CROI 2019
Selected PMTCT, Pediatric, Adolescent, and Maternal/Adult Abstracts

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For webinar 04/01/2019
March 21 2019
Pregnancy, ARV Drugs, Viral Suppression, Pregnancy Outcome
Randomized trial of RAL+2NRTI vs EFV+2NRTI in 408 pregnant ART-naïve women S America, Africa, Thailand and US presenting to ANC at ≥28-36 weeks (later expanded to ≥ 20 weeks) gestation. Primary endpoint is virologic response (VL <200) at delivery.

<table>
<thead>
<tr>
<th>Delivery</th>
<th>Efavirenz</th>
<th>Raltegravir</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VL &lt;200</td>
<td>84% (151/179)</td>
<td>94% (174/183)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enrolled 20 to &lt;28 wks</td>
<td>97% (87/90)</td>
<td>96% (85/88)</td>
<td>NS</td>
</tr>
<tr>
<td>Enrolled 28 to &lt;37 wks</td>
<td>71% (64/89)</td>
<td>93% (89/95)</td>
<td>0.05</td>
</tr>
</tbody>
</table>
More Rapid VL Decline with RAL than EFV  
*Mirochnick M et al. CROI, 2019 Seattle Abs. 39LB*

- VL decline was greater in raltegravir arm than efavirenz arm at study weeks 2, 4 and 6.
- Both regimens well-tolerated; no difference AE, stillbirth, preterm.
- 1 raltegravir and 6 efavirenz infants were infected (p=0.06).

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<thead>
<tr>
<th></th>
<th>Efavirenz</th>
<th>Raltegravir</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>VL ↓ by wk 2 and sustained to delivery</td>
<td>84/131 (64%)</td>
<td>121/132 (92%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VL ≥2.0 log ↓decline or &lt;200 by wk 2</td>
<td>91/131 (69%)</td>
<td>123/132 (93%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VL &lt;1,000 all time pt after wk 4</td>
<td>117/123 (95%)</td>
<td>115/120 (96%)</td>
<td>NS</td>
</tr>
<tr>
<td>Stayed on study drug through delivery</td>
<td>129/131 (98%)</td>
<td>131/132 (99%)</td>
<td>NS</td>
</tr>
</tbody>
</table>
DTG vs EFV When Starting ART in Late Pregnancy
Khoo S et al. CROI 2019 Seattle, WA Abs. 40LB

- Open-label randomized trial of DTG+2NRTI vs EFV+2NRTI in 268 pregnant ART-naïve women presenting to antenatal clinic at ≥28-36 weeks gestation in Kampala and Cape Town.
- Primary endpoint is virologic response (VL <50) at delivery.

Analysis at delivery (ITT): 122 DTG, 115 EFV
- Median GA at enrollment, 31 wks; median d on ART prior to delivery, 55 d
- No difference in baseline VL (median 4.4 log), CD4 (median 445), prior obstetric history, gestation, BMI
**More Rapid VL Decline with Dolutegravir than Efavirenz**  
*Khoo S et al. CROI 2019 Seattle, WA Abs 40LB*

- **Primary outcome**
  - Time on medication before delivery, median 55 days

<table>
<thead>
<tr>
<th>Delivery</th>
<th>Dolutegravir</th>
<th>Efavirenz</th>
<th>aRR DTG vs EFV*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VL &lt;50</td>
<td>73.8% (90/122)</td>
<td>42.6% (49/115)</td>
<td>1.66 (1.2, 2.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VL &lt;1000</td>
<td>92.6% (113/122)</td>
<td>82.6% (95/115)</td>
<td>1.11 (1.0, 1.2)</td>
<td>0.0513</td>
</tr>
</tbody>
</table>

*Adjusted for age, country, VL (<> 100,000), CD4 (<>200), GA at start ART

![Percent VL <50 c/mL](chart.png)

- Lower efficacy both at high RNA
- Preterm rates similar (17% DTG, 16% EFV, similar to Botswana 18%)
- 4 stillbirths – all DTG arm
- 3 infant infections at birth (thought IU infection) – all DTG arm
- 8,539 pregnant women age >15 years (median 29 years); 38% ART naïve (63% RAL, 49% EFV), 42% ART >2 years.
- VL <50 c/mL 2-6 months after first prescription in pregnancy: overall 77%
  - Multivariate analysis, compared to EFV ART, 36% higher odds of suppression if on RAL (aOR 1.36, 1.1-1.7) and 49% lower odds suppression if using LPV/r (aOR 0.51, 0.4-0.7)

### Other factors associated with suppression:
- Lower baseline VL
- Higher baseline CD4
- Older age
- Higher education level
- Lower time on ART
Maternal HIV RNA After Delivery is Correlated with Infected Infant Pre-Treatment HIV RNA

Sakol-Moethl M et al. CROI 2019 Seattle, WA Abs.797

- Data from 40 mother-infant pairs from the Early Infant Treatment Study enrolled at <7 days from delivery (median 2 d).
- All infants received sdNVP at birth and AZT BID per MOH protocol until HIV dx, when changed to ART.
- Maternal RNA done at infant enrollment (median 2 d PP); infant RNA at baseline prior to ART.
- Higher maternal RNA correlated with higher pre-treatment infant RNA.
- Lowest infant RNA values in those exposed IU to DTG.

### Table

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<tbody>
<tr>
<td>No ART exposure (n=17)</td>
<td>42%</td>
<td>NA</td>
<td>64,072 [547,491512]</td>
<td>31,708 [&lt;40, &gt;10000000]</td>
</tr>
<tr>
<td>EFV-based ART (n=10)</td>
<td>25%</td>
<td>14 [1, 39]</td>
<td>10,259 [67, 144729]</td>
<td>1749 [1005, 1111950]</td>
</tr>
<tr>
<td>DTG-based ART (n=11)</td>
<td>27.5%</td>
<td>11 [1, 29]</td>
<td>56 [&lt;40, 85697]</td>
<td>310[79, 389270]</td>
</tr>
<tr>
<td>LPV/r-based ART (n=2)</td>
<td>5%</td>
<td>NA*</td>
<td>29,085 [23912, 34257]</td>
<td>80,430 [17244, 143616]</td>
</tr>
<tr>
<td>Total (n=40)</td>
<td>2.5 [0, 40]</td>
<td>24,789 [&lt;40, 491512]</td>
<td>11,335 [&lt;40, &gt;10000000]</td>
<td>0.63 / &lt;0.001</td>
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</table>

* by Spearman’s correlation, * not applicable because of small sample size (n=2).
Dolutegravir and Other Integrase Strand Transfer Inhibitors (InSTI) in Pregnancy
Antiretroviral Pregnancy Registry (APR):
Integrase Inhibitors (InSTI) and Neural Tube Defects (NTD)
*Albano J et al.  CROI 2019 Seattle, WA Abs. 747*

- Through 31 Jul 2018: includes 20,064 pregnancies and 10,072 1st trimester exposures.
- APR reports come from North America (75%), Europe (8%), Africa (7%), South America (6%) and Asia (4%).

