unicef
for every child

Understanding and Improving
Viral Load Suppression in Children with HIV
in Eastern and Southern Africa

HIV Viral Load Suppression (VLS) in Children

Dr. Geoffrey Chipungu
HIV/AIDS Specialist
UNICEF ESARO

20 April 2021

unicef | for every child

Outline

- Background
- Methodology
- Findings
- Conclusion
- Taking Action

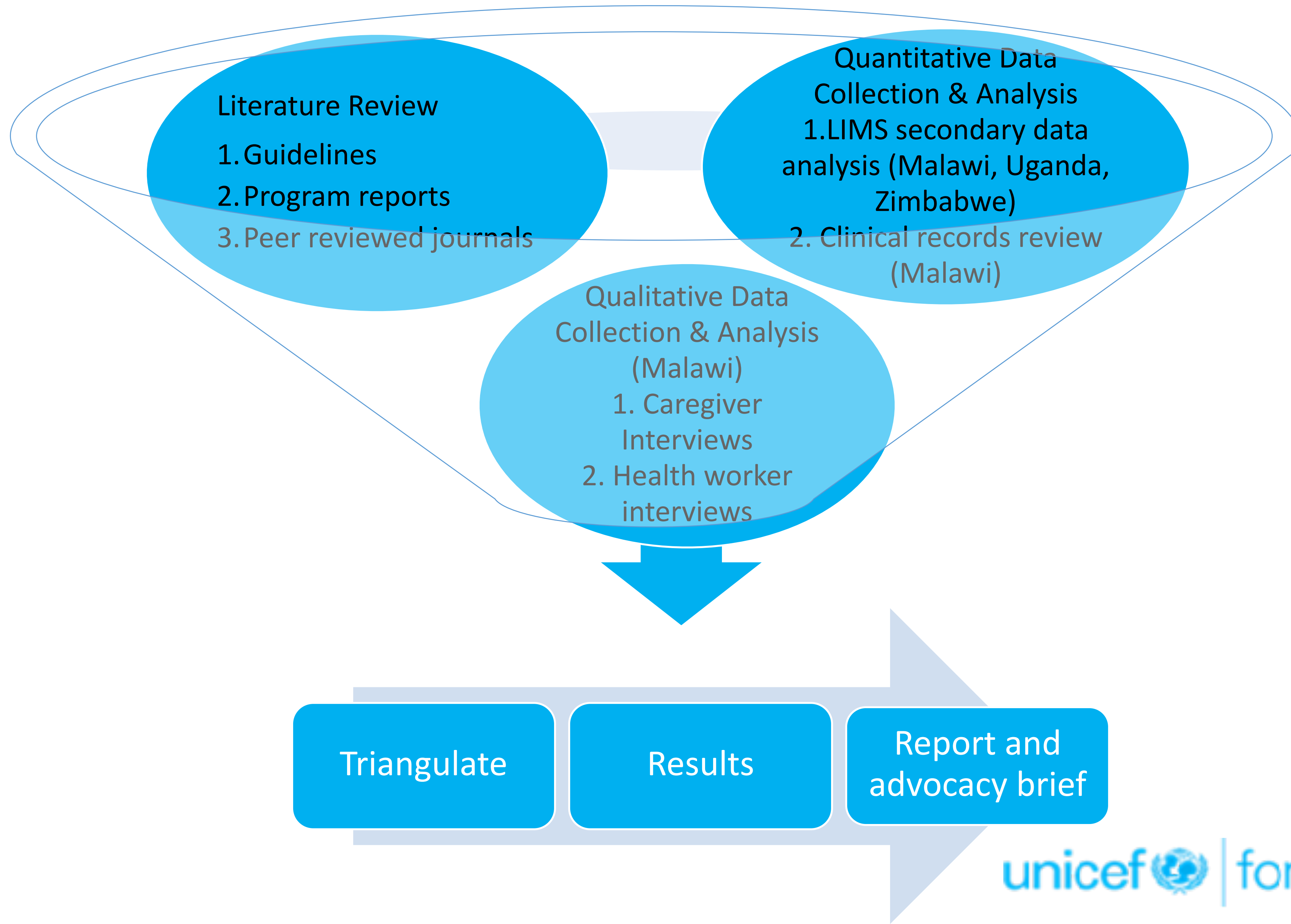
Why this study?

Children are lagging behind adults in viral load suppression[4]

Malawi: Children at **42%** vs adults at 67%
Uganda: Children at **39%** vs adults at 84%
Zimbabwe: Children at **47%** vs adults at 86%

- VLS indicates successful virologic, immunologic and clinical outcomes.
- Population-based studies found sub-optimal VLS for children with HIV (0-14 years), especially compared to adult VLS.
- VLS among children with HIV falls short of the 3rd 95 of the UNAIDS 95-95-95 targets.
- We set out to explore the rates, trends and factors associated with VLS to inform paediatric HIV policies and programmes

Study Framework



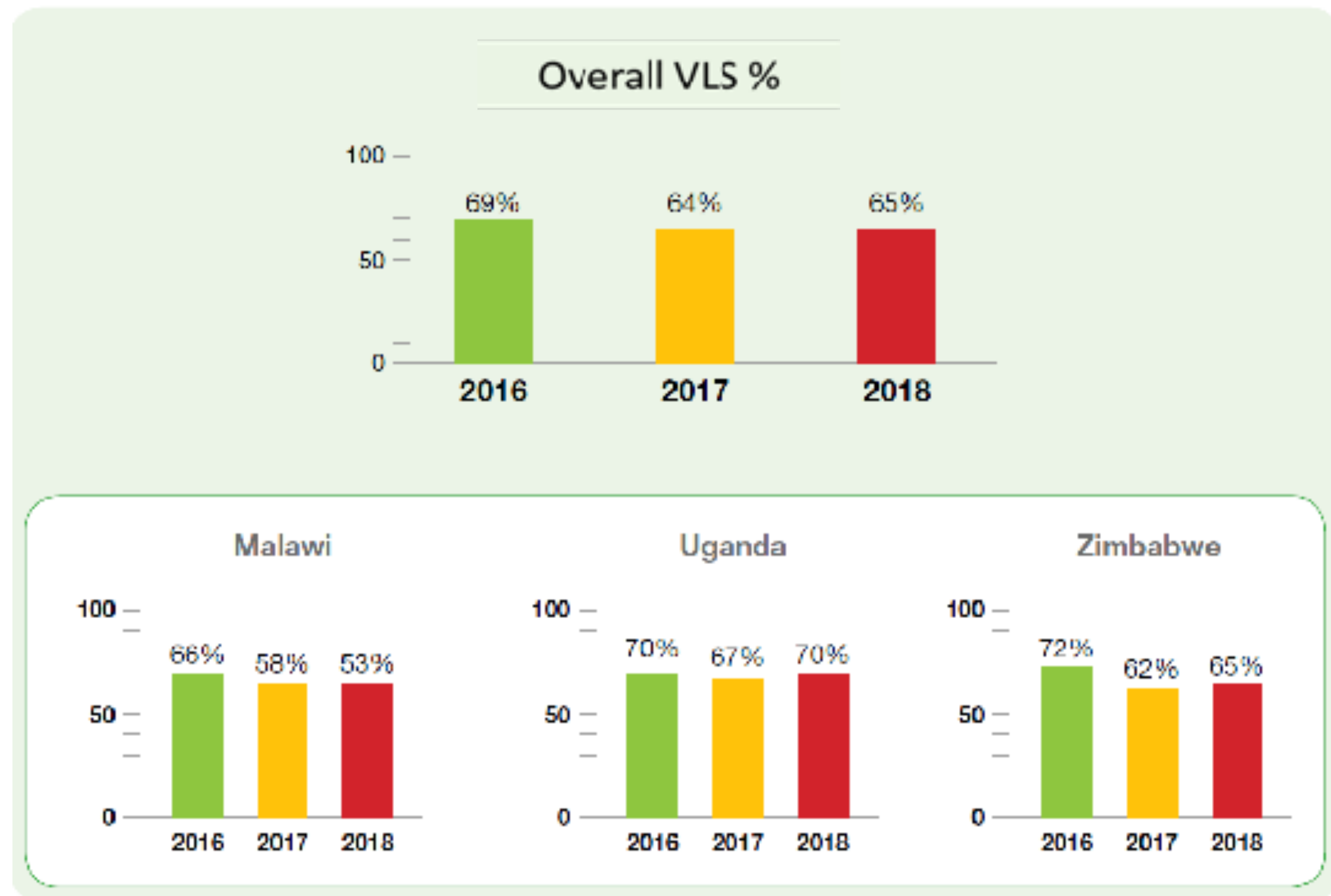
unicef | for every child

Viral load volumes and data quality

Finding	2016	2017	2018
# of VL eligible for analysis for <15 y.o.	66,158	71,941	121,370
The reason for viral load test was not always indicated	93%	81%	82%
ART regimen was not always indicated	68%	59%	57%
Duration of ART was not always indicated	75%	66%	71%
Disproportionately few viral loads were done post IAC	1.2%	3.9%	4.2%
Yet fewer VL were done for suspected treatment failure	0.3%	0.2%	0.1%

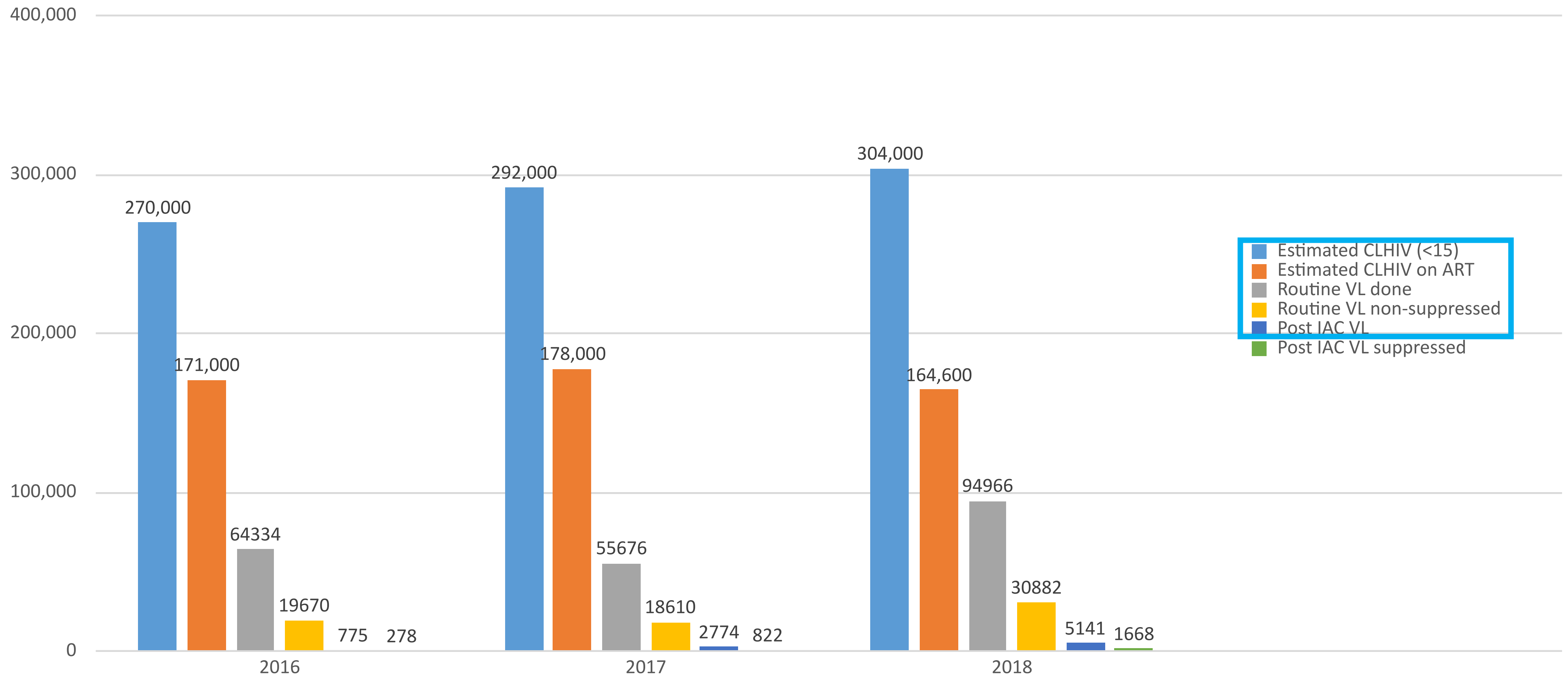
Viral Load Suppression Trends in children

The study found that one out of every three children who had a viral load test had not achieved viral load suppression.



unicef | for every child

Combined VL Cascade for CLHIV for the 3 countries



https://data.unicef.org/resources/dataset/hiv-aids-statistical-tables/

unicef | for every child

Factors associated with VLS

- Duration on ART
  - 70% (5-9 years) vs 65% (<5 years)
- ARV formulation
  - Initial 74% vs Switched 60%
- Adherence
  - Clinic appointments: 64% vs 59% VLS
- Nutrition status (n=66)
  - Normal 87%, moderate 50%, severe 77%
- Health facility-related
  - Schedules, staff shortage, perceived child-unfriendly setup, space
- Psychosocial support for the caregiver and child

Conclusion

- To reach the third 95 target much more needs to done on VL coverage and follow-up.
- Children are more likely to achieve VLS when they and their caregivers have support from families, communities and health workers.
- Drug regimens and formulations continue to impede children's VLS.
- Health care quality, accessibility and affordability have a direct impact on children's adherence.
- Multi-sectoral challenges (food security, poverty) affect treatment success.
- Lack of documentation, storage and utilization of data in both the LIMS and patient records was common.

