Dolutegravir (DTG) has arrived! Where are we now?

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The contents of this presentation are the author's and do not necessarily reflect the views of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), the U.S. Agency for International Development (USAID), or the U.S. Government.

— Dolutegravir (DTG) has arrived! Where are we now and what is next?

WHAT TED ASKED ME TO COVER….

- DTG is in which countries and for which ages? We could probably get that from CHAI.
- What portions of those populations have transitioned?
- What can you say about outcomes (if anything)?
- Any lessons learned from the rollout, from implementation perspective? Stockouts, dissemination, etc?
- OK to restrict to PEPFAR supported, of course.
- Had imagined this primarily about children, but if you had data on pregnant women that'd be great.

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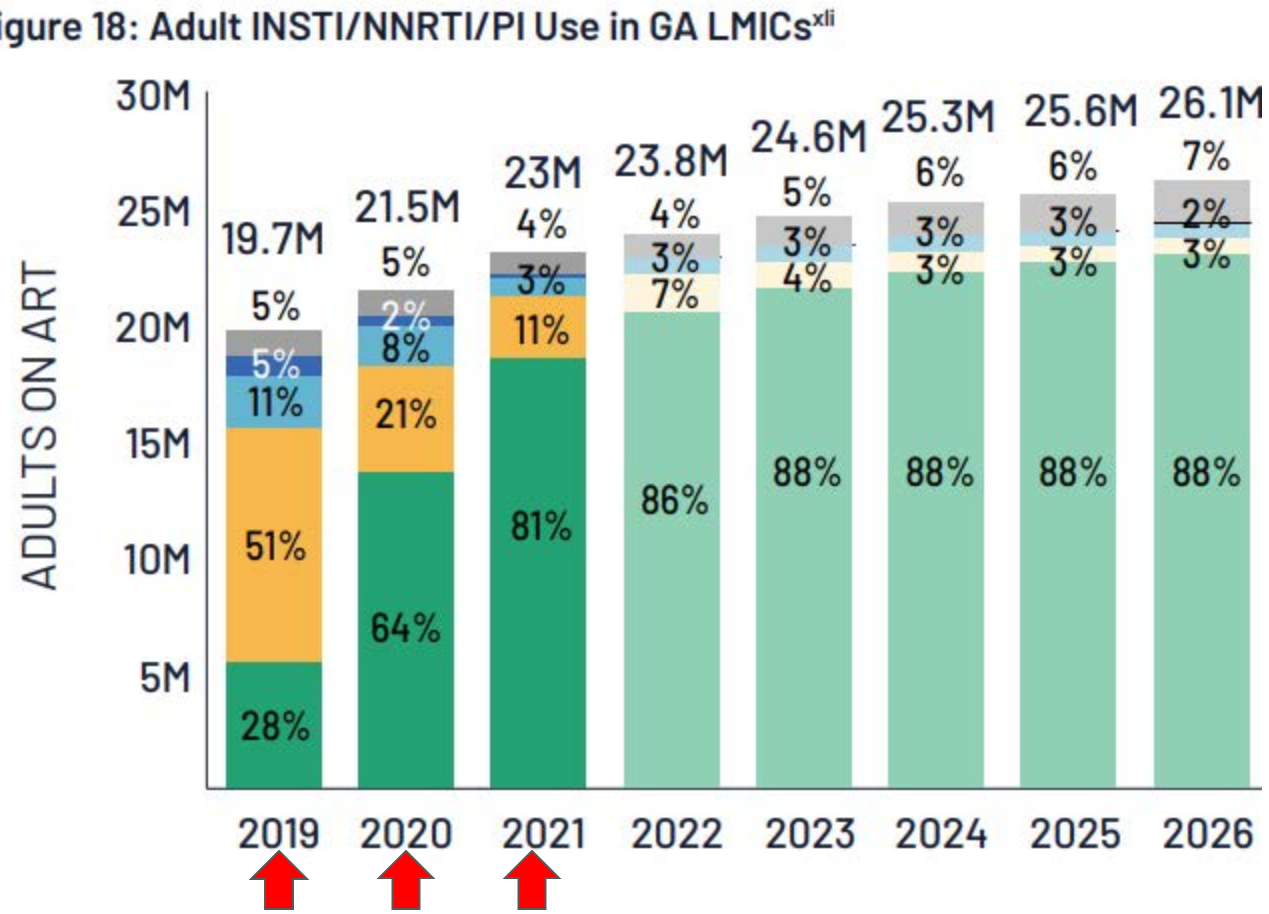
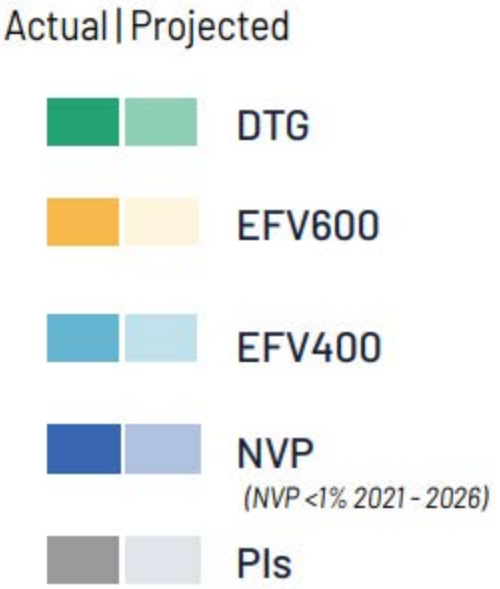
Rapid Scale-up of Adult DTG globally (CHAI 2022)

Figure 18: Adult INSTI/NNRTI/PI Use in GA LMICs[xli]



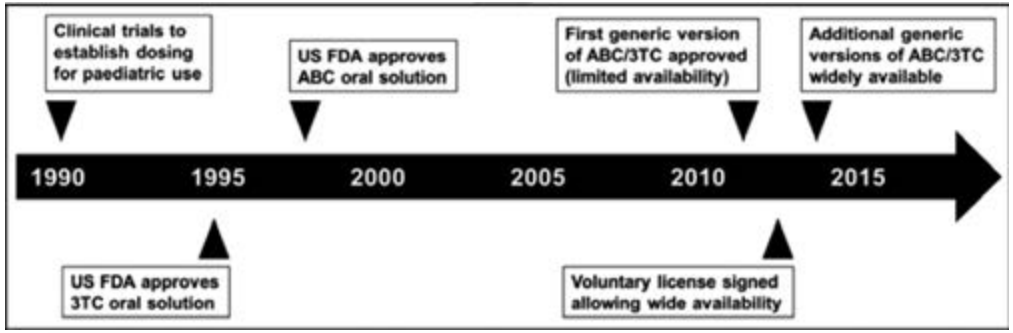


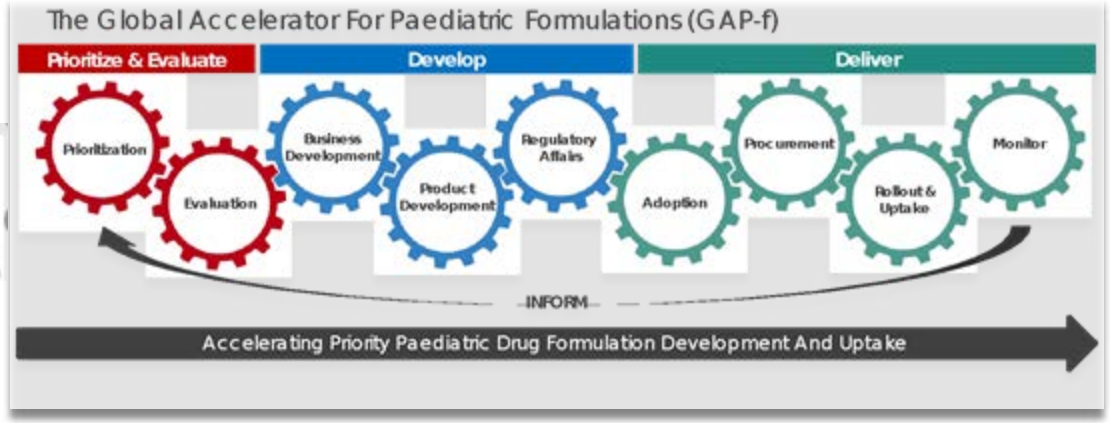
https://chai19.wpenginepowered.com/wp-content/uploads/2022/12/2022-CHAI-HIV-Market-Report-12.8.22.pdf

COMMENTARY

Shortening the decade-long gap between adult and paediatric drug formulations: a new framework based on the HIV experience in low- and middle-income countries

Martina Penazzato[1,*], Linda Lewis[2], Melynda Watkins[2], Vineet Prabhu[2], Fernando Pascual[3], Martin Auton[4], Wesley Kreft[5], Sébastien Morin[6], Marissa Vicari[6], Janice Lee[7], David Jamieson[8] and George K Siberry[9]





WHO Initiative: Global Accelerator for Pediatric formulations (GAP-f).
Originally for HIV, now for all drugs important for children in LMICs

Golin R et al. Journal of the International AIDS Society 2020, 23:e25660
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25660/full | https://doi.org/10.1002/jia2.25660

JIAS
JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

VIEWPOINT

The promise of paediatric dolutegravir

Rachel Golin, Jeffrey M Samuel, B Ryan Phelps, Udita Persaud, Christine Y Malati and George K Siberry

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*These authors have contributed equally to the work.

