IAS 2022 & Pediatric HIV Workshop
Selected PMTCT, Pediatric, Adolescent, and Maternal/Adult Abstracts

Lynne M. Mofenson MD
8/17/2022
Update on Epidemiology of Pediatric HIV 2022

International Workshop on HIV & Pediatrics 2022
ART Coverage in Pregnant Women Was 81% in 2021 – A Slight Decline Since Peak of 83% in 2019

→ 81% of pregnant women with HIV received ART in 2021.

→ No meaningful increase in pregnant women ART coverage since 2014!

Regional differences: West/Central Africa coverage only 60% 2021; 43% of pregnant women not on ART from this region

Source: UNAIDS epidemiological estimates 2022: aidsinfo.unaids.org
Minimal Decline in New Pediatric Infections in 2021

Maternal ART and New Infections in Children Globally, 2010-2021

160,000 new pediatric HIV infections estimated in 2020

Minimal change in new infections since 2015 – either no change or only 10,000 decline/year

If assume only 10,000 decline/year, will take 14 years (2035) to meet our 2020 target of 20,000 new infections

Source: UNAIDS epidemiological estimates 2022: aidsinfo.unaids.org
Causes of New Child Infections Globally 2021

Primary gaps in PMTCT globally in 2021:

- Globally 75,000 new child infections still occur because pregnant women are not diagnosed and started on treatment
- Regional (and country) differences:
  - Almost half of those not receiving treatment are in west/central Africa
  - Over half of the incident infections that lead to vertical transmission are in east/southern Africa

Source: UNAIDS epidemiological estimates 2022: aidsinfo.unaids.org
Early Infant Diagnosis Declined Slightly Globally from 63% in 2020 to 62% in 2021

→ Globally, 62% of infants had EID by 8 week in 2021, a slight decrease from 63% in 2020

→ EID in west/central Africa remains at 25%, having actually decreased between 2019 and 2020

→ EID in east/southern Africa is 71%, but this is a slight decrease from 74% in 2020
ART Coverage in Children in 2021 Has Not Improved; Consistently Lower ART Coverage in Children vs Adults

- ART coverage in children 0-14 years **remain 52%**, consistently lower than in adults which increased to 76% from 74% in 2020.

- 60% of children **not** on ART are **aged 5-14 years**

- EID is not enough; need for home-testing and/or self-testing to identify older children living with HIV
Despite New, More Potent ARV Availability, Decline in Deaths Among Young People Age 15-24 Years Has Slowed

- AIDS-related mortality in adults continues to decrease, higher in males than females
- AIDS-related mortality in young people has minimal decline since 2013, higher in females than males
Pediatric ART Optimization, DTG Transition & VL Implementation Data
Good Viral Suppression on Children on DTG ART in Africa

Bacha J et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 4; AIDS 2022 Abs.OAB0202

- Retrospective review from 7 BIPAI sites in 6 countries on 11,799 enrolled in care and prescribed DTG ART
  - Majority $\geq$10 years (3% 0-<5; 18% 5-<10; 40% 10-<15; 40% 15-<20)
  - Most ART-experienced (naïve 21%; switch NNRTI 44%; switch PI 34%; 3rd line 1%); **95% virally suppressed (<1000) at baseline before DTG**
  - Mean FU on DTG ART 22.4 months (SD 12.4 months); VL results ranged from 6-60 months post DTG ART – however, sample size at $>$24 mo FU limited (only show results to 24 mo)

- No real difference in suppression by sex, age group, or NRTI backbone

<table>
<thead>
<tr>
<th>Cohort of CALHIV</th>
<th>VLS rate after SDS with DTG by chronological VL test among previously unsuppressed cohort</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>First post-DTG VL</td>
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<tr>
<td>All CALHIV</td>
<td></td>
</tr>
<tr>
<td>(n=210, 5.5%)</td>
<td>79.9% (115/144)</td>
</tr>
<tr>
<td>ABC-based SDS</td>
<td>80.0% (76/95)</td>
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<tr>
<td>(n=141, 6.4%)</td>
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<tr>
<td>AZT-based SDS</td>
<td>83.3% (10/12)</td>
</tr>
<tr>
<td>(n=18, 3.6%)</td>
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<tr>
<td>TDF-based SDS</td>
<td>78.4% (29/37)</td>
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<tr>
<td>(n=51, 4.6%)</td>
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</tbody>
</table>

- Limited numbers but suppression in ~80% maintained over time, no difference by NRTI backbone
Shifting from PI-Based ART to DTG-ART Achieves and Maintains Viral Suppression

Bacha J et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 21; AIDS 2022 Ab)AB0203

- Retrospective review from 7 BIPAI sites in 6 countries on 1,475 children enrolled in care and optimized from PI- to DTG-based ART
  - Median age 14.0 year (range 3.6-19.9 years)
  - Time on PI (72% LPV/r, 28% ATV/r) ART prior to switch to DTG 9.8 years
  - Suppression (VL <1,000) on PI ART 88.9%
- FU on DTG 212 days (7-1017 days); post-DTG VL suppression 89.8%, with no difference by PI
- 118 youth were unsuppressed on PI; 68% suppressed after switch to DTG
- VL suppression was lower for both PI and DTG ART in females and adolescents 15-19 years
  - Switch from PI to DTG ART effective at maintaining and achieving viral suppression.
  - Continued attention to support females and older adolescents needed.
Transition to DTG-Based ART is Associated with Sex and Viral Load Access in West African Children and Adolescents

Desmonde S et al. International Pediatric HIV Workshop, Montreal Jul 2022, Abs. 22

- Evaluated transition to DTG-based ART among 2,787 children/youth aged 0-24 years on ART with ≥1 visit since 2019 in 7 clinics contributing to the pediatric IeDEA West African cohort.

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Transitions to DTG Since 2019

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<tr>
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<tbody>
<tr>
<td>CIF (%)</td>
<td>2.6</td>
<td>23.2</td>
<td>43.8</td>
</tr>
<tr>
<td>95% CI</td>
<td>[2.0 – 3.2]</td>
<td>[21.5 – 24.9]</td>
<td>[41.2 – 46.2]</td>
</tr>
</tbody>
</table>

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Factors Associated with DTG Transition

- Sex: Male/female: 2.19, 95%CI [1.91-2.40]
- Access to viral load: RR for DTG transition (ref: VL<500 copies/mL)
  - VL >500 copies: 1.08, 95%CI [0.92-1.27]
  - No VL: 0.41, 95%CI [0.35-0.48]

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Slow transition to DTG; 44% by June 2021.

Access to DTG associated with male sex (pregnancy concern?); access to VL testing; age >5 yrs (later DTG formulation availability for <5 yrs) and being on 2nd line ART.
Uptake of RAL Granules in Newborns Diagnosed with HIV in Zimbabwe During COVID-19 Pandemic

Denoend-Ndam L et al. AIDS 2022, Montreal, Canada, Abs. EPB203

- RAL granules introduced in 14 health facilities with capacity for POC HIV birth testing in Zimbabwe; HCW were trained on RAL use and caregiver counseling on preparation/administration of RAL.
- Study population included all infants exposed to HIV born at project sites from June 2020- June 2021
  
  Lower than expected birth testing uptake and RAL usage observed
  - Inconsistent supply chain POC EID testing cartridges, RAL granules, ped AZT/3TC
  - Shortage of trained healthcare workers due to strikes and high staff turnover
  - Documentation gaps of data points not recorded or not maintained in registers
  
  → Need to address health systems gaps for supply chain; staffing (training, retention, mentorship, supervision); and ability to track newborns and maintain documentation of weight and RAL dosing

- 59% infants started on RAL ART; started earlier than those starting other ART regimens (4 vs 6 d)
- Day 28 (when switch to non-RAL ART recommended) available for 85% of 27 started on RAL – 18 (78%) switched to non-RAL ART as recommended
- Weight check for dosing did not appear to be done often (7 d, 37%; 28 d, 22%)

Point-of-care birth testing, ART initiation, and RAL treatment cascade; N=6989 neonates exposed to HIV in 14 health facilities in Zimbabwe.