Taking Action

- Provide multi-year support to caregivers and children with HIV.
- Promote paediatric viral load testing and adopt efficacious, child-friendly regimens.
- Strengthen paediatric service delivery coverage, accessibility and quality.
- Improve case management with multi-sectoral linkages and referrals.
- Work toward smarter paediatric HIV data management systems.
- Generate useful paediatric HIV implementation research.

unicef for every child

New study offers insights and recommendations for improving viral suppression among children with HIV

Methodology

http://www.childrenandaids.org/vls-clhiv

unicef | for every child

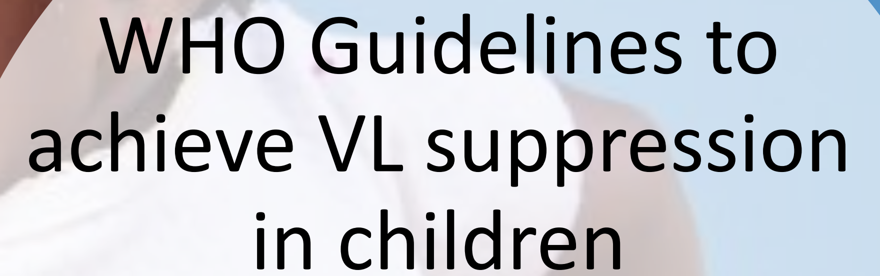
Acknowledgements

- Children, caregivers and health workers who participated in the study
- Respective Ministries of Health
- UNICEF ESARO and country offices
- Kundai Moyo and Edward Chigwedere, V and E Consultants
- Judith Sherman, Independent Consultant

unicef | for every child

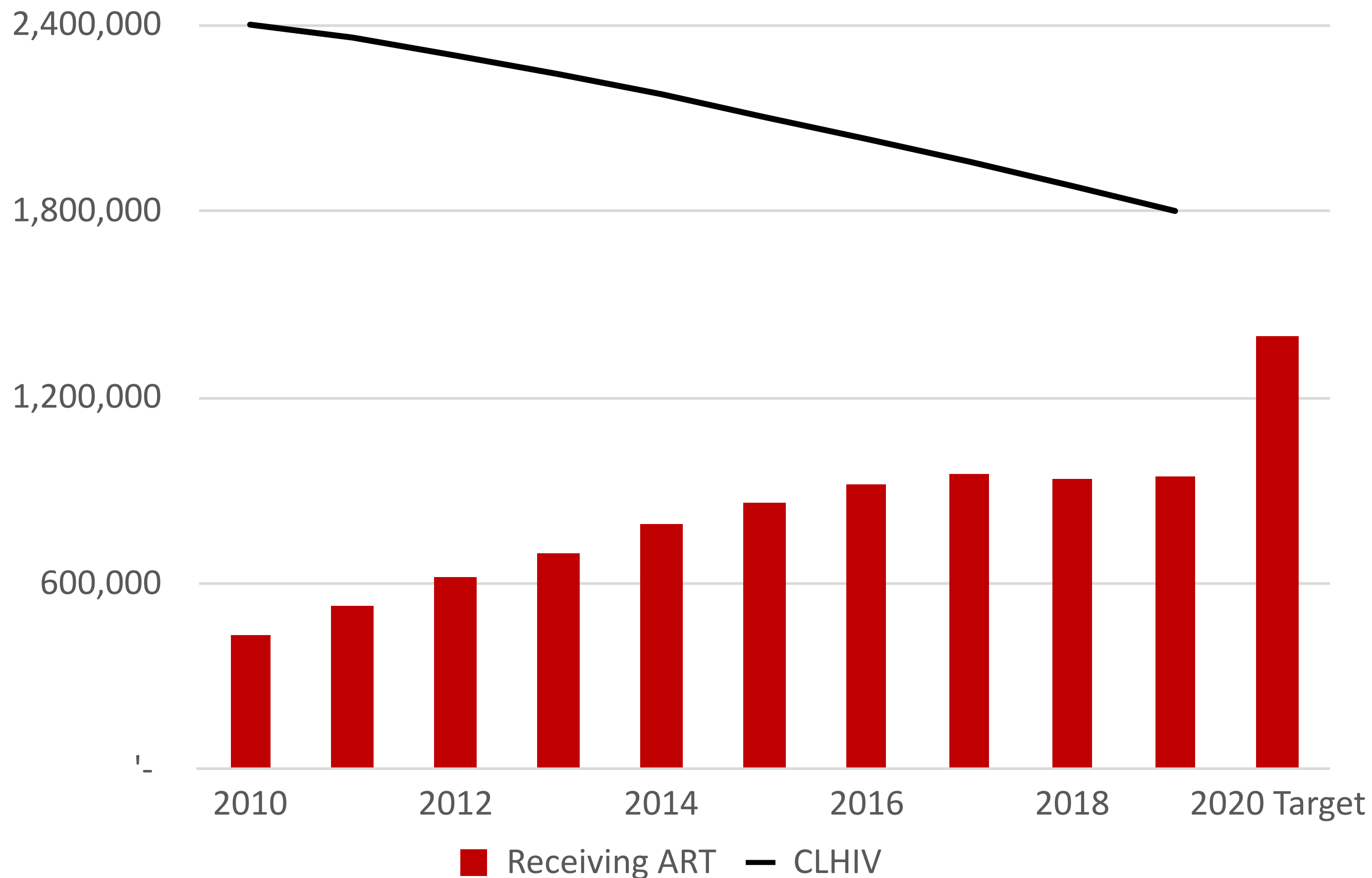
unicef
for every child

WHO Guidelines to achieve VL suppression in children



Dr Martina Penazzato
Paediatric HIV lead
HIV Hepatitis and STI programme
WHO Geneva

53% of children living with HIV are receiving treatment compared to 68% of adults



- Only 950,000 children receiving treatment in 2019
- Children living with HIV is declining with reduction in new infections and as children age into adulthood
- Most recent data suggest lower numbers in mid-2020

Source: UNAIDS 2020 Estimates

Treatment optimization

Starting	Changing	Transitioning	Switching
children on preferred regimens in optimal formulations	formulations as children grown and can take more optimal formulations	to better regimens and formulations as improved regimens are available	to appropriate 2nd or 3rd line regimens in optimal formulations when VL failure

For the benefit of the individual and the programme!

World Health Organization

Starting

children on preferred regimens in optimal formulations

Switching

to appropriate 2nd or 3rd line regimens in optimal formulations when VL failure

Table 1. Summary of preferred and alternative first-line ART for neonates and children

	Neonates	Children
Preferred	AZT+3TC+RAL[a]	ABC + 3TC + DTG
Alternatives	AZT+3TC+NVP	ABC + 3TC + LPVr TAF[c] + 3TC (or FTC) + DTG ABC + 3TC + RAL[d]
Special circumstances[d]	AZT+3TC+LPVr[b]	ABC + 3TC + EFV[e] (or NVP[f]) AZT + 3TC + EFV[e] (or NVP[f]) AZT + 3TC + LPVr (or RAL)

Additional evidence in support of WHO guidelines

Presented @CROI!

WHO Guidelines ALREADY recommend DTG for ALL children in need of 1st or 2nd line ART

Table 2. Summary of sequencing options for ART for children

First-line ART	Second-line ART[a]	Third-line ART
Two NRTIs + LPVr	Two NRTIs + DTG	DRV/r + DTG[b] with or without one or two NRTIs. Where possible, consider optimization using genotyping
Two NRTIs + EFV or NVP	Two NRTIs + DTG	
Two NRTIs + DTG or RAL	Two NRTIs + LPVr or ATVr	

[a]An optimized NRTI backbone should be used: AZT following TDF or ABC failure and vice versa.
[b]DTG-based third-line ART following the use of an integrase inhibitor must be administered with DTG twice daily

World Health Organization

Per protocol analysis over 96 weeks

Estimated risk difference (DTG-SOC) [95% CI] p-value:

	Estimate	[95% CI]	p-value
Primary: Total	-8.0%	[-13.5%,-2.6%]	p=0.004
Per-protocol: Total	-6.8%	[-12.2%,-1.4%]	p=0.01
Primary: ODYSSEY A	-12.5%	[-20.6%,-4.3%]	p=0.003
Per-protocol: ODYSSEY A	-12.6%	[-21.1%,-4.1%]	p=0.004
Primary: ODYSSEY B	-4.6%	[-11.8%,2.7%]	p=0.22
Per-protocol: ODYSSEY B	-2.3%	[-9.5%,4.9%]	p=0.53

Total NI margin

A/B NI margin

-24 -20 -16 -12 -8 -4 0 4 8 12

Difference in proportion with failure

DTG better SOC better

No significant difference in treatment effects by sex, weight, age, stratification factors, baseline VL or baseline CD4

Turkova et al. CROI 2021

Penta

$ Excluding all patients who did not meet eligibility criteria & censoring follow-up in both arms for switch to 3rd agent for protocol deviation, toxicity or pregnancy, or stop of ART for >31 days

Accelerated development of a DTG 10 mg dispersible scored tablet will provide scalable access to a generic pediatric DTG formulation for children under 20kg

DTG 10mg
Dispersible

Suppliers	Dosage
Mylan MacLeods	10mg

Groundbreaking Agreement Reduces by 75% the Cost of HIV Treatment for Children in Low-and Middle-Income Countries

Courtesy of CHAI

POLICY BRIEF – JULY 2020

CONSIDERATIONS FOR INTRODUCING NEW ANTIRETROVIRAL DRUG FORMULATIONS FOR CHILDREN

Dosing of DTG below 20 kg is now available and NO FURTHER guidance is needed on the formulations (including BD for children on TB Tx)

Formulation	3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg		25–29.9 kg		≥30 kg	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
ABC/3TC 120/60 mg scored dispersible tablet	1		1.5		2		2.5		3		1 adult tab (600/300 mg)		1 adult tab (600/300 mg)	
LPV/r 40/10 mg pellets (capsules)	2	2	3	3	4	4	5	5	6	6	–		–	
LPV/r 40/10 mg granules (sachets)	2	2	3	3	4	4	5	5	6	6	–		–	
LPV/r 100/25 mg tablets	–	–	–	–	2	1	2	2	2	2	3	3	3	3
4-in-1 ABC/3TC/LPV/r 30/15/40/10 mg (capsules)	2	2	3	3	4	4	5	5	6	6	–	–	–	–
DTG 5 mg dispersible tablets*	1		3		4		5		–		–		–	
DTG 10 mg scored dispersible tablet	0.5		1.5		2		2.5		–		–		–	
DTG 50 mg tablet	–		–		–		–		1		1		1	
TDF/3TC (or FTC)/DTG 300/300 (or 200)/50 mg tablet	–		–		–		–		–		–		1	

* This dosing was reviewed and confirmed by the Pediatric ARV Working Group on June 19, 2020.

New ARV Optimal Formulary and Limited Use List

Changing formulations as children grown and can take more optimal formulations

POLICY BRIEF

THE 2021 OPTIMAL FORMULARY AND LIMITED-USE LIST FOR ANTIRETROVIRAL DRUGS FOR CHILDREN

- Since 2011, the publication of the Optimal Formulary and Limited-use List has provided clear guidance to country programmes, procurement entities and funding agencies on the essential antiretroviral therapy (ART) dosage forms for children needed to deliver WHO-recommended ART regimens for all lines of treatment.
- The products included are regularly reviewed against a specific list of criteria that considers current WHO recommendations, supply constraints and programmatic realities to support programmes in taking a pragmatic approach to implementing WHO guidelines
- This sixth edition of the Optimal Formulary and Limited-use List is intended to support the transition and implementation of preferred and alternative ART regimens recommended for infants and children across all lines of treatment.

