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

→ 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

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

Distribution pregnant women with HIV not on ART by region, 2020

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

→ 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

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

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%

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

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

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

- Missed target by 800,000 in 2020


Distribution children with HIV not on ART by age, 2020

- 0-4 years: 37%
- 5-9 years: 23%
- 10-14 years: 40%
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.
→ Only 40% [29–51%] of all children with HIV were virally suppressed in 2020.

→ If focus specifically on suppression in children or adults with known HIV on ART, 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

→ 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.

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](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

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

ODYSSEY A: First-line ART
N=311 (44%)

DTG N=154
SOC N=157
92% EFV

ODYSSEY B: Second-line ART
N=396 (56%)

DTG N=196
SOC N=200
98% PI

FU: until last patient reaches 96 wks
Primary endpoint: viral or clinical failure

• 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
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


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

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

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

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


<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>DTG N=42</th>
<th>SOC N=43</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse event</td>
<td>15 (11%)</td>
<td>19 (11%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Grade 3 or above</td>
<td>36 (19%)</td>
<td>34 (21%)</td>
<td>0.79</td>
</tr>
<tr>
<td>ART modifying event</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

- 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.
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 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

<table>
<thead>
<tr>
<th></th>
<th>DTG</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODYSSEY A: first line</td>
<td>11 (7%)</td>
<td>30 (19%)</td>
</tr>
<tr>
<td>ODYSSEY B: second-line</td>
<td>31 (16%)</td>
<td>40 (20%)</td>
</tr>
</tbody>
</table>

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.
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 2\textsuperscript{nd} Line ART, ODYSSEY
Kityo C et al. International Pediatric HIV Workshop Abs 10/IAS Virtual Abs PEBLB 17 July 2021

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

- Resistance with viral failure on 2\textsuperscript{nd} 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 2\textsuperscript{nd} 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 [solid line] (2 consecutive VL <200 c/mL) or ART switch [dashed line] following viral failure (>400 c/mL)

- ~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).

*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)
DTG had high genetic resistance barrier in children.

In children failing 1\textsuperscript{st} line DTG ART, there was no post-failure resistance to any drug class.

Among those on 2\textsuperscript{nd} 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-suppression in DTG arm.

However, none of the children with InSTI resistance had resuppressed by end of trial.

Supports use of DTG for both 1\textsuperscript{st} and 2\textsuperscript{nd} line ART - but ongoing adherence support is needed, especially if child is on 2\textsuperscript{nd} 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

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

- 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

- Differences were similar by 1\textsuperscript{st} vs 2\textsuperscript{nd} 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.
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.

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)
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).

**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

- 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

2. Cepheid Xpert VL in Hub

3. VL Counseling Script

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

<table>
<thead>
<tr>
<th>Retention and Viral Load Resuppression Among Children Provided Daily ART Reminder and VEAC, May-Sept 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>CALHIV with High VL offered Intervention Accepted Active as at end of September 2020 Completed 3 months Had repeat VL test VL results available Resuppressed VL</td>
</tr>
<tr>
<td>152 121 (80%) 121 (100%) 93 (77%) 68 (73%) 58 (85%) 39 (67%)</td>
</tr>
</tbody>
</table>

→ 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
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.
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
- Third round: Nov 2020 – Aug 2021 (planned)
Of those who switched, 81% (2,009/2,488) switched to a DTG-based regimen within 6 mos. Regimens prior to switch to DTG: 80% NNRTI, 17% PI, 3% NNRTI + PI or other.

However, 16% (319/2,009) of children switched to DTG then switched to other regimens within 6 mos. Regimens switched to after DTG: 84% stayed on DTG, 16% switched.

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).
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.
1\textsuperscript{st} - 2\textsuperscript{nd} 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 \( \geq 3 \) months** (median 11.0 months).