13 Infants NOT initiated on ART
- AZT/3TC out of stock 4
- No record available 4
- Transferred for ART start another facility 2
- Died day birth before start 1
- Mother disappeared before start 1
- Pharmacy closed 1

ART regimen initiated in HIV+ neonates
- AZT/STC + RAL
- AZT/STC+NVP
- AZT/STC + LPV/r
- ABC/STC + LPV/r
- ABC/STC + DTG

58.7% of neonates initiated on ART received RAL-based regimens

N=6989 neonates exposed to HIV in 14 health facilities in Zimbabwe.
Evaluated viral load testing in >40,000 HIV+ children age <5 years in 2019, 2020 and 2021 in 11 countries with >500 children on ART at USAID-supported sites at middle 2021 (and hence eligible for VL testing by end 2021).

Coverage lower in children age <5 yr than adults in all 3 years

Coverage by country and age show significant variation

General VL testing barriers identified in countries:

- **Patient factors** including reduced clinic attendance due to COVID, distance/transport/poverty/stigma, poor treatment literacy re: VL monitoring
- **Health facility performance challenges** such as missed opportunities for testing, form completion errors, phlebotomy errors; staffing
- **Specimen transport problems** such as fuel cost, security issues, COVID disruption
- **Shortages & stock-out** reagents, other VL commodities
- **Lab challenges** such as equip malfunction; staff shortages; power outages; sample backlog
- **Information systems issues** such as problems with lab/clinic interface; internet downtime; data lost; lack data entry EMR
Examples of Country Facilitators of VL Testing in Children
Frost K et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 19

Community VL Sample Collection Helps Improve Access
- COVID led to rapid expansion of community and home-based services, including community VL sample collection
- VL sample collection is done via home visits and visits to other community locations
- Samples (blood or DBS) collected by clinical staff, CHW or OVC providers

OVC Case Managers & Other Community Workers Help to Reduce Patient Barriers and Improve Access
- ~70% (range 28-91%) of CLHIV <5 yr on ART in these 11 countries are currently enrolled in OVC programs
- OVC services continue to evolve with stronger facility-community integration and services

Point-of-Care Testing to Reduce Turn-Around Time For Results
- Several countries have been rolling out POC VL testing for pregnant/BF women and now extending to children – at least 10 countries plan to implement in 2023
- POC VL requires venous blood (not DBS) so plans need to include pediatric phlebotomy supplies when implementing

Optimize Family-Centered DSD and MMD Models to Improve Access and Convenience
- COVID led to rapid expansion DSD and MMD models including in children
- Family-centered DSD models including VL testing implemented in Kenya1, Nigeria2, South Africa3, showing improved coverage and viral suppression children

Simplify Pediatric Sample Collection with Better Phlebotomy Supplies and/or DBS
- Pediatric phlebotomy supplies for venous blood collection (>4 countries): butterfly needles and small EDTA tubes
- DBS sample collection (>8 countries): easier to collect than venous samples in infants, young children

→ Despite increased risk of morbidity & mortality, children age <5 years are substantially less likely than adults to receive VL testing.
→ There are several promising strategies being tested to improve VL testing among young children
→ Tracking of the speed, coverage and fidelity of the scale-up of these key interventions is critical to access success and impact.
Pediatric HIV Disease Course in the ART Era
EARTH-EPIICAL cohort of 212 HIV+ infants started on ART age <3 months in Mozambique, Mali and South Africa, being followed to age 4 years.

Pneumonia 6/12 (50%)
Diarrhea/Malnutrition 3/12 (25%)
Tuberculosis 2/12 (17%)
Neuromalaria 1/12 (8%)
Pneumonia 3/11 (27%)
Unknown 1/11 (27%)
Sepsis 2/11 (18%)
Severe immune suppression 3/12 (25%)
AIDS-defining disease 9/12 (75%)
Febrile Seizure 1/12 (9%)
Diarrhea 1/11 (9%)

23 patients (10.8%) died
- at 1 year = 11% (CI95%, 6 to 15)
- at 2 years = 12% (CI95%, 7 to 17)

Due to AIDS-related causes = 5.7%
Due to non-AIDS related causes = 1.4%

Mortality in African Infants Starting ART at Age <3 Months

Brehin C. International Pediatric HIV Workshop, Montreal July 2022, Abs.15; AIDS 2022 Abs.OAB0205
Used data from tracing and linkage studies in Southern Africa to correct mortality for LTFU in children receiving ART

- LTFU: No visit for >180 d and no recorded death or transfer
- True LTFU: Traced/linked & not found or known deceased

### Tracing Cohort
Tracing done on stratified random sample of clinic participants

- N=972
- N=171 (18%) File not found, can’t be traced
- N=121 (12%) Documented transfer
- N=680 (70%) Tracing by text, phone, home visit
- N=218 (32%) Tracking unsuccessful

### Linkage Cohort
Unique patient IDs used to assess if a patient lost at one site has any linkage to another; National death register to ID deaths

- Logistic and GAM models predicted probability of being included in tracing sample and found by tracer
- Inverse probability weights assumes that those found represent all of whom were traced & not found/ traced; patients not lost given weight of 1

- 1,456 recorded as LTFU
- Of these, 72% could be linked
- Of these, 898 (65%) vital status ascertained
Mortality in Children and Youth on ART Who Are Lost-to-Follow-Up in Southern Africa: Linkage vs Tracing

Nyakato P et al. AIDS 2022, Montreal, Canada, Abs.OAC0304

→ Mortality was 2-2.5 times higher with additional outcomes in those LTFU
→ Linkage and tracing results were similar
→ Program level mortality in HIV+ children is underestimated without additional ascertainment
HIV Testing and Case Finding
National Implementation of Validated Pediatric HIV Testing Eligibility Screening Tool and Expansion of Index Testing, Uganda

Mabirizi D et al. International Pediatric HIV Workshop, Montreal July 2022, Abs.16

- Analyzed HIV testing data for 3,283 PEPFAR-supported sites in Uganda, pre-HRAT (2019) and post-HRAT+expanded index testing (2021) to explore changes in testing in children age 1-14 yrs; number needed to test (NNT) to identify one new child with HIV calculated

- **All Testing Modalities**
  - Ped testing ↓ by 13%
  - HIV diagnosis ↑ 1.8%
  - NNT ↓ from 55 to 47

- **Outpatient Testing**
  - Ped testing ↓ by 8.5%
  - HIV diagnosis ↑ 46.9%
  - NNT ↓ from 54 to 40

- **Index Testing**
  - Ped testing ↑ by 89.6%
  - HIV diagnosis ↑ 41.6%
  - NNT ↑ from 35 to 46

- Use of validated HRAT and ↑ index testing can ↑ pediatric HIV testing and case identification among children with the highest risk, especially in high volume, low HIV prevalence settings

- Use of HRAT resulted in significant reduction in NNT, making OPD testing slightly more efficient than ped index testing (NNT 40 vs 46)
Pediatric HIV Risk Screening Tool Evaluation in Uganda, Tanzania, Malawi

