IAS 2020
Selected PMTCT, Pediatric, Adolescent, and Maternal/Adult Abstracts

Lynne M. Mofenson MD
7/22/20 webinar set
Update on Epidemiology of Pediatric HIV

2020
New Infections in Children Globally, 2000-2019
Significant Decline New Infections Since 2000 – But Progress Has Stalled

Most of the decline in transmission occurred between 2004 to 2012

Since 2015, slope of decline has SLOWED - and is almost flat between 2018 (160,000) to 2019 (150,000)

→ At current rate of decline it will take >13 years to decrease new infections in children to our 2020 target of 20,000

We have missed 2018 (and 2020) targets

Source: UNAIDS epidemiological estimates, 2020 (see https://aidsinfo.unaids.org/).
What are the Primary Missed Opportunities in 2019 for Prevention of Mother-to-Child Transmission Globally?

- **27%** of new infections in children were linked to **lack of maternal ART** during pregnancy or breastfeeding (likely because women were not diagnosed or not linked to treatment).

- **27%** of new infections in children were linked to **acute infection** pregnancy or breastfeeding.

- **24%** of new infections in children were linked to **mothers losing access to HIV care/lack of retention in care** either during pregnancy or breastfeeding.

→ Resolving these 3 program gaps would reduce MTCT by 78% - from 150,000 to 33,000
As a Result of These Missed Opportunities, Few Countries Have Achieved Overall MTCT Rates <5%

13 of the 21 focus countries in Africa continue to have MTCT rates of 10% or higher

About half of this transmission occurs during breastfeeding

Even in countries with high treatment coverage for pregnant women, gaps in retention, adherence and HIV prevention result in MTCT rates >5%

Source: UNAIDS epidemiological estimates, 2020 (see https://aidsinfo.unaids.org/).
Although Number of Children on ART Has More Than Doubled Since 2010, All Pediatric Treatment Targets Have Been Missed

2019: 1.8 million children 0-14 years living with HIV

Number children accessing ART globally 2000-2019 and 2018 and 2020 targets

Percentage of HIV+ Children Receiving ART

Treatment coverage in children in 2019 was 53% compared to 68% for adults

Plateauing in numbers of children on ART since 2017

Source: UNAIDS epidemiological estimates, 2020 (see https://aidsinfo.unaids.org/).
Pediatric HIV – We Are Not Done Yet!

Martina Penazzato, Plenary

Why is it okay that...

Today

400 children acquired HIV

260 children died of AIDS-related conditions

We need to...
ACT NOW

Do more operational...
RESEARCH

Keep...
INNOVATING
Testing the children of individuals living with HIV is an inexpensive, high yield intervention. Why is this not being done more?

Wolf HT et al. IAS Virtual July 2020 Abs. OAB0703

Pediatric index testing: 12% of index tests done but accounted for 28% of positive tests

12 PEPFAR African Countries

0-4 years  4.5% yield
5-9 years  2.8% yield
10-14 years  2.7% yield

Irrnovations to Speed Diagnosis

Point of care EID proven to result in more rapid diagnosis and ART start. Why not implement now?

Screening
For TB, cryptococcal disease, developmental delay

Optimize
ART start within 7 d, optimal regimen, counseling

Treat
For TB, cryptococcal disease, severe pneumonia

Prevent
TB, PJP, cryptococcal pneumonia and catch-up immunizations

Stop AIDS! screen, treat, optimize, prevent

30% of children and youth with HIV still present with severe immune suppression

Fourth 90: Health and Well-Being with HIV

Optimize Treatment

DTG available for children as young as age 4 weeks. NOW is the time to implement!

Screen
Developmental delay, cardiac, lung and renal disease, cervical cancer (after sexual debut)

Refer and Link
Clinical specialties, disability, rehabilitation, community psychosocial support

Assess and Manage
Psychosocial status and mental health with appropriate management

Nutrition
Ensure optimal nutrition

Nurturing Care
HIV touch points optimized to deliver simple interventions for early childhood development

Attention to quality of life for children we hope will live a long life needs more attention

We need a 4th “90”!
Need for Operational Research

Learn From What You Are Doing

COVID-19: a stress test for change
Reframing the way we delivery care and support to children and adolescents

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children &lt;10</td>
<td>10/37</td>
<td>23/37</td>
</tr>
<tr>
<td>Adolescents 10-19</td>
<td>14/37</td>
<td>26/37</td>
</tr>
</tbody>
</table>

O'Keefe M et al. COVID-19 IAS Virtual July 2019 Track C

Identify and Test Solutions in Multiple Settings

Learn what works, take to scale, adapting to local context

Lessons we learn from response to COVID-19 pandemic can improve care for children and youth in the future

Critical needs:
- Collaboration
- Capacity building
- Political support
- Resources
Innovate

COVID-19 Has Taught Us We can Do Things Differently

→ New adaptive trial designs can rapidly ID new treatments
→ Provide access to children/pregnant women rapidly
→ Rapidly develop trials in children & pregnant women
→ Multi-group/company collaborations can work

Promote New Technologies for Children

- Dispersible tablets (DTs)
- Oro-dispersible tablets (ODTs)
- Multi-particulates (MPs)
- Mini-tablets (1-3 mm)
- Long-acting depot injections*
- Suppositories
- Taste-masking technologies
- Enhanced bioavailability

Gilead’s Insights Regarding COVID-19 Disease Medications

Gilead to Test Antiviral Drug Remdesivir in Pediatric Patients with COVID-19

Solidarity Call to Action

Access to COVID-19 Tools (ACT) Accelerator

Commitment to Quicken Development of New Therapies and Vaccines

Partner for Innovation and Efficiency

The Global Accelerator for Pediatric Formulations (GAP-f)
Dolutegravir, TAF

New Clinical Trials

Efficacy but Toxicity as Well – Adults, Adolescents

Pregnancy, DTG and Neural Tube Defects
More Rapid Viral Suppression with DTG, Similar Long-Term Efficacy to EFV

**ADVANCE**
- 1053 ART-naive pt with RNA >500
- 59% Female
- 192 Weeks

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>HIV RNA &lt;50 c/mL at 96 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG + TAF/FTC</td>
<td>351</td>
<td>73.9% (n=310; 96 wk n=277)</td>
</tr>
<tr>
<td>DTG + TDF/FTC</td>
<td>351</td>
<td>72.3% (n=303; 96 wk n=263)</td>
</tr>
</tbody>
</table>

**NAMSAL**
- 613 ART-naive RNA <1000
- 67% Female

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>HIV RNA &lt;50 c/mL at 96 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG/TDF/3TC</td>
<td>310</td>
<td>73.9% (n=310; 96 wk n=277)</td>
</tr>
<tr>
<td>EFV400/TAF/3TC</td>
<td>303</td>
<td>72.3% (n=303; 96 wk n=263)</td>
</tr>
</tbody>
</table>

- Fewer SAE DTG than EFV, 6 vs 9%
- Fewer Grade 3/4 AE DTG than EFV, 15-17% vs 27%
- More NRTI/NNRTI emergent resistance with EFV failure
- AE similar btn arms
- Emergent resistance only with EFV failure

Sokhela S et al. IAS Virtual July 2020 Abs. OAXLB0104
Kouanfack C et al. IAS Virtual July 2020 Abs. OAB0402
Both RCT Show Excess Weight Gain with DTG, Especially with TAF

ADVANCE Trial (DTG/TAF or TDF/FTC vs EFV/TDF/FTC): Week 144-Weight Gain over Time by Sex

ADVANCE trial weight: Women

ADVANCE trial weight: Men
Both RCT Show Excess Weight Gain with DTG, Especially with TAF

**ADVANCE Trial** (DTG/TAF or TDF/FTC vs EFV/TDF/FTC): Week 144-Weight Gain over Time by Sex

- **ADVANCE trial weight: Women**
  - No real plateau in weight gain
  - Weight ↑ greater any DTG, greatest with TAF-DTG vs EFV, esp women

- **ADVANCE trial weight: Men**
  - Highest in women
  - TAF>EFV metabolic syndrome

**NAMSAL Trial** (DTG/TDF/FTC vs EFV400/TDF/FTC): Week 96-Weight Gain over Time by Sex

- **NAMSAL trial weight: Women**
  - Weight ↑ greater with DTG/TDF/FTC than EFV/TDF/FTC, esp women

- **NAMSAL trial weight: Men**
  - Weight ↑ greater with TDF/FTC vs TDF/EFV, esp women
ADVANCE: Estimates of Adverse Pregnancy Outcomes (APO) with Pre-Pregnancy Weight Gain

Sokhela S et al. IAS Virtual July 2020 Abs OAXLB0104

- Used ADVANCE ART-related emergent obesity rates and data on relationship of obesity with APO to estimate RR for APO by ART regimen.

