference:	0.38%

Higher the bar, the more deaths prevented

South Africa, Zimbabwe, Uganda, Mozambique, Cote d'Ivoire

- 1: Current
- 2: CTX for 3mths
- 3: CTX for 6mths
- 4: CTX for 9mths
- 5: CTX for 12mths
- 6: CTX once positive

Highest EID coverage, lowest MTCT rate → Lowest EID coverage, highest MTCT rate

Varying model assumptions (Zimbabwe)

2.02%

Main model, CTX uptake (65%), MTCT (20%) CTX uptake (65%), Low EID (20%), MTCT (20%)

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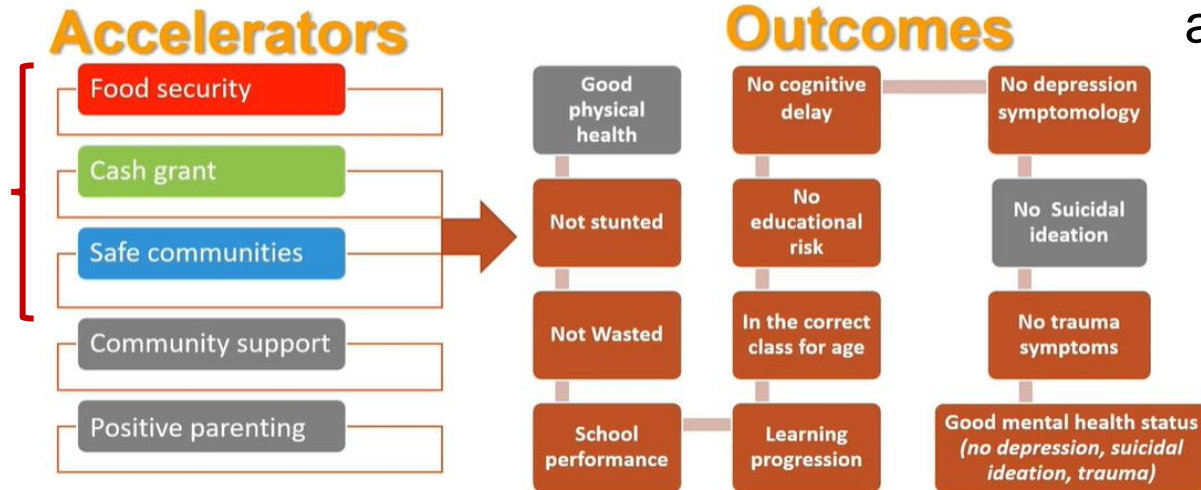
Accelerators community support and positive parenting were associated with mental health outcomes, however the other 3 accelerators had greater impact on several child outcomes.