Machekano R et al. International Pediatric HIV Workshop, Montreal July 2022, Abs.17

- Evaluated performance of Zimbabwe HIV Risk Screening Tool (Z-HRST) in Uganda (n=3482, 1.6% HIV+), Tanzania (n=14,812, 0.4% HIV+) and Malawi (n=9245, 0.8% HIV+); evaluate alternative tools selected through machine-learning approaches (training set and validation set data)
- Testing performance varied between countries
- Selected optimal tool based on 3 questions:
  1. Child had growth problems (adolescents: Child sickly in last 3 months)
  2. >1 biologic parent/sibling HIV+ (or unknown status)
  3. Recurring skin problems

- However, tool had poor discrimination for older adolescents (15-19 yrs)

- Including maternal HIV status ↑ sensitivity

- Variable sensitivity of tool based on HIV prevalence in country
- Tool more beneficial for ID in children <15 yr than adolescents
- Performance was better in OPD than in community settings
Caregiver-Assisted Oral HIV Screening of Children Age 18 Months-14 Years, Uganda and Zambia

Stecker CC et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 18

- Evaluated acceptability, feasibility and effectiveness of implementing caregiver-assisted oral fluid-based HIV screening for children as part of index testing for HIV+ adults in cross-sectional cluster sampling design, 32 facilities in 16 districts Uganda, 15 facilities in 2 provinces Zambia

**Acceptability**
- 96.8% (3931/4059) of eligible index parents/caregivers accepted oral test kits
- 7593 test kits sent home; 97.6% (7413) children tested and returned results

**Feasibility**
- 1.6% (119 children) had reactive oral test kit result
- 97.5% (116 children) completed blood-based testing at facility
- ↓ need for facility-based testing by 98.4%

**Effectiveness**
- 43/116 (37.1%) of children confirmed HIV+
- 97.7% (42/43) children had same-day ART initiation
- 0.4% of children had minor reaction to oral test kit

→ New acceptable/feasible addition to HIV testing “tool kit” for identification of HIV+ children

→ Can help decongest facilities
HIV Self-Testing Models: STAR III, Nigeria

Adepoju A et al. AIDS 2022, Montreal, Canada, Abs.OAE0103

→ HIVST distribution is acceptable & feasible across diverse settings, populations, and age groups in Nigeria, & reach high risk persons not tested previously

→ Positivity rate optimized by one-stop shops serving key populations

→ Achieving high result return possible enabling support/linkage based on result

→ Lower rates of confirmatory testing and LTC with pharmacy distribution warrants further exploration
Implications for Programming – Paediatric HIV

• EARLY ART with DTG as FIRST LINE must be scaled up urgently
  – Field experience confirms DTG working well even for kids switching from PI 1st line
  – DTG levels not affected by food in children (unlike adults)
  – Even in infants treated as early as 3 months, mortality is highest in first 6 months
  – DSD called for, especially among older adolescents 15-19 years

• VL TESTING COVERAGE NEEDS TO IMPROVE
  – VL testing less accessible to children especially those below 5 years.
  – DTG switch provides an opportunity to increase access to VL testing for children
  – Other promising strategies – community VL test collection and POC

• FIND THE CHILDREN USING MULTIMODAL APPROACHES!
  – Supported Oral HIV self tests are widely accepted and have been used as home-based tests for index testing to identify children
  – Risk assessment tools are reducing costs and increasing case finding
Pregnancy, ARV Drugs and Infant Outcomes
Pregnancy Outcomes with DTG vs EFV in 5 Clinical Trials

Hill A et al. AIDS 2022, Montreal, Canada Symposium 7/30/22

→ Meta-analysis of 1,074 pregnancy outcomes from DolPHIN-1 (PK), DolPHIN-2 (DTG vs EFV late pregnancy), IMPAACT 2010/VESTED (DTG vs EFV after 1st trimester), and pregnancies in ADVANCE and NAMSAL trials

→ No significant differences overall in risk of stillbirth, neonatal death or MTCT rates between DTG and EFV arms

→ Some differences in outcomes btn trials – in DolPHIN-2 non-significant trend for more stillbirths and neonatal death on DTG arm while in VESTED non-significant trend for more stillbirths and neonatal deaths on EFV

→ 5 cases of MTCT DTG (4 with early + test [day 2-5], 1 with only 3 wk DTG duration = all in utero) vs 1 case EFV (breastfeeding)
Cohort study 23 sites in Kenya identified 198 women receiving DTG periconception between Jul 2017-Jul 2019, matched to 392 women receiving EFV periconception, matched by age, LMP and facility type.

Adverse outcomes were common (>25% of births) both DTG and EFV.

No significant differences adverse pregnancy outcome between periconception DTG vs EFV, and no NTD identified.

No NTD either group; 1 case cleft lip/palate EFV exposure.
Data from Belgium, France, Italy, Poland, Portugal, Spain, UK, Ukraine, and Canada on women who received DTG-based regimen during pregnancy.

Analysis included 138 DTG-exposed pregnancies
- 92 exposed to DTG 1st trimester; 77 of these had preconception exposure
- 16 miscarriages/abortions and 2 stillbirths (all 1st trimester exposure)
- 131 live births (8 multiple pregnancies)
- No difference LBW, VLBW, PTD, VPTD by trimester
- 5 birth defects seen (none in stillbirths) (No NTD)
  - ASD
  - Small umbilical hernia
  - Cutaneous hemangioma
  - Left hydronephrosis
  - Suspicion pelvicalyceal system enlargement
- No significant difference birth defects 1st vs 2nd/3rd trimester exposure

<table>
<thead>
<tr>
<th></th>
<th>Any Trimester</th>
<th>1st Trimester</th>
<th>2nd-3rd Trimester</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnancy outcomes</strong></td>
<td>N=138</td>
<td>N=92</td>
<td>N=46</td>
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</tr>
<tr>
<td>Induced abortion</td>
<td>7/138 (5.1%)</td>
<td>7/92 (7.6%)</td>
<td>0/46</td>
<td>0.095</td>
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<tr>
<td>Spontaneous abortion</td>
<td>9/138 (6.5%)</td>
<td>9/92 (9.8%)</td>
<td>0</td>
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<tr>
<td><strong>Birth outcomes</strong></td>
<td>N=133</td>
<td>N=85</td>
<td>N=48</td>
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<tr>
<td>Stillbirth</td>
<td>2 (1.5%)</td>
<td>2 (2.4%)</td>
<td>0</td>
<td>0.535</td>
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<tr>
<td>Live birth</td>
<td>131 (98.5%)</td>
<td>83 (97.6%)</td>
<td>48 (100%)</td>
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<tr>
<td>LBW</td>
<td>20/116 (17.2%)</td>
<td>10/69 (14.5%)</td>
<td>10/47 (21.3%)</td>
<td>0.453</td>
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<tr>
<td>VLBW</td>
<td>5/116 (0.9%)</td>
<td>2/69 (2.9%)</td>
<td>3/47 (6.4%)</td>
<td>0.394</td>
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<td>PTD</td>
<td>20/116 (17.2%)</td>
<td>10/69 (14.5%)</td>
<td>10/47 (21.3%)</td>
<td>0.453</td>
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<td>VPTD</td>
<td>5/116 (4.3%)</td>
<td>2/69 (2.9%)</td>
<td>3/47 (6.4%)</td>
<td>0.394</td>
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<tr>
<td>Birth defect live birth</td>
<td>5/131 (3.8%)</td>
<td>4/83 (4.8%)</td>
<td>1/48 (2.1%)</td>
<td>0.652</td>
</tr>
<tr>
<td>Birth defect stillbirth</td>
<td>0/2</td>
<td>0/2</td>
<td>0/0</td>
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</tr>
</tbody>
</table>
Surface birth outcomes surveillance by trained hospital midwives at sentinel sites in Botswana, covering 70% all births in country.