- Based on RR of APO in obese vs normal BMI per meta-analysis (table), predicted potential APO ↑ (including gestational diabetes, pre-eclampsia, LGA infant, and neonatal death) due to ART-induced obesity:
  - TAF/FTC/DTG: 9.9% increase
  - TDF/FTC/DTG: 5.2% increase
  - TDF/FTC/EFV: 0.9% increase

<table>
<thead>
<tr>
<th>APO</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational DM</td>
<td>4.31</td>
<td>3.2, 5.9</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>4.06</td>
<td>3.1, 5.3</td>
</tr>
<tr>
<td>LGA infant</td>
<td>2.48</td>
<td>1.0, 2.5</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>1.57</td>
<td>1.2, 5.6</td>
</tr>
</tbody>
</table>
Switch to DTG in Adolescents with Viral Suppression Associated with ↑ in BMI and Odds of Overweight, Eswatini

Kay A et al.  IAS Virtual July 2020 Abs. OAB0106

- 605 HIV+ adolescents age 10-19 years with HIV RNA <200 c/mL who were transitioned to DTG – evaluated weight and height before and after transition DTG

- 73% on NVP ART prior to transition and 88% started TDF/3TC-based DTG ART.

- After transition to DTG, there was a significant change in BMI annual increase that was above normal expected BMI increase in youth.

- Significant increase in BMI z-score after DTG initiation.

- Adjusting for sex, NRTI backbone, prior ART regimen & age at DTG start, after DTG transition, odds of becoming overweight/obese increased by ~1% per day.

- Driven by larger ↑ in youth categorized as thin prior to DTG.
DTG in Pregnancy
Prospective cohort of 1257 pregnant women and newborns from 21 sites in US with 1st ART regimen in pregnancy DTG (120), ATVr (464), DRVr (185), RPV (243), RAL (86), or EVG (159).

Comparison Viral Suppression and Adverse Pregnancy Outcomes Between DTG and Other Regimens

→ DTG ART viral suppression rates 97-98%, comparable to DRVr, RPV, EVG but better than ATVr and RAL.

→ Comparable rates of overall adverse birth outcomes between regimens, ranging between 22-27%.
Viral Suppression with DTG vs EFV in Pregnancy and MTCT
Meta-Analysis of 5 Clinical Trials in 1074 Pregnant Women

Asif SF et al. IAS Virtual July 2020 Abs.OABL0195

- Meta-analysis of 1074 pregnant women from 5 trials; 3 enrolled late pregnancy (DolPHIN 1/2, VESTED), while 2 (NAMSAL, ADVANCE) had women became pregnant on study drug.

- Significantly higher viral suppression with DTG > EFV. OR 2.9 (1.5-5.5)
- Differences between trials in the extent of suppression reflect timing ART initiation
- While DTG had superior virologic efficacy than EFV, all 5 infant infections with DTG (all with ART started in pregnancy).
- Safety profile of DTG and EFV (and TAF and TDF) generally similar in meta-analysis but only shows short-term effects of DTG, and most started drugs during pregnancy as opposed to preconception.
- LT safety requires further assessment.

- No significant difference SGA DTG vs EFV
- No significant difference AE mother/infants with DTG vs EFV
- No significant difference AE mother/infants with TAF vs TDF
Women Starting or Transitioning to DTG-Based ART in Kenya

Viral Suppression

Humphrey J et al. IAS Virtual July 2020 Abs. PEC0394

Retrospective study 5,155 women age 15-49 starting DTG ART at AMPATH-affiliated HIV clinics in Kenya
- 89% transitioned from EFV or NVP to DTG (95% started TLD)
- 61% using any contraception at time starting DTG (primarily condom, only 10% using DMPA, oral contraceptive or IUD with little change from pre to post DTG signal).

12 months post-DTG start
- 87% remained on DTG through 12 mos
- 12% changed back from DTG to EFV or NVP

Viral suppression high and similar in those who stayed on DTG or switched back to EFV
Counseling About DTG and EFV Among Women of Reproductive Age Receiving ART in Kenya

Bernard C et al. IAS Virtual July 2020 Abs. PEB0286

- Telephone interviews between May 2019-May 2020 with 1,245 HIV+ women of reproductive age who initiated DTG between Oct 2017-Apr 2019 in AMPATH HIV clinics, Kenya
- Surveys included questions about knowledge of ever having taken DTG (n=1,028) and counseling they received from HCW about risks of DTG and EFV.
  - Only 33% of 1,028 ever DTG users recalled receiving counseling about potential teratogenic risk of DTG
  - Only 13% of 289 ever EFV users reported receiving counseling about potential EFV interaction with contraceptive implant.
  - 21% of women who self-reported ever DTG use reported switching off DTG
What Are New Data on Neural Tube Birth Defects and Preconception DTG?
Tsepamo: Evolution of NTD Prevalence with Preconception DTG

Zash R et al. IAS Virtual July 2020 Abs. OAXLB0102

Significant prevalence difference between DTG preconception and all other exposure groups (0.82 to 0.94)
Prevalence difference DTG vs EFV preconception
0.12 (0.0, 0.32)

Prevalence difference DTG vs non-DTG preconception
0.09 (-0.03, 0.30%)

Prevalence difference DTG vs uninfected
0.12 (0.01, 0.32)
After a period of decline since the original safety signal, prevalence of NTD among infants born to women on DTG at conception appears to be stabilizing at a low prevalence level.
### Update: Prospective Antiretroviral Pregnancy Registry InSTI and Neural Tube Defects through January 2020

#### Overall Birth Defects/Neural Tube Defects and Timing Earliest InSTI Exposure

<table>
<thead>
<tr>
<th></th>
<th>Periconception</th>
<th>Later 1&lt;sup&gt;st&lt;/sup&gt; Trimester</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt;/3&lt;sup&gt;rd&lt;/sup&gt; Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall birth defects</td>
<td>Defects/outcomes</td>
<td>Defect/outcomes</td>
<td>Defects/outcomes</td>
</tr>
<tr>
<td>Exposure to any InSTI</td>
<td>33/1008 (3.3%)</td>
<td>3/159 (1.9%)</td>
<td>27/674 (4.0%)</td>
</tr>
<tr>
<td>DTG</td>
<td>14/382 (3.7%)</td>
<td>2/73 (2.7%)</td>
<td>12/285 (4.2%)</td>
</tr>
<tr>
<td>1/382 NTD (0.26%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVG</td>
<td>11/298 (3.7%)</td>
<td>0/25 (0%)</td>
<td>1/68 (1.5%)</td>
</tr>
<tr>
<td>RAL</td>
<td>11/327 (3.4%)</td>
<td>2/95 (2.1%)</td>
<td>15/399 (3.8%)</td>
</tr>
<tr>
<td>0 NTD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIC</td>
<td>0/25 (0%)</td>
<td>0/3</td>
<td>0/12</td>
</tr>
<tr>
<td></td>
<td>0 NTD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

→ One NTD in prospective APR with periconception DTG, rate 0.26%
Neural Tube Defects and Adverse Pregnancy Outcome After Maternal Exposure to DTG During Pregnancy, US 2013-2017

Hoover KW, et al. IAS Virtual July 2020 Abs. PEB0356

- Analyzed IBM MarketScan commercial/Medicaid databases including clinical diagnoses, procedure and medications to ID maternal exposure to ARV; NTD; adverse pregnancy outcome (APO).
- Compared prevalence of NTD and APO among HIV-negative women and HIV+ women by type ARV

→7,168 HIV+ pregnancies, 235 on DTG.
→There were no NTD among 1,234 HIV+ women on InSTI, including DTG.
→NTD prevalence was 0.48-0.58/1000 (0.05-0.06%) among 6.4 million HIV-uninfected women.
→Prevalence stillbirth, spontaneous and induced abortion higher in HIV+ women (particularly those on no ARV) compared to HIV-uninfected women; not associated with specific ARV use.
Pediatric Antiretroviral Therapy
85% of Children Living with HIV and Viral Failure in Kenya Have Drug Resistance Mutations Requiring Regimen Change

Abuogi L et al. IAS Virtual July 2020 Abs. LBPEB08

- 704 HIV+ children age 1-14 years on ART enrolled from 5 facilities Kenya 3/19-12/19 and randomized to SOC or intervention (POC VL q 3 mo with targeted DR monitoring if VL >1000).

