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

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

- Eastern and southern Africa: 42,000
- Western and central Africa (excluding Nigeria): 65,000
- Nigeria: 47,000
- Remaining regions: 43,000

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

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**

![Graph showing decrease in number of children with HIV receiving ART from 2010 to 2020.](source)

**Source:** UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).
Lower ART Coverage in Children and Adolescents vs Adults

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

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

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

Source: Special analysis of UNAIDS 2021 epidemiological estimates.
In 2020, ART coverage in children 0-14 years was 54% [37–69%], significantly lower than 74% [57–90%] ART coverage in adults.

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

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

Source: Special analysis of UNAIDS 2021 epidemiological estimates.
→ 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.

In 2020:
- Worldwide, 1.7 million children were living with HIV; 530,000 a third of these, are aged ≤5 years
- 5.4 million children aged ≤5 years are HIV-exposed and uninfected & 1.3 million births/year to HIV+ women, most of whom will be uninfected.
- In Botswana, Eswatini, Lesotho and South Africa, more than one in five children are HIV-exposed and uninfected.
Move from 90-90-90 to **95-95-95**:
- HIV knowledge
- HIV+ on ART
- HIV+ on ART have suppression

*Including pregnant and BF women and children*

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

https://aidstargets2025.unaid.org
DTG in Children
New Clinical Trial Data
DTG-Based ART Shown Superior to SOC in Older Children ≥14 kg Living with HIV: ODYSSEY
Turkova A et al. CROI March 2021 Abs 174

**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

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

**ODYSSEY A:** First-line ART
- N=311 (44%)
- DTG N=154 (92% EFV)
- SOC N=157 (98% PI)

**ODYSSEY B:** Second-line ART
- N=396 (56%)
- DTG N=196
- SOC N=200

- Enrolled Sept 2016-June 2018
- 96 wk FU completed April 2020
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 1\textsuperscript{st} line, 13 (15%) 2\textsuperscript{nd} 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>
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Difference between arms driven by virologic, as opposed to clinical, endpoints

→ Differences between arms only first emerge after one year (48 weeks) on ART
Viral or Clinical Failure by 96 Weeks Lower with DTG vs SOC in Pooled Analysis


Difference in Proportion with Viral/Clinical Failure DTG vs SOC

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)

Primary Efficacy Analysis Bayesian analysis:
- 11% less failure DTG
- Test of heterogeneity of treatment effect between ≥14kg and <14kg: p=0.24

DTG better
SOC better
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>
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<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>
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</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.

Change Total Cholesterol from Baseline

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

Mean change from baseline, mg/dL (% change)

Weeks from randomisation

- DTG arm  - SOC arm
- 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

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 (1<sup>st</sup> line): Major resistance mutations post-failure of 1<sup>st</sup> line ART

- No resistance mutations with failure of DTG 1<sup>st</sup> line ART.
- In SOC 1<sup>st</sup> 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 PE BLB 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 or ART Switch Post-Failure in Children in the ODYSSEY Trial

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

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

- ~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 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-suppression in DTG arm.

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

Supports use of DTG for both 1st and 2nd line ART - but ongoing adherence support is needed, especially if child is on 2nd line DTG.
Neuropsychiatric and Sleep Disturbances
DTG vs SOC in the ODYSSEY Trial

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

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

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<thead>
<tr>
<th></th>
<th>DTG</th>
<th>SOC</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=350</td>
<td>N=357</td>
<td>N=707</td>
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</table>

- All neuropsychiatric adverse events, N [N participants]
- Serious Adverse Events
  - DTG-modifying AEs
  - Hazard Ratio for time to first RAEP (95% CI)
    - 0.87 (0.75, 1.01) / 1 (ref) / 0.164

- No significant difference DTG vs SOC sleep data

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

- No difference “low mood” or anxiety, but more participants/carers report symptoms of self-harm, “life was not worth living” or suicidal thoughts in DTG arm. Most transient, none required ART change.
Weight Gain and Change in BMI in Children on DTG vs SOC in the ODYSSEY Trial

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

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

Change from Baseline in Weight and Height DTG vs SOC

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

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

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

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

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

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

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

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

**RAPID-VL: 3 component intervention**

- **1. Viral load flow sheet tool**
  - **Today’s Visit**
    - ART Start Date
    - Last Viral Load
    - Date Given to Patient
    - ART Status
    - Adherence
    - VL Counseling Done?
    - Ordering VL Today?
    - Type of Test
  - **Today’s Date**
    - Date Drawn
    - Result (circle one or enter value)
      - <40 c/mL
      - >=1000 c/mL
      - Result invalid
      - No prior VL
      - Result Value:
  - **VL Counseling Script**
    - New patient
    - Established patient
    - VL Undetectable
    - VL Detectable
  - **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</td>
</tr>
<tr>
<td>Accepted</td>
</tr>
<tr>
<td>Active as at end of September 2020</td>
</tr>
<tr>
<td>Completed 3 months</td>
</tr>
<tr>
<td>Had repeat VL test</td>
</tr>
<tr>
<td>VL results available</td>
</tr>
<tr>
<td>Resuppressed VL</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
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.
390 children/youth enrolled in a community-based ART (CBART) trial in rural Zimbabwe enrolled 2018-2019; **184 had switched to TLD as of July 2020** (median age 15 years, IQR 11-19 years).