Between August 2014 and March 2022, 224,251 deliveries occurred at study sites, of which 223,797 (99.8%) had evaluable infant surface examination.

- 9,460 exposed to DTG from conception
- 23,664 exposed to non-DTG ART from conception (14,432 to EFV)
- 6,551 started DTG during pregnancy
- 170,723 born to women without HIV

156 neural tube defects identified (100 with photo, 56 description only)

- DTG from conception: 10 NTD/9,460 births (0.11%; 95% CI 0.06-0.19%)
- Non-DTG from conception: 25 NTD/23,664 births (0.11%; 95% CI 0.07-0.16%)
- EFV from conception: 11 NTD/14,432 births (0.08%; 95% CI 0.04-0.14%)
- DTG during pregnancy: 4 NTD/6,551 births (0.06%; 95% CI 0.02-0.16%)
- Women without HIV: 108 NTD/170,723 births (0.07%; 95% CI 0.05-0.08%)

<table>
<thead>
<tr>
<th>Exposure vs Comparison Groups</th>
<th>Prevalence Difference (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>DTG conception vs non-DTG conception</td>
<td>0.00 (-0.07, 0.10)</td>
</tr>
<tr>
<td>DTG conception vs EFV conception</td>
<td>0.03 (-0.05, 0.12)</td>
</tr>
<tr>
<td>DTG conception vs DTG during pregnancy</td>
<td>0.04 (-0.06, 0.14)</td>
</tr>
<tr>
<td>DTG conception vs Women without HIV</td>
<td>0.04 (-0.01, 0.13)</td>
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The prevalence of NTD in infants born to women on DTG at conception has declined slightly to 0.11% and does not substantially differ from other exposure groups.
Prevalence of Adverse Birth Outcomes and External Birth Defects Among Women Living with HIV in Malawi

Smith-Sreen J et al. AIDS 2022, Montreal, Canada, Abs.OAC405

- Implemented Tsepamo-like data collection for birth defect surveillance at 4 high volume delivery sites in high HIV prevalence districts in Malawi.
- Data for Dec 2016-Dec 2021 excluding COVID suspension period Jun 2020-Jun 2021 (Note: not yet analyzed by specific maternal ART regimen or timing).
- 173,618 births; 10% (17,410) to HIV+ women; 17,079 on ART, 331 not on ART

Rate of PTD and LBW highest among HIV+ women not on ART, demonstrating importance of testing and early ART in HIV+ women

Rate of PTD and LBW slightly higher among HIV+ women on ART than HIV-negative women

688 defects, overall prevalence 38.5/10,000 (0.39%)
Most common: clubfoot 0.172%; hypospadias 0.076%; NTD 0.057%

Non-significant defect ↑ in HIV+ women on ART vs HIV-negative women
- Overall defects, prevalence ratio HIV+ is 1.23 (95% CI 0.96-1.6), 0.078
- NTD prevalence ratio HIV+ is 1.65 (95% CI 0.95-2.9), p=0.076
Prenatal PrEP and Growth/Neurodevelopment in Kenyan Infants at 24-36 Months

Gomez L et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 12; AIDS 2022 Abs.OAC0502

No differences in growth or neurodevelopment between children with and without prenatal PrEP exposure

Support safety of PrEP use in pregnancy

Child Growth Indicators

- Median (IQR) for Weight and Length
- % with Underweight or Stunting

Child Neurodevelopment Indicators

- ASQ-SE score
- Abnormal score

PrEP exposure during pregnancy

Characteristic

Maternal age, years
Child age, months
Currently married
Maternal education, years
Number of living children
Preterm birth
Partner known to be living with HIV

Median (IQR)

- Any (n=119)
- None (n=545)

Adjusted Coeff (95% CI)

P-value

Association:

- Adjusted for maternal age, partner HIV status, syphilis diagnosis in pregnancy, and gestational age at birth, and clustered by site
- Among n=449 30-month visits with socio-emotional development data
- Among n=278 36-month visits with socio-emotional development data

Prenatal PrEP exposure not associated with any adverse growth outcomes at 24-36 months

Prenatal PrEP exposure not associated with adverse developmental outcomes at 30-36 months
Low Birth Weight is More Common in HIV+ than HIV-Uninfected Women Even in the Universal ART Era

Zotova N et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 25

- Using data from Central Africa International Epidemiology Database to Evaluate AIDS (CA-IeDEA) sites in Rwanda, evaluated birth outcomes among all women who gave birth 2012-2020 at these sites.

### Pregnancy Outcome by HIV Status

![Graph showing pregnancy outcomes by HIV status]

### Factors Associated with LBW

<table>
<thead>
<tr>
<th>HIV status</th>
<th>N</th>
<th>OR (95% CI)</th>
<th>aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>9,473</td>
<td>1.35 (0.98, 1.89)</td>
<td>1.47 (0.85, 2.56)</td>
</tr>
<tr>
<td>Positive</td>
<td>1,006</td>
<td>2.61 (1.31, 5.19)</td>
<td>2.07 (0.88, 4.87)</td>
</tr>
</tbody>
</table>

- Even in age of universal ART, HIV+ women remain more likely to have LBW babies
- Lower weight and primigravida status were independently associated with LBW – supplementary nutrition to women living with HIV may reduce LBW risks especially in those of low weight and primigravida?
PMTCT Cascade Issues:

- bNAb Infant Prophylaxis
- Dual HIV/Syphilis Elimination
- Gaps in Care and Interventions
CEPAC Model: A strategy is **cost-effective** if it resulted in the greatest projected clinical benefit and was cost-saving or had an ICER ≤50% of a country’s annual GDP per capita.

- **Standard of care strategy (SOC)** = infants with known HIV exposure are offered WHO-recommended oral antiretroviral prophylaxis

- Modeled offering bNAbs to one of three target populations:

- Infants getting bNAb were offered one of three dosing approaches:

### Methods: Key bNAb assumptions

<table>
<thead>
<tr>
<th>Input parameter</th>
<th>Value</th>
<th>Rationale</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy against intrapartum and postnatal HIV acquisition</td>
<td>70%</td>
<td>Assumption based on existing data on efficacy against sensitive virus in adults (AMP trial) and neutralization coverage of single bNAbs</td>
<td>Ceperri et al. NEJM, 2021; Lichtenste et al., 2020</td>
</tr>
<tr>
<td>Effect duration/dosing interval</td>
<td>3 mo.</td>
<td>VRC01LS and VRC07-523LS infant PK data</td>
<td>Capistran et al., CROI 2021; NFIX Trail et al., Infait HIV, 2021</td>
</tr>
<tr>
<td>Uptake (range by age)</td>
<td>56% - 96%</td>
<td>Country-specific routine infant vaccination uptake</td>
<td>WHO, 2021</td>
</tr>
<tr>
<td>Cost, per dose</td>
<td>$20</td>
<td>Estimated costs of monoclonal antibody production and vaccine delivery in low- and middle-income countries</td>
<td>Anderson et al. 2019, 2021; Bugnaga et al., Vaccine, 2013; Ceperri et al., The Lancet Infectious Diseases, 2013; COVID-19 Vaccine Task Force, 2021</td>
</tr>
</tbody>
</table>
> Offering bNAb to infants with **known HIV exposure** was cost-effective in Côte d’Ivoire & Zimbabwe and offering bNAb to **all infants** was cost-effective in South Africa, where maternal HIV prevalence and incidence are relatively higher.

