



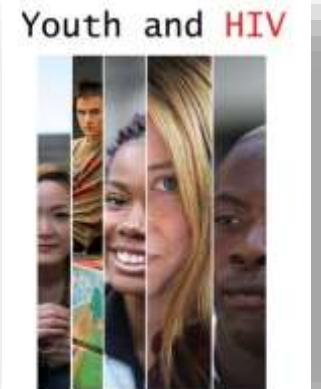
IAS 2020

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



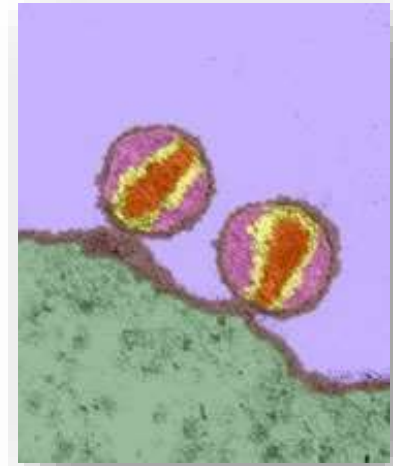
Lynne M. Mofenson MD

7/21/20 Long set



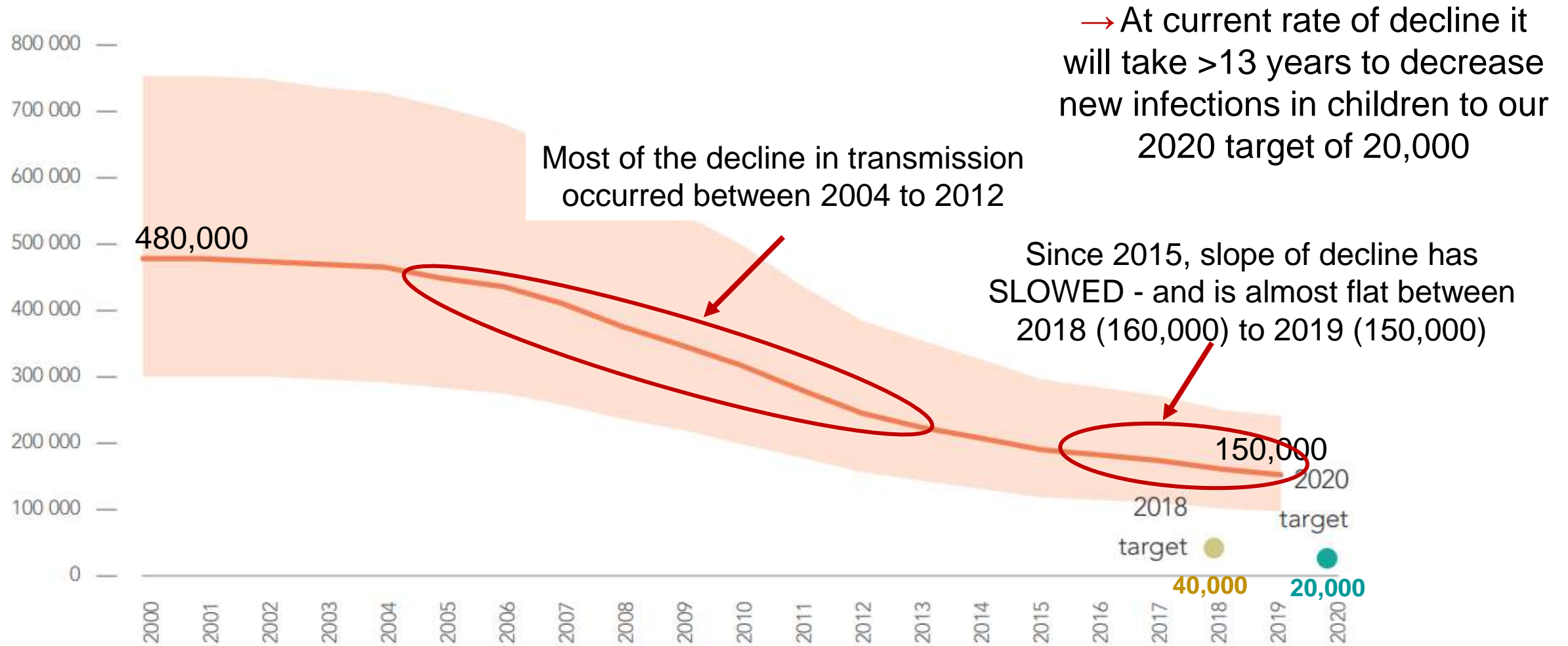


Update on Epidemiology of Pediatric HIV 2020



New Infections in Children Globally, 2000-2019

Significant Decline New Infections Since 2000 – But Progress Has Stalled

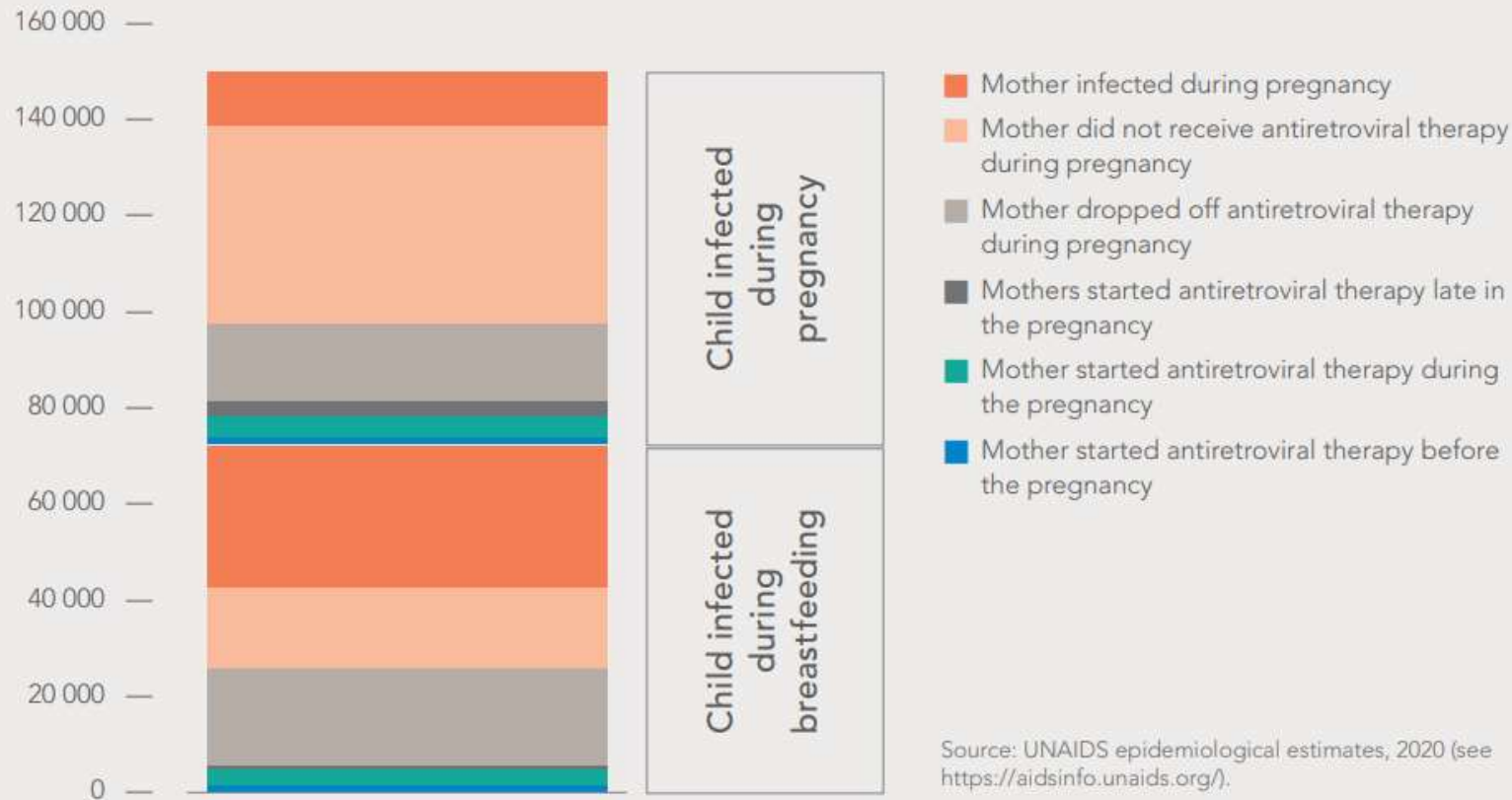


Source: UNAIDS epidemiological estimates, 2020 (see <https://aidsinfo.unaids.org/>).

We have missed
2018 (and 2020) targets

Causes of New Child Infections Globally 2019

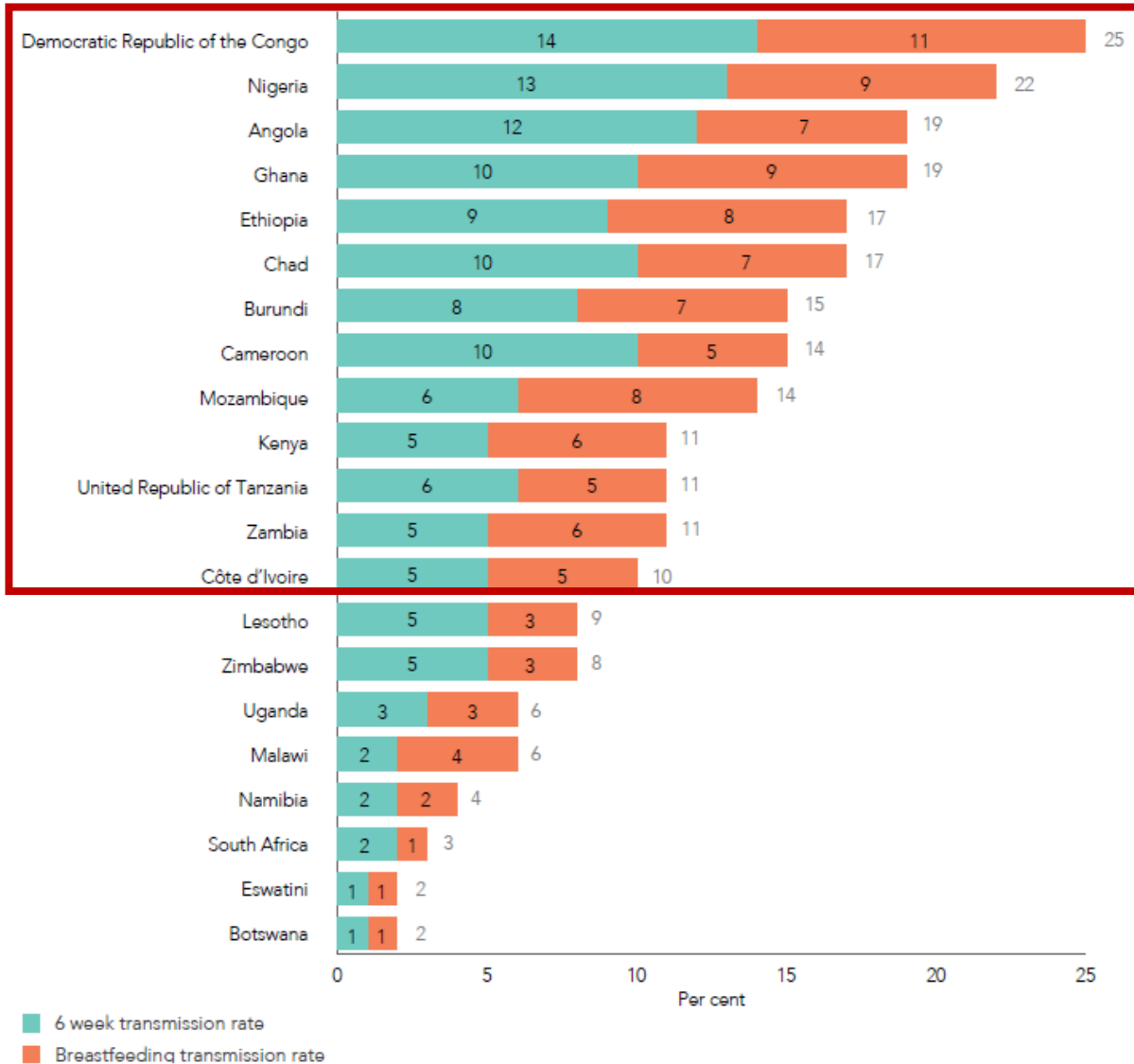
New child HIV infections by prevention of vertical transmission intervention, global, 2019



Primary gaps in PMTCT:

- **27%** of new infections in children were linked to **lack of maternal ART** during pregnancy or breastfeeding (likely not diagnosed or linked to treatment).
- **27%** of new infections in children were linked to **acute infection** pregnancy or breastfeeding.
- **24%** of new infections in children were linked to **mothers losing access to HIV care/lack of retention in care** either during pregnancy or breastfeeding

As a Result of These Missed Opportunities, Few Countries Have Achieved Overall MTCT Rates <5%

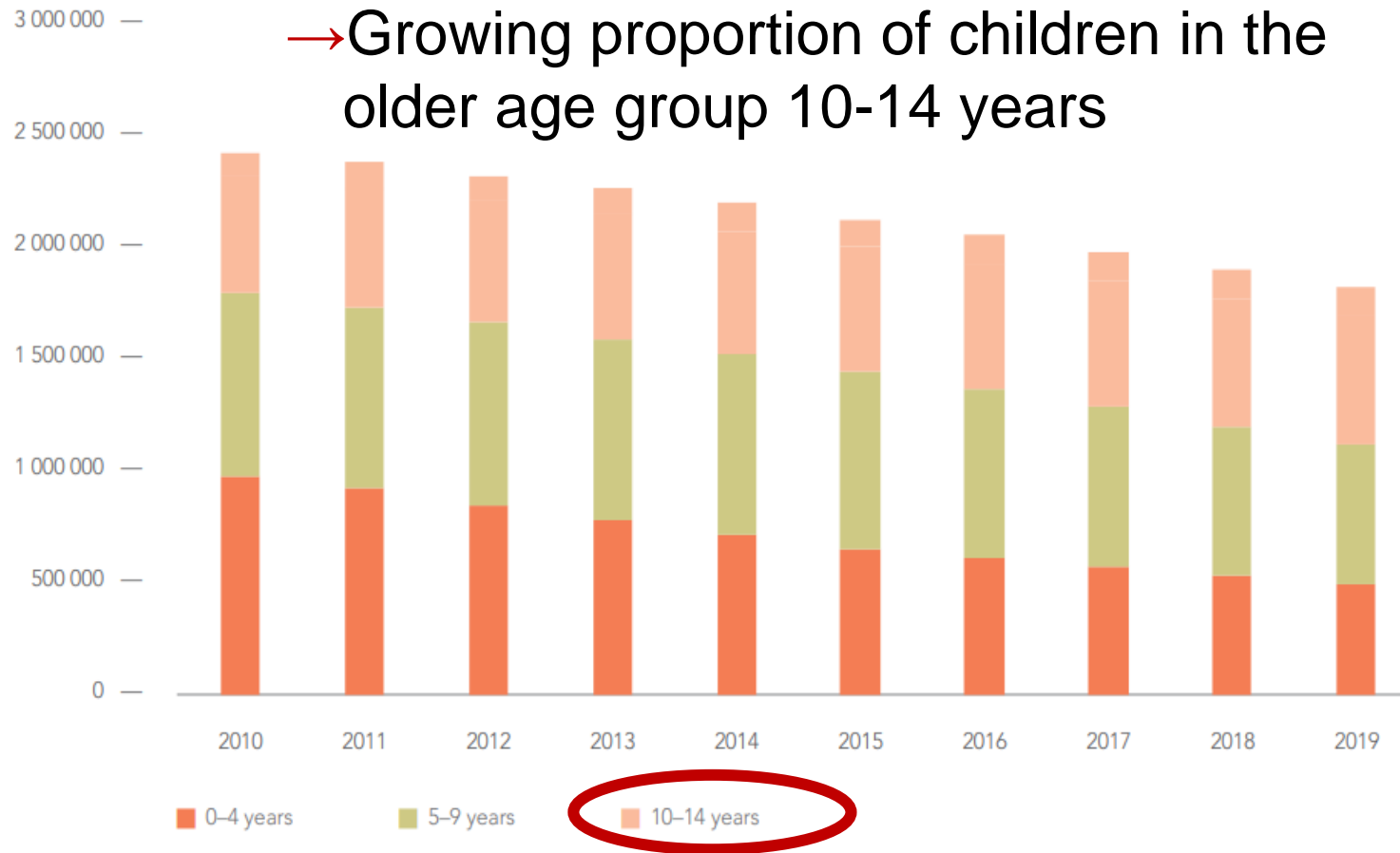


- 13 of the 21 focus countries in Africa continue to have MTCT rates of 10% or higher
- About half of this transmission occurs during breastfeeding
- Even in countries with high treatment coverage for pregnant women, gaps in retention, adherence and HIV prevention result in MTCT rates >5%

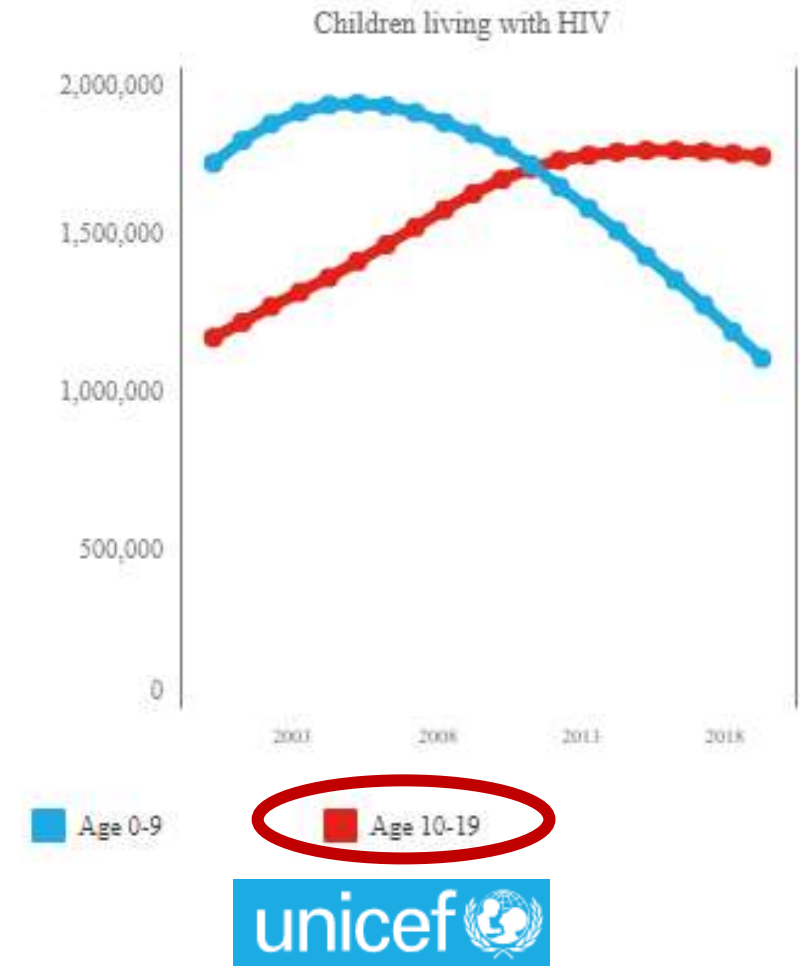
Number of Children 0-14 Years Living with HIV by Age 2010-2019

1.8 Million Children Living with HIV in 2018

Number of children living with HIV, by age, global, 2010–2019



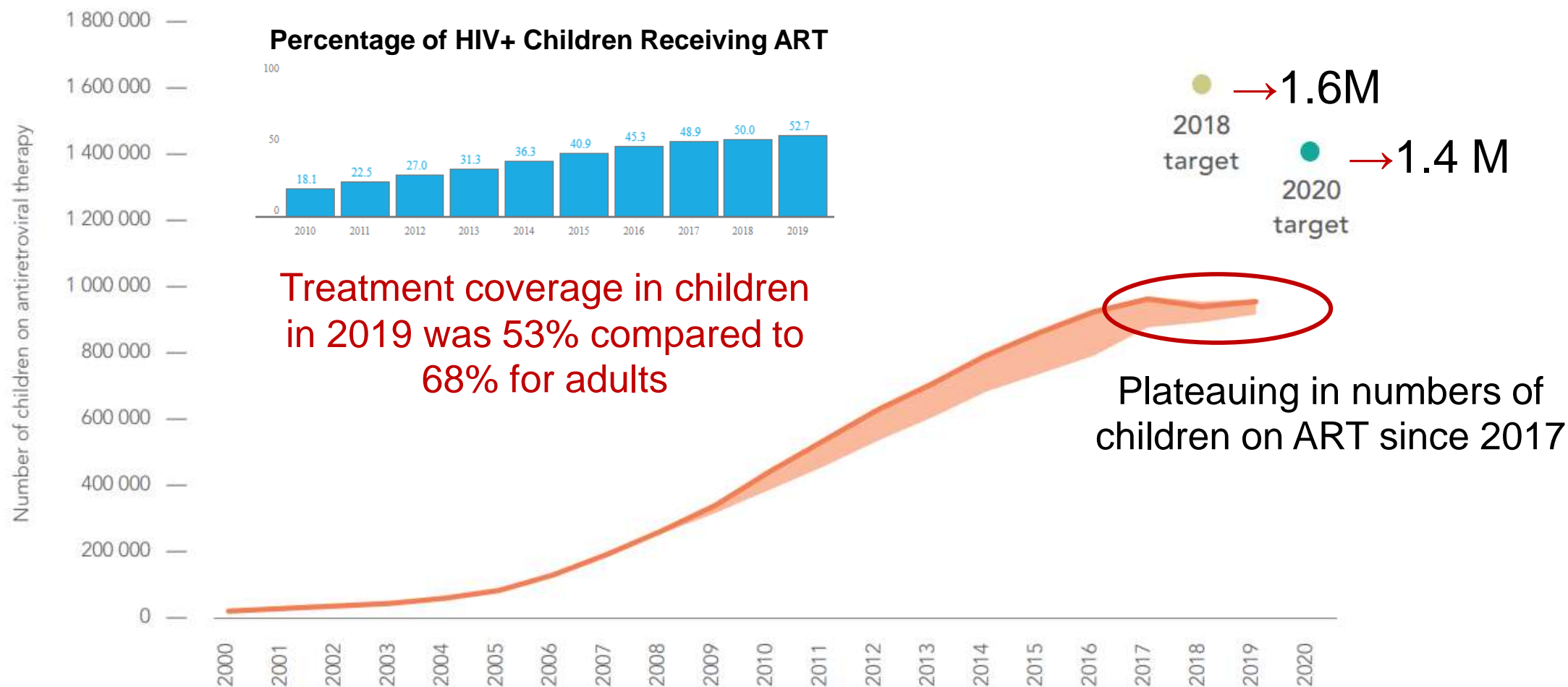
Source: UNAIDS epidemiological estimates, 2020 (see <https://aidsinfo.unaids.org/>).



<https://data.unicef.org/resources/hiv-estimates-for-children-dashboard/>

Although Number of Children on ART Has More Than Doubled Since 2010, All Pediatric Treatment Targets Have Been Missed

Number of children (aged 0–14 years) accessing antiretroviral therapy, global, 2000–2019 and 2018 and 2020 targets





Pediatric HIV – We Are Not Done Yet!

Martina Penazzato, Plenary



Why is it okay that...

Today



400 children acquired HIV



260 children died of
AIDS-related conditions

We need to...

ACT NOW



Do more operational...

RESEARCH



Keep...

INNOVATING



Index Testing



12 PEPFAR African Countries

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

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

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

Testing the children
of individuals living
with HIV is an
inexpensive, high
yield intervention.

Why is this not
being done more?

ACT NOW

Addressing Advanced Disease

SCREEN

For TB, cryptococcal
disease, developmental
delay

OPTIMIZE

ART start within 7 d,
optimal regimen,
counseling



TREAT

For TB, crypto
disease, severe
pneumonia

PREVENT

TB, PJP, cryptococcus,
pneumonia and catch-up
immunizations



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

Stop AIDS! screen,
treat, optimize,
prevent

Innovations to Speed Diagnosis



Point of care EID
results in more
rapid diagnosis
and ART start.

Why not
implement now?

Fourth 90: Health and Well-Being with HIV

SCREEN

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

REFER AND LINK

Clinical specialties,
disability, rehabilitation,
community psychosocial
support

NURTURING CARE

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

NUTRITION

Ensure optimal nutrition

ASSESS AND MANAGE

Psychosocial status and
mental health with
appropriate management

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

We need a 4th
"90"!

Optimize Treatment

DTG plus ABC/3TC in dispersible tablets can be
given to all children from 4 weeks of age

- DTG 5 mg DT US FDA approved* on June 12th
- DTG 10 mg scored tablets submitted for approval

DTG available for
children as young
as age 4 weeks.

NOW is the time
to implement!



Need for Operational Research



Learn From What You Are Doing

COVID-19: a stress test for change

Reframing the way we deliver care and support to children and adolescents

COVID-19 and ↑ # Countries Permitting
≥ 3Mo MMD in Children and Adolescents

	Before	After
Children <10	10/37 → 23/37	
Adolescents 10-19	14/37 → 26/37	

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

Policies to support multi-month
dispensing for children and
adolescents



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

Identify and Test Solutions in Multiple Settings

Effect of a differentiated service delivery model on
virological failure in adolescents with HIV in Zimbabwe
(Zvandiri): a cluster-randomized controlled trial

Wendy Mwaikwa, Nicola Willes, Juliet Mufuka, Sarah Berridge, Maureen Dikuma, Colin Mangwani, Hendramonah Mahomane, Walter Mangoni, Tazir Apollis, Ricardo Araya, Helen A Bliss, Frances M Cowan



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



Critical needs:

- Collaboration
- Capacity building
- Political support
- Resources

Innovate

COVID-19 Has Taught Us We can Do Things Differently



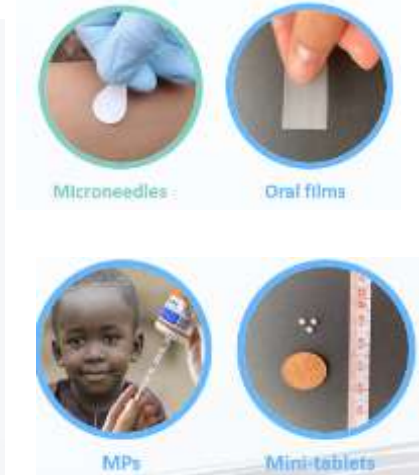
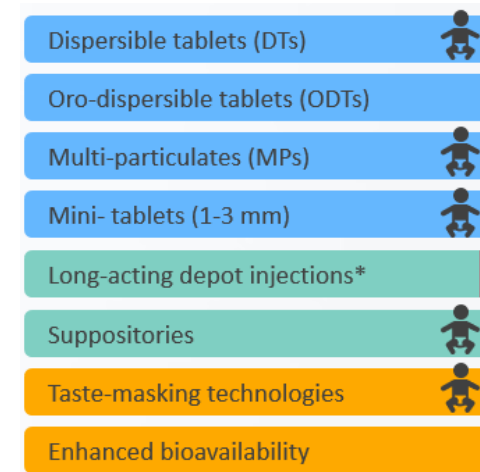
→ New adaptive trial designs can rapidly ID new treatments

→ Provide access to children/pregnant women rapidly

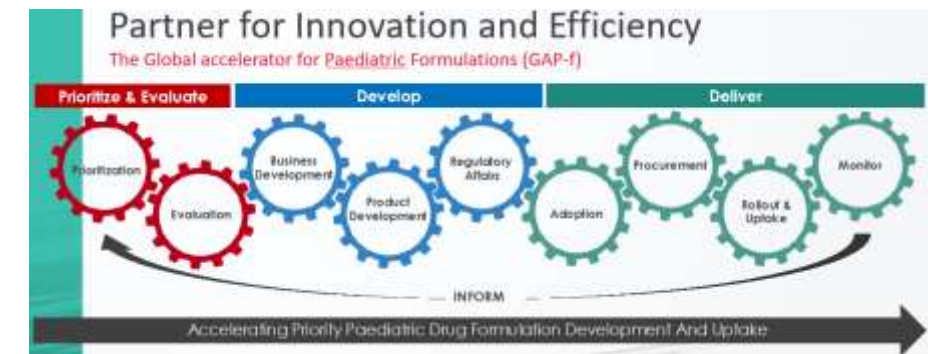
→ Rapidly develop trials in children & pregnant women

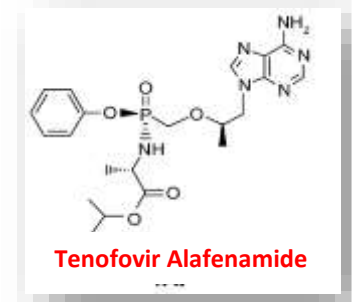
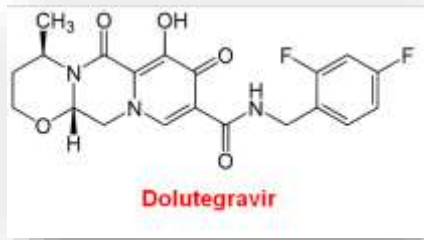
→ Multi-group/company collaborations can work

Promote New Technologies for Children



Speed New Drug Development for Children



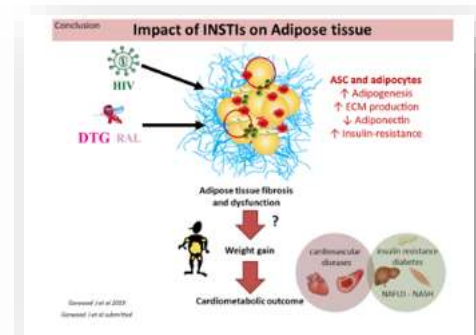
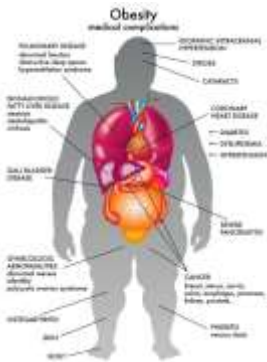


Dolutegravir, TAF



New Clinical Trials

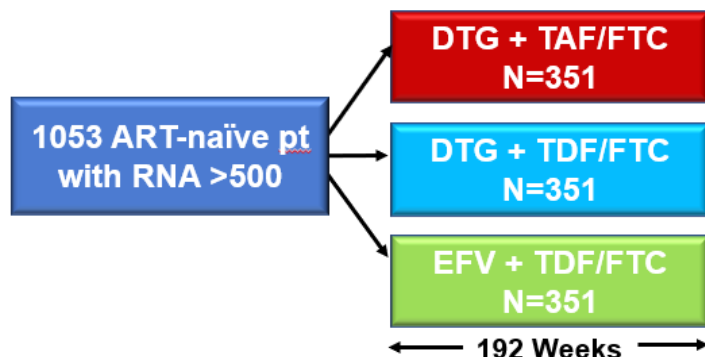
Efficacy but Toxicity as Well – Adults, Adolescents
Pregnancy, DTG and Neural Tube Defects



ADVANCE Trial: DTG + TDF or TAF vs EFV 1st Line ART

No Significant Difference Viral Efficacy at 96 Weeks

Sokhela S et al. IAS Virtual July 2020 Abs. OAXLB0104



Treatment Emergent Resistance

	TAF/FTC+DTG (n=351)	TDF/FTC+DTG (n=351)	TDF/FTC/EFV (n=351)
VF with resistance data at baseline & failure	12 (3%)	16 (5%)	21 (6%)
NRTI	0/12 (0%)	2/16 (13%)	9/21 (43%)
NNRTI	0/12 (0%)	0/16 (0%)	10/21 (48%)
Total: NRTI or NNRTI	0/12 (0%)	2/16 (13%)*	13/21 (62%)
INSTI	0/12 (0%)	0/16 (0%)	0/21 (0%)

*M184V mutations in both cases

Adverse Events

	TAF/FTC+DTG (n=351)	TDF/FTC+DTG (n=351)	TDF/FTC/EFV (n=351)
Number of patients with:			
Serious Adverse Events	22 (6%)	20 (6%)	31 (9%)
Grade 3 and 4 AEs	54 (15%)	60 (17%)	96 (27%)*
Drug-related Grade 1-4 AEs	212 (60%)	246 (70%)	267 (76%)
Death	1 (0%)	2 (1%)	2 (1%)

*higher rates of Grade 3 or 4 adverse events in EFV arm mainly from short-term elevations in liver enzymes

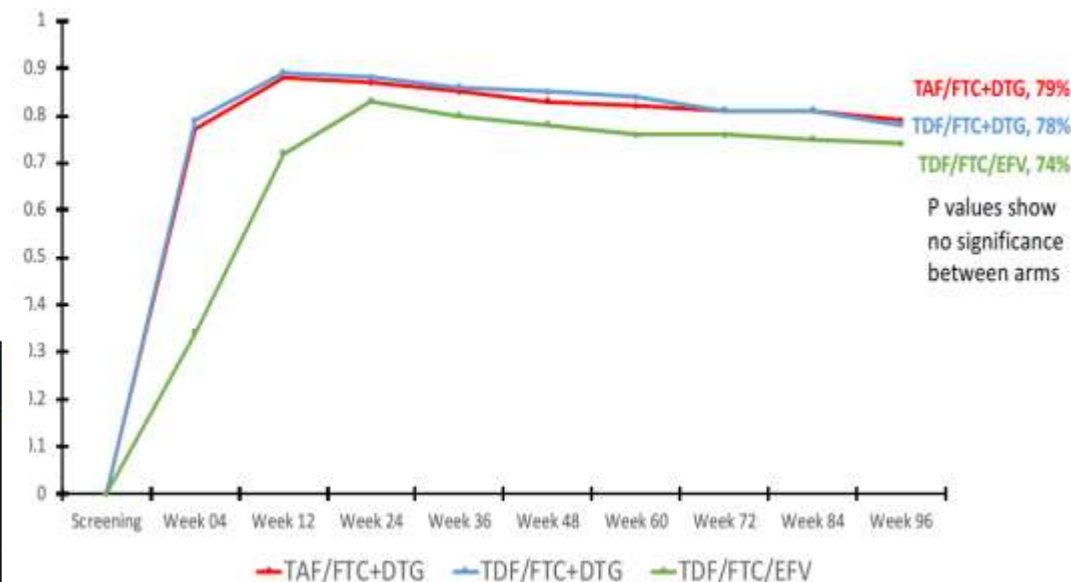
Grade 3/4 Renal Events, Renal Markers, CrCl

	TAF/FTC+DTG (n=351)	TDF/FTC+DTG (n=351)	TDF/FTC/EFV (n=351)
Renal	1 (0%)	2 (1%)	3 (1%)
Acute kidney injury	0 (0%)	0 (0%)	1 (0%)
Haematuria	0 (0%)	0 (0%)	1 (0%)
Hydronephrosis	0 (0%)	0 (0%)	1 (0%)
Lupus nephritis	0 (0%)	1 (0%)	0 (0%)
Proteinuria	0 (0%)	1 (0%)	0 (0%)
Renal impairment	1 (0%)	0 (0%)	0 (0%)
Creatinine clearance			
Grade 3 or 4	6 (2%)	46 (13%)	14 (4%)

Bone DXA at 96 Weeks

	TAF/FTC+DTG (n=351)	TDF/FTC+DTG (n=351)	TDF/FTC/EFV (n=351)
Hip			
Normal	291/307 (95%)	290/315 (92%)	260/293 (89%)
Osteopenia	16/307 (5%)	25/315 (8%)	33/293 (11%)
Lumbar Spine			
Normal	258/307 (84%)	252/315 (80%)	228/293 (78%)
Osteopenia	49/307 (16%)	63/315 (20%)	65/293 (22%)