Prior to switch, 63% (n=115) were receiving 1\textsuperscript{st} line NNRTI (83% on TLE, 17% ABC/3TC/EFV or NVP); and 38% (n=69) were on 2\textsuperscript{nd} line PI ART (81% ATV/r) primarily with ABC/3TC (only 6% receiving TDF).

Prior to TLD switch, **76% (139/184) had VL <1,000**.

After median duration 6.9 mos (IQR 5-9.1) on TLD, **95% (174) had VL <1,000**.

Of the 10 patients with VL \(\geq 1,000\) on TLD, 9/10 had VL >1,000 on prior regimen.

Being on prior **PI-based ART regimen** more likely to fail compared to prior 1\textsuperscript{st} line NNRTI ART (10.1% vs 2.6%, \(p=0.042\)).

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

Of children switched:
- 80% (2,009/2,488) switched to a DTG-based regimen within 6 mos.
- 16% (319/2,009) switched to other regimens within 6 mos.

Regimens prior to switch to DTG:
- 80% (NNRTI)
- 17% (PI)

Regimens switched to after DTG:
- 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).
▪ 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.
1,121 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.

<table>
<thead>
<tr>
<th>VL Result N (%)</th>
<th>VL Pre-DTG</th>
<th>VL Post DTG ≥ 3mos</th>
</tr>
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<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 ≥1000</td>
<td>485 (49.1)</td>
<td>205 (20.7)</td>
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Retrospective review from 7 Baylor sites in 6 countries in 2,655 children 0-19 years enrolled in care and switched to DTG ART without modifying NRTI backbone from Jan17-Dec 20; most children (96%) were suppressed at time of switch.

→ Those suppressed at baseline remained suppressed after switch.

→ 83% of the 88 children not suppressed at baseline became suppressed after switch.

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

→ Those who were suppressed generally maintained suppression.

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

→ Supports programmatic switch to DTG in settings without pre-switch VL testing.
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
  
  - 15% Resistance

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

  **#3: Transition to DTG with VL-based switch NRTI**
  
  - 70% suppressed on ABC/3TC/EFV
  
  - Switch to ABC/3TC/DTG ($25)

  - VL Test, wait 3 mo for result

  - Switch to AZT/3TC/DTG ($14/mo)

  - Efficacy: 96%
  
  - Late failure: 0.4%/mo

  - Reason for prior failure
  
  - 15% Adherence
  
  - 15% Resistance

  - 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.
Pediatric ART
New ARV Drug Formulation/Regimens in Children
PK and Safety of Dispersible and Whole Tablet FDC ABC/3TC/DTG in Children ≥14 kg: IMPAACT 2019

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

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

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

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

→ Long-term data through week 48 and PK/safety data on children <14 kg are forthcoming.
PK, Safety, and Acceptability of Single-Dose ABC/3TC/LPV/r (4-in-1) Fixed-Dose Granule Formulation in Newborns: PETITE Study
Cressey T et al. International Pediatric HIV Workshop Abs 5/IAS Virtual Abs PEBLB16 July 2021

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

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

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

### Safety

- No deaths of life-threatening events occurred: 16 participants had 35 AEs
- Only 1 SAE with a participant requiring hospitalization

### ABC/3TC Pharmacokinetics

- ABC and 3TC plasma concentrations were as expected (slightly higher than older children)
- →Very low LPV/r levels of concern (rtv BLQ in 4/120 (3%) samples)
- →Protocol amendment will evaluate separate LPV/r granules (40/10 mg) and ABC/3TC dispersible tablet

### Acceptability

- Administration 4-in-1 to neonates
- Capsule opened and suspended in milk and given by syringe or cup
- 4-in-1 was found easy to swallow

### LPV Pharmacokinetics

- Adult tablet formulation (RALETRA package insert)
- Infants liquid formulation (Chadwick et al, PIDI 2009)
Once-Daily NNRTI-Sparing ART Regimen DRV/r + InSTI is Non-Inferior to SOC in Virally-Suppressed Children – PENTA-17

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

- PENTA-17 SMILE trial: phase 2/3 multicenter, open-label non-inferiority trial
  - Enrolled 318 children from 31 sites in 11 countries
  - Median age 14.7 years
  - Median CD4 count 782
  - Median cumulative ART exposure 11 years
  - ART prior to randomization
    - NNRTI 59%, PI 41%
    - ABC/3TC 36%, AZT/3TC 33%, TDF/FTC 18%

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

- Primary Endpoint: Viral failure at 48 weeks (non-inferiority margin 10%)

- Enrolled 318 children from 31 sites in 11 countries
  - Median age 14.7 years
  - Median CD4 count 782
  - Median cumulative ART exposure 11 years
  - ART prior to randomization
    - NNRTI 59%, PI 41%
    - ABC/3TC 36%, AZT/3TC 33%, TDF/FTC 18%