2021 Optimal formulary Launched today!

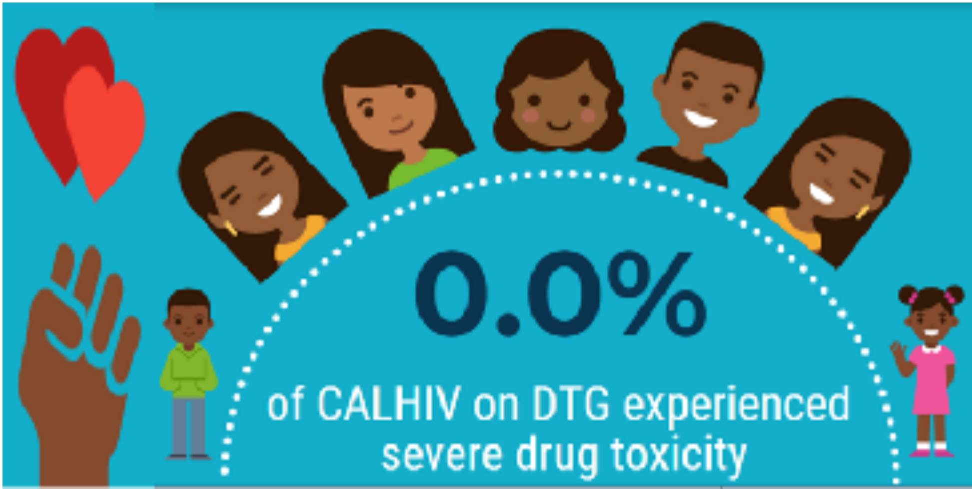
2021 Paediatric ARV Optimal Formulary and Limited-use List

2021		
DRUG	FORMULATION	DOSE
DTG	Tablet, disp, scored	10 mg
ABC/3TC	Tablet, disp, scored	120/60 mg
AZT	Oral liquid	50 mg/5 mL, 240 mL
NVP	Oral liquid	50 mg/5 mL, 100 mL
LPV/r	Tablet, heat-stable	100 mg/25 mg
LPV/r	Oral granules	40/10 mg
AZT/3TC	Tablet, disp, scored	60/30 mg
DTG 50 mg for children ≥ 20 kg		

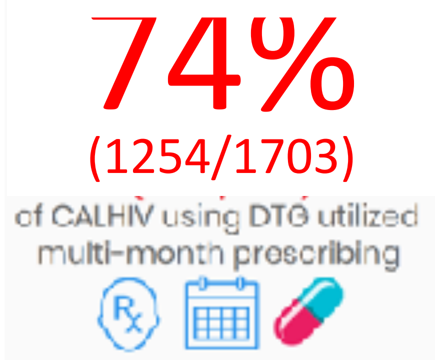
2021 Limited-use List		
DRUG	FORMULATION	DOSE
NVP	Tablet, disp, scored	50 mg
3TC	Oral liquid	50 mg/5mL
RAL	Granules for suspension	100 mg
LPV/r	Oral pellets	40/10 mg
DRV	Tablet	75 mg, 150 mg
RTV	Tablet	25 mg

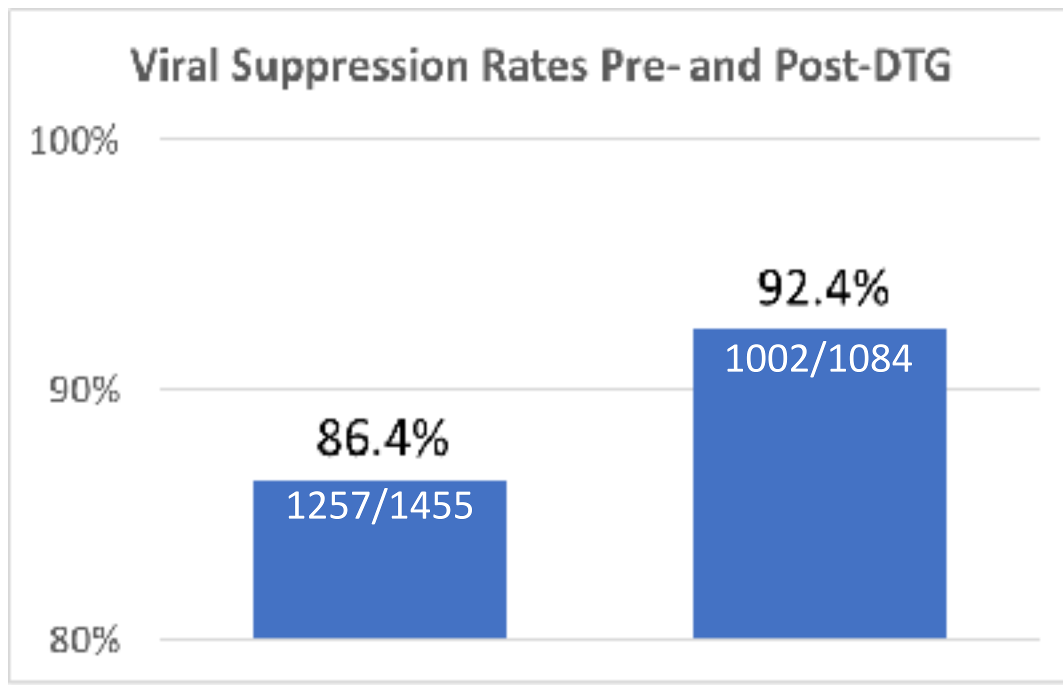
Transitioning to better regimens and formulations as improved regimens are available

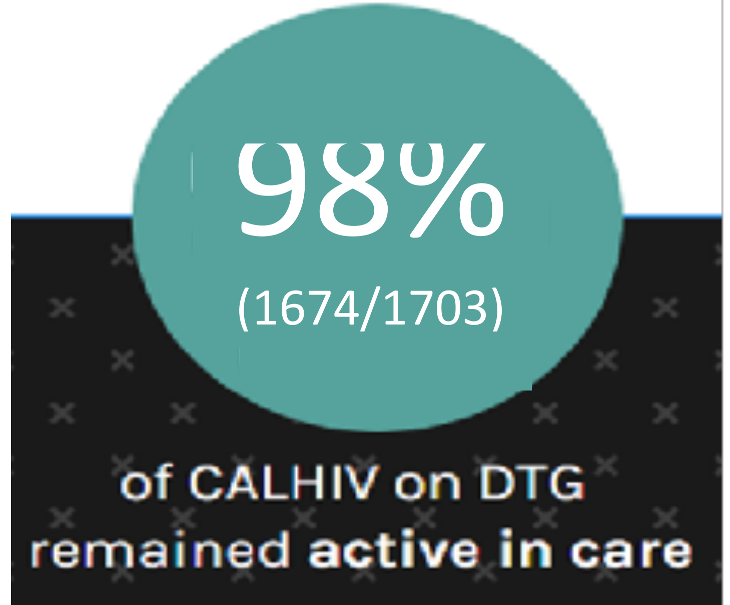
Bacha J et al. HIV Paediatrics Workshop Nov 2020

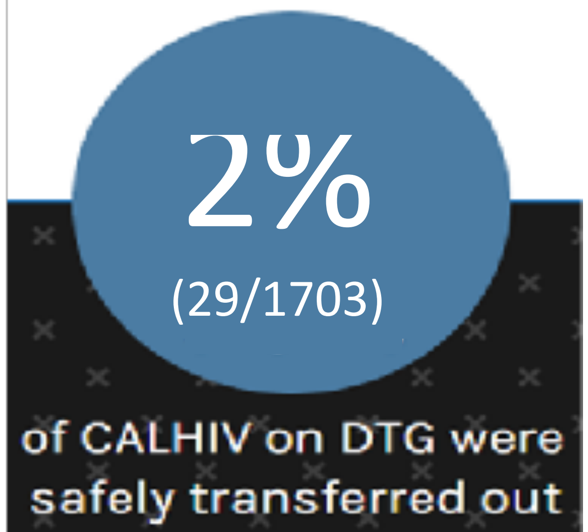


74%
(1254/1703)

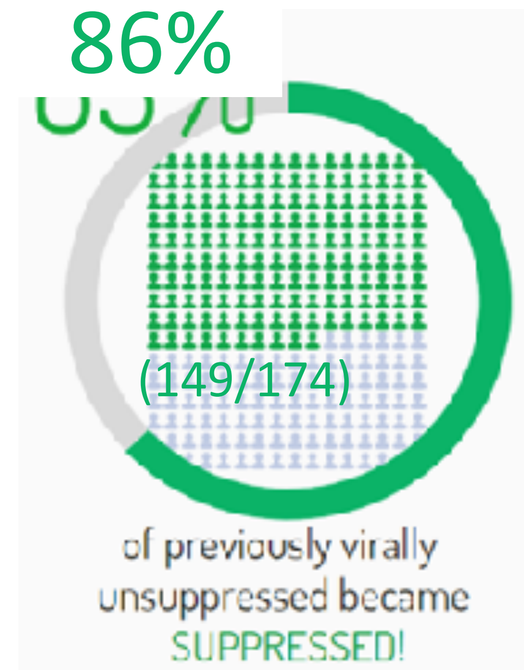


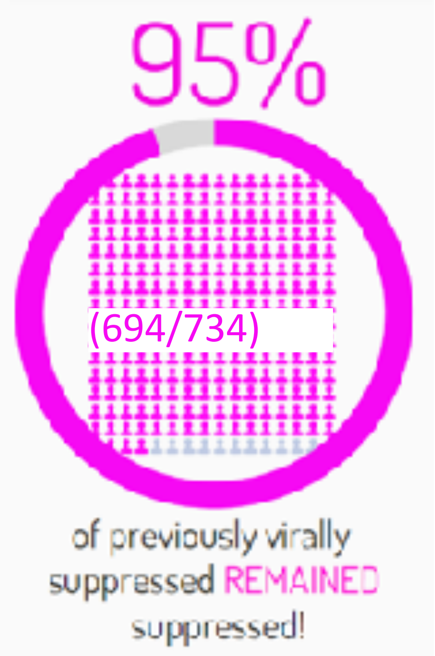






86%





Transitioning to better regimens and formulations as improved regimens are available

PAWG advice on transition to DTG for children established on 1st or 2nd line ART

The PAWG encourages rapid transition to DTG-based regimens for ALL infants and children (older than 4 weeks and weighting at least 3 kg) established on 1st and 2nd line ART irrespective of their current regimen. Timing of transition to DTG-based regimens for these infants and children should account for:

- Availability and anticipated supply of paeds DTG and, in case of inadequate supplies to provide DTG to all children, the need to prioritize children who most need DTG considering:
    1. The urgency to transition children off NNRTI-based regimens
    2. The importance of transitioning children who need to start TB treatment
    3. The anticipated benefits to transitioning children on LPVr solid formulations, particularly where those continue to present challenges in administration and/or challenges with attaining optimal VL suppression
- Viral load testing is not be considered a precondition to undertaking programmatic or individual transition to DTG-based regimens. While viral load monitoring remains a good practice to deliver appropriate care to children living with HIV, infants and children should not have their transition to DTG delayed due to lack of documented viral load.

Fully endorsed by PAWG in March 2021 and to be included in 2021 WHO ARV Consolidated Guidelines

World Health Organization

Treatment monitoring in children and adolescents is critical to preserve future treatment options

Less likely to be virologically suppressed

More likely to acquire HIVDR from their mother

More likely to fail with multi-drug resistance

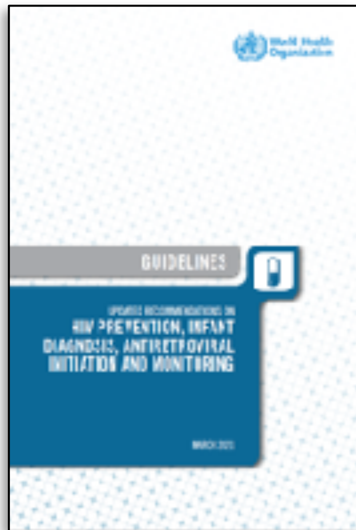
Less treatment options

Life-long treatment

Timely identification of virological failure and switch to appropriate 2nd line can minimize selection of drug resistance and optimize future treatment optiojn improving overall clinical outcomes in children and adolescents

World Health Organization

2021 Updated treatment monitoring algorithm



https://apps.who.int/iris/handle/10665/340190

World Health Organization

Treatment monitoring algorithm

Routine viral load monitoring for early detection of treatment failure: obtain and review result by 6 months after ART initiation, 12 months after ART initiation and yearly thereafter

- Undetectable (≤50 copies/ml) → Maintain ARV drug regimen
- Viral load >50 to ≤1000 copies/ml → Provide enhanced adherence counselling; repeat viral load testing after 3 months[c]
- Viral load >1000 copies/ml → If on NNRTI-based regimen, switch to appropriate regimen[a,b]; Provide enhanced adherence counselling; repeat viral load testing after 3 months[c]

After repeat viral load testing:

- Undetectable (≤50 copies/ml) → Maintain ARV drug regimen
- Viral load >50 to ≤1000 copies/ml → Maintain ARV drug regimen, but continue enhanced adherence counselling and repeat viral load testing after 3 months[d]
- Viral load >1000 copies/ml → Switch to appropriate regimen

2021 Point-of-care viral load recommendations

Recommendation

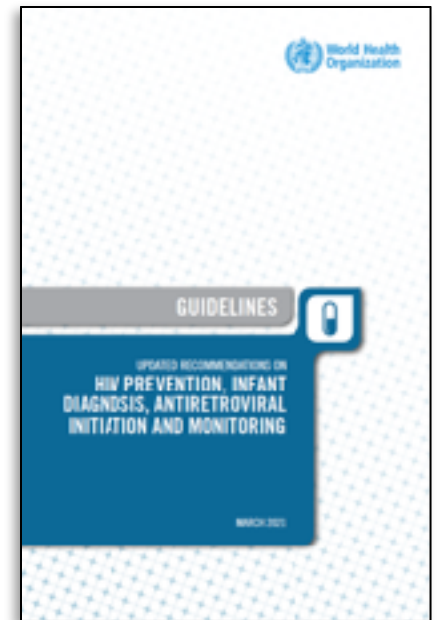
Point-of-care viral load may be used to monitor treatment among people living with HIV receiving ART.