**APR Primary Analysis**
Prevalence = \( \frac{\text{number of defects}}{\text{number of live births}} \)

**Compared to:**
- MACDP* 3/100 live births
- TBDR* 4/100 live births
- 1st trimester vs. 2nd & 3rd trimester

*MACDP = Metropolitan Atlanta Congenital Defects Program; TBDR = Texas Birth Defects Registry*
Prospective Antiretroviral Pregnancy Registry (APR): Integrase Inhibitors (InSTI) and Neural Tube Defects (NTD)  
Albano J et al.  CROI 2019 Seattle, WA Abs. 747

- 1,193 live births with InSTI exposure at any time in pregnancy; 604 periconceptional exposure, including 174 DTG, 186 EVG, 244 RAL.
- 2 CNS defect cases were reported with InSTI exposure at any time (both DTG, one 1\textsuperscript{st} trimester, one 2\textsuperscript{nd}/3\textsuperscript{rd} trimester).
- There were \textbf{no NTD} among \textit{prospective cases} for any InSTI drug.

<table>
<thead>
<tr>
<th>Earliest Trimester of Exposure – Prospective Cases</th>
<th>Periconception</th>
<th>1\textsuperscript{st} Trimester</th>
<th>2\textsuperscript{nd}/3\textsuperscript{rd} Trimester</th>
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<tbody>
<tr>
<td>Defects/live birth</td>
<td>Defect/live birth</td>
<td>Defects/live birth</td>
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<tr>
<td>Exposure to any INSTI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16/604 (2.6%)</td>
<td>4/135 (3.0%)</td>
<td>17/452 (3.8%)</td>
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<tr>
<td>Dolutegravir</td>
<td>6/174 (3.4%)</td>
<td>2/55 (3.6%)</td>
<td>4/137 (2.9%)</td>
</tr>
<tr>
<td>Elvitegravir</td>
<td>5/186 (2.7%)</td>
<td>0/27 (0%)</td>
<td>0/57 (0%)</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>5/244 (2.0%)</td>
<td>4/68 (5.9%)</td>
<td>13/290 (4.5%)</td>
</tr>
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</table>

\textit{Can be more than one organ system for a defect}

\textbf{No Neural Tube Defects}

\textbf{CNS}: 2: (lissencephaly – neural migration disorder) with preconception DTG; 1 (ventriculomegaly) with 2\textsuperscript{nd}/3\textsuperscript{rd} trimester DTG exposure.

- Face, ear, face, neck: 2
- Cleft lip/palate: 2
- Respiratory: 1
- Cardiac/circulatory: 11
- Lower GI: 1
- Renal: 4
- Musculoskeletal: 8
- Chromosome abnl: 2
- Other organ systems: 1
- Specified syndromes 1
There were 7 NTD plus 2 encephalocele cases reported with InSTI exposure in retrospective reports to the APR (reported after delivery with defect that has occurred, no denominator, not included in prospective data review).

### Summary of Retrospective NTD and Encephalocele Cases with InSTI Drug Exposure through July 2018

<table>
<thead>
<tr>
<th>Dolutegravir [timing of exposure, country]</th>
<th>Raltegravir [timing of exposure, country]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iniencephaly [P, BW]</td>
<td>Myelomeningocele [T2, UK]</td>
</tr>
<tr>
<td>Encephalocele [P, BW]</td>
<td></td>
</tr>
</tbody>
</table>

P = periconception, T2 = second trimester, unk = unknown; BW = Botswana, PR = Puerto Rico, UK = United Kingdom, US = United States
Shamsuddin, Poster 745: Merck review of database on pregnancies with RAL exposure:
- **Prospective**: 456 periconception RAL: no NTD
- **Retrospective**: 435 retrospective reports, 1 NTD, 1 encephalocele with RAL preconception exposure

Farrow, P030, Glasgow HIV Conf Oct 2018: Gilead of database on pregnancies with EVG or BIC exposure:
- **Prospective**: 155 preconception EVG, no NTD
  18 preconception BIC exposures, no NTD
- **Retrospective**: 318 reports, 2 NTD preconception EVG

Sibiude, Poster 744: French Perinatal Cohort Study
- **Prospective**: 218 preconception exposures to RAL, 41 to DTG and 42 to EVG: no NTD reported
Fetal and Infant Growth Similar Regardless of HIV Exposure or DTG vs EFV ART Exposure
CROI 2019 Seattle, WA Abs. 750 and 751

**Abs. 750 Masasa et al. Botswana**
- Ultrasound fetal biometry in 435 pregnant women 16-36 weeks GA
  - 167 HIV-uninfected (mean 26 wk GA)
  - 268 HIV (mean 28 wk GA) (176 DTG 92 EFV ART)
- No significant differences between uninfected and HIV+ women on ART
- No significant differences HIV+ women on DTG and EFV ART

**Abs. 751 Kgole S et al. Botswana**
- Birth anthropometry in 463 infants:
  - 275 HIV-exposed, 158 DTG/117 EFV
  - 188 HIV-unexposed
- No significant difference in WAZ or LAZ between HEU/HUU or DTG/EFV.
Ugandan Clinic Experience Following Potential NTD Signal with Preconception Dolutegravir

Arnold AS et al. CROI 2019 Seattle, WA Abs. 748

- Following clinical safety alert, clinic response plan developed; all women <55 years on DTG identified and contacted → group counseling session (15/grp)
- Women childbearing potential referred for pregnancy testing, evaluation of pregnancy intention in next 12 mos, and effective FP offered.
- Women intending to conceive offered EFV-ART; women could choose to remain on DTG without FP signing informed choice declaration.

9% (692/7963) were women on DTG, 95% (658) reviewed by 9/2018
510 women of reproductive potential (med age 37 yr, med duration DTG 4.3 mos)
5% (23/510) HCG+, all initial ultrasounds no deformities

Regimen Choice After Counseling

- Switched off DTG to EFV based regimen: 19% (97)
- Kept on DTG: 79% (402)

Contraceptive Choice for Women Staying on DTG

N=402

40% Effective contraception
60% condom/none
Modeling Impact of DTG Introduction on NNRTI Resistance, South Africa

Hauser A et al. CROI 2019 Seattle, WA Abs. 538

- Epidemiologic modeling to investigate development of pre-ART NNRTI drug resistance (DR) under different scenarios of DTG introduction.
- Assumes DTG efficacy similar to NNRTI and dx and treatment rates constant from 2018.