- Preliminary results on resistance testing in intervention arm presented
  - 365 randomized; 60 had VL >1000 and underwent ≥1 resistance test.
  - 51/60, 85%, had drug resistance mutations to NNRTI, NRTI or both.
  - K103N NNRTI and M184V NRTI most common.

→Children with VF likely to have DR and therefore efforts to ↑ adherence will likely not result in viral suppression.

→Early drug resistance testing with VF to determine appropriate ART regimen change rather than ↑ adherence counseling desirable.

Median age 12.7 yrs; prior 2nd line ART 85% PI-based (LPV/r 67%, ATV/r 18%).

Median VL at switch 4.7 log copies/mL; 81% switched for confirmed resistance.

- 98% had ≥1 resistance mutations, with 71% >3 TAMs and 52% PI mutations.

Viral response to 3rd line: of those with VL post-switch, suppression to VL <1000 was 75% (45/66) at 6 mos and 78% (32/41) at 12 mos on 3rd line ART (<50, 46% and 51%).
Evaluated factors associated with viral suppression using pre-enrollment VL data from 704 children age <15 years recruited into Opt4Kids randomized trial, along with their caregivers.

→ Biologic mother most common caregiver
→ 80% caregivers were HIV+
  • 45% reported viral suppression
→ 78% of children had viral suppression

→ Children in care of biologic mother compared to other caregivers more likely to have suppression.

→ Children who had virally suppressed caregivers were 7.5 times more likely to have suppression.

Table 1: Children and caregiver characteristics (N=704 children)

<table>
<thead>
<tr>
<th>Caregiver characteristics</th>
<th>Median (IQR) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of caregiver</td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>484 (68.4)</td>
</tr>
<tr>
<td>Father</td>
<td>56 (8.3)</td>
</tr>
<tr>
<td>Other</td>
<td>184 (23.2)</td>
</tr>
<tr>
<td>At least primary education</td>
<td></td>
</tr>
<tr>
<td>Caregiver HIV positive</td>
<td>56 (80.4)</td>
</tr>
<tr>
<td>Viral load suppressed</td>
<td>318 (44.9)</td>
</tr>
<tr>
<td>Median age</td>
<td>35 (31-43)</td>
</tr>
</tbody>
</table>

Children characteristics

<table>
<thead>
<tr>
<th>Gender (female)</th>
<th>343 (48.3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age</td>
<td>9.5 (1.1)</td>
</tr>
<tr>
<td>Median time on ART (years)</td>
<td>6.3 (3.9)</td>
</tr>
<tr>
<td>Viral load suppressed</td>
<td>78</td>
</tr>
</tbody>
</table>

ARV basis:

- NNRTI based: 444 (51.6)
- PI based: 30 (36.0)
- Integrate based: 9 (1.1)
Factors Associated with Non-Adherence to ART in Adolescents in Masaka Uganda

Jjuuko G et al. IAS Virtual July 020 Abs. OAD0804.

- The AIDS Support Organization (TASO) in Masaka Uganda providing adolescent clinic services explored factors associated with poor adherence among non-suppressed (VL >1000) **school-going** adolescents (age 10-19) with adherence <95% from both rural and peri-urban areas of Masaka district.

- Of 325 youth, 127 (39%) were non-suppressed (63% girls, 37% boys).

- 110/127 (87%) had adherence <95%.

→ Concluded there was a need for HIV school-related interventions targeting both teachers and students to create flexible and conducive environment for HIV+ students.

→ Majority reasons cited were school-related issues.
Viral Non-Suppression in Youth is Associated with Overlapping Significant Life Events

Mwangwa F et al. IAS Virtual July 2020 Abs. OAB0702

- 900 HIV+ youth 15-24 yr (83% female, 51% <20 yr) from 14 clinics in rural Uganda and Kenya participating in SEARCH-Youth intervention trial between Feb-Oct 2019
- Cross sectional analysis of baseline data including recent life events to identify associations with viral suppression (<400).

Multivariate Analysis of Predictors of Viral Suppression

<table>
<thead>
<tr>
<th>Predictor of viral suppression</th>
<th>Prevalence in YLHIV</th>
<th>Adjusted Odds Ratios (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overlapping (2 or more) recent events</td>
<td>151/900 (17%)</td>
<td>0.52 (0.35-0.77), p=0.001</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>155/900 (17%)</td>
<td>0.56 (0.38-0.84), p=0.004</td>
</tr>
<tr>
<td>Increasing age</td>
<td>n/a</td>
<td>1.08 (1.02-1.15), p=0.011</td>
</tr>
<tr>
<td>Disclosure of HIV status to family</td>
<td>727/900 (81%)</td>
<td>2.00 (1.4-2.8), p&lt;0.001</td>
</tr>
<tr>
<td>Disclosure of HIV status to partner</td>
<td>483/900 (54%)</td>
<td>1.71 (1.2-2.4), p=0.001</td>
</tr>
</tbody>
</table>

Less likely suppressed
More likely suppressed

Overlapping recent life events, alcohol use and lack of disclosure to family and partner were significantly independently associated with viral non-suppression and can identify those most vulnerable patients needing attention.
HIV Testing and Case Finding
Outbreak primarily spread through parenteral route linked to unsafe injection and blood transfusion practices – need to invest in improving blood service and injection practices.
Distribution of Multiple HIV-Self Test to High-Risk HIV-Uninfected Women Led to Increased Partner/Couple Testing and ID HIV+ Partners

Thirmurthy H et al. IAS Virtual July 2020 Abs. OACL0105

- Cluster randomized trial 2,090 participants: 66 pair-matched clusters from beach communities and hotspots randomized to intervention or control (~30 women per cluster); mean FU 19 mos, >85% retention each visit
  - Age >18 yr, HIV negative, >2 sexual partners in last 4 weeks

  - HIV testing and surveys q 6 mo to 24 mo

  → High risk women were able to distribute self-tests to sex partners; ~50% of tests given to partners, 50% used themselves

  → Provision of multiple self-tests led to significant (p<0.001) 35% ↑ in primary partner & 45% ↑ in couples testing and identified 1.8 times more HIV+ sex partners/pt (0.26 vs 0.14 partners/pt).

  → ↑ condom use at 6 but not 12 and 24 mos; incidence IPV similar.

→ No effect on HIV incidence; additional HIV prevention interventions needed
Pediatric Index Testing to Improve Identification of HIV+ Children
12 PEPFAR-Supported Countries

Wolf HT et al. IAS Virtual July 2020 Abs. OAB0703

- Evaluated PEPFAR program HIV testing data from children aged 1-14 years in 12 African countries from Oct 2017-Sept 2018 and Oct 2018-Sept 2019 to determine proportion of HIV+ children identified through index testing.

  → 8/12 countries had significant increase in index testing of children.
  → % tests in 2019 that were done through index testing ranged from 4%-29%.
  → % HIV+ children ID by index testing ranged from 9-68%, with 8 countries identifying >25% and 3 countries >50% of HIV+ children through index testing.

 → Significant ↑ 2018 to 2019 index testing and significant proportion of HIV+ children identified through index testing.
Community-Based Parenting Program, Rural Lesotho Increases HIV Testing of Children

**Tomlinson M et al. IAS Virtual July 2020 Abs. OAD0506**

- Community based, integrated child health and development intervention – including HIV - delivered to caregivers by trained community health workers, rural Lesotho.