Proportion with HIV RNA <50 c/mL at 96 Weeks



ADVANCE Trial: DTG + TDF or TAF vs EFV 1st Line ART

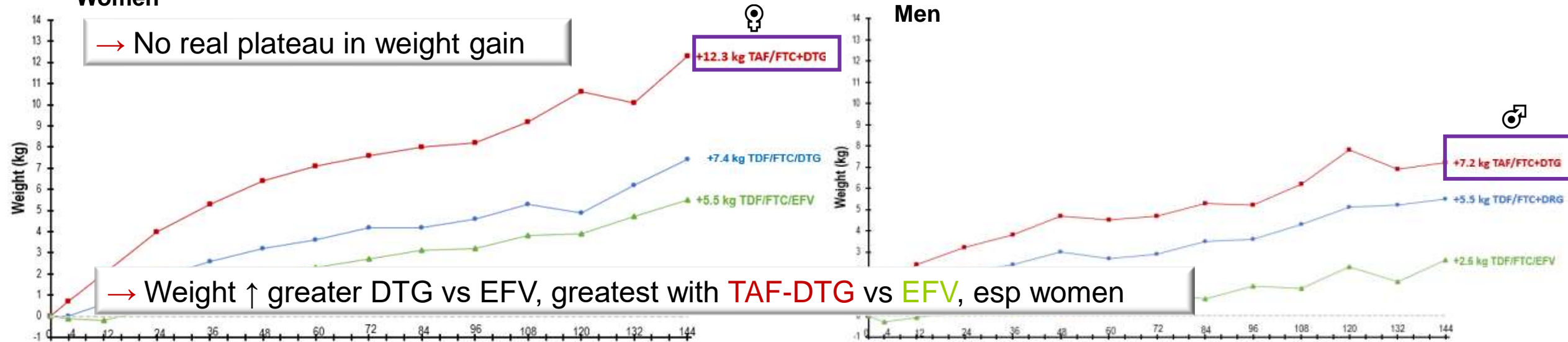
Excess Weight Gain with DTG-TAF

Sokhela S et al. IAS Virtual July 2020 Abs. OAXLB0104

Women

Mean Weight Gain through Week 144

Men



Change Body Composition to Week 96

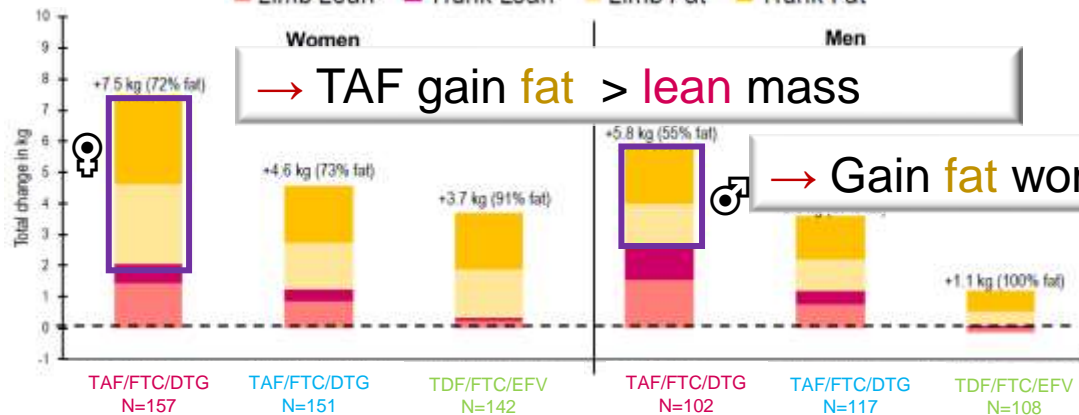
■ Limb Lean ■ Trunk Lean ■ Limb Fat ■ Trunk Fat

Women

Men

→ TAF gain fat > lean mass

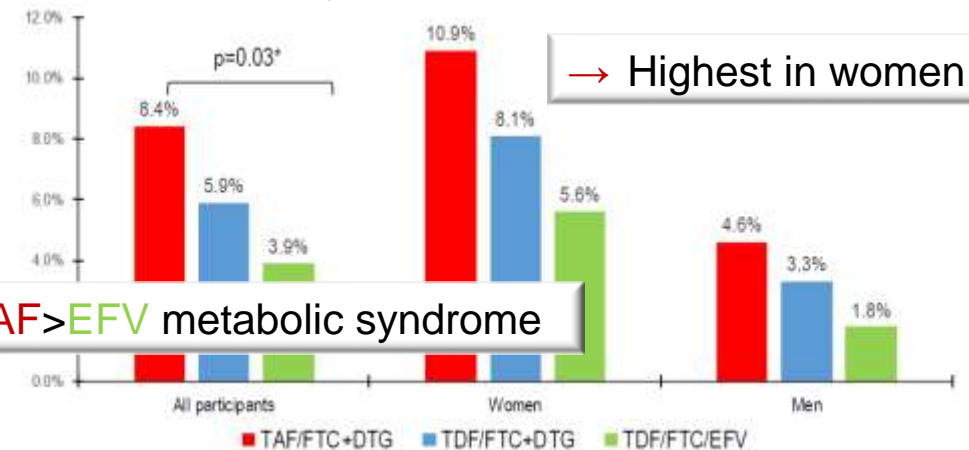
→ Gain fat women > men



Treatment Emergent Metabolic Syndrome to Week 96

→ Highest in women

→ TAF > EFV metabolic syndrome



NAMSAL Trial, 96 Weeks: DTG vs Low Dose EFV400 1st Line ART

Similar Viral Efficacy, Weight Gain More with DTG

Kouanfack C et al. IAS Virtual July 2020 Abs. OAB0402



613 ART-naive
RNA <1000

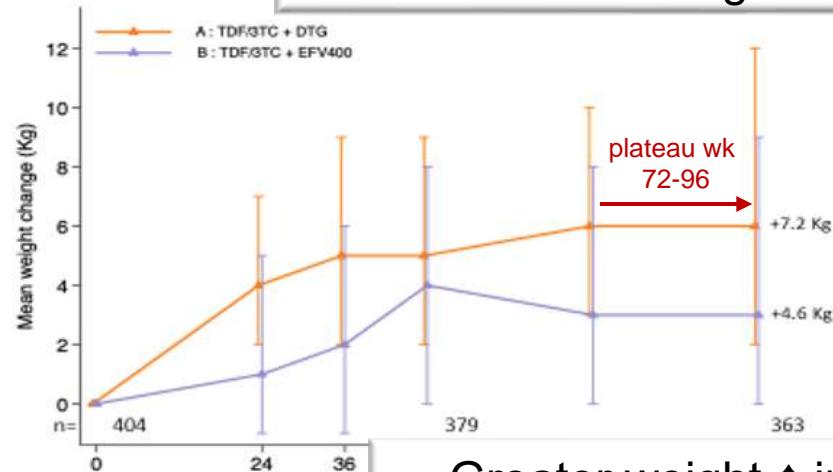
DTG/TDF/3TC (n=310; 96 wk n=277)

EFV400/TAF/3TC (n=303; 96 wk n=263)

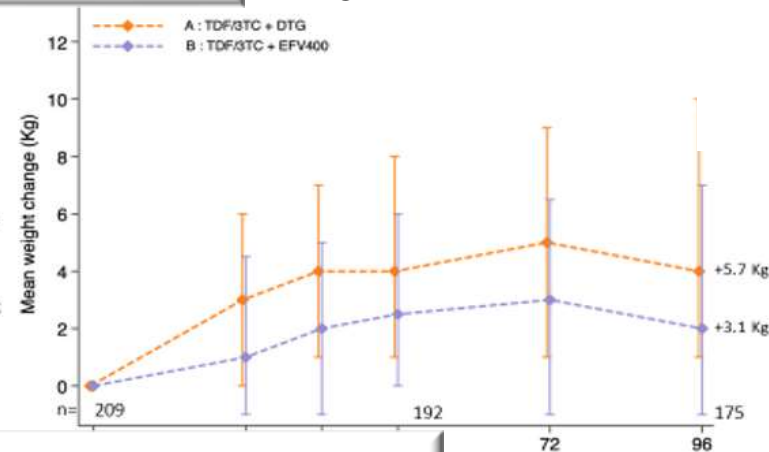
Mean Weight Change through Week 96

→ Persistent weight ↑ greater DTG vs EFV through week 96

Women

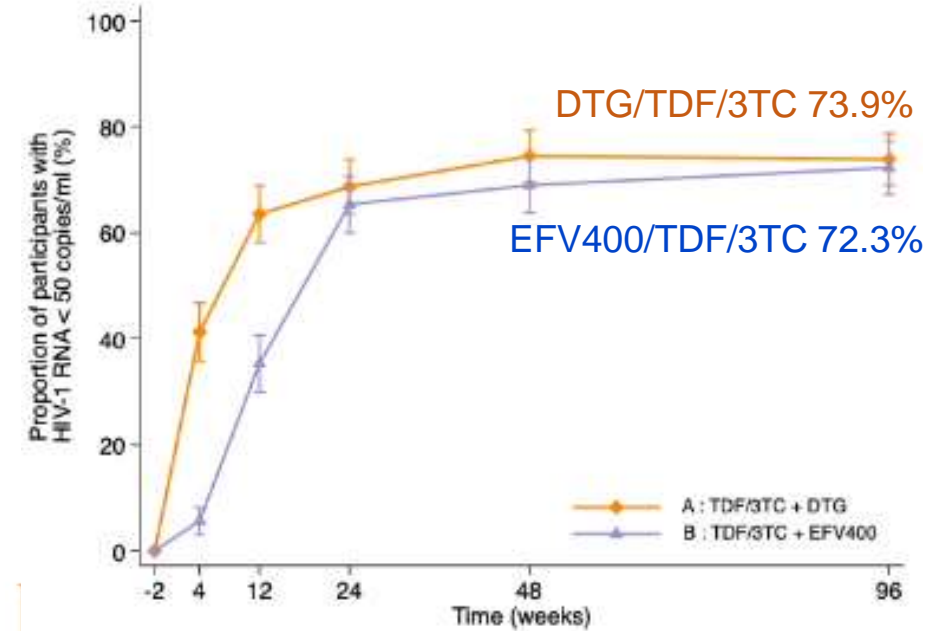


Men



→ Greater weight ↑ in women vs men

% with HIV RNA <50 c/mL at 96 Weeks



Weight Change, 96 Weeks

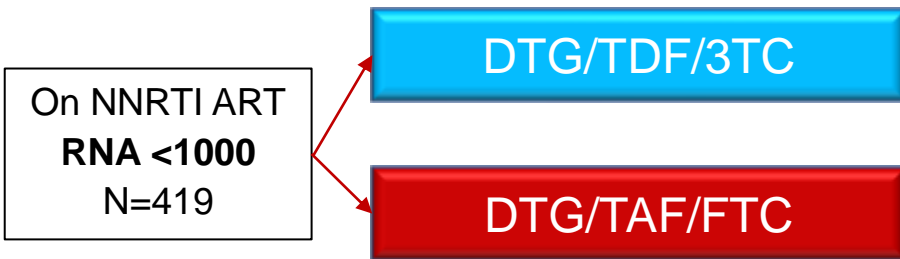
	DTG	EFV400	Total	Superiority test p-value
Evolution (W96-BL)	n=275	n=263	n=538	
Weight (kg)	+6.7 (+1.0; +11.0)	+4.2 (-1.0; +8.0)	+5.5 (+0.0; +10.0)	<0.001
Weight (% de BL)	+10.7 (+2.0; +16.7)	+6.9 (-1.4; +12.3)	+8.8 (+0.0; +15.5)	<0.001
Weight gain ≥ 5%	187 (68%)	123 (47%)	310 (58%)	<0.001
Extreme weight gain ≥ 10%	124 (45%)	87 (33%)	211 (39%)	0.004

VISEND Study 36 Week Results: **Switch** to DTG with TDF or TAF

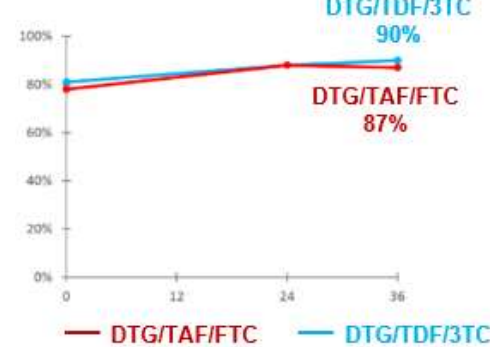
Similar Viral Efficacy But Higher Weight Gain with TAF

Hill A et al. IAS Virtual July 2020 Abs. LBPEB07

- Evaluated switch from NNRTI ART to DTG-based ART in HIV+ adults, randomized by viral suppression or not at time of switch; 24-week data on RNA %<50 and weight gain.

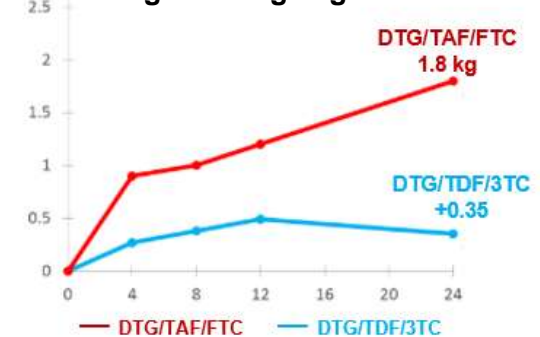


% RNA <50 c/mL

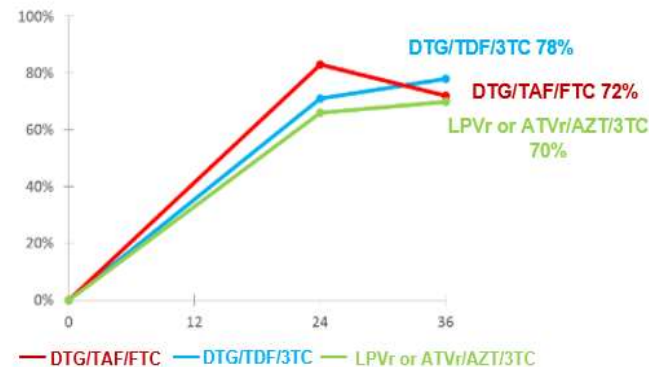
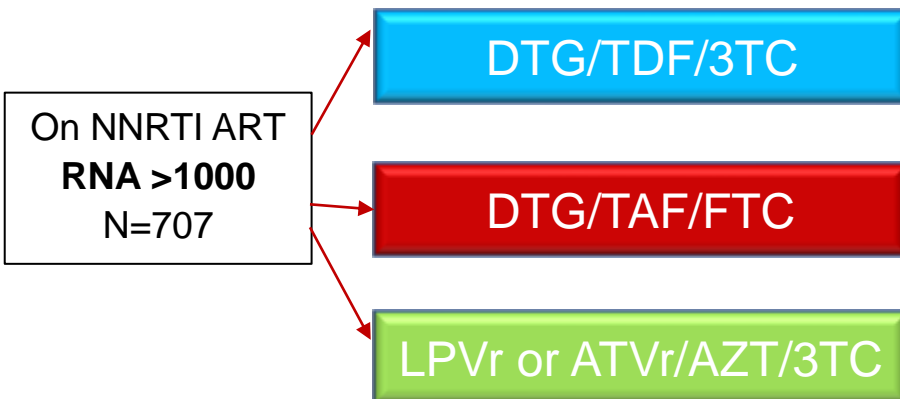


→ Similar viral efficacy

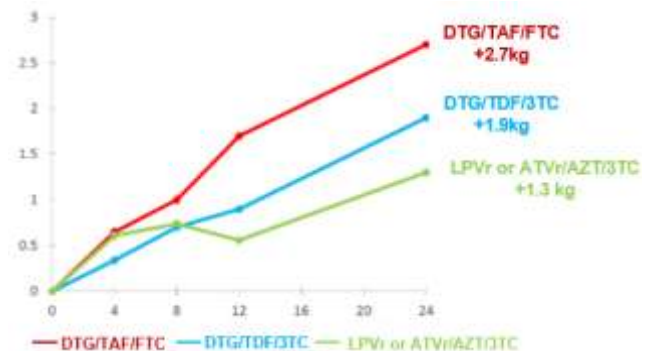
Weight Change kg



→ Higher wt gain with DTG+**TAF** > **TDF**



→ Similar viral efficacy



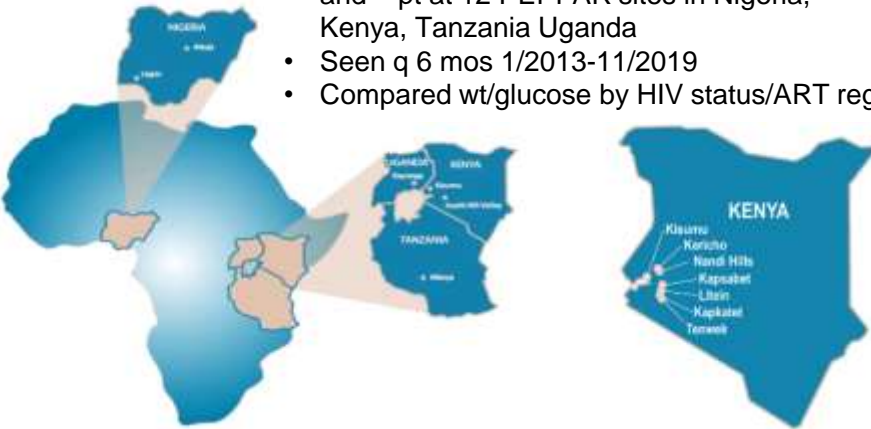
→ Higher wt gain with **TAF** > **TDF** or **PI**

Weight Gain and Hyperglycemia During DTG Transition in Africa

Ake J et al. IAS Virtual July 2020 Abs. OAB0602

AFRICOS Enrollment Sites

- AFRICOS cohort study enrolled 3,514 HIV+ and – pt at 12 PEPFAR sites in Nigeria, Kenya, Tanzania Uganda
- Seen q 6 mos 1/2013-11/2019
- Compared wt/glucose by HIV status/ART regimen



- BMI evaluation: 1,954 HIV+ adults; 742 TLD, 1212 noTLD
 - Define: High BMI ≥ 25 kg/m² (obese ≥ 30 kg/m²)
- Hyperglycemia: 2262 HIV+ adults: 653 TLD, 1609 no TLD
 - Define: Fasting glucose >99 mg/dL, any glucose >199 mg/dl or receiving hypoglycemic medication
- Excluded those with high BMI or hyperglycemia at baseline
- Significant risk differences by geographic area, sex, age

Adjusted Hazard Ratio for Time to High BMI

	Unadjusted		Adjusted ¹	
	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Non-TLD ART	Ref		-	
ART-Naïve	0.43	0.26-0.69	0.45	0.28-0.74
On TLD	1.51	1.01-2.25	1.85	1.24-2.76

¹Adjusted for gender, study site, age, and depression

- ART-naïve pt had ↓ risk high BMI compared to pt on non-TLD ART or TLD ART.
- TLD ART associated with independent significant 1.85-fold ↑ in developing high BMI

Adjusted Hazard Ratio for Time to Hyperglycemia

	Unadjusted		Adjusted ¹	
	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Non-TLD ART	Ref		-	
ART-Naïve	0.20	0.11-0.38	0.22	0.12-0.43
On TLD	1.47	0.95-2.28	1.27	0.82-1.97

¹Adjusted for study site, gender, age at enrollment, and BMI

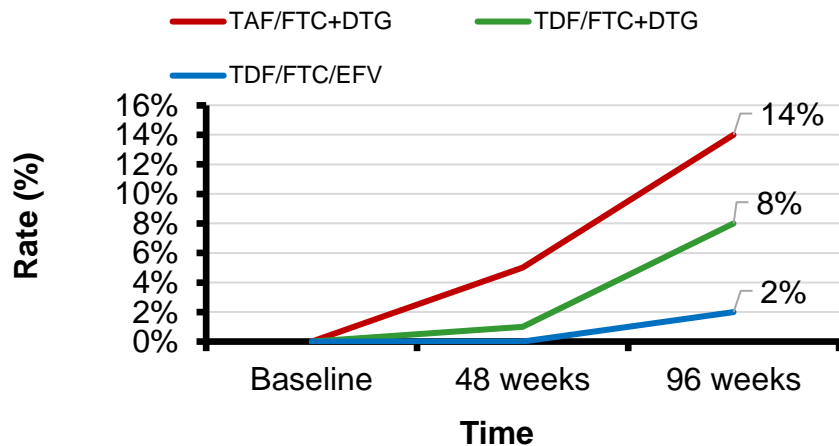
- ART-naïve pt had ↓ risk hyperglycemia compared to pt on non-TLD ART or TLD ART.
- TLD ART associated with non-significant trend to ↑ risk of developing hyperglycemia (most often mild)

ADVANCE: Estimates of Adverse Pregnancy Outcomes (APO) with Pre-Pregnancy Weight Gain

Sokhela S et al. IAS Virtual July 2020 Abs OAXLB0104

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

ART-Related Obesity Rates
(in women with normal BMI baseline)



APO	RR	95% CI
Gestational DM	4.31	3.2, 5.9
Pre-eclampsia	4.06	3.1, 5.3
LGA infant	2.48	1.0, 2.5
Neonatal death	1.57	1.2, 5.6

- Based on RR of APO in obese vs normal BMI per meta-analysis (table), predicted potential APO ↑ (including gestational diabetes, pre-eclampsia, LGA infant, and neonatal death) due to ART-induced obesity:

- **TAF/FTC/DTG:** 9.9% increase
- **TDF/FTC/DTG:** 5.2% increase
- **TDF/FTC/EFV:** 0.9% increase

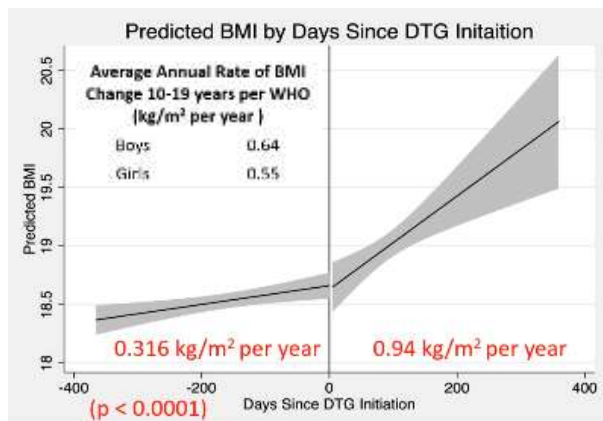


Baylor Eswatini

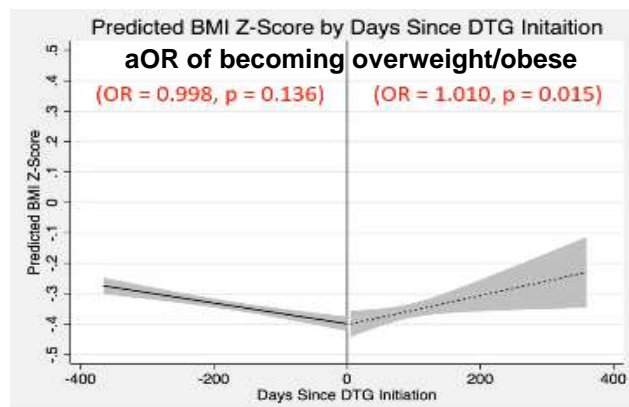
Switch to DTG in Adolescents with Viral Suppression Associated with ↑ in BMI and Odds of Overweight, Eswatini

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

- 605 HIV+ adolescents age 10-19 years with HIV RNA <200 c/mL who were transitioned to DTG – evaluated weight and height before and after transition DTG
- 73% on NVP ART prior to transition and 88% started TDF/3TC-based DTG ART.



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



- Significant increase in BMI z-score after DTG initiation.
- Adjusting for sex, NRTI backbone, prior ART regimen & age at DTG start, after DTG transition, odds of becoming overweight/obese increased by ~1% per day.
- Driven by larger ↑ in youth categorized as thin prior to DTG.



DTG in Pregnancy



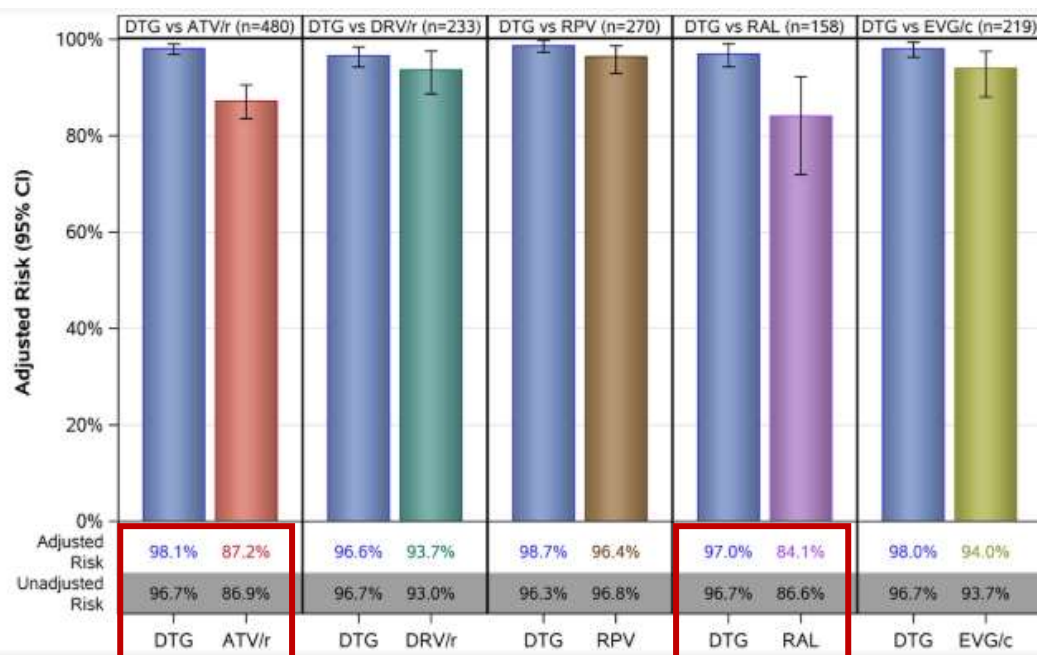
Viral Suppression by Delivery and Birth Outcomes in Pregnant HIV+ Women on DTG ART in the U.S.

Patel K et al. IAS Virtual July 2020 Abs. PEB0278

- Prospective cohort of 1257 pregnant women and newborns from 21 sites in US with 1st ART regimen in pregnancy DTG (120), ATVr (464), DRVr (185), RPV (243), RAL (86), or EVG (159)

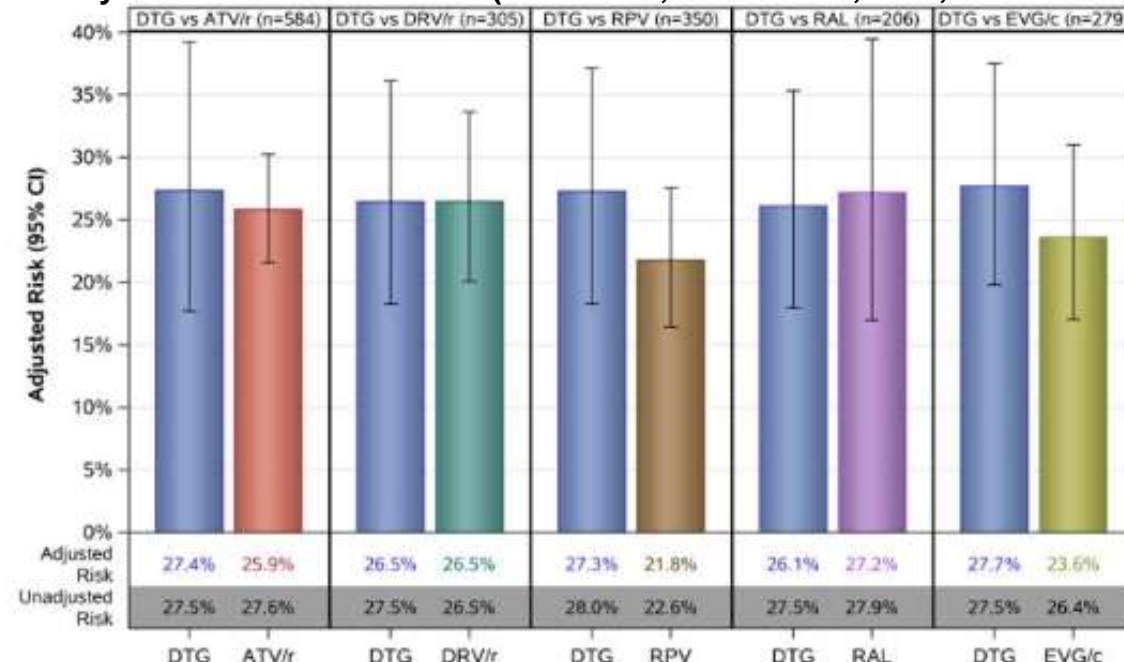
Comparison Viral Suppression and Adverse Pregnancy Outcomes Between DTG and Other Regimens

Adjusted Risk of Viral Suppression by Delivery



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

Any Adverse Birth Outcome (PTD/VPTD, LBW/VLBW, SGA, neonatal death)



→ Comparable rates of overall adverse birth outcomes between regimens, ranging between 22-27%.

Viral Suppression with DTG vs EFV in Pregnancy and MTCT

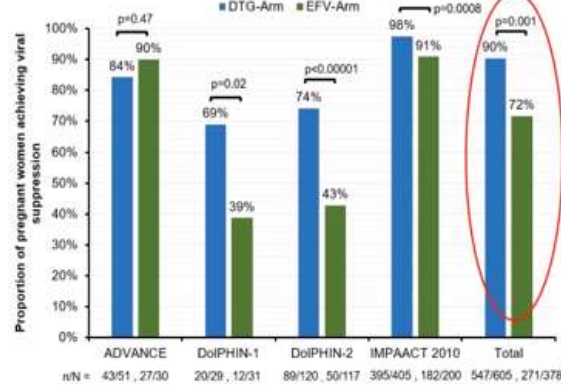
Meta-Analysis of 5 Clinical Trials in 1074 Pregnant Women

Asif SF et al. IAS Virtual July 2020 Abs.OABLB0195

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

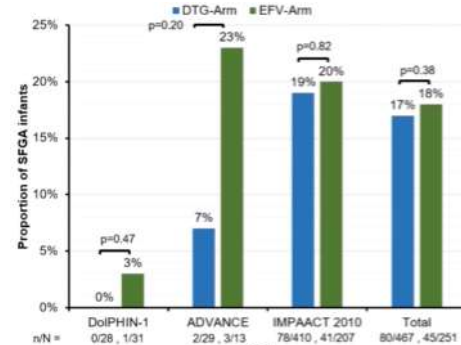
Trial	Location	Treatment Arms	Sample Size (pregnant women)	
			DTG-Arm	EFV-Arm
DolPHIN-1 (enrolled in 3rd trimester)	South Africa, Uganda	TDF/XTC+DTG vs TDF/XTC/EFV	29	31
DolPHIN-2 (enrolled in 3rd trimester)	South Africa, Uganda	TDF/XTC+DTG vs TDF/XTC/EFV	137	131
NAMSAL (from conception)	Cameroon	TDF/3TC+DTG vs TDF/3TC/EFV	13	12
ADVANCE (from conception)	South Africa	TAF/FTC+DTG vs TDF/FTC+DTG vs TDF/FTC/EFV	26 25	30
IMPAACT 2010 (enrolled in 3rd trimester)	Brazil, Botswana, India, Tanzania, Thailand, South Africa, USA, Zimbabwe	TAF/FTC+DTG vs TDF/FTC+DTG vs TDF/FTC/EFV	216 213	211

Viral Suppression



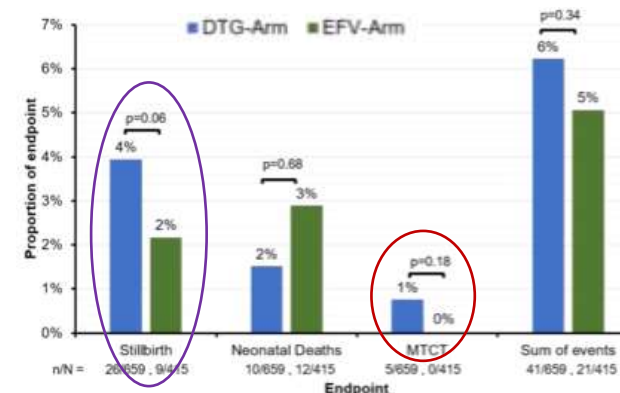
- Differences between trials in the extent of suppression reflect timing ART initiation
- Significantly **higher viral suppression** with **DTG** > **EFV**, OR 2.9 (1.5-5.5)

SGA



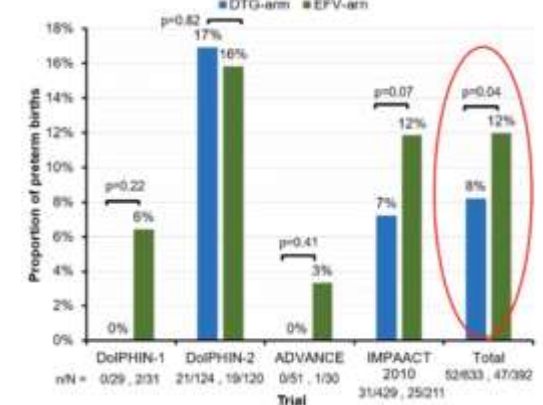
- No difference SGA DTG vs EFV**

Stillbirth, Neonatal Death, MTCT



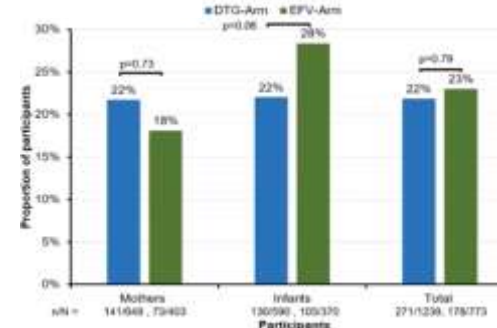
- No significant difference** neonatal death or **MTCT** (despite faster suppression) **DTG** vs **EFV**; **borderline trend** ↑ stillbirths with **DTG**

Preterm



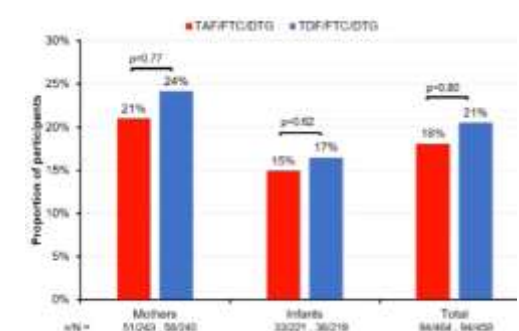
- Higher rate PTD with EFV**

Adverse Events



- No significant difference** AE mother/infants with **DTG** vs **EFV**

Adverse Events TAF vs TDF



- No significant difference** AE mother/infants with **TAF** vs **TDF**

→ While **DTG** had superior virologic efficacy than **EFV**, all 5 infant infections with **DTG** (all with ART started in pregnancy).

→ Safety profile of **DTG** and **EFV** (and **TAF** and **TDF**) generally similar in meta-analysis but only shows short-term effects of DTG, and most started drugs during pregnancy as opposed to preconception.

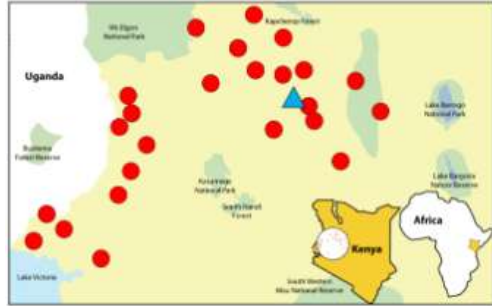
→ LT safety requires further assessment.