- 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

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

Adjusted probability and adjusted RD (% points) of having SDG-aligned child outcomes with <u>three combined</u> accelerator provision
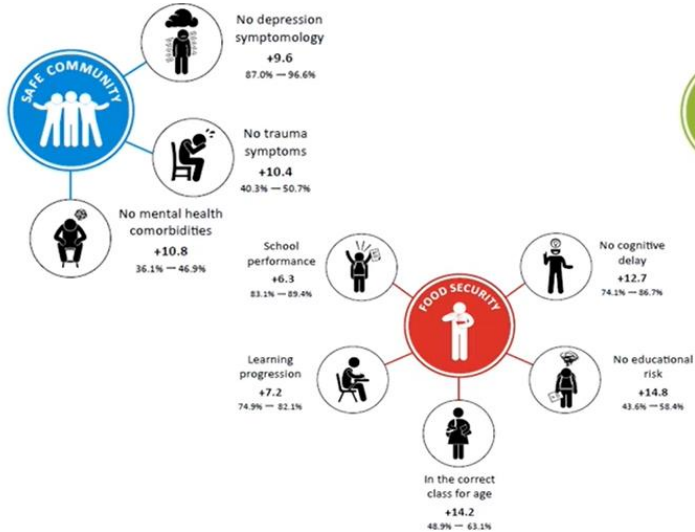
→Significant association of individual accelerator provision with decrease in adverse child and **increase in positive outcomes**
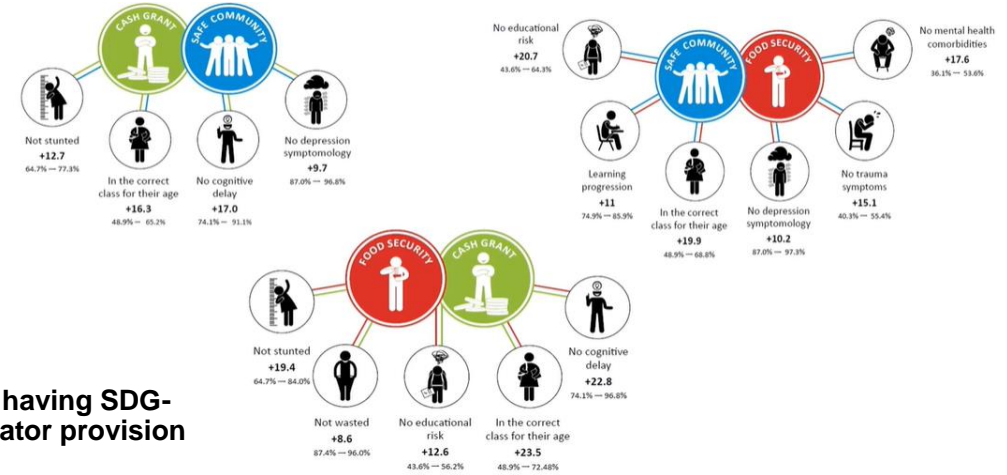
→Additive value of having two accelerators provision with further improved child outcomes
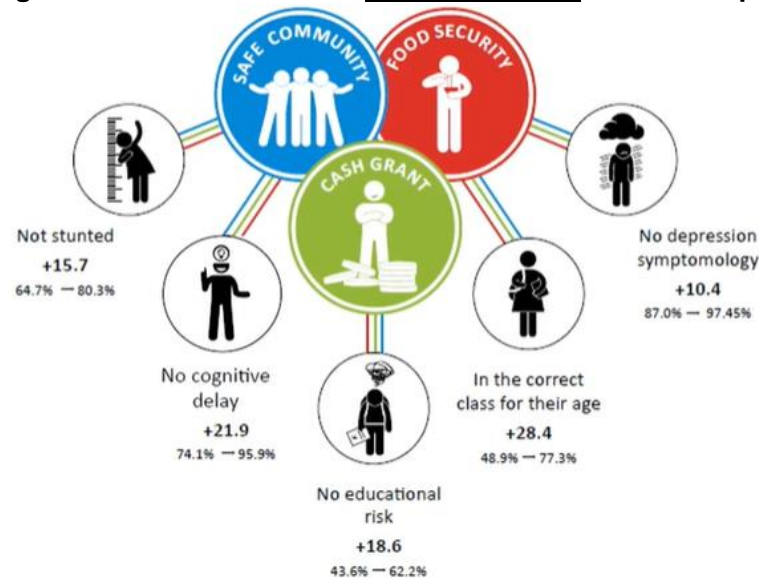
→A combination delivery of these 3 accelerators results in highest probability of positive child outcomes and was superior to provision of individual components alone.
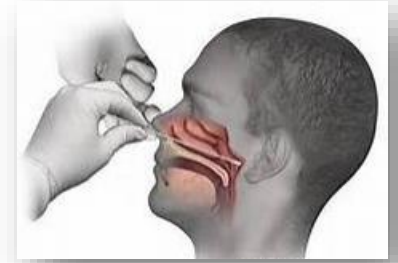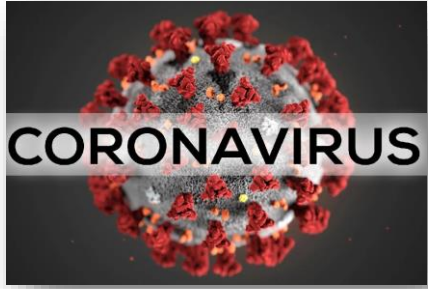
Effects of COVID-19-Related Mitigation Practices on Programs
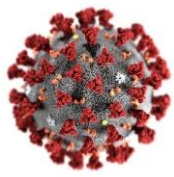
Effect of COVID-19 Pandemic on HIV Services in Africa