**Intervention**

- "early morning star" Mphathalatsane intervention
- Community based, integrated child health and development intervention – including HIV - delivered to caregivers by trained community health workers
- Caregivers with children age 1-5 yrs - 2 age groups: 12-30 mos, 31-60 mos
- Group session (5-6 caregivers) - Hosted at local preschool center - Delivered by community health workers
- 8 weekly sessions - 5th top up session - Community health day HIV-specific: education, storybook, song, film

**Trial Design**

- Cluster randomized controlled trial
- 94 villages (clusters)
- Intervention (17) N=531 children and caregivers
- Control (17) N=509 children and caregivers
- 8 weekly sessions
- 5th top up session
- Community health day
- HIV-specific: education, storybook, song, film

**Endpoints**

- HIV testing rates of children
- Caregiver report
- Early Childhood Vigilance Task (ECVT)
- MacArthur Communicative Development Inventory (CDI)
- Mullen Scale infant Development
- Peabody Picture Vocabulary

<table>
<thead>
<tr>
<th>Tested for HIV</th>
<th>Control</th>
<th>Intervention</th>
<th>Effect (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>115 (23:0)</td>
<td>153 (30:0)</td>
<td>1.56 (1:04 to 2:33)</td>
<td>0:029</td>
</tr>
<tr>
<td>12 months</td>
<td>207 (42:8)</td>
<td>313 (61:4)</td>
<td>1.78 (1:12 to 2:81)</td>
<td>0:013</td>
</tr>
</tbody>
</table>

- Significant increase in children receiving HIV testing with intervention at 3- and 12-month post-intervention follow-up

→ While most mother’s HIV status known, only ~ half of children’s status known at baseline
Determinants of HIV Testing for Young People 15-24 Years in Uganda
Kalibbala D et al. IAS Virtual July 2020 Abs. PEC0549

- Mixed methods study in 650 young persons (397 rural and 253 urban) 15-24 years from Wakiso district Uganda (selected by stratified cluster random sampling).
- Questionnaires and in-depth interview (n=16) regarding HIV testing.
- 61% female; 47% 15-19 and 53% 20-24 yr; 80% <5km to nearest HIV testing site.

Factors Associated with HIV Testing in Ugandan Youth

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Crude Prevalence ratio [95%CI]</th>
<th>Adjusted Prevalence ratio [95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>1.12 (1.02-1.24) 1.09 (1.01-1.18)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>20-24</td>
<td>1.38 (1.26-1.52) 1.26 (1.15-1.37)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Married/Widowed</td>
<td>1.26 (1.18-1.34) 1.02 (1.01-1.04)</td>
<td></td>
</tr>
<tr>
<td>Ever had sexual intercourse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>1.13 (1.08-1.19) 1.13 (1.08-1.19)</td>
<td></td>
</tr>
<tr>
<td>Distance to nearest HIV testing site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5km</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>5-10km</td>
<td>1.04 (0.94-1.15) 1.06 (0.97-1.16)</td>
<td></td>
</tr>
<tr>
<td>&gt;10 km</td>
<td>0.77 (0.59-1.01) 0.77 (0.59-0.99)</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ever</td>
<td>1.16 (1.07-1.24) 1.05 (0.97-1.13)</td>
<td></td>
</tr>
<tr>
<td>Encouraged by Peers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>1.19 (1.08-1.30) 1.28 (1.09-1.28)</td>
<td></td>
</tr>
<tr>
<td>Perceived HIV testing services as Youth-friendly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>1.13 (0.99-1.28) 1.12 (1.01-1.25)</td>
<td></td>
</tr>
</tbody>
</table>

→Prevalence of “ever HIV test” 80.2%; higher in females (83.6%) than males (74.8%).
→On adjusted analysis, factors associated with testing in youth: female sex, age >20 years, marriage, history of sex, peer-encouragement, and positive perception of youth-friendly health services.
→Interviews revealed 5 emergent themes related to HIV testing in youth:
  - Decisions on testing related to **self-evaluation of risk**
  - **Fears** of positive test deferred some from testing
  - Engagement with **other health services** facilitated testing for HIV
  - **Barriers** include fear injection, insufficient confidentiality, facilities not youth-friendly
  - Mixed feeling on **mobile testing**, lack of privacy a concern
LEOPARD (Latency and Early neonatal Provision of AntiRetroviral Drugs) enrolled 73 neonates with confirmed *in utero* infection in Johannesburg; ART was initiated within 1st 14 days of life.

Of 61 infant remaining on study, 46 (75%) attained VL <50.

14/46 (30%) had a **negative diagnostic PCR after ART start**; in 10/14 (71%) last PCR remained negative.

Infants with suppression and negative PCR had **higher CD4% pre-ART** and **higher cycle threshold values** on birth PCR; age at ART start, BW and pre-ART RNA were **not** associated with PCR negativity (table).

> Clinicians need to be alert to the possibility of false negative PCR test in infants started on early ART to avoid confusion about infant HIV status.
Multi-Month ART Dispensing
6-Month ART Dispensing is Non-Inferior to SOC for 24-Month Retention and Viral Suppression

*Cassidy T et al. IAS Virtual July 2020 Abs. OAELB0102*

- Cluster randomized non-inferiority trial of 6-month MMD in Ubuntu ARV Clinics in Khayelitsha South Africa.
- Enrolled 2,150 ART-experienced virally suppressed adults in Adherence Clubs (977 Intervention, 1173 SOC) (77% female, median time ART 7.3 yr, median age 42 years)
- First study visits Oct-Nov 2017, database closure Jan 2020
PMTCT Cascade
Described uptake of PMTCT and outcomes in 2,576 HIV+ mothers attending ANC (HIV prevalence 31%) with live-born infants in 2017 using electronic medical records with unique patient ID and linked mother-infant pairs.

- 88% knew HIV status at 1st ANC and 78% already on ART.
- 95% women diagnosed antepartum started ART; 88% suppressed in the 85% tested.
- 94% infants had 1st EID test by 10 wks
  - 80% tested at birth; if negative only 58% returned for test at 10 weeks

- Overall 12-month MTCT only 1.6% (however, 10% of infant lacked 12-month HIV outcome).

- Risk factors for infant infection
  - Starting ART during pregnancy vs preconception
  - First diagnosed with HIV at delivery or postpartum
  - No antenatal suppression or no VL test antepartum

**Population** | # HIV+/total # | 12 mo MTCT
--- | --- | ---
Overall cohort | 41/2576 | 1.6%
No infant HIV outcome | 249/2576 (9.7%) |
All with known outcome | 41/2327 | 1.8%
Dx before ANC | 31/2273 | 1.4%
Dx during ANC | 6/263 | 2.3%
Dx delivery/PP | 4/40 | 10%
Factors Associated with Interruption HIV Care and Treatment in Pregnant and Postpartum Women in Kabeho Cohort, Rwanda

Nawar E et al. IAS Virtual July 2020 Abs. PDD0407

- Kabheo Study observational prospective cohort of 608 HIV+ pregnant /early PP women in PMTCT program at 14 high volume facilities in Rwanda, enrolled 2013-14 and FU 2016-17.
- Most women who interrupted care eventually returned to care; evaluated factors associated with missed visit in women who later returned to care.

<table>
<thead>
<tr>
<th>Facility-level characteristic</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ANC, PMTCT, and ART services offered all 5 days per week</td>
<td>0.54</td>
<td>0.32, 0.92</td>
</tr>
<tr>
<td>Not offered all 5 days</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>2 Retention support¹</td>
<td>0.30</td>
<td>0.12, 0.76</td>
</tr>
<tr>
<td>No retention support</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>3 Peer counseling</td>
<td>0.31</td>
<td>0.23, 0.42</td>
</tr>
<tr>
<td>No peer counseling</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>4 Infant feeding counseling</td>
<td>0.20</td>
<td>0.15, 0.28</td>
</tr>
<tr>
<td>No infant feeding counseling</td>
<td>Reference</td>
<td></td>
</tr>
</tbody>
</table>

1 Interruptions are defined as missing at least 1 monthly visit followed by returning to care
2 Retention support includes telephone reminders, transportation reimbursement/support, or default tracing systems.

- Individual factors such as age, education, marital status, CD4 count, HIV disclosure status, travel time to clinic, number in household were not significantly associated with missed visit.

- **Health facility factors** had strong association with reduced care/treatment interruptions – including # days ANC available and availability of retention support, peer counseling, infant feeding counseling.

- These health system factors may be effective target for interventions to improve retention.
TB and HIV

- Pregnancy
- Pediatrics
P1078: IPT immediate start >1st T pregnancy vs deferral to 12 wk PP in HIV+ women on ART (85% EFV, 12% NVP), LFT 1 mo → risk hepatic toxicity (Gr ≥3 LFT or ≥2 ALT/bili or ALT/sx) in 945 with ≥1 LFT. → 6% had ≥1 hepatotoxicity event, similar by arm

- Incidence 48 wk: 5.8/100 PY immediate, 6.7/100 PY deferred

→ ALT increase PP and peaks at 12 wk PP both arms

- Toxicity: 8% AP, 8% within 1 wk PP, 84% >1 wk PP

Factors Associated with Hepatic Toxicity
Type ART/timing, CTx use PP, CYP2B6 slow genotype

→ CD4, HIV RNA, age, BMI, NAT2 genotype, HBsAG positivity & duration/timing of ART not significant.