The NEW ENGLAND JOURNAL of MEDICINE
N Engl J Med 2021;385:2531-43.

ORIGINAL ARTICLE

Dolutegravir as First- or Second-Line Treatment for HIV-1 Infection in Children

A. Turkova, E. White, H.A. Mujuru, A.R. Kekitiinwa, C.M. Kityo, A. Violari, A. Lugemwa, T.R. Cressey, P. Musoke, E. Variava, M.F. Cotton, M. Archary, T. Puthanakit, O. Behuhuma, R. Kobbe, S.B. Welch, M. Bwakura-Dangarembizi, P. Amuge, E. Kaudha, L. Barlow-Mosha, S. Makumbi, N. Ramsagar, C. Ngampiyaskul, G. Musoro, L. Atwine, A. Liberty, V. Musiime, D. Bbuye, G.M. Ahimbisibwe, S. Chalermpantmetagul, S. Ali, T. Sarfati, B. Wynne, C. Shakeshaft, A. Colbers, N. Klein, S. Bernays, Y. Saïdi, A. Coelho, T. Grossele, A. Compagnucci, C. Giaquinto, P. Rojo, D. Ford, and D.M. Gibb, for the ODYSSEY Trial Team*

Dolutegravir (DTG) efficacious, once-daily, palatable, dispersible tablet, high barrier to drug resistance – and recommended by WHO for all 3+kg/4+weeks old!

WHO Consolidated HIV Recommendations (July 2021)

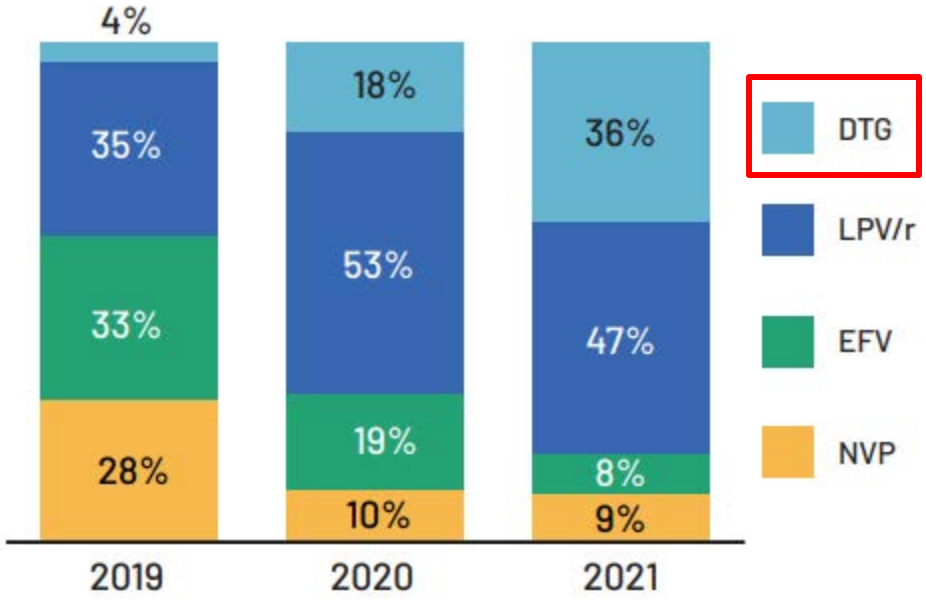
Populations	Preferred first-line regimen
Adults and adolescents	TDF + 3TC (or FTC) + DTG[a,b]
Children	ABC + 3TC + DTG[d]
Neonates	AZT (or ABC) + 3TC + RAL[h]

Table 4.4 Transition to optimal ARV drug regimens for children who are established on ART[a]

Current regimen	Weight	Optimal regimen for transition	Considerations
AZT + 3TC + NVP AZT + 3TC + EFV	<30 kg	ABC + 3TC plus DTG	As long as above 3 kg and four weeks old
ABC + 3TC + NVP ABC + 3TC + EFV ABC + 3TC + LPV/r AZT + 3TC + LPV/r	>30 kg	TLD	-

[a]See Chapter 7 for definition of being established on ART.

Estimated Pediatric Third-Position Drug Use in GA LMICs CHAI 2022



Adults 28% ->81% over same 3-year time period

https://chai19.wpenginepowered.com/wp-content/uploads/2022/12/2022-CHAI-HIV-Market-Report-12.8.22.pdf

A WORD ABOUT PEPFAR DATA

- Monitoring, Evaluation, and Reporting (MER) Indicators for reporting results
  - Summary and description of MER indicators: https://www.state.gov/pepfar-fy-2023-mer-indicators/
  - Publicly accessible PEPFAR data: https://data.pepfar.gov/
  - Rich set of routinely reported data covering all aspects of PEPFAR-supported programming globally
  - **Aggregate data with disaggregates - NO LINKED DATA or RELATIONAL DATABASE**
- In many countries, there are national digital health systems, electronic medical records and implementing partner (IP) databases related to HIV services - but these data are not routinely available to PEPFAR at HQ

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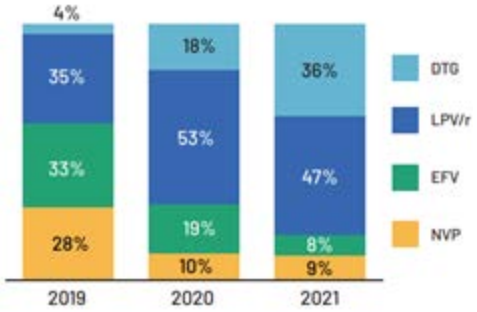
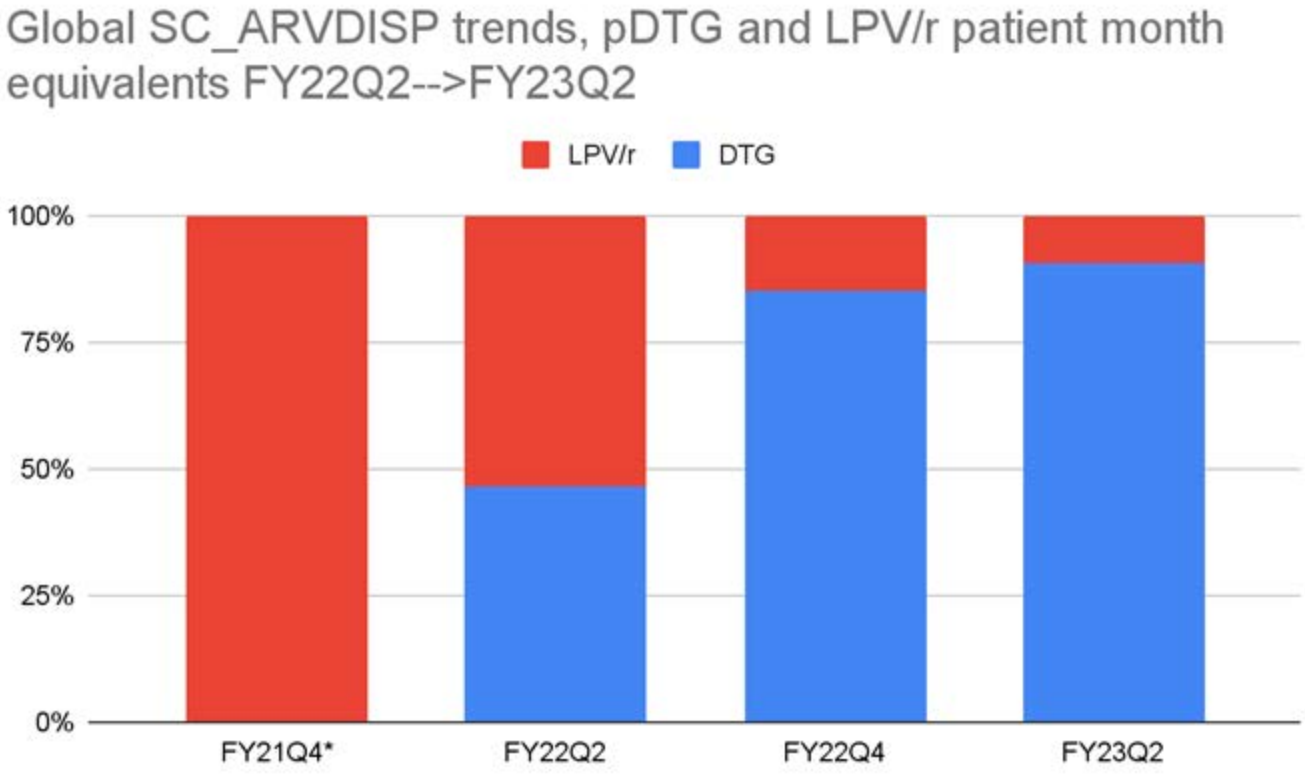
Shift in proportion of LPVr vs DTG dispensed for children

SC_ARVDISP: The number of adult and pediatric ARV bottles (units) dispensed by ARV drug category …

By March 2023, DTG almost completely replaced LPVr dispensing for children in PEPFAR-supported programs