- DTG to all pt regardless gender and treatment status results in lowest NNRTI resistance, 8.2%, in 2035.
- DTG limited to men (or men+women non-childbearing age) results in increase in NNRTI DR to ~17% in 2035.
- Including men and women using contraception will stabilize resistance at 11.8%.
HIV- and ARV-Exposed Uninfected Children
SHINE: 2x2 factorial trial community cluster-based RCT compared effect of improved infant feeding, improved hygiene, or both vs SOC on outcomes, including growth and neurodevelopment.

Women were eligible if they lived permanently in trial clusters (catchment area of 1-4 village health workers) and were confirmed pregnant. Clusters randomized 1:1:1:1 to:

- **Control:** VHW encouraged early ANC, PMTCT uptake and EBF
- **IYCF:** VHW visited with interactive module for improved complementary feeding and 20gm nutri-butter per day between 6-18 mo/o
- **WASH:** ventilated improved pit latrine, handwashing stations, soap, chlorine, play space, hygiene counselling
- **COMBINED IYCF + WASH**

Included 738 HIV-exposed and 3989 HIV-unexposed infants.
SHINE trial (2012-2015), compared outcomes 738 HEU & 3989 HUU.

Evans C. Abs. 790 – Mortality/Growth: HEU had worse outcomes than HUU; 39% higher 18-mo mortality & more growth abnl, esp stunting.

Chandna J. Abs. 784 – Development: HEU lower total development, motor, language scores than HUU; no difference object permanence or self-control.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HEU (N=738)</th>
<th>HUU (N=3989)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-Month Mortality</td>
<td>7%</td>
<td>5%</td>
<td>0.04</td>
</tr>
<tr>
<td>Stunting</td>
<td>45.9%</td>
<td>30.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Underweight</td>
<td>17.4%</td>
<td>9.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wasting</td>
<td>4.7%</td>
<td>2.5%</td>
<td>0.001</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>9.5%</td>
<td>5.0%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Malawi Developmental Assessment Tool (MDAT): Gross and fine motor, language, and social components, adapted for rural Zimbabwean households

MacArthur Bates Communicative Development Inventory (CDI): Vocabulary and grammar checklist, translated and validated in Shona
Zimbabwe SHINE Trial: HEU Children: Are Outcomes Improved by Intervention?

- **Chasekwa B. Abs. 791 - Growth**: 668 HEU evaluated at 18 months; Infant/Young Child Feeding (ICYF) but not WASH significantly decreased rate of stunting and anemia among HEU.

  - HEU in ICYF group had ↓ stunting vs non-ICYF groups (40% vs 50%, RR 0.81)
  - HEU in ICYF group had ↓ prevalence anemia vs non-ICYF groups (7% vs 14%, RR 0.52)

- **Ntozini R. Abs. 42 – Development**: 323 HEU in early child development (ECD) substudy, administered by trained nurses age 2 years. Significantly improved development with the **combined** infant feeding and sanitation intervention (ICYF+WASH) (but not individual interventions alone).
Maternal Health Issues
Incident Infection in Pregnancy, Botswana
Mayondi GK et al.  CROI 2019 Seattle, WA Abs. 733

- As part of Tsepamo birth surveillance study, HIV status abstracted from all women delivering 8 hospitals Botswana.
- Analyzed women not known to be infected at start of pregnancy for seroconversion.

- 39 seroconversions in 15,490 pregnant women with $\geq 2$ tests = HIV incidence 6.5/1000 person years
- Median GA at seroconversion was 29 weeks; 90% started ART before delivery.
- Among 5,547 women without a 3rd trimester test, estimate 10 seroconversions may have been missed due to lack of testing

- As MTCT rates among women with known HIV infection decrease, the proportion of MTCT due to seroconversion during pregnancy will be increasingly important.
Prevalence of STI in HIV+ and HIV-Uninfected Pregnant Women, South Africa

Davey DJ et al. CROI 2019 Seattle, WA Abs. 1003

- Cross-sectional study 242 pregnant women attending public ANC in Cape Town (106, 44% HIV+), testing for STI at 1st ANC visit.
- Overall STI prevalence 33%: HIV+ 39%, HIV- 28% (p=0.04)

Factors associated with STI, adjusting for GA and age: unmarried/not cohabiting; HIV infection; recent STI symptoms.
Potential Concern for Timing of DMPA Injection in Women Treated for HIV and TB  
Mngqibisa R et al.  CROI 2019 Seattle, WA Abs. 78

- Study to evaluate whether concurrent use of EFV and RIF will decrease clearance of MPA resulting in potential reduced contraceptive efficacy.
- Estimate optimal dosing frequency for DMPA based on target serum MPA level of >0.1 ng/mL.

42 women with HIV/TB, not pregnant, stable on EFV ART >4 weeks, & on continuation phase of TB treatment (INH/RIF)

- MPA levels ≥0.1 ng/mL all through week 8.
- At week 10, 1 woman (2.4%) had level <0.1 ng/mL.
- At week 12, 5 women (11.9%) level <0.1 ng/mL.
- However, progesterone stayed low suggesting no ovulation.
- Consider shortening DMPA interval from 12→8-10 week with EFV/RIF coadmin?
PMTCT Cascade - Male Partner Testing
Self-tests for at-home partner self-testing offered to 758 HIV-uninfected women seeking routine ANC at 10 facilities in Kenya.

- Instructed on use and received ≥2 or more oral-fluid tests.
- Data on outcomes assessed at 1 month in person FU visit.

63% of women with partner with unknown status accepted HIVST kits; of 390 with FU data, 76% had offered to partner; of 296 with partner data, 93% had tested.
Outcome and Cost of Three Methods to Increase Male Partner Testing, South Africa

Medley A et al. CROI 2019 Seattle, WA Abs. 928

- 1,100 pregnant women with partner HIV- or unknown offered 3 options for partner testing – facility, home (trained counselor), self-test, Jan 2017-Oct 2017; incentives for post-test counseling (airtime vouchers for texting counselor)

- Women: mean age 28 years, 72% single, 37% 1st pregnancy
- HIV prevalence women 21%
- Facility: 223 men tested, 20 (9%) HIV+, 18 linked to care
- Home: 28 men tested, 2 (7%) HIV+, 1 linked to care
- Self test: 668 men tested - even with incentives, only 60% received post-test counseling, 23 (6%) self report HIV+, 14 confirmatory test, 14 LTC

→ HIVST most popular but most expensive per HIV dx; need operational research to improve linkage to confirmatory testing and care.
Randomized Trial on Index HIV Self-Testing for Partners of ART Clients, Malawi

Dovel K et al. CROI 2019 Seattle, WA Abs.93

3 district hospitals Malawi; new ART clients ≥15 yrs with partner ≥15 yr, unknown HIV status, no hx IPV, lives in catchment area.