→ Critical to monitor for hepatic toxicity PP when most events occur; consider ARV regimen and CTX use.
Pediatric TB Clinical Cascade in HIV+ Children on ART, 16 Countries

Patel MR et al. IAS Virtual July 2020 Abs. OAB0504


**Median TB Cascade Indices in CLHIV on ARV Stratified by Pediatric TB incidence, CLHIV Burden and Region**

- **Screening** was high overall, but screening positivity was lower than expected given CLHIV.
- **TB diagnosis** was unclear among CLHIV on ART because data are not age disaggregated.
- **TB treatment initiation** was low, regardless of region, number CLHIV or TB incidence.
- **TPT initiation** was very low regardless of region, number CLHIV or TB incidence.
- **TPT completion** was high in Eastern but low in Southern and Western Africa.

How to Address the Gaps

Children and adolescents need to be specifically considered and included in national, subnational, and clinic-level efforts for...
Biomarkers of Infant Adherence to INH Prophylaxis in a TB Prevention Trial in Kenya

LaCourse S et al. IAS Virtual July 2020 Abs. OAB0704

- Standardized adherence questionnaire at FU
- Urine collected each visit to test for INH metabolite using new INH dipstick

![Image of Infant Tuberculosis Prevention Study (iTIPS)]

**Primary outcome:** Mtb infection INH 7.0 vs. No INH 13.4 per 100 PY HR 0.53 (95%CI 0.24-1.14), p=0.11

**INH Dipstick Result by Caregiver-Reported Adherence**

<table>
<thead>
<tr>
<th>% of Participants</th>
<th>INH present</th>
<th>INH not present</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Optimal</strong></td>
<td>48.9</td>
<td>51.1</td>
</tr>
<tr>
<td><strong>Suboptimal</strong></td>
<td>52.5</td>
<td>47.5</td>
</tr>
<tr>
<td><em>Overall Use</em></td>
<td>48.5</td>
<td>51.5</td>
</tr>
<tr>
<td><em>Timing of Last INH Dose</em></td>
<td>61.9</td>
<td>38.1</td>
</tr>
<tr>
<td><em>Missed Doses in Past 3 Days</em></td>
<td>47.1</td>
<td>52.9</td>
</tr>
<tr>
<td><strong>YES</strong></td>
<td>73.7</td>
<td>26.3</td>
</tr>
</tbody>
</table>

Only ~50% of infants with caregiver-reported adherence had a positive urine INH test

- Urine biomarker assessment suggests over-reported infant INH adherence
- Maternal education and viral suppression associated with infant adherence
  - Advances maternal understanding of medication rationale and success in their own medication use predicts infant adherence
- Biomarker monitoring may be useful to evaluate and motivate infant medication adherence
  - Low cost real-time objective measure aid in counseling

- Development of low-cost urine INH dipstick - modified Arkansas method
  - Potassium dichromate + chloramine T → oxynin chloride
  - Splits INH metabolite (isonicotinic acid + glucuronosylhydride derivative)
  - Coneness with trinitrobenzene → dark blue polyethylene dye
  - Color change with INH metabolite detection within 30 hours of ingestion
Adolescents and HIV
New HIV infection rates vary across and between regions.

In sub-Saharan Africa, incidence of HIV among AGYW (aged 15-24 years) is generally highest in southern Africa, but subnational data show districts cross the region with very high rates of HIV infection.

The high incidence of HIV among AGYW across Africa points toward the critical need to improve prevention interventions for this group.
Survey of 8,236 in- and out-of-school AGYW age 10-24 years in 20 selected districts in Uganda; 50.3% in-school.

Findings suggest need for 1) keeping girls in school and b) to develop specific prevention interventions to target out-of-school girls.
Evaluation of DREAMS project in Zimbabwe, targeted at YWSS age 18-24 yr.

Non-randomized design recruited 1204 in 2 intervention and 1227 in 4 comparison sites; 24 mo FU.

While HIV incidence was lower in DREAMS sites, on adjustment no longer statistically significant.

YSSW used clinical services more over time – but few accessed non-clinical DREAMS services.

Most SW in DREAMS sites offered PrEP and ~1/3 self-reported initiation but retention suboptimal and HIV incidence similar those who never started PrEP.

Still need approaches to strengthen use integrated social/clinical services in YWSW.

Baseline HIV prevalence: 19.5% DREAMS, 26.3% non-DREAMS sites; yearly HIV testing in those HIV-negative

% with 24-mo FU: 56% DREAMS (n=538), 53% non-DREAMS (n=479)

Differences in demographics between sites adjusted for in analysis.

HIV Incidence in Young Sex Workers HIV-Negative at Enrollment

<table>
<thead>
<tr>
<th></th>
<th>Number of incident infections/person-years (95% CI)</th>
<th>Rate per 100 person-years</th>
<th>Age-adjusted rate ratio (95% CI) p-value</th>
<th>Fully adjusted rate ratio (95% CI) p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-DREAMS (N=479)</td>
<td>48.9/07.62</td>
<td>5.29</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>DREAMS (N=538)</td>
<td>31/9/88.14</td>
<td>3.14</td>
<td>0.59 (0.34-0.93)</td>
<td>0.74 (0.43-1.25)</td>
</tr>
</tbody>
</table>

*Adjusted for age, highest education level, marital status, self-identification as female sex worker, STI symptoms, number sex partners last month, baseline HIV prevalence.
Lack of Impact of DREAMS on HSV-2 Acquisition Among AGYW in Rural KwaZulu Natal South Africa

Mthiyane N et al. IAS Virtual July 2020 Abs.OAC0104

Africa Health Research Institute (AHRI) enrolled cohort of 2184 adolescent girls age 13-22 years rural South Africa; 78% (1,702) completed 2-year FU.

Annual:
- Face-to-face interview and self-filled questionnaire
  - Socio-demographics
  - General health
  - Awareness and uptake of DREAMS interventions
  - Sexual behaviour
- Dried blood spot for HSV-2 testing


Baseline Characteristics

Non-Significant ↓ HSV-2 Incidence in DREAMS Recipients Age 18-22 Yr

High Incidence HSV-2 Overall

<table>
<thead>
<tr>
<th></th>
<th>Number with HSV-2 Infection</th>
<th>Person time (years)</th>
<th>Incidence/100 person-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (N=1397)</td>
<td>241</td>
<td>1652</td>
<td>15.4 (13.6 - 17.5)</td>
</tr>
<tr>
<td>Non-DREAMS beneficiary (N=590)</td>
<td>109</td>
<td>648</td>
<td>16.8 (13.9 - 20.3)</td>
</tr>
<tr>
<td>DREAMS beneficiary (N=807)</td>
<td>132</td>
<td>914</td>
<td>14.4 (12.2 - 17.1)</td>
</tr>
</tbody>
</table>

Adjusted RR of HSV-2 DREAMS vs non-DREAMS

Adjusted for Age, 2008 child formulation, migration and sexual initiation
As part of DREAMS in Tanzania, Sauti project instituted core package of services:
- Biomedical – VCT/condom, TB/STI screen/rx, screen and referral for GBV, alcohol, drug abuse
- Behavioral – peer-led sessions addressing HIV risk, gender, reproductive health
- Structural – economic empowerment community banking, health and parenting ed

Cluster RCT, communities with ≥110 AGYW age 15-23 yr out-of-school randomized to unconditional cash transfer (quarterly mobile money transfer US $31 for 18 mos) or not, all in combination with Sauti interventions; primary endpoint HSV-2 seroconversion status.