- Of these children, 1,085 had VL results available after \( \geq 3 \) 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 \( \geq 3 \) mos

<table>
<thead>
<tr>
<th>VL Result N (%)</th>
<th>VL Pre-DTG</th>
<th>VL Post DTG ( \geq 3 )mos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undetectable VL &lt;50</td>
<td>414 (41.9)</td>
<td>698 (70.7)</td>
</tr>
<tr>
<td>Suppressed VL 50-&lt;1000</td>
<td>89 (9.0)</td>
<td>85 (8.6)</td>
</tr>
<tr>
<td>Unsuppressed VL ( \geq 1000 )</td>
<td>485 (49.1)</td>
<td>205 (20.7)</td>
</tr>
</tbody>
</table>
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
    - Continue on current ART until failure
    - Switch to PI-based 2nd line ART ($22/mo)
  - #2: Transition all children to DTG
    - 30% failing on ABC/3TC/EFV
    - Switch all to ABC/3TC/DTG ($14/mo)
    - Reason for prior failure
      - 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
    - 70% suppressed on ABC/3TC/EFV
    - Switch to AZT/3TC/DTG ($9/mo)
    - 70% viral suppression
    - Reason for prior failure
      - 15% Adherence
        - Efficacy 50% Late failure 0.2%/mo
      - 15% Resistance
        - Efficacy 90% Late failure 0.4%/mo
    - VL Test, wait 3 mo for result
    - Switch to ABC/3TC/DTG ($25)

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

* efficacy better when resistance because here you change NRTI
** late failure higher with twice daily AZT
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.
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
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 with ART Regimen Switch Over Time
Proportion with Viral Failure Over Time

Proportion of study outcomes:
- First VL within 1 year < 50 copies/mL: 76% (Rapid), 69% (Intermediate), 75% (Delayed)
- First VL within 1 year < 200 copies/mL: 82% (Rapid), 82% (Intermediate), 75% (Delayed)
- VF after ART initiation: 11% (Rapid), 5% (Intermediate), 15% (Delayed)
- Switching to Second line therapy: 4% (Rapid), 7% (Intermediate), 5% (Delayed)
- Death: 1% (Rapid), 2% (Intermediate), 3% (Delayed)
- Lost to follow-up: 9% (Rapid), 9% (Intermediate)

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

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

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

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Pre-Intervention</th>
<th>Post-Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 14</td>
<td>284/765</td>
<td>285/760</td>
</tr>
<tr>
<td>15 to 19</td>
<td>285/760</td>
<td>245/819</td>
</tr>
<tr>
<td>20 to 24</td>
<td>709/1526</td>
<td>709/2484</td>
</tr>
</tbody>
</table>

Percentage with VL Result of Those Eligible for VL Check

<table>
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<tr>
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<th>Pre-Intervention</th>
<th>Post-Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 14</td>
<td>225/765</td>
<td>230/761</td>
</tr>
<tr>
<td>15 to 19</td>
<td>740/819</td>
<td>806/991</td>
</tr>
<tr>
<td>20 to 24</td>
<td>492/1772</td>
<td>492/1794</td>
</tr>
</tbody>
</table>

Percentage with Viral Suppression of Those Tested

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Pre-Intervention</th>
<th>Post-Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 14</td>
<td>390/586</td>
<td>286/552</td>
</tr>
<tr>
<td>15 to 19</td>
<td>611/749</td>
<td>700/884</td>
</tr>
<tr>
<td>20 to 24</td>
<td>1155/2030</td>
<td>1690/2384</td>
</tr>
</tbody>
</table>

P value <0.001

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)