> Cost-effective bNAb strategies would substantially reduce projected MTCT compared to the current standard of care.

> The potential clinical impact and cost-effectiveness of bNAb infant prophylaxis should motivate further bNAb research.
Globally, estimated 1 million cases of syphilis in pregnant women cause 350,000 adverse birth outcomes/yr

Syphilis is 2nd leading infectious cause of stillbirth globally (64% in Africa)

Despite this, significant disparity between national coverage for HIV vs syphilis testing in pregnant women globally

Nigeria 2021 national policy change: HIV and syphilis testing should be offered to pregnant women seeking antenatal care in all settings

- ↑ pregnant women tested for HIV from 67% to 95% by 2022
- Plan ↑ pregnant women tested for syphilis from 10% to 60% by 2026

Recent WHO data show 33% (63/194) reporting countries have reported adoption of dual HIV/syphilis testing for pregnant women in ANC
Mbeko+Men: Impact of Community-Based Intervention on Maternal Mental Health and Care-Seeking in Rural Zimbabwe

Webb K et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 13

- Cluster randomized trial in 8 rural health facilities enrolling 457 women who had given birth in the prior 6 months (11% HIV+) and 242 male co-parents
- Did before/after implementation surveys to measure impact on maternal mental health (Edinburgh Postnatal Depression Score, EPDS, >12=depression) and male engagement in care/support

Reduction in EPDS score (↓ depression) in both intervention and control arms, but decline in mean EPDS score was 34% greater in intervention vs control arm (aRR 0.66, 95% CI 0.48-0.90, p=0.008)

Improvement ANC indicators in intervention group

- Significant impact of Mbeko+Men intervention on sub-measures of:
  - Overall relationship dynamics (Intimate Bond Measure)
  - Men’s gender attitudes (Gender Equitable Men)
  - Men’s practical support for women and babies (cooking, accompanying to ANC/birth/infant illness, playing with baby)

Low-intensity gender-synchronized intervention positively impacted maternal mental health, ANC cascade and improved couple’s relationships

Women living with HIV and survivors intimate partner violence need targeted mental health support
Impact of ART Status on Gaps in HIV Care in Women Living with HIV in Khayelitsha, South Africa

Phillips T et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 28

- Examined differences in HIV care gaps (>270 days without evidence of HIV care) between delivery to 24 mos postpartum by maternal ART history at time of pregnancy in Khayelitsha ART cohort

- 6,877 women age 15-59 yr with ≥1 live birth between Apr 2013-Mar 2019

Changing % Women on ART, Restarting ART, and Newly Starting ART by Year of Delivery

Cumulative incidence of PP gap HIV care:
- 1 yr PP: 16.0% (95% CI 15-17)
- 2 yr PP: 30.9% (95% CI 30-32)

- Increasing % of HIV+ women presenting for ANC are on ART
- Women newly starting ART in pregnancy have ↑ risk of having PP gap in HIV care
- Small but growing % of women re-entering HIV care/restarting ART in pregnancy who have ↑ ↑ risk of having PP gap in HIV care
- Assessment of ART history during ANC can facilitate support interventions to optimize sustained PP retention in care
HIV-Exposed Uninfected Infants

16 million

>20% of children born in multiple countries including South Africa are HEU

80% of brain growth happens by 3 years
Increased Risk Long-Term Risk Hospitalization and Chronic Disease in HEU vs HUU, Montreal, Canada

**Centre maternel et infantil sur le SIDA (CMIS) Cohort:** established in 1988 at CHU Sainte-Justine in Montreal, follow-up mother-infant pairs from pregnancy to early childhood; 93% mothers on ARV in pregnancy, mostly PI-based (70%)

- Matched 1:3 with control children in RAMQ universal health system database selected randomly after matching for age, gender, and postal code (neighborhood)

**Summary Of Chronic Conditions**

-Congenital anomalies: 40 (5.5) vs 76 (3.5); RR 1.58 (1.09 - 2.3), p=0.016
-Neuro-psychiatric disorders: 241 (33.3) vs 566 (26.1); RR 1.28 (1.13 - 1.45), p<0.001
-Diabetes mellitus, metabolic and immunity disorders: 79 (10.9) vs 340 (15.7); RR 0.70 (0.55 - 0.88), p=0.002
-Respiratory diseases: 161 (22.3) vs 559 (25.8); RR 0.66 (0.74 - 1.01), p=0.06
-Cardiovascular system diseases: 21 (2.9) vs 75 (3.5); RR 0.84 (0.52 - 1.35), p=0.47
-Malignancy: 12 (1.7) vs 45 (2.1); RR 0.58 (0.43 - 1.5), p=0.89

**Product-Limit Failure Curves**

- CHEU vs CHUU

**Excluding prolonged birth hospitalization**

- HR= 1.42 [1.26-1.61], p<0.001
- aHR for gestational age: 1.23 [1.08-1.40], p=0.001

- HR= 1.21 [1.06-1.40], p=0.006
- aHR for gestational age: 1.14 [0.99-1.31], p=0.078
Retrospective study of mother-infant pairs with available clinical samples in the SIME Montreal Cohort; tested for CMV by Allostar CMV PCR; prevalence of CMV in general population is 0.5%.

- HIV-infected infants had highest risk of cCMV.
- **HEU had 3-fold ↑ risk of** CMV compared to general population.
- Highest risk among HEU with low birth weight or mothers with detectable RNA or low CD4 – would be highest priority for screening for cCMV.
- Given risk neurodevelopmental delay in HEU and known association with cCMV, suggests that all HEU should be tested for cCMV at birth.
Implications for Programming – Elimination of vertical transmission and infants who are HIV exposed

• DTG should be offered to all women including of child-bearing age
  – No difference in adverse birth outcomes for women on DTG vs EFV at conception
  – Continued strong evidence on more rapid and better viral suppression

• Innovation for elimination of vertical transmission
  – PrEP safe in pregnancy (no difference in birth outcomes), and should be promoted with DSD for at risk populations
  – Promising strategies to increase VL testing – community maternal VL test collection and POC
  – Broadly Neutralizing Antibodies for injectable infant prophylaxis on the horizon
At 12 mos, the 6-month PrEP dispensing with interim HIVST was non-inferior compared with SOC PrEP dispensing at 12 mos.

It simplified PrEP delivery reducing number clinic visits without compromising HIV testing, retention or adherence.

Among single women, the intervention increased PrEP adherence.

HIVST should be considered to support PrEP continuation and increase health system efficiencies.
Pilot randomized trial of adherence support intervention vs control in 200 HIV-negative pregnant women initiating TDF/FTC PrEP at single site Malawi, evaluating retention and TFV-DP levels.