→ No overall effect cash transfer on HSV-2 conversion (RR adjusted for matching pairs: RR 1.0 (95% CI 0.8-1.3 p=0.98)

<table>
<thead>
<tr>
<th>Age</th>
<th>Human</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>1542</td>
<td>1544</td>
</tr>
<tr>
<td>n=1542</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19 years</td>
<td>555 (35.9%)</td>
<td>773 (50.1%)</td>
</tr>
<tr>
<td>20-23 years</td>
<td>927 (62.0%)</td>
<td>771 (49.9%)</td>
</tr>
<tr>
<td>HIV prevalence</td>
<td>3.1%</td>
<td>4.6%</td>
</tr>
<tr>
<td>HSV-2 prevalence</td>
<td>32.8%</td>
<td>31.2%</td>
</tr>
</tbody>
</table>

Reported to be sexually active: 73.8% vs 77.1%
Of sexually active: reported transactional sex (6 months) 26.9% vs 23.8%
Of sexually active: reported sex work (6 months) 16.6% vs 17.1%
Of sexually active: reported intergenerational sex (6 months) 11.9% vs 13.0%

No significant baseline differences between study arms

→ However, when stratified by community HIV risk and setting, cash transfer appeared that it may be effective in rural communities with low HIV risk
Effect Economic Support/Community Dialogue on Adolescent Sexual Behavior, Zambia

Hegdahl HK et al. IAS Virtual July 2020 Abs.OAC0103

- Cluster randomized trial in 12 districts to evaluate effectiveness of economic support +/- community intervention on sexual behavior, knowledge and norms in girls in grade 7 in schools, intervention 2 yrs, with FU 4 yrs

- Unconditional cash transfer q mo to girls, annual to parents, pay school fees gr 8-9

- Plus community meeting parents 6x yr; youth clubs q 2 wks, focus SRH

Data collection
- Baseline survey
- Biannual follow-up interviews
- Face-to-face and ACASI
- Trained, local research assistants

Mean age 13.6 years (SD 1.39)
- 9% had ever had boyfriend
- 2% had ever used contraceptives
- Most had some knowledge of SRH
- Low levels of pregnancy and marriage

- No effect on contraceptive use.
- However, significant effect of economic support and community intervention on deceeding self-reported sexual behavior.

### Comparing Groups:

<table>
<thead>
<tr>
<th></th>
<th>Combined vs Control</th>
<th>Economic vs Control</th>
<th>Combined vs Economic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Currently using modern contraceptive methods</td>
<td>1.00 (0.81 – 1.24)</td>
<td>1.03 (0.82 – 1.30)</td>
<td>0.98 (0.80 – 1.21)</td>
</tr>
<tr>
<td>Good knowledge of modern contraceptive methods</td>
<td>1.16 (0.95 – 1.43)</td>
<td>0.99 (0.80 – 1.23)</td>
<td>1.17 (1.00 – 1.36)</td>
</tr>
<tr>
<td>Sexually active last 4 weeks</td>
<td>0.60 (0.47 – 0.78)</td>
<td>0.71 (0.54 – 0.94)</td>
<td>0.83 (0.65 – 1.11)</td>
</tr>
</tbody>
</table>
Effectiveness of Sista2Sista Program on Improving Sexual/Reproductive Health Outcomes AGYW Zimbabwe

Hanisch D et al. IAS Virtual July 2020 Abs. OADLB0104

- Structured peer group behavioral intervention aimed at improving health outcomes among vulnerable in- and out-of-school AGWY.
- Led by female mentors and organized by age 10-14; 15-19; 20-24 yrs.
- Programs led by 130 mentors running groups in 23 districts in Zimbabwe.
- Analyzed program data for 91,612 AGYW age 10-24 yrs who were enrolled btn 2013-2019 to evaluate program exposure and HIV testing, marriage, school attendance, FP, and sexual abuse; mean age 15 yr, 81% in school, attrition rate <0.5%, with 64% attending at least 75% sessions.
- FU 4,612 graduates 1 year after graduation to assess sustainability.

→ Sista2Sista was an effective behavioral intervention to improve HIV and other SRH outcomes, with better outcomes at higher thresholds of program completion:
  - >75% sessions associated with increased odds HIV testing uptake & decreased odds school drop-out/child marriage; >85%, also more likely to return to school; and 100%, also more likely to use FP and report sexual abuse.

→ Augmenting group exercises with individual sessions increased likelihood program completion.
→ Outcomes related to school attendance and use FP were sustainable up to 1-year post-intervention.
PrEP Effectiveness and Use by Adolescents and Pregnant Women
Incorporating PrEP into SOC Prevention in Clinical Trial is Associated with Reduced HIV Incidence – ECHO Trial

Donnell D et al. IAS Virtual July 2020 Abs.OAC0105

- ECHO was RCT comparing HIV incidence in 7,829 women randomized to IM DMPA, copper IUD or levonorgesteral implant, conducted Dec 2015-Oct 2018.

**HIV Prevention Provided as Part of Study**
- At each 3 month visit, participants received a comprehensive package of HIV prevention, including HIV testing and risk reduction counselling, condoms, partner and participant STI testing and management, and referrals for pre-exposure prophylaxis (PrEP), as it became a part of national standard of prevention.
- All South African sites implemented on-site provision of PrEP between March and June 2018 (last year of the study)

**Two approaches** to limit confounding of PrEP access and calendar time:
- **Study visit method:** include only study visits with on-site PrEP access
- **Calendar time method:** include study visits within 6 mos before on-site PrEP access

**Objective:** Evaluate impact PrEP access on HIV incidence in S Africa sites by when on-site PrEP access began – comparing overall HIV incidence BEFORE and AFTER PrEP access in women on study at that time.
- Overall HIV incidence in ECHO women in South Africa was 4.5%
- 2,043 women had FU after PrEP access began; of these, 25% (543) initiated PrEP (had characteristics of higher HIV risk)

**PrEP Access and HIV Incidence South Afric**

<table>
<thead>
<tr>
<th>Study visit method</th>
<th>Infection/Person Years</th>
<th>Incidence rate</th>
<th>IRR (95% CI)</th>
<th>p-value</th>
<th>Adjusted* IRR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before PrEP access</td>
<td>133/2850</td>
<td>4.65%</td>
<td>0.45 (0.25, 0.81)</td>
<td>0.0076</td>
<td>0.45 (0.25, 0.82)</td>
<td>0.0085</td>
</tr>
<tr>
<td>On-site PrEP access</td>
<td>12/556</td>
<td>2.16%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calendar time method</th>
<th>Infection/Person Years</th>
<th>Incidence rate</th>
<th>IRR (95% CI)</th>
<th>p-value</th>
<th>Adjusted* IRR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before PrEP access</td>
<td>46/919</td>
<td>5.00%</td>
<td>0.45 (0.23, 0.86)</td>
<td>0.016</td>
<td>0.43 (0.22, 0.84)</td>
<td>0.014</td>
</tr>
<tr>
<td>On-site PrEP access</td>
<td>11/481</td>
<td>2.29%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*adjusted for age, new partner since last visit, unprotected sex and partner has other partners

→ ~ 25% of women started PrEP at South African sites when offered on-site.
→ Overall HIV incidence decreased by ~ 50% after on-site PrEP access implemented, despite no change in HIV risk profile before and after, and with findings robust using either analysis method.
PrEP is main DREAMS prevention component, implemented in 15 countries.

- Of 168,000 PrEP initiations in women, 51% were in AGYW, with 2.5-fold ↑ from FY 2018 to 2019.
- Uptake in AGYW similar to that of key populations (30% each in 2019)
- Of 129,280 PrEP starts in AGYW, 99% were in DREAMS countries.
- Despite COVID, DREAMS countries have newly started 43,197 AGYW on PrEP in FY 2020.
Tu’Washindi Intervention to Increase PrEP Use in AGYW at Risk of IPV
Pilot Study Results, Kenya

Roberts S et al. IAS Virtual July 2020 Abs. OADLB103

Nested in DREAMS in Kenya: 3 components over 6 months

- 103 HIV-negative, median age 22 yr
- 58% married
- 48% ever PrEP use; 34% currently on PrEP
- 62% any IPV; 46% last 3 months
- Balanced between arms

IPV non-significantly lower in intervention group

97% retention at exit, similar between arms

Intervention:
- 100% attended ≥1 support club
- 90% attended Buddy Day, 80% with partners
- 31% partner attend community sensitization

PrEP Uptake Higher Among 67 Not On PrEP

- PrEP uptake higher intervention
- But PrEP adherence poor, with only 3 pt having Wisepill opening on >85% d
- However, #d with opening was better in intervention, 25% vs 13%, p=0.02

Adjusted rate ratio*: 2.28
95% CI: 1.50 - 4.38
p<0.01
PrEP continuation rates were low but AGYW who concurrently started PrEP and FP were more likely to continue than those starting PrEP alone, and those entering through peer network or at drop-in or private facility were more likely to continue.
Cohort of 374 HIV-negative pregnant and postpartum women recruited at 1st ANC visit in primary care clinic in community with high HIV prevalence, Aug 2019-Mar 2020 (median age 25 yr, median GA 21 wk).