### Transition Readiness Scoring

<table>
<thead>
<tr>
<th>Variable</th>
<th>Categories</th>
<th>Beta (W-Ref)</th>
<th>Reference Value (W)</th>
<th>Beta (W-Ref)/Beta (W-Ref)*</th>
<th>Points = Beta(W-Ref)/Beta (W-Ref)*&lt;1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen line</td>
<td>Second line*</td>
<td>2.63</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>First line</td>
<td>1</td>
<td>2.63</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Disclosed</td>
<td>No*</td>
<td>1.01</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>1</td>
<td>1.01</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HARTS Score</td>
<td>2-20*</td>
<td>0.05</td>
<td>11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>21-30</td>
<td>0.05</td>
<td>25.5</td>
<td>0.73</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>31-39</td>
<td>0.05</td>
<td>35</td>
<td>1.20</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>40-56</td>
<td>0.05</td>
<td>48</td>
<td>1.85</td>
<td>4</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>No*</td>
<td>-1.23</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>1</td>
<td>-1.23</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Age at ART Initiation</td>
<td>0-5</td>
<td>-0.21</td>
<td>2.5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>6-8</td>
<td>-0.21</td>
<td>7</td>
<td>-0.95</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>9-15</td>
<td>-0.21</td>
<td>12</td>
<td>-2.0</td>
<td>4</td>
</tr>
<tr>
<td>Sex</td>
<td>Male*</td>
<td>-0.91</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>1</td>
<td>-0.91</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Factors Associated with Viral Suppression 1 Year Post Transition

<table>
<thead>
<tr>
<th>Covariate</th>
<th>AOR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line ART</td>
<td>13.9</td>
<td>4.2 - 46.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Disclosed HIV Status</td>
<td>2.8</td>
<td>1.2 - 6.2</td>
<td>0.015</td>
</tr>
<tr>
<td>HARTS score (per unit score)</td>
<td>1.6</td>
<td>1.2 - 2.2</td>
<td>0.004</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.3</td>
<td>0.1 - 0.7</td>
<td>0.004</td>
</tr>
<tr>
<td>Age at ART initiation (years)</td>
<td>0.8</td>
<td>0.7 - 0.9</td>
<td>0.004</td>
</tr>
<tr>
<td>Female</td>
<td>0.4</td>
<td>0.2 - 0.9</td>
<td>0.018</td>
</tr>
</tbody>
</table>

### Transition Readiness

- **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

- **Acceptability:** More ring pt felt ring acceptable vs oral

- **Compliance:** >50% highly adherent over 12 mos

- **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)
  - 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 not represented 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.
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.

### Factors Associated with HIV-Free Survival

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

The most rapid decline in HFS occurs between birth to 6 months, plateauing at age 1 year.
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.

- 22,930 HIV+ pregnant women enrolled 226 sites 2015-2017
- 9,140 (40%) missing infant data
- 13,790 (60.1%) documented infant data

- 5,327 no infant outcome (transfer, stillbirth, maternal death LTFU)
- 3,826 missing data

- 2,295 documented transfer 1981 neg HIV test <15 mo
- 4,604 (20%) missing final MTCT status

- 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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Univariable, N = 7483</th>
<th>Multivariable Complete case, N = 7483</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude odds ratio</td>
<td>p-value</td>
</tr>
<tr>
<td>Age at start of PMTCT care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 years</td>
<td>1.02 (0.53, 1.99)</td>
<td>0.91</td>
</tr>
<tr>
<td>20-29 years</td>
<td>0.95 (0.76, 1.18)</td>
<td>0.61</td>
</tr>
<tr>
<td>30-39 years</td>
<td>1 [referent]</td>
<td></td>
</tr>
<tr>
<td>40+ years</td>
<td>1.11 (0.70, 1.80)</td>
<td></td>
</tr>
<tr>
<td>Gestational age, weeks&lt;13 (first trimester)</td>
<td>1.59 (1.15, 2.19)</td>
<td>0.0001</td>
</tr>
<tr>
<td>≥13 (second trimester)</td>
<td>2.18 (1.50, 3.17)</td>
<td></td>
</tr>
<tr>
<td>Advanced HIV disease versus none</td>
<td>1.00 (0.78, 1.27)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Time enter ANC
HIV disease
Timing ART Start
Clinic volume

Factors Associated with Odds of HIV-Free Survival

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Univariable, N = 7483</th>
<th>Multivariable Complete case, N = 7483</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude odds ratio</td>
<td>p-value</td>
</tr>
<tr>
<td>Patient characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at start of PMTCT care</td>
<td></td>
<td></td>
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<td>Advanced HIV disease versus none</td>
<td>1.00 (0.78, 1.27)</td>
<td>0.99</td>
</tr>
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</table>

When ART was started
Before PMTCT enrolment
At PMTCT enrolment
31+ days after enrolment
NNRT Inhibitor ART backbone versus Protease Inhibitor
Female versus male infants
Health facility attributes
PMTCT clients' volume
1-10 women per year
11-100 women per year
101-515 women per year
Couple HIV testing rate of 50% at first ANC visit versus <50%

<0.0001* | 0.0001* | 0.0002* |
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.