Standard of Care (N=135): Passive partner referral slip
Index take slip home to partner; slip asks partner to attend nearest health facility; disclosure counseling

Randomized 1:2.5
75% (365) index client 4 wk FU survey:
107 SOC, 258 HIVST
62% (161) partners completed FU survey

Index HIVST (N=349): Oraquick HIV ST
Index given SOC and HIVST kit; demonstration of HIVST, local tailored HIVST instructions; counseling

Distributed to partner
HIV testing in partners
HIV+ partner test

Similar partner distribution More partners tested Similar HIV+ prevalence

→ HIVST tested more partners
→ HIVST identified more HIV+ partners
→ HIVST needed better instruction
→ But linkage to care and ART start was poor

ART initiation in HIV+ partner
6-month ART initiation, medical chart review: (n=23 facilities)

Population SOC HIVST
Total 3/4 (25%) 7/30 (23%)
Male Partner 3/4 (75%) 6/27 (22%)
Female Partner 0/0 (0%) 0/1 (0%)
Youth (15-24) 0/0 (0%) 1/2 (50%)

Partner return for ART start poor (23%)

Ease of test use (self-report)
Reported by index partners who used HIVST (n=122)

Variable Total Female Partner Male Partner
ART client helped with HIVST 65% (79/122) 76% (31/41) 59% (48/81)
Unable to interpret result 8% (10/122) 5% (2/41) 10% (8/81)
Accepting results 8% (10/122) 7% (3/41) 9% (7/81)
Keeping results private 1% (1/122) 2% (1/41) 0% (0/81)

65% partners needed help and 7% couldn’t interpret
ARV Drugs in Children
**Dolutegravir in Children**

**CROI 2019 Seattle, WA**

- **Frange P. Abs. 828 (France)**
  - 109 children (92% ART-exp, 11% prior InSTI) 5-18 yrs starting DTG
  - Pre-DTG suppression 58.7%; switch DTG ↑ to 79.8%, similar rates all ages
  - Low rate AE

- **Ruel T. Abs. 829LB (P1093)**
  - Age ≥6 mos-<2 yr and ≥2 yr-<6 yr
  - PK study of higher dosing of dispersible tablet (DT)
  - Increased wt band DTG-DT dosing met pre-specified AUC24 and C24 targets both age groups.

- **Bollen P. Abs. 830LB (ODYSSEY)**
  - PK evaluation of 50 mg DTG tab and 30 mg DTG-DT in children 20-<25 kg (EMA rec dose 25 mg tab 20-<30kg).
  - Daily 50 mg DTG and 30 mg DT had similar PK profiles but Cmax (6.07-7.42 mg/L) was slightly higher than adults (5.41 mg/L).

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**Good suppression >5 yr/o with switch to DTG**

<table>
<thead>
<tr>
<th>Duration of follow-up (months) (median, range)</th>
<th>Total (n=109)</th>
<th>Group 1 (5-12 years) (n=53)</th>
<th>Group 2 (12-18 years) (n=51)</th>
<th>Group 3 (≥18 years) (n=25)</th>
</tr>
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<tbody>
<tr>
<td>Viral load follow-up</td>
<td></td>
<td>12 (6-36)</td>
<td>24 (6-54)</td>
<td>24 (6-48)</td>
</tr>
<tr>
<td>Sustained virological success (n, %)</td>
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<tr>
<td>VL &lt;50 copies/mL at the last visit (without ARV change) (n, %)</td>
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<tr>
<td>Emergence of R463L in patients with virological failure (n, %)</td>
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<tr>
<td>Safety</td>
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<tr>
<td>Grade II clinical events</td>
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<tr>
<td>Grade III/IV biological events</td>
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<tr>
<td>Stop for intolerance</td>
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**Dosing for 6mo-6 yrs defined**

<table>
<thead>
<tr>
<th>Weight Band (kg)</th>
<th>Revised Dose (mg)</th>
<th>Dose (mg/kg) for Weight Range</th>
<th>Dosage previously tested (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-&lt;10</td>
<td>15</td>
<td>2.50/1.50</td>
<td>10</td>
</tr>
<tr>
<td>10-&lt;14</td>
<td>29</td>
<td>2.00/1.43</td>
<td>15</td>
</tr>
<tr>
<td>14-&lt;20</td>
<td>25</td>
<td>1.79/1.25</td>
<td>15</td>
</tr>
</tbody>
</table>

**DTG trough by age cohort**

**Adult dose for >20kg?**

**DTG levels over time: 30 mg DT, 50 mg tab, 25 mg tab**
**Bunglawala FS. Abs.827**

- Simulation of DTG dosing for neonates based on PK of RAL (metabolized UGT1A1) and midazolam (CYP3A4) in neonates.
- Different DTG dosing strategies simulated; target achieve levels ~ to those observed in pediatric ($C_{trough}$ 0.99 mg/L; $AUC_{24}$ 50.1 mg.h.L).  

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Total Dose (mg)</th>
<th>Dose* (mg/kg)</th>
<th>$C_{max}$ (mg/L)</th>
<th>$AUC_{av}$ (mg.h/L)</th>
<th>$C_{max}$ (mg/L)</th>
<th>$AUC$ (mg.h/L)</th>
<th>$C_{trough}$ (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too high</td>
<td>1</td>
<td>5 QD</td>
<td>1.4 (1.7 - 1.1)</td>
<td>3.99 ± 1.1</td>
<td>66.1 ± 22.9</td>
<td>2.3 ± 1.1</td>
<td>47.8 ± 14.3</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>4 QD</td>
<td>1.1 (1.3 - 0.9)</td>
<td>3.3 ± 0.6</td>
<td>47.0 ± 14.1</td>
<td>1.7 ± 0.6</td>
<td>35.1 ± 10.5</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>3 QD</td>
<td>0.85 (1 - 0.7)</td>
<td>2.4 ± 0.6</td>
<td>35.2 ± 13.4</td>
<td>1.3 ± 0.7</td>
<td>27.3 ± 9.2</td>
</tr>
<tr>
<td>Too low</td>
<td>4</td>
<td>2 QD</td>
<td>0.55 (0.7 - 0.4)</td>
<td>1.6 ± 0.3</td>
<td>23.5 ± 6.6</td>
<td>0.8 ± 0.3</td>
<td>18.0 ± 6.4</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Day 1-7 = 2 QD, Day 8-28 = 3 QD</td>
<td>0.7 (1 - 0.4)</td>
<td>1.8 ± 0.7</td>
<td>30.5 ± 11.7</td>
<td>1.3 ± 0.7</td>
<td>25.9 ± 7.6</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Day 1-7 = 2 QD, Day 8-28 = 3.5 QD</td>
<td>0.8 (1.2 - 0.4)</td>
<td>2.2 ± 1.4</td>
<td>35.4 ± 17.2</td>
<td>1.6 ± 1.1</td>
<td>28.8 ± 8.4</td>
</tr>
</tbody>
</table>

*Median (Range), neonate weight range in the model is 3.0 - 4.5kg. $C_{max}$: Maximum plasma concentration over 28 day simulations; $C_{max}$: Maximum plasma concentration after final dose has been administered; $AUC_{av}$: Average area under curve over 28 day simulations; $AUC$, Area under curve after final dose; $C_{trough}$: Minimum plasma concentration after final dose.