92% (344) opted to start PrEP at 1st ANC visit

Retention: 71% at 1 mo, 59% at 3 mo

Persistence: Of those who returned, % reported taking PrEP >5 d in past week: 89% 1 mo, 85% 3 mo

Early PrEP retention and persistence associated with:
- Older age (>25 yr)
- STI + at baseline
- >1 sex partner
- Sex partner HIV status unknown
- Alcohol use before/during pregnancy
- More frequent sex acts
The Future:

New PrEP Options

IAS results!

Results anticipated 2021
PrEP with Long-Acting Injectable Cabotegravir (CAB LA) Safe and More Effective than Oral TDF/FTC in MSM/TGW

Landovitz R et al. IAS Virtual July 2020 Abs. OAXLB0101

- Phase 3 study comparing IM CAB LA with oral TDF/FTC for HIV prevention in MSM/TGW >18 yrs at risk for HIV

Daily oral CAB vs PL X 5 weeks
IM CAB q 2 mo + oral placebo vs IM placebo q 2 mo + oral TDF/FTC X 3 years
Daily TDF/FTC both arms (cover tail CAB) X 1 year

52 HIV infections in 6,389 PY FU (median per-pt FU 1.4 yr)
Pooled HIV incidence 0.81 per 10 PY

Cumulative HIV Incidence by Study Arm

66% Better Efficacy for Prevention Compared to TDF/FTC PrEP!
PrEP with Long-Acting Injectable Cabotegravir (CAB LA) Safe and More Effective than Oral TDF/FTC in MSM/TGW

Landovitz R et al. IAS Virtual July 2020 Abs. OAXLB0101

- Of the 13 incident CAB LA infections:
  - 2 were infected prior to drug administration
  - 5 were infected after a prolonged hiatus from CAB
  - 3 occurred during the oral lead-in phase
  - Only 5 occurred despite continuous on-time CAB injections

- Of the 39 incident TDF/FTC infections:
  - 3 were infected prior to drug administration
  - 3 had intermittent visit adherence
  - The remainder occurred during TDF/FTC (random sampling TFV levels found >75% had levels consistent with at least 4 doses/wk, still to examine those who became infected)
81% of CAB (vs 31% placebo IM) had injection reactions, most mild or moderate; 47 (2.2%) of CAB participants permanently discontinued CAB due to injection-related AE, with severity of AE strongly associated.

- ↓ CrCl more frequent in TDF/FTC than CAB (72 vs 69%), while ↑ glucose more frequent with CAB than TDF/FTC (9 vs 5%), as was pyrexia (5 vs 3%), usually within 7 d of injection.

- **Weight gain was higher in CAB** (+1.3 kg/yr) than TDF/FTC (+0.31 kg/yr) (p<0.001), although most of this difference was during first year.
Key Take-Aways IAS Virtual - HIV

- New findings on weight gain with DTG & potential clinical effects need further evaluation.
- The NTD safety signal with preconception DTG has stabilized at low prevalence level, supporting use of DTG in women of reproductive potential.
- Critical need for evaluation of 3rd line ART in children given high prevalence of resistance among those with viral failure.
- HIV testing innovations (self- and index- testing) may improve identification of children and adults.
- TB cascade in children remains problematic.
- Need continued evaluation of new interventions to prevent incident HIV infection in AGYW given lack of success of many programs.
- PrEP uptake and adherence in young people remains suboptimal and need improved interventions to support.
- New long-acting PrEP option very relevant for AGYW, await trial results in women; pharmacovigilance for pregnancy outcomes will be important.
Selected Abstracts Relevant to Children and Women
Effects of COVID-19-Related Mitigation Practices on Programs
HIV-Self Testing During the COVID Pandemic, Eswatini

Dekova R et al. IAS Virtual July 2020 Abs. OAXLB0103

- Oral HIV self-tested piloted in 2017, and STAR project began to evaluate; testing scale up in 2019 multiple implementing partners and in facilities.

- National lockdown due to COVID-19 March 28; non-essential business closed; pharmacies, health care facilities and food stores open.

- Community HTS paused as HIVST kit distribution channels inaccessible and few clients accessing health facilities.

- MOH recommended community distribution of HIV self-test kits in community by HTS counselors using only pharmacies and shops as channels for distribution.
HIV-Self Testing During the COVID Pandemic, Eswatini

Dekova R et al. IAS Virtual July 2020 Abs. OAXLB0103

- HIV self-testing ↑ post lockdown and community distribution; males as well as females

**April-May 2020**

- 49% were males
- 17% of those reached had never tested for HIV in past, highest among males.

- Follow-up calls after test distribution April-May 2020
  - 89% used the test kit
  - 3% (151) were HIV+
  - Of the 151 HIV+, 45% were new diagnoses, 59% started on ART as of May

**Concluded**
- HIVST playing important role in normalizing testing, decreasing stigma and creating demand.
- Enabled reaching clients wouldn’t normally through standard targeted testing.
PEPFAR Countries Adapting Increase in Multi-Month Dispensing (MMD) of ART During COVID-19 Pandemic

O’Keefe M et al. COVID-19 IAS Virtual July 2019 Track C

→ Rapid evaluation of MMD policies in 37 PEPFAR countries before and after COVID-19 pandemic.

Prior to COVID 19, ~one-third persons on ART (5/15 million) had adopted ≥ 3-month MMD.

Prior to COVID-19 children were excluded from MMD more frequently than adults; participation was 22% if <15 years compared to 38% adult men and 35% adult women.

Number of Countries Permitted ≥3Mo MMD by Patient Group Before and After COVID-19

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Breastfeeding women</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>Children &lt;10</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>Adolescents 10-19</td>
<td>14</td>
<td>26</td>
</tr>
</tbody>
</table>

→ Policies before COVID excluded MMD in pt with TB treatment, children, adolescents and pregnant and breastfeeding women

→ Significant expansion MMD in the during COVID-19 pandemic

→ As of June 2020, 24/37 (65%) of countries have modified MMD policies due to COVID-19

→ Recommend maintaining the expanded MMD after COVID-19 for benefit of both patients and health system efficiency
Drop in PrEP Retention and Persistence During COVID-19 Lockdown

Davey DJ et al. IAS Virtual July 2020 Abs. LBPEC24

- Cohort of 422 HIV-negative pregnant and postpartum women recruited at 1\textsuperscript{st} ANC visit in primary care clinic in community with high HIV prevalence Cape Town South Africa, Aug 2019-May 2020 (median age 25 yr, median GA 21 wk).
- 91\% (n=382) started PrEP at 1\textsuperscript{st} ANC.
- Compared retention and persistence on PrEP at 1 & 3 mos before (through Mar 26 2020) and during lockdown (Mar 27-May 15 2020)

\[ \rightarrow 33\% \text{ decrease in retention and study refills after lockdown; 2.4-fold } \uparrow \text{ odds missing study visit during lockdown} \]

| Table. Retention in PrEP in pregnancy study before COVID-19 lockdown and during lockdown, Cape Town, South Africa (n=414 women on PrEP) |
|---|---|---|
| 1m visit | 3m visit |
| | | |
| Pre COVID lockdown (Aug-Mar 27, 2020) | 207 | 84 | 71\% | 113 | 60 | 59\% |
| During lockdown (Mar 28-Jun 1) | 19 | 32 | 37\% | 51 | 62 | 45\% |
| Total retention | | | | | | |
| Pre-COVID lockdown | 340 | 201 | 63\% |
| During lockdown | 110 | 152 | 42\% |

Implications and Next Steps

- Barriers to accessing facility-based maternal PrEP services existed prior to lockdown (esp. in postpartum women).
- Maternal PrEP programs may require differentiated care to optimize maternal PrEP use, including:
  - Community-based or home PrEP delivery
  - SMS reminders
  - Telephonic phone adherence counselling
- Maternal PrEP differentiated care should be considered during and following the COVID-19 lockdown

\[ \text{Commonly cited barriers to study attendance included (during telephonic interviews):} \]
\[ \text{=} \text{Fear of COVID infection (for self/infant),} \]
\[ \text{=} \text{Fear of police,} \]
\[ \text{=} \text{Limited transportation or funds for transport and} \]
\[ \text{=} \text{Long queuing at facility} \]
Declining Trends in Maternal and Child Health Service Use During COVID-19 in Guatemala