Women Starting or Transitioning to DTG-Based ART in Kenya

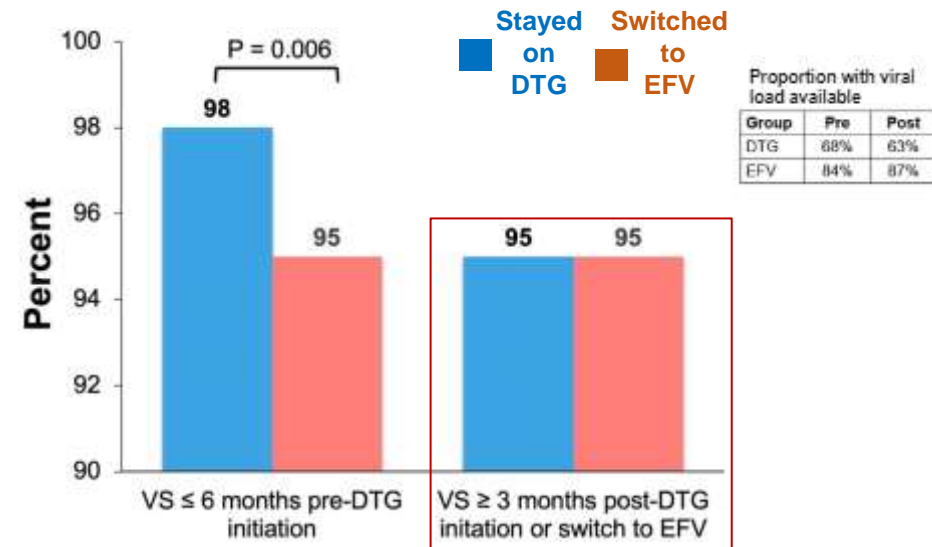
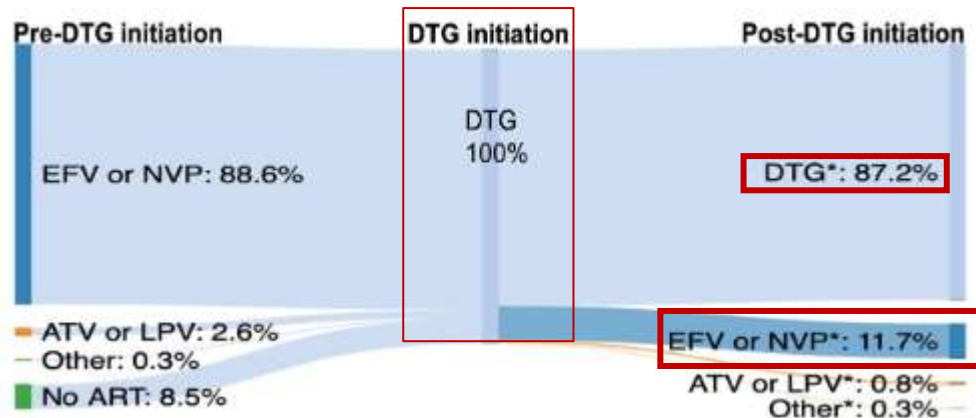
Viral Suppression



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



- Retrospective study 5,155 women age 15-49 starting DTG ART at AMPATH-affiliated HIV clinics in Kenya
 - 89% transitioned from EFV or NVP to DTG (95% started TLD)
 - 61% using any contraception at time starting DTG (primarily condom, only 10% using DMPA, oral contraceptive or IUD with little change from pre to post DTG signal).
- 12 months post-DTG start
 - 87% remained on DTG through 12 mos
 - 12% changed back from DTG to EFV or NVP
- Viral suppression high and similar in those who stayed on DTG or switched back to EFV

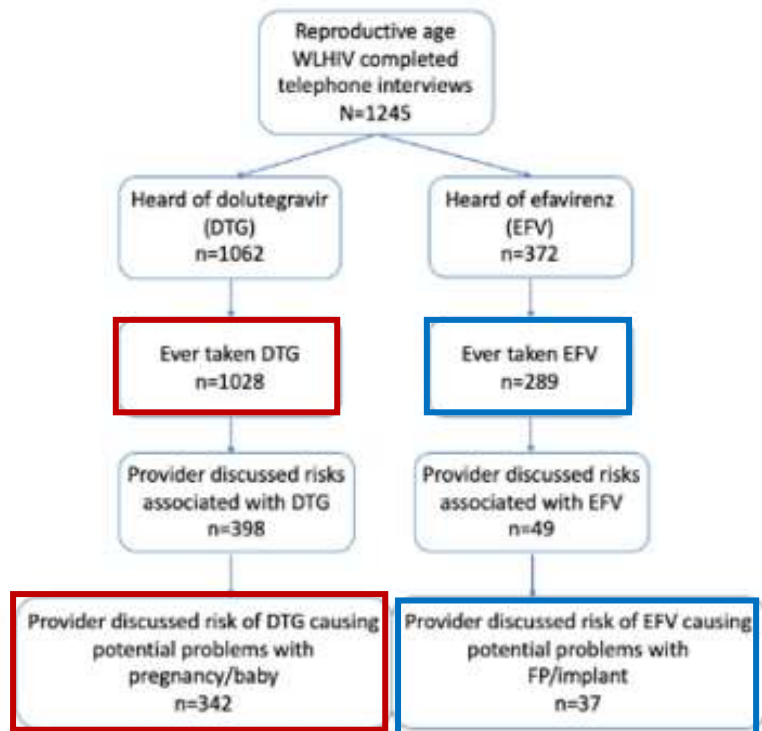


Counseling About DTG and EFV Among Women of Reproductive Age Receiving ART in Kenya

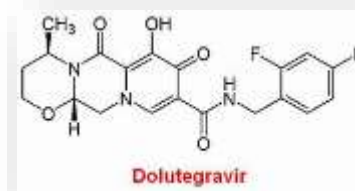


Bernard C et al. IAS Virtual July 2020 Abs. PEB0286

- Telephone interviews between May 2019-May 2020 with 1,245 HIV+ women of reproductive age who initiated DTG between Oct 2017-Apr 2019 in AMPATH HIV clinics, Kenya
- Surveys included questions about knowledge of ever having taken DTG (n=1,028) and counseling they received from HCW about risks of DTG and EFV.



- Only 33% of 1,028 **ever DTG** users recalled receiving counseling about potential teratogenic risk of DTG
- Only 13% of 289 **ever EFV** users reported receiving counseling about potential EFV interaction with contraceptive implant.
- 21% of women who self-reported ever DTG use reported switching off DTG



Open spinal bifida
(Copp & Greene, 2016,
Encyclopedia of Life Sciences,
John Wiley)

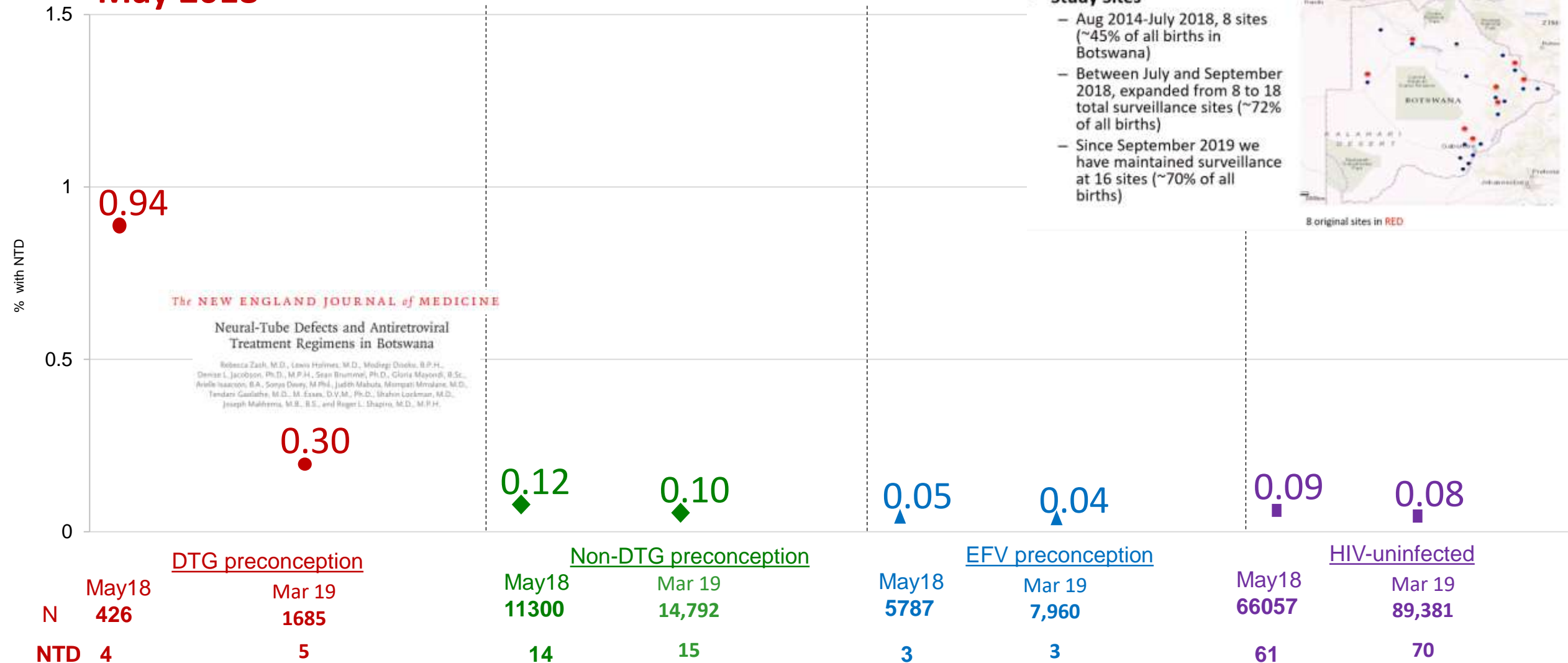
What Are New Data on Neural Tube Birth Defects and Preconception DTG?



Tsepamo: Evolution of NTD Prevalence with Preconception DTG

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

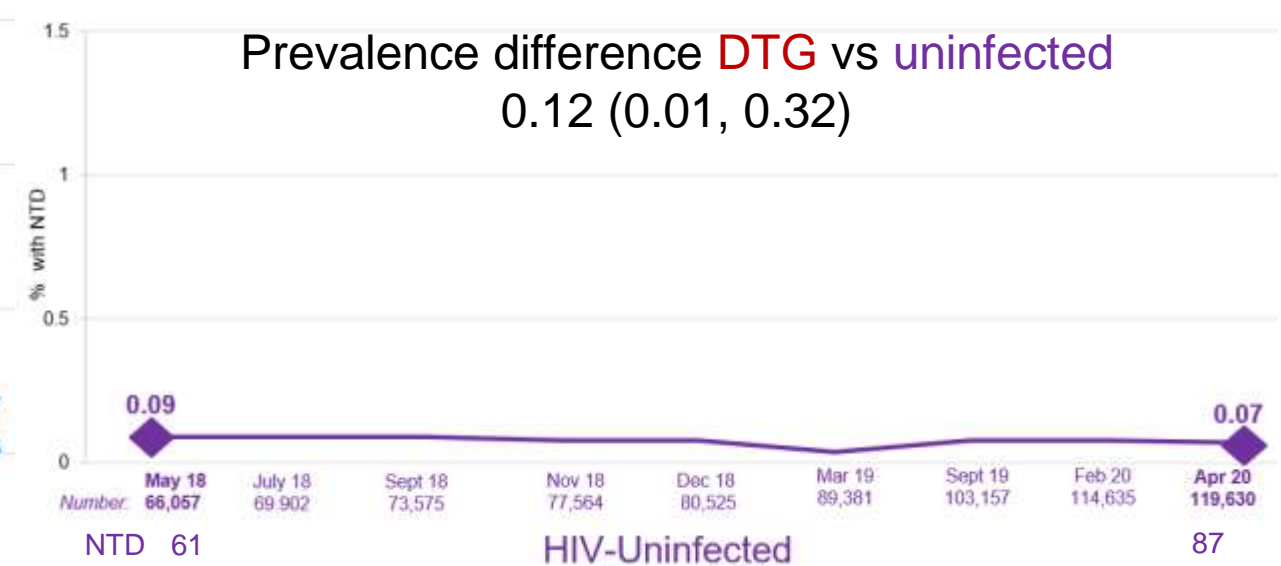
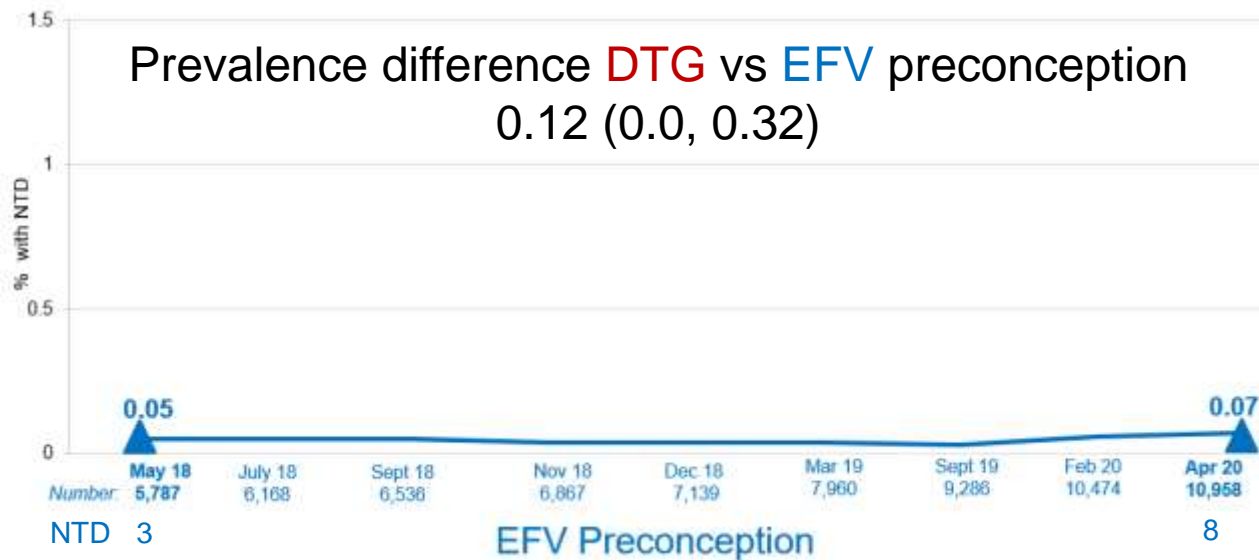
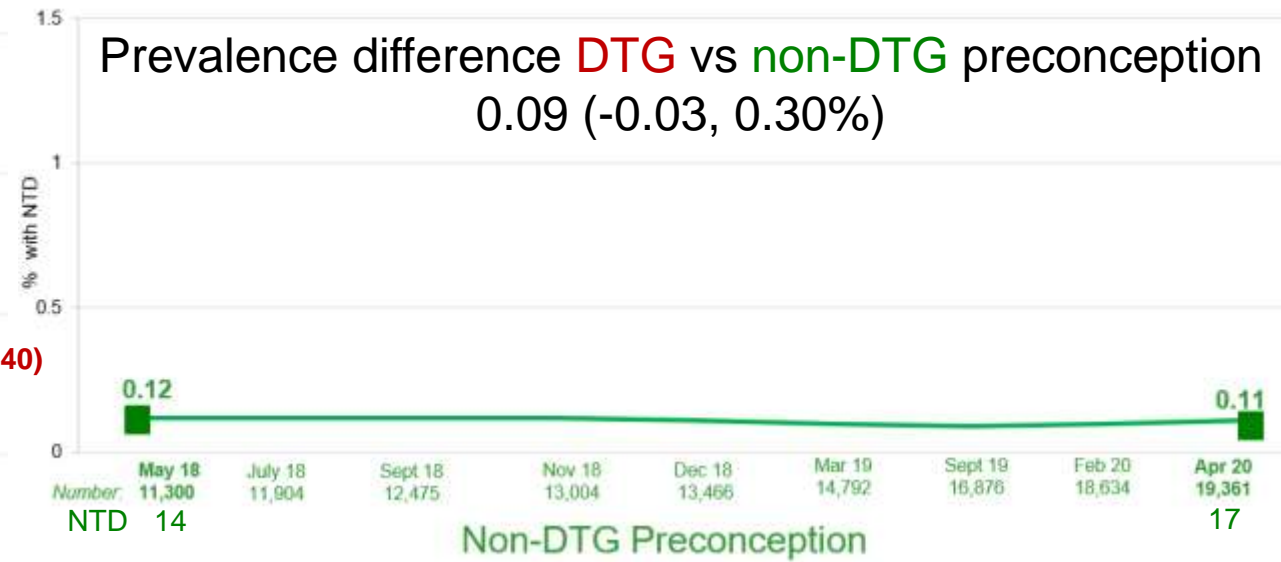
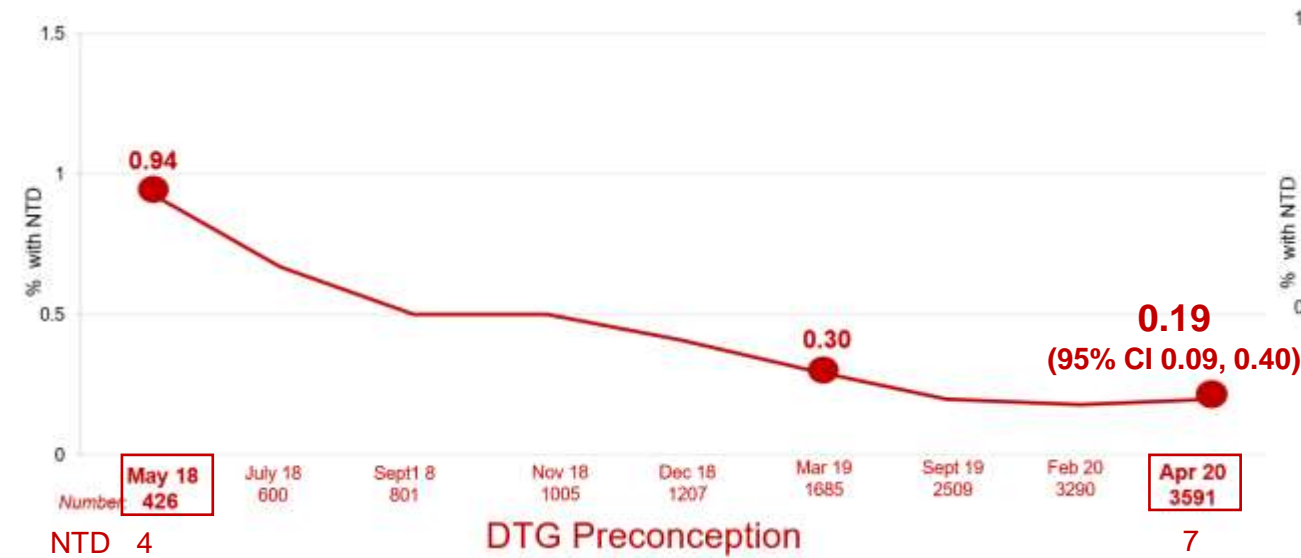
May 2018



→ Significant prevalence difference between DTG preconception and all other exposure groups (0.82 to 0.94)

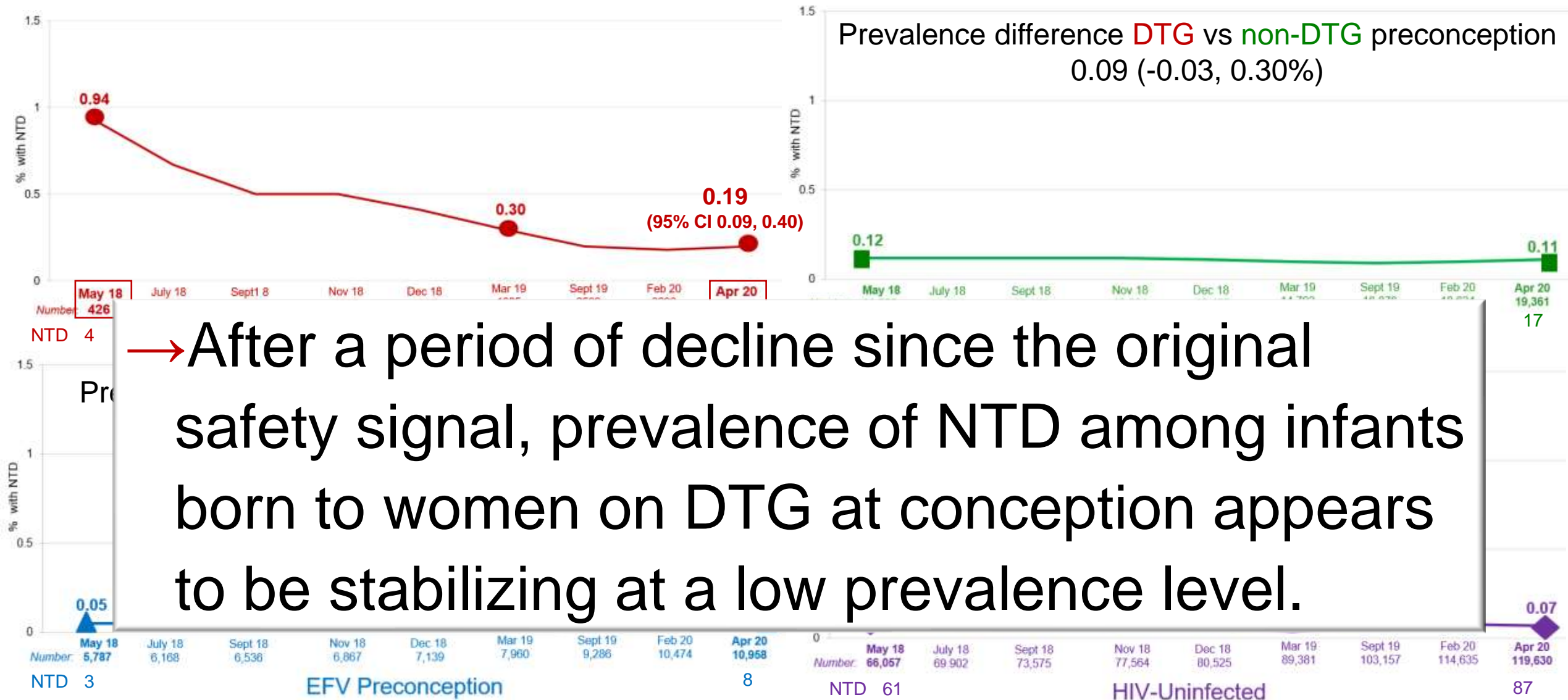
Tsepamo: Evolution of NTD Prevalence with Preconception DTG

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



Tsepamo: Evolution of NTD Prevalence with Preconception DTG

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



Update: Prospective Antiretroviral Pregnancy Registry InSTI and Neural Tube Defects through January 2020

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

	Earliest Trimester of Exposure – <u>Prospective</u> Cases		
	Periconception	Later 1 st Trimester	2 nd /3 rd Trimester
Overall birth defects	Defects/outcomes	Defect/outcomes	Defects/outcomes
<i>Exposure to any InSTI</i>	33/1008 (3.3%)	3/159 (1.9%)	27/674 (4.0%)
DTG	14/382 (3.7%) 1/382 NTD (0.26%)	2/73 (2.7%)	12/285 (4.2%)
EVG	11/298 (3.7%) 0 NTD	0/25 (0%)	1/68 (1.5%)
RAL	11/327 (3.4%) 0 NTD	2/95 (2.1%)	15/399 (3.8%)
BIC	0/25 0 NTD	0/3	0/12

→ One NTD in prospective APR with periconception DTG, rate 0.26%



1 Jan 1989 -
31 Jan 2020



Neural Tube Defects and Adverse Pregnancy Outcome After Maternal Exposure to DTG During Pregnancy, US 2013-2017

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

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

→ 7,168 HIV+ pregnancies, 235 on DTG.

→ There were no NTD among 1,234 HIV+ women on InSTI, including DTG.

→ NTD prevalence was 0.48-0.58/1000 (0.05-0.06%) among 6.4 million HIV-uninfected women.

→ Prevalence stillbirth, spontaneous and induced abortion higher in HIV+ women (particularly those on no ARV) compared to HIV-uninfected women; not associated with specific ARV use.

Table. Prevalence of neural tube defects (NTDs) and pregnancy outcomes per 1,000 women exposed to dolutegravir (DTG) and other antiretroviral (ARV) medications by ARV class — United States, 2013-2017

Commercial insurance					
Outcome	Women without HIV	Women with HIV			
		No ARV	DTG	Other INSTI	Non-INSTI
Pregnancies (N)	3,752,373	1,257	46	256	1,079
NTDs*	0.48 (0.46-0.51)	1.59 (0.19-5.74)	0.00	0.00	0.00
Live births *	704.2 (703.7-704.6)	604.6 (577.0-631.8)	478.3 (328.9-630.5)	535.2 (472.0-597.5)	711.8 (683.7-738.7)
Stillbirths*	3.8 (3.7-3.8)	4.8 (1.8-10.4)	0.0	7.8 (1.0-27.9)	5.6 (2.0-12.1)
Spontaneous abortions*	49.8 (49.6-50.1)	117.7 (100.4-136.9)	108.7 (36.3-235.7)	89.8 (57.8-131.8)	84.3 (68.4-102.5)
Induced abortions*	18.8 (18.6-18.9)	96.3 (80.5-113.9)	43.5 (5.3-148.4)	31.3 (13.6-60.6)	33.4 (23.5-45.9)
Medicaid insurance					
Pregnancies (N)	2,593,751	1,882	189	743	1,716
NTDs*	0.58 (0.55-0.61)	0.53 (0.01-2.96)	0.00	0.00	1.75 (0.36-5.10)
Live births *	746.2 (745.6-746.7)	800.2 (781.4-818.1)	761.9 (694.7-820.7)	732.2 (688.8-763.7)	828.7 (810.0-846.2)
Stillbirths*	4.5 (4.4-4.6)	8.5 (4.9-13.8)	5.3 (0.1-29.1)	13.5 (6.5-24.6)	8.7 (4.9-14.4)
Spontaneous abortions*	38.5 (38.3-38.8)	52.6 (43.0-63.7)	42.3 (18.5-81.7)	80.8 (62.2-102.7)	36.7 (28.3-46.7)
Induced abortions*	1.6 (1.5-1.6)	3.7 (1.5-7.7)	0.0	1.3 (0.0-7.5)	4.1 (1.6-8.4)

*Prevalence per 1,000 pregnancies [95% confidence interval; those in bold blue text had confidence intervals that did not overlap confidence intervals for the prevalence in women without HIV.



Photo credit: Paul Jeffrey, World Council of Churches

Pediatric Antiretroviral Therapy and New ARV Drugs in Children



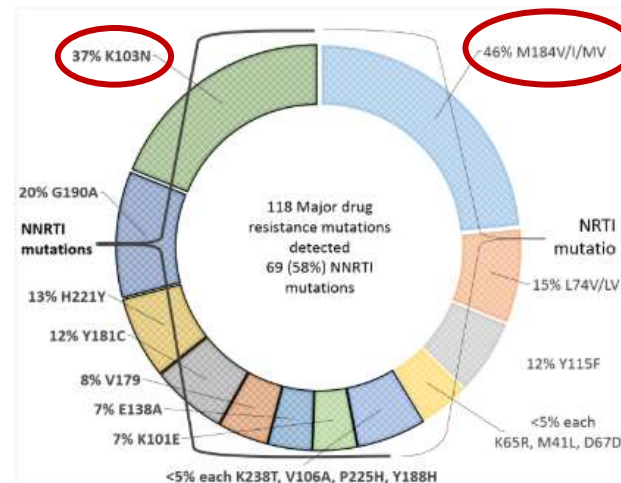


85% of Children Living with HIV and Viral Failure in Kenya Have Drug Resistance Mutations Requiring Regimen Change

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

- 704 HIV+ children age 1-14 years on ART enrolled from 5 facilities Kenya 3/19-12/19 and randomized to SOC or intervention (POC VL q 3 mo with targeted DR monitoring if VL >1000).
- Preliminary results on resistance testing in intervention arm presented
 - 365 randomized; 60 had VL >1000 and underwent ≥ 1 resistance test.
 - 51/60, **85%**, had **drug resistance mutations** to NNRTI, NRTI or both.
 - K103N NNRTI and M184V NRTI most common.

Drug Class	Number of CLHIV with DRMs by class	Proportion of CLHIV with DRMs by class
Non-nucleoside reverse transcriptase (NNRTI)	48	80%
Nucleoside reverse transcriptase inhibitor (NRTI)	36	60%
Both NNRTI and NRTI	33	55%
No resistance	9	15%



- Children with VF likely to have DR and therefore improved adherence will not result in viral suppression.
- Early drug resistance testing with VF to determine appropriate ART regimen change rather than adherence counseling may be desirable.

HIV+ Children on Third-Line ART in Africa: New Horizons DRV/r, ETR Drug Donation Program

Tiam A et al. IAS Virtual July 2020 Abs. PDB0403

- Observational cohort 169 children age 0-24 years on DRV/r or ETR 3rd-line ART in Eswatini, Kenya, Lesotho, Uganda, and Zambia as part of New Horizon's Program Dec 2018-Mar 2020.
- Median age 12.7 yrs; prior 2nd line ART 85% PI-based (LPV/r 67%, ATV/r 18%).
- Median VL at switch 4.7 log copies/mL; 81% switched for confirmed resistance.
 - 98% had ≥ 1 resistance mutations, with 71% >3 TAMs and 52% PI mutations.

Figure 1: Nonnucleoside/nucleotide reverse transcriptase mutations (N=102)

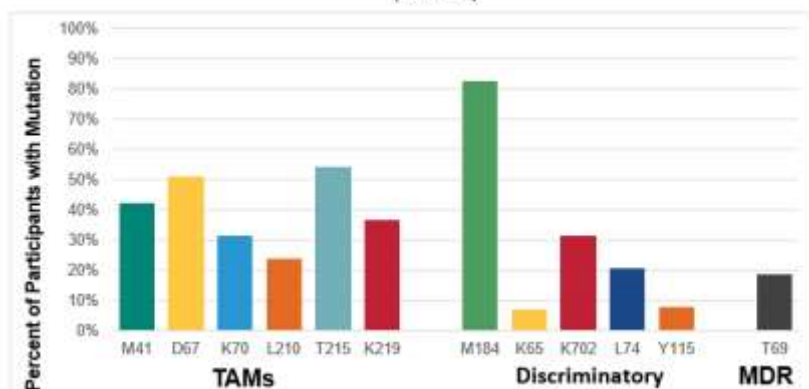
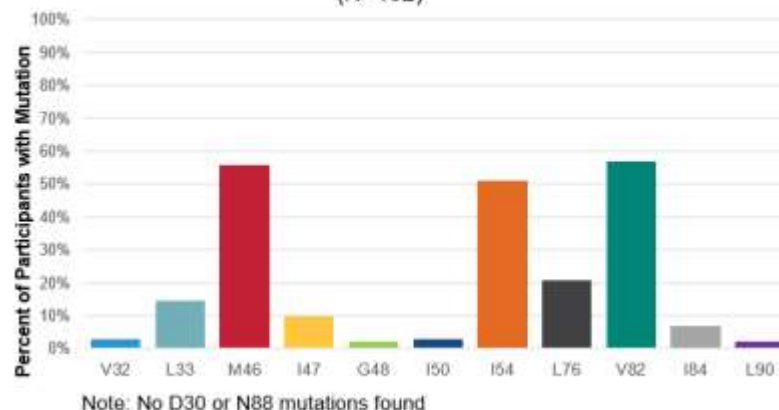


Figure 2: Protease Inhibitors Mutations (N=102)



- Viral response to 3rd line: of those with VL post-switch, suppression to VL <1000 was 75% (45/66) at 6 mos and 78% (32/41) at 12 mos on 3rd line ART (<50, 46% and 51%).

Viral Suppression of Caregivers Living with HIV and Type of Caregiver Associated with Viral Suppression in HIV+ Children, Kenya



Odeny B et al. IAS Virtual July 2020 Abs. PDD405

- Evaluated factors associated with viral suppression using pre-enrollment VL data from 704 children age <15 years recruited into Opt4Kids randomized trial, along with their caregivers.

Table 1: Children and caregiver characteristics (N=704 children)	
	Median (IQR) N (%)
Caregiver characteristics	
Type of caregiver	
Mother	484(68.4)
Father	59(8.3)
Other	164(23.2)
At least primary education	486(68.8)
Caregiver HIV positive	568(80.4)
Viral load suppressed	318 (44.9)
Median age	36 (31-43)
Children characteristics	
Gender (female)	342(48.3)
Median age	9(6-11)
Median time on ART (years)	6(3-9)
Viral load suppressed	(78)
ART base:	
NNRTI based	440(51.6)
PI based	307(36.0)
Integrase based	9(1.1)

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

Table 2: Viral load suppression and caregiver and pediatric characteristics				
	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Caregiver characteristics				
Caregiver relationship to child				
Mother	Ref			
Father	1.25(0.23-23.19)	0.833	1.03(0.19-19.28)	0.976
Other	0.39(0.15-1.04)	0.053	0.26(0.08-0.82)	0.016
Education (primary)	0.61(0.17-1.72)	0.382	0.43(0.9-1.43)	0.211
Caregiver VL suppressed	10.71(2.27-56.44)	0.003*	7.53(1.32-43.03)	0.0173
Children characteristics				
Gender				
Female	Ref			
Male	1.35(0.53-3.60)	0.529	0.93(0.31-2.69)	0.890
Median age	0.91(0.79-1.04)	0.178	0.84(0.69-0.99)	0.061
ART base class (current)				
NNRTI	Ref			
PI	0.99(0.82-1.20)	0.942	0.993(0.81-1.22)	0.946
Integrase	1.01(0.06-4.47)	0.993	1.02(0.06-4.71)	0.984

- Children in care of biologic mother compared to other caregivers more likely to have suppression.
- Children who had virally suppressed caregivers were 7.5 times more likely to have suppression.

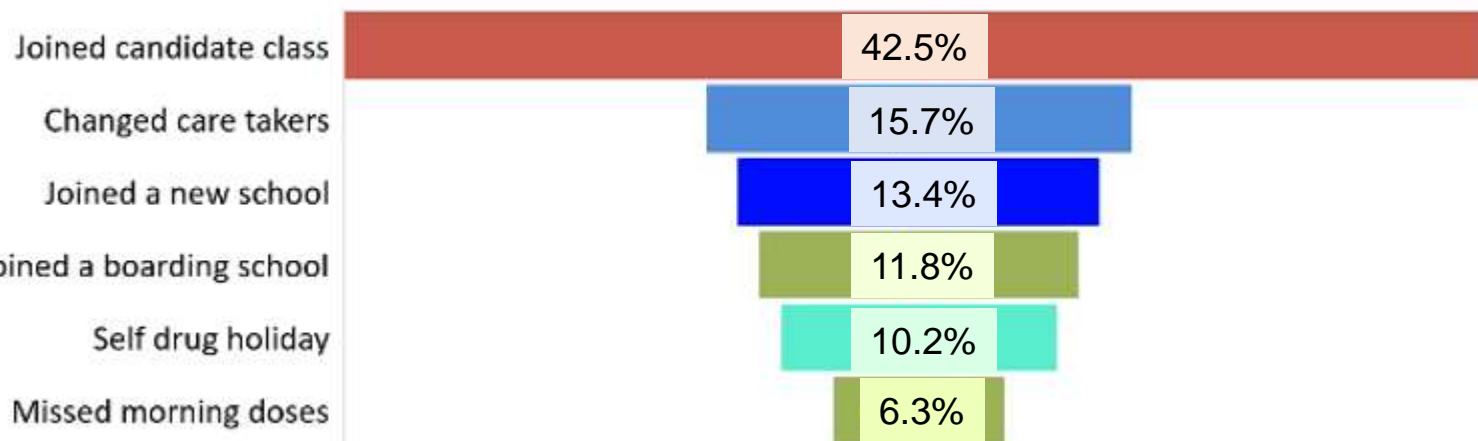


Factors Associated with Non-Adherence to ART in Adolescents in Masaka Uganda

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

- The AIDS Support Organization (TASO) in Masaka Uganda providing adolescent clinic services explored factors associated with poor adherence among non-suppressed (VL >1000) **school-going** adolescents (age 10-19) with adherence <95% from both rural and peri-urban areas of Masaka district.
- Of 325 youth, 127 (39%) were non-suppressed (63% girls, 37% boys).
- 110/127 (87%) had adherence <95%.

Reasons for poor adherence among adolescents with non suppressed viral load

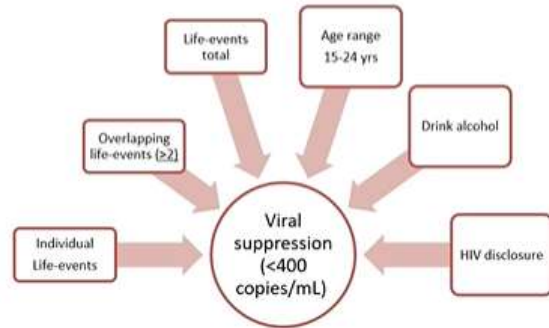


→ Concluded there was a need for HIV school-related interventions targeting both teachers and students to create flexible and conducive environment for HIV+ students.

Viral Non-Suppression in Youth is Associated with Overlapping Significant Life Events

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

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



Recent life-events:

- Start/stop school or employment 9%
- Change in residence 16%
- Divorce/separation or relationship strife 8%
- New sexual partner 8%
- Family death 8%
- Sickness 9%
- Incarceration 0%
- Pregnancy or birth 16%

Behaviors – Alcohol use and HIV status disclosure

17% Family 81% Partner 54%

Multivariate Analysis of Predictors of Viral Suppression

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

Less likely suppressed

More likely suppressed

→ Overlapping recent life events, alcohol use and lack of disclosure to family and partner were significantly independently associated with viral non-suppression and can identify those most vulnerable patients needing attention.