Risk factors for lack 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.

<table>
<thead>
<tr>
<th></th>
<th>VL &lt;1000 (p=0.898)</th>
<th>SOC</th>
<th>POC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>188/200 (94.0%)</td>
<td>178/201 (88.6%)</td>
<td></td>
</tr>
<tr>
<td>6-months</td>
<td>125/130 (96.2%)</td>
<td>124/136 (91.2%)</td>
<td></td>
</tr>
<tr>
<td>12-months</td>
<td>127/135 (94.1%)</td>
<td>131/143 (91.6%)</td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>128/136 (94.1%)</td>
<td>115/122 (94.3%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>VL &lt;200 (p=0.701)</th>
<th>SOC</th>
<th>POC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>179/200 (89.5%)</td>
<td>174/201 (86.6%)</td>
<td></td>
</tr>
<tr>
<td>6-months</td>
<td>121/130 (93.1%)</td>
<td>116/136 (85.3%)</td>
<td></td>
</tr>
<tr>
<td>12-months</td>
<td>115/135 (85.2%)</td>
<td>118/143 (82.5%)</td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>116/136 (85.3%)</td>
<td>104/122 (85.3%)</td>
<td></td>
</tr>
</tbody>
</table>

- 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.

→ 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)**

<table>
<thead>
<tr>
<th>Age group (in years)</th>
<th>Sample distribution (n=17 909)</th>
<th>Percent virally suppressed (95% CI) 2017</th>
<th>Percent virally suppressed (95% CI) 2019</th>
<th>Unadjusted OR</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>3 200 (22.3)</td>
<td>56.1 (56.1–56.9)</td>
<td>56.4 (56.6–56.2)</td>
<td>0.6 (0.6–0.7)</td>
<td>0.7 (0.6–0.8)</td>
</tr>
<tr>
<td>25-34</td>
<td>12 709 (77.7)</td>
<td>66.8 (66.7–66.8)</td>
<td>66.3 (67.2–66.3)</td>
<td>Ref</td>
<td>Ref</td>
</tr>
</tbody>
</table>

**Province of ANC care**

- Eastern Cape: 2,705 (16.1)
- Free State: 1,370 (8.2)
- Western Cape: 2,441 (14.3)
- KwaZulu-Natal: 5,095 (30.1)
- Limpopo: 859 (5.3)
- Mpumalanga: 1,702 (10.6)
- North West: 1,082 (6.5)
- Northern Cape: 248 (1.5)
- Gauteng: 2,441 (14.3)

**Timing of ART start**

- Before pregnancy: 12,700 (69.8)
- During pregnancy: 2,441 (29.2)
- 0.6 (0.5–0.7)
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