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.
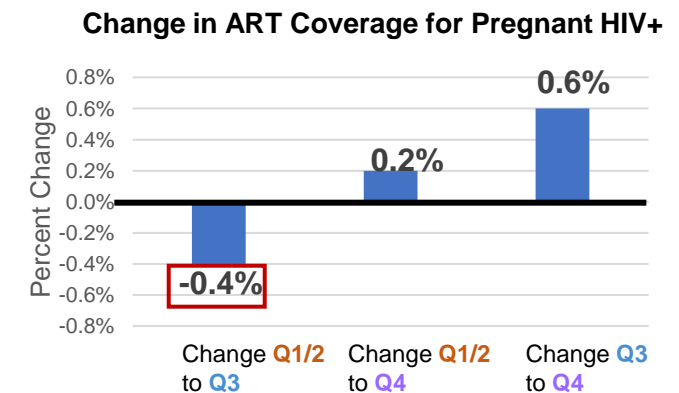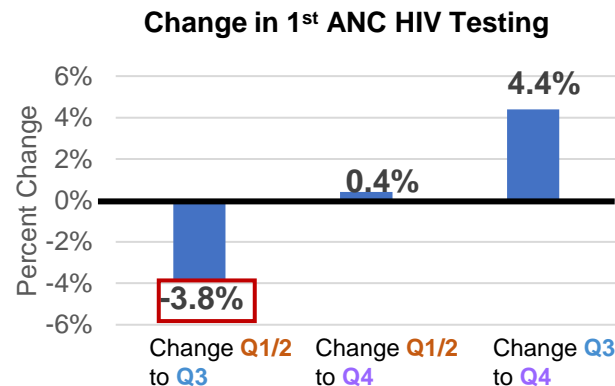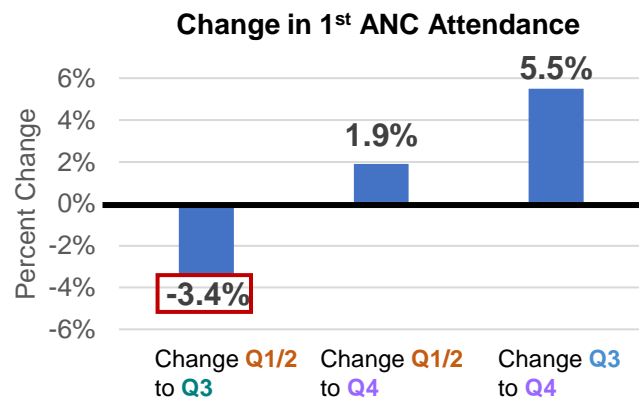
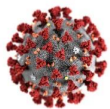**Pre-COVID-19**　　　　　　　　　　**During COVID-19**

| 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.**

Change in 1st ANC Attendance

Change in 1st ANC HIV Testing

Change in ART Coverage for Pregnant HIV+

- **Early infant diagnosis and linkage to care during COVID-19**:

  During COVID-19
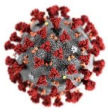
  | Q3: Oct 2019-Mar 2020 | Q4: Apr 2020-Sep 2020 |

  – 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.

2-month EID coverage by country—FY2020

Source: PEPFAR MER Data.
■ Oct. 2019 to Mar. 2020   ■ Apr. 2020 to Sep. 2020   ● Percent change
*Data are from 20 regions.

Infants with HIV linked to ART by country—FY2020

Source: PEPFAR MER Data.
■ Oct. 2019 to Mar. 2020   ■ Apr. 2020 to Sep. 2020   ● Percent change

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 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