Adherence at 3 & 6 Months According to TFV-SP Drug Level Scores

Clinical Outcomes

- Oral PrEP adherence consistently low even in trial setting, with daily dosing by <12% of pregnant women.
- Unfortunately, the combination adherence support did not increase retention or adherence to oral PrEP.
- Will injectable PrEP result in improved retention and adherence?
Adaptive PrEP Adherence Interventions for Young South African Women

Velloza J et al. AIDS 2022, Montreal, Canada, Abs.OAC0504

- Endpoint TFV-DP >700 fmol/punch
  - Primary randomization (SMS vs WhatsApp)
  - Secondary randomization (drug level feedback vs monthly counseling)
- Optimal adherence of 4 dynamic treatment strategies:
  - No significant differences between intervention or dynamic treatment strategies – had similar impact on adherence
  - Did not compare to SOC – and PrEP adherence actually higher than comparable cohorts
  - Challenging to re-engage non-responders after 2 mos
- Individual level interventions may be insufficient to overcome structural barriers to PrEP for AGYW – long-acting formulations may have promise
HPTN 084 Updated Results CAB vs TDF/FTC for PrEP

Delany-Moretiwe S et al. AIDS 2022, Montreal, Canada, Abs.OALBX0107

- NEJM: HIV incidence CAB 0.20 vs TDF/FTC 1.85 per 100 PY, HR 0.12 (0.05-0.31)
- Blinded portion of trial stopped Nov 2020; pt continued on randomized regimen pending protocol amendment for open-label CAB – report on HIV infections during the 12-month period following the unblinding

→ CAB continues to be superior to TDF/FTC in preventing infections in women, with 89%↓ risk; no new safety concerns

Pregnancy Incidence CAB vs TDF/FTC, Blinded and Unblinded Periods

→ Pregnancy incidence ↑ in unblinded period; confirms importance of evaluating CAB safety and PI in pregnancy during HPTN 084 open label extension
Cost-Effectiveness of CAB-LA vs Oral PrEP, South Africa
Thembisa Modeled Analysis

Jamieson L et al. AIDS 2022, Montreal, Canada, Abs.OAE0304


<table>
<thead>
<tr>
<th>Oral Prep (TDF/FTC)</th>
<th>CAB-LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium coverage</td>
<td>High coverage</td>
</tr>
<tr>
<td>Coverage 5% (AGYW, FSW, ABYM); 15% (FSW, MSM)</td>
<td>10% (AGYW, FSW, ABYM); 30% (FSW, MSM)</td>
</tr>
<tr>
<td>Coverage 5% (AGYW, FSW, ABYM); 15% (FSW, MSM)</td>
<td>10% (AGYW, FSW, ABYM); 30% (FSW, MSM)</td>
</tr>
<tr>
<td>Effectiveness 65% (AGYW, FSW); 85% (ABYM, MSM)</td>
<td>95% (all populations)</td>
</tr>
<tr>
<td>Annual cost per person initiated</td>
<td>Calculation</td>
</tr>
<tr>
<td>$76-78 (AGYW, FSW, ABYM); $116 (MSM)</td>
<td>$78-81 (AGYW, FSW, ABYM); $122 (MSM)</td>
</tr>
<tr>
<td>$131-137 (AGYW, FSW, ABYM, MSM 1st year); $105 (MSM 2nd year)</td>
<td></td>
</tr>
</tbody>
</table>

Oral Prep
- Duration 5-11 mo
- Coverage 5-15 % or 10-30% (hi)
- Effectiveness 65-85%
- Cost $76-78 ($116 MSM as includes syphilis test)

CAB-LA
- Duration same as oral or 12-24 mo
- Coverage 10-25% % or 20-50% (hi) min duration
- Coverage 20-40% or 35-67% (hi) max duration
- Effectiveness 95%
- Cost varies $78-81 or $31-137 depending on duration

Impact on HIV
- At baseline HIV incidence declining from 0.39% to 0.17%
- By 2041, CAB-LA min (and max) reduces incidence, averts more infections and AIDS deaths than TDF/FTC
- HIV incidence decreased to
  - 0.15-0.16% TDF/FTC
  - 0.10-0.13% CAB-LA
- HIV infections averted
  - Max 8900-16300/yr TDF/FTC
  - Max 26400-52000/yr CAB-LA
- AIDS deaths averted; over 20 yrs
  - 6500 -2400 TDF/FTC
  - 21500-43400 CAB-LA
Cost-Effectiveness of CAB-LA vs Oral PrEP, South Africa

Thembisa Modeled Analysis

Jamieson L et al. AIDS 2022, Montreal, Canada, Abs.OAE0304

### Cost-Effectiveness over 20 Years

**Medium coverage scale-up for PrEP interventions**

<table>
<thead>
<tr>
<th>Scenario</th>
<th>New HIV infections</th>
<th>% averted over 20 yrs</th>
<th>Life years lost due to AIDS</th>
<th>% saved over 20 yrs</th>
<th>CAB-LA drug cost relative to oral PrEP</th>
<th>Total cost of HIV program (November 2021 USD)</th>
<th>Incremental cost effectiveness (2021 USD)</th>
<th>Cost of infection averted</th>
<th>Cost/infection year saved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>3.01</td>
<td>37.34</td>
<td>41.29</td>
<td>0</td>
<td>1x</td>
<td>$4,051</td>
<td>2,029</td>
<td>2,029</td>
<td>2,029</td>
</tr>
<tr>
<td>Oral PrEP</td>
<td>2.90</td>
<td>37.02</td>
<td>42.08</td>
<td>2%</td>
<td>2x</td>
<td>$4,051</td>
<td>2,029</td>
<td>2,029</td>
<td>2,029</td>
</tr>
<tr>
<td>CAB-LA minimum duration</td>
<td>2.58</td>
<td>36.19</td>
<td>43.25</td>
<td>3%</td>
<td>3x</td>
<td>$4,471</td>
<td>$4,471</td>
<td>2,713</td>
<td>2,713</td>
</tr>
<tr>
<td>CAB-LA maximum duration</td>
<td>2.44</td>
<td>35.81</td>
<td>46.24</td>
<td>4%</td>
<td>4x</td>
<td>$4,471</td>
<td>$4,471</td>
<td>3,240</td>
<td>3,240</td>
</tr>
</tbody>
</table>

→ To be more CE than TDF/FTC, CAB-LA needs to be same (1x) price; at slightly higher (2x) as TDF/FTC is less CE

- CAB-LA is highly effective in preventing HIV transmission
  - Estimated 3-5-fold ↑ in averting HIV infection/AIDS deaths over 20 yrs

- Cost of CAB-LA drug needs to be <$9/injection (hi coverage) or <$15/injection (med coverage) for it to be similarly or more CE than TDF/FTC in South Africa

- Current US list price: $3700/injection – unaffordable for LMIC

- Voluntary licensing terms with Medicines Patent Pool under negotiation with Viiv

### Impact on Cost of HIV Programs

- By 2041, number of HIV+ pt on ART vs baseline
  - Reduced 1-2% TDF/FTC
  - Reduced 4-8% CAB-LA

- Total HIV program cost higher with CAB-LA despite less need for ART, likely due to assumed higher uptake compared to TDF/FTC

### Threshold Analysis

<table>
<thead>
<tr>
<th>What Would Be Cost of CAB-LA/Injection to be as CE as Oral PrEP?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minimal duration scenario</strong></td>
</tr>
<tr>
<td>Cost per CAB-LA injection (2021 USD)</td>
</tr>
<tr>
<td>Equal ICERS for cost/HIV infection averted</td>
</tr>
<tr>
<td>Equal ICERS for cost/life year saved</td>
</tr>
</tbody>
</table>

→ Acceptable range of cost/injection to be as CE as TDF/FTC is $9-15
Implications for Programming – PrEP

• New Models for PrEP show promise
  – 6 mo prescriptions and HIV self-testing reduced the need for clinic visits
  – “Adaptive” strategies to improve adherence eg PrEP plus SMS work but don’t always overcome structural barriers

• Long-acting Cabotegravir for PrEP
  – It’s coming, and it will be highly efficacious
  – But cost is a challenge. It would have to be >200 fold cheaper than current price
Adolescents and HIV
Cohort study of 1046 adolescents living with HIV seen at >70 health facilities in Eastern Cape South Africa interviewed yearly for 3 years and health data collected from facilities; retention 94%, mortality 3.4%.