- 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

<table>
<thead>
<tr>
<th>Factors Associated with Recent Infection</th>
<th>Positive syphilis rapid test</th>
<th>Partner HIV+ or HIV status unknown</th>
<th>Unmarried</th>
<th>Overnight travel past 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>342 (98.0)</td>
<td>39 (88.6)</td>
<td>1.</td>
<td>1.</td>
</tr>
<tr>
<td>Positive</td>
<td>7 (2.0)</td>
<td>5 (11.4)</td>
<td>6.26</td>
<td>1.90-20.68 0.003</td>
</tr>
<tr>
<td>Primary male partner characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partner HIV status</td>
<td>257 (73.6)</td>
<td>18 (49.0)</td>
<td>1.</td>
<td>1.</td>
</tr>
<tr>
<td>HIV positive</td>
<td>7 (2.0)</td>
<td>5 (11.4)</td>
<td>10.20</td>
<td>2.04-35.35 0.001</td>
</tr>
<tr>
<td>HIV status unknown</td>
<td>85 (24.4)</td>
<td>21 (47.7)</td>
<td>3.53</td>
<td>1.79-6.93 0.001</td>
</tr>
<tr>
<td>Participate and primary partner are married</td>
<td>336 (96.4)</td>
<td>78 (96.6)</td>
<td>4.95</td>
<td>2.85-7.12 0.001</td>
</tr>
<tr>
<td>Not married</td>
<td>11 (3.2)</td>
<td>6 (10.5)</td>
<td>4.04</td>
<td>2.42-6.63 0.002</td>
</tr>
<tr>
<td>Overnight travel outside home (past 6 mo.)</td>
<td>160 (48.8)</td>
<td>11 (25.0)</td>
<td>1.</td>
<td>1.</td>
</tr>
<tr>
<td>No-participant and partner travel</td>
<td>177 (51.2)</td>
<td>33 (75.0)</td>
<td>2.86</td>
<td>1.41-5.88 0.004</td>
</tr>
<tr>
<td>Any participant or partner travel</td>
<td></td>
<td></td>
<td>3.09</td>
<td>1.43-6.67 0.004</td>
</tr>
</tbody>
</table>
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.

- 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.
- 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.
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


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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Oct-Dec 2019 (pre-tool use)</th>
<th>Oct-Dec 2020 (during tool use)</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td># women screened</td>
<td>12,350</td>
<td>18,342</td>
<td>+49%</td>
</tr>
<tr>
<td># children tested</td>
<td>2,500</td>
<td>4,075</td>
<td>+63%</td>
</tr>
<tr>
<td># children testing HIV+</td>
<td>78</td>
<td>123</td>
<td>+58%</td>
</tr>
</tbody>
</table>

- 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

[Impact ICT Screening Tool on Screening, Testing and Ped Case ID Pre- and Post-Tool Use]
Pediatric HIV Care
and
HIV-Exposed Uninfected Children
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.

- 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.

- Prior receipt of INH prophylaxis did not ↓ incidence
- Poor household conditions associated with infection
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.

**Model Structure**

- **HIV test at 6 wks**
- **Postnatal MTCT**
- **HIV test at 9 mo**
- **HIV+ started on ART**

**Factor Associated with Risk Mortality**

- Death (6wks to 2 years):
  - HIV exposed, uninfected
  - HIV positive, no ART
  - HIV positive, ART

**Primary Model assumptions 1**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Assumption</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV transmission (by end of breastfeeding)</td>
<td></td>
<td>South Africa: 4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zimbabwe: 8.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cote d’Ivoire: 13.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mozambique: 14%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uganda: 6%</td>
</tr>
<tr>
<td>Early HIV test (by 6 wks)</td>
<td></td>
<td>South Africa: 83%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zimbabwe: 63%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cote d’Ivoire: 53%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mozambique: 71%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uganda: 56%</td>
</tr>
<tr>
<td>Received 9-month/end of breastfeeding test</td>
<td></td>
<td>EXPERT OPINION</td>
</tr>
<tr>
<td>if have early HIV test</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>if no early HIV test</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Death (6wks to 2 years):</td>
<td></td>
<td>Arikawa CID 2018</td>
</tr>
<tr>
<td>HIV exposed, uninfected</td>
<td>3.7%</td>
<td>Evans CID 2021 (SHINE)</td>
</tr>
<tr>
<td>HIV positive, no ART</td>
<td>53.6%</td>
<td>Becquet PLOS One 2012</td>
</tr>
<tr>
<td>HIV positive, ART</td>
<td>6.5%</td>
<td>Cotton Lancet 2013 (CHER)</td>
</tr>
<tr>
<td>ART uptake</td>
<td>80%</td>
<td>JIAS, Dunning</td>
</tr>
</tbody>
</table>