(conditional recommendation; moderate-certainty evidence)

Box 2. Priorities for point-of-care viral load testing

Point-of-care viral load testing should be given priority for the following populations:

- Pregnant and breastfeeding women
- Infants, children and adolescents
- People requiring a repeat viral load after a first elevated viral load
- People for whom treatment failure is suspected
- People presenting sick, living with advanced HIV disease or having a known opportunistic infection (TB, cryptococcal infection, etc.)
- First scheduled viral load test for people re-entering care

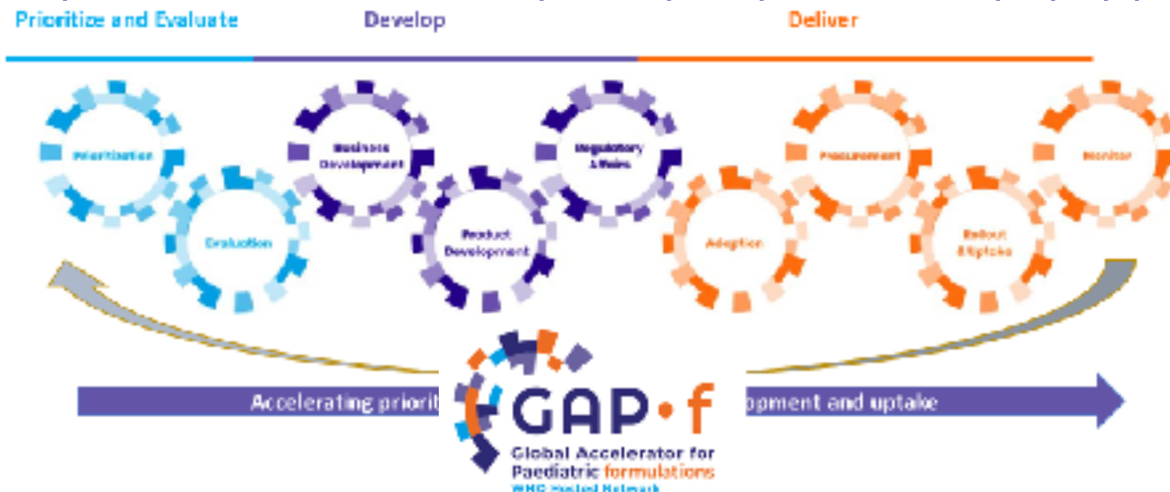


https://apps.who.int/iris/handle/10665/340190

World Health Organization

Collaboration and Political are needed to move the needle

- **GAP-f network** set up as a collaboration platform to accelerate investigation, development and introduction of better medicines for children with pDTG as a proof of concept of "what we can do together" when we are aligned and join forces
- The **"Vatican Platform"** generated political momentum and elevated the technical work of many stakeholders generating acceleration or strengthening to develop and roll out pediatric HIV testing and treatment. The initiative's robust monitoring and reporting system promote



World Health Organization

AIDS Free targets

Provide 1.4 million children (aged 0–14) and 1 million adolescents (aged 15–19) with lifelong HIV treatment by 2020 [Reach 95% of all children and adolescents living with HIV]

WHO and Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) are the co-conveners leading the AIDS Free Working Group of stakeholders working to reach the "super fast-track" targets.

The toolkit consists of the latest normative guidance, technical guidelines, policy briefs, case studies and advocacy resources to support efforts to achieve the AIDS Free targets in high-burden countries.

Materials included in this toolkit represents the work of several members of this group, including Adolescent Treatment Coalition (ATC), Clinton Health Access Initiative (CHAI), Children's Investment Fund Foundation (CIFF), ELMA Philanthropies, United States President's Emergency Plan for AIDS Relief (US PEPFAR), Joint United Nations Programme on HIV and AIDS (UNAIDS), United National Children's Fund (UNICEF), Unitaid,

Thank you

WHO

20, Avenue Appia
1211 Geneva

Switzerland

www.who.int

www.gap-f.org/

www.who.int/hiv/pub/paediatric/aids-free-toolkit/en/

www.who.int/hiv/pub/research-dev-toolkit-paediatric-arv-drug-formulation/en/

Global AIDS response for children

Where are the gaps?

Unicef Webinar

20 April 2021

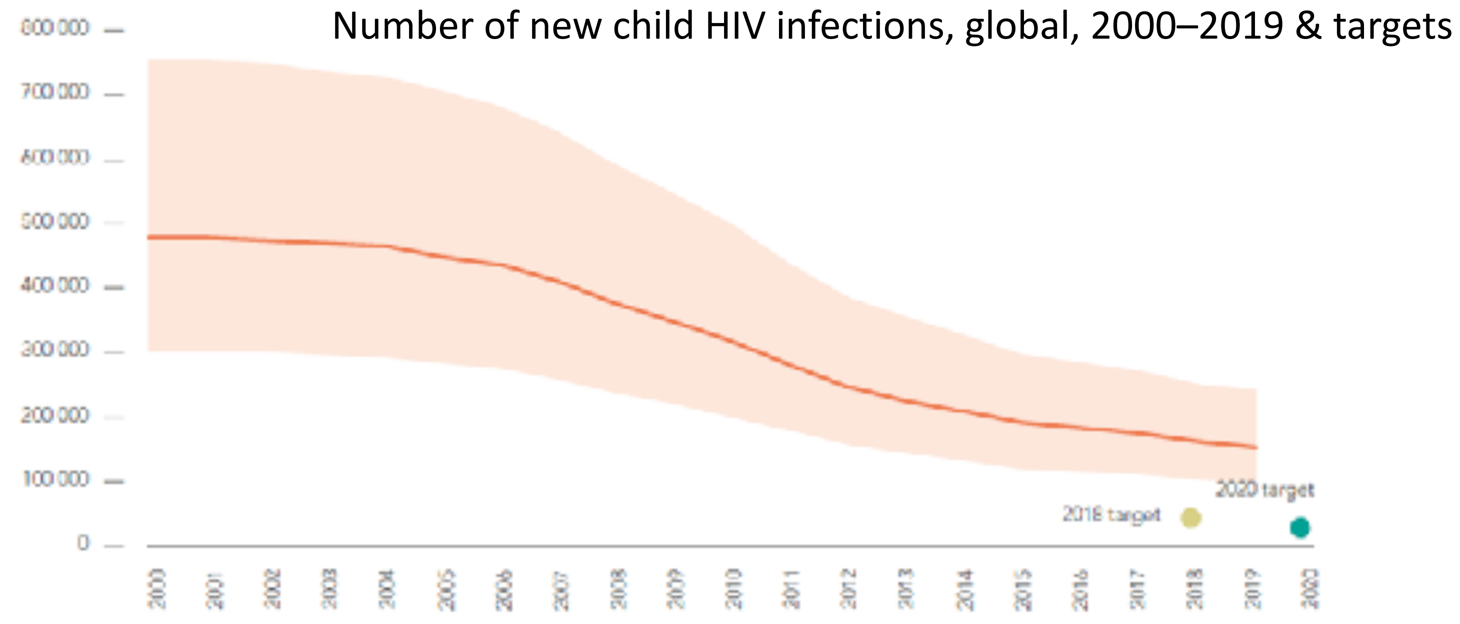
2021

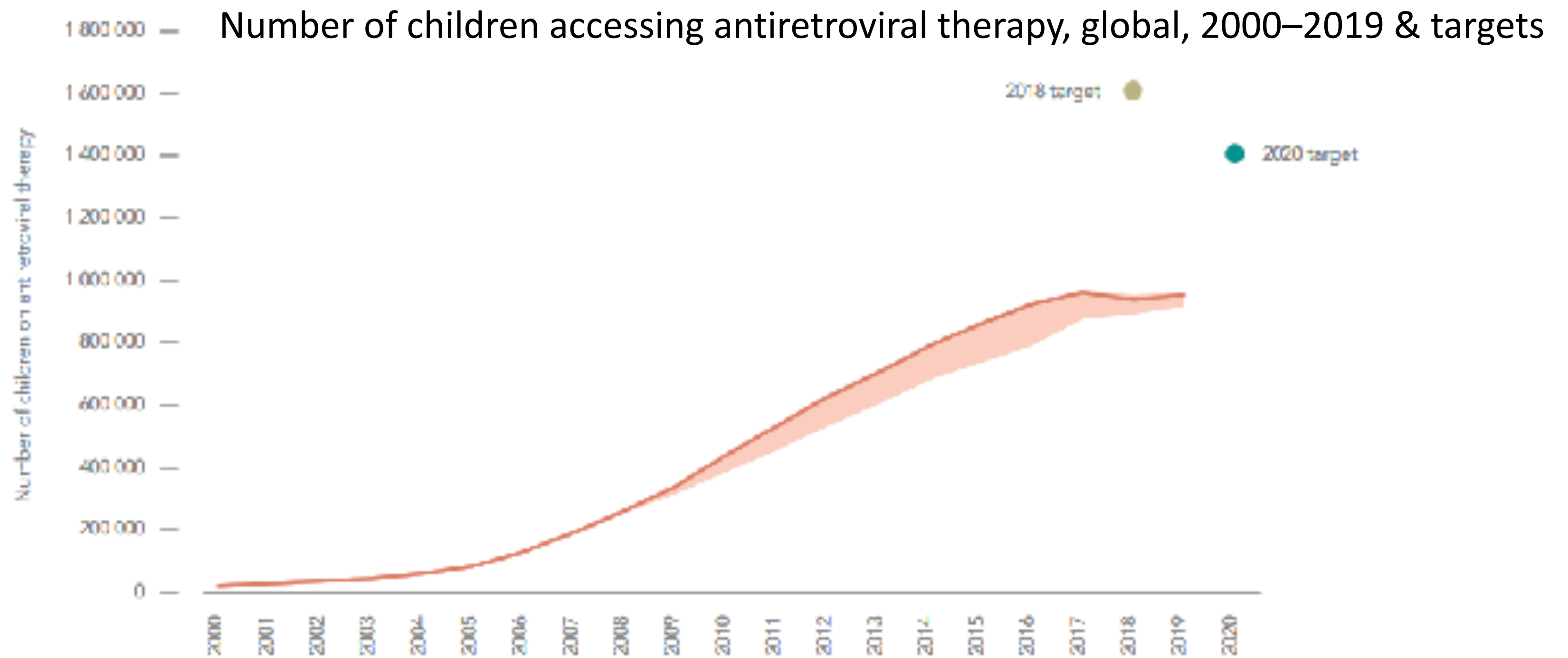
END INEQUALITIES. END AIDS. GLOBAL AIDS STRATEGY 2021-2026