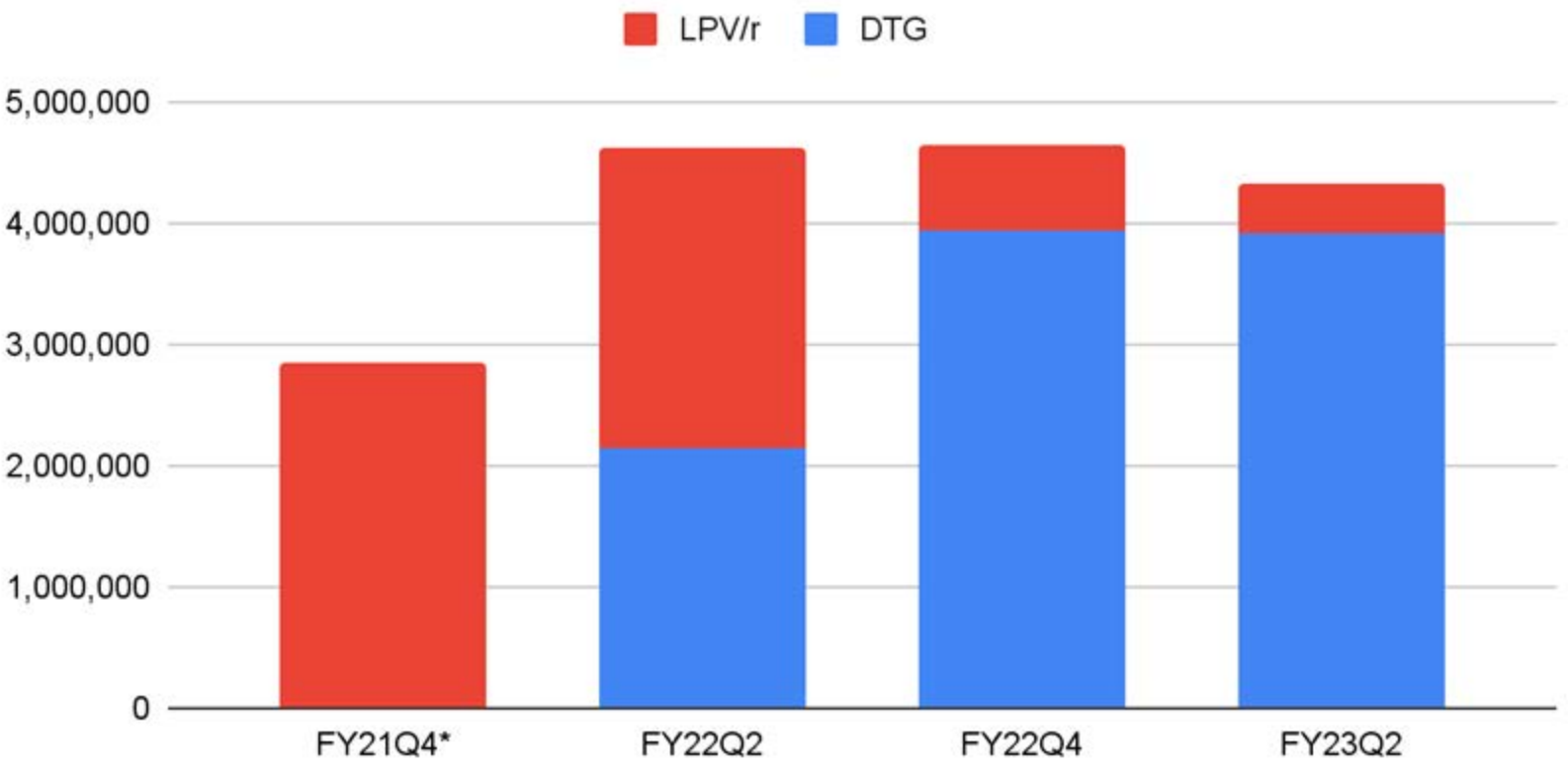
[Reminder below of global DTG uptake thru 2021]





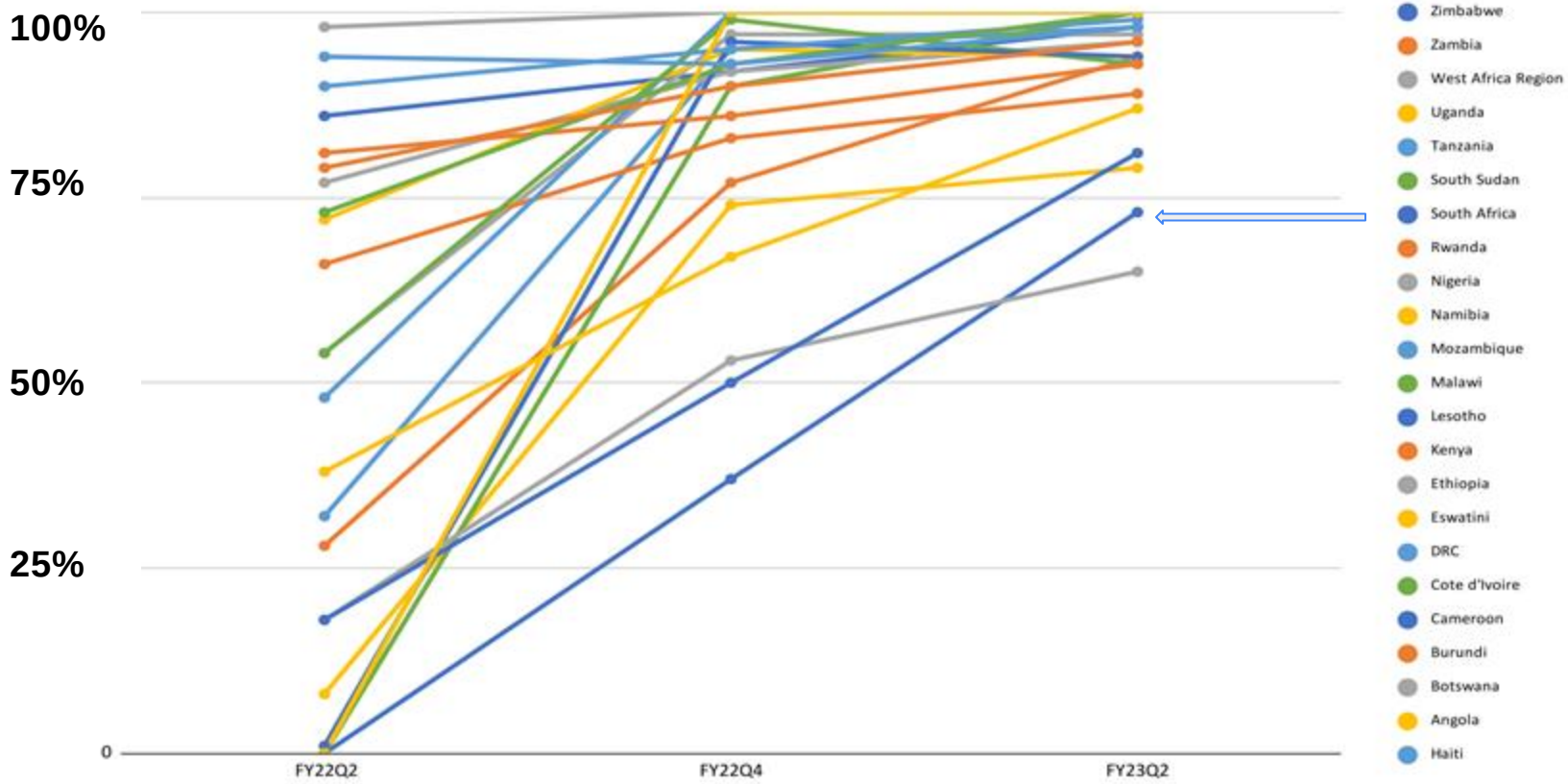
Data from USAID Adult MMD workbook in Tableau FY23Q3 workbook