- Regimens 2, 3, 5 and 6 (>2 to 4 mg QD) result in PK parameters comparable to those in pediatric patients.

**Figure 1** PK profile showing average concentration of DTG ($C_{av}$) from 0-28 days, (inset) DTG PK profile of daily doses.
Early Infant Treatment (EIT) Study
Broncano PG et al. CROI 2019 Seattle, WA Abs. 43

- Screened 10,600 newborns, identified 44 HIV+ infants (0.4%) → 42 enrolled in EIT and start immediate ART (AZT/3TC/NVP then change at 2-5 weeks to AZT/3TC/LPV/r).

- 10 infants have complete testing at 84-96 weeks; compared to control infants starting at 1-12 mo and suppressed adults

Cross-Sectional Comparison: EIT, Control, Adults

→ Significant decline cell-associated provirus with early ART compared to control and adults on LT suppressive therapy

→ At 84-96 wks, with early ART saw an increase in defective proviral DNA and decrease in intact DNA, with levels of both lower in early treatment compared to control and adults on LT suppressive therapy
Neonatal ART Started <7 vs 7-28 Days Reduces Time to Viral Suppression

*Rodriguez SD et al. CROI 2019 Seattle, WA Abs. 44*

- Compared VL decline in 25 infants started at <7 days vs 19 started at 7-28 days of life.

- While overall probability of suppression at 48 weeks similar, the probability **early** suppression (by 3-6 mos) decreased by 35% for each week elapsed prior to starting ART.

\[
\text{HR} = 0.65 \ (0.46, \ 0.92)
\]
Adolescents and HIV, Including PrEP in Adolescents and Women
Recent HIV Infection Adolescent Girls and Young Women, Malawi

Payne D et al. CROI 2019 Seattle, WA Abs. 831

- Nov 2017-July 2018 enrolled pregnant women age 15-24 years newly dx with HIV at 1\textsuperscript{st} ANC visit at 121 facilities; recent infection testing algorithm (RITA) used to define recent infection.

- Among 54,643 attending 1\textsuperscript{st} ANC, HIV prevalence 4.3%; 1,159 had new HIV dx and eligible for study, 589 (50.9%) enrolled in study.

- 11.7% with new dx had recent infection → annualized incidence of 0.59%.

- Incidence higher among those aged 20-24 years (vs 15-19 years); Blantyre residence

![Estimated of HIV incidence in pregnant adolescent girls and young women Malawi 2017-2018](image)
Similiar findings across all projects:

- PrEP interest and uptake is high (>90%) (data from HPTN 082).
- Risk score of PrEP acceptors high
- STI prevalence ~30%
- IPV in past year 30-50%
- Depressive symptoms 42%
- Limited contraceptive taking experience

- PrEP should be offered as **part of comprehensive youth-friendly services** (flexible hours non-judgmental)
- Delivered as a part of a **package of sexual and reproductive health services** (including ongoing choice in context of changing risk, refills for PrEP/contraception, add STI testing)
- Respond to greatest health needs (including screen for IPV, referral for mental health services)
Persistence with PrEP Use in Adolescent and Young Women Initiating PrEP in MCH and FP Clinics

Mugwanya K et al. CROI 2019 Seattle, WA Abs.993

- Women 15-45 years seeking routine ANC, PNC and FP in 16 high volume facilities in Kenya screened for HIV risk and willingness to initiate PrEP; 2304 women initiated on PrEP.
- Median age 24; 58% had partner unknown HIV status, 96% reported recent condomless sex.
- Continuation at 1, 3 and 6 months was 38%, 21% and 10% overall; similar by delivery point.
- Continuation of PrEP use at 3 months was independently higher among women with HIV positive male partners (p<0.01) and older women 35 years and above (p=0.02); only partner HIV status independently associated with continuation at month 6.
- Commonly reported reasons for stopping PrEP included low perceived risk of HIV (23%), experiencing side effects (19%), pill burden (17%), and that partner is HIV negative (17%).

2,304 women on PrEP

<table>
<thead>
<tr>
<th>Age-Years</th>
<th>N (%) or median (interquartile range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;24 years</td>
<td>1086 (47%)</td>
</tr>
<tr>
<td>≥24 years</td>
<td>1218 (53%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Marital status</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>1837 (79%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Delivery point</th>
<th>N (%) or median (interquartile range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal care</td>
<td>912 (40%)</td>
</tr>
<tr>
<td>Postnatal care</td>
<td>1114 (48%)</td>
</tr>
<tr>
<td>Family planning</td>
<td>278 (12%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Partner HIV status</th>
<th>N (%) or median (interquartile range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>758 (33%)</td>
</tr>
<tr>
<td>Positive</td>
<td>215 (9%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1327 (58%)</td>
</tr>
</tbody>
</table>

PrEP continuation by delivery point

<table>
<thead>
<tr>
<th>Month 1</th>
<th>Month 3</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>38%</td>
<td>21%</td>
</tr>
<tr>
<td>ANC</td>
<td>34%</td>
<td>18%</td>
</tr>
<tr>
<td>PNC</td>
<td>39%</td>
<td>6%</td>
</tr>
<tr>
<td>FP</td>
<td>41%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Correlates continuing PrEP at 3 Mos

<table>
<thead>
<tr>
<th>Age groups</th>
<th>N (%)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 years</td>
<td>362</td>
<td>23%</td>
</tr>
<tr>
<td>20-24 years</td>
<td>872</td>
<td>18%</td>
</tr>
<tr>
<td>25-34 years</td>
<td>877</td>
<td>22%</td>
</tr>
<tr>
<td>≥35 years</td>
<td>193</td>
<td>37%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reported Partner HIV status</th>
<th>N (%)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>1327</td>
<td>19%</td>
</tr>
<tr>
<td>Negative</td>
<td>758</td>
<td>18%</td>
</tr>
<tr>
<td>Positive</td>
<td>215</td>
<td>52%</td>
</tr>
</tbody>
</table>
High Adherence in Young Women, Cape Town South Africa, in First 3 Months After PrEP start

- Adherence at 3 months assessed by tenofovir-diphosphosphate (TFV-DP) in dried blood spots. High adherence: TFV-DP >700 fmol/punch (>4 doses/wk); Medium: 350-700 fmol/punch (2-3 doses/wk).

- **Celum CL. Abs. 994:** 3 Ps for Prevention Study (Perception, Partners, Pills) enrolled 200 sexually active women 16-25 years; median age 19 years.
  - Retention 89% at 3 mos; 50% had high and 80% had ≥medium adherence at 2 and 3 months.
  - High adherence associated with: partner unknown or HIV+, disclosure of PrEP use.