2016-2020 Start Free Stay Free AIDS Free Super Fast-Track strategy

Two commitments for children

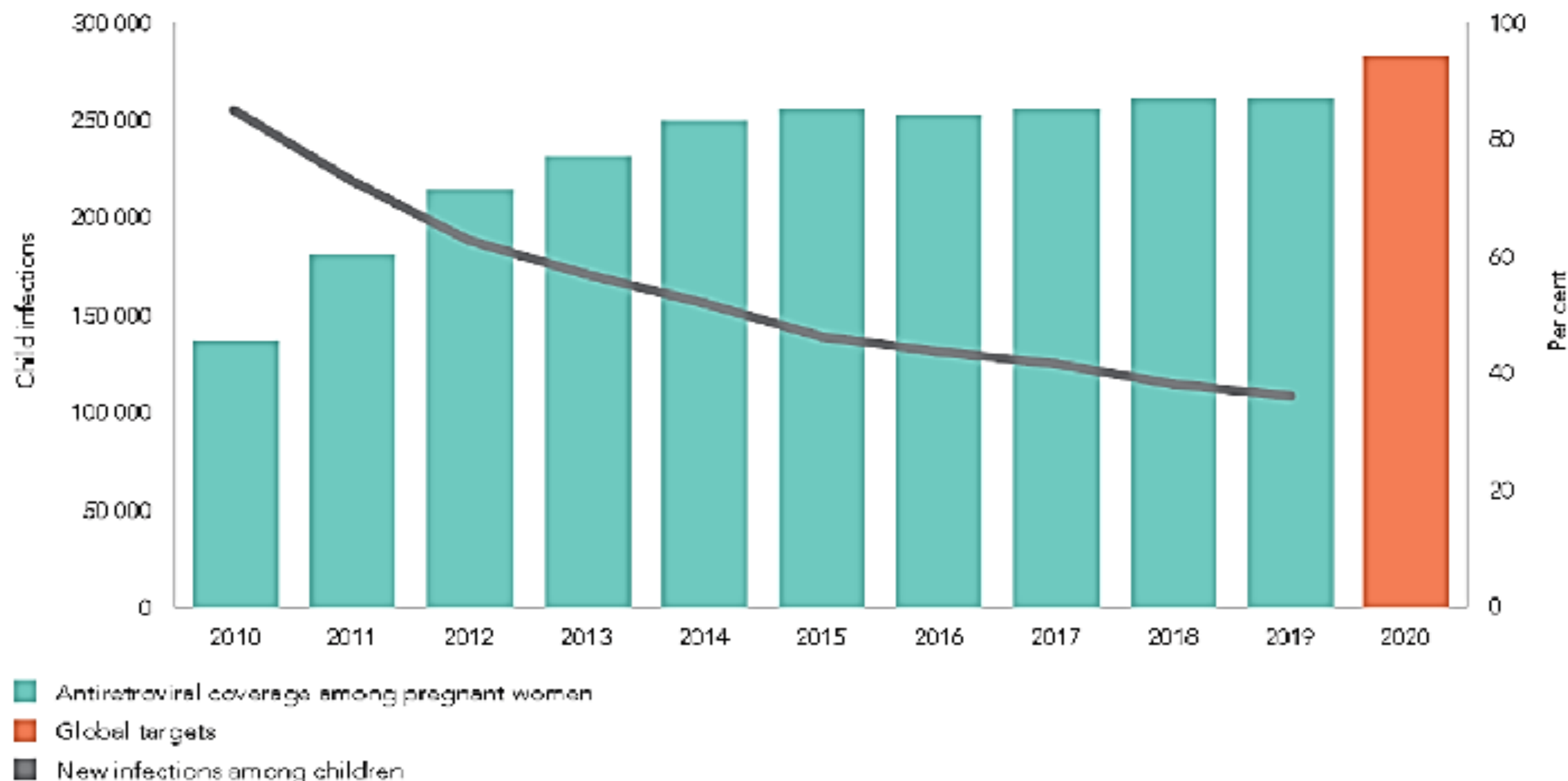
We will miss them both





Source: UNAIDS estimates & Global AIDS monitoring 2020 see https://aidsinfo.unaids.org/

Despite high ART coverage for pregnant women living with HIV (85%), new child infections persist

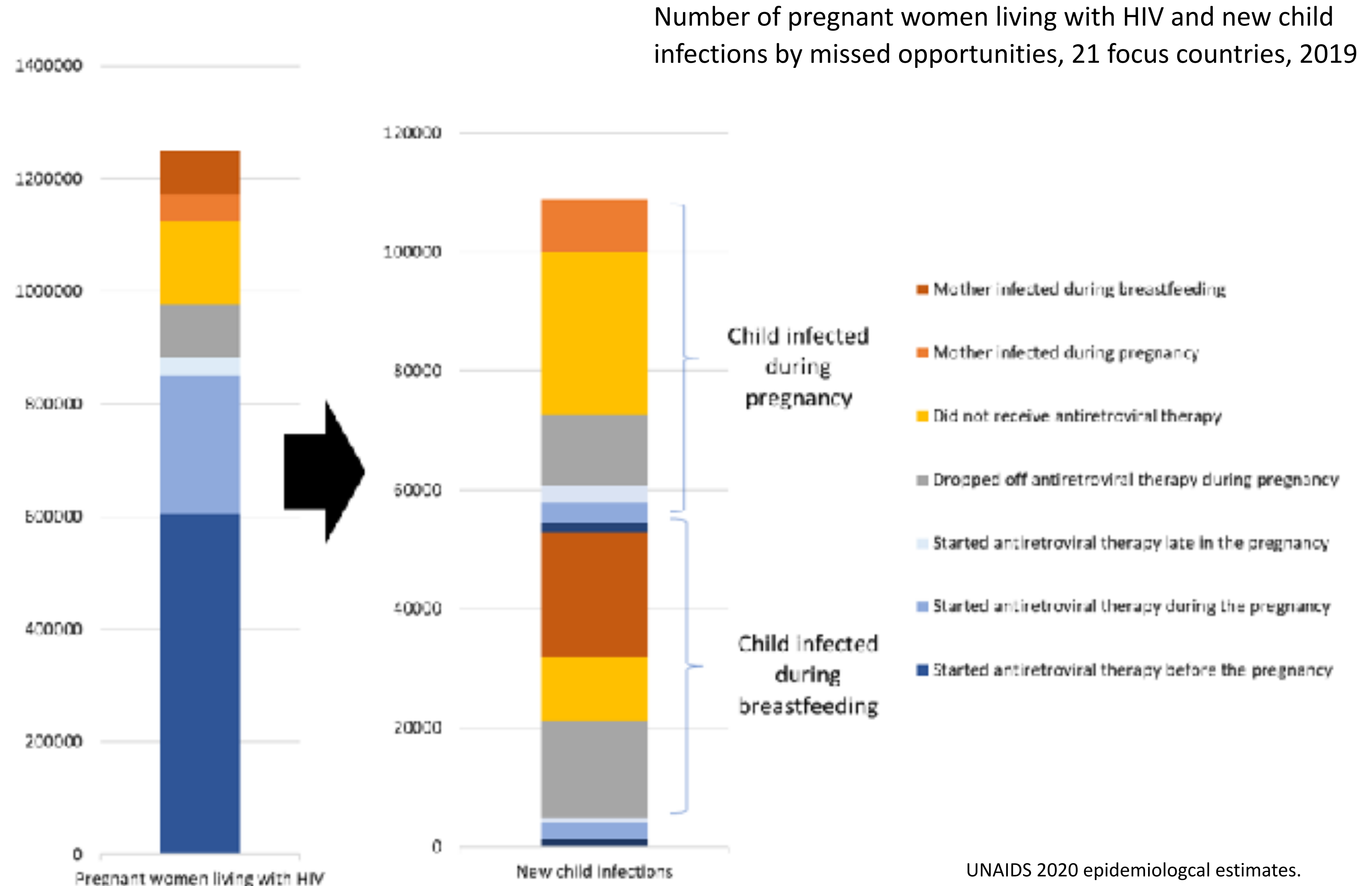


Why do new child infections continue to occur?

Inequalities:

- Poor access to HIV testing & treatment before or early enough in pregnancy
- Women become newly infected with HIV during pregnancy & breastfeeding
- Women do not have the support they need and drop of HIV treatment during pregnancy & breastfeeding

Number of pregnant women living with HIV and new child infections by missed opportunities, 21 focus countries, 2019

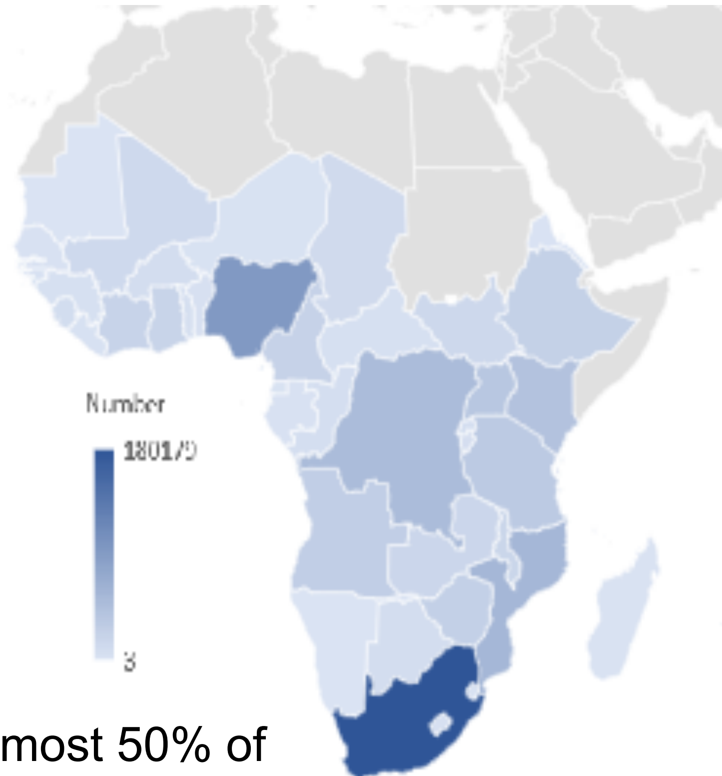


UNAIDS 2020 epidemiologcal estimates.

Inequalities:

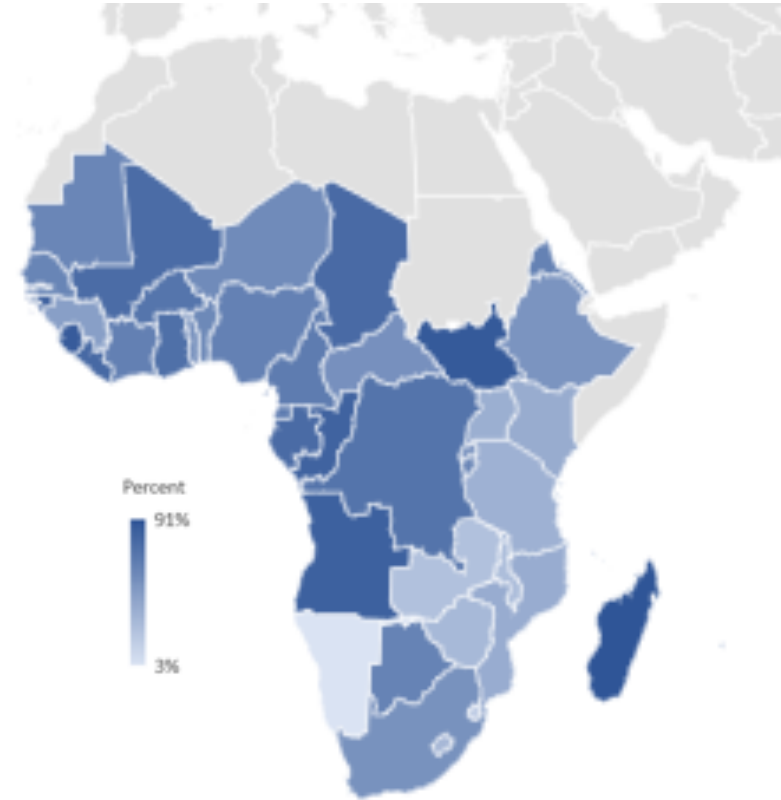
Where are the missing children?