SAME RESULTS PRESENTED AS **VOLUME** OF MONTHS of DRUG DISPENSED



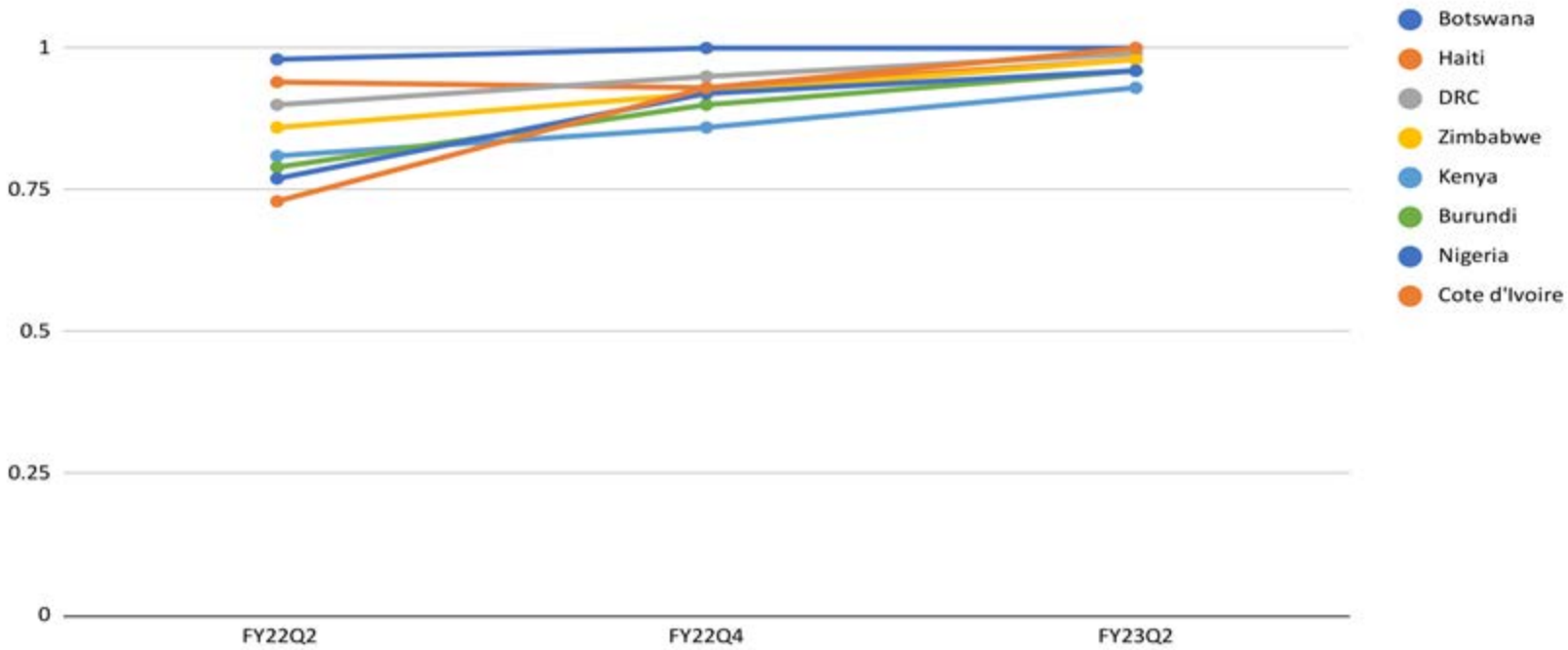
Data from USAID Adult MMD workbook in Tableau FY23Q3 workbook

pDTG Percentage of SC_ARVDISP trend by Country, FY22Q2--FY23Q2



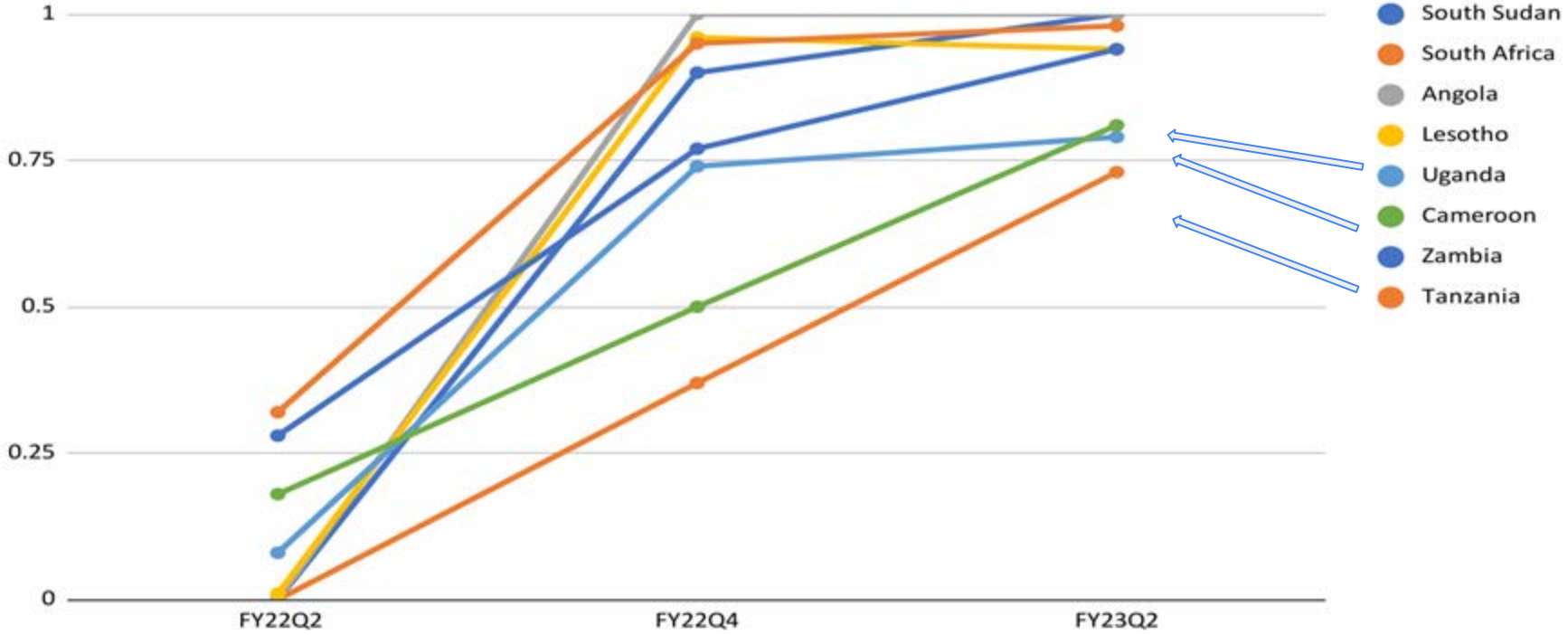
Data from USAID Adult MMD workbook in Tableau FY23Q3 workbook

Early Adopters Percentage pDTG of SC_ARVDISP by Country, FY22Q2-->FY23Q2



Data from USAID Adult MMD workbook in Tableau FY23Q3 workbook

Rapid Transition Percentage pDTG of SC_ARVDISP by Country, FY22Q2-->FY23Q2



Data from USAID Adult MMD workbook in Tableau FY23Q3 workbook

CONTEMPORANEOUS TRENDS

- Since we can't directly link ARV dispensed or other regimen information to individual patient data, we can only look at how relevant aggregate results changed over the same time period
  - TX_CURR = Number on ART (fine age disaggregates)
  - TX_PVLS
    - VLC: Proxy measure of viral load coverage, based on VL tests sent and number on ART for at least 3 months
    - VLS: Proxy measure of viral load suppression, based on number of VL <1000 out of all VL tests sent
  - MMD (disagg of TX_CURR) = multi month dispensing (at least 3 months of drug at a time) (<15 vs 15+ yrs old)

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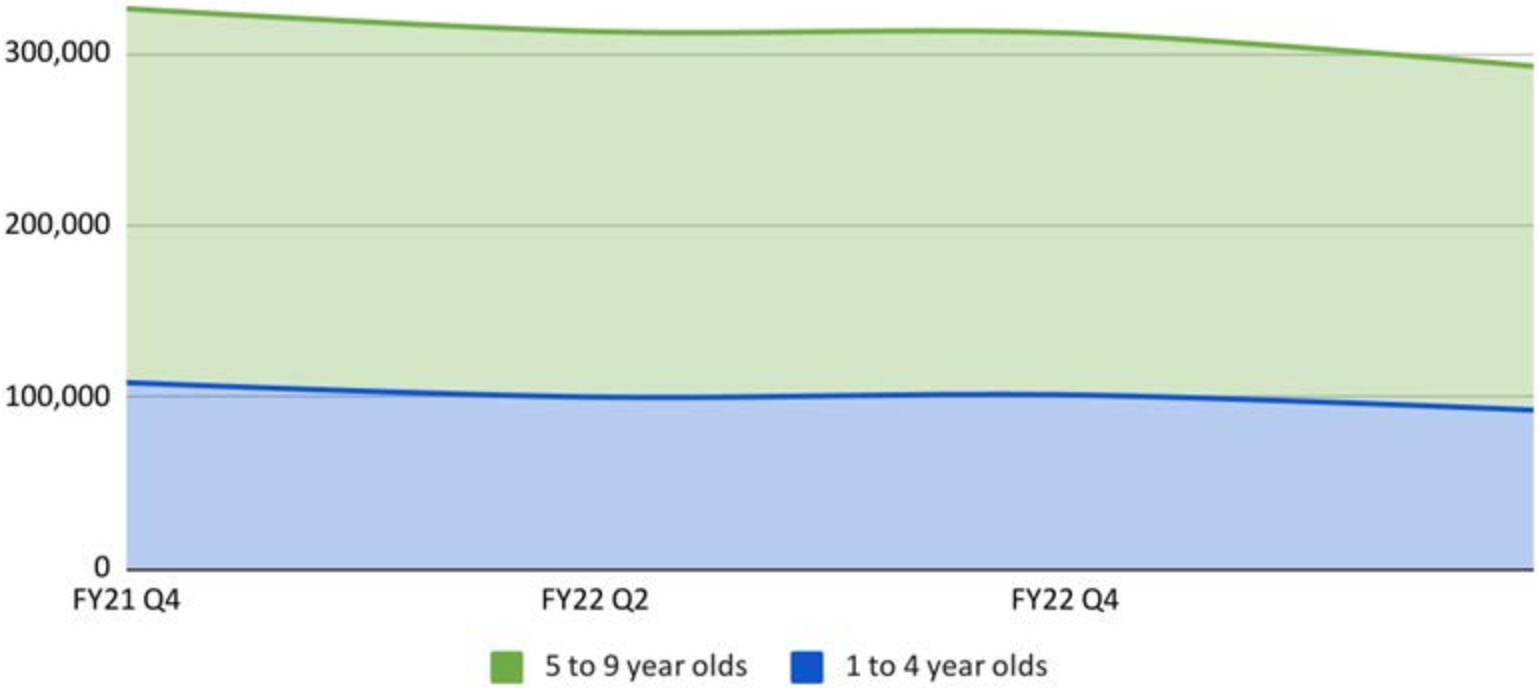
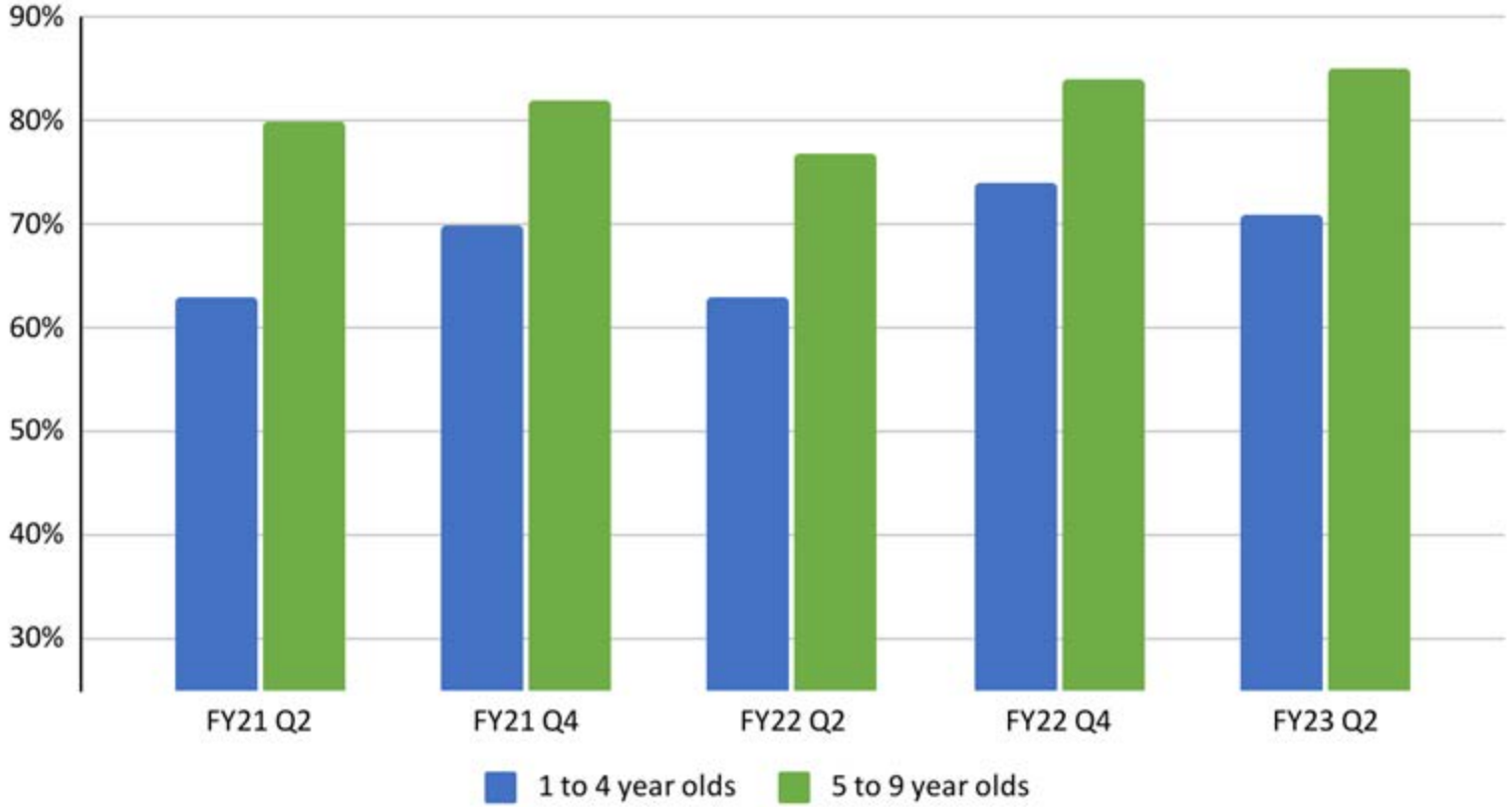
GLOBAL TRENDS for CHILDREN on ART, 1-4 and 5-9 years old, FY21Q4 -> FY23Q2



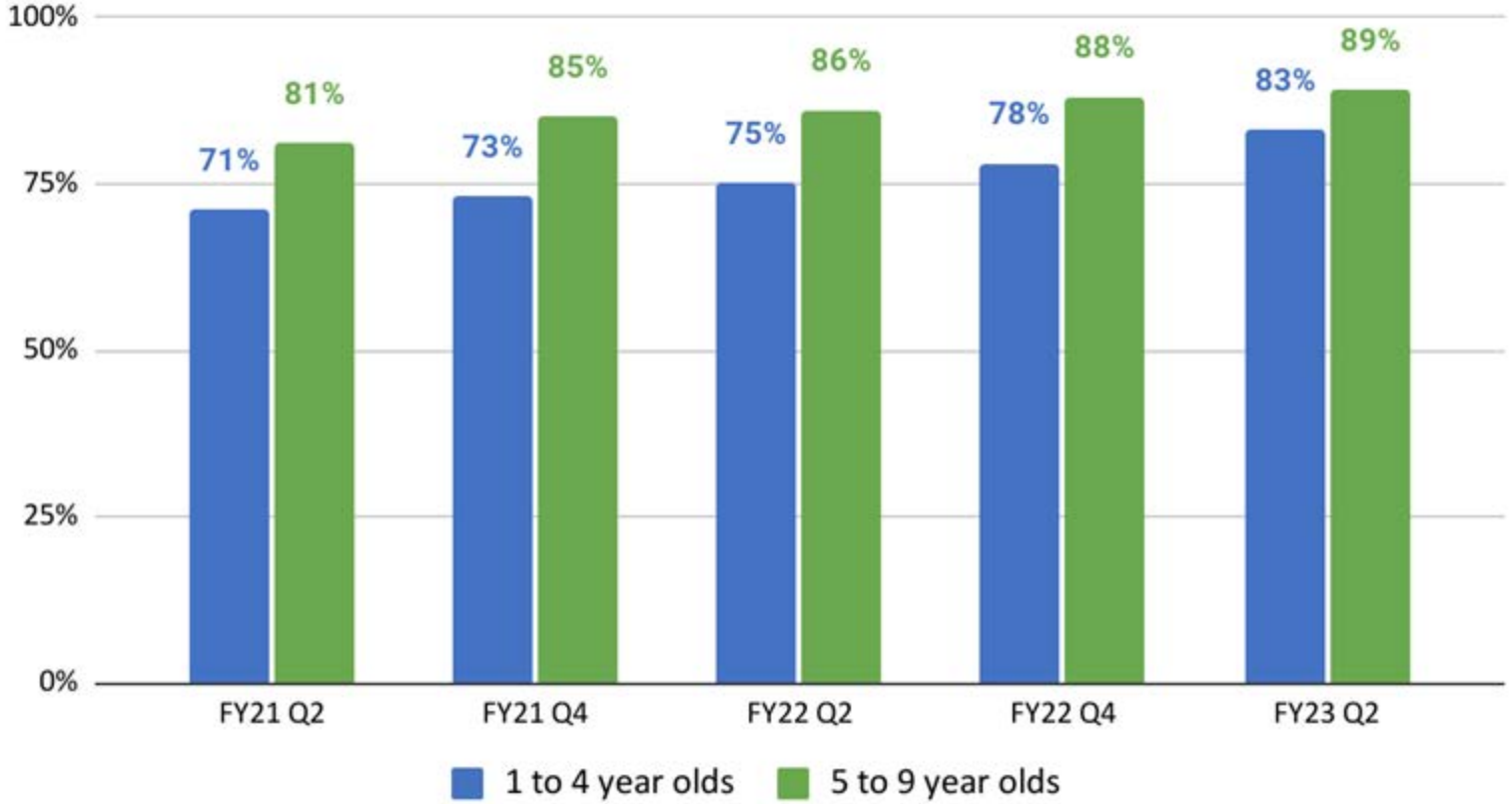
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

GLOBAL Viral Load Coverage (VLC) IN CLHIV, 1-4 and 5-9 years old, FY21Q2->FY23Q2



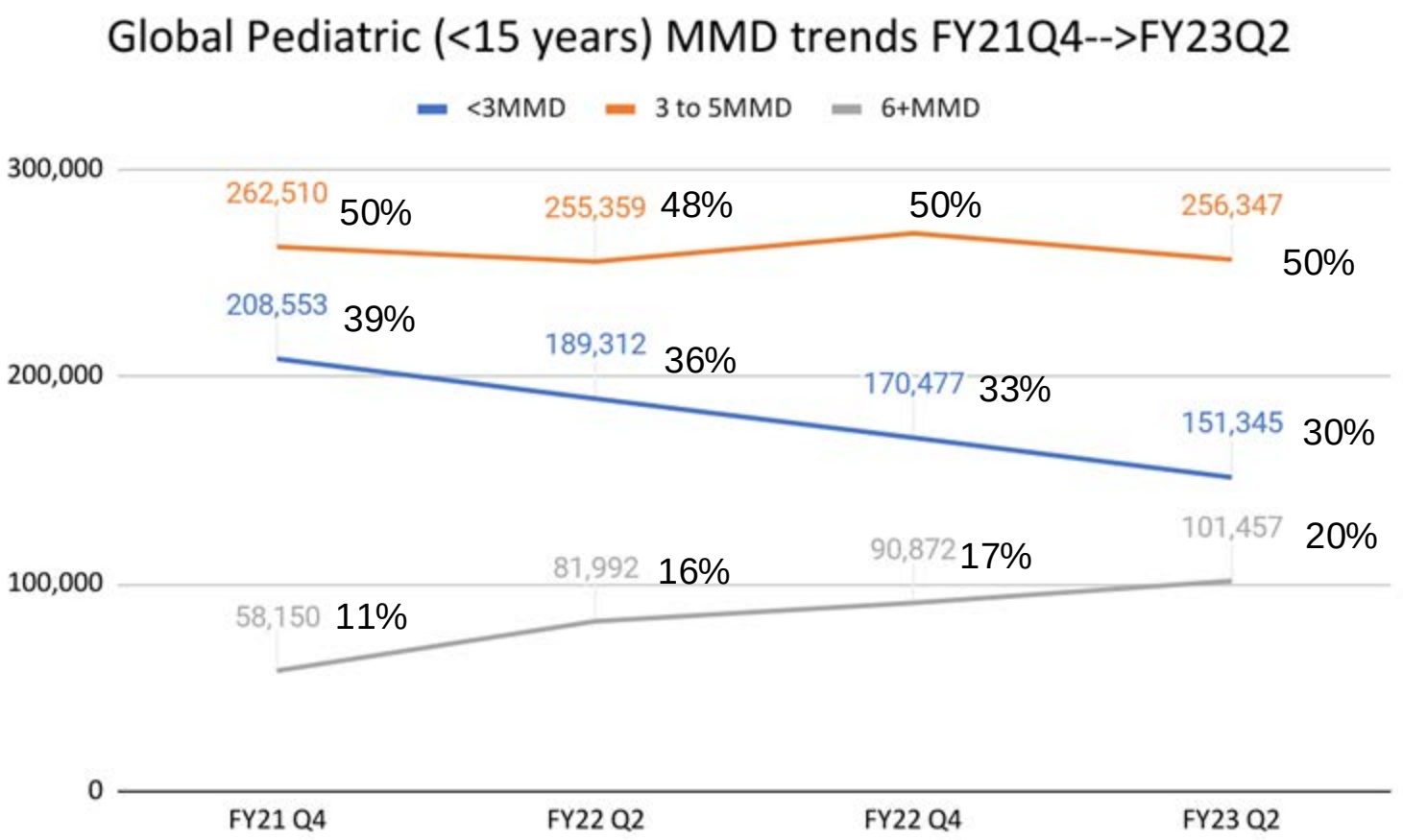
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

GLOBAL Viral Load Suppression (VLS) IN CLHIV, 1-4 and 5-9 years old, FY21Q2->FY23Q2



Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

NO MMD DATA FROM RSA



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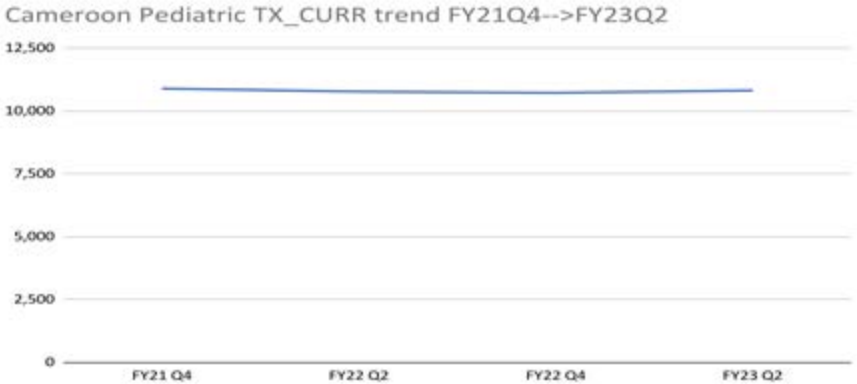
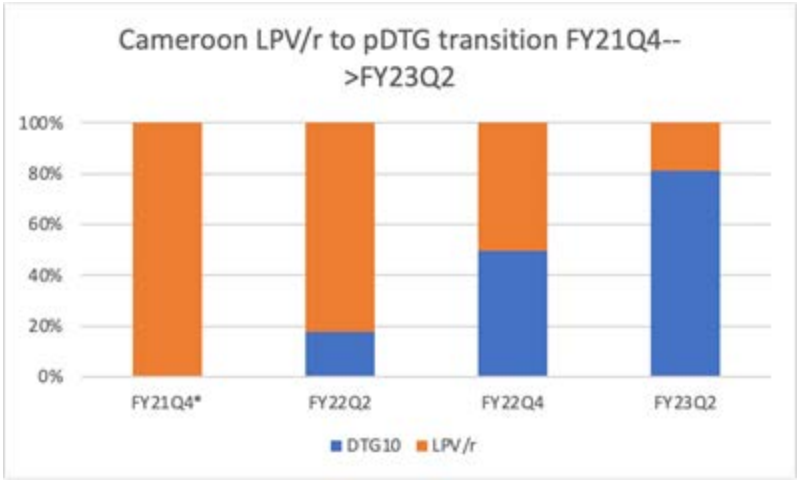
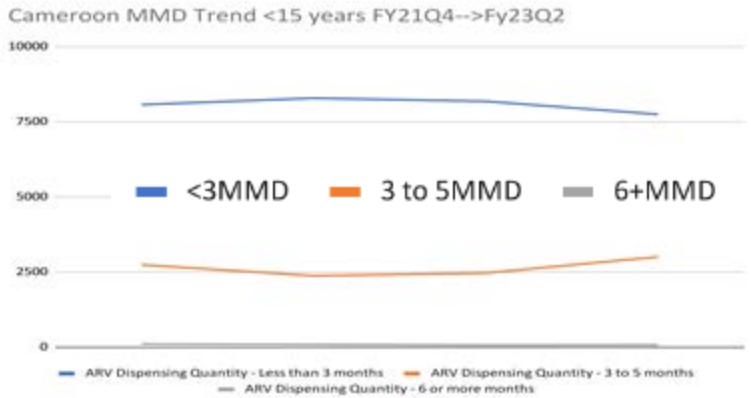
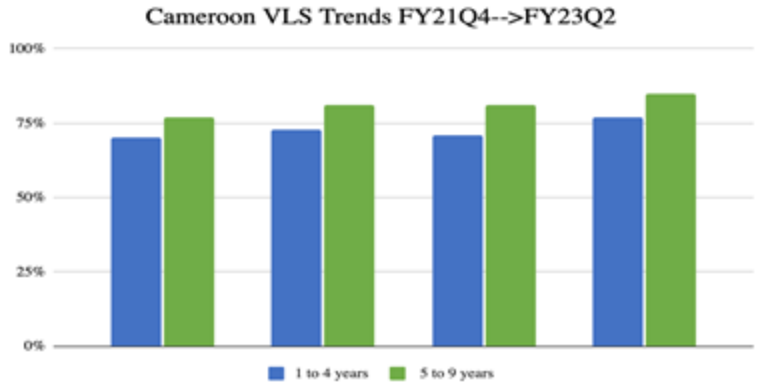
COUNTRY PROFILES

CAMEROON



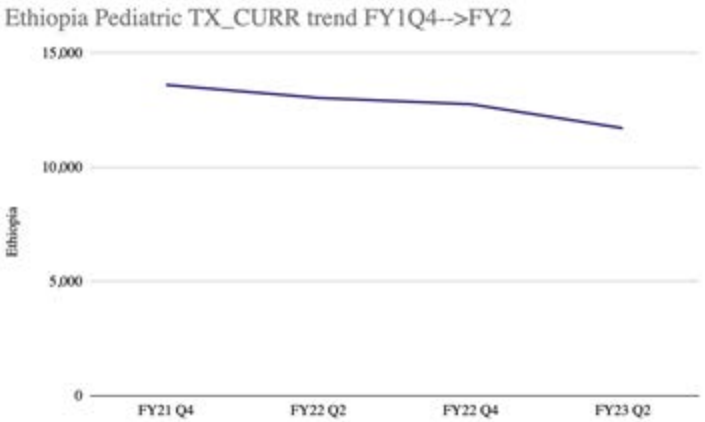


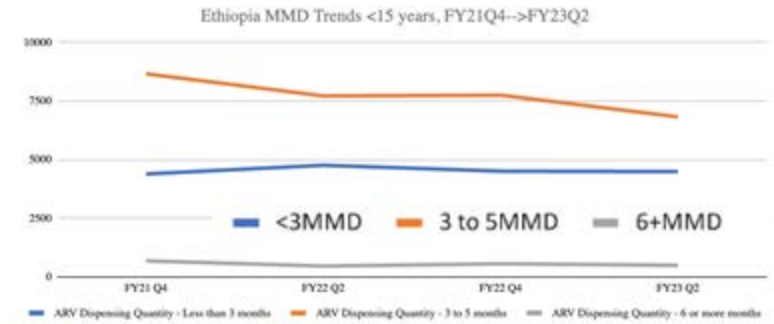


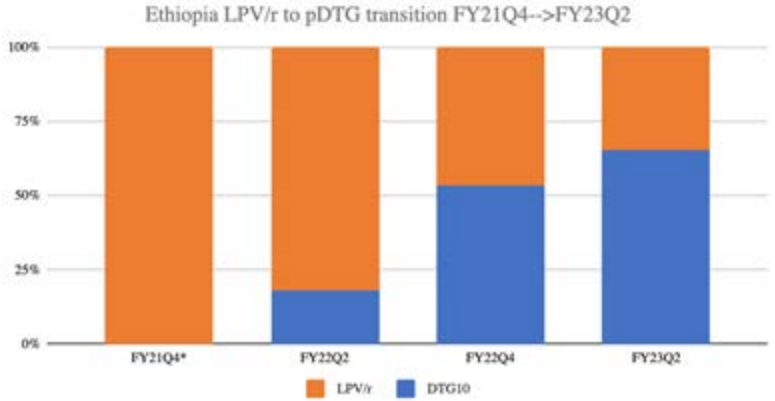


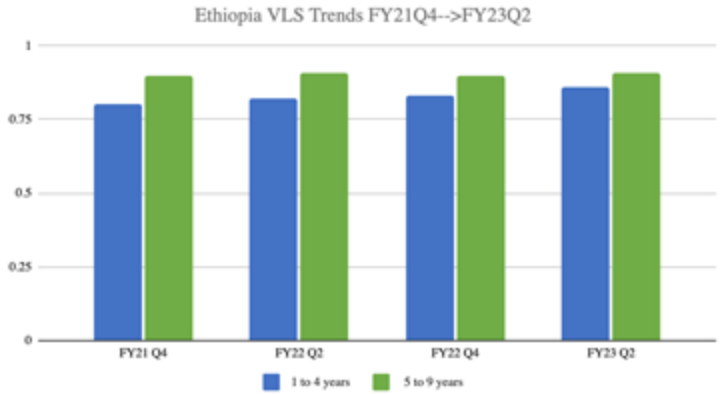
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

Ethiopia









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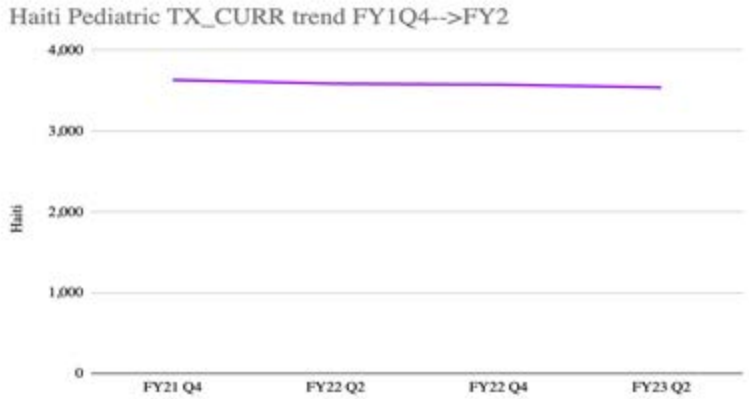
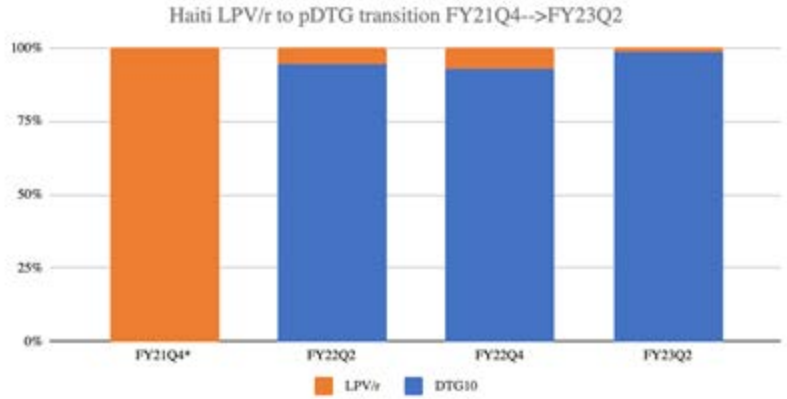
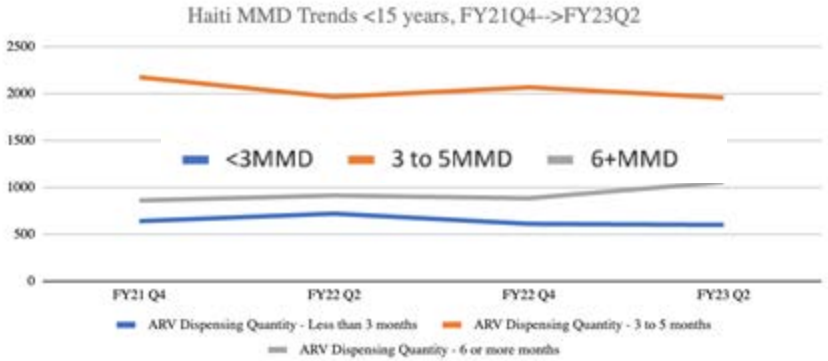
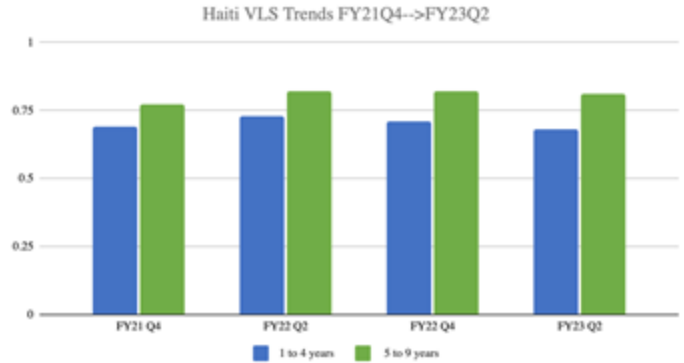
Haiti









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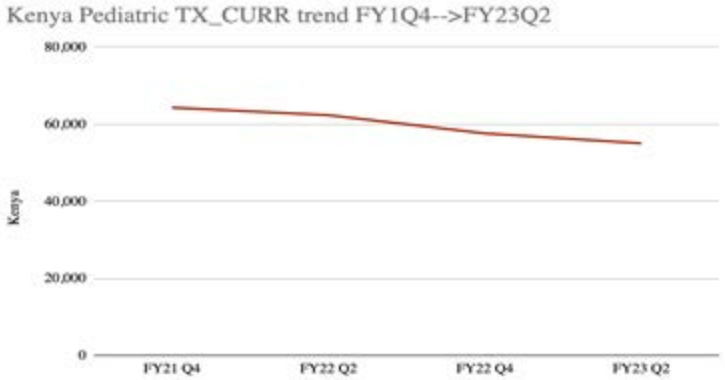
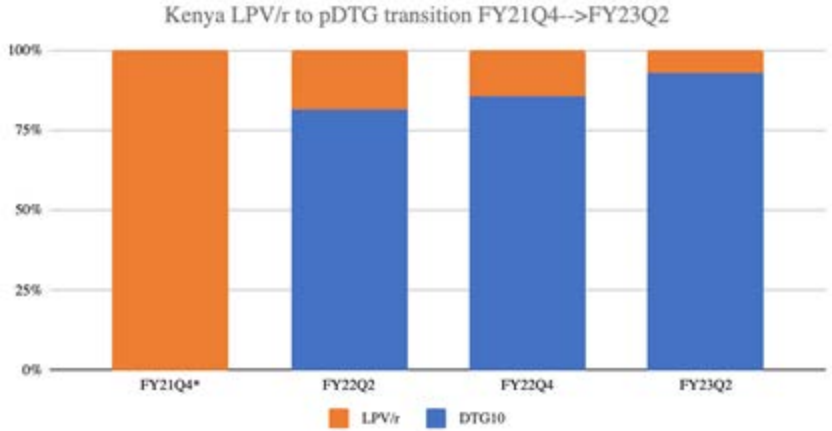
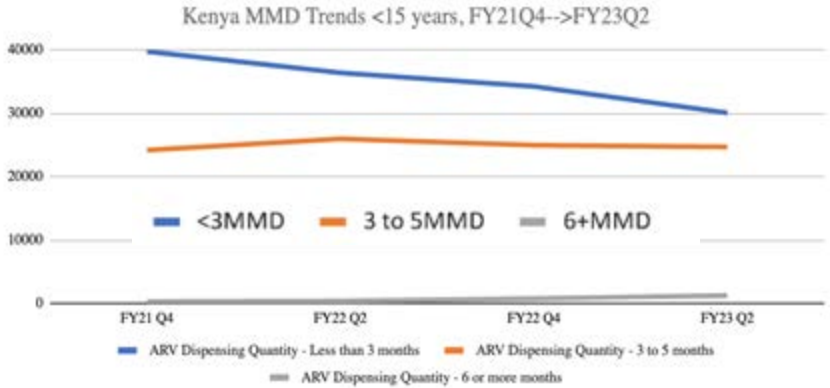
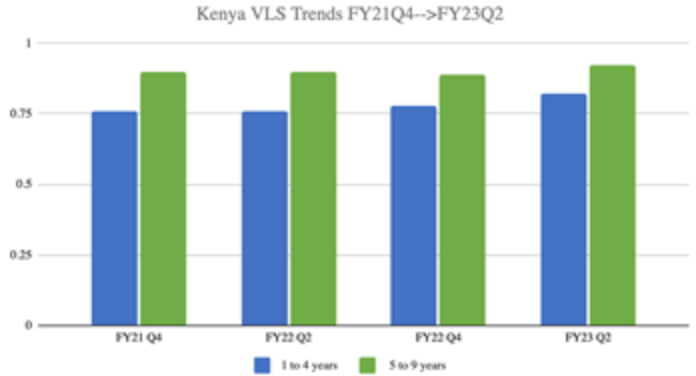
Kenya









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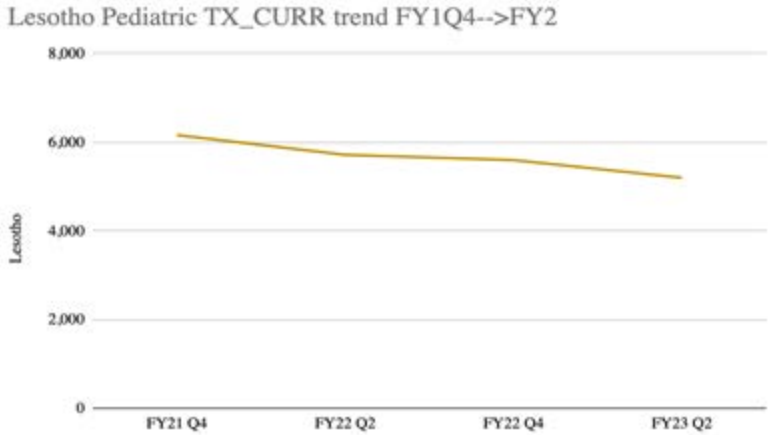
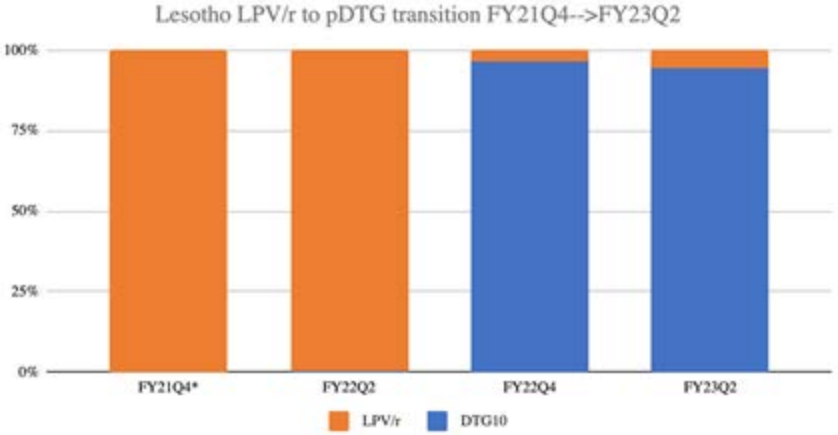
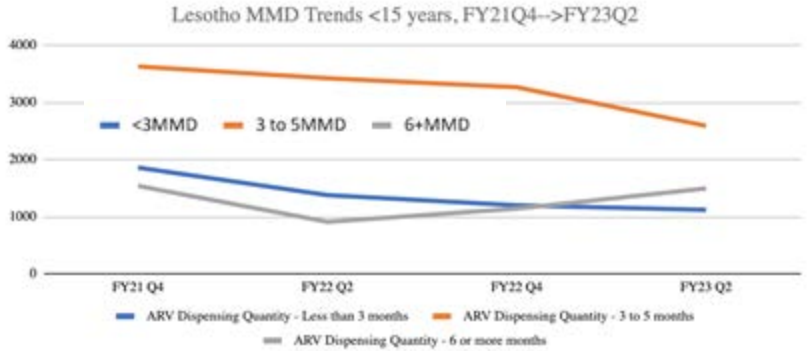
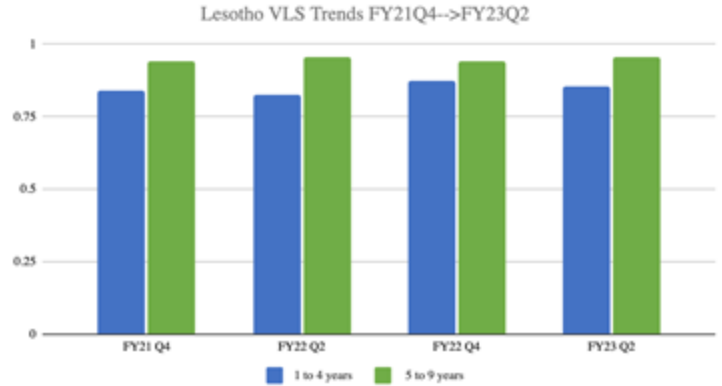
Lesotho



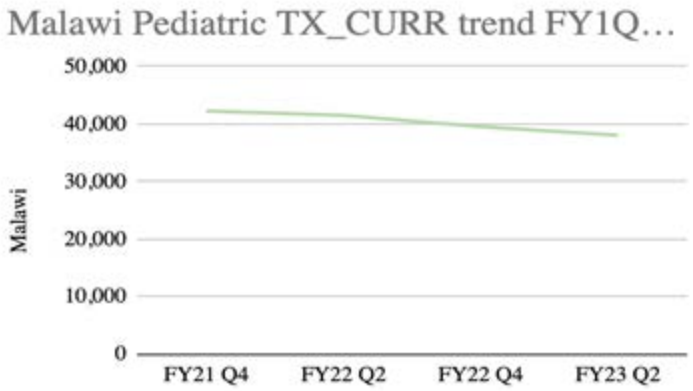


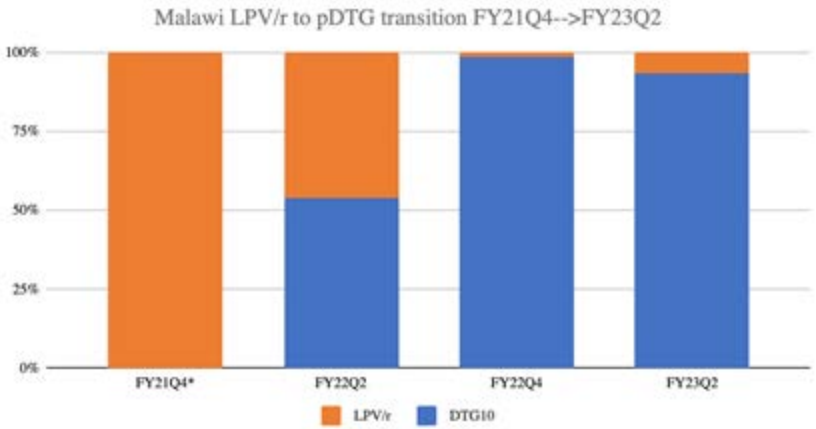


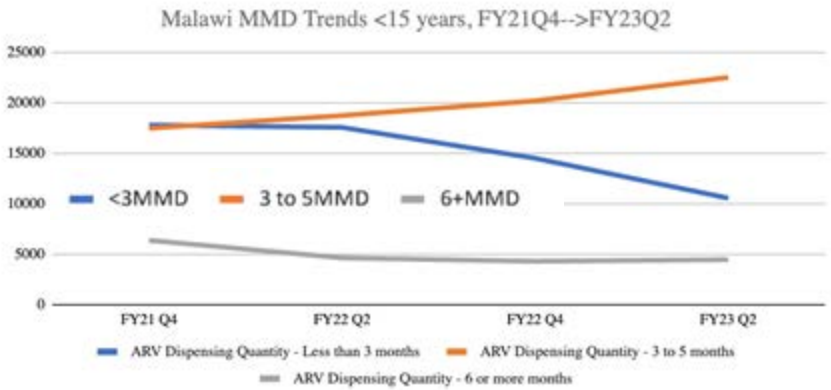


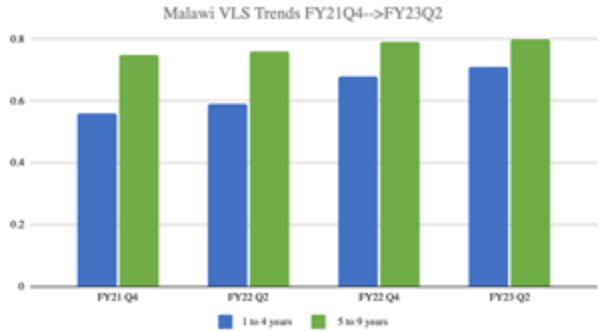
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

Malawi



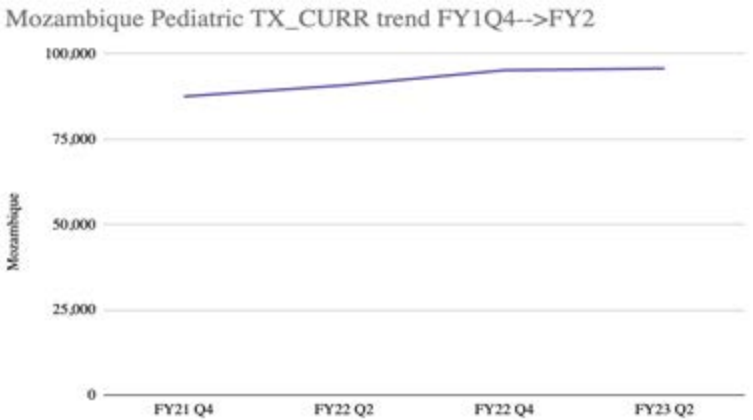