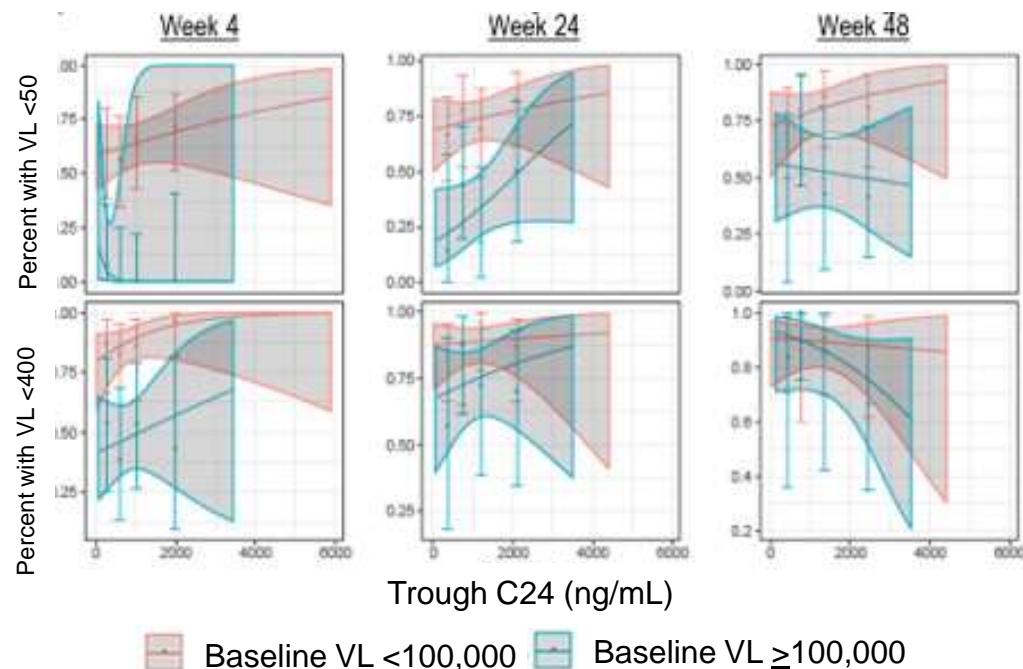
- ≥2 overlapping events: 17%
- ≥3 overlapping events: 4%

DTG Plasma Exposure-Viral Load Response in Children

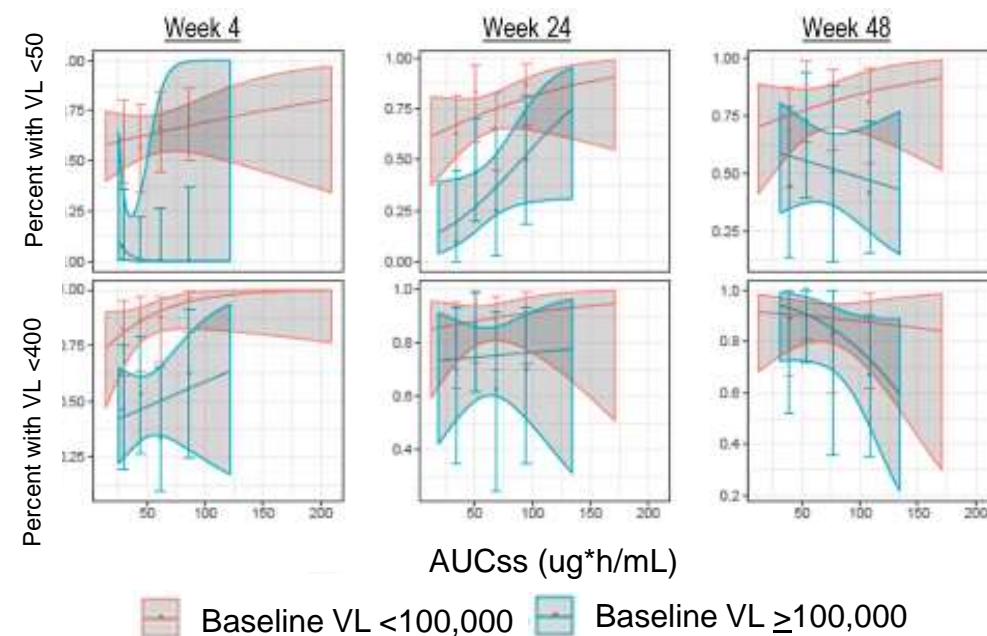
Singh R et al. IAS Virtual July 2020 Abs. OAB07046

- Determine if DTG drug exposures in 181 children in IMPAACT P1093 PK study at wks 4, 24 and 48 were predictive of virologic outcomes (VL <50 or <400).

VL Response to <50 or <400 VL by DTG Trough C24 Level
Stratified by Baseline VL < or >100,000



VL Response to <50 or <400 VL by DTG Steady State AUC
Stratified by Baseline VL < or >100,000



→ No relationship between DTG trough (C24) or steady state AUC level and VL response at doses studied (and now approved for use) suggests that **doses are already at maximum of the dose-viral response curve.**



24-Week Safety, Tolerability and Efficacy of DTG Dispersible Tablet In Children 4 Weeks to <6 Years



Ruel T et al. IAS Virtual July 2020 Abs. PEB0293

- P1093 enrolled 51 children into 3 age cohorts: 4 weeks to <6 months; 6 months to <2 years; and 2 years to <6 years; 71% already on ART, 29% ART-naïve.

Regimen	n (%)
ABC, 3TC	24 (47%)
7DV, 3TC	10 (20%)
ZDV, 3TC, LPV/r	6 (12%)
ABC, 3TC, LPV/r	5 (10%)
ABC, FTC	2 (4%)
D4T, 3TC, LPV/r	2 (4%)
D4T, 3TC	1 (2%)
3TC, EFV, DRV/r	1 (2%)

→ All received optimized background including ≥ 2 drugs with ≥ 1 having genotype-predicted activity.

DTG Dispersible Tablet Dosing by WHO Weight Band

Age	Weight Band (kg)	DTG DT Dose (mg)	# tabs
≥ 4 weeks to < 6 months of age	3 to < 6	5	1
	6 to < 10	10	2
≥ 6 months of age	6 to < 10	15	3
	10 to < 14	20	4
	14 to < 20	25	5

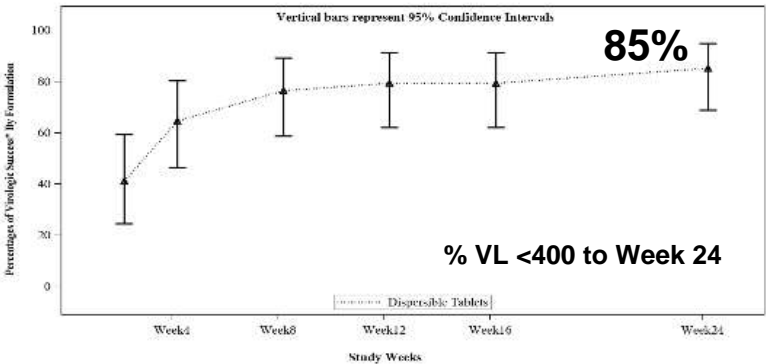
→ Weight-band based once daily dosing was used.

24 Week Outcome by Age Cohort

Age Group	4 wks to <6 mo (n=17)	6 mo to <2 yrs (n=9)	2 yrs to <6 yrs (n=8)
HIV RNA <50c/mL*	41% [18, 67]	67% [30, 93]	63% [25, 92]
HIV RNA <400c/mL*	88% [64, 99]	89% [52, 100]	75% [35, 97]

*Proportion (95% confidence interval); *Median (interquartile range) change from baseline

→ Good virologic response all age cohorts in this primarily ART- experienced group, with overall 85% VL <400 at week 24.



Number (%) with ≥ 1 Grade 3 or 4 Adverse Event by 24 Weeks

	4 wks to <6 mo (n=23)	6 mo to <2 yrs (n=12)	2 yrs to <6 yrs (n=16)
# with grade 3 or greater clinical event(s), overall	3 (13%)	2 (17%)	1 (6%)
# with grade 3 or greater laboratory event(s), overall	13 (57%)	4 (33%)	3 (19%)

→ No AE attributed to study drug and no drug discontinuation for toxicity.



24-Week Safety, Tolerability and Efficacy of DTG Dispersible Tablet In Children 4 Weeks to <6 Years



Ruel T et al. IAS Virtual July 2020 Abs. PEB0293

- P1093 enrolled 51 children into 3 age cohorts: 4 weeks to <6 months; 6 months to <2 years; and 2 years to <6 years. 9% ART-naïve.

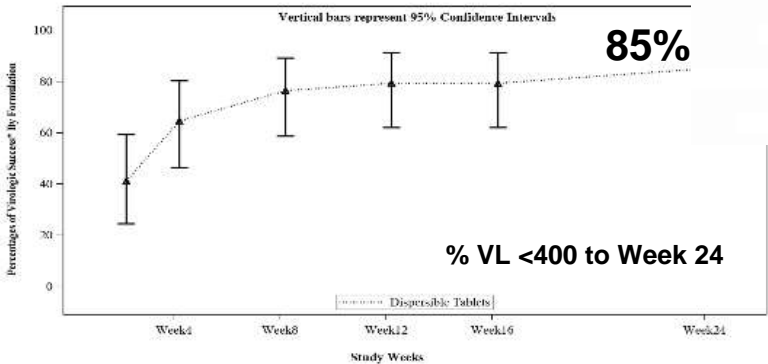
Regimen	n (%)
ABC, 3TC	24 (47%)
7DV, 3TC	10 (20%)
ZDV, 3TC, LPV/r	6 (12%)
ABC, 3TC, LPV/r	5 (10%)
ABC, FTC	2 (4%)
D4T, 3TC, LPV/r	2 (4%)
D4T, 3TC	1 (2%)
3TC, EFV, DRV/r	1 (2%)

→ All received c background in drugs with ≥1 genotype-prec

24 Week Outcome by Age Cohort

Age Group	4 wks to <6 mo (n=17)	6 mo to <2 yrs (n= 9)
HIV RNA <50c/mL*	41% [18, 67]	67% [30, 93]
HIV RNA <400c/mL*	88% [64, 99]	89% [52, 100]

*Proportion (95% confidence interval); *Median (interquartile range) change from base



WHO Weight Band

Weight Band (kg)	DTG DT Dose (mg)	# tabs
< 6	5	1
6 - 10	10	2
10 - 15	15	3
< 14	20	4
< 20	25	5

→ Weight-band based once daily dosing was used.

Use all age cohorts in this primarily group, with overall 85% VL <400

Adverse Event by 24 Weeks

Age Group	4 wks to <6 mo (n=12)	6 mo to <2 yrs (n=16)
event(s), overall	1 (17%)	1 (6%)
# with grade 3 or greater laboratory event(s), overall	4 (33%)	3 (19%)

→ No AE attributed to study drug and no drug discontinuation for toxicity.

Safety, PK, Efficacy of Low Dose EVG/COBI/FTC/TAF in Children

Age ≥ 2 Year on ART with Virologic Suppression

Natukunda E et al. IAS Virtual July 2020 Abs.OALB0101

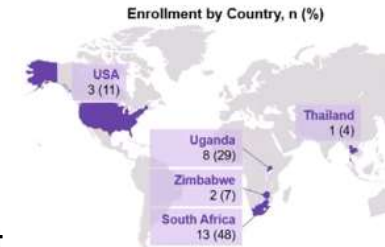


Eligibility Criteria

- HIV-1 RNA <50 copies/mL for ≥ 6 mo
- CD4 count ≥ 400 cells/ μ L
- eGFR ≥ 90 mL/min/1.73 m² (Schwartz)



- Enrolled 27 children, median age 6 yrs, most on 2 NRTI/PI > NNRTI



Pharmacokinetics

PK Parameter*	Cohort 3 ≥ 2 y; ≥ 14 kg N=27	E/C/F/TAF-Treated Adults N=1193†	Children/Adults %GLSM Ratio (90% CI)
EVG			
AUC _{0-24h} h·ng/mL	29900	21600	139 (112, 172)
C _{max} ng/mL	2850	2000	143 (113, 180)
C _{24h} ng/mL	195	248	78.9 (53.1, 117)
TAF			
AUC _{0-24h} h·ng/mL	344	178	193 (166, 224)
C _{max} ng/mL	218	145	150 (116, 195)

*Geometric least squares mean (GLSM). †EVG, n=19 from intensive PK data (1 Phase 2 study in adults with HIV, TAF: n=539 from population PK data (2 Phase 3 studies in adults with HIV).

- EVG/TAF AUC ~2-fold higher children than adults
- EVG trough lower in children but 9-fold above IC50 wild type
- EVG, TAF, COBI, FTC exposures within safe and efficacious range of historical data in adults and adolescents

Viral response

- Viral suppression maintained in all participants at week 16, and 16/17 (94%) at week 24
- No change CD4 %
- None met criteria for resistance testing

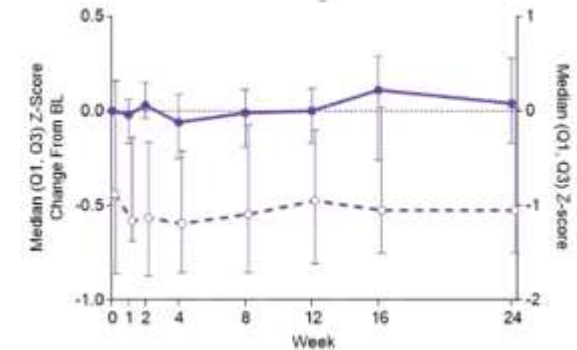
Bone DXA

	BMD	
Median (Q1, Q3)	Spine	TBLH
Baseline	0.436 g/cm ² (0.391, 0.468)	0.478 g/cm ² (0.442, 0.513)
% Change at Week 24 (n=12)	+4.243 (0.701, 6.852)	+4.224 (2.120, 5.379)

BMD, bone mineral density; TBLH, total body less head

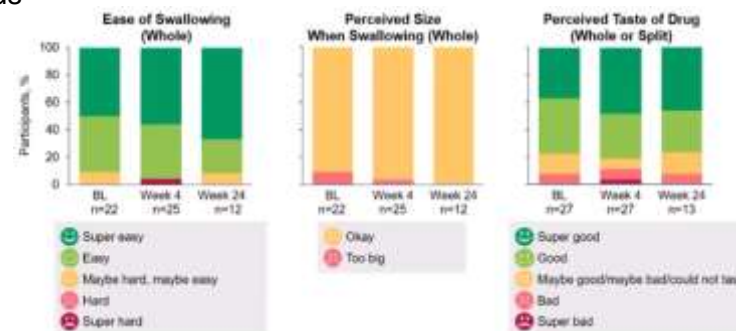
- No pt had >4% decline spine or TBLH BMD

Weight



- Minimal change in body weight over 24 weeks, and was consistently ~ minus -1 z-score below normal

Acceptability



- Ease of swallowing and acceptability excellent tablet good

Conclude

→ In virally suppressed children age ≥ 2 yr and weight ≥ 14 -25 kg, switch to E/C/F/TAF low strength tablet had PK within range seen in adults, was well-tolerated without significant toxicity or weight gain, good viral response and excellent adherence.



HIV Testing and Case Finding



Pediatric HIV Infection and Unsafe Injection Practice, Sindh, Pakistan

Mir F et al. IAS Virtual July 2020 Abs. OACLB0102

Background

- Larkana District, Sindh
 - High prevalence of HIV in Key Populations eg PWID
 - Prior outbreaks 2003 and 2016
- April 2019
 - Local GP reported 12 children HIV+
 - Outbreak reported on national TV
- National and international response
 - April-Dec 1167 children and 219 adults tested positive
 - Clinical crisis - treatment center for children, sustainability of resources for testing/treating/continuum of care
 - Epidemiological investigation



- Household-based individually matched case-control study (with HIV,HBV/HCV test child and HIV test mother):

- 401 cases: HIV+ age 0-15 yr registered for HIV care
- 401 controls: HIV negative matched to case on age, sex and home location

		Controls, n (%)	Cases, n (%)
N		401	401
Sex	Male	249 (62.1)	249 (62.1)
	Female	152 (37.9)	152 (37.9)
Age (years)	0-2	135 (33.7)	133 (33.2)
	3-4	139 (34.7)	138 (34.4)
	5-8	89 (22.2)	91 (22.7)
	9-15	38 (9.5)	39 (9.7)
	Negative	394 (98.3)	369 (92.0)
Mother's HIV status	Positive	0	28 (7.0)
	Unknown, mother dead	7 (1.7)	4 (1.0)

Risk factors for HIV in multivariate model

Variable	Category	Controls, n (%)	Cases, n (%)	Adjusted OR (95% CI)	p-value
Number of visits to government hospital	0	287 (71.6)	312 (77.8)	1	<0.001
	1	87 (21.7)	312 (77.8)	0.56 (0.07, 4.61)	
	>1	27 (6.7)	78 (19.5)	19.81 (2.55, 153.8)	
Number of visits to private clinic	0	112 (27.9)	75 (18.7)	1	<0.001
	1-2	101 (25.2)	19 (4.7)	1.38 (0.18, 10.45)	
	3-5	119 (29.7)	56 (14.0)	1.95 (0.25, 15.49)	
	6-10	49 (12.2)	72 (18.0)	9.40 (1.01, 87.65)	
	>10	20 (5.0)	179 (44.6)	55.84 (3.99, 781.5)	
Number of injections/infusions in past 6 months (analysed as continuous)	0	200 (49.9)	42 (10.5)	1	0.001
	1 or more	201 (50.1)	359 (89.5)	1.50 (1.18, 1.92)	
Had blood transfusion	No	398 (99.3)	345 (86.0)	1	0.001
	Yes	3 (0.7)	56 (14.0)	114.8 (6.35, 2074)	

Adjusted for mother's occupation

		Controls, n (%)	Cases, n (%)	Univariate OR (95% CI)	P-value
HBsAg (Hepatitis B)	Negative	380 (94.8)	328 (81.8)	1	<0.001
	Positive	21 (5.2)	73 (18.2)	4.47 (2.55, 7.82)	

		Controls, n (%)	Cases, n (%)	Univariate OR (95% CI)	P-value
Anti-HCV (Hepatitis C)	Negative	397 (99.0)	375 (93.5)	1	<0.001
	Positive	4 (1.0)	26 (6.5)	6.50 (2.27, 18.62)	

→ Outbreak primarily spread through parenteral route linked to unsafe injection and blood transfusion practices – need to invest in improving blood service and injection practices

Distribution of Multiple HIV-Self Test to High-Risk HIV-Uninfected Women

Led to Increased Partner/Couple Testing and ID HIV+ Partners

Thirmurthy H et al. IAS Virtual July 2020 Abs. OACLB0105



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



Siaya County, Kenya

HIVST intervention group

- 5 self tests at enrollment and additional tests on 3-monthly basis
- Test kits included use instructions
- Participants trained on self-test use
- Encouragement to offer self-tests to current & potential partners with whom unprotected sex was likely

Control group

- Multiple referral cards for HIV testing at local testing venues
- Referral cards designed to encourage women and their partners to seek HIV testing services

- HIV testing and surveys q 6 mo to 24 mo

	HIV self-test	VCT referral card
	Intervention	Control
Used by participant	7.1	4.4
Given to sexual partners	7.9	7.9
Given to others	0.4	0.9
Unused	1.5	3.3
Total	16.8	16.3

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

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

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

→ **No effect on HIV incidence**; additional HIV prevention interventions needed

	Overall	Intervention	Control
HIV-positive cases	34	19	15
Person-years of follow-up	3,147.8	1531.2	1616.6
Incidence per person-year of follow-up	1.1	1.2	0.9

Unadjusted hazard ratio: 1.16; 95% CI 0.54, 2.49; $p = 0.70$

Pediatric Index Testing to Improve Identification of HIV+ Children



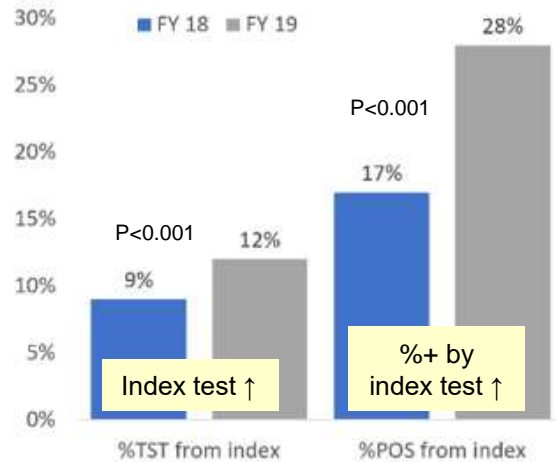
12 PEPFAR-Supported Countries



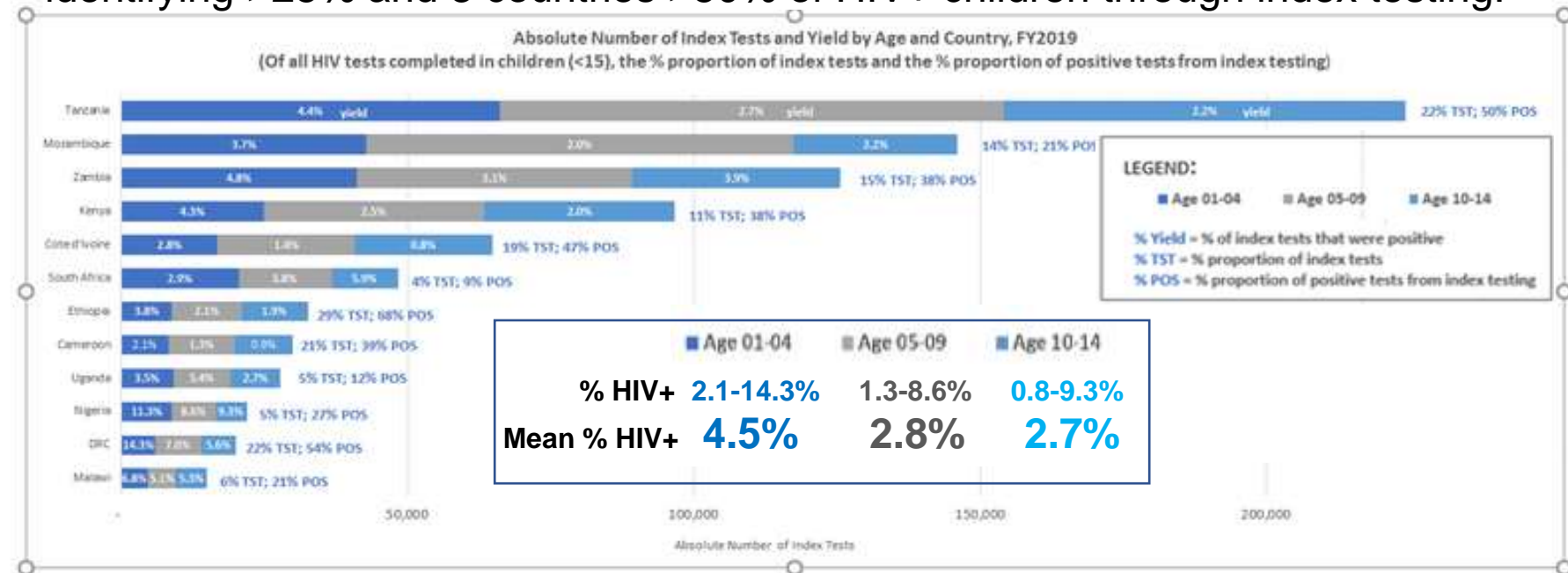
Wolf HT et al. IAS Virtual July 2020 Abs. OAB0703

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

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



- Significant ↑ 2018 to 2019 index testing and significant proportion of HIV+ children identified through index testing.



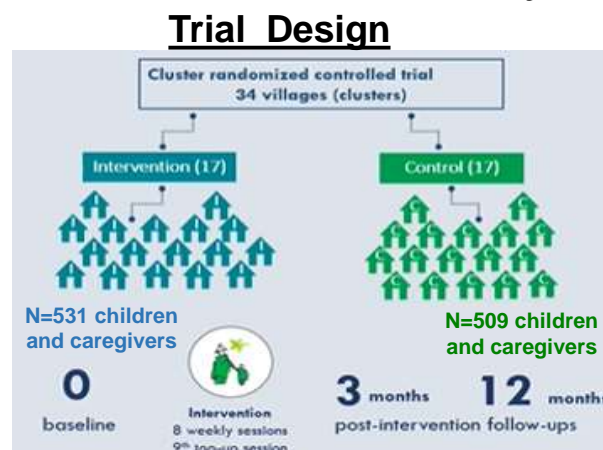
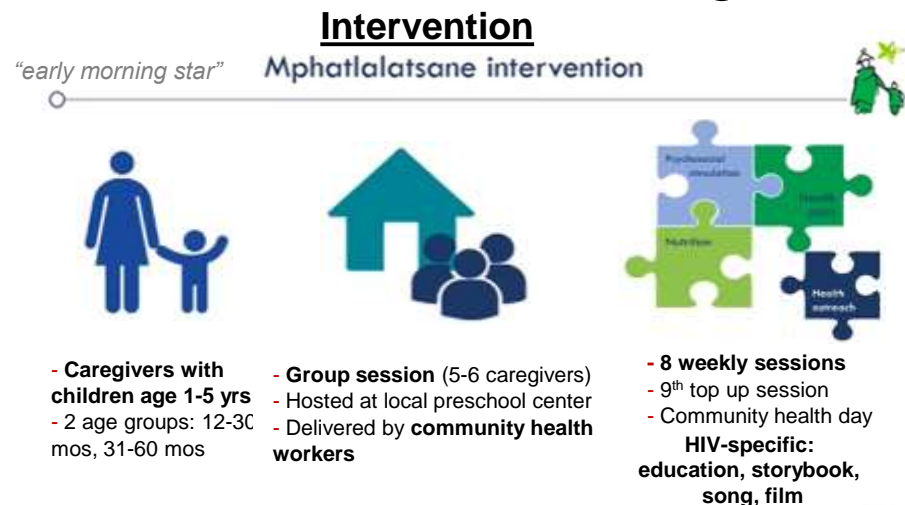


Community-Based Parenting Program, Rural Lesotho Increases HIV Testing of Children



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

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



12-month FU 98% both arms

Endpoints		
HIV testing rates of children 	Child Attention 	Child Language
Caregiver report	Early Childhood Vigilance Task (ECVT)	MacArthur Communicative Development Inventory (CDI) Mullen Scale Infant Development Peabody Picture Vocabulary



		Control	Intervention	Effect (95% CI)	p
Tested for HIV					
	3 months	115 (23.0)	153 (30.0)	1.56 (1.04 to 2.33)	0.029
	12 months	207 (42.8)	313 (61.4)	1.78 (1.12 to 2.81)	0.013

→ While most mother's HIV status known, only ~ half of children's status known at baseline

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

Determinants of HIV Testing for Young People 15-24 Years in Uganda

Kalibbala D et al. IAS Virtual July 2020 Abs. PEC0549

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

Factors Associated with HIV Testing
in Ugandan Youth

Characteristics	Crude Prevalence ratio [95%CI]	Adjusted Prevalence ratio [95%CI]
Sex		
Male	1	1
Female	1.12(1.03-1.21)	1.09 (1.01-1.18)
Age		
15-19	1	1
20-24	1.38(1.26-1.49)	1.26(1.15-1.37)
Marital status		
Single	1	1
Married/Widowed	1.26(1.18-1.34)	1.07(1.01-1.14)
Ever had sexual Intercourse		
No	1	1
Yes	1.31(1.18-1.45)	1.13 (1.01-1.26)
Distance to nearest HIV testing site		
<5km	1	1
5-10km	1.04(0.94-1.15)	1.06 (0.97-1.16)
>10 km	0.77(0.59-1.01)	0.77 (0.59-0.99)
Alcohol		
Never	1	1
Ever used	1.16 (1.07-1.24)	1.05 (0.97-1.13)
Encouraged by Peers		
No	1	1
Yes	1.19(1.08-1.28)	1.18(1.09-1.28)
Perceived HIV testing services as Youth-friendly		
No	1	1
Yes	1.13(0.99-1.28)	1.12(1.01-1.25)

- Prevalence of “ever HIV test” 80.2%; higher in females (83.6%) than males (74.8%).
- On adjusted analysis, factors associated with testing in youth: female sex, age ≥ 20 years, marriage, history of sex, peer-encouragement, and positive perception of youth-friendly health services.
- Interviews revealed 5 emergent themes related to HIV testing in youth:
 - Decisions on testing related to self-evaluation of risk
 - Fears of positive test deferred some from testing
 - Engagement with other health services facilitated testing for HIV
 - Barriers include fear injection, insufficient confidentiality, facilities not youth-friendly
 - Mixed feeling on mobile testing, lack of privacy a concern



Negative Diagnostic PCR Results Among Very Early Treated Infants in South Africa

Burke M et al. IAS Virtual July 2020 Abs. PEB0290

- LEOPARD (Latency and Early neOnatal Provision of AntiRetroviral Drugs) enrolled 73 neonates with confirmed in utero infection in Johannesburg, where ART was initiated within 1st 14 days of life
- Of 61 infant remaining on study, 46 (75%) attained VL <50.
- 14/46 (30%) had a **negative diagnostic PCR after ART start**; in 10/14 (71%) last PCR remained negative.
- Infants with suppression and negative PCR had higher CD4% pre-ART and higher cycle threshold values on birth PCR; age at ART start, BW and pre-ART RNA were not associated with PCR negativity (table).

Infant Characteristics and PCR Negative Tests

Infant Characteristics	Total (N=46)	Ever PCR negative (N=14)	Never PCR negative (N=32)	p-value
Age at ART start, N (%)				
0 to <= 48 hours	29 (63.0)	10 (71.4)	19 (59.4)	0.52
>48 hours to 14 days	17 (37.0)	4 (28.6)	13 (40.6)	
Birth Weight (grams), Median (IQR)	2,750 (2,425 – 3,180)	2,673 (2,120 – 3,160)	2,750 (2,530 – 3,265)	0.45
Pre-ART HIV RNA (copies/ml), Median (IQR)	11,908 (901 – 116,138)	11,910 (901 – 31,445)	10,725 (910 – 317,660)	0.75

→ Clinicians need to be alert to the possibility of false negative PCR test in infants started on early ART to avoid confusion about infant HIV status



Multi-Month ART Dispensing



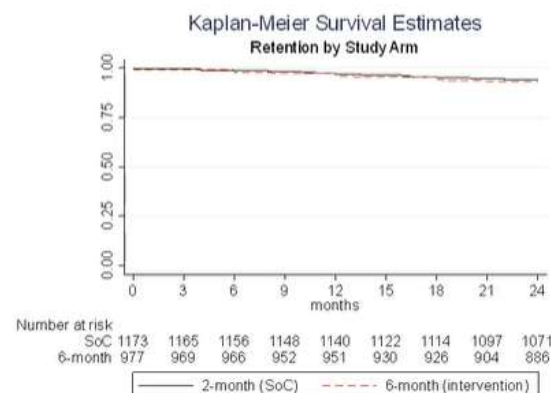
6-Month ART Dispensing is Non-Inferior to SOC for 24-Month Retention and Viral Suppression

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

- Cluster randomized non-inferiority trial of 6-month MMD in Ubuntu ARV Clinics in Khayelitsha South Africa.
- Enrolled 2,150 ART-experienced virally suppressed adults in Adherence Clubs (977 Intervention, 1173 SOC) (77% female, median time ART 7.3 yr, median age 42 years)
- First study visits Oct-Nov 2017, database closure Jan 2020

	Standard of care ACs	Intervention ACs (6-months refills)
Units of care	Groups of 25-30	Groups of 25-30
Frequency of AC visits/ART dispensing interval	4 x 2-month + 1 x 4-month AC visits (5 per year including blood draw and clinical visit)	2 x 6-month AC visits + one blood draw (3 per year including blood draw and clinical visit)
Grace period	5-days	5-days
Clinical visit frequency	Annual	Annual
Buddy ART refill collection	Allowed every 2 nd visit	Not permitted
Peer-based support	Strong emphasis	Strong emphasis
Patient self-management	Strong emphasis	Strong emphasis
ART packing and dispensing	Pre-packed by central dispensing unit, delivered to the clinic pharmacy, dispensed at AC visit	Pre-packed at the clinic pharmacy with support from research staff, dispensed at AC visit
Management of clinical complications	Up-referral to clinic clinicians – if unstable patient exits AC and returns to routine clinic appointments	Up-referral to clinic clinicians – if unstable patient exits AC and returns to routine clinic appointments

Retention was high in both arms



24-month retention

Intervention: 93.1%
(95% CI: 91.2-94.7%)

SoC: 94.0%
(95% CI: 92.4-95.2%)

Hazard ratio:

1.09 (95% 0.54-2.19)

Viral load completion

Non-inferior VL completion at 24-months

SoC VL completion:
89.3%
[CI 85.6-92.1%]

Intervention VL completion:
94.5%
[CI 92.9-95.8%]

Viral load suppression

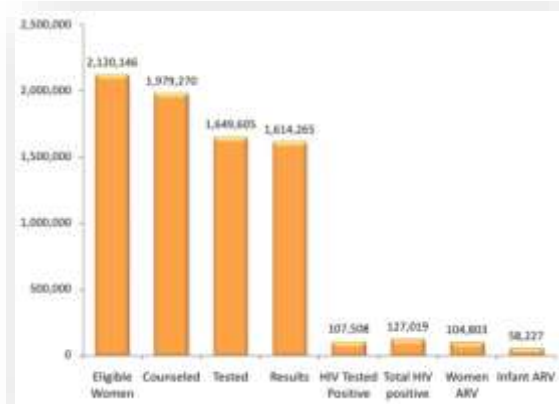
Non-inferior VL suppression at 24-months

SoC VL suppression:
97.5%
[CI 96.4-98.3%]

Intervention VL suppression:
96.3%
[CI 94.6-97.58%]



PMTCT Cascade





Declining HIV MTCT in Brazil 2010-2017

Da Silveira LN et al. IAS Virtual July 2020 Abs. OAC0704

- Using national electronic medical record system on ART and VL to identify number of infected children <1 year old to estimate number children infected with HIV yearly.
- Number pregnant women with HIV identified from national register minus pregnancy losses (estimated from data collected during national surveillance on NTD)
 - Estimated 107,734 pregnant HIV+ women with live births over 7 years
 - Identified 4,765 HIV infected children, for overall transmission 4.4%.

Table 1: Number of infected-children, exposed children and mother to child transmission rate by year of birth. Brazil, 2010-2018

	2010	2011	2012	2013	2014	2015	2016	2017
Infected-children	684	651	607	602	556	517	507	361
Exposed	11.354	11.503	11.654	11.807	11.962	12.119	12.278	12.454
MTCT rate	6,0%	5,7%	5,2%	5,1%	4,6%	4,3%	4,1%	2,9%

15% decline 38% decline
MTCT rate decreased 52% p-value<0.001



PMTCT in National HIV Care Centers in Columbia

Buitrago EM et al. IAS Virtual July 2020 Abs. OAC073

- VIHCOL group is nationwide network of HIV care centers in Columbia with clinical data from 25,000 patients in 23 centers and 11 cities.
- Included 362 women with complete clinical record whose pregnancy was diagnosed Jan 2014 or later and outcome of pregnancy known by Dec 2019
 - 26% known HIV status before pregnancy; 4% diagnosed in delivery/PP
 - 1st VL in pregnancy was <1000 in 49%, ↑ to 91% by delivery, with 72% <50.
 - All received ART (48% LPV/r, 12% RAL, 5% NVP, 4% EFV, 25% other)
 - 353 live births; 97% formula fed.
 - **No confirmed infant HIV infections** in this network of HIV sites in Columbia over this 5-year period (official national MTCT for country in 2018 was 2.1%)

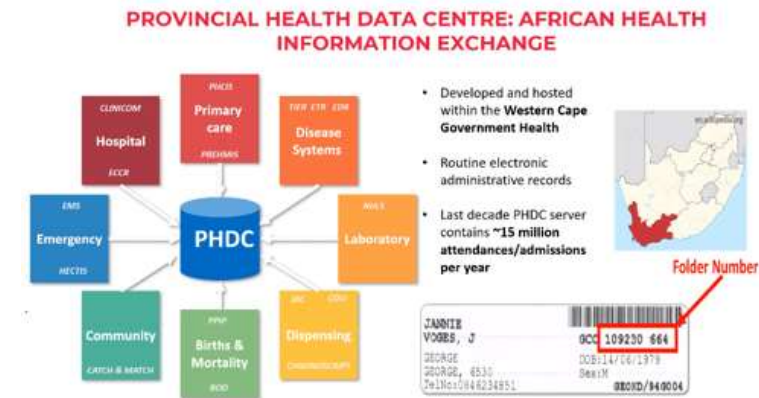
Mother to child transmisión (n, %)		
Confirmed	0	0
No MTCT	281	77.7
Indetermined (only one VL in chart)	9	2.5
LFU	9	2.5
Infant death before 2nd VL obtained	3	0.83
No data	60	16.6

MTCT at Age 12 Months in Khayelitsha South Africa 2017

Phelayane F et al. IAS Virtual July 2020 Abs. OAC0705

- Described uptake of PMTCT and outcomes in 2,576 HIV+ mothers attending ANC (HIV prevalence 31%) with live-born infants in 2017 using electronic medical records with unique patient ID and linked mother-infant pairs.