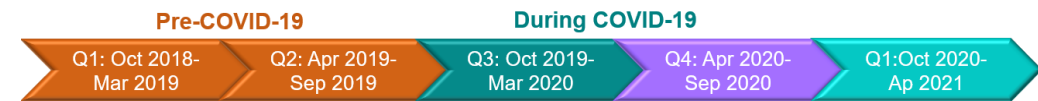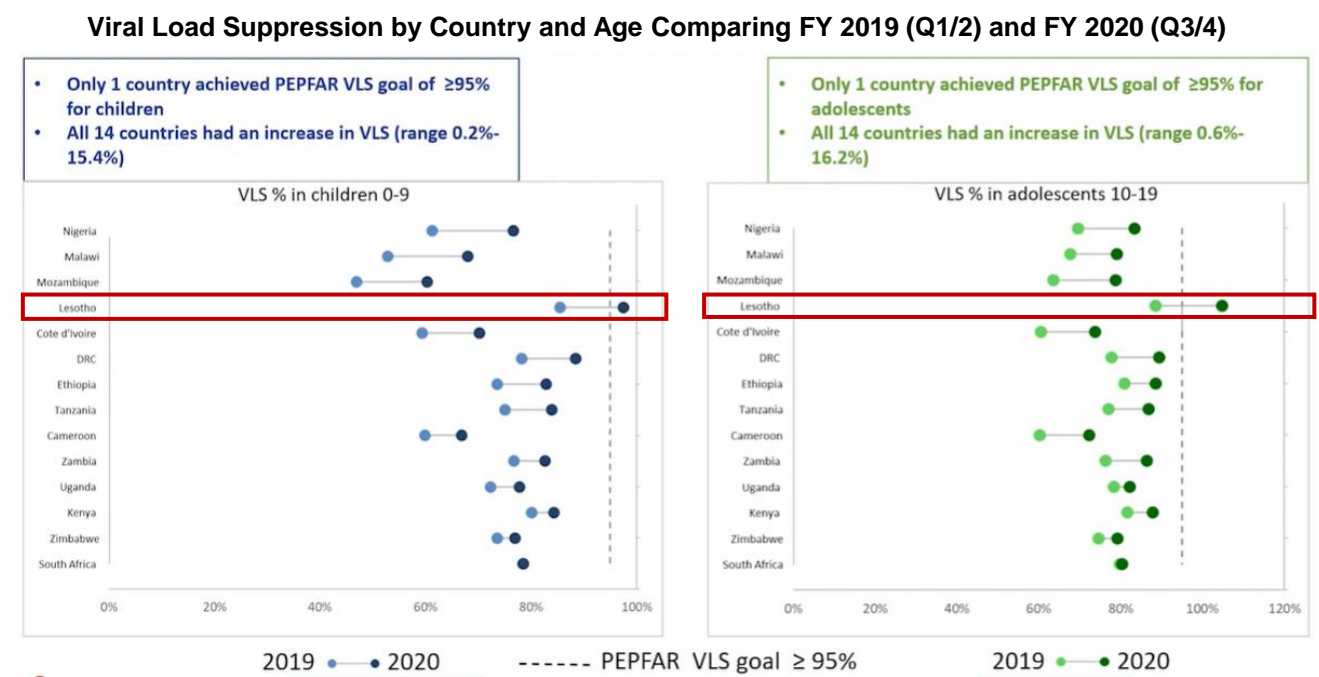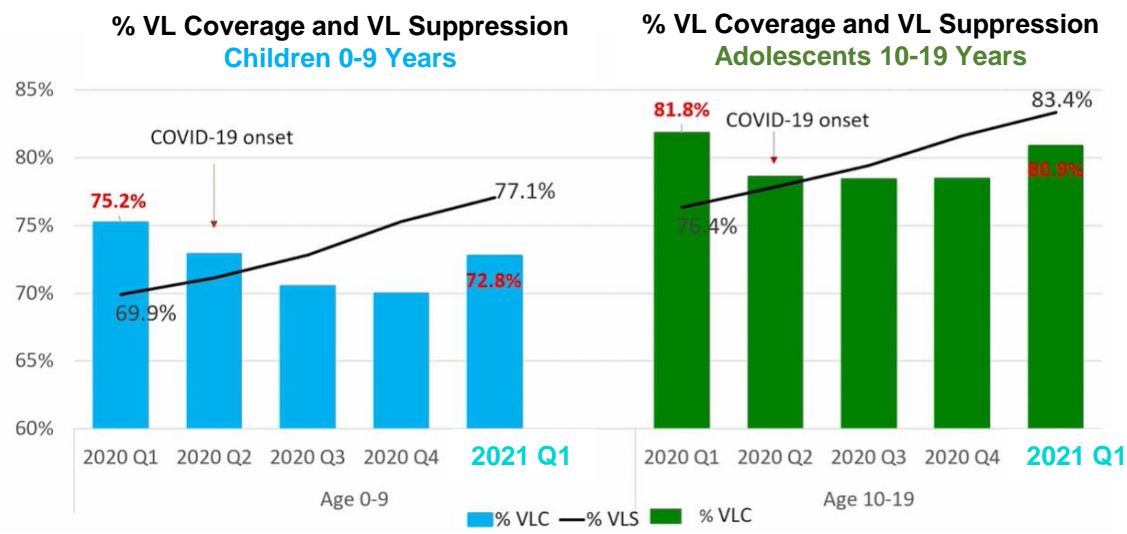- Viral load suppression paradoxically increased during COVID-19 in both Q3 and Q4.
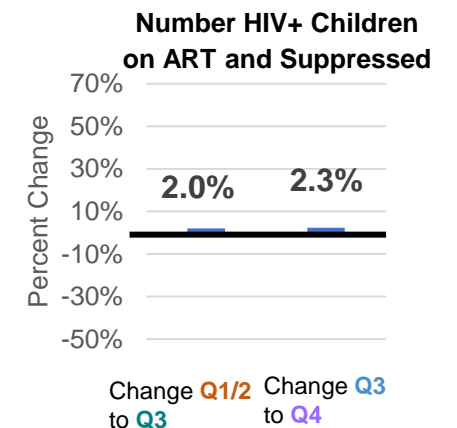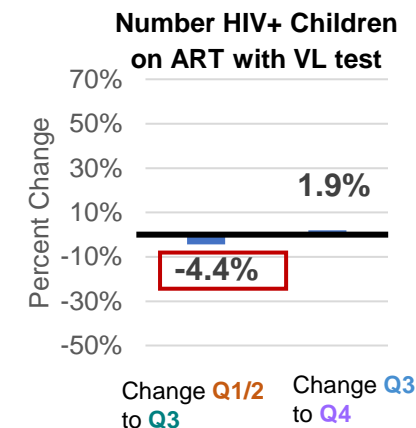