Number of children living with HIV not on treatment



Almost 50% of missing children are in South Africa, Nigeria, Mozambique, DR Congo, and Kenya

Percent of children living with HIV not on treatment



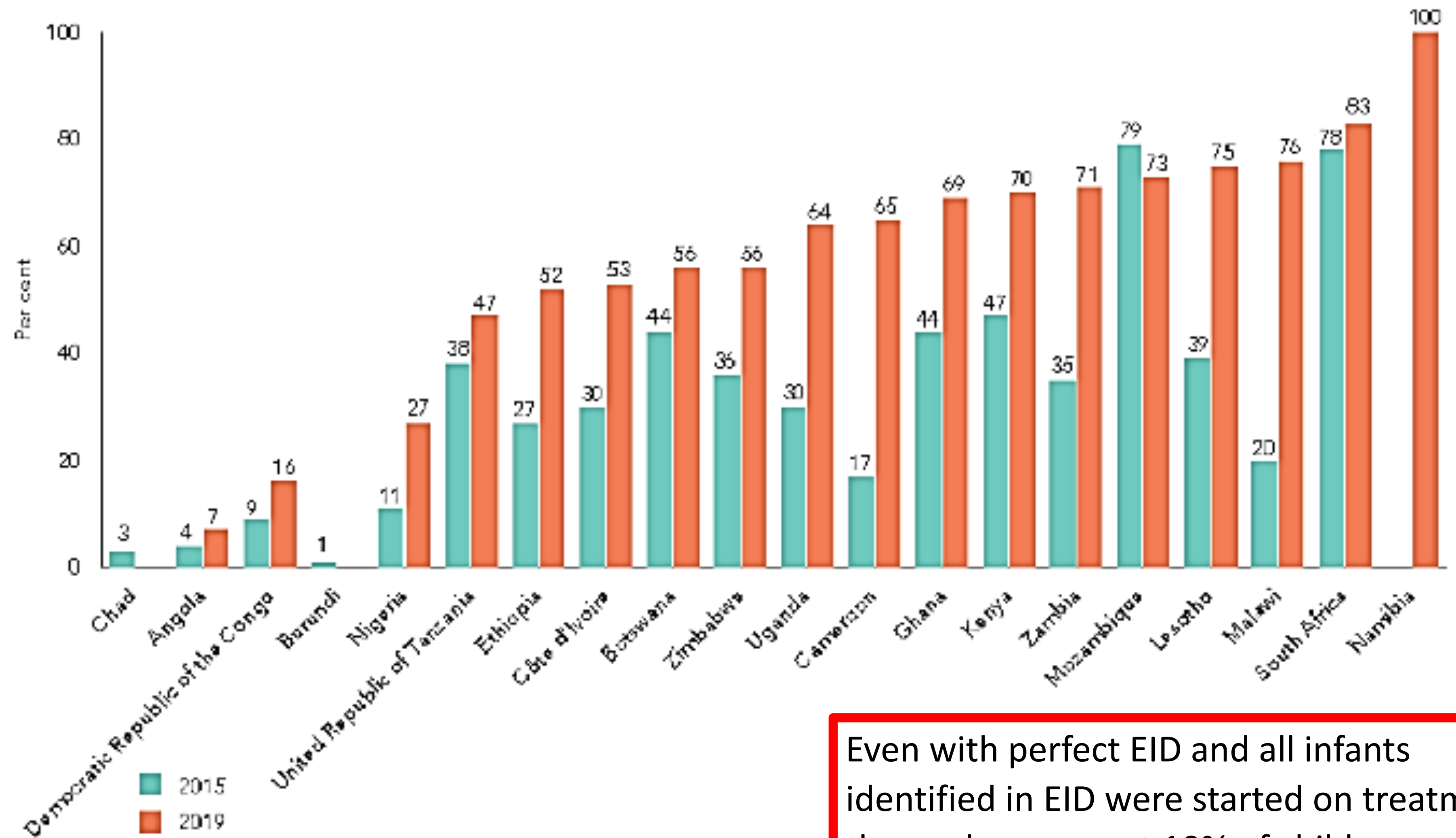
Absolute number and percent of children living with HIV not receiving treatment

Global	850,000	47%
Eastern and southern Africa	490,000	42%
Western and central Africa	290,000	67%
Asia and the Pacific	48,000	35%
Latin America	17,000	54%
Caribbean	6,400	56%
Middle East and North Africa	5,600	58%

Early infant diagnosis is still surprisingly low

Inequalities:

- Some gains since 2015 but not fast enough & many countries lagging
- Move to POC EID
- Use available tools



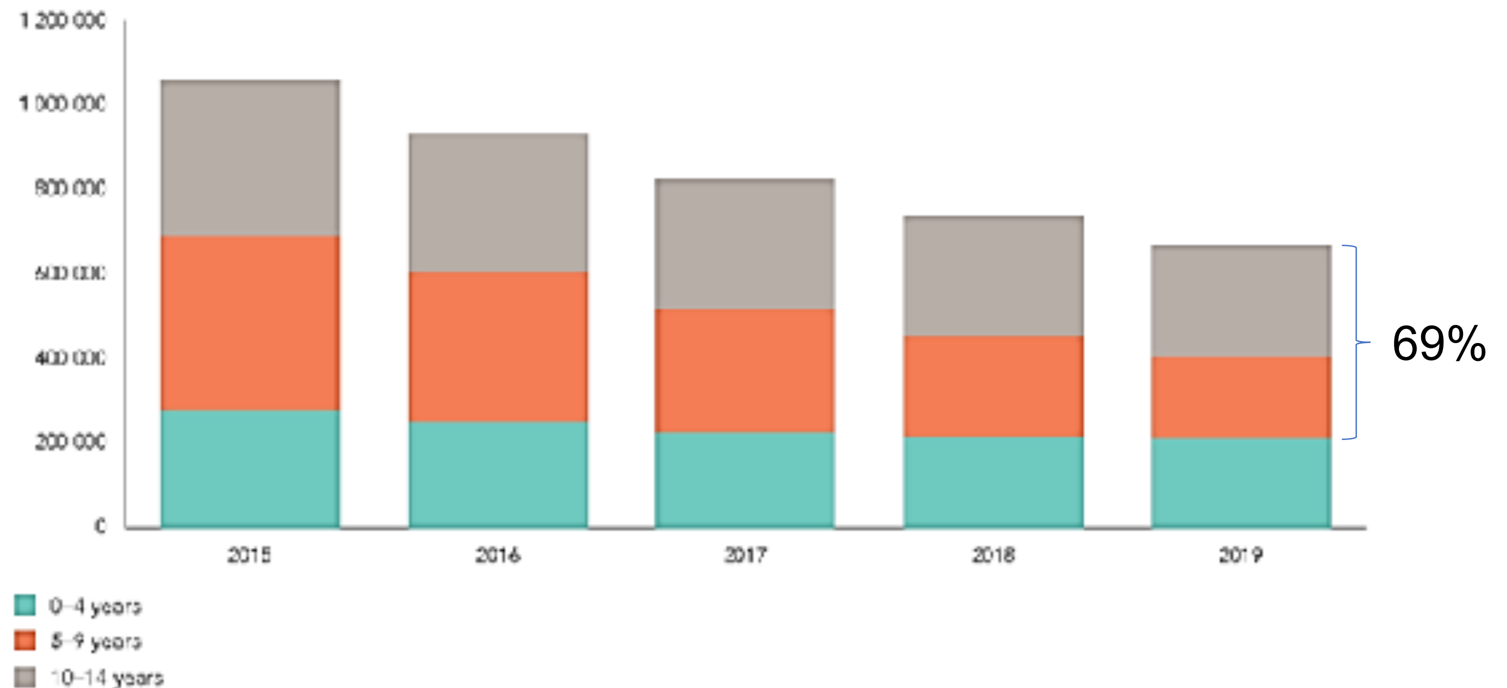
Even with perfect EID and all infants identified in EID were started on treatment, they only represent 10% of children not currently on treatment

Two thirds of children not on treatment are >5 years

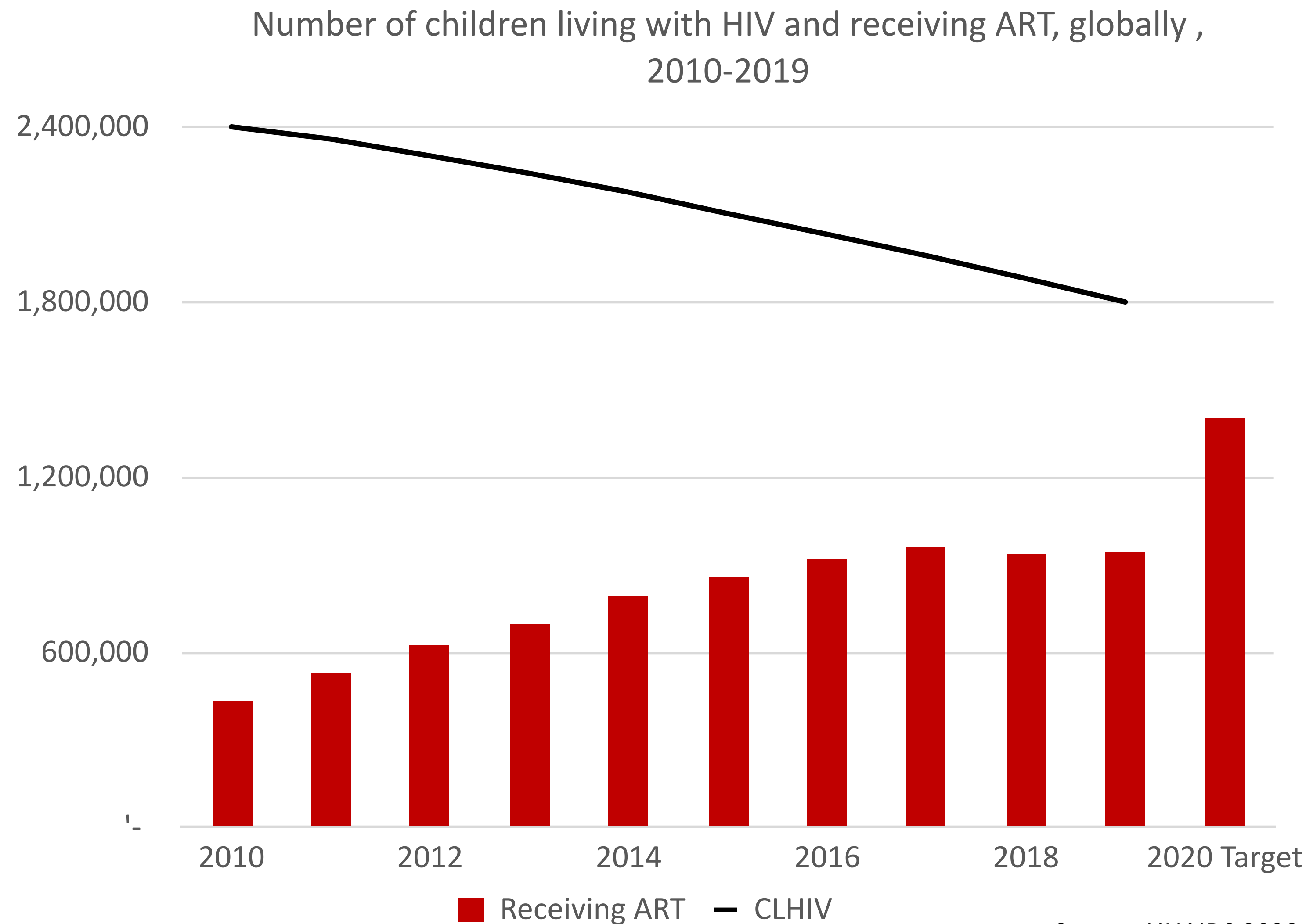
Inequalities:

- Inadequate use of index, family, household, community and self testing to identify older children not yet on treatment
- Slow scale-up of optimized treatment options & formulations to improve retention in care
- Adolescents are vulnerable to dropping off treatment & lack the additional support needed during this transition to adult care

Children living with HIV **not on ART** by age group, focus countries, 2015-2019



Inequalities:
Children living with HIV much less likely to receive treatment than adults or pregnant women globally
(53% v 68% v 85%)