- 88% knew HIV status at 1st ANC, 78% on ART.
- 95% women diagnosed antepartum started ART; 88% suppressed in the 85% tested.
- 94% infants had 1st EID test by 10 wks
 - 80% tested at birth; if negative only 58% returned for test at 10 weeks
- **Overall 12-month MTCT only 1.6%** (however, 10% of infant lacked 12-month HIV outcome).
- Risk factors for infant infection
 - Starting ART during pregnancy vs preconception
 - First diagnosed with HIV at delivery or postpartum
 - No antenatal suppression or no VL test antepartum



Population	# HIV+/total #	12 mo MTCT
Overall cohort	41/2576	1.6%
No infant HIV outcome	249/2576 (9.7%)	
All with known outcome	41/2327	1.8%
<i>Dx before ANC</i>	31/2273	1.4%
<i>Dx during ANC</i>	6/263	2.3%
<i>Dx delivery/PP</i>	4/40	10%

Factors Associated with Interruption HIV Care and Treatment in Pregnant and Postpartum Women in Kabeho Cohort, Rwanda

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

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

Adjusted odds ratios (OR) and 95% confidence intervals (95% CI) for interruptions¹ among women enrolled in the Kabeho Study.

Facility-level characteristic		OR	95% CI
1	ANC, PMTCT, and ART services offered all 5 days per week	0.54	0.32, 0.92
	Not offered all 5 days	Reference	
2	Retention support ²	0.30	0.12, 0.76
	No retention support	Reference	
3	Peer counseling	0.31	0.23, 0.42
	No peer counseling	Reference	
4	Infant feeding counseling	0.20	0.15, 0.26
	No infant feeding counseling	Reference	

¹ Interruptions are defined as missing at least 1 monthly visit followed by returning to care

² Retention support includes telephone reminders, transportation reimbursement/support, or default tracing systems

NOTE: Individual characteristics were not associated with interruptions (results not shown)

- Individual factors such as age, education, marital status, CD4 count, HIV disclosure status, travel time to clinic, number in household were not significantly associated with missed visit.
- **Health facility factors** had strong association with reduced care/treatment interruptions – including **# days ANC available** and availability of **retention support, peer counseling, infant feeding counseling**.
- These health system factors may be effective target for interventions to improve retention.



Effect of Early Childhood Development Programs in Very Early Treated Infants in South Africa

Strehlau R et al. IAS Virtual July 2020 Abs. PEB0327

- LEOPARD (Latency and Early neonatal Provision of AntiRetroviral Drugs) enrolled 73 neonates with confirmed *in utero* infection with ART was initiated within 1st 14 days of life.
- 36 infants were also enrolled in an early childhood stimulation trial: 12-month program to stimulate infant development, while 36 received standard of care; at 12 mos Bayley assessment conducted on 28 intervention and 24 control children.

Home Stimulation Program

- The home stimulation programme was initiated within the first month of life.
- At birth, infants enrolled in the IG were provided a standardised set of age-appropriate, developmentally stimulating toys. Additional items were provided every three months through the first year of life (Table 1).
- The child's caregiver received an information card which was created in a South African setting as part of a developmental activity programme for use in children receiving outpatient care for cardiac disorders.
- The information card included illustrations and information explaining what a child is expected to do at certain ages in terms of physical, cognitive, language and socio-emotional development.
- Additional information included on the caregiver information card included information on how to stimulate the child, as well as warning signs which may indicate developmental delay.
- A new information card was provided three monthly according to the age of the child.
- The information contained in the caregiver information card was explained to the caregiver. Ideas on child play and stimulation using the toys provided were also discussed.

Assessment Subscale	Intervention Group	Observation Group	P
Age at time of BSID-III assessment (days), mean (SD)	345.47 (66.2)	352 (27)	0.6535
Cognitive subscale			
Scaled Score, mean (SD)	11 (2.57)	11 (2)	1.000
Composite Score, mean (SD)	105 (12.84)	103 (9)	0.5252
Language Subscale			
Receptive Communication, Scaled Score, mean (SD)	10.96 (2.35)	9 (4)	0.0331
Expressive Communication, Scaled Score, mean (SD)	10.75 (2.08)	10 (2)	0.1931
Language Subscale, Composite Score, mean (SD)	105.21 (2.35)	100 (17)	0.1904
Motor Subscale			
Fine Motor, Scaled Score, mean (SD)	10.5 (2.08)	10 (2)	0.3833
Gross Motor, Scaled Score, mean (SD)	9.25 (2.10)	10 (2)	0.1954
Motor Subscale, Composite Score, mean (SD)	99.46 (9.24)	99 (11)	0.8705

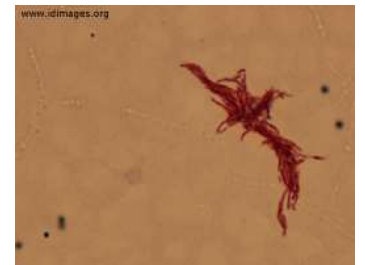
- We found 12-month old infants infected with HIV and having started ART within the first week of life to achieve good scores when assessed using the Bayley Scales of Infant and Toddler Development (3rd Ed.).
- However, in conjunction with having started ART at a very early age, at 12-months, infants having participated in a year-long, home-based developmental stimulation programme achieved higher scores on the cognitive, language and motor assessment subscales.

- Composite scores for cognitive, language and motor subscales are within test average (100) range for all.
- The intervention group had trend to higher composite scores in all 3 language subscales
- Language receptive communication score significant greater in intervention group, while 1 child in observation group had developmental delay on language subscale.



TB and HIV

- Pregnancy
- Pediatrics



Risk Factors for Hepatotoxicity in Pregnant and Postpartum HIV+ Women Receiving INH Prophylaxis

Gupta A et al. IAS Virtual July 2020 Abs. OAB0505

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

→ 6% had ≥ 1 hepatotoxicity event, **similar by arm**

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

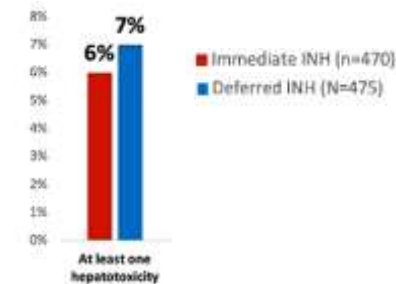
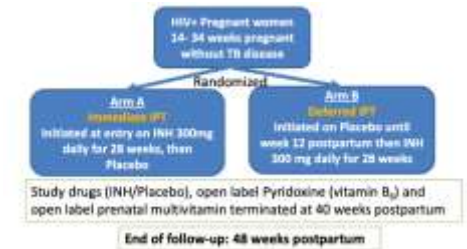
→ ALT increase PP and peaks at 12 wk PP both arms

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

Factors Associated with Hepatic Toxicity

Type ART/timing, CTx use PP, CYP2B6 slow genotype

Characteristic	Group	Estimated risk ratio	95% CI	p
INH/ARV regimen interaction				
EFV: Immediate vs Deferred (ref)	PP toxicity	0.73	(0.41, 1.27)	0.028
NVP: Immediate vs Deferred (ref)	AP toxicity	8.67	(1.06, 70.81)	
Hepatitis C positive serology		3.60	(0.88, 14.88)	0.077
Mid upper arm circumference (ref: obesity)	Malnutrition <23	0.37	(0.05, 2.77)	0.420
	Normal: 23-31	0.77	(0.45, 1.32)	
Initiated cotrimoxazole after week 12 pp (vs never initiated or initiated before week 12 pp)		4.57	(1.80, 11.47)	0.001
CYP2B6 Genotype (ref: slow)	Fast	0.37	(0.16, 0.84)	
	Intermediate	0.44	(0.23, 0.82)	0.017



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

→ Critical to monitor for hepatic toxicity PP when most events occur; consider ARV regimen and CTX use.

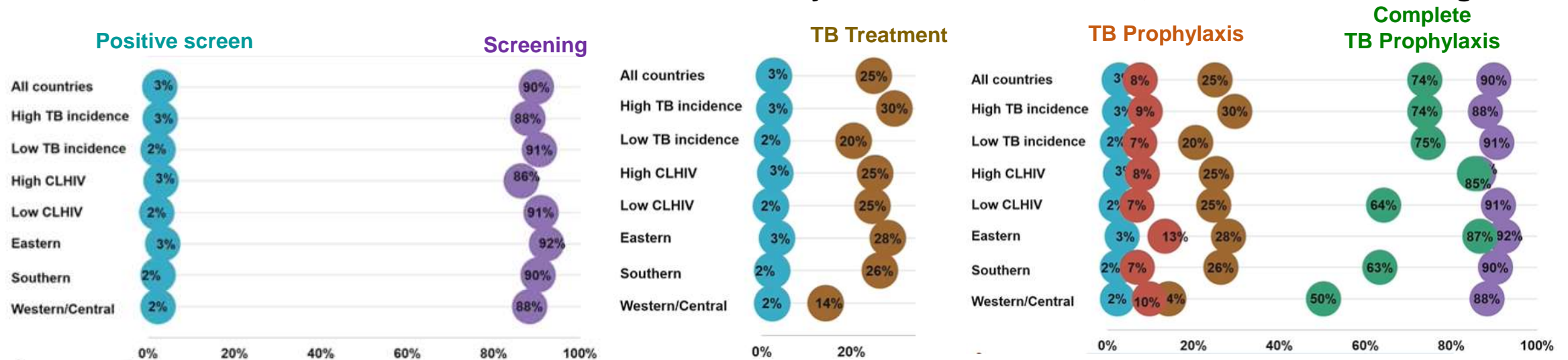


Pediatric TB Clinical Cascade in HIV+ Children on ART, 16 Countries

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



- Evaluated TB cascade among CLHIV age <15 years in 16 African countries Apr-Sept 2019
- Median TB Cascade Indices in CLHIV on ARV Stratified by Pediatric TB incidence, CLHIV Burden and Region**

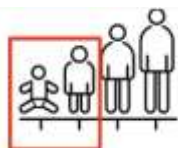


- Screening was high overall, but screening positivity was lower than expected given CLHIV
- TB diagnosis was unclear among CLHIV on ART because data are not age disaggregated

- TB treatment initiation was low, regardless of region, number CLHIV or TB incidence

- TPT initiation was very low regardless of region, number CLHIV or TB incidence
- TPT completion was high in Eastern but low in Southern and Western Africa

How to Address the Gaps

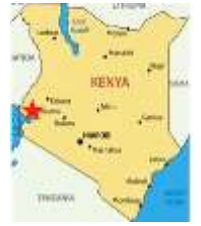


Children and adolescents need to be specifically considered and included in national, subnational, and clinic-level efforts for...



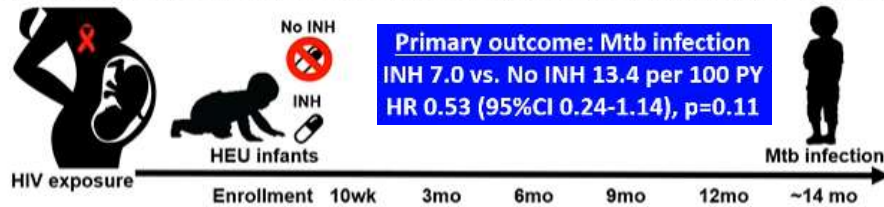
Biomarkers of Infant Adherence to INH Prophylaxis in a TB Prevention Trial in Kenya

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



Infant Tuberculosis Prevention Study (iTIPS)

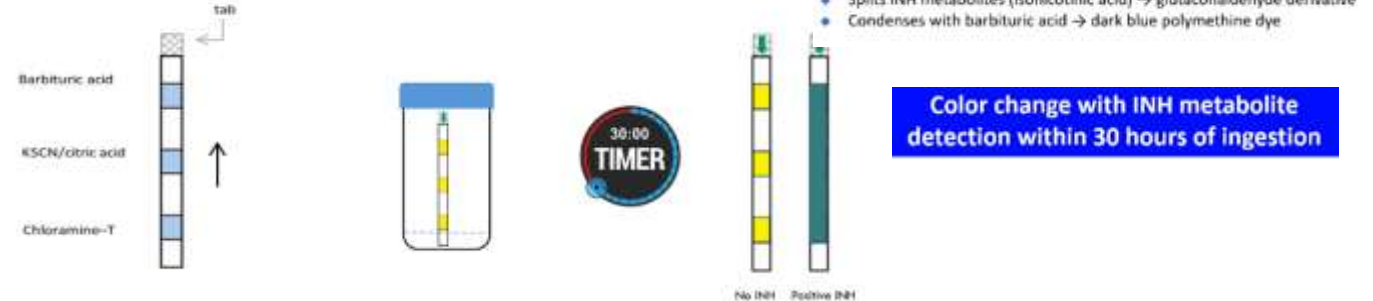
Non-blinded RCT of INH efficacy for Mtb infection primary prophylaxis



LaCourse et al, CID 2020

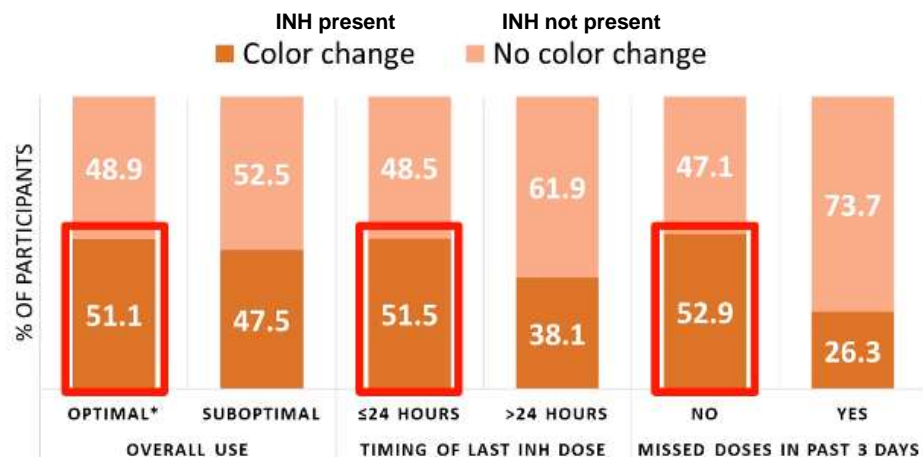
Development of low-cost urine INH dipstick - modified Arkansas method

Kilburn Am Rev Res Dis 1972, Schouffrageel Chest 1990, Eidvitz-Markus Chest 2003, Amlobu JTCO 2014



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

INH Dipstick Result by Caregiver-Reported Adherence



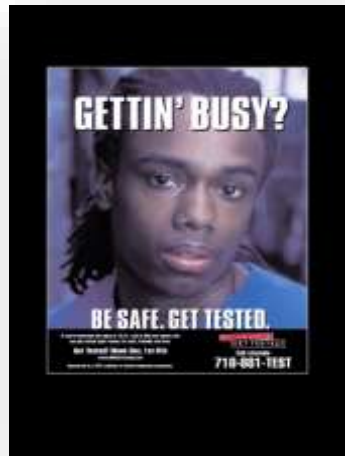
Caregiver reported measure of adherence

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

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



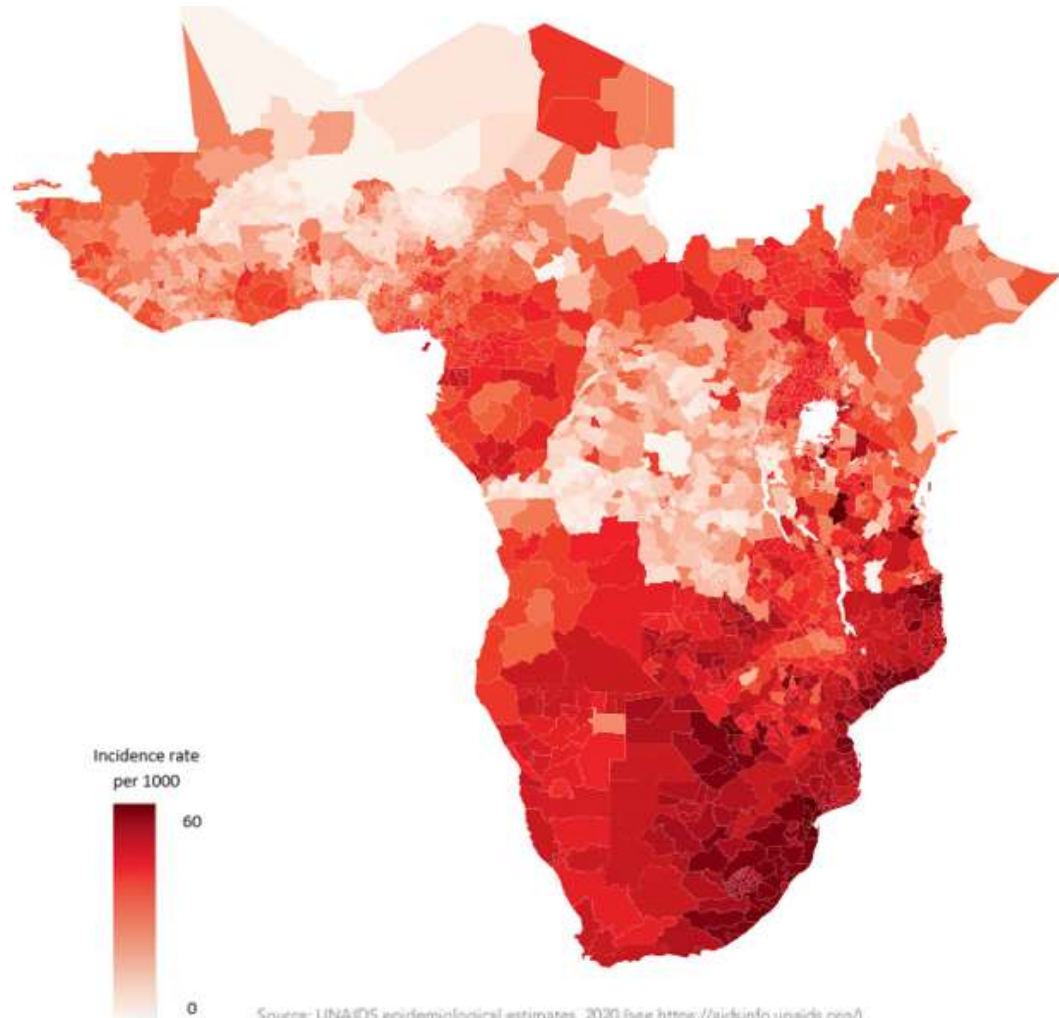
Adolescents and HIV



HIV Incidence in Adolescent Girls and Young Women Aged 15-24 Years

Subnational Levels, Sub-Saharan Africa, 2019 →

Critical Need For Effective Prevention Interventions



- New HIV infection rates vary across and between regions.
- In sub-Saharan Africa, incidence of HIV among AGYW (aged 15-24 years) is generally highest in southern Africa, but subnational data show districts cross the region with very high rates of HIV infection.
- The high incidence of HIV among AGYW across Africa points toward the critical need to improve prevention interventions for this group.

Source: UNAIDS epidemiological estimates, 2020 (see <https://aidsinfo.unaids.org/>)
Note: HIV incidence estimated as new HIV infections per 1000 person-years at risk.
Countries: For selected countries in SSA that had the data required to produce subnational HIV estimates. See table A1, Methods section.
Methods: See Methods section.

National Uganda Survey of In- and Out-of-School AGYW HIV, Syphilis and Sexual Risk Behavior Prevalence

Matovu JKB et al. IAS Virtual July 2020 Abs. PDC0403

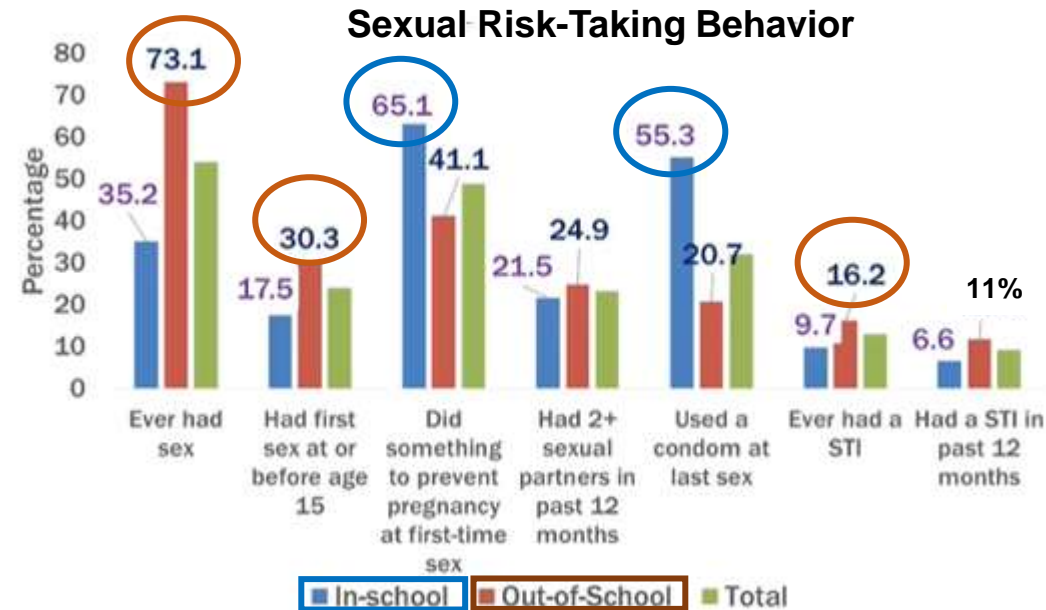


- Survey of 8,236 in- and out-of-school AGYW age 10-24 years in 20 selected districts in Uganda; 50.3% in-school.



Weighted HIV/Syphilis Prevalence
N=8,236; 50.3% in-school

	HIV (%)	Syphilis (%)	Total (%)
School status			
In-school	0.6	0.6	4,139 (50.3)
Out-of-school	1.6	1.9	4,097 (49.7)
Age-group			
10-14	0.3	0.7	1,297 (15.8)
15-19	0.8	1.1	3,644 (44.2)
20-24	2.4	2.0	3,295 (40.0)
Overall weighted sero-prevalence	1.0	1.2	



→ Findings suggest need for 1) **keeping girls in school** and b) to **develop specific prevention interventions to target out-of-school girls**



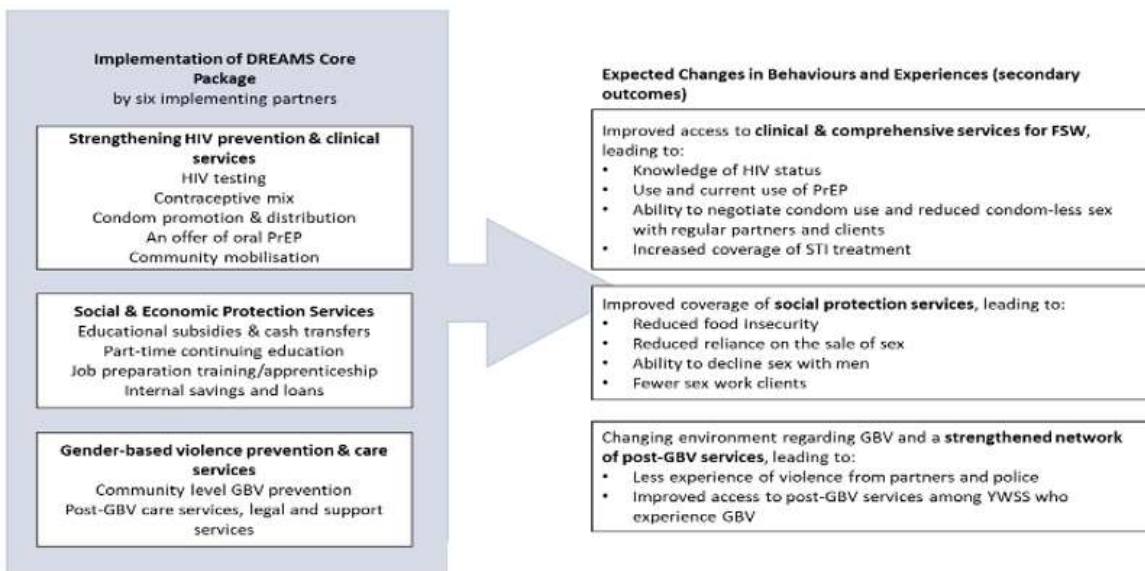
DREAMS and HIV Incidence in Young Women Sex Workers, Zimbabwe

Chabata ST et al. IAS Virtual July 2020 Abs. OAC0102

Zimbabwe

- Evaluation of DREAMS+PrEP among most vulnerable AGYW, using the Sisters platform for cohorts of YWSS and HIV testing in 2 intervention & 4 comparison sites [Partner: LSTM with CeSHHAR]

- Evaluation of DREAMS project in Zimbabwe, targeted at YWSS age 18-24 yr.
- Non-randomized design recruited 1204 in 2 intervention and 1227 in 4 comparison sites; 24 mo FU.



HIV Incidence in Young Sex Workers HIV-Negative at Enrollment

	Number of seroconversions/person-years of follow-up	Rate per 100 person-years	Age-adjusted rate ratio (95%CI) p-value	Fully adjusted rate ratio (95%CI) ¹ p-value
Non-DREAMS (N=479)	48/907.62	5.29	1.0	1.0
DREAMS (N=538)	31/988.14	3.14	0.59 (0.38-0.93) p=0.022	0.74 (0.43-1.29) p=0.287

*Adjusted for age, highest education level, marital status, self-identification as female sex worker, STI symptoms, number sex partners last month, baseline HIV prevalence

- Baseline HIV prevalence: 19.5% DREAMS, 26.3% non-DREAMS sites; yearly HIV testing in those HIV-negative
- % with 24-mo FU: 56% DREAMS (n=538), 53% non-DREAMS (n=479)
- Differences in demographics between sites adjusted for in analysis.

- While HIV incidence was lower in DREAMS sites, on adjustment no longer statistically significant.
- YSSW used clinical services more over time – but few accessed non-clinical DREAMS services.
- Most SW in DREAMS sites offered PrEP and ~1/3 self-reported initiation but retention suboptimal and HIV incidence similar those who never started PrEP.
- Still need approaches to strengthen use integrated social/clinical services in YWSW.

Lack of Impact of DREAMS on HSV-2 Acquisition Among AGYW in Rural KwaZulu Natal South Africa

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

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

Annual:

- Face-to-face interview and self-filled questionnaire

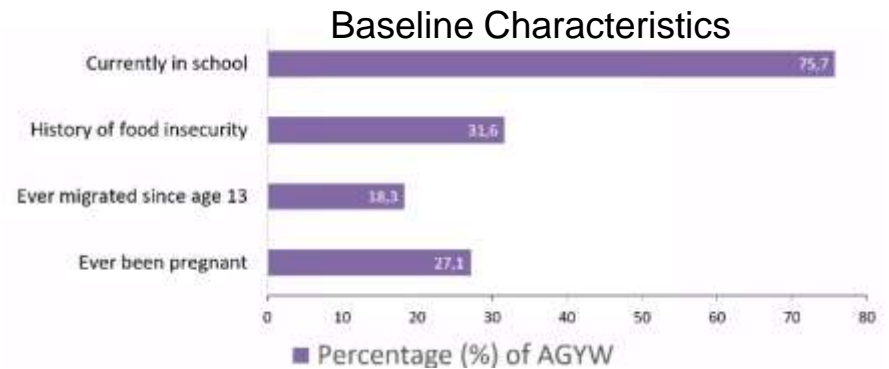
- ☐ Socio-demographics
- ☐ General health
- ☐ Awareness and uptake of DREAMS interventions
- ☐ Sexual behaviour

- Dried blood spot for HSV-2 testing

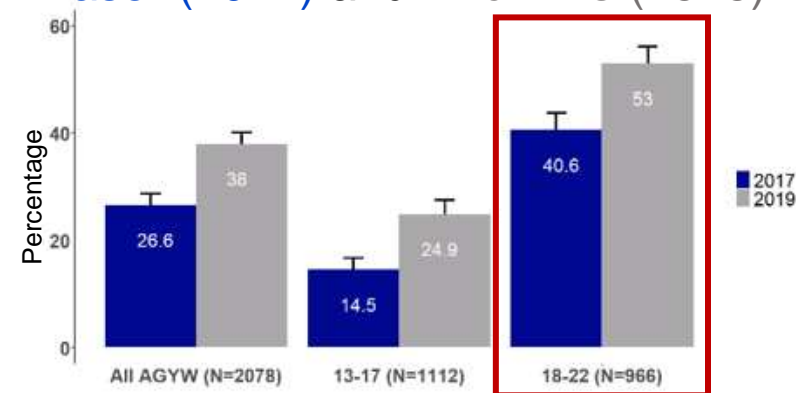
- AGYW considered DREAMS beneficiaries if reported either:

1. Receiving an invitation to participate in a DREAMS activity
2. Participating in services provided by local DREAMS implementing organizations in the past 12 months

- HSV-2 incidence: Calculated for AGYW with a first negative test plus ≥ 1 follow-up test



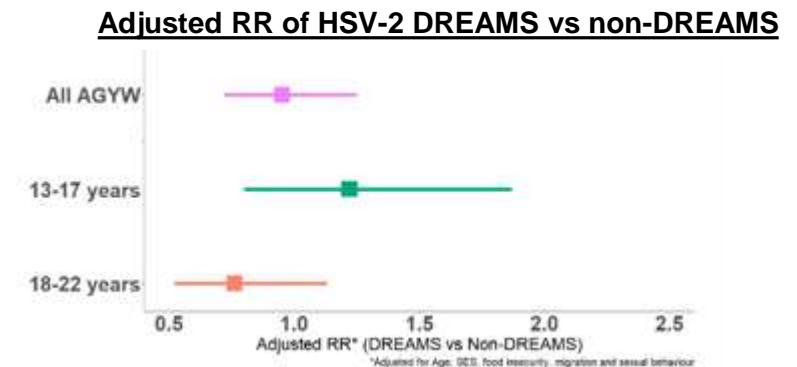
Very High HSV-2 Prevalence Base- (2017) and End-Line (2019)



High Incidence HSV-2 Overall

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

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





No Effect of Cash Transfer Added to Combination Prevention Intervention to AGYW to Reduce Sexual Risk Behavior, Tanzania

Materu J. IAS Virtual July 2020 Abs. LBPEC18

- As part of DREAMS in Tanzania, Sauti project instituted core package of services:
 - Biomedical – VCT/condom, TB/STI screen/rx, screen and referral for GBV, alcohol, drug abuse
 - Behavioral – peer-led sessions addressing HIV risk, gender, reproductive health
 - Structural – economic empowerment community banking, health and parenting ed
- Cluster RCT, communities with ≥ 110 AGYW age 15-23 yr **out of school** randomized to unconditional cash transfer (quarterly mobile money transfer US \$31 for 18 mos) or not, all in combination with Sauti interventions; primary endpoint **HSV-2 seroconversion status**.

Baseline

Factor	Intervention n=1482	Control n=1544
Age		
15-19 years	555 (37.5%)	773 (50.1%)
20-23 years	927 (62.6%)	771 (49.9%)
HIV prevalence	3.1%	4.0%
HSV-2 prevalence	32.8%	31.2%
Reported to be sexually active	73.8%	77.1%
Of sexually active: reported transactional sex (6 months)	28.9%	31.8%
Of sexually active: reported sex work (6 months)	16.7%	17.1%
Of sexually active: reported intergenerational sex (6 months)	11.9%	13.0%

No significant baseline differences between study arms

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

RR HSV-2 Conversion to + by Community Stratum

	Intervention Group	Control Group	Crude RR †	Adjusted RR ‡
High HIV risk, urban stratum	9.4%	5.2%	1.84 (1.01-3.35)	1.46 (0.71-2.98)
High HIV risk, rural stratum	14.0%	8.1%	1.77 (1.05-2.97)	1.69 (0.90-3.17)
Low HIV risk, rural stratum	9.4%	17.8%	0.53 (0.34-0.83)	0.47 (0.30-0.74)

*Adjusted for age, matching pairs baseline HSV-2

→ However, when stratified by community HIV risk and setting, cash transfer appeared that I may be effective in **rural communities with low HIV risk**

Effect Economic Support/Community Dialogue on Adolescent Sexual Behavior, Zambia

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

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

Control group
31 schools
999 girls

Economic support
63 schools
2004 girls

Combined support
63 schools
1919 girls

- Unconditional cash transfer q mo to girls, annual to parents, pay school fees gr 8-9
- Plus community meeting parents 6x yr; youth clubs q 2 wks, focus SRH

Data collection

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

Mean age 13.6 years (SD 1.39)

9% had ever had boyfriend

2% had ever used contraceptives

Most had some knowledge of SRH

Low levels of pregnancy and marriage

	RR (95% CI)					
	Combined vs Control		Economic vs Control		Combined vs Economic	
Currently using modern contraceptive methods	1.00	(0.81 – 1.24)	1.03	(0.82 – 1.30)	0.98	(0.80 – 1.21)
Good knowledge of modern contraceptive methods	1.16	(0.95 – 1.43)	0.99	(0.80 – 1.23)	1.17	(1.00 – 1.36)
Sexually active last 4 weeks	0.60	(0.47 – 0.78)	0.71	(0.54 – 0.94)	0.85	(0.65 – 1.11)

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



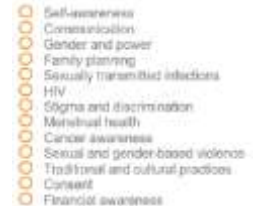
Effectiveness of Sista2Sista Program on Improving Sexual/Reproductive Health Outcomes AGYW Zimbabwe



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

- Structured peer group behavioral intervention aimed at improving health outcomes among vulnerable in- and out-of-school AGYW.
 - Led by female mentors and organized by age 10-14; 15-19; 20-24 yrs.
 - Programs led by 130 mentors run groups in 23 districts in Zimbabwe.
 - Analyzed program data for 91,612 AGYW age 10-24 yrs who were enrolled b/n 2013-2019 to evaluate program exposure and HIV testing, marriage, school attendance, FP, and sexual abuse; mean age 15 yr, 81% in school, attrition rate <0.5%, with 64% attending at least 75% sessions.
 - FU 4,612 graduates 1 year after graduation to assess sustainability.
- Sista2Sista was an effective behavioral intervention to improve HIV and other SRH outcomes, with better outcomes at higher thresholds of program completion:
- **≥75%** sessions associated with **increased odds HIV testing uptake** & **decreased odds school drop-out/child marriage**; **≥85%**, also more likely to **return to school**; and **100%**, also more likely to **use FP and report sexual abuse**.
- Augmenting group exercises with individual sessions increased likelihood program completion.
- Outcomes related to school attendance and use FP were sustainable up to 1-year post-intervention.

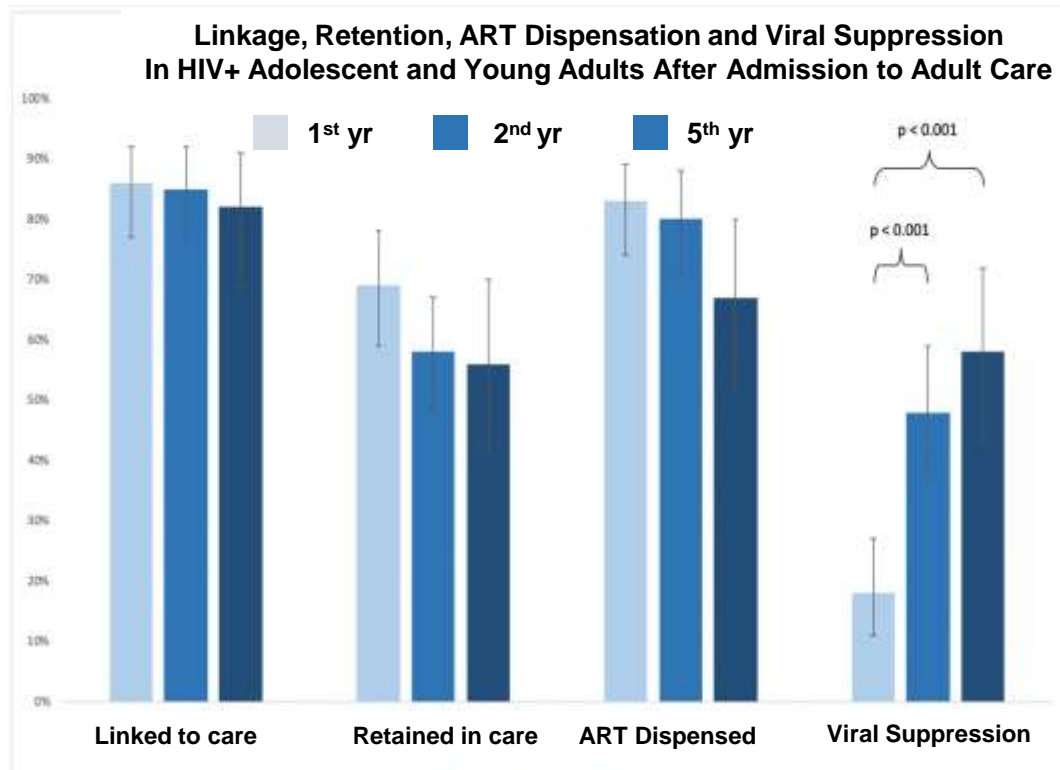
Sista2Sista peer groups meet weekly over the course of one year, following a 40-exercise curriculum that is guided by a Mentor's Manual. Girls who complete at least 30 (75%) exercises are considered graduates of the program.