- FU weeks 4, 12, 24, 36, 48 and every 12-16 weeks thereafter
Once-Daily NNRTI-Sparing ART Regimen DRV/r + InSTI is Non-Inferior to SOC in Virally-Suppressed Children – PENTA-17
Compagnucci A et al. International Pediatric HIV Workshop Abs 1/IAS Virtual Abs PEB201 July 2021

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

### Change CD4 to Week 48

- InSTI+DRV/r vs SOC

### Lipids changes from randomisation to weeks 24 and 48

- Total cholesterol (mg/dL)
- HDL (mg/dL)
- LDL (mg/dL)
- triglycerides (mg/dL)

### Difference in Proportion with VF Week 48

- InSTI+DRV/r better
- SOC better

### Probability failure (95% CI)

- InSTI+DRV/r: 5% (1.7, 8.4)
- SOC: 7.6% (3.5, 11.7)

### Difference (InSTI+DRV/r – SOC)

- 2.5% (-7.7, +2.6); **p value 0.335**

### Failure (RNA ≥50 c/mL)

- InSTI+DRV/r n=158
- SOC n=160

- 8
- 12

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

- In virologically suppressed children without PI/InSTI resistance, switching to NNRTI-sparing regimen InSTI+DRV/r was **non-inferior** virologically and clinically
Long-Term Safety and Efficacy of Bictegravir/FTC/TAF in Virally Suppressed Adolescents and Children

Natukunda E et al. International Pediatric HIV Workshop Abs 2

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

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

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

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

→Formulation for children <2 years planned.
Long-Term Safety and Efficacy Elvitegravir/Cobicistat/FTC/TAF in Virally Suppressed Adolescents and Children

Anugulruengkitt S et al. International Pediatric HIV Workshop Abs 4

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

None of children met criteria for resistance testing 12-<18 yr; >35 kg N=50 6-<12 yr, >25 kg N=52 >2 yr; 14-<25 kg N=27

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

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

In virologically suppressed children and adolescents through 96 weeks and young children through 48 weeks FU, EVG/COBI/F/TAF maintained viral suppression with no resistance; acceptable bone and renal safety profile; both formulations well tolerated.
Adolescents and HIV
Rapid ART Initiation in Adolescents in Thailand Associated with Improved Clinical Outcome

Teeraananchai S et al. International Pediatric HIV Workshop Abs 31

- Thailand national ARV database and National Death Registry data to assess treatment outcome among 19,825 HIV+ youth aged 15-24 years initiating NNRTI-based ART (89% EFV-based) from 2014-May 2019 with FU data to May 2020

- Classified youth into 3 categories based on timing ART start post diagnosis:
  - Rapid – <1 month (n=12,216)
  - Intermediate – 1-3 months (n=4,275)
  - Delayed >3 months (n=3,337)

![Graph showing proportion with ART regimen switch and viral failure over time]

- 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.
### 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>37%</td>
<td>99%</td>
</tr>
<tr>
<td>15 to 19</td>
<td>38%</td>
<td>99%</td>
</tr>
<tr>
<td>20 to 24</td>
<td>46%</td>
<td>99%</td>
</tr>
</tbody>
</table>

**P value <0.001**

### Percentage with VL Result of Those Eligible for VL Check

<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>33%</td>
<td>90%</td>
</tr>
<tr>
<td>15 to 19</td>
<td>30%</td>
<td>81%</td>
</tr>
<tr>
<td>20 to 24</td>
<td>28%</td>
<td>72%</td>
</tr>
</tbody>
</table>

**P value <0.001**

### 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>67%</td>
<td>82%</td>
</tr>
<tr>
<td>15 to 19</td>
<td>52%</td>
<td>83%</td>
</tr>
<tr>
<td>20 to 24</td>
<td>68%</td>
<td>85%</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)

Factors Associated with Viral Suppression 1 Year Post Transition

<table>
<thead>
<tr>
<th>Transition Readiness Scoring</th>
<th>Beta (W-Rref)</th>
<th>Points = Beta(W-Rref/Ref)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen line</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second line*</td>
<td>2.63</td>
<td>0</td>
</tr>
<tr>
<td>First line</td>
<td>1</td>
<td>1.63</td>
</tr>
<tr>
<td>Disclosed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No*</td>
<td>1.01</td>
<td>1.01</td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HARTS Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21–30</td>
<td>0.05</td>
<td>11</td>
</tr>
<tr>
<td>31–39</td>
<td>0.73</td>
<td>1</td>
</tr>
<tr>
<td>40–56</td>
<td>1.85</td>
<td>1</td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No*</td>
<td>-1.23</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>-1.23</td>
</tr>
<tr>
<td>Age at ART initiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–5</td>
<td>-0.21</td>
<td>2.5</td>
</tr>
<tr>
<td>6–8</td>
<td>-0.95</td>
<td>0</td>
</tr>
<tr>
<td>9–15</td>
<td>2.0</td>
<td>1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male*</td>
<td>-0.91</td>
<td>0</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>0.91</td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td>-8 to 11</td>
</tr>
</tbody>
</table>