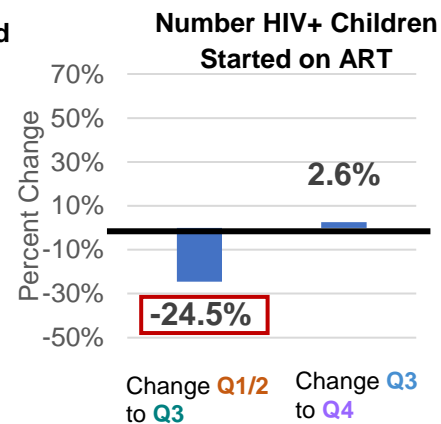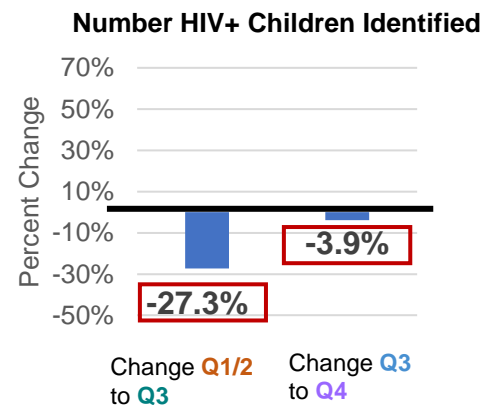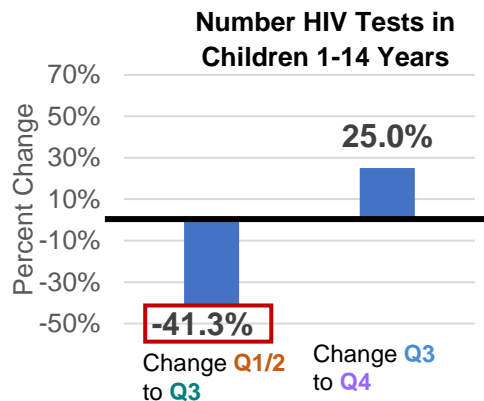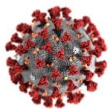
Number HIV Tests in Children 1-14 Years
- 25.0%
- -41.3%
- Change Q1/2 to Q3
- Change Q3 to Q4