Sustainability of HIV Care Cascade in Adolescents and Young Adults with HIV Transitioning to Adult HIV Care

Antonio MB et al. IAS Virtual July 2020 Abs. PEB0339

- Retrospective cohort of 108 HIV+ youth referred from pediatric to adult HIV care clinics in Sao Paulo Brazil between Jan 2001 and Dec 2019; evaluated linkage, retention and suppression at 1, 2 and 5 years in all youth with ≥ 1 visit in adult care.
- Median age at transition to adult care was 19 years.



- Overall, linkage (defined as record of ≥ 1 VL measurement), retention (defined as record of ≥ 2 VL thereafter) and ART use were below desirable levels and percent with undetectable VL was very low (18%) in the **1st year** after admission to adult care.
- In the **2nd and 5th** years after transition, although the linkage, retention and ART use did not change significantly, the % with undetectable VL increased significantly.
- However only 58% had undetectable VL in the 5th year after admission to adult care.

Rates of Cervical Lesions by Age and Prior Screening Status



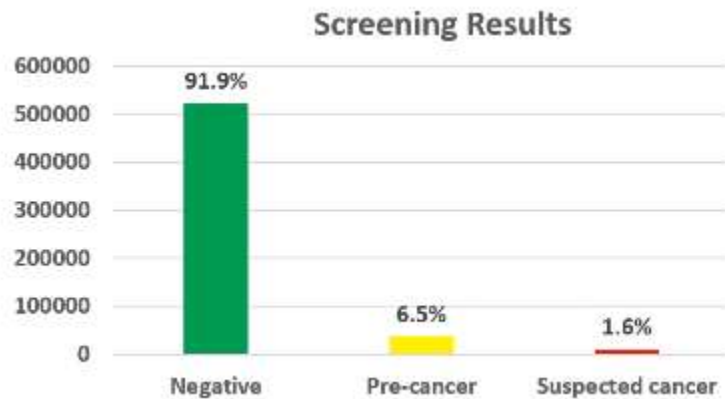
Go Further Partnership



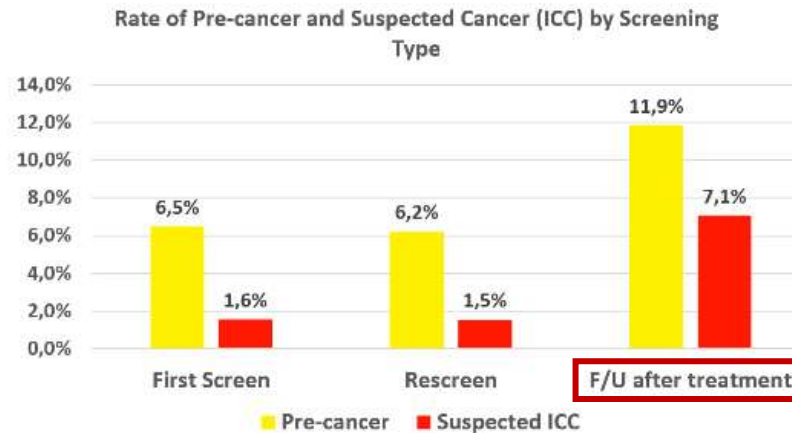
Watts DH et al. IAS Virtual July 2020 Abs. OAB07045

- 8 countries funded for bi-annual cervical cancer screening with visual inspection with acetic acid (VIA) for HIV+ women >25 yr; data collection includes age; type screen (1st, rescreen, FU treatment); VIA findings; and treatment

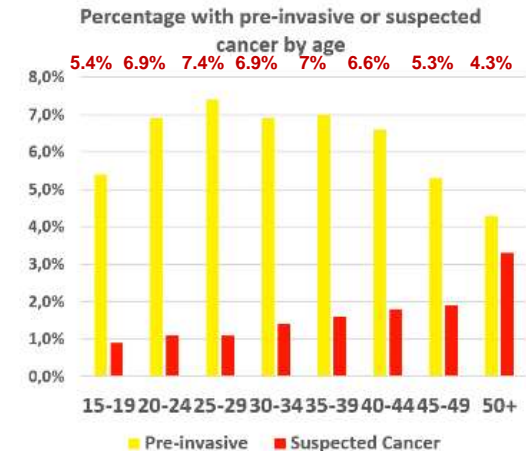
- Through Sept 2019, 568,311 screenings
 - 489,810 was 1st screening
 - 73,499 was for repeat screening
 - 5,052 was FU after treatment for abnl



- Women with prior treatment for cervical abnl have high rates **suspected cancer** at FU test despite prior treatment



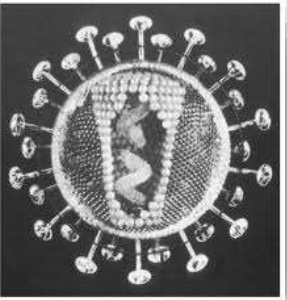
- Rate **suspected cancer** increased with age but seen in **every age group**, including youngest 15-19 years



- Women treated for precancer lesions high risk recurrence & should have repeat evaluation sooner than 12 mos
- Pre-invasive lesions seen in $\geq 5\%$ all HIV+ women; screening earlier in HIV+ women: onset sex or age 18
- Rates of treatment were <80% target, need to increase availability cryotherapy or thermal ablation + Loop Electrosurgical Excision Procedure (LEEP)



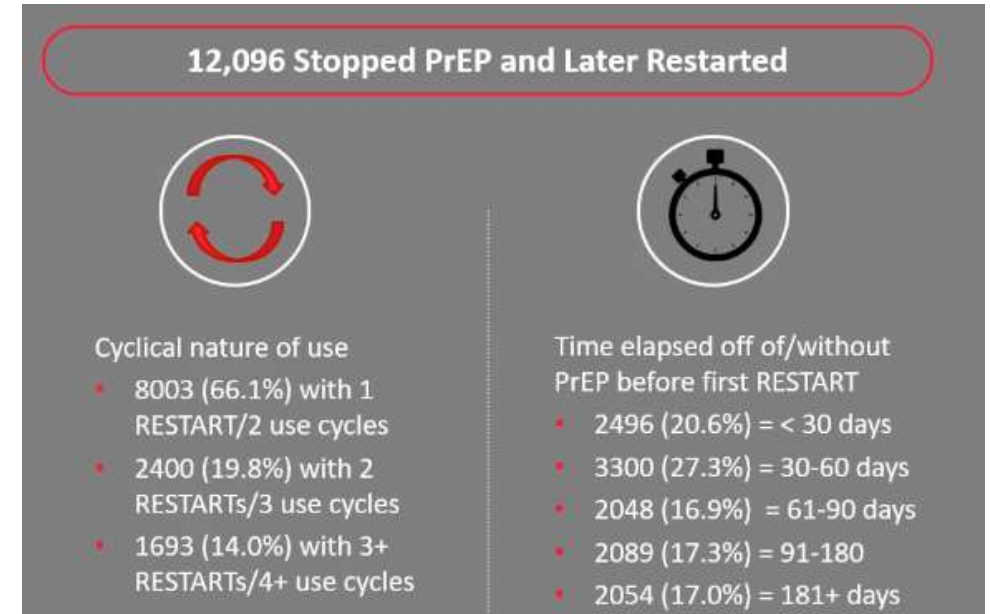
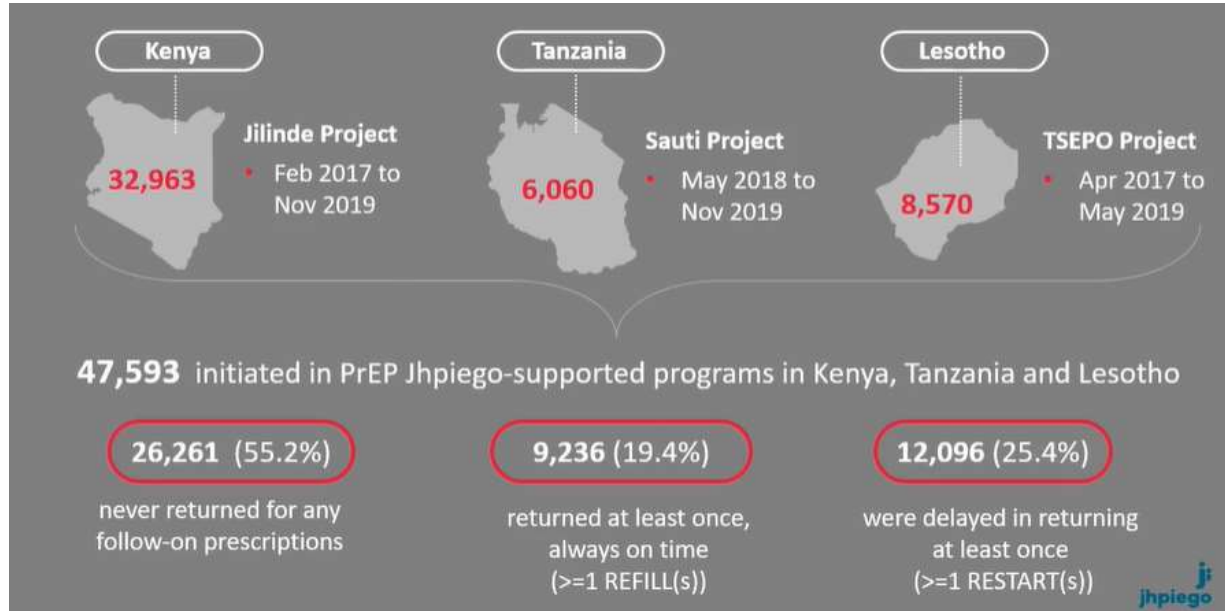
PrEP Effectiveness and Use by Adolescents and Pregnant Women



Patterns of PrEP Use in >40,000 Clients in Sub-Saharan Africa

Mutegi J et al. IAS Virtual July 2020 Abs. OAE0704

- Evaluated patterns of PrEP use in three Jhpigo projects in 3 countries.



- With each increase in cycle number, clients were less likely to stay off PrEP for an extra month between cycles in all three programs, after adjustment*
 - Independent predictors of using PrEP a greater number of cycles, after adjustment*, included:
 - Age (older), sex (female) and risk group (MSM, FSW, serodiscordant relationship vs, general population) - Jilinde (Kenya)
 - Sex (female) - Sauti (Tanzania)
 - Age (older), marital status (married) and risk group (MSM, FSW vs. general population) - TSEPO (Lesotho)
- * number of use cycles, time observed, age, sex, marital status, risk group, district/county, prior PrEP use, STI diagnosis

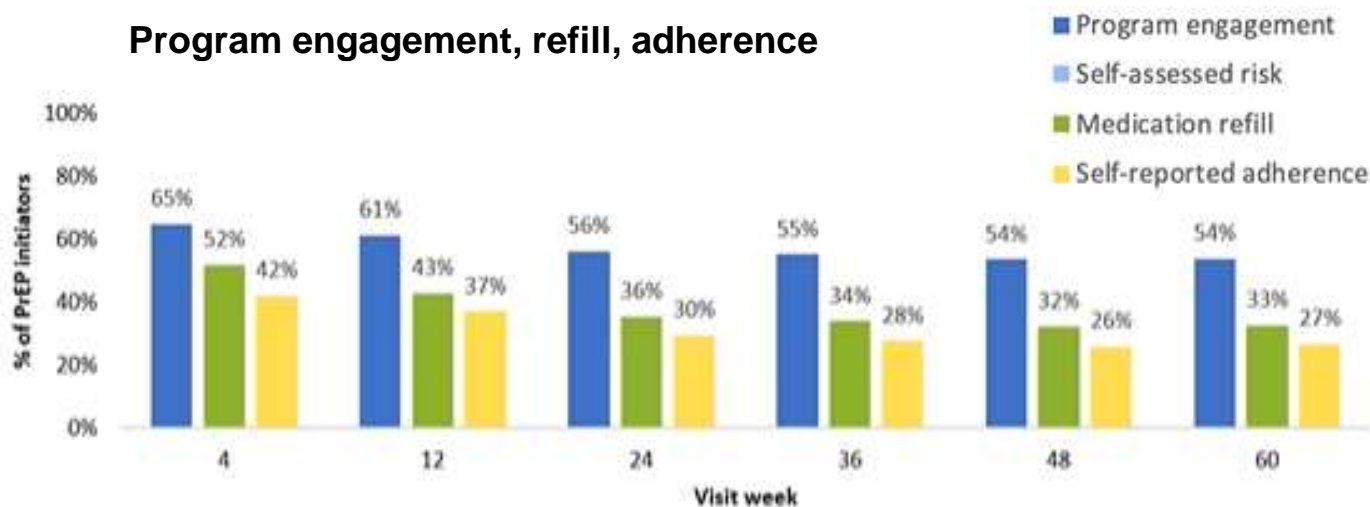
- While pt frequently stop PrEP many restart at a later date, and cycling use on and off common
- **Providers should anticipate episodic use** and messages should more clearly address stop and restart of PrEP and **facilitate rapid, easy re-entry particularly for younger pt with known risk factors**

Interim Results SEARCH: Population-Based PrEP Study in Rural Kenya/Uganda - Reduction HIV Incidence

Koss C et al. IAS Virtual July 2020 Abs. OAC0805



- SEARCH: 16 communities,
 - Universal access PrEP for persons at elevated HIV risk (serodifferent, risk score or self-identified);
 - Rapid or same-day start at health fairs or nearby clinics, ongoing basis 2016-2019;
 - Flexible delivery system with FU visit clinic, home, community
 - HIV antibody testing enrollment and 4, 12 and q12 weeks to week 144
- 74,541 ≥ 15 yr tested negative in 16 communities \rightarrow 15,632 (21%) assessed to be at elevated risk \rightarrow 5,447 (35%) started PrEP \rightarrow 4,260 (78%) had at least 1 HIV test



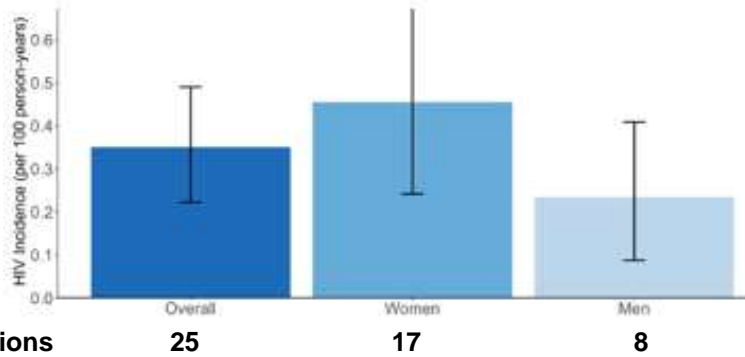
- \rightarrow At Week 4, 2/3 PrEP initiators seen
- \rightarrow By Week 24, 30% still on PrEP then stable
- \rightarrow 83% stopped PrEP at least once but half later restarted.
- \rightarrow **Of those reporting current HIV risk, at least 90% got PrEP refill and 70% reported adherence.**

Interim Results SEARCH: Population-Based PrEP Study in Rural Kenya/Uganda – Reduction HIV Incidence

Koss C et al. IAS Virtual July 2020 Abs. OAC0805



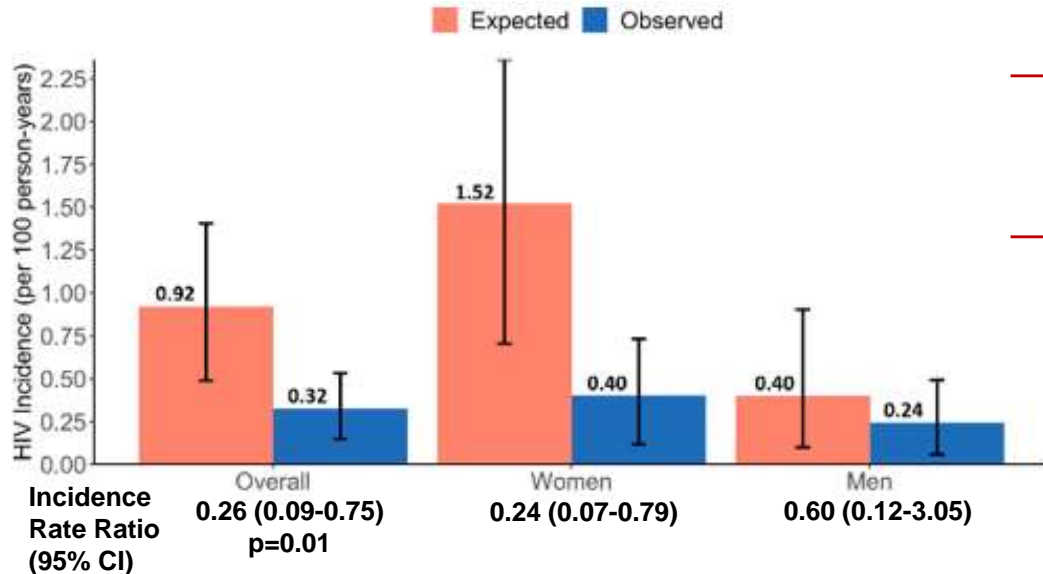
HIV Incidence Stratified by Sex



Seroconversions

Incidence Rate/
100 PY (95% CI)

Expected HIV Incidence Stratified by Sex



- 25 seroconversions, higher in women than men
- 18 (72%) reported PrEP non-adherence for >30 d before
- 7 reported taking at least 1 dose PrEP within 30 d: 4 reported intermittent adherence last 3 mos; 2 seroconverted at week 4 (acute infection enrollment?); 1 had virus with 2-drug class resistance (NNRTI, M184V)
- Estimated incidence in 8 communities with propensity score recent historical controls
- **74% reduction in incidence with PrEP compared to expected rate in matched recent controls**
 - 76% reduction in incidence among women
 - 40% reduction in incidence among men

Incorporating PrEP into SOC Prevention in Clinical Trial is Associated with Reduced HIV Incidence – ECHO Trial

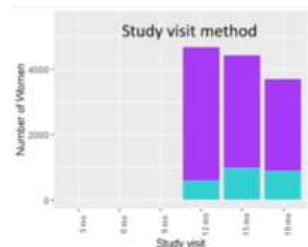
Donnell D et al. IAS Virtual July 2020 Abs.OAC0105

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

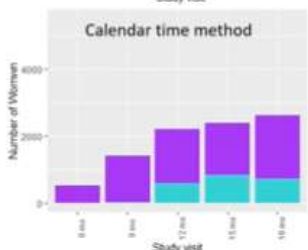
HIV Prevention Provided as Part of Study

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

Two approaches to limit confounding of PrEP access and calendar time:



- Study visit method:** include only study visits with *on-site* PrEP access



- Calendar time method:** include study visits within 6 mos before on-site PrEP access

Objective: Evaluate impact PrEP access on HIV incidence in S Africa sites by when on-site PrEP access began – comparing **overall** HIV incidence **BEFORE** and **AFTER** PrEP access in women on study at that time.

- Overall HIV incidence in ECHO women in South Africa was 4.5%
- 2,043 women had FU after PrEP access began; of these, 25% (543) initiated PrEP (had characteristics of higher HIV risk)

PrEP Access and HIV Incidence South Afric

		Infection/ Person Years	Incidence rate	IRR (95% CI)	p-value	Adjusted* IRR (95% CI)	p-value
Study visit method	Before PrEP access	133/2860	4.65%	0.45 (0.25, 0.81)	0.0076	0.45 (0.25, 0.82)	0.0085
	On-site PrEP access	12/556	2.16%				
Calendar time method	Before PrEP access	46/919	5.00%	0.45 (0.23, 0.86)	0.016	0.43 (0.22, 0.84)	0.014
	On-site PrEP access	11/481	2.29%				

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

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



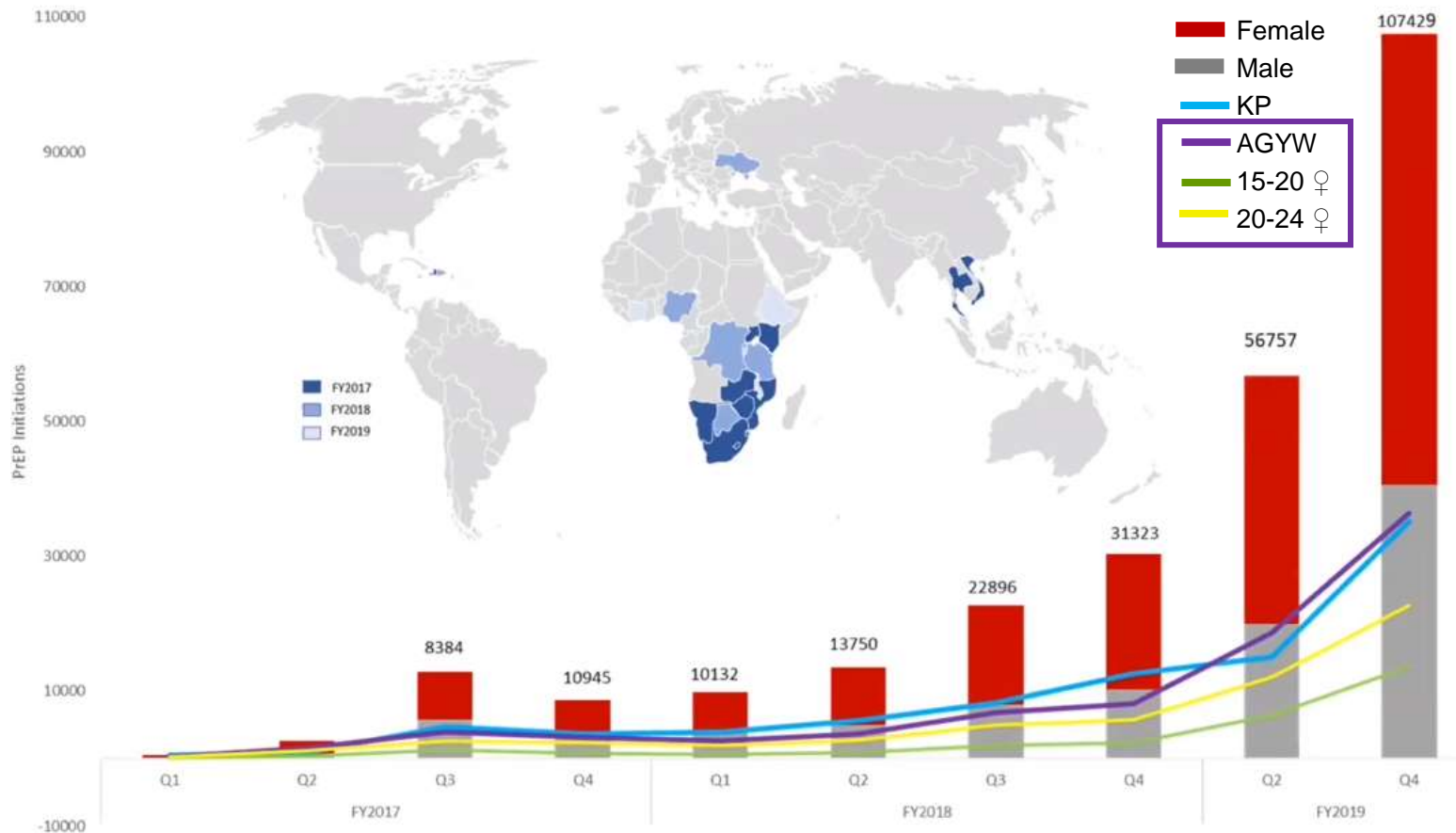
Uptake Of PrEP in Adolescent Girls/Young Women in PEPFAR-Supported Countries

Patel P et al. IAS Virtual July 2020 Abs. OAC0803



- PrEP is main DREAMS prevention component, implemented in 15 countries.

PrEP Uptake in 24 PEPFAR Countries, 2017-2019



- Of 168,000 PrEP initiations in women, 51% were in AGYW, with 2.5-fold ↑ from FY 2018 to 2019.
- Uptake in AGYW similar to that of key populations (30% each in 2019)
- Of AGYW, women 20-24 represent higher proportion of those starting PrEP than adolescent girls 15-19.
- Of 129,280 PrEP starts in AGYW, 99% were in DREAMS countries.
- Despite COVID, DREAMS countries have newly started 43,197 AGYW on PrEP in FY 2020.

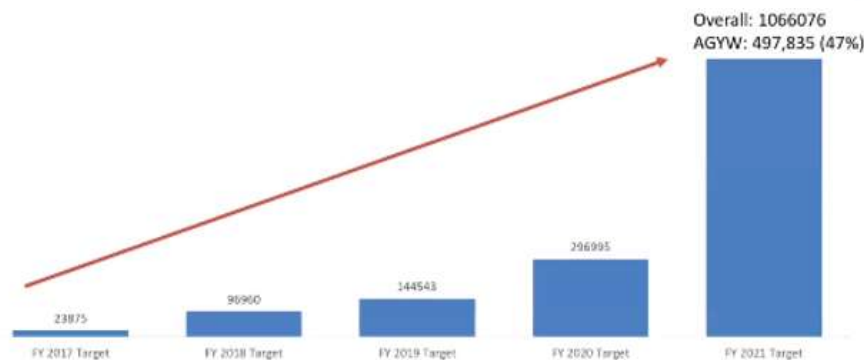
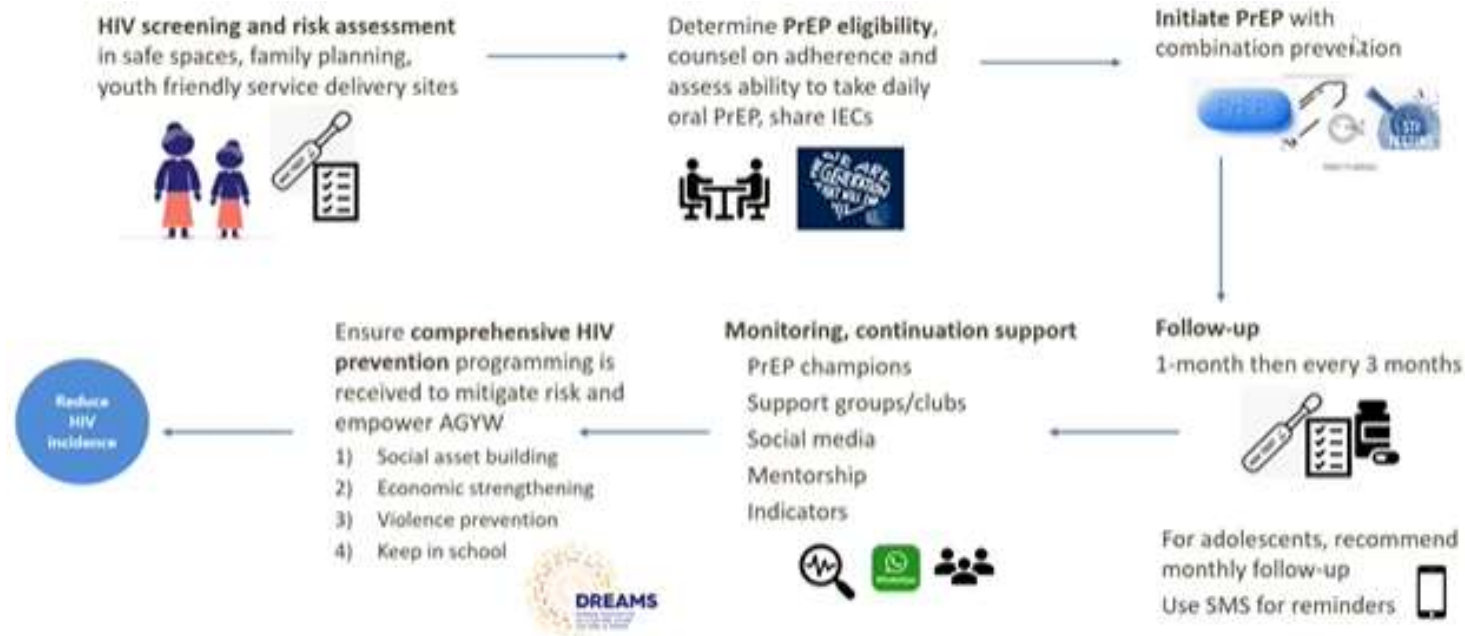


Uptake Of PrEP in Adolescent Girls/Young Women in PEPFAR-Supported Countries

Patel P et al. IAS Virtual July 2020 Abs. OAC0803



DREAMS PrEP Program



- PEPFAR plans substantial increase in PrEP targets in FY 2021, to starting >1 million persons on PrEP, 47% of whom are targeted to be AGYW

Tu'Washindi Intervention to Increase PrEP Use in AGYW at Risk of IPV

Pilot Study Results, Kenya

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

■ Nested in DREAMS in Kenya: 3 components over 6 months

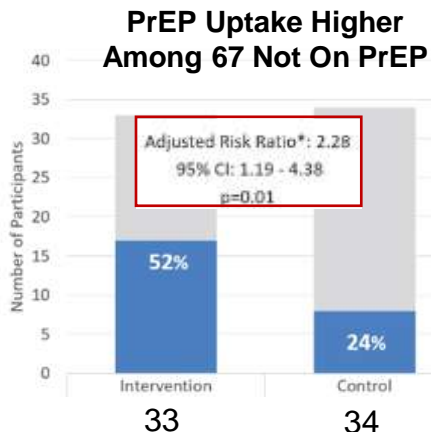
Pilot Cluster Randomized Trial



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

*Selected and pair-matched on geography (urban, rural, fishing), size, and % on PrEP

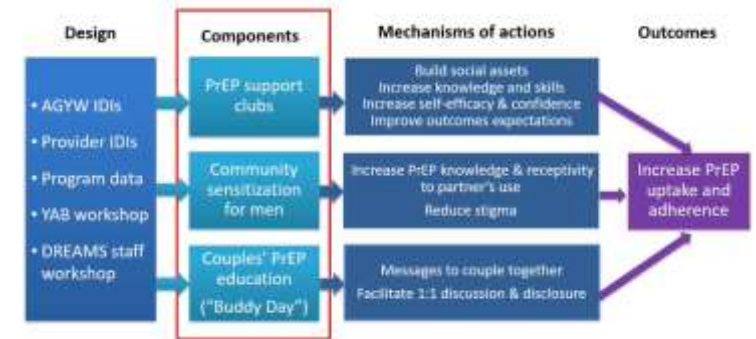
- 97% retention at exit, similar between arms
- Intervention:
 - 100% attended ≥ 1 support club
 - 90% attended Buddy Day, 80% with partners
 - 31% partner attend community sensitization



→ **PrEP uptake higher intervention**

→ But PrEP adherence poor, with only 3 pt having Wisepill opening on $>85\%$ d

→ However, #d with opening was better in intervention, 25% vs 13%, $p=0.02$



→ **IPV non-significantly lower in intervention**

g Any reportable IPV

Events per participant	Intervention N (%)	Control N (%)
0	38	41
1	9	6
2	1	3
3	0	2
Total events	11	18

Adjusted rate ratio*: **0.66**
95% CI: 0.27 - 1.62
 $p=0.37$

IPV resulting in physical injury

Events per participant	Intervention N (%)	Control N (%)
0	46	44
1	2	5
2	0	3
Total events	2	11

Adjusted rate ratio*: **0.20**
95% CI: 0.04 - 1.02
 $p=0.05$



Tu'Washindi is safe, feasible, and shows promise in promoting PrEP uptake and adherence among AGYW



Still unknown: Do these gains translate to increases in protective levels of PrEP adherence? Can the intervention reduce IPV risk?



Next steps: Acceptability and feasibility results forthcoming



Future plans: Evaluate intervention effects on IPV and biomarkers of PrEP use with fully-powered RCT

Oral PrEP and Family Planning Integration to Improve PrEP Continuation Among AGYW in Kenya

Were D et al. IAS Virtual July 2020 Abs. OAE0705



THE JILINDE PROJECT

- 5 year project to develop an effective model for scaling up oral PrEP in low resource settings
- Implemented in 10 out of 47 counties in Kenya
- PrEP provided to AGYW in one County (Migori) through:
 - 9 public health facilities
 - 2 private health facilities
 - 2 drop in centers (DICES)
 - 5 community safe spaces

- Demand creation for PrEP and FP was conducted by peer educators (PEs) and community health volunteers (CHVs) at the community
- PEs and CHVs refer AGYW who express interest to the diverse service delivery points for uptake and follow-up monitoring
- PrEP and FP services are integrated and offered concomitantly by the same provider
- Follow-up visits are synchronized



- May 2017-Mar 2020, 3,238 AGYW started PrEP
- 46.6% returned at 1 mo
- 13.8% returned at 3 mos

Factors Associated with PrEP Discontinuation at 1 Month

Variable	Category	Discontinued at Month 1 (n=1732/3238; 53.4%)	O.R. (95% C.I.)	Sig.
Age	15-19 Years	766/1433 (53.5%)	1.00(0.87-1.15)	0.971
	20-24 Years	966/1805 (53.5%)	Ref.	
Marital Status	Single/Never Married	1174/2233 (52.6%)	0.89(0.76-1.03)	0.120
	Married/ Ever Married	558/1005 (55.5%)	Ref.	
Entry Channel	Peer Networks	697/1492 (46.7%)	0.60(0.52-0.69)	<0.001
	Non-Peer	1035/1746 (59.3%)	Ref.	
Facility Type	DICE and Private	242/849 (28.5%)	0.24(0.20-0.29)	<0.001
	Public and safe spaces	1490/2389 (62.4%)	Ref.	
On Family Planning	No	1172/2135 (54.9%)	1.18(1.02-1.37)	0.026
	Yes	560/1103(50.8%)	Ref.	
HIV positive partner	No	1707/3202(53.3%)	0.50(0.25-1.02)	0.058
	Yes	25/36 (69.4%)	Ref.	

Less likely
dc

More likely
dc

Factors Associated with PrEP Discontinuation at 3 Months

Variable	Category	Discontinued at Month 3 (n=2496/2900; 86.2%)	O.R. (95% C.I.)	Sig.
Age	15-19 Years	1119/1306 (85.7%)	0.93(0.75-1.15)	0.488
	20-24 Years	1380/1594 (86.6%)	Ref.	
Marital Status	Single/Never Married	1672/1980 (84.4%)	0.61(0.48-0.78)	<0.001
	Married/ Ever Married	827/920 (89.9%)	Ref.	
Entry Channel	Peer Networks	1180/1401 (84.2%)	0.73(0.59-0.90)	0.003
	Non-Peer	1319/1499 (88.0%)	Ref.	
Facility Type	DICE and Private	467/746 (62.6%)	0.10(0.08-0.13)	<0.001
	Public and Safe spaces	2029/2154 (94.3%)	Ref.	
On Family Planning	No	1705/1950 (87.4%)	1.37(1.10-1.70)	0.005
	Yes	794/950 (83.6%)	Ref.	
HIV positive partner	No	2469/2865 (86.2%)	1.04(0.40-2.69)	0.937
	Yes	30/35 (85.7%)	Ref.	

Less likely
dc

More likely
dc

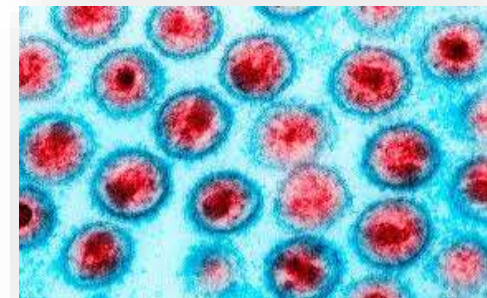
- PrEP continuation rates were low but AGYW who concurrently started PrEP and FP were more likely to continue than those starting PrEP alone, and those entering through peer network or at drop-in or private facility were more likely to continue.