- **Celum CL. Abs 995:** 451 sexually active HIV-negative women ages 16-25 were enrolled; 427 accepted PrEP (412 at enrollment, 15 after enrollment); median age 21 years (6% <18 years).
  - 84% had TFV/DP detectable at mo 3; 25% high & 48% ≥medium adherence
  - Predictors high vs low adherence: attend adherence support group, no depression, # sex partners
Pooled analysis comparative data on efficacy and safety of TAF vs TDF in women (stratified by ART naïve vs virally suppressed).

- Viral response (96 wks) same with TAF but bone and renal toxicity improved compared to TDF.
F/TAF Non-Inferior to F/TDF for PrEP, MSM/TGW: Discover Study

Hare CB et al. CROI 2019 Seattle, WA Abs. 104LB

F/TAF 200/25 mg QD N=2694

F/TDF 200/300 mg QD N=2693

96 Weeks

Primary analysis: HIV incidence/100 PY after 100% complete wk 48 and 50% complete wk 96

Non-inferiority margin upper 95% CI <1.62

Expected incidence 1.44/100 PY (IPrEx; PROUD; IPERGAY)

- F/TAF non-inferior to F/TDF for prevention HIV infection in MSM/TGQ
- Both well tolerated, low d/c
- F/TAF had better bone and renal outcomes
TB and HIV

- Pregnancy
- Pediatrics
- General
Prospective cohort pregnant HIV+ women with and without TB disease in Soweto, S Africa, January 2011-July 2014, FU pregnancy to 12 mo PP for MTCT, pregnancy outcomes, maternal/infant mortality and TB.

Evaluated outcomes by IPT use (non-randomized, self-reported).
IPT use in 2nd/3rd trimester during pregnancy was not associated with a higher rate of poor maternal or infant outcomes in this cohort of 152 women, after controlling for CD4, VL, ART, maternal age, BMI and anemia.

**Adverse Pregnancy Outcome by IPT Use**

- **Fetal Demise:** 1% (1/11) vs. 1% (1/23) (p=0.06)
- **Prematurity:** 10% (1/10) vs. 15% (1/6) (p=0.09)
- **LBW:** 9% (1/18) vs. 22% (2/9) (p=0.06)
- **Birth defect:** 1% (1/11) vs. 2% (2/23)
- **Composite:** 27% (6/23) vs. 22% (2/9)

**TB disease:**
- Maternal: 1 case (no IPT)
- Infant: No cases

*Adjusted for CD4, VL, ART type, maternal age, anemia

→ Higher risk adverse pregnancy outcome: no IPT, low CD4, anemia
Tshepiso Cohort vs APPRISE RCT Trial

Salazar-Austin N et al. CROI 2019, Seattle, WA Abs. 77

**Tshepiso**: Observational 2\textsuperscript{nd}/3\textsuperscript{rd} trimester IPT (self-reported); 152 deliveries (69 IPT, 82 no IPT)

**APPRISE**: RCT of immediate (2\textsuperscript{nd}/3\textsuperscript{rd} trimester) IPT vs deferred (12 wk postpartum) IPT; 962 deliveries (460 Immediate, 466 Deferred)

**Adverse Pregnancy Outcome by IPT Use**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>IPT (N=69)</th>
<th>No IPT (N=82)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal Death</td>
<td>1%</td>
<td>1%</td>
<td>1.00</td>
</tr>
<tr>
<td>Prematurity</td>
<td>10%</td>
<td>10%</td>
<td>0.06</td>
</tr>
<tr>
<td>LBW</td>
<td>9%</td>
<td>10%</td>
<td>0.60</td>
</tr>
<tr>
<td>Birth defect</td>
<td>1% 2%</td>
<td>15%</td>
<td>1.00</td>
</tr>
<tr>
<td>Composite</td>
<td>22%</td>
<td>27%</td>
<td>0.09</td>
</tr>
</tbody>
</table>

**No. events**
- Fetal Death: 1 1 (p=1.00)
- Prematurity: 7 18 (p=0.06)
- LBW: 6 10 (p=0.60)
- Birth defect: 1 2 (p=1.00)
- Composite: 11 23 (p=0.09)

**TB disease**:  
Maternal: 1 case (no IPT)  
Infant: No cases

**Death**:  
Maternal: 0 (IPT), 1 (no IPT)  
Infant: 1 (IPT), 0 (no IPT)

**Adverse Pregnancy Outcome by Immediate vs Deferred IPT**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Immediate IPT (N=460)</th>
<th>Deferred PP IPT (N=466)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal death</td>
<td>4%</td>
<td>2%</td>
<td>0.09</td>
</tr>
<tr>
<td>Prematurity</td>
<td>11% 9%</td>
<td>10%</td>
<td>0.29</td>
</tr>
<tr>
<td>LBW</td>
<td>14%</td>
<td>10%</td>
<td>0.07</td>
</tr>
<tr>
<td>Birth defect</td>
<td>2% 13%</td>
<td>2%</td>
<td>0.26</td>
</tr>
<tr>
<td>Composite</td>
<td>23%</td>
<td>17%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**No. events**
- Fetal death: 17 9 (p=0.09)
- Prematurity: 48 40 (p=0.29)
- LBW: 62 46 (p=0.07)
- Birth defect: 10 6 (p=0.26)
- Composite: 106 78 (p=0.01)

**TB disease**:  
Maternal: 3 (immediate), 3 (deferred)  
Infant: 0 (immediate), 1 (deferred)

**Death**:  
Maternal: 2 (immediate), 4 (deferred)  
Infant: 11 (immediate), 17 (deferred)

**Severe pregnancy outcome composite**:  
Immediate: 6.3%  
Deferred: 4.6%  
P=0.27
Improving Child TB Contact Management, Lesotho – PREVENT Study
Hirsch-Moverman Y et al. CROI 2019 Seattle, WA Abs.79

- Cluster-randomized trial of community-based intervention (10 clinics) vs SOC (10 clinics) to improve identification and screening of child contacts.
- All adult TB pt newly registered at clinics Jan 2017-June 2018 and child contacts included, with data collection from medical records.