**Primary Model assumptions 2**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Assumption</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTX uptake</td>
<td>100%</td>
<td>Assumption</td>
</tr>
<tr>
<td>Relative risk for death: CTX vs no CTX</td>
<td></td>
<td>CHAP NEJM 2013</td>
</tr>
<tr>
<td>Infants with HIV</td>
<td>0.57</td>
<td>Lockman Lancet GH 2017</td>
</tr>
<tr>
<td>Infants without HIV</td>
<td>1.00</td>
<td>Daniels Lancet GH 2019</td>
</tr>
</tbody>
</table>
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

- 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 and 10 were associated with accelerators.

Accelerators community support and positive parenting were associated with mental health outcomes, however the other 3 accelerators had greater impact on several child outcomes.
Combined Interventions to Accelerate Delivery on Outcomes for Young Children Affected by HIV in Southern Africa

Mebrahtu H et al. IAS Virtual Abs

Adjustment probability and adjusted risk differences (RD, % points) of having SDG-aligned child outcomes with single accelerator provision

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

Adjustment probability and adjusted RD (% points) of having SDG-aligned child outcomes with two combined accelerator provision

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

Adjustment probability and adjusted RD (% points) of having SDG-aligned child outcomes with three combined accelerator provision

→ 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.

**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.

<table>
<thead>
<tr>
<th>Pre-COVID-19</th>
<th>During COVID-19</th>
</tr>
</thead>
</table>

**Change in 1st ANC Attendance**

- Q1/2 to Q3: -3.4%
- Q1/2 to Q4: 1.9%
- Q3 to Q4: 5.5%

**Change in 1st ANC HIV Testing**

- Q1/2 to Q3: -3.8%
- Q1/2 to Q4: 0.4%
- Q3 to Q4: 4.4%

**Change in ART Coverage for Pregnant HIV+**

- Q1/2 to Q3: -0.4%
- Q1/2 to Q4: 0.2%
- Q3 to Q4: 0.6%
**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.

**Graphs:**
- 2-month EID coverage by country—FY2020
- Infants with HIV linked to ART by country—FY2020

Source: PEPFAR MER Data.
- **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 both Q3 and Q4.
  - Viral load suppression paradoxically increased during COVID-19 in both Q3 and Q4.
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

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

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

<table>
<thead>
<tr>
<th>FY20 Quarters</th>
<th>CLHIV on Treatment</th>
<th>&lt;3MMD (%)</th>
<th>3-5MMD (%)</th>
<th>6MMD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY20Q1</td>
<td>176,516</td>
<td>108,210 (65.6%)</td>
<td>52,769 (32.0%)</td>
<td>3,919 (2.4%)</td>
</tr>
<tr>
<td>FY20Q2</td>
<td>181,123</td>
<td>109,186 (60.6%)</td>
<td>65,510 (36.4%)</td>
<td>5,453 (3.0%)</td>
</tr>
<tr>
<td>FY20Q1/Q2</td>
<td>178,820</td>
<td>108,698 (63.1%)</td>
<td>59,140 (34.2%)</td>
<td>4,668 (2.7%)</td>
</tr>
<tr>
<td>FY20Q1/Q3</td>
<td>182,914</td>
<td>82,304 (46.3%) **</td>
<td>84,725 (47.6%) **</td>
<td>10,869 (6.1%) *</td>
</tr>
<tr>
<td>FY20Q2/Q4</td>
<td>185,357</td>
<td>7,944 (46.5%) **</td>
<td>80,673 (45.9%) *</td>
<td>15,774 (9.0%) **</td>
</tr>
</tbody>
</table>

Country: DRC, Ethiopia, Eswatini, Haiti, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Tanzania, Uganda, Zambia, Zimbabwe

p<0.01

p<0.001

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

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

- 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

**Ilatravir**
First-in-Class NNRTI 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
Thank You For Your Attention!

Questions?

ANY QUESTIONS?

CAN THE RED DOT EVER BE CAUGHT?