Experience with sexual violence

- 37% lifetime exposure to IPV or sexual abuse
- 23% females reported lifetime IPV or sexual abuse
- 5% females reported both lifetime IPV and sexual abuse
- 11% exposure in past 2 years

Impact of Sexual Violence on ART Adherence

- 72% no IPV or sexual abuse
- 50% sexual abuse only
- 52% IPV only
- 30% both IPV and sexual abuse

Multivariable Associations Between IPV, Sexual Abuse, and Past-Week ART Adherence Among Adolescents (N=980, observations 1960)

<table>
<thead>
<tr>
<th>Adolescent victimisation</th>
<th>aOR 95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPV (past-year)</td>
<td>0.36 (0.21-0.72)</td>
<td>0.003</td>
</tr>
<tr>
<td>Sexual abuse (past-year)</td>
<td>0.54 (0.29-0.99)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

→ Need to ask about IPV and sexual violence
→ Need to make referrals where possible
→ Scale up prevention programs and response services

Integrating and Scaling Up Evidence Based Violence Prevention Interventions
Behavior-Based Intervention on Effects of Preventive Sexual Violence Curriculum on Improving Male Attitudes Toward Women, S Africa

**Madubela N et al. AIDS 2022, Montreal, Canada, Abs.OAD0502**

- No Means No curriculum implemented in priority districts in South Africa
- Trained 16 male program facilitators to conduct the COVID-adapted 8-hr curriculum for adolescent boys and young men (10-24 yr) in 4 subdistricts – target 280 in each subdistrict.

**8-hour intervention for men and boys**
- Class 1: Introduction to sources of strength (SOS)
- Class 2: Introduction to the Man Box and Cycle of Force
- Class 3: Your moments of truth
- Class 4: Introduction to intervention

**Focus**
- Personal safety
- Redefining gender roles
- Debunking rape myths
- Consent
- Bystander intervention

**Conducted Aug 2021-Mar 2022; pre-and post-questionnaires to evaluate effect on attitudes toward women and gender-based violence**

---

**Changes in Knowledge and Attitudes Toward Women**

<table>
<thead>
<tr>
<th>Implementing Partner</th>
<th>Knowledge</th>
<th>Attitudes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% with desired response</td>
<td>% with desired response</td>
</tr>
<tr>
<td></td>
<td>PRE</td>
<td>POST</td>
</tr>
<tr>
<td>Childline Gauteng</td>
<td>61%</td>
<td>89%</td>
</tr>
<tr>
<td>Aramidla</td>
<td>65%</td>
<td>91%</td>
</tr>
<tr>
<td>Childline North West</td>
<td>44%</td>
<td>71%</td>
</tr>
<tr>
<td>Hope Africa</td>
<td>65%</td>
<td>100%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>60%</td>
<td>85%</td>
</tr>
</tbody>
</table>

---

*Men should not show emotions* and *It is important to get help when raped or attacked* are two statements that students across implementing partners were found to struggle with.
Cluster randomized trial, 2,068 HIV+ adolescents 15-24 yrs in 28 clinics in Kenya and Uganda Mar 2019-Mar 2022; effect multi-level intervention effect on viral suppression (RNA <400) at 2 yrs

Intervention Utilization/Fidelity

- Alternative clinic access selected by many participants
- Choices varied by clinic
- Useful during COVID periods

Alternative Clinic Site Visits by Clinic Site

- Off site appointment
  - Off site
  - Not off site
- Phone appointment
  - Phone app
  - No phone app
- Off-hours appointment
  - Off hr app
  - No off hr app
- Off-site drug delivery
  - Off site drug
  - No off site drug

Number Life stage Assessments During Study

- 84.5% of 785 participants remaining in region during 2-year period had ≥4 life-stage assessments

Mean VL Delivery Time (days)

- Mean time results delivery was 38.4 hours
- In 13/14 clinics, 80% of results delivered within 72 h
SEARCH-Youth Multilevel Health System Intervention to Improve Viral Suppression in HIV+ Adolescents/Young Adults Kenya, Uganda

Mwangwa F et al. AIDS 2022, Montreal, Canada, Abs.OALBE0102

- 15% ↑ suppression in intervention vs 5% ↑ control
- 2-year suppression 88% intervention, 80% control
- Relative effect 1.10 (95% CI 1.03-1.2), p=0.002

### Viral Suppression (<400) at 2 Years

**Engagement in care status at baseline**
- 34% recent engagement (start ART in prior 6 mo/enrollment)
- 62% engaged (start ART >6 mos, with clinic visit prior 6 mos)
- 4% re-engaging (start ART >6 mos, without clinic visit prior 6 mos)

**Improvements with intervention across subgroups defined by baseline care status**
- Particularly impressive in those re-engaging in care: 85% intervention vs 53% control, relative effect 1.60 (95% CI 1.00-2.6), p=0.03

### Viral Suppression (<400) at 2 Years by Age and Sex

**Relative effect**

<table>
<thead>
<tr>
<th>Women</th>
<th>Relative effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>1.06 (1.00-1.13); p=0.026</td>
</tr>
<tr>
<td>15-19 years</td>
<td>1.13 (1.01-1.26); p=0.015</td>
</tr>
<tr>
<td>20-24 years</td>
<td>1.05 (0.99-1.11); p=0.040</td>
</tr>
</tbody>
</table>

- Improvement by regardless of age and sex
- Largest effect in younger age (15-19 yrs)

→ Intervention increased viral suppression compared to SOC overall, in key subgroups & during period DTG transition and COVID-19

→ Added to current efforts, life stage-based assessment, allowing alternatives to clinic appts & rapid VL test/feedback could help AYAH achieve goal of universal suppression

- Study during DTG transition, switching similar both arms
- Intervention was associated with higher probability suppression in both youth who switched and did not:
  - DTG: 92% intervention, 88% control
  - No switch: 70% intervention, 64% control
Implications for Programming – Adolescents with HIV

- Counselling for GBV should be part of ART adherence for adolescents
  - IPV and sexual abuse strongly associated with poor adherence
  - Interventions targeting adolescent boys and young men can help to reduce GBV

- Adherence strategies must be multilayered
  - Phone support and community delivery of ARVs improved adherence for adolescents and young people
DSD Initiation
How Soon Should Eligibility for DSD Happen?

Jamieson L et al. AIDS 2022, Montreal, Canada, Abs.OAE0104

- Zambia, EMR medical record review to ask is enrollment into DSD <6 mos after ART start associated with increased LTFU (no interaction with health system between 15-21 mos after ART start)?
  - Early enrollers (20%): DSD with <6 mos ART (N=6,340, 45% 0-3 mos; 55% 4-6 mo)
  - Established enrollers (80%): DSD with >6 mos ART (N=25,857)
  - No difference age (median, 37 yr), sex (61% female), setting (64% urban)

- Across most DSD models and all ART dispensing intervals, early enrollers had similar or lower rates of LTFU 18 mos after ART initiation

- Early enrollers risk LTFU lower than established pt for most models care and all dispensing intervals including those enrolled 0-3 mos after ART start.
- Potential bias re: early entry may be associated with pt with better adherence
- Despite this, DSD models do work for some early ART patients, suggesting blanket exclusion of those on ART <6 mos should be reconsidered
SARS-CoV-2/COVID-19, HIV, and Impact on HIV/TB Services
Incidence of SARS-CoV-2 Infection in Children and Adolescents Living with HIV in Europe

Chappell E et al. International Pediatric HIV Workshop, Montreal July 2022, Abs. 6

- Pediatric HIV cohorts from European Pregnancy and Pediatric Infections Cohort Collaboration (EPPICC) included if they had FU data through 2020 and were able to report COVID-19 data
- 11 cohorts including 1,718 children with HIV from 9 countries; **129 (8%) diagnosed with SARS-CoV-2 infection** (91% on ART): **47/1000 PY** (95% CI 40-56)
- Only 39 (30%) had additional clinical descriptive data available: 22/38 (61%) had symptoms, all mild; 3/39 (8%) hospitalized, no deaths

→ Incidence SARS-CoV-2 was relatively low and generally mild, as seen in children without HIV; slightly more common in HIV+ older children and those not virally suppressed.

Bertagnolio S et al. AIDS 2022, Montreal, Canada, Abs.OAB0404

- Symptoms similar to HIV-negative except less frequent cough
- PLWH more frequent underlying conditions (>1 underlying condition, 59% of PLWH vs 45% in HIV-negative (p<0.0001); 52% PLWH had 1-2 and 7% ≥3 underlying conditions)

Risk Factors for In-Hospital Mortality in PLWH

<table>
<thead>
<tr>
<th>Risk factors for in-hospital mortality</th>
<th>aHR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>1.04 (0.89-1.19)</td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td>1.43 (1.24-1.65)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1.05 (1.01-1.09)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.02 (1.00-1.04)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.01 (0.98-1.05)</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, comorbidities (TB, DM, hypertension, pulmonary disease, chronic kidney disease)

→ Risk in-hospital mortality was 52% higher than HIV-negative, adjusting for age, gender, underlying conditions
→ Independent mortality risk factors: older age, chronic kidney disease, diabetes, hypertension, VL & CD4 <200 (regardless of VL status)
→ Decrease in mortality with Omicron seen in both PLHIV and HIV-negative but decrease was much less in HIV+
How Outreach Mobile Health Clinics Maintained HIV Testing and Linkage to Services in the Face of COVID-19, Malawi

Khozomba N et al. AIDS 2022, Montreal, Canada, Abs.OAE0202

- Malawi used Mobile Health Clinics to maintain HIV services during COVID

**Overall HIV Testing Malawi 2008-2022**

- New positive
- HIV negative
- HIV self-test

New diagnosis yield (%)

**GAIA Mobile Health Clinics**

- 7 clinics operating in 3 districts

**Expanding access to care through Mobile Health Clinics**

- Pre-COVID tests/clinic: 1042
- Mean positivity rate: 3.6%
- National average: 2.9%

- Post-COVID tests/clinic: 1272, 22% ↑
- Mean positivity rate: 2.8%
- National average: 2.3%

**Lessons Learned**

- Community based care effectively blunted impact COVID in rural and remote populations
Impact of COVID-19 Prevention Measures on Lives of Young People Living with HIV, Uganda

Ssekajja B et al. AIDS 2022, Montreal, Canada, Abs.OAD0202

- Quantitative (mobile web survey) and qualitative (focus group) study of HIV+ young people

Underlying Reasons for Difficulty in Accessing STI/HIV Services

1. Afraid of COVID-19
   - 34% of males and 29% of females afraid to catch COVID-19 infection from health facility
   - 55% of those in need of STI/HIV testing and/or treatment could access the services within the COVID-19 pandemic
   - 10% lacked access to medications

2. Lack of transport
   - Was reported by 25% of male respondents and 26% of female respondents

3. Health facility closed
   - Was reported by 11% of male respondents and 9% of female respondents

4. Curfew
   - Was reported by almost 12% of males and 5% of female respondents

5. Stock out of medicine
   - Was reported by 25% of the respondents

Recommendations from Young HIV+ People

- HIV prevention, care and treatment services should remain crucial during all times, including in case of a pandemic
- Prioritize the mental health of YPLHIV
- Combat stigma
- Address stock-outs, distribution, and adherence issues around ARVs
- Ensure access to PreP and PEP
- Integrate sexuality education in online learning
- Provide economic support for young people including those living with HIV

Increased vulnerability across all groups of young people

- Young People in Schools
  - Limited access to sexuality education
- Sex Workers
  - Increased physical and psychological abuse
- LGBTQI+
  - Increased harassment, rights violation and economic hardships
- Teenage Mothers
  - Increased economic hardships
The Global Alliance to end AIDS in children by 2030

A new global initiative to accelerate evidence-based action at scale
The Global Alliance is the successor to the Global Plan and the 3-Frees

A 9-year global strategic initiative in 3-year phases with the goal of ending AIDS in Children by 2030

<table>
<thead>
<tr>
<th>PILLARS</th>
<th>POPULATIONS</th>
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</thead>
<tbody>
<tr>
<td>I. Early testing and comprehensive, high-quality treatment &amp; care for children and adolescents living with HIV and perinatally exposed children</td>
<td>I. Children (0-14 years) and Adolescents (15-19 years) Living with HIV</td>
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<tr>
<td>II. Closing the treatment gap and optimizing continuity of treatment for pregnant and breastfeeding women living with HIV</td>
<td>II. Children perinatally exposed to HIV</td>
</tr>
<tr>
<td>III. Preventing new HIV infections among pregnant and breastfeeding women</td>
<td>III. Pregnant and Breastfeeding Girls and Women who are Living with HIV including marginalized and key populations</td>
</tr>
<tr>
<td>IV. Addressing rights, gender equality, and the social &amp; structural barriers that hinder access</td>
<td>IV. Pregnant and Breastfeeding Girls and Women who are HIV-negative but at risk of HIV</td>
</tr>
</tbody>
</table>
Learning from the past, the new Global Alliance will take some novel approaches

Build momentum over a longer period – 9 years from 2022 to 2030 in three phases, each will involve leadership of different regional and national partners.

Promote country leadership and community ownership with the participation of national programmes and affected communities of children, adolescents and mothers living with HIV, to lead, develop and execute plans.

Boost existing initiatives to end AIDS in children, with the commitment to coordinate, collaborate and celebrate shared successes.

Increase advocacy and ensure senior high-level engagement from partners including countries, UN agencies, global networks of PLHIV, implementers, PEPFAR and GF to drive support for the initiative;

Address programme gaps AND structural barriers that are hampering progress for children especially for marginalized communities including key populations.

Use data to target and focus our attention.

LESSONS LEARNED

- Country buy-in
- Senior political leadership
- Donor alignment
- Focused action
- Community engagement
Following the Launch at AIDS 2022, we committed to an Alliance kick-off in Abuja for the 12 Phase 1 partner countries:

- Angola
- Cameroon
- Cote d’Ivoire
- Democratic Republic of Congo
- Kenya
- Mozambique
- Nigeria
- South Africa
- Tanzania
- Uganda
- Zambia
- Zimbabwe
Each 3 year phase of the Alliance will be an opportunity to take stock and re-align our efforts.

Phase 1: 2022 to 2024
- Launch
- Co-creation of strategy with partners
- Focus on high burden countries

Phase 2: 2025 to 2027
- Building on success
- Expanded focus on additional countries including those with low prevalence or concentrated epidemics

Phase 3: 2028 to 2030
- Countdown to 2030
- Stocktaking & strategy adjustment
- Focused on closing remaining country gaps

For more information including joining the alliance as a Member – visit: https://www.childrenandaids.org/global-alliance
Thank You For Your Attention!

Questions?