<table>
<thead>
<tr>
<th>Comparison of Study Interventions</th>
<th>SOC</th>
<th>CBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three I’s training</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Child contact screening for TB</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>PT provision to child contacts</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Child screening and PT provision training according to clinical algorithm</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Nurse mentorship and monitoring</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Health education in facilities and community for caregivers using PT literacy curriculum</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Community-based village health workers (VHW) working with facility-based VHW to link to services</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Consistent community support via VHW</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

**Identification:** # child contacts/adult case was low, not significantly different

**Screening:** More child contacts/adult case screened with CBI but not statistically significant

**Yield:** Non-significant trend for higher yield at CBI sites

- Adult TB cases in register 973 (64% male, 68% HIV+)
  - CBI (N=490) TB card located, contact filled out 484 (99%)
  - SOC (N=483) TB card located, contact filled out 314 (65%)
- Child contact ID per TB case
  - CBI 216 (44%), 4/10 cases
  - SOC 163 (34%), 3/10 cases
- Child contact ID and screened per TB case
  - CBI 204 (94%), 4/10 cases
  - SOC 101 (62%), 2/10 cases

*p=0.08*
Nevirapine PK is Modified by TB Therapy with Rifampin in Young Children

Kwara A et al. CROI 2019 Seattle, WA Abs.825

- HIV+ children with (N=30) or without TB (N=23) aged 3-35 months or <10 kg started on NVP 200 mg/m² + 2NRTI with 2-week lead in.
- Proportion of children with NVP $C_{\text{min}} <3$ mg/L was 61% in HIV/TB coinfected children on RIF and 31% in HIV only (p=0.03) or off RIF.
- In multivariate analysis, TB coinfection and CYP2B6 516TT genotype influenced NVP PK.

In 14 HIV/TB children with PK on and off RIF, NVP $C_{\text{min}}$, $C_{\text{max}}$, and $AUC_{0-12h}$ was significantly ↓ & CL/F ↑ during co-administration of NVP/RIF.
Test and Treat, Viral Load Testing, Viral Suppression
Impact of Universal Testing and Treatment in Zambia and South Africa – HPTN 071

Hayes RJ et al. CROI 2019, Seattle, WA Abs. 92LB

- Universal test and treat – 21 communities randomized to one of 3 arms (7 communities per arm); primary outcome HIV incidence.

**Pop-ART Combination Intervention**

**Viral Suppression by Arm**

<table>
<thead>
<tr>
<th></th>
<th>Pop-ART Immediate</th>
<th>Pop-ART National guide</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral suppression</td>
<td>1531/2159 (72%)</td>
<td>1318/1891 (68%)</td>
<td>1480/2183 (60%)</td>
</tr>
<tr>
<td>Adjusted prevalence ratio*</td>
<td>1.16 (0.99, 1.36)</td>
<td>1.08 (0.92, 1.27)</td>
<td>1</td>
</tr>
<tr>
<td>VS compared to SOC</td>
<td>16% increase</td>
<td>8% increase</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.07</td>
<td>0.30</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age category, sex
Impact of Universal Testing and Treatment in Zambia and South Africa – HPTN 071
Hayes RJ et al. CROI 2019, Seattle, WA Abs. 92LB

Primary endpoint: Incidence PC12 to PC36 by Community

- PopART achieved first 2 UNAIDS 90-90 targets
- PopART with ART by local guidelines reduced incidence by 30% in these high burden settings
- Community-based services for universal HIV testing and linkage are key component of global combination prevention

Primary endpoint: Incidence in PC12-PC36

<table>
<thead>
<tr>
<th></th>
<th>Pop-Art Immediate</th>
<th>Pop-Art National guide</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV incidence</td>
<td>198/12,990 (1.45%)</td>
<td>157/14,149 (1.06%)</td>
<td>198/12,563 (1.55%)</td>
</tr>
<tr>
<td>Adjusted rate ratio*</td>
<td>0.93 (0.74, 1.18)</td>
<td>0.70 (0.55, 0.88)</td>
<td>1</td>
</tr>
<tr>
<td>Incidence compared to SOC</td>
<td>7% reduction</td>
<td>30% reduction</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.51</td>
<td>0.006</td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted for age category, sex and baseline community HIV prevalence; reported numbers include imputation for PC12 and PC24 missed visits
Impact of Universal Testing and Treatment Botswana

Wirth K et al. CROI 2019 Seattle, WA Abs.95

- Pair-matched communities randomized trial 30 communities Botswana, October 2013, interventions ended March 2018, FU completed April 2018

**Intervention (15 communities)**
- Community mobilization
- Home-based and mobile HIV testing campaigns, targeted testing
- Linkage to care support: scheduled clinic visits, SMS reminder, active tracing is missed apt
- Early ART (universal from June 2016 at 1st visit)
- Strengthened VMMC

**SOC (15 communities)**
- ART if CD4 <350 or WHO III/IV or pregnant until June 2016 when moved to universal ART

- Selected 1 pair of communities per region

Intervention uptake assessed through end-of-study survey in communities not in longitudinal cohort
HIV Diagnosis, ART, Suppression and VMMC Increased in Both Arms, with Greater Increase in Intervention

Wirth K et al. CROI 2019 Seattle, WA Abs.95

- Significant increase across cascade with intervention.

### HIV Diagnosis

**HTC coverage** = documented HIV-negative test result in past 12 months or awareness of HIV-positive status among all participants

- **Baseline** Standard of Care: 43%
- **Study End** Standard of Care: 35%
- **Baseline** Intervention: 40%
- **Study End** Intervention: 88%

<table>
<thead>
<tr>
<th>Intervention effect</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.29</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>(1.17, 1.43)</td>
<td></td>
</tr>
</tbody>
</table>

**HIV diagnosis** = documented awareness of HIV-positive status among all HIV-positive participants

- **Baseline** Standard of Care: 86%
- **Study End** Standard of Care: 88%
- **Baseline** Intervention: 84%
- **Study End** Intervention: 93%

<table>
<thead>
<tr>
<th>Intervention effect</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.08</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>(1.04, 1.13)</td>
<td></td>
</tr>
</tbody>
</table>

### ART Coverage

**ART coverage** = documented current receipt of ART among all HIV-positive participants (regardless of prior diagnosis)

- **Baseline** Standard of Care: 76%
- **Study End** Standard of Care: 72%
- **Study End** Intervention: 90%

<table>
<thead>
<tr>
<th>Intervention effect</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.11</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>(1.07, 1.17)</td>
<td></td>
</tr>
</tbody>
</table>

### Viral Suppression

**Viral suppression** = VL <400 copies/mL on ART among all HIV-positive participants (regardless of diagnosis/ART status)

- **Baseline** Standard of Care: 75%
- **Study End** Standard of Care: 83%
- **Study End** Intervention: 88%

<table>
<thead>
<tr>
<th>Intervention effect</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.12</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>(1.09, 1.16)</td>
<td></td>
</tr>
</tbody>
</table>

### VMMC

**Male circumcision** = self-reported receipt of circumcision among HIV-negative men aged 18-49 years

- **Baseline** Standard of Care: 33%
- **Study End** Standard of Care: 35%
- **Study End** Intervention: 40%

<table>
<thead>
<tr>
<th>Intervention effect</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.26</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>(1.17, 1.35)</td>
<td></td>
</tr>
</tbody>
</table>
Factors Associated with Persistent Viremia with Universal Test and Treat, Uganda

Patel EU et al. CROI 2019 Seattle, WA Abs.96

- Rakai Community Cohort Study of adults 15-49 years, 5 surveys Nov 2011 and Feb 2017
- HIV VL measured in all HIV+ persons in 2011, 2015 and 2016