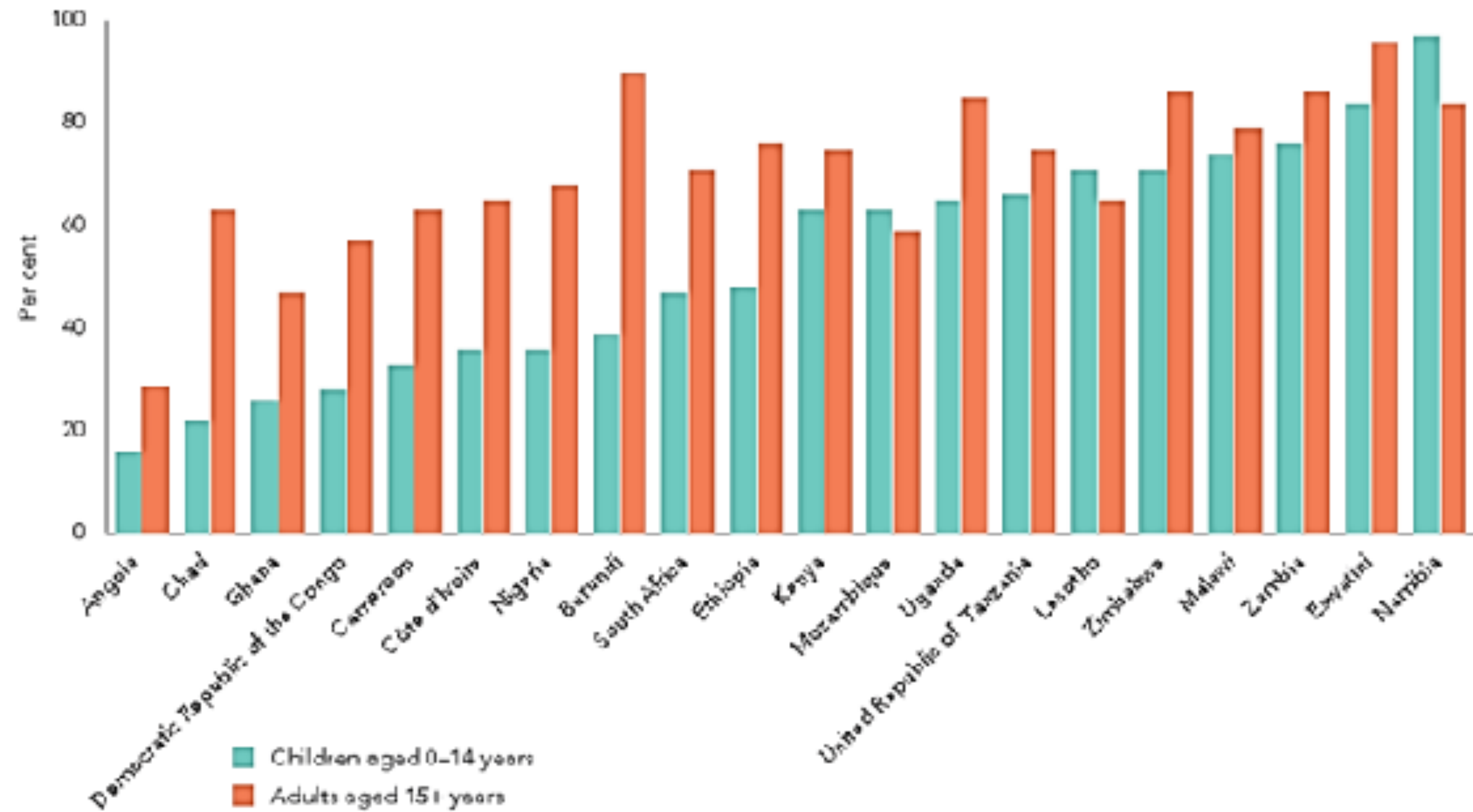
Source: UNAIDS 2020 Estimates

- Numbers of children living with HIV declining as children age into adulthood
- **850,000** children living with HIV ***NOT ON TREATMENT*** in 2019
- COVID-19 hasn't helped.

Paediatric ART is still far behind adult coverage in 17 of 20 focus countries

Inequalities: Children living with HIV much less likely to receive treatment than adults in most focus countries

Figure 9. Antiretroviral therapy coverage among people aged 0–14 and 15+ years for 20 focus countries, 2019



Data for Botswana were not available at the time of publication.
Source: UNAIDS epidemiological estimates, 2020.

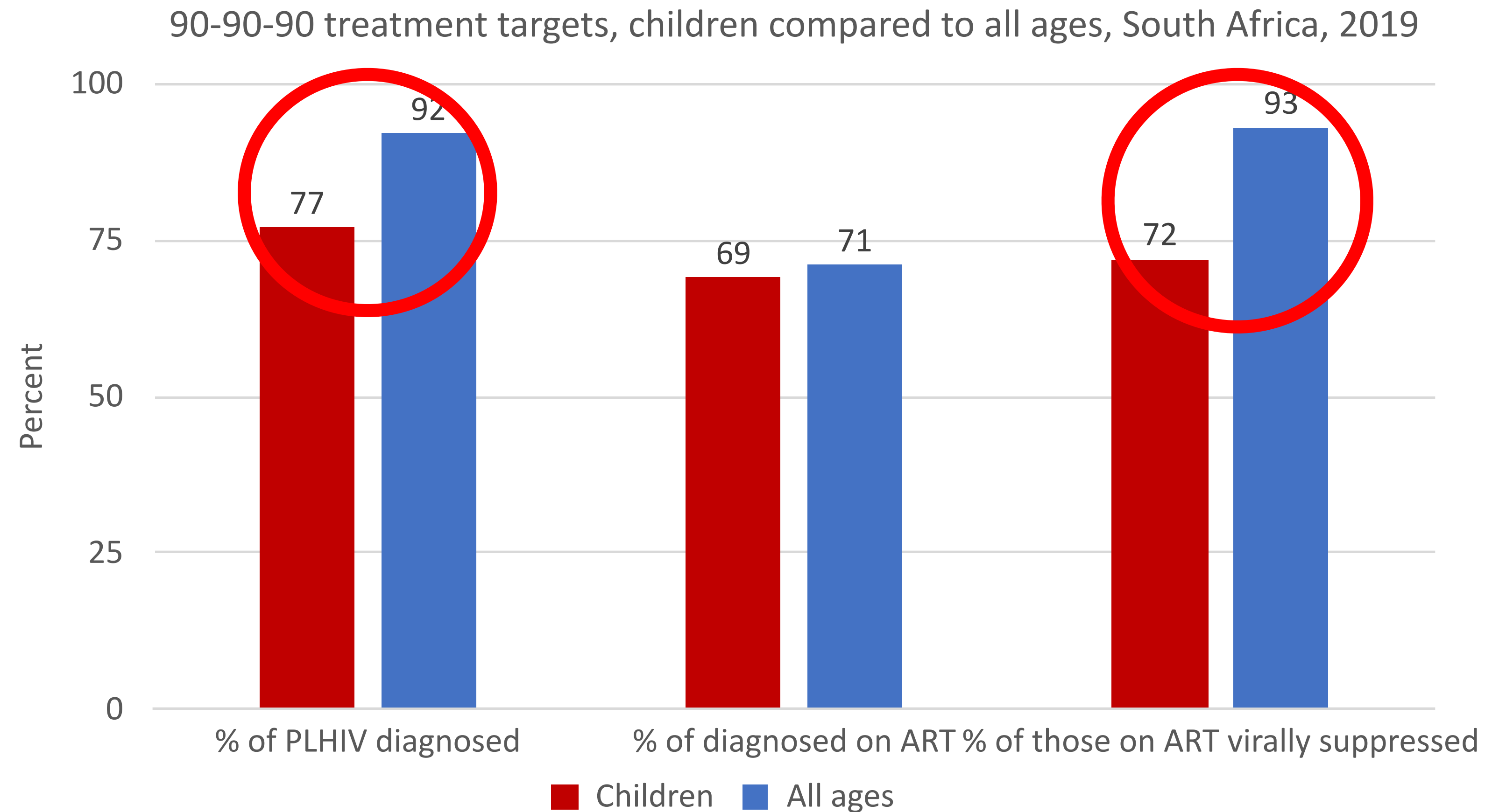
Inequalities:

90-90-90 coverage compared to adults

Children less likely to be diagnosed with HIV

Children on HIV treatment are less likely to have suppressed viral loads

Gaps to the 90-90-90 targets for children v adults: 1st & 3rd 90s



Only 37% of all children living with HIV were virally suppressed in 2019, compared to 60% of adults

Source: Thembisa Model 2020.

End Inequalities. End AIDS
Global AIDS Strategy 2021-2026

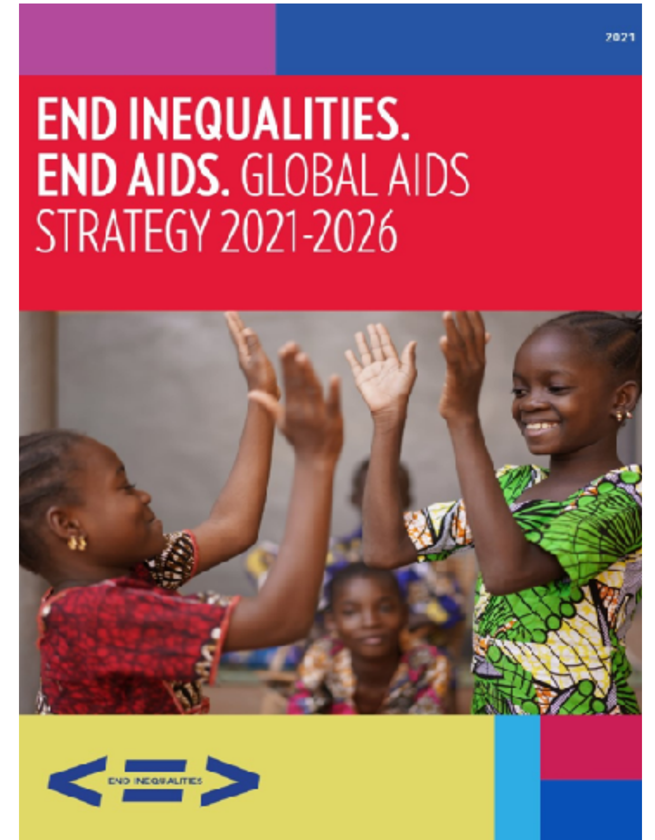
#GlobalAIDSStrategy

#EndInequalities

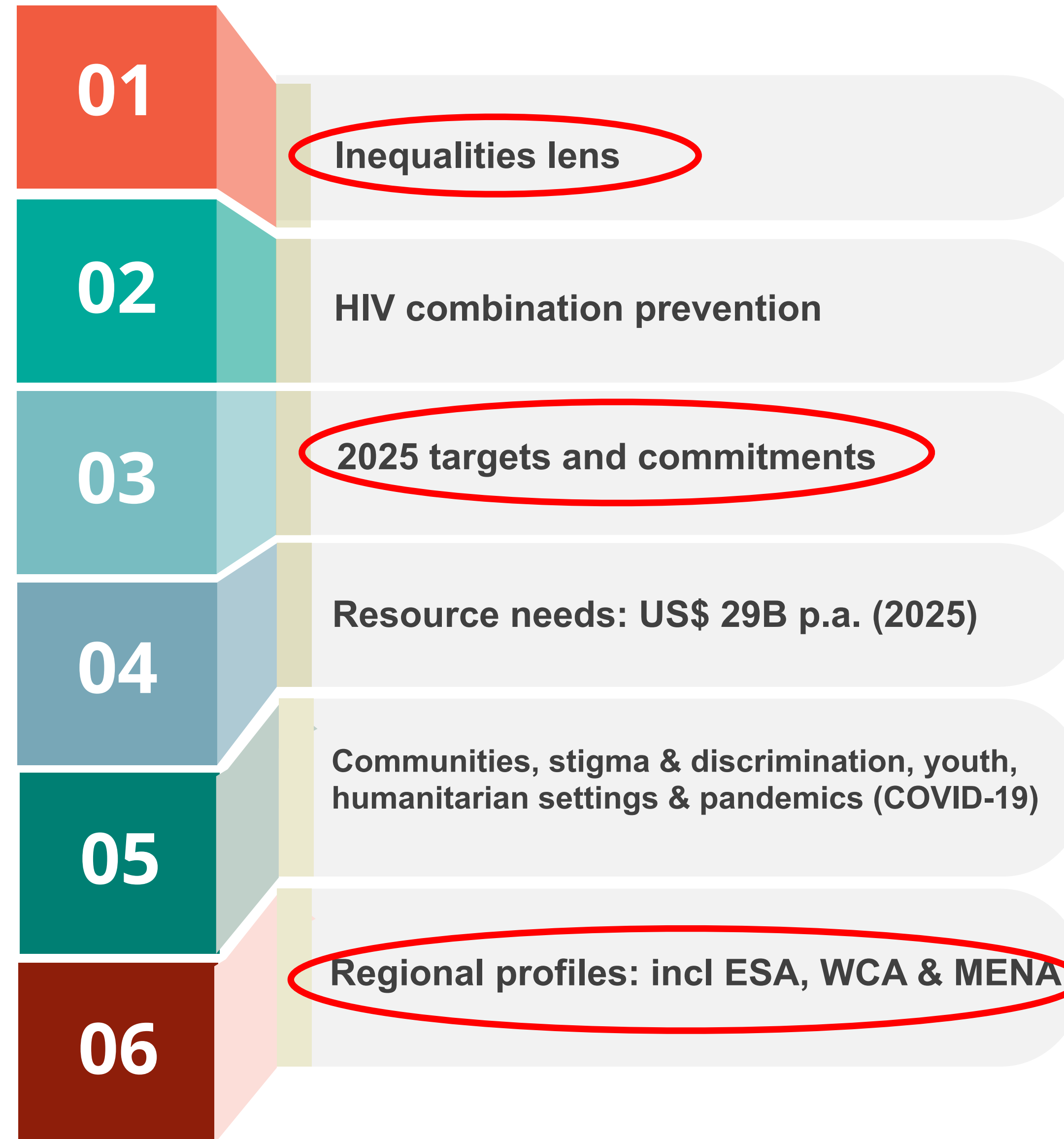
#OntracktoEndAIDS

The Global AIDS Strategy aims to end the inequalities that prevent progress to ending AIDS.

The Strategy features new bold targets and evidence-based actions for 2025 to get every country and every community on-track to end AIDS as a public health threat by 2030.