High-Risk Pregnant Women Initiate and Persist on PrEP, Cape Town

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

- Cohort of 374 HIV-negative pregnant and postpartum women recruited at 1st ANC visit in primary care clinic in community with high HIV prevalence, Aug 2019-Mar 2020 (median age 25 yr, median GA 21 wk).
- **92%** (344) opted to start PrEP at 1st ANC visit
- **Retention:** 71% at 1 mo, 59% at 3 mo
- **Persistence:** Of those who returned, % reported taking PrEP >5 d in past week: 89% 1 mo, 85% 3 mo
- **Early PrEP retention and persistence associated with:**
 - Older age (>25 yr)
 - STI + at baseline
 - >1 sex partner
 - Sex partner HIV status unknown
 - Alcohol use before/during pregnancy
 - More frequent sex acts



The Future: New PrEP Options



IAS results!

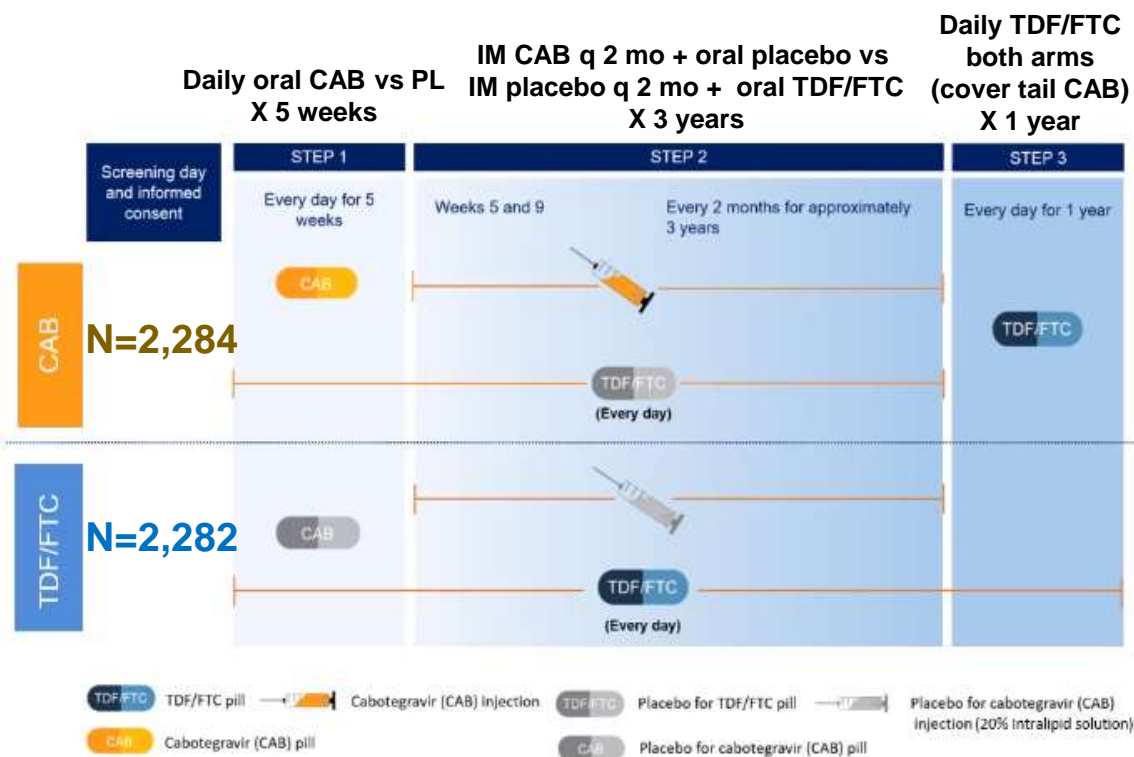


Results anticipated 2021

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

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

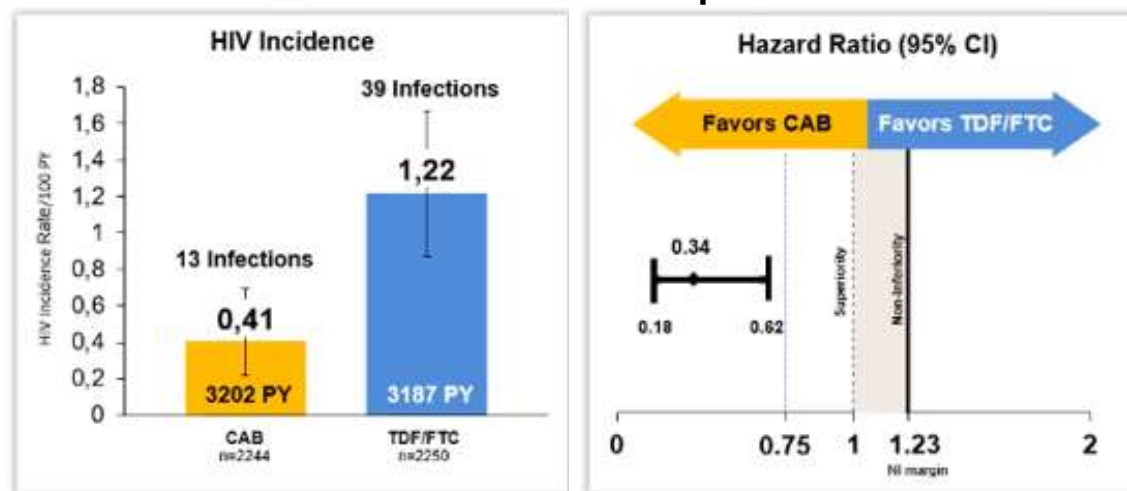
- Phase 3 study comparing IM CAB LA with oral TDF/FTC for HIV prevention in MSM/TGW >18 yrs at risk for HIV



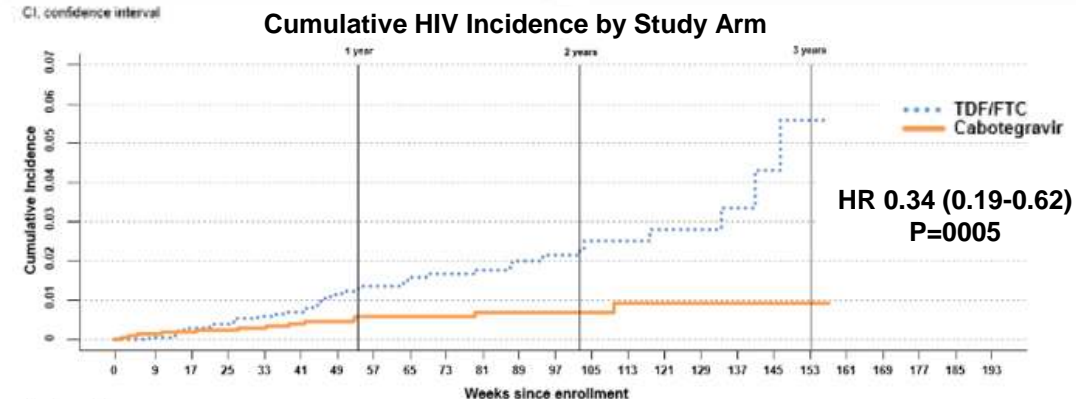
52 HIV infections in 6,389 PY FU

(median per-pt FU 1.4 yr)

Pooled HIV incidence 0.81 per 10 PY



**66% Better Efficacy for Prevention
Compared to TDF/FTC PrEP!**





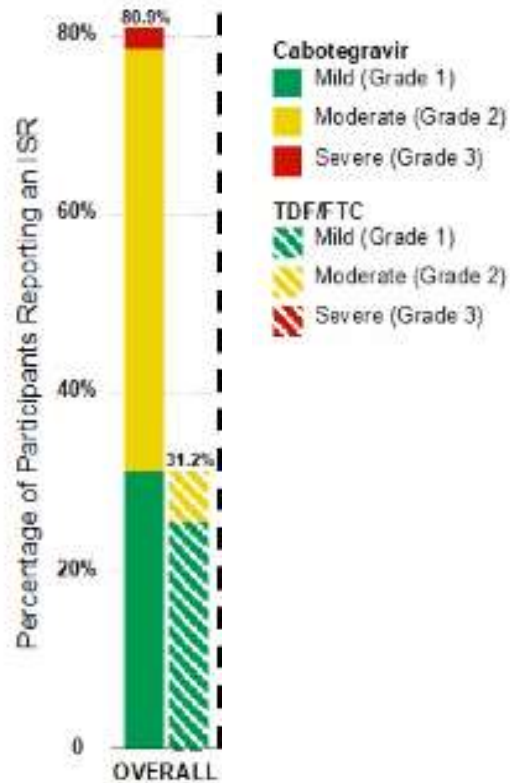
PrEP with Long-Acting Injectable Cabotegravir (CAB LA) Safe and More Effective than Oral TDF/FTC in MSM/TGW

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

- Of the 13 incident CAB LA infections:
 - 2 were infected prior to drug administration
 - 5 were infected after a prolonged hiatus from CAB
 - 3 occurred during the oral lead-in phase
 - Only 5 occurred despite continuous on-time CAB injections
- Of the 39 incident TDF/FTC infections:
 - 3 were infected prior to drug administration
 - 3 had intermittent visit adherence
 - The remainder occurred during TDF/FTC (random sampling TFV levels found >75% had levels consistent with at least 4 doses/wk, still to examine those who became infected)

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

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



- 81% of CAB (vs 31% placebo IM) had injection reactions, most **mild** or **moderate**; 47 (2.2%) of CAB participants permanently discontinued CAB due to injection-related AE, with severity of AE strongly associated.
- ↓ CrCl more frequent in TDF/FTC than CAB (72 vs 69%), while ↑ glucose more frequent with CAB than TDF/FTC (9 vs 5%), as was pyrexia (5 vs 3%), usually within 7 d of injection.
- **Weight gain was higher in CAB** (+1.3 kg/yr) than TDF/FTC (+0.31 kg/yr) ($p < 0.001$), although most of this difference was during first year.

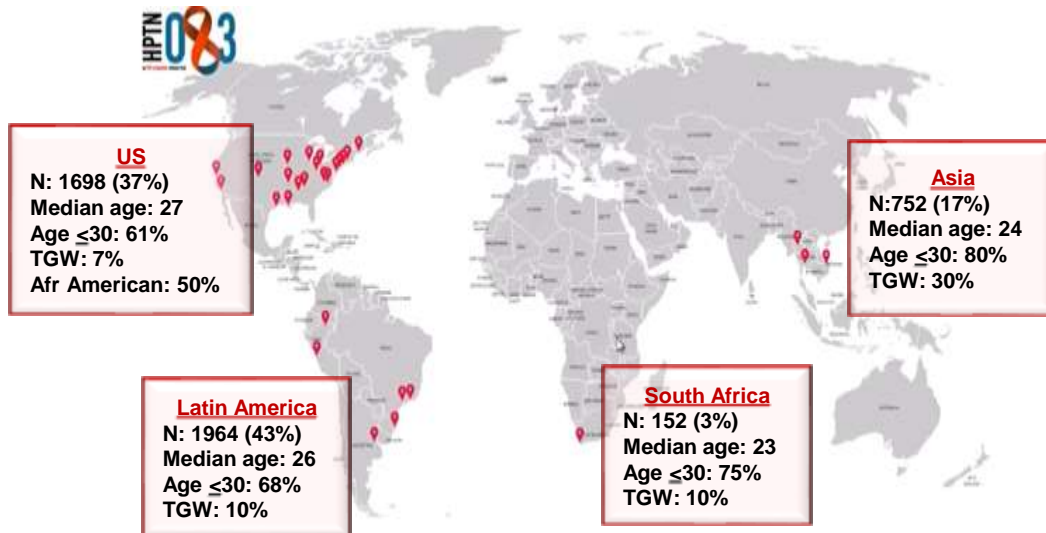
Efficacy of CAB LA PrEP Maintained Across Regions and Subpopulations



Grinsztejn B et al. IAS Virtual July 2020 Abs. OACLB0101

- HPTN 83 enrolled in 43 sites across 4 regions

Africa: S Africa
Asia: Thailand, Vietnam
Latin America: Argentina, Brazil, Peru
US

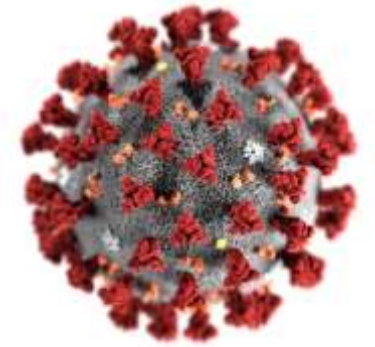
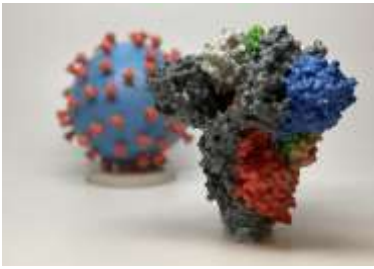


- Enrolled MSM/TGW across all regions were young and in US, high % African American

OVERALL
N: 4566
Median age: 26
Age ≤30: 67%
TGW: 12%

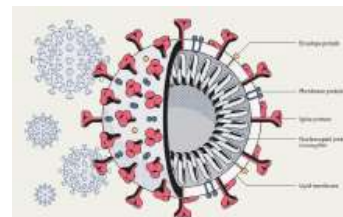
- Effect of IM CAB LA compared to oral TDF/FTC maintained across populations by age, cohort, race and region

Subgroup	CAB Events/PY (IR%)	TDF/FTC Events/PY (IR%)	HR (95%CI)	Hazard ratios (95%CI)
Age				
≤30	11/2185 (0.50)	33/2114 (1.56)	0.32 (0.16, 0.63)	
>30	2/1016 (0.20)	6/1071 (0.56)	0.33(0.07, 1.61)	
Cohort				
TGW	2/368 (0.54)	7/383 (1.83)	0.29 (0.06, 1.41)	
MSM	11/2829 (0.39)	32/2800 (1.14)	0.34 (0.17, 0.67)	
Race				
Black/African-American	4/686 (0.58)	15/711 (2.11)	0.28 (0.10, 0.83)	
Non-Black/African-American	0/837 (0.00)	5/790 (0.63)	0.09 (0.00, 2.06)	
Region				
US	4/1523 (0.26)	20/1501 (1.33)	0.19 (0.07, 0.56)	
Latin America	6/1016 (0.59)	11/1007 (1.09)	0.54 (0.20, 1.46)	
Asia	2/569 (0.35)	6/580 (1.03)	0.34 (0.07, 1.66)	
Africa	1/92 (1.08)	2/96 (2.08)	0.52 (0.05, 5.77)	



IAS COVID-19

Selected Abstracts Relevant
to Children and Women





HIV, TB and COVID-19 in Adults, South Africa

Davies MA et al. IAS Virtual July 2020 Abs OAXLB0106



- Used Western Cape routine public sector data (unique ID) in 3.4 million adults >20 yrs (unique ID) to look at risk factors for COVID-19 death in 625 of 22,308 adults with confirmed COVID-19 who died; 11/625 (18%) HIV+.



Provincial Health Data Center
3.5 million pt records

→ How much more likely to are you to die from COVID-19 if you have vs don't have a risk factor?

Adjusted HR for dying from COVID-19 (all active public sector patients); n=3.5m

	Adjusted HR	95% CI	
Sex			Sex
female	Ref		female
male	1.45	1.23; 1.70	male
Age			Age
20-39 years	Ref		age 20-39
40-49 years	2.83	1.92; 4.15	age 40-49
50-59 years	7.78	5.51; 10.98	age 50-59
60-69 years	11.54	8.11; 16.42	age 60-69
≥70 years	16.79	11.69; 24.11	age ≥70
Diabetes			Diabetes
none	Ref		no comorbidities
diabetes HbA1c <7%	5.37	3.96; 7.27	diabetes HbA1c <7%
diabetes HbA1c 7 - 8.9%	8.53	6.60; 11.02	diabetes HbA1c 7-8.9%
diabetes HbA1c ≥9%	12.07	9.70; 15.02	diabetes HbA1c ≥9%
diabetes no HbA1c measurement	2.91	2.18; 3.89	diabetes no HbA1c
Other non-communicable diseases			Other non-communicable disease
hypertension	1.31	1.09; 1.57	hypertension
chronic kidney disease	1.86	1.49; 2.33	chronic kidney disease
chronic pulmonary disease / asthma	0.93	0.73; 1.17	chronic pulmonary disease/asthma
Tuberculosis			Tuberculosis
never tuberculosis	Ref		previous tuberculosis
previous tuberculosis	1.51	1.18; 1.93	current tuberculosis
current tuberculosis	2.70	1.81; 4.04	HIV
HIV			HIV positive
negative	Ref		
positive	2.14	1.70; 2.70	

No real difference in risk by viral suppression (e.g., <1000 or >1000)

	Adjusted HR	95% CI
HIV negative	Ref	
HIV "well" VL <1000 copies/ml (last 15 mo) & recent ART	2.61	1.98; 3.43
HIV "probably well" VL <1000 copies/ml (2yr to 15 mo ago) OR recent ART & VL <1000 copies/ml >2yr ago	1.76	0.96; 3.24
HIV "not well" VL ≥ 1000 copies/ml or CD4 <200 cells/μl	3.35	1.83; 6.12
Unknown viraemia, ART & CD4	1.33	0.85; 2.07



HIV, TB and COVID-19 in Adults, South Africa

Davies MA et al. IAS Virtual July 2020 Abs OAXLB0106

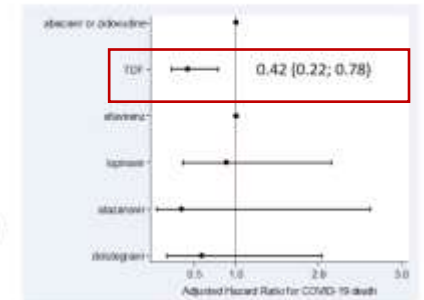


- Preliminary analysis on type of ARV suggests TDF-based ART may be associated with lower risk mortality but confounded by fact TLE (now TLD) is standard ART for all and only 2nd line receives non-TDF and may have other risks.
- Older age and comorbidities increased risk of COVID-19 death – particularly uncontrolled diabetes, hypertension and renal disease.
- Modest ~2 times ↑ risk of COVID 19 death associated with HIV and TB; may be over-estimate if residual confounding (e.g., overweight, SES).
- Effect HIV or TB smaller than effect of other comorbidities; those with HIV and TB tend to be younger, where overall risk of COVID-19 death is lower.
- Overall, <10% of COVID-19 deaths are due to HIV.

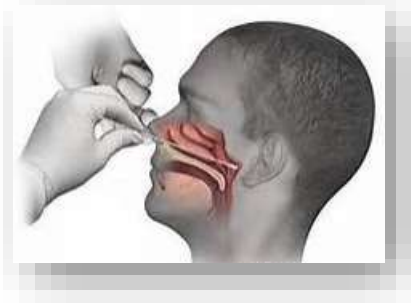
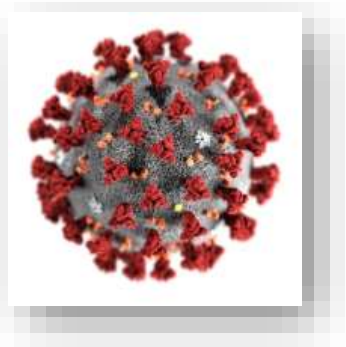
Effect of different ARVs on COVID-19 death among cases with HIV on ART

Until January 2020

- First-line: TDF + XTC + EFV unless renal failure
- Second-line: ZDV + XTC + LPV
- DTG introduced from January 2020



*Adjusted for all variables in the previous table as well as urban/rural location & subdistrict within Cape Town Metro



Effects of COVID-19-Related Mitigation Practices on Programs





- STAR project evaluating oral-self-testing scale-up in 2019 in community and facilities.
- National lockdown due to COVID-19 March 28; non-essential business closed; only pharmacies, health care facilities and food stores open.
- Community HTS paused but MOH recommended community distribution of HIV self-test kits in community by HTS counselors using only pharmacies and shops as channels for distribution.

Distribution in front of pharmacies; grocery stores



MODALITY:

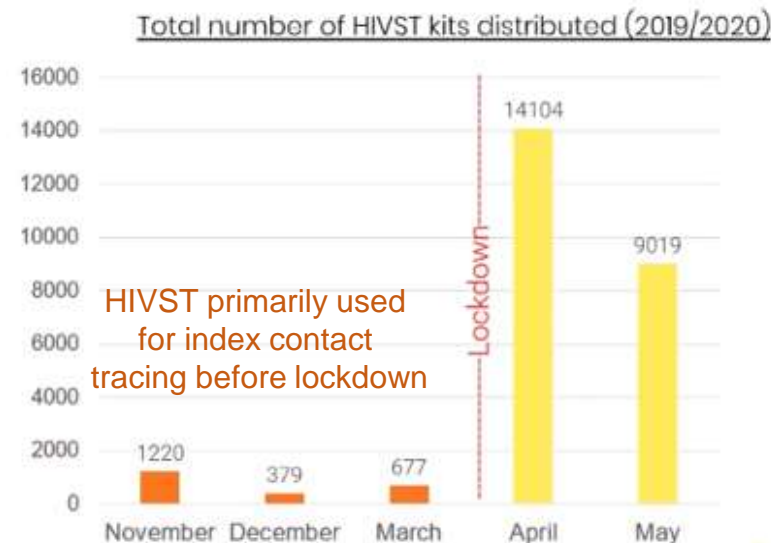
Primary & secondary distribution at pharmacies and food shops

- Eligibility screening and risk assessment is conducted
- Consent for follow up
- Phone call for follow up support, including linkage to prevention and HIV treatment

HIV-Self Testing During the COVID Pandemic, Eswatini

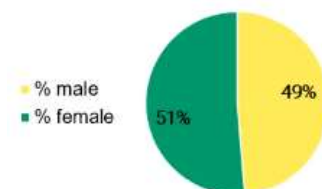
Dekova R et al. IAS Virtual July 2020 Abs. OAXLB0103

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



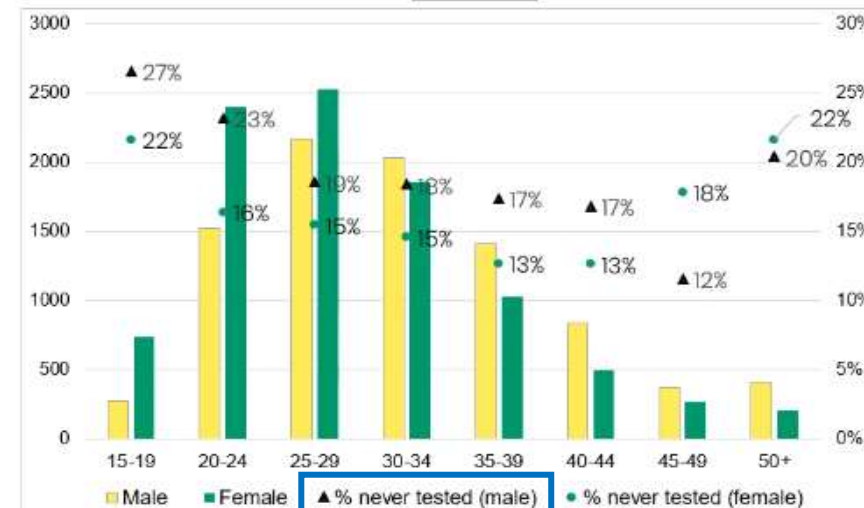
April-May 2020

Primary HIVST distribution by sex (n=18,564)

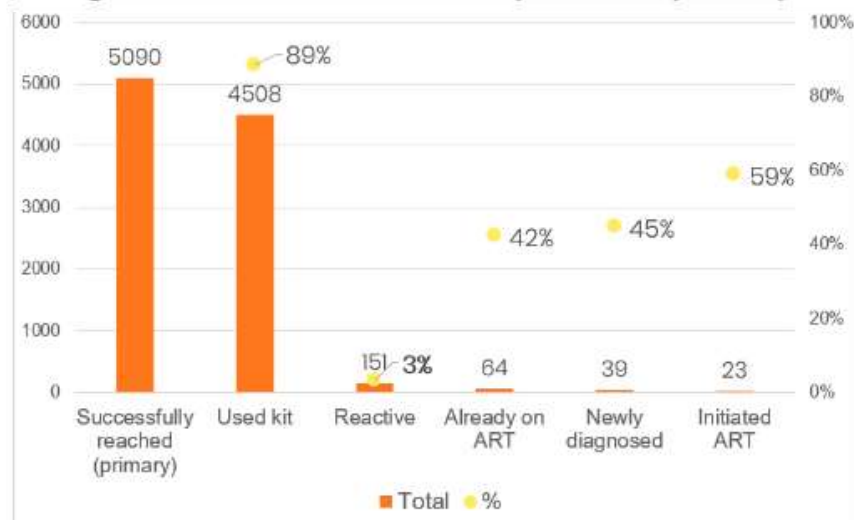


- 49% were males
- 17% all reached had **never tested** for HIV in past, highest among males.

Primary HIVST distribution by age, sex and testing frequency (n=18,564)



Linkage to care cascade: follow-up calls in April, May 2020



→ Follow-up calls after test distribution April-May 2020

- 89% used the test kit
- 3% (151) were HIV+
- Of the 151 HIV+, 45% were new diagnoses, 59% started on ART as of May

Concluded

- HIVST playing important role in normalizing testing, decreasing stigma and creating demand.
- Enabled reaching clients that wouldn't normally be accessed through standard targeted testing.

PEPFAR Countries Adapting Increase in Multi-Month Dispensing (MMD) of ART During COVID-19 Pandemic

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

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

Proportions of MMD Category by Patient Type as of December 2019
(Figure 1)



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

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

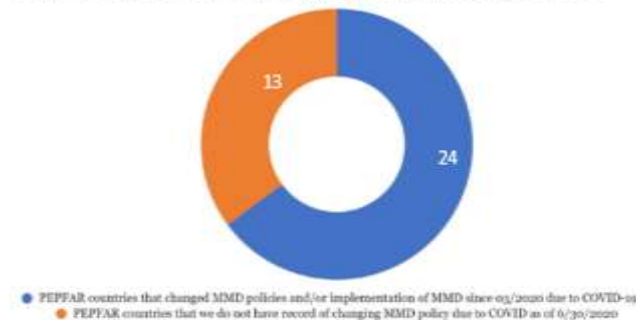
Number of Countries Permitted ≥ 3 Mo MMD by Patient Group Before and After COVID-19

	Before	After
TB	3	14
Pregnant women	7	14
Breastfeeding women	11	18
Children <10	10	23
Adolescents 10-19	14	26

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

→ Significant expansion MMD in the during COVID-19 pandemic

PEPFAR Countries Changing MMD Policy or Implementation due to COVID-19



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

→ Recommend maintaining the expanded MMD after COVID-19 for benefit of both patients and health system efficiency



Drop in PrEP Retention and Persistence During COVID-19 Lockdown

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

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

Table. Retention in PrEP in pregnancy study before COVID-19 lockdown and during lockdown, Cape Town, South Africa (n=414 women on PrEP)

	1m visit			3m visit		
	Attended	Missed	% retained	Attended	Missed	% retained
Pre COVID lockdown (Aug-Mar 27, 2020)	207	84	71%	113	80	59%
During lockdown (Mar 28-Jun 1)	19	32	37%	51	62	45%
Total retention						
	Attended	Missed	% retained			
Pre-COVID lockdown	340	201	63%			
During lockdown	110	152	42%			

→ **33% decrease in retention and study refills after lockdown; 2.4-fold ↑ odds missing study visit during lockdown**

Implications and Next Steps

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

- Commonly cited barriers to study attendance included (during telephonic interviews):
 - ✓ Fear of COVID infection (for self/infant),
 - ✓ Fear of police,
 - ✓ Limited transportation or funds for transport and
 - ✓ Long queuing at facility

Bold p<0.05

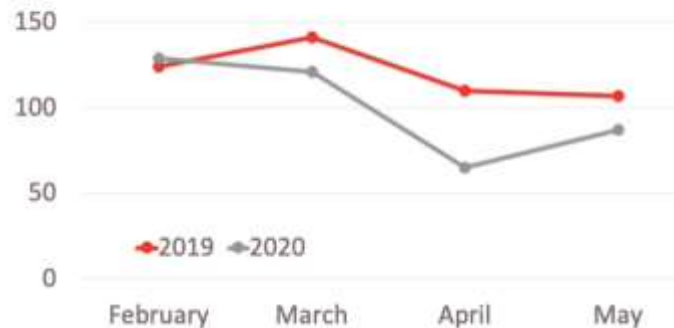
Declining Trends in Maternal and Child Health Service Use During COVID-19 in Guatemala



Endyke-Doran C et al. COVID-19 IAS Virtual July 12019 Track x

- Management Science for Health project start 2019 to promote group ANC for Mayan women in Quetzaltenango, Guatemala; with COVID-19 restrictions no longer able to bring together groups but encourage to continue prenatal care
- With MOH, evaluated key maternal and child service use data Feb-May 2020 and 2019

Number of women receiving postpartum care visits



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

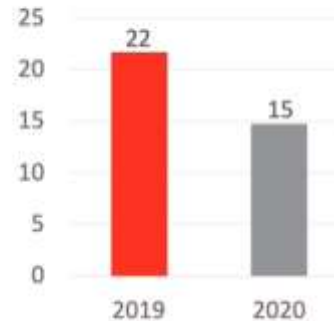
Review of health statistics

Are COVID-19 restrictions resulting in decreases in essential antenatal (ANC) services?

Participating stakeholders:	<ul style="list-style-type: none">Department of health of Quetzaltenango (DASQ)MSH Quetzaltenango
Key maternal and child service data analyzed:	<ul style="list-style-type: none">First ANC visitPostpartum careVaccination coverage
Time period analyzed:	<ul style="list-style-type: none">February-May 2019February-May 2020
Number of health facilities:	10

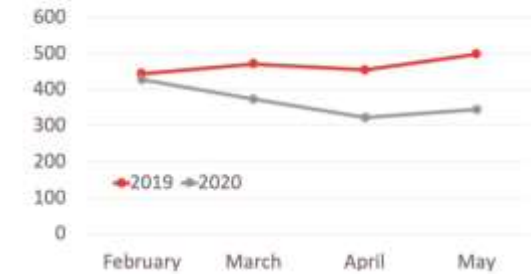
DPT3 percent coverage to date

January – May 2019 vs. 2020



- 7% drop in children receiving 3rd DPT booster in 2020 vs 2019 in 10 health facilities

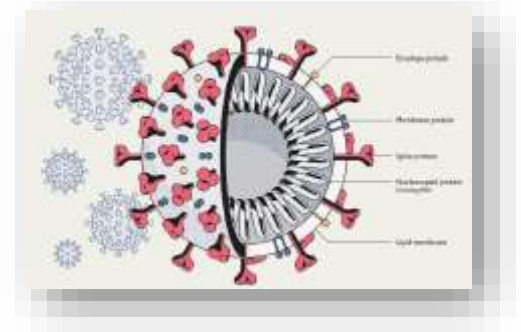
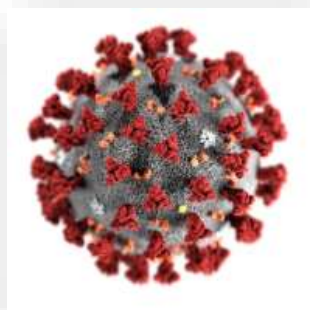
Number of women receiving their first ANC visit



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

Next steps

- Identify mitigating strategies to maintain essential maternal and child health services to save lives
- Maximize safety for health care workers and clients
- Risk communication and community engagement to dispel fears
- Improve data access and quality for use and decision making.



COVID-19 Treatment – Pregnant Women and Children



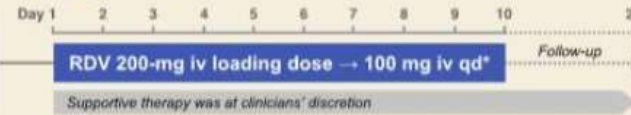


Remdesivir Compassionate Use in 86 Pregnant and Postpartum Women with Severe COVID 19

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

RDV Compassionate-Use Program

Hospitalized pregnant women with severe COVID-19 (rtPCR confirmed) and:
• SpO₂ ≤94% while breathing room air
or
• Need for O₂ support

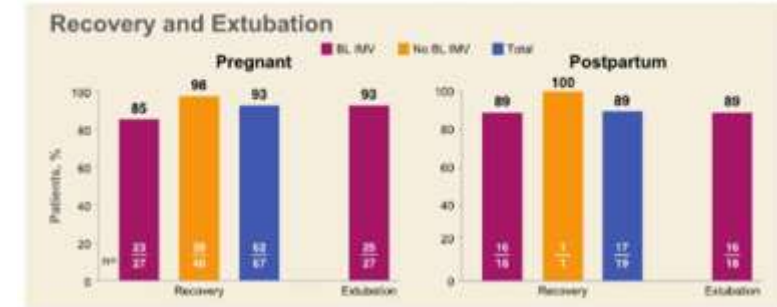


*Recommended dosing; not all patients received 10 d of treatment. rtPCR, reverse transcriptase–polymerase chain reaction; SpO₂, peripheral oxygen saturation.

Baseline Demographic and Clinical Characteristics*

	Pregnant: n=87	Postpartum: n=19	All: N=86
Age, y	33 (21–43)	34 (20–41)	33 (20–43)
<35 y	40 (60)	11 (58)	51 (60)
Gestational age, wk	28 (14, 39)	30 (27, 36)	29 (14, 39)
Gestational age category, wk			
<24	12 (18)	0	12 (14)
24–32	44 (66)	13 (72)	57 (67)
>32	11 (16)	5 (28)	16 (19)
Duration of hospitalization, d	3 (2, 5)	3 (2, 6)	3 (2, 5)
Invasive	27 (40)	18 (95)	45 (52)
IMV	27 (40)	17 (90)	44 (51)
ECMO	0	1 (5)	1 (1)
O ₂ -support category			
Noninvasive	40 (60)	1 (5)	41 (48)
NIPPV	2 (3)	0	2 (2)
High-flow O ₂	10 (15)	1 (5)	11 (13)
Low-flow O ₂	25 (37)	0	25 (29)
Room air	3 (4)	0	3 (3)
ICU setting	44 (67)	19 (100)	63 (74)
Duration of symptoms before RDV, d	9 (7, 11)	9 (6, 11)	9 (2, 26)
Any medical condition history	45 (67)	10 (53)	55 (64)
Obesity*	11 (16)	4 (21)	14 (16)
Asthma	9 (13)	1 (5)	10 (12)
Gestational diabetes	7 (10)	2 (11)	9 (10)
Chronic hypertension	6 (9)	1 (5)	7 (8)
Diabetes mellitus†	7 (10)	—	7 (8)
Hypothyroidism	4 (6)	2 (11)	6 (7)
Preeclampsia	0	0	0
Laboratory values			
ALT, U/L	24 (15, 36)	34 (18, 43)	26 (15, 39)
AST, U/L	30 (24, 48)	42 (31, 67)	32 (25, 56)

28-Day Clinical Recovery Was High Among Both Pregnant and Postpartum Women



- 93% of pregnant women and 89% of PP women recovered
- Highest rate improvement in pregnant women **not needing mechanical ventilation** vs women **needing mechanical ventilation**

♦ Deliveries were early (67% at <32-wk gestational age), and mostly by CD (82%) and emergent CD (86%) due to the severity of COVID-19 illness

♦ No new safety signals were identified; the most common AEs were due to underlying disease and most laboratory abnormalities were Grades 1–2

– There was 1 maternal death unrelated to RDV (ARDS, cytokine storm) and 1 17-wk miscarriage (methicillin-sensitive *Staphylococcus aureus* endocarditis/sepsis, including septic joint)

- 86 women, 67 (78%) pregnant, 19 postpartum
- More postpartum women needed invasive support
- 64% had ≥1 comorbidity



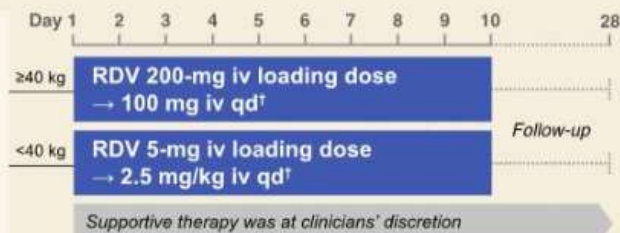
Remdesivir Compassionate Use in 77 Children with Severe COVID 19

Chiltos K et al. COVID-19 IAS Virtual July 2019 Track B

RDV Compassionate-Use Program

Hospitalized children (aged <18 y) with severe COVID-19 (rtPCR confirmed) including:

- SpO₂ ≤94% while breathing ambient air
- or
- Need for O₂ support*



*Severity determined by treating physician, with input from Gilead medical monitors; some children without need for O₂ support were approved for RDV if they had severe extrapulmonary manifestations or high-risk comorbidities. [†]Recommended dosing and duration; not all patients received 10 d of treatment. rtPCR, reverse transcriptase-polymerase chain reaction assay; SpO₂, peripheral oxygen saturation.