Endyke-Doran C et al. COVID-19 IAS Virtual July 2019 Track x

→ Management Science for Health project start 2019 to promote group ANC for Mayan women in Quetzaltenango, Guatemala; with COVID-19 restrictions no longer able to bring together groups but encourage to continue prenatal care

→ With MOH, evaluated key maternal and child service use data Feb-May 2020 and 2019

→ 21% drop in women having ≥1 ANC visit in March 2020 vs 2019 and 29% drop in April 2020 vs April 2019

→ 54% drop in women having attending postpartum care in April 2020 vs 2019

→ 7% drop in children receiving 3rd DPT booster in 2020 vs 2019 in 10 health facilities
COVID-19 Treatment – Pregnant Women and Children
Remdesivir Compassionate Use in 86 Pregnant and Postpartum Women with Severe COVID 19

Burwick R et al. COVID-19 IAS Virtual July 2019 Track B

93% of pregnant women and 89% of PP women recovered

Highest rate improvement in pregnant women not needing mechanical ventilation vs women needing mechanical ventilation

86 women, 67 (78%) pregnant, 19 postpartum

More postpartum women needed invasive support

64% had >1 comorbidity

Deliveries were early (57% at <32-wk gestational age), and mostly by CD (82%) and emergent CD (86%) due to the severity of COVID-19 illness

No new safety signals were identified: the most common AEs were due to underlying disease and most laboratory abnormalities were Grades 1–2
- There was 1 maternal death unrelated to RDV (ARDS, cytokine storm) and 1 17-wk miscarriage (methicillin-sensitive Staphylococcus aureus endocarditis/sepsis, including septic joint)
Remdesivir Compassionate Use in 77 Children with Severe COVID 19
Chiltos K et al.  COVID-19 IAS Virtual July 2019 Track B

Clinical recovery in 80% children on ventilators/ECMO and 87% not on invasive oxygen support

Recovery similar all age groups (may be better >12 years but more children with COVID-19 were >12 years to begin with)

4 deaths (5%) (reported as due to COVID in 2, multiorgan failure 1, brain herniation 1)

No new safety concerns

Mild transaminase elevations, most Grade 1 or 2, rarely required drug dc

→ 77 children, 51% requiring ventilation
→ Primarily older children (53% >12 yr)
→ 79% had existing medical condition, most common neurologic/genetic, obesity 13%
Issues Related to Potential SARS-CoV-2 Mother-to-Child Transmission
Prospective study of women with confirmed COVID-19 admitted to Milan hospital; assessed presence of SARS-CoV-2 in blood, vaginal and rectum.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
<th>Type specimen</th>
<th>SARS-CoV-2 PCR Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive NP swab</td>
<td>62</td>
<td>Plasma (n=53)</td>
<td>2/53 (4%) – both 3rd trimester pregnant women, 1 critical (vent), 1 severe (sub-ICU)</td>
</tr>
<tr>
<td>Non-pregnant women</td>
<td>6</td>
<td>Vagina (n=60)</td>
<td>0/60</td>
</tr>
<tr>
<td>Pregnant</td>
<td>56</td>
<td>Rectum (n=44)</td>
<td>11/44 (25%) 45% with positive rectal swab had GI sx during hospitalization</td>
</tr>
<tr>
<td>1st trimester</td>
<td>4</td>
<td>Newborn NP swab (n=45)</td>
<td>0/45</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd trimester</td>
<td>46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mode delivery</td>
<td>Vaginal 31, CS 14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

→ 56 pregnant women: 20 aSx, 13 mild, 16 moderate, 6 severe, 1 critical
→ 6 non-pregnant women: 2 milk, 3 moderate, 1 severe

Viremia rare and only in severely ill women
No virus in vaginal secretions but 25% in rectal sample
No evidence infant infection
31 pregnant women with COVID-19 third trimester evaluated for possible MTCT
- 14/31 positive CXR, 4 severe disease
- 25 (81%) vaginal delivery (6 induced due to COVID), 6 cesarean (3 for severe maternal COVID)
- 1 PTD; 1 low Apgar scores, 2 NICU admission
Of 31 infants born to mother with COVID-19:

- **Possible in utero infection, 2 infants**

  → Preterm infant (34 wk), vaginal: **maternal viremia**, IgM/G antibody; positive vaginal/placental swab; **infant viremia**, no IgM but +IgG Ab (from mother); infant had + NP PCR delivery but **negative at 1 wk**; **no sx or abnormal lab**.

  → Term, vaginal: mild maternal disease; negative virus maternal blood, vaginal/placental swab and infant blood but **SARS-CoV-2 IgM antibody** in neonatal blood; infant has + NP PCR at delivery, **negative 3 d**; **no sx or abnormal lab**.

- SARS-CoV-2 viremia found in another mother with severe disease, but negative vaginal/placenta/umbilical/infant specimens, infant negative NP PCR, no symptoms.
Of 31 women
- 1/11 breast milk samples positive rtPCR and IgM (not IgG) antibody

Mother with severe disease but no virus blood, vaginal/placental swab, infant specimens but breast milk + PCR for virus and IgM antibody. Infant negative NP at birth, no symptoms, no abnormal lab.

Placentas of 3 women including cases prior slide examined; “altered inflammatory profile gene expression” reported – but was strongest in woman with no viral detection in placenta with IgM+ infant.

Cytokine studies in 3 mother-infant pairs found “hyper-active inflammatory profile” in both maternal and infant blood (however, could be transplacental maternal-fetal cytokine transfer).
SARS-CoV-2 Secretory IgA Response in Human Milk Following COVID-19 in Lactating Women

Powell RL. COVID-19 IAS Virtual July 2019 Track A

- Compared milk from 15 breastfeeding women recovered from COVID-19 (8 confirmed, 7 suspect) to repository of milk from 10 women prior to pandemic.
- 13/15 were infected postpartum, and 87% were >1 mo postpartum (1-32 mos).
  → All milk samples from COVID-19 recovered donors contained significant levels of SARS-CoV-2 specific IgA, while all controls were negative; not necessarily correlated with presence SARS-CoV-2 specific IgG.
  → 80% of milk samples from COVID-19 recovered donors had IgA and secretory antibody reactivity against SARS-CoV-2 spike receptor binding domain vs none control.

- Unclear if this would provide protection for breastfed infants; need larger sample size and long-term FU to better understand SARS-CoV-2 immunity in milk.
Potential SARS-CoV-2 Mother-to-Child Transmission

### Intrauterine Infection
- Viremia rare in mother (<3%)
- Virus rare in amniotic fluid

### Perinatal Infection
- Vaginal secretions rarely positive
- Vaginal delivery = potential viral exposure in maternal feces (~40%)
- Potential exposure to maternal respiratory secretions after birth

### Breast Milk Infection
- Virus rarely found in milk
- When found appears transient
- SARS-CoV-2 IgA and IgG may be present in milk

### Placental Infection
- May be more likely in mothers with severe COVID-19
  - Higher prevalence viremia
  - More likely placental barrier disruption due to thrombosis
- Placenta, amniotic fluid, and/or neonatal blood viral test positive

### Intrapartum or horizontal transmission possible, but seems uncommon
- Exposure to maternal fecal virus or virus in respiratory secretions most likely source
- Most infants no symptoms

**Blumberg DA et al, Am J Perinatol 2020 Jun 5**
Summary

- While COVID-19 mitigation interventions have had unwanted negative consequences, there are lessons to be learned that may improve HIV programs in the future.
- It is encouraging that new treatments are being studies in pregnant women and children more rapidly than previously.
- SARS-CoV-2 mother-to-child transmission may occur but in utero infection likely rare, and transmission in the peripartum period (including horizontal transmission) more likely.
- Breast milk may rarely have SARS-CoV-2 virus detected by PCR but infectivity unclear; milk also contains antibody to SARS CoV-2 but protective aspects are unclear.
Questions?

THANKS FOR YOUR ATTENTION
PLEASE CLAP AND DO NOT ASK TOUGH QUESTIONS

Sometimes I question my sanity
Occasionally it replies

THANK YOU FOR YOUR ATTENTION
ANY QUESTIONS SEARCH IN GOOGLE

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