Transition readiness

<table>
<thead>
<tr>
<th>Transition readiness</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive PV</th>
<th>Negative PV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (≤2) vs intermediate-high (&gt;2)</td>
<td>96.4%</td>
<td>27.7%</td>
<td>50.0%</td>
<td>91.2%</td>
</tr>
<tr>
<td>High (≥5) vs intermediate-high (&lt;5)</td>
<td>56.0%</td>
<td>86.6%</td>
<td>75.8%</td>
<td>72.4%</td>
</tr>
</tbody>
</table>

- **High readiness (≥5):** likely ready to transition to adult care
- **Intermediate readiness (3-4):** may benefit from additional time in ped clinic and additional interventions/resources before transition
- **Low readiness (≤2):** should have additional time in ped clinic; should receive additional interventions/resources prior to transition
Adherence to the Dapivirine Ring and Oral PrEP Among Adolescent Girls/Young Women – Interim REACH

*Nair G et al. IAS Virtual July 2021 Abs OALC01LB01*

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

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

**Adherence**
- >50% highly adherent over 12 mos
- More ring pt fully compliant (leaves ring full mo) vs oral PrEP (6+ doses/wk, >1200 fmol/punch)

**Acceptability**
- 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
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.
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.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of exposed children</td>
<td>652</td>
<td>570</td>
<td>1222</td>
</tr>
<tr>
<td>Number infected 24 months</td>
<td>17/607, 2.8%</td>
<td>10/507, 2.0%</td>
<td>27/1114, 2.4%</td>
</tr>
<tr>
<td>Number of deaths</td>
<td>57, 8.7%</td>
<td>59, 10.4%</td>
<td>116, 9.5%</td>
</tr>
<tr>
<td>Deaths minus stillbirths</td>
<td>38, 6.0%</td>
<td>33, 6.1%</td>
<td>71, 6.1%</td>
</tr>
<tr>
<td>HIV-free survival; # alive and HIV free, % [95% CI]</td>
<td>582, 91.8% [89.4 – 93.8]</td>
<td>499, 92.4% [89.8 – 94.5]</td>
<td>1081, 92.1% [90.4 – 93.6]</td>
</tr>
</tbody>
</table>

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>Age group</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>2.41 [1.36 – 4.26]</td>
<td>0.002</td>
</tr>
<tr>
<td>25 – 48 years</td>
<td>809</td>
<td>772 (95.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age</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></td>
<td></td>
</tr>
<tr>
<td>Breastfeeding ≥ 6 mos</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></td>
<td></td>
</tr>
<tr>
<td>Disclosed HIV status to partner</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></td>
<td></td>
</tr>
</tbody>
</table>
HIV-Free Survival in Era of Universal ART: Data from Tanzania

Lyatuu GW et al. IAS Virtual Abs PEC345 July 2021

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

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

Factors Associated with Odds of HIV-Free Survival

<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><strong>Patient characteristics</strong></td>
<td></td>
<td></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>1 (referent)</td>
</tr>
<tr>
<td>40+ years</td>
<td>1.11 (0.70, 1.78)</td>
<td>1.12 (0.70, 1.80)</td>
</tr>
<tr>
<td>Gestational age, weeks†</td>
<td></td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>&lt;13 (first trimester)</td>
<td>1 (referent)</td>
<td>1 (referent)</td>
</tr>
<tr>
<td>13-27 (second trimester)</td>
<td>1.59 (1.15, 2.19)</td>
<td>1.52 (1.10, 2.09)</td>
</tr>
<tr>
<td>28 (third trimester)</td>
<td>2.18 (1.50, 3.17)</td>
<td>2.10 (1.44, 3.06)</td>
</tr>
<tr>
<td>Advanced HIV disease versus none</td>
<td>1.00 (0.78, 1.27)</td>
<td>0.99</td>
</tr>
<tr>
<td>When ART was started</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before PMTCT enrolment</td>
<td>0.83 (0.50, 1.39)</td>
<td>0.58 (0.44, 0.76)</td>
</tr>
<tr>
<td>At PMTCT enrolment</td>
<td>1 (referent)</td>
<td>1 (referent)</td>
</tr>
<tr>
<td>31+ days after enrolment</td>
<td>9.69 (0.81, 116.25)</td>
<td>6.73 (0.55, 82.35)</td>
</tr>
<tr>
<td>NNRT Inhibitor ART backbone versus Protease Inhibitor</td>
<td>1.24 (0.44, 3.51)</td>
<td>0.69</td>
</tr>
<tr>
<td>Female versus male infants</td>
<td>1.12 (0.91, 1.39)</td>
<td>0.28</td>
</tr>
<tr>
<td><strong>Health facility attributes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PMTCT clients’ volume</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-10 women per year</td>
<td>1 (referent)</td>
<td></td>
</tr>
<tr>
<td>11-100 women per year</td>
<td>0.58 (0.37, 0.86)</td>
<td>0.81 (0.40, 1.49)</td>
</tr>
<tr>
<td>&gt;101 women per year</td>
<td>0.31 (0.19, 0.50)</td>
<td>0.36 (0.22, 0.63)</td>
</tr>
<tr>
<td>Couples HIV testing rate of 50%+ at first ANC visit versus &lt;50%</td>
<td>1.56 (0.96, 2.54)</td>
<td>0.076</td>
</tr>
</tbody>
</table>

Time enter ANC
HIV disease
Timing
ART
Start
Clinic volume

22,930 HIV+ pregnant women enrolled 226 sites 2015-2017

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

9,186 (40.1%) final MTCT/vital status

2,295 documented transfer 1981 neg HIV test <15 mo

2,390 missing final MTCT status 2,160 neg HIV test <15 mo

159 (1.7%) infants HIV+ (18 mos)

300 (3.3%) infants died

18-month HIV-free survival 95%
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.

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.

- 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.
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>Province of ANC care</th>
<th>Age</th>
<th>Timing of ART* initiation</th>
<th>Coverage</th>
<th>gap to 95% target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pendulo</td>
<td>0-14</td>
<td>Before pregnancy</td>
<td>96.0%</td>
<td>84%</td>
</tr>
<tr>
<td></td>
<td>15-24</td>
<td>86.6%</td>
<td>64.2%</td>
<td>43.8%</td>
</tr>
<tr>
<td></td>
<td>25-29</td>
<td>97.0%</td>
<td>66.0%</td>
<td>29.0%</td>
</tr>
</tbody>
</table>

### Province

- Eastern Cape
- Free State
- Gauteng
- KwaZulu Natal
- Limpopo
- Mpumalanga
- North West
- Northern Cape
- Western Cape

### Timing of ART Start

- Before pregnancy
- During pregnancy

### Province

- 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)

- Province
- Age
- Timing of ART* initiation

### Coverage

- Pregnant women who knew their HIV-positive status
- Pregnant women receiving ART
- Pregnant women virally suppressed

### gap to 95% target

- Pregnant women who knew their HIV-positive status
- Pregnant women receiving ART
- Pregnant women virally suppressed
Baseline HIV testing with validated algorithm for recency (Limiting Antigen Avidity EIA \( \text{OD} \leq 1.5 \) 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**

<table>
<thead>
<tr>
<th>Female characteristics</th>
<th>HIV negative ((N=349))</th>
<th>Recent ((N=44))</th>
<th>Unadjusted OR</th>
<th>95% CI</th>
<th>p-value</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>342 (98.0)</td>
<td>39 (88.6)</td>
<td>1.1</td>
<td></td>
<td></td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>7 (2.0)</td>
<td>5 (11.4)</td>
<td>6.26</td>
<td>1.90-20.68</td>
<td>0.003</td>
<td>5.57</td>
<td>1.43-21.76</td>
<td>0.014</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary male partner characteristics</th>
<th>HIV negative ((N=349))</th>
<th>Recent ((N=44))</th>
<th>Unadjusted OR</th>
<th>95% CI</th>
<th>p-value</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partner HIV status</td>
<td>257 (73.6)</td>
<td>18 (40.9)</td>
<td>1.1</td>
<td></td>
<td></td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV positive</td>
<td>7 (2.0)</td>
<td>5 (11.4)</td>
<td>10.20</td>
<td>2.94-35.35</td>
<td>&lt;0.001</td>
<td>7.84</td>
<td>2.12-28.88</td>
<td>0.002</td>
</tr>
<tr>
<td>Status unknown</td>
<td>85 (24.4)</td>
<td>21 (47.7)</td>
<td>3.53</td>
<td>1.79-6.93</td>
<td>&lt;0.001</td>
<td>4.46</td>
<td>2.16-9.20</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Couple characteristics</th>
<th>HIV negative ((N=349))</th>
<th>Recent ((N=44))</th>
<th>Unadjusted OR</th>
<th>95% CI</th>
<th>p-value</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participate and primary partner are married</td>
<td>338 (96.9)</td>
<td>38 (86.4)</td>
<td>1.1</td>
<td></td>
<td></td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>11 (3.2)</td>
<td>6 (13.6)</td>
<td>4.85</td>
<td>1.70-13.86</td>
<td>0.003</td>
<td>4.04</td>
<td>1.24-13.08</td>
<td>0.020</td>
</tr>
<tr>
<td>Not married</td>
<td>241 (69.2)</td>
<td>20 (45.5)</td>
<td>1.1</td>
<td></td>
<td></td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overnight travel outside home (past 6 mo.)</td>
<td>177 (51.2)</td>
<td>33 (75.0)</td>
<td>2.86</td>
<td>1.41-5.88</td>
<td>0.004</td>
<td>3.09</td>
<td>1.43-6.67</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Factors Associated with Recent Infection

→ Positive syphilis rapid test
→ Partner HIV+ or HIV status unknown
→ Unmarried
→ Overnight travel past 6 months
BMD in PP Mother on DTG/TDF/FTC, DTG/TAF/FTC or EFV/TDF/3TC and Their Infants – IMPAACT 2010 Trial

Mbengeranwa T et al. International Pediatric HIV Workshop Abs 12

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

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

**Infant:** No significant difference BMD z-scores between treatment arms for whole body; but significantly lower spine BMC in EFV/TDF/3TC arm
Pregnant women randomized 2:1 to monthly dapivirine ring or daily TDF/FTC starting at 36-37 wk gestation – interim analysis.