Number HIV+ Children Identified
- -3.9%
- -27.3%
- Change Q1/2 to Q3
- Change Q3 to Q4

Number HIV+ Children Started on ART
- 2.6%
- -24.5%
- Change Q1/2 to Q3
- Change Q3 to Q4

Number HIV+ Children on ART with VL test
- 1.9%
- -4.4%
- Change Q1/2 to Q3
- Change Q3 to Q4

Number HIV+ Children on ART and Suppressed
- 2.0%
- 2.3%
- Change Q1/2 to Q3
- Change Q3 to Q4

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

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	Q1:Oct 2020- Ap 2021

  - − 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%.

% VL Coverage and VL Suppression Children 0-9 Years

% VL Coverage and VL Suppression Adolescents 10-19 Years

Viral Load Suppression by Country and Age Comparing FY 2019 (Q1/2) and FY 2020 (Q3/4)

- Only 1 country achieved PEPFAR VLS goal of ≥95% for children
- All 14 countries had an increase in VLS (range 0.2%-15.4%)

- Only 1 country achieved PEPFAR VLS goal of ≥95% for adolescents
- All 14 countries had an increase in VLS (range 0.6%-16.2%)

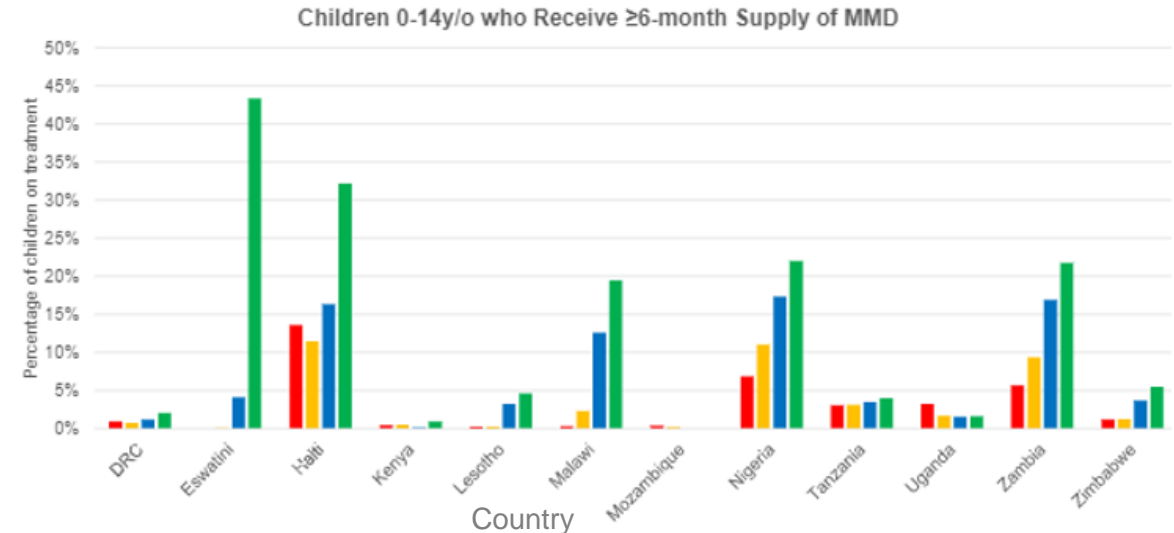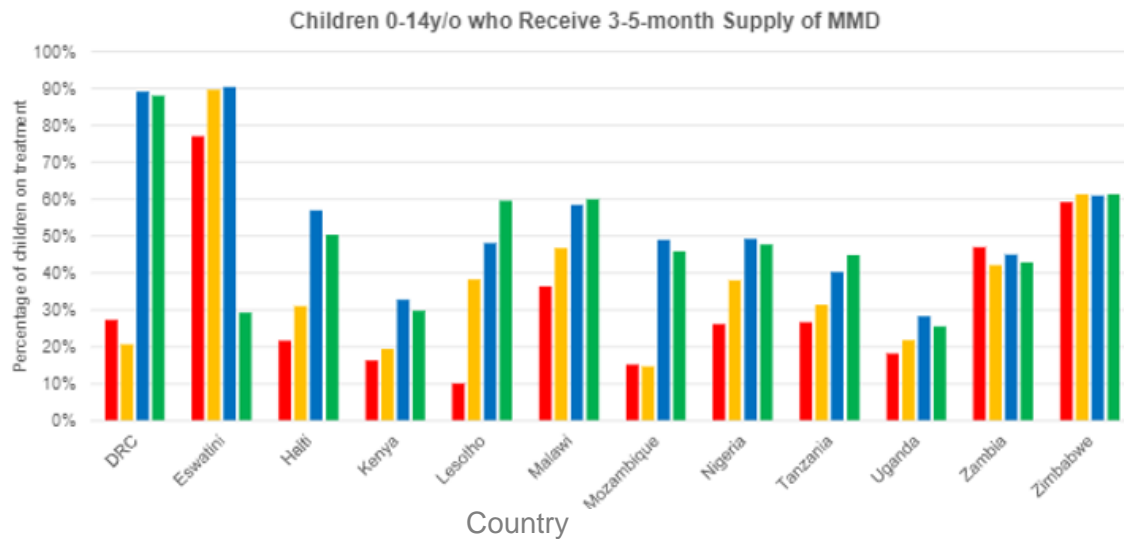# Multi-Month ART Dispensing in Children During the COVID-19 Pandemic, 12 PEPFAR Focus Countries