Baseline Demographics and Clinical Characteristics

	Invasive O ₂ n=39	No Invasive O ₂ n=38	Total n=77
Median age, y (range)	11 (0–17)	15 (0–17)	14 (0–17)
Age, n (%)			
<2 mo	4 (10)	0	4 (5)
2 mo–<1 y	5 (13)	3 (8)	8 (10)
1–<5 y	3 (8)	1 (3)	4 (5)
5–12 y	11 (28)	9 (24)	20 (26)
>12 y	16 (41)	25 (66)	41 (53)
Gender, n (%)			
Male	23 (59)	23 (61)	46 (60)
Female	16 (41)	15 (39)	31 (40)
Median duration of symptoms, d (Q1, Q3)	7 (5, 8)	9 (7, 12)	8 (6, 10)
Median duration of hospitalization, d (Q1, Q3)	4 (3, 5)	4 (2, 7)	4 (3, 5)
Median duration of invasive O ₂ support, d (Q1, Q3)	2 (2, 3)	0	2 (2, 3)
ALT ≤50 U/L, n (%)	25 (66)	31 (84)	56 (75)
Median ALT, U/L (Q1, Q3)	33 (21, 69)	31 (20, 44)	32 (20, 51)
Any reported medical history	29 (74)	32 (84)	61 (79)

- 77 children, 51% requiring ventilation
- Primarily older children (53% >12 yr)
- 79% had existing medical condition, most common neurologic/genetic, obesity 13%

Recovery by Age



- Clinical recovery in 80% children on ventilators/ECMO and 87% not on invasive oxygen support
- Recovery similar all age groups (may be better >12 years but more children with COVID-19 were >12 years to begin with)

Safety

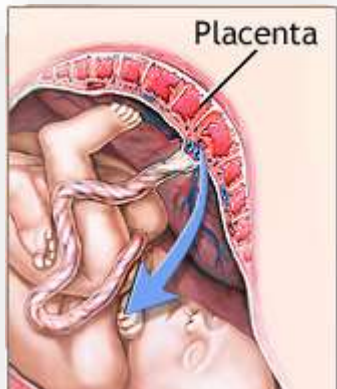
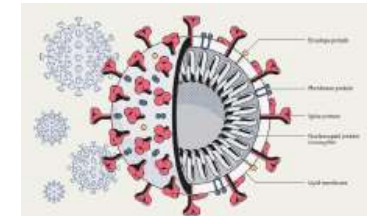
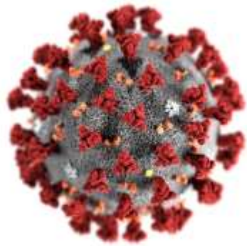
	Patients, n (%)	Invasive O ₂ n=39	No Invasive O ₂ n=38	Total n=77
Adverse Events*	Any AE	15 (38)	10 (26)	25 (32)
	Any serious AE	8 (21)	4 (11)	12 (16)
	Death	2 (5) [†]	2 (5)	4 (5) [†]
	AE occurring in >1 patient			
Laboratory Abnormalities	Anemia	2 (5)	0	2 (3)
	Any Grade	30 (77)	31 (82)	61 (79)
	ALT increased	14 (36)	23 (61)	37 (48)
	AST increased	23 (64)	18 (47)	41 (55)
	Creatinine increased	15 (38)	15 (39)	30 (39)
	Grade 3–4 (>5x ULN)	15 (38)	11 (29)	26 (34)
	ALT increased	5 (13)	5 (13)	10 (13)
	AST increased	11 (28)	4 (11)	15 (19)
	Creatinine increased	8 (21)	6 (16)	14 (18)

*AEs were reported by clinician; [†]1 death occurred at Day 33. [‡]Cases of death were reported as COVID-19 for 2 patients, brain herniation, and multi-organ failure in context of COVID-19 + nonfatal events. ALT, aspartate aminotransferase.

- 4 deaths (5%) (reported as due to COVID in 2, multiorgan failure 1, brain herniation 1)
- No new safety concerns
- Mild transaminase elevations, most Grade 1 or 2, rarely required drug dc



Issues Related to Potential SARS-CoV-2 Mother-to-Child Transmission



SARS-CoV-2 in Blood and Secretions of Pregnant Women with COVID-19

Di Giminiani et al. COVID-19 IAS Virtual July 2019 Track C

- Prospective study of women with confirmed COVID-19 admitted to Milan hospital; assessed presence of SARS-CoV-2 in blood, vaginal and rectum.

Characteristic	Number
Positive NP swab	62
Non-pregnant women	6
Pregnant	56
1 st trimester	4
2 nd trimester	6
3 rd trimester	46
Mode delivery (45 delivered)	Vaginal 31, CS 14

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

Type specimen	SARS-CoV-2 PCR Positive
Plasma (n=53)	2/53 (4%) – both 3 rd T pregnant 1 critical (vent), 1 severe (sub-ICU)
Vagina (n=60)	0/60
Rectum (n=44)	11/44 (25%) 45% with positive rectal swab had GI sx during hospitalization
Newborn NP swab (n=45)	0/45

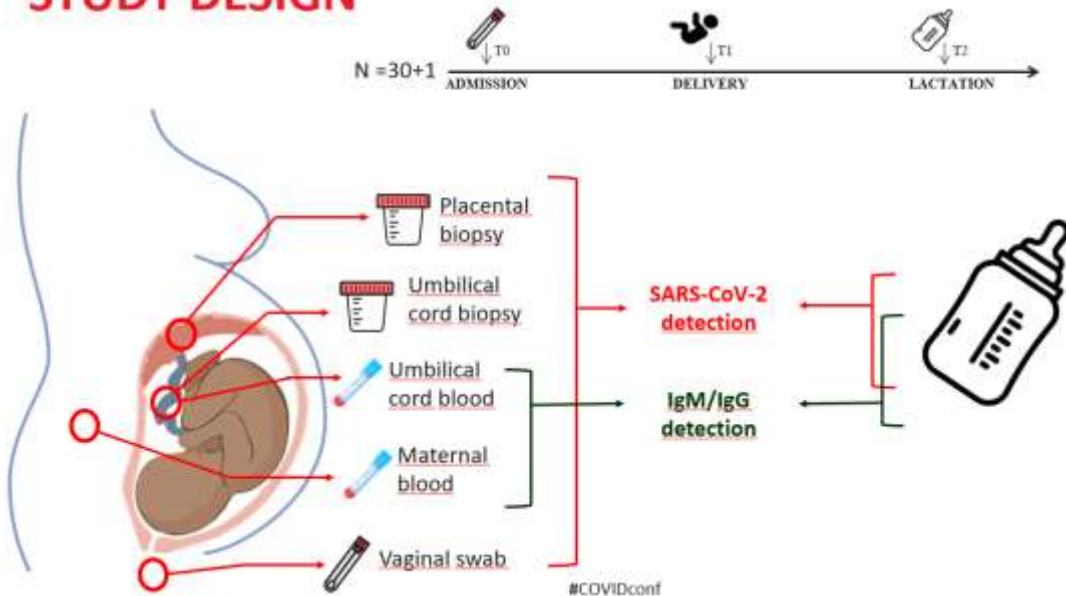
- Viremia rare and only in severely ill women
- No virus in vaginal secretions but 25% in rectal sample
- No evidence infant infection

Possible Mother-to-Child SARS-CoV-2 Transmission, Italy

Fenizia C et al. COVID IAS Virtual July 2020 Track A

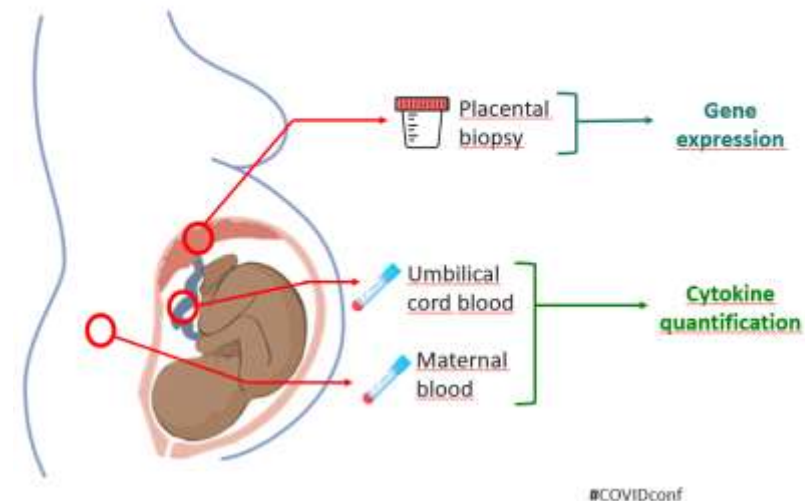
- 31 pregnant women with COVID-19 third trimester evaluated for possible MTCT
 - 14/31 positive CXR, 4 severe disease
 - 25 (81%) vaginal delivery (6 induced due to COVID), 6 cesarean (3 for severe maternal COVID)
 - 1 PTD; 1 low Apgar scores, 2 NICU admission

STUDY DESIGN



STUDY DESIGN – INFLAMMATORY PROFILE

3 selected cases



Possible Mother-to-Child SARS-CoV-2 Transmission

Fenizia C et al. COVID IAS Virtual July 2020 Track A

subject n.	clinical outcome	Δ T1-T0 (days)	maternal plasma			vaginal swab	Placenta	Umbilical cord plasma			umbilical cord	Milk		
			virus	IgM	IgG			virus	IgM	IgG		virus	IgM	IgG
1	SEVERE	2	-	-	-	-	-	-	-	-	-	+	+	-
2	MILD	1	-	-	-	-	-	N/A	N/A	N/A	-	-	-	-
3	MILD	1	-	-	-	-	-	-	-	-	-	-	-	N/A
4	SEVERE	2	+	-	+	-	-	-	-	-	-	-	-	-
5	MILD	7	-	-	-	-	-	-	-	-	-	N/A	N/A	N/A
6	MILD	1	-	+	+	-	-	-	-	-	-	-	N/A	-
7	MILD	12	-	+	+	-	-	-	-	-	-	-	-	-
8	SEVERE	6	-	+	+	-	-	-	-	-	-	N/A	N/A	N/A
9	MILD	1	N/A	N/A	N/A	-	-	-	-	-	-	-	-	-
10	MILD	1	-	-	-	-	-	-	-	-	-	-	-	-
11	MILD	5	-	-	-	-	-	-	-	-	-	-	-	-
12	MILD	4	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
13	MILD	3	-	-	+	-	-	-	-	+	-	-	-	-
14	MILD	3	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
15	MILD	4	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
16	MILD	2	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
17	SEVERE	6	+	+	+	+	+	+	-	+	N/A	N/A	N/A	N/A
18	MILD	2	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
19	MILD	9	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
20	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
21	MILD	13	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
22	MILD	10	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
23	MILD	9	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
24	MILD	12	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
25	MILD	17	-	+	+	-	-	-	+	+	N/A	N/A	N/A	N/A
26	MILD	13	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
27	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
28	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
29	MILD	2	-	-	+	-	-	-	-	-	N/A	-	-	-
30	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
31	recovered	N/A	-	-	+	N/A	-	-	-	+	N/A	N/A	N/A	N/A

2/30

1/30

1/31

1/31

1/31

1/8

Possible Mother-to-Child SARS-CoV-2 Transmission

Fenizia C et al. COVID IAS Virtual July 2020 Track A

subject n.	clinical outcome	Δ T1-T0 (days)	maternal plasma			vaginal swab	Placenta	Umbilical cord plasma			umbilical cord	Milk		
			virus	IgM	IgG			virus	IgM	IgG		virus	IgM	IgG
1	SEVERE	2	-	-	-	-	-	-	-	-	-	+	+	-
2	MILD	1	-	-	-	-	-	N/A	N/A	N/A	-	-	-	-
3	MILD	1	-	-	-	-	-	-	-	-	-	-	-	N/A
4	SEVERE	2	+	-	+	-	-	-	-	-	-	-	-	-
5	MILD	7	-	-	-	-	-	-	-	-	-	N/A	N/A	N/A
6	MILD	1	-	+	+	-	-	-	-	-	-	-	N/A	-
7	MILD	12	-	+	+	-	-	-	-	-	-	-	-	-
8	SEVERE	6	-	+	+	-	-	-	-	-	-	N/A	N/A	N/A
9	MILD	1	N/A	N/A	N/A	-	-	-	-	-	-	-	-	-
10	MILD	1	-	-	-	-	-	-	-	-	-	-	-	-
11	MILD	5	-	-	-	-	-	-	-	-	-	-	-	-
12	MILD	4	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
13	MILD	3	-	-	+	-	-	-	-	+	-	-	-	-
14	MILD	3	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
15	MILD	4	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
16	MILD	2	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
17	SEVERE	6	+	+	+	+	+	+	-	+	N/A	N/A	N/A	N/A
18	MILD	2	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
19	MILD	9	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
20	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
21	MILD	13	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
22	MILD	10	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
23	MILD	9	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
24	MILD	12	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
25	MILD	17	-	+	+	-	-	-	+	+	N/A	N/A	N/A	N/A
26	MILD	13	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
27	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
28	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
29	MILD	2	-	-	+	-	-	-	-	-	N/A	-	-	-
30	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
31	recovered	N/A	-	-	+	N/A	-	-	-	+	N/A	N/A	N/A	N/A

Infant (GA 34 wk):
NP pos birth
NP neg 7 d

No Sx
Lab normal
Not BF

Possible Mother-to-Child SARS-CoV-2 Transmission

Fenizia C et al. COVID IAS Virtual July 2020 Track A

subject n.	clinical outcome	Δ T1-T0 (days)	maternal plasma			vaginal swab	Placenta	Umbilical cord plasma			umbilical cord	Milk		
			virus	IgM	IgG			virus	IgM	IgG		virus	IgM	IgG
1	SEVERE	2	-	-	-	-	-	-	-	-	-	+	+	-
2	MILD	1	-	-	-	-	-	N/A	N/A	N/A	-	-	-	-
3	MILD	1	-	-	-	-	-	-	-	-	-	-	-	N/A
4	SEVERE	2	+	-	+	-	-	-	-	-	-	-	-	-
5	MILD	7	-	-	-	-	-	-	-	-	-	N/A	N/A	N/A
6	MILD	1	-	+	+	-	-	-	-	-	-	-	N/A	-
7	MILD	12	-	+	+	-	-	-	-	-	-	-	-	-
8	SEVERE	6	-	+	+	-	-	-	-	-	-	N/A	N/A	N/A
9	MILD	1	N/A	N/A	N/A	-	-	-	-	-	-	-	-	-
10	MILD	1	-	-	-	-	-	-	-	-	-	-	-	-
11	MILD	5	-	-	-	-	-	-	-	-	-	-	-	-
12	MILD	4	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
13	MILD	3	-	-	+	-	-	-	-	+	-	-	-	-
14	MILD	3	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
15	MILD	4	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
16	MILD	2	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
17	SEVERE	6	+	+	+	+	+	+	-	+	N/A	N/A	N/A	N/A
18	MILD	2	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
19	MILD	9	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
20	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
21	MILD	13	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
22	MILD	10	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
23	MILD	9	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
24	MILD	12	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
25	MILD	17	-	+	+	-	-	-	+	+	N/A	N/A	N/A	N/A
26	MILD	13	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
27	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
28	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
29	MILD	2	-	-	+	-	-	-	-	-	N/A	-	-	-
30	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
31	recovered	N/A	-	-	+	N/A	-	-	-	+	N/A	N/A	N/A	N/A

Infant (GA 39 wk):
NP pos birth
NP neg 48 hr

No Sx
No lab abnl
Not BF

Possible Mother-to-Child SARS-CoV-2 Transmission

Fenizia C et al. COVID IAS Virtual July 2020 Track A

subject n.	clinical outcome	Δ T1-T0 (days)	maternal plasma			vaginal swab	Placenta	Umbilical cord plasma			umbilical cord	Milk		
			virus	IgM	IgG			virus	IgM	IgG		virus	IgM	IgG
1	SEVERE	2	-	-	-	-	-	-	-	-	-	+	+	-
2	MILD	1	-	-	-	-	-	N/A	N/A	N/A	-	-	-	-
3	MILD	1	-	-	-	-	-	-	-	-	-	-	-	N/A
4	SEVERE	2	+	-	+	-	-	-	-	-	-	-	-	-
5	MILD	7	-	-	-	-	-	-	-	-	-	N/A	N/A	N/A
6	MILD	1	-	+	+	-	-	-	-	-	-	-	N/A	-
7	MILD	12	-	+	+	-	-	-	-	-	-	-	-	-
8	SEVERE	6	-	+	+	-	-	-	-	-	-	N/A	N/A	N/A
9	MILD	1	N/A	N/A	N/A	-	-	-	-	-	-	-	-	-
10	MILD	1	-	-	-	-	-	-	-	-	-	-	-	-
11	MILD	5	-	-	-	-	-	-	-	-	-	-	-	-
12	MILD	4	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
13	MILD	3	-	-	+	-	-	-	-	+	-	-	-	-
14	MILD	3	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
15	MILD	4	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
16	MILD	2	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
17	SEVERE	6	+	+	+	+	+	+	-	+	N/A	N/A	N/A	N/A
18	MILD	2	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
19	MILD	9	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
20	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
21	MILD	13	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
22	MILD	10	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
23	MILD	9	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
24	MILD	12	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
25	MILD	17	-	+	+	-	-	-	+	+	N/A	N/A	N/A	N/A
26	MILD	13	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
27	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
28	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
29	MILD	2	-	-	+	-	-	-	-	-	N/A	-	-	-
30	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
31	recovered	N/A	-	-	+	N/A	-	-	-	+	N/A	N/A	N/A	N/A

Infant
Neg NP birth
No Sx
Lab normal

Possible Mother-to-Child SARS-CoV-2 Transmission

Fenizia C et al. COVID IAS Virtual July 2020 Track A

subject n.	clinical outcome	Δ T1-T0 (days)	maternal plasma			vaginal swab	Placenta	Umbilical cord plasma			umbilical cord	Milk		
			virus	IgM	IgG			virus	IgM	IgG		virus	IgM	IgG
1	SEVERE	2	-	-	-	-	-	-	-	-	-	+	+	-
2	MILD	1	-	-	-	-	-	N/A	N/A	N/A	-	-	-	-
3	MILD	1	-	-	-	-	-	-	-	-	-	-	-	N/A
4	SEVERE	2	+	-	+	-	-	-	-	-	-	-	-	-
5	MILD	7	-	-	-	-	-	-	-	-	-	N/A	N/A	N/A
6	MILD	1	-	+	+	-	-	-	-	-	-	-	N/A	-
7	MILD	12	-	+	+	-	-	-	-	-	-	-	-	-
8	SEVERE	6	-	+	+	-	-	-	-	-	-	N/A	N/A	N/A
9	MILD	1	N/A	N/A	N/A	-	-	-	-	-	-	-	-	-
10	MILD	1	-	-	-	-	-	-	-	-	-	-	-	-
11	MILD	5	-	-	-	-	-	-	-	-	-	-	-	-
12	MILD	4	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
13	MILD	3	-	-	+	-	-	-	-	+	-	-	-	-
14	MILD	3	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
15	MILD	4	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
16	MILD	2	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
17	SEVERE	6	+	+	+	+	+	+	-	+	N/A	N/A	N/A	N/A
18	MILD	2	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
19	MILD	9	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
20	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
21	MILD	13	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
22	MILD	10	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
23	MILD	9	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
24	MILD	12	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
25	MILD	17	-	+	+	-	-	-	+	+	N/A	N/A	N/A	N/A
26	MILD	13	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
27	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
28	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
29	MILD	2	-	-	+	-	-	-	-	-	N/A	-	-	-
30	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
31	recovered	N/A	-	-	+	N/A	-	-	-	+	N/A	N/A	N/A	N/A

Infant
Neg NP birth
No Sx
Lab normal

Possible Mother-to-Child SARS-CoV-2 Transmission

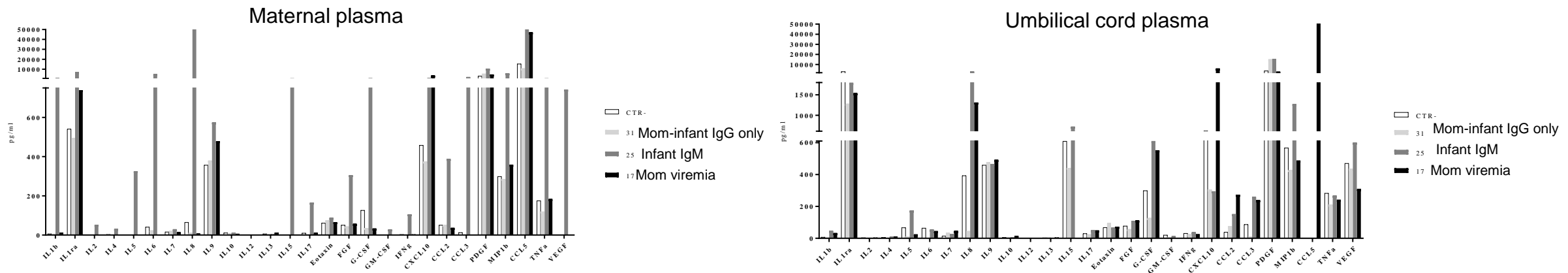
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subject n.	clinical outcome	Δ T1-T0 (days)	maternal plasma			vaginal swab	Placenta	Umbilical cord plasma			umbilical cord	Milk		
			virus	IgM	IgG			virus	IgM	IgG		virus	IgM	IgG
1	SEVERE	2	-	-	-	-	-	-	-	-	-	+	+	-
2	MILD	1	-	-	-	-	-	N/A	N/A	N/A	-	-	-	-
3	MILD	1	-	-	-	-	-	-	-	-	-	-	-	N/A
4	SEVERE	2	+	-	+	-	-	-	-	-	-	-	-	-
5	MILD	7	-	-	-	-	-	-	-	-	-	N/A	N/A	N/A
6	MILD	1	-	+	+	-	-	-	-	-	-	-	N/A	-
7	MILD	12	-	+	+	-	-	-	-	-	-	-	-	-
8	SEVERE	6	-	+	+	-	-	-	-	-	-	N/A	N/A	N/A
9	MILD	1	N/A	N/A	N/A	-	-	-	-	-	-	-	-	-
10	MILD	1	-	-	-	-	-	-	-	-	-	-	-	-
11	MILD	5	-	-	-	-	-	-	-	-	-	-	-	-
12	MILD	4	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
13	MILD	3	-	-	+	-	-	-	-	+	-	-	-	-
14	MILD	3	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
15	MILD	4	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
16	MILD	2	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
17	SEVERE	6	+	+	+	+	+	+	-	+	N/A	N/A	N/A	N/A
18	MILD	2	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
19	MILD	9	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
20	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
21	MILD	13	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
22	MILD	10	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
23	MILD	9	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
24	MILD	12	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
25	MILD	17	-	+	+	-	-	-	+	+	N/A	N/A	N/A	N/A
26	MILD	13	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
27	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
28	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
29	MILD	2	-	-	+	-	-	-	-	-	N/A	-	-	-
30	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
31	recovered	N/A	-	-	+	N/A	-	-	-	+	N/A	N/A	N/A	N/A

Possible Mother-to-Child SARS-CoV-2 Transmission

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- Placentas of women with COVID-19 identified “altered inflammatory profile gene expression” – strongest in woman with no viral detection in placenta but IgM infant.
- Cytokine studies found “hyper-active inflammatory profile” in both maternal and infant blood (however, could be transplacental maternal-fetal cytokine transfer).



- Possible in utero infection in 1 infant: positive placenta and maternal/infant viremia; report NP positive PCR delivery but negative at 1 wk; no sx or abnormal lab.
- 1 infant had SARS-CoV-2 IgM antibody in neonatal blood but negative virus placenta, vagina and infant blood; NP positive at delivery, negative 3 d; no sx.
- 1/11 breast milk samples positive rtPCR and IgM (but not IgG) antibody.

SARS-CoV-2 Secretory IgA Response in Human Milk Following SARS-CoV-2 Infection in Pregnant Women

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

- Part of study recruiting lactating women to provide milk, including women who have recovered from COVID 19 illness.

Methodology

- A SARS-CoV-2 ELISA using blood plasma was recently developed and validated at Mount Sinai and we have adapted this assay for use with human milk
- Plates were coated with the full trimeric SARS-CoV-2 Spike protein or the Receptor Binding Domain (RBD) of the Spike
- Samples were tested in duplicate in 3 unique experiments for separate assays measuring IgA, IgG, IgM, and secretory-type Ab reactivity (the secondary Ab used in this assay is specific for free and bound SC)
- The 10 pre-pandemic control undiluted milk samples were used to determine positive cutoff values for each assay, calculated as the mean OD + 2*SD
- ~30mL of milk was obtained from consented study participants using electronic or manual pumps.
- Participants either had a laboratory-confirmed COVID-19 infection, or highly likely infection based on close contact with a confirmed COVID-19 case and/or symptoms of infection such as cough, anosmia, malaise, diarrhea, and fever.
- Milk was obtained ~14-30 days after symptoms had resolved.
- Milk was pumped by the participants and frozen in their homes until sample pickup.
- Pre-pandemic negative control milk samples were obtained in accordance with IRB-approved protocols prior to December 2019 for other studies, and had been stored in laboratory freezers at -80C
- Milk samples were centrifuged at 800g for 15 min, fat was removed, and supernatant transferred to a new tube. Centrifugation was repeated 2x to ensure removal of all cells and fat.

~90% of human milk antibody is IgA and ~8% IgM, nearly all in secretory form complexed to j-chain and secretory component proteins

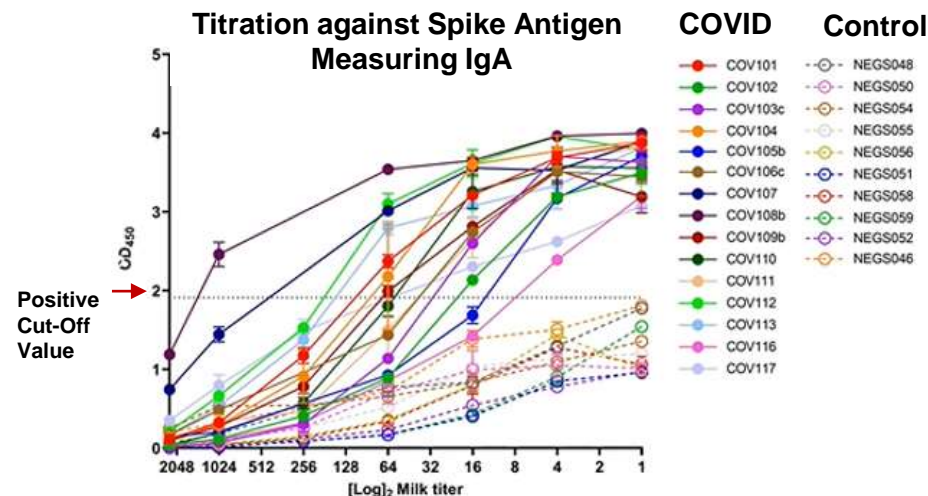
Participants with COVID-19

Sample ID	COVID-19 Confirmed or Suspected (C/S)	Months Post-partum	Infected ante- or post-partum (A/P)
COV101	C	4	P
COV102	C	1	A [#]
COV103c	C	4	P
COV104	S	23	P
COV105b	S	6	P
COV106c	S	8	P
COV107	S	32	P
COV108b	C	4	P
COV109b	S	3	P
COV110	S	14	P
COV111	S	7	P
COV112	C	1	A [#]
COV113	C	7	P
COV116	C	6	P
COV117	C	4	P

→ 8 women had confirmed, 7 suspected COVID-19

→ Majority (87%) were >1 mo PP (1-32 mos)

→ Majority (87%) infected postpartum

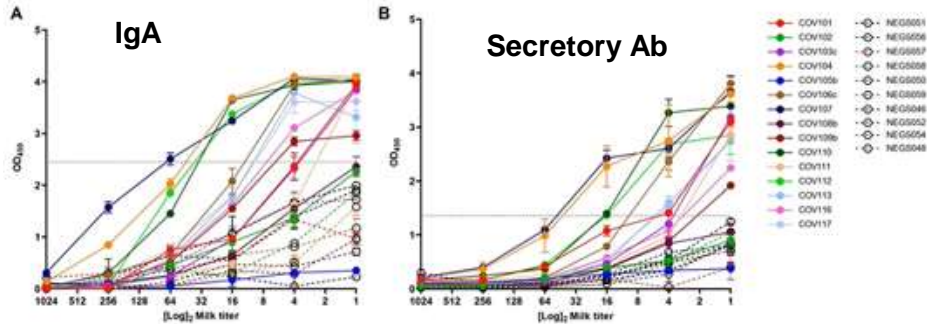


→ All milk samples from COVID-19 recovered donors contained significant levels of SARS-CoV-2 specific IgA, while all controls were negative

SARS-CoV-2 Secretory IgA Response in Human Milk Following SARS-CoV-2 Infection in Pregnant Women

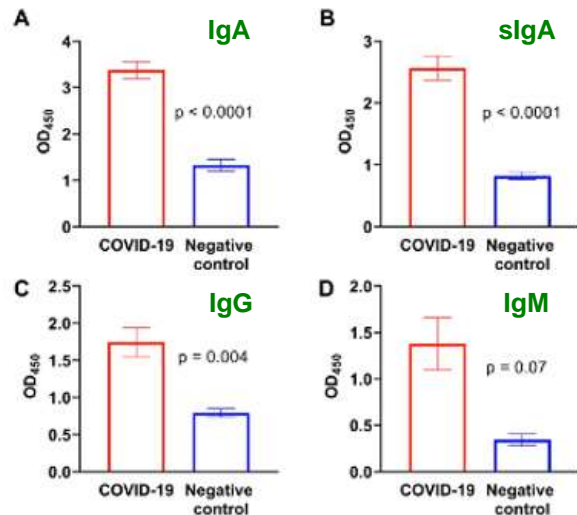
Powell RL. COVID-19 IAS Virtual July 2019 Track A

Titration against Receptor Binding Domain of Spike



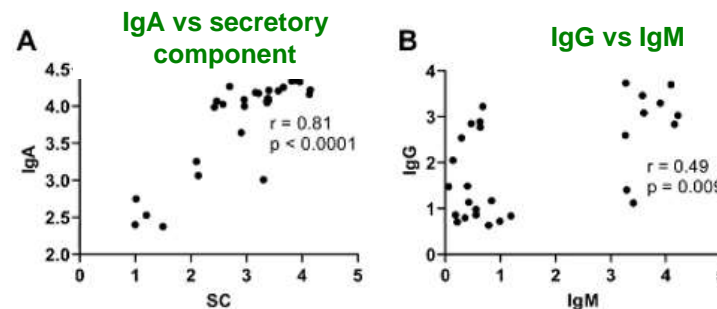
- 80% of milk samples from COVID-19 recovered donors had IgA and secretory Ab reactivity against the receptor binding domain of SARS-CoV-2 spike vs none controls
- The IgA response in milk was dominant and not necessarily concurrent with measurable IgG or IgM response

Grouped Optical Density Values for Undiluted Milk



- Milk from COVID-19 recovered donors has significantly greater IgA, secretory antibody and IgG binding against receptor binding domain of spike protein than controls

Optical Density Values for Undiluted Milk by Ab Subclass

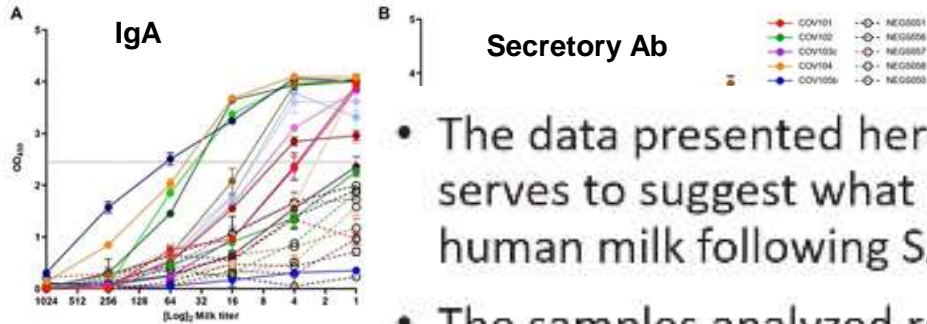


- IgA and secretory Ab OC values for undiluted milk highly correlated, IgG and IgM values modestly correlated.

SARS-CoV-2 Secretory IgA Response in Human Milk Following SARS-CoV-2 Infection in Pregnant Women

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

Titration against Receptor Binding Domain of Spike

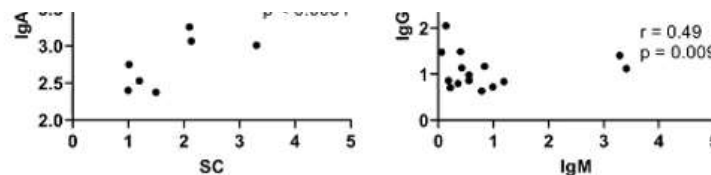
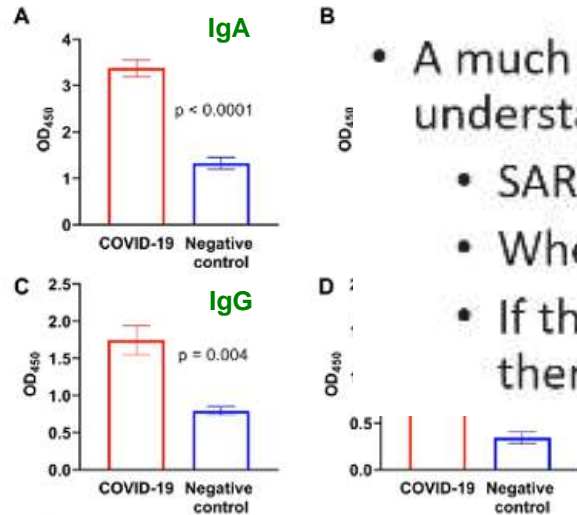


→ 80% of milk samples from COVID-19 recovered donors had IgA and secretory Ab reactivity against the receptor binding

- The data presented herein is preliminary using a small sample size and only serves to suggest what might be the typical range of the antibodies generated in human milk following SARS-CoV-2 infection.
- The samples analyzed represent only a snapshot of what is likely a dynamic immune response.
- A much larger sample size and long-term follow-up study is needed to better understand:
 - SARS-CoV-2 immunity in milk
 - Whether a typical response is truly protective for breastfed babies
 - If this response would generate sufficient Abs to be purified and used therapeutically to treat COVID-19.

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Grouped Optical Density



IC values for
related, IgG
tly correlated.

Brazil Recommendations for Women with COVID-19

Who Desire to Breastfeed

Ortelan N et al. COVID-19 IAS Virtual July 2019 Track C

- To date, no evidence of SARS-CoV-2 transmission in breast milk from women with confirmed COVID-19 to their infant in review literature
- Benefits of breast milk outweigh risk of SARS CoV 2 transmission, safe breastfeeding should be promoted.

→ To reduce risk of transmission to child, preventive procedures are advisable.



- In hospitals/maternity units, room should be isolated, infant crib at least 2 meters from mother's head and *potential* use of physical barrier between.
- If maternal health impaired, neonate managed separately and fed expressed breast milk (pasteurization not required).
- Individualized decision regarding separation mother-baby but note that interferes with mother-child relationship and establishment of lactation.

Potential SARS-CoV-2 Mother-to-Child Transmission

Intrauterine Infection

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



In Utero Infection

EARLY EXPOSURE

- NP rtPCR positive at <24 hr and/or amniotic fluid or cord/neonatal blood

PERSISTENCE

- NP rtPCR positive at ≥24-36 hr
- IgM positive during wk 1 life

Superficial Exposure/Contamination or Transient Viremia

EARLY EXPOSURE

- NP rtPCR positive at <24 hr and/or amniotic fluid or cord blood

NO PERSISTENCE/ IMMUNE RESPONSE

- NP rtPCR negative ≥24 hr
- IgM negative during 2 wk post birth

Placental infection rare

May be more likely in mothers with severe COVID-19

- Higher prevalence viremia
- More likely placental barrier disruption due to thrombosis

Placenta, amniotic fluid, and/or neonatal blood viral test positive

Perinatal Infection

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



Intrapartum or Immediate Postnatal Infection

- NP rtPCR negative at <24 hr BUT positive 1-14 d
- IgM positive at 2-3 weeks

Intrapartum or horizontal transmission possible, but seems uncommon

- Exposure to maternal fecal virus or virus in respiratory secretions most likely source
- Most infants no symptoms

Blumberg DA et al, Am J Perinatol 2020 Jun 5

Breast Milk Infection

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



Infection through viral presence in breast milk is unlikely

More likely is horizontal transmission through respiratory secretion contact