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

Table 1. Enrollment characteristics of participants

<table>
<thead>
<tr>
<th>N (%) or Median (IQR)</th>
<th>PREP Unexposed (n=3,437)</th>
<th>PREP Exposed (n=549)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>24 (21, 28)</td>
<td>25 (21, 30)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Partner living with HIV</td>
<td>1%</td>
<td>19%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Partner HIV status unknown</td>
<td>30%</td>
<td>42%</td>
<td>0.01</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>24 (20, 30)</td>
<td>24 (19, 28)</td>
<td>0.01</td>
</tr>
<tr>
<td>Positive Results</td>
<td>1%</td>
<td>2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Syphilis Test - Transmisional sex</td>
<td>2%</td>
<td>3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>STI diagnosis</td>
<td>2%</td>
<td>5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intimate partner violence</td>
<td>6%</td>
<td>14%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Median (IQR)</th>
<th>PREP Unexposed (n=3471)</th>
<th>PREP Exposed (n=548)</th>
<th>Adjusted Coeff (95% CI)*</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg) 6-week</td>
<td>5.0 (4.5, 5.4)</td>
<td>5.0 (4.5, 5.4)</td>
<td>0.03 (-0.06, 0.11)</td>
<td>0.52</td>
</tr>
<tr>
<td>6-month</td>
<td>7.7 (7.0, 8.5)</td>
<td>7.8 (7.2, 8.7)</td>
<td>0.22 (0.08, 0.36)</td>
<td>0.004</td>
</tr>
<tr>
<td>9-month</td>
<td>8.6 (7.9, 9.6)</td>
<td>8.6 (8.0, 9.5)</td>
<td>0.09 (-0.04, 0.21)</td>
<td>0.16</td>
</tr>
<tr>
<td>Length (cm) 6-week</td>
<td>55.0 (54.0, 57.0)</td>
<td>55.3 (54.0, 57.2)</td>
<td>-0.60 (-2.01, 0.81)</td>
<td>0.39</td>
</tr>
<tr>
<td>6-month</td>
<td>66.0 (64.0, 68.0)</td>
<td>66.0 (64.0, 69.0)</td>
<td>0.31 (-0.51, 1.13)</td>
<td>0.44</td>
</tr>
<tr>
<td>9-month</td>
<td>70.0 (68.7, 72)</td>
<td>70.5 (68.6, 72.0)</td>
<td>-0.02 (-1.32, 1.28)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Results were similar when analyzed separately by trimester of PrEP initiation
HIV Testing and Case Finding
Prior HIV Diagnosis in Children with HIV from 6 Countries from Population HIV Incidence Assessments (PHIA)

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

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

- 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.

Definition Diagnosed vs 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

\[ \text{26\% of women screened had at least 1 untested child} \]

\[ \text{Of 60,944 children identified, 23\% were untested} \]

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

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

<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>
Pediatric HIV Care
and
HIV-Exposed Uninfected Children
Insulin Resistance and Metabolic Syndrome in Children with Perinatal HIV Infection South Africa

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

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

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

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

→ No significant differences seen between HEU and HUU children.
Increased Infectious-Cause Hospitalizations in HIV-Exposed Uninfected Infants Compared to HIV-Unexposed Infants, S Africa

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

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

<table>
<thead>
<tr>
<th></th>
<th>HUU n=458</th>
<th>HEU n=455</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-neonatal hospitalization</td>
<td>32 (7%)</td>
<td>58 (13%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Etiology: infectious</td>
<td>27 (6%)</td>
<td>47 (10%)</td>
<td>0.014</td>
</tr>
<tr>
<td>Very severe infection</td>
<td>12 (3%)</td>
<td>27 (6%)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Among infants hospitalized between 2-12 mos:
- 30% previously hospitalized as neonates
- 20% preterm
- 77% hospitalizations associated with infections
- 84% infectious causes respiratory tract

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

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

→ Other independent associated factors:
  - Preterm birth
  - Lower duration of breastfeeding
Infant Tuberculosis Prevention Study (iTIPS)
Extended Post-Trial Follow-Up: Factors Associated with TB Infection Age <2 Years
LaCourse SM et al. IAS Virtual Abs OAB0205 July 2021

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

- 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
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.

\[\begin{align*}
  &\text{Correlates of 24-month cumulative } Mtb \text{ infection} \\
  &\begin{array}{l|c|c|c}
    & RR (95\% CI) & p \\
    \hline
    \text{Infant Characteristics} & & \\
    Study arm (INH) & 0.8 (0.4-1.4) & 0.38 \\
    Female & 1.5 (0.8-2.7) & 0.22 \\
    WAZ (kg) & 1.0 (0.7-1.3) & 0.79 \\
    \hline
    \text{Maternal Characteristics} & & \\
    HIV viral load >1000 & 1.5 (0.5-4.4) & 0.42 \\
    History of TB & 1.0 (0.4-2.6) & 0.99 \\
    Ever IPT & 0.9 (0.5-1.7) & 0.67 \\
    Current IPT & 0.5 (0.2-1.3) & 0.14 \\
    \hline
    \text{Household Characteristics} & & \\
    No flush toilet & -- & <0.001 \\
    No running water & 3.9 (1.3-12.4) & 0.02 \\
  \end{array}
\]

\[\begin{align*}
  &\rightarrow 24\text{-mo cumulative } Mtb \text{ infection high in HEU (8.6%/yr)} \\
  &\rightarrow \text{Prior receipt of INH prophylaxis did not } \downarrow \text{ incidence} \\
  &\rightarrow \text{Poor household conditions associated with infection}
\]
Moiled 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)**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Positive EID (6 wks)</th>
<th>No positive EID result (6 wks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: No CTX (Base case)</td>
<td>No CTX</td>
<td>No CTX</td>
</tr>
<tr>
<td>1: CTX for all (current guidelines)</td>
<td>CTX</td>
<td>CTX until EoB</td>
</tr>
<tr>
<td>2: CTX for 3 mths</td>
<td>CTX</td>
<td>CTX until 3 months</td>
</tr>
<tr>
<td>3: CTX for 6 mths</td>
<td>CTX</td>
<td>CTX until 6 months</td>
</tr>
<tr>
<td>4: CTX for 9 mths</td>
<td>CTX</td>
<td>CTX until 9 months</td>
</tr>
<tr>
<td>5: CTX for 12 mths</td>
<td>CTX</td>
<td>CTX until 12 months</td>
</tr>
<tr>
<td>6: CTX once positive result</td>
<td>CTX</td>
<td>No CTX</td>
</tr>
</tbody>
</table>

**Model Structure**

- Child born to mother living with HIV
- Model starts when child is 6 weeks old
- 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**

<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>South Africa: 4%</td>
<td>UNAIDS Factsheets 2019; Dunning JIAS</td>
</tr>
<tr>
<td>Cote d’Ivoire: 13.3%</td>
<td>Mozambique: 14%</td>
<td></td>
</tr>
<tr>
<td>Uganda: 6%</td>
<td>South Africa: 83%</td>
<td></td>
</tr>
<tr>
<td>Zimbabwe: 63%</td>
<td>Cote d’Ivoire: 53%</td>
<td></td>
</tr>
<tr>
<td>Mozambique: 71%</td>
<td>Uganda: 56%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Assumption</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early HIV test (by 6 wks)</td>
<td>50%</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>30%</td>
<td>Arikawa CID 2018</td>
<td></td>
</tr>
<tr>
<td>Evans CID 2021 (SHINE)</td>
<td>Bcquetc PLOS One 2012</td>
<td></td>
</tr>
<tr>
<td>Cotton Lancet 2013 (CHER)</td>
<td></td>
<td></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>ART uptake</td>
<td>80%</td>
<td>JIAS Dunning</td>
</tr>
</tbody>
</table>

**HIV test by 6 wks**

- Postnatal MTCT
- HIV test at 9 mo
- HIV+ started on ART
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.

- 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 single accelerator provision

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

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

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

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

Adjusted probability and adjusted RD (% points) of having SDG-aligned child outcomes with three combined accelerator provision
Effects of COVID-19-Related Mitigation Practices on Programs
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.
**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.
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>
<thead>
<tr>
<th>Table 1. MMD among &lt;15y/o across 12 PEPFAR-supported countries, October 2019 - September 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY20 Quarters</td>
</tr>
<tr>
<td>FY20Q1</td>
</tr>
<tr>
<td>FY20Q2</td>
</tr>
<tr>
<td>FY20Q1/Q2</td>
</tr>
<tr>
<td>FY20Q3</td>
</tr>
<tr>
<td>FY20Q4</td>
</tr>
</tbody>
</table>

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

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

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

<table>
<thead>
<tr>
<th>Year</th>
<th>Untreated/sub-optimally treated</th>
<th>Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-2019</td>
<td>86/1297 (6.6%)</td>
<td>17/1297 (1.3%)</td>
</tr>
<tr>
<td>2020 May-Dec</td>
<td>12/155 (7.7%)</td>
<td>5/155 (3.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mode</th>
<th>2015-2019</th>
<th>2020 May-Dec</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDU</td>
<td>32/236 (13.6%)</td>
<td>6/23 (26.1%)</td>
</tr>
<tr>
<td>Heterosexual contact</td>
<td>30/803 (3.7%)</td>
<td>5/97 (5.2%)</td>
</tr>
</tbody>
</table>
HIV Infection is Independently Associated with COVID-19 Disease Severity and In-Hospital Mortality in Adults

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

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

Long-Acting ART and PrEP Options

Islatravir

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

Lenacapavir

LEN: first-in-class HIV capsid inhibitor
High Rates Drug Resistance (DR) in PrEP Failures
Kenya, Zimbabwe, Eswatini, S Africa
Parikh U et al. IAS Virtual July 2021 Abs LB-02361

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

### Resistance vs PrEP Adherence

<table>
<thead>
<tr>
<th>MUTATION PROFILE</th>
<th># PARTICIPANTS</th>
<th>LOW &lt;350 fmol/punch &lt;2 doses/week</th>
<th>MODERATE 350-699 fmol/punch 2-3 doses/week</th>
<th>HIGH ≥700 fmol/punch 4-7 doses/week</th>
</tr>
</thead>
<tbody>
<tr>
<td>No resistance mutations</td>
<td>65/118 (55%)</td>
<td>34/41 (82%)</td>
<td>1/41 (2%)</td>
<td>6/41 (15%)</td>
</tr>
<tr>
<td>Not associated with PrEP NNRTI DR only</td>
<td>26/118 (22%)</td>
<td>12/20 (60%)</td>
<td>1/20 (5%)</td>
<td>7/20 (35%)</td>
</tr>
<tr>
<td>PrEP-associated (K65R, K70E, M184V)</td>
<td>27/118 (23%)</td>
<td>2/18 (11%)</td>
<td>2/18 (11%)</td>
<td>14/18 (78%)</td>
</tr>
</tbody>
</table>

- 78% of pt with PrEP-related resistance had drug levels associated with high adherence, while 82% of those with no resistance had drug levels associated with low adherence.
- 50% of PrEP-related resistance cases had K65R and/or M184IV mutations only.

### PrEP-Associated Resistance

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

- Seroconversions on PrEP small (0.2%)
- 23% had DR TDF/3TC, most having high adherence
- 22% only NNRTI mutations = background transmitted DR

### Time from PrEP Start to Seroconversion

- 58% start to seroconvert within 0-3 months
- 22% start to seroconvert within 1-3 months
- 18% start to seroconvert 6-12 months
- 18% start to seroconvert 12+ months
- 8% unknown

- 78% of pt with PrEP-related resistance had drug levels associated with high adherence, while 82% of those with no resistance had drug levels associated with low adherence.
New Long-Acting Drugs for ART and PrEP – Studies in Adults

**Lenacapavir**
- 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.

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

- 26-week data, all on SC LEN

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

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

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

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

- Important agent for person with multi-drug resistance
Efficacy & Safety of Long-Acting Subcutaneous Lenacapavir (LEN) in ART-Naïve Adults

Gupta S et al. IAS Virtual July 2021 Abs OALB0302

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

- Adverse events: no SAE or grade 4 AE related to study drug, no clinically relevant Grade ≥3 lab with no discontinuations for AE.

- 61% had no injection site reactions (ISR); 83% of IRS were Grade 1 and resolved in days; 1 Grade 3 ISR (nodule), no Grade 4.

→ LEN SC or orally with F/TAF = safe, well-tolerated, with high suppression (94% <50 c/mL) at week 28
→ Continued study in ART-naïve, ART-experienced and for PrEP

28-week data

Week 28
% RNA <50 c/mL

Proportion with RNA <50 c/mL over time
Lenacapavir (LEN) for PrEP Studies
Das M et al. IAS Virtual July 2021 Session SA15

LEN for PrEP Cisgender Women
LEN for PrEP MSM/TGW

“Roots” – Underpinning Studies
Proof of concept capsid inhibitors prevent HIV in non-human primates
Robust PK and safety database in persons with and without HIV

Phase I PK  LEN mucosal PK  Highly ART-experienced  ART naive
Safety and PK of Oral Ilatravir (ISL)
Once Monthly for PrEP – Phase IIA Safety-Dose Finding
Hillier S et al. IAS Virtual July 2021 Abs OALCo1LB03

- Phase 2a placebo-controlled study of 2 doses of monthly oral ISL for PrEP in 242 low-risk adults, reporting on week 24 data
  - Most AE mild (74%), similar to placebo arm, and did not lead to d/c study drug
  - Rates drug-related AE <3% and no drug-related SAE

ISL-TP levels with 60 or 120 mg q month doses were all above prespecified PK threshold of 0.05 pmol/10⁶ PBMC

- ISL well-tolerated, most AE mild and no drug-related SAE; lab >Grade 3 rare.
- ISL triphosphate in PBMC remained above the pre-specified PK threshold for HIV prevention through at least 8 weeks after last dose.
- 2 ongoing PrEP trials in MSM/TGW and cis-gender females
Islatravir (ISL) Orally Once Monthly for PrEP Phase III Studies

Robertson M et al. IAS Virtual July 2021 Session SA15

IMPOWER 022 Trial in Women: Study Schema

IMPOWER 024 Trial in MSM and TGW: Study Schema
Thank You For Your Attention!

Questions?