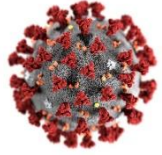*Fernando N et al. Pediatric HIV Workshop Abs 116/IAS Virtual Abs PEB209 July 2021*

■ **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	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]	185,357	7,944 (45.2%) **	80,673 (45.9%) *	15,774 (9.0%) **

p<0.01 ↕ p<0.001 ↕

→ *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**

Children 0-14y/o who Receive 3-5-month Supply of MMD

Children 0-14y/o who Receive ≥6-month Supply of MMD

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.
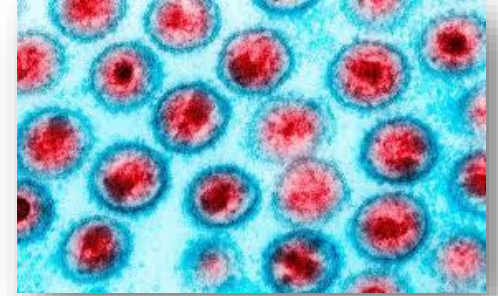
The Future:

Long-Acting
ART and PrEP Options

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

Lenacapavir
LEN: first-in-class HIV capsid inhibitor

EC₅₀, 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

Translocation Inhibition
- Translocation inhibition prevents opening of the RT nucleotide binding site
- Nucleotides cannot be incorporated into vDNA
- **Viral replication is inhibited**

Delayed Chain Termination
- ISL changes vDNA structure such that nucleotide incorporation is prevented
- As ISL is not in the RT active site, it is not susceptible to resistance-conferring mutations
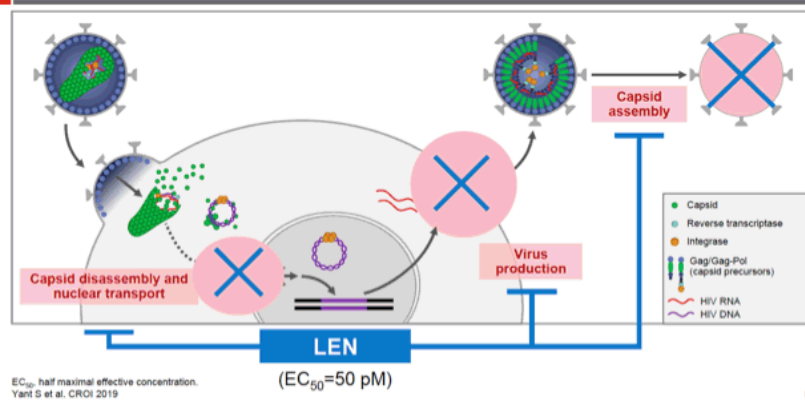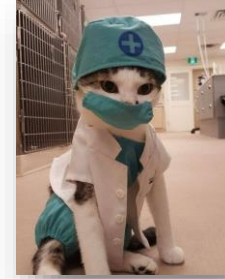- **Viral replication is inhibited**

- 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

Thank You For Your Attention!

Questions?