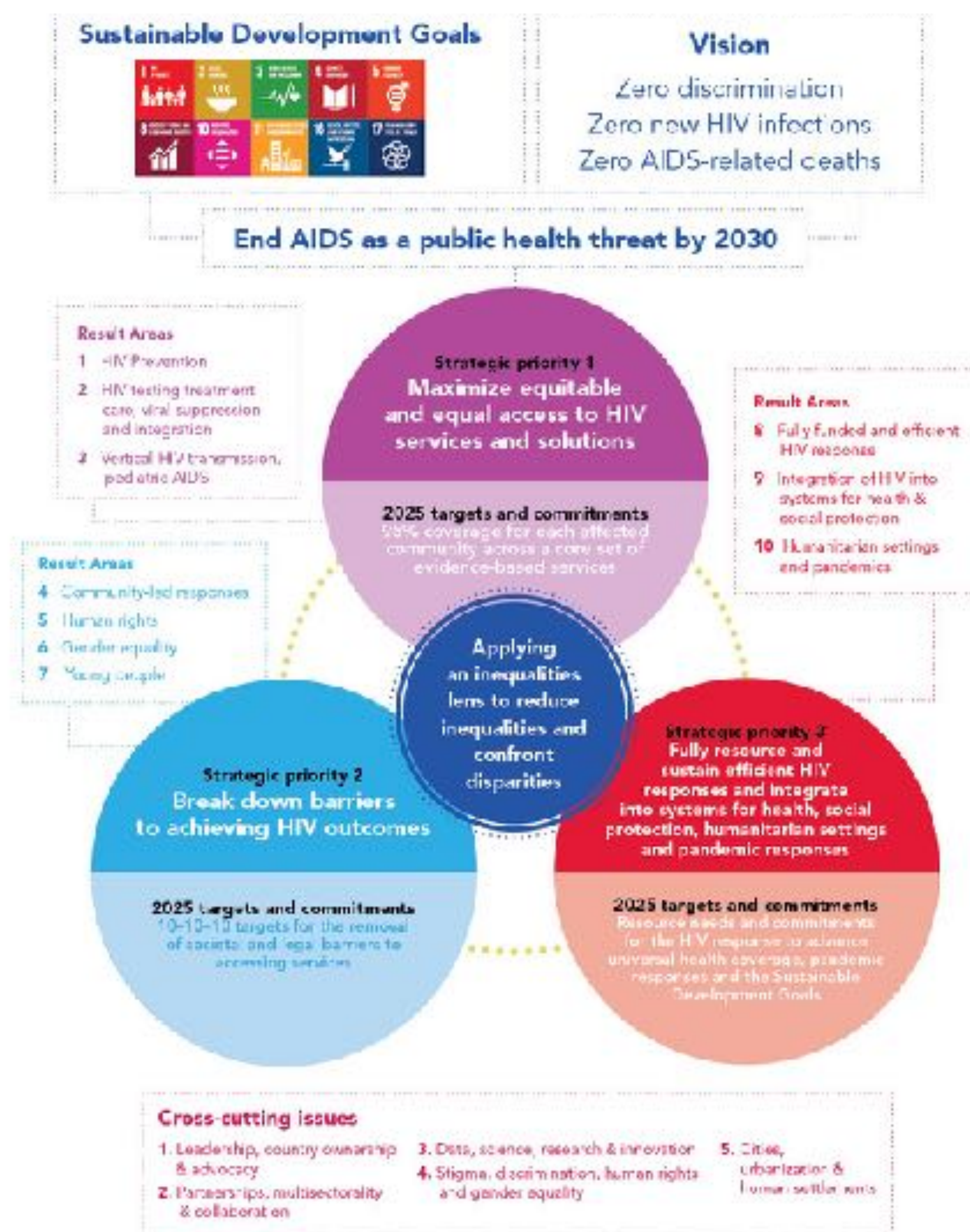


Global AIDS Strategy 2021-2026: What is New / Prioritized



End Inequalities
End AIDS
Global AIDS Strategy 2021-2026:

Framework



UNAIDS

Global AIDS Strategy and targets – child focused

- Inequality lens will focus targets on children and adolescents
- Result areas identify clear actions for children and adolescents

Result Area 2: **Adolescents, youth** and adults living with HIV, especially key populations and other priority populations, know their status and are immediately offered and retained in quality, integrated HIV treatment and care that optimize health and well-being

Result Area 3: Tailored, integrated and differentiated **vertical transmission** and **paediatric** service delivery for **women and children**, particularly for **adolescent girls and young women** in locations with high HIV incidence

Result Area 7: **Young people** fully empowered and resourced to set new direction for the HIV response and unlock the progress needed to end inequalities and end AIDS

Result Area 9 **Integrated systems for health and social protection** schemes that support wellness, livelihood and enabling environments for people living with, at risk of and affected by HIV to reduce inequalities and allow them to live and thrive

DETAILED TARGETS: vertical transmission and paediatrics

Population	Target
Women of reproductive age in high HIV prevalence settings, within key populations and living with HIV	95% have their HIV prevention and sexual and reproductive health service needs met
Pregnant and breastfeeding women	95% of pregnant women are tested for HIV, syphilis and hepatitis B surface antigen at least once and as early as possible. In high HIV burden settings, pregnant and breastfeeding women with unknown HIV status or who previously tested HIV-negative should be re-tested during late pregnancy (third trimester) and in the post-partum period.
Pregnant and breastfeeding women living with HIV	90% of women living with HIV on antiretroviral therapy before their current pregnancy
	All pregnant women living with HIV are diagnosed and on antiretroviral therapy, and 95% achieve viral suppression before delivery
	All breastfeeding women living with HIV are diagnosed and on antiretroviral therapy, and 95% achieve viral suppression (to be measured at 6–12 months)
Children (aged 0–14 years)	95% of HIV-exposed infants receive a virologic test and parents provided the results by age 2 months
	95% of HIV-exposed infants receive a virologic test and parents provided the results after the cessation of breastfeeding
	95–95–95 testing and treatment targets achieved among children living with HIV

2030 | Ending the AIDS epidemic

***2023 Interim Target: 75% treatment coverage fo children

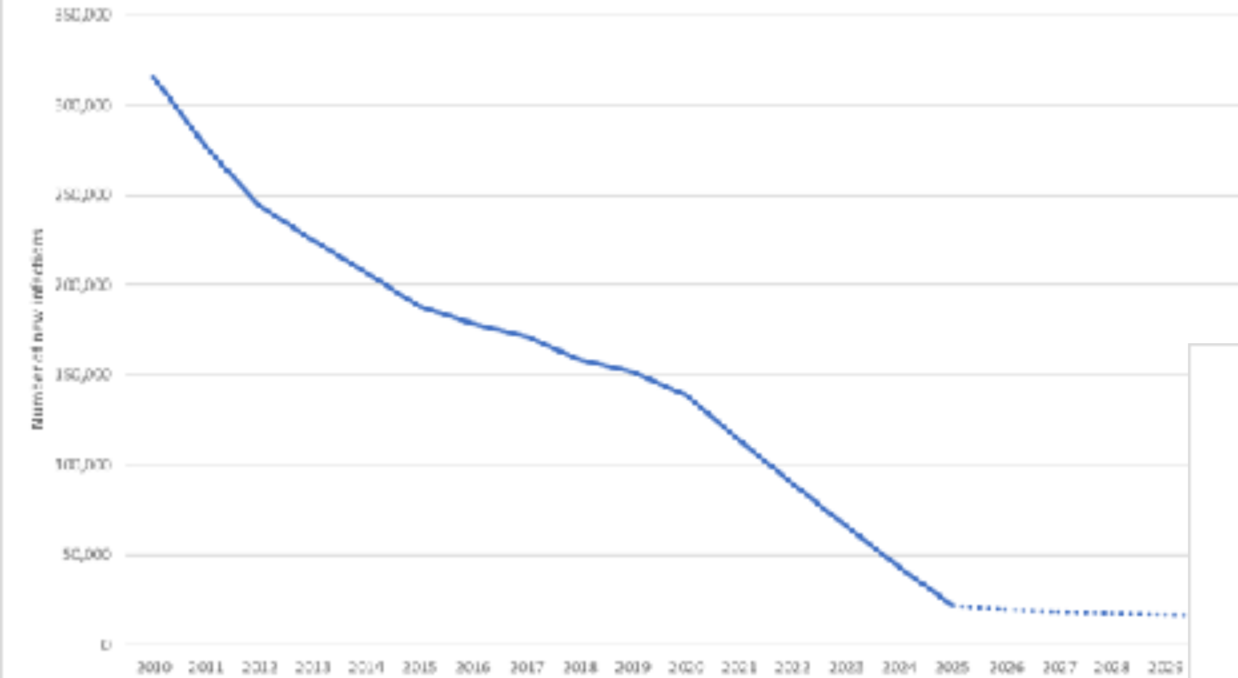
Impact of reaching the strategy’s targets and commitments

Reaching the 2025 targets will reduce new HIV infections to **under 370 000 in 2025**

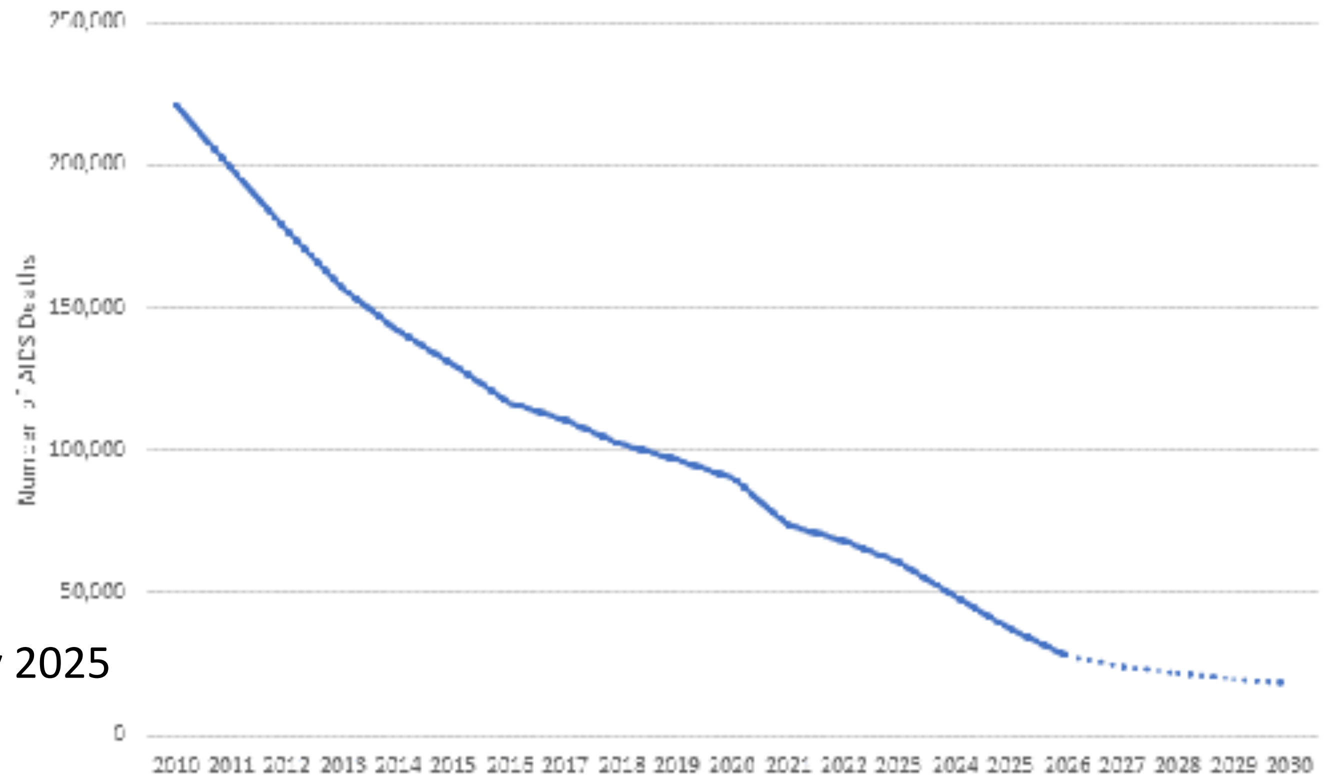
Reaching the 2025 targets will reduce AIDS-related deaths to **under 250 000 in 2025**

This degree of success in the HIV response will put the international community firmly on-track to end the AIDS epidemic in all settings and for all populations by 2030

Impact of reaching the strategy's targets and commitments for children aged 0-14 years



New child infection reduced < 22 000 by 2025



AIDS-related deaths in children reduced to < 37 000 by 2025

NEW YORK | 8–10 JUNE 2021

High-Level Meeting on AIDS
END INEQUALITIES. END AIDS.

Co-facilitators: Namibia, Australia

Multi-stakeholder Task Team Hearing: 23 April

2020 Results Report

2030 | Ending the AIDS epidemic

UNAIDS

Thank you!

Acknowledgements

- Shannon Hader
- Mary Mahy
- Tim Rwabuhemba