Factors associated with persistent viremia included:
- Being young (<29 years)
- Being Male
- Never Married
- Recent in-migration
Point of Care Viral Load Testing Improves Viral Suppression and Retention in Care

Drain PK et al. CROI 2019 Seattle, WA Abs. 53LB

- RCT at public clinic in Durban S Africa in adults >18 years presenting for 6 month post ART start FU visit
  - Intervention: POC viral load testing (Xpert) and same day counseling with task shifting to nurse for stable pt
  - SOC: lab viral load testing and care from nurse)

Primary outcome: 12 mo viral suppression and retention (pick up drugs)

<table>
<thead>
<tr>
<th></th>
<th>Intervention Arm</th>
<th>Standard-of-care Arm</th>
<th>Absolute Risk Difference</th>
<th>Non-inferiority (1-side 95% CI) P value</th>
<th>Superiority (2-side 95% CI) P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral suppression (&lt;200 copies/ml) and Retention in care at study clinic</td>
<td>89.7% (175/195)</td>
<td>75.9% (148/195)</td>
<td>13.9%</td>
<td>(≥7.6) &lt;0.001</td>
<td>(6.4-21.2) &lt;0.001</td>
</tr>
</tbody>
</table>

After 12 mo clinical FU, the intervention increased viral suppression and retention in care at the study clinic by 13.9% (95% CI 6.4-21.2%)
Secondary outcomes

Viral suppression <50 c/mL and retention

<table>
<thead>
<tr>
<th></th>
<th>Intervention Arm (N=195)</th>
<th>Standard-of-Care Arm (N=195)</th>
<th>Absolute Risk Difference</th>
<th>Superiority P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral suppression (&lt;200 copies/ml)</td>
<td>93.3%</td>
<td>83.1%</td>
<td>10.3%</td>
<td>0.003</td>
</tr>
<tr>
<td>Retention in care at study clinic</td>
<td>92.3%</td>
<td>84.6%</td>
<td>7.7%</td>
<td>0.026</td>
</tr>
<tr>
<td>Viral suppression ≤50 copies/mL and retention in care</td>
<td>85.6%</td>
<td>71.3%</td>
<td>14.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Viral suppression &lt;200 copies/ml and retention in care at any clinic</td>
<td>90.8%</td>
<td>78.5%</td>
<td>12.3%</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Entry VL and Communication of Results

<table>
<thead>
<tr>
<th></th>
<th>Intervention Arm</th>
<th>Standard-of-Care Arm</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entry of viral load result into health information system</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Median [IQR] days to enter viral load result in health information system</td>
<td>0 [0-0]</td>
<td>2 [1-4]</td>
<td>2 days</td>
</tr>
<tr>
<td>Communication of viral load result to patient</td>
<td>99.8%</td>
<td>81.5%</td>
<td>18.3%</td>
</tr>
<tr>
<td>Median [IQR] days to communicate viral load result to patient</td>
<td>0 [0-0]</td>
<td>28 [28-54]</td>
<td>28 days</td>
</tr>
</tbody>
</table>

Follow-Up HIV Care and Treatment

<table>
<thead>
<tr>
<th></th>
<th>Intervention Arm</th>
<th>Standard-of-Care Arm</th>
<th>Cox Hazard Ratio</th>
<th>Superiority P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switch to second-line ART after viral failure (&gt;1,000 copies/ml x2)</td>
<td>6/6 (100%)</td>
<td>4/9 (44%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Median [IQR] days to switch to second-line ART after viral failure</td>
<td>1 [0-7]</td>
<td>76 [20-134]</td>
<td>10.9</td>
<td>0.005</td>
</tr>
<tr>
<td>Referral into community-based ART delivery program</td>
<td>116 (60%)</td>
<td>52 (27%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Median [IQR] days to referral into community-based ART program</td>
<td>168 [168-175]</td>
<td>261 [231-281]</td>
<td>3.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Healthcare Utilization

<table>
<thead>
<tr>
<th></th>
<th>Intervention Arm</th>
<th>Standard-of-Care Arm</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total clinic visits per patient</td>
<td>5.2 ±1.6</td>
<td>6.1 ±1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinic visits with a Professional Nurse per patient</td>
<td>4.2 ±1.8</td>
<td>5.6 ±1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinic visits with an Enrolled Nurse per patient</td>
<td>0.9 ±0.9</td>
<td>0.4 ±0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of viral load tests per patient</td>
<td>2.0 ±0.3</td>
<td>1.9 ±0.5</td>
<td>0.006</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Point-of-care Test</th>
<th>Centralized Laboratory Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per HIV viral load test</td>
<td>$21.53</td>
<td>$25.98</td>
</tr>
<tr>
<td>Total over 5 years testing per patient</td>
<td>$129.18</td>
<td>$155.88</td>
</tr>
</tbody>
</table>
Some Key Take-Aways

- **Pregnancy:**
  - InSTI (RAL/DTG) particularly important ARV for use in late presenters for rapid VL decrease
  - Data on DTG and other InSTI on birth defects/birth outcomes reassuring but insufficient numbers of preconception exposures to draw conclusions regarding NTD
  - Infants infected despite maternal ART, particularly women on DTG with low VL at delivery, may have low infant VL which may complicate diagnosis
  - Incident infection increasingly important as cause of new infant infections

- **Maternal health:**
  - High rates of STI in HIV+ women
  - Concomitant EFV with RIF TB treatment may decrease DMPA levels requiring shorter DMPA interval (to q12 to q8-10 wk) during dual use

- **HEU:**
  - Worse outcomes of HEU vs HUU children for mortality, growth, development, but may be improved by better nutrition and sanitation

- **Pediatric treatment:**
  - DTG dosing for younger children evaluated; adult dose may be able to be used in children >20 kg
  - Very early ART decreases viral reservoir in children & earlier (<7 d) is better
Some Key Take-Aways

- **Adolescents:**
  - Incident infection in young girls remains a problem
  - PrEP is acceptable by young girls but adherence and retention seems to vary between studies, S Africa data showing good adherence by drug measurement but Kenya not as measured by patient retention
  - TAF seems to be effective as PrEP in MSM/TGW (not yet studies heterosexual tx), which has potential advantages for women compared to TDF in terms bone/renal toxicity

- **TB:**
  - IPT after 1st trimester of pregnancy appeared safe in one study, but associated with potential increase in adverse pregnancy outcome in APPRISE trial (CROI last year and in press)
  - Still need better ways to optimize child TB contact tracing
  - RIF given with NVP in children may decrease NVP levels

- **Testing and treatment:**
  - HIV self-testing improves male partner testing but linkage for confirmatory testing and ART remains suboptimal
  - The universal test and treatment approach appears to work to improve identification, treatment, suppression and decrease HIV incidence
  - POC viral load testing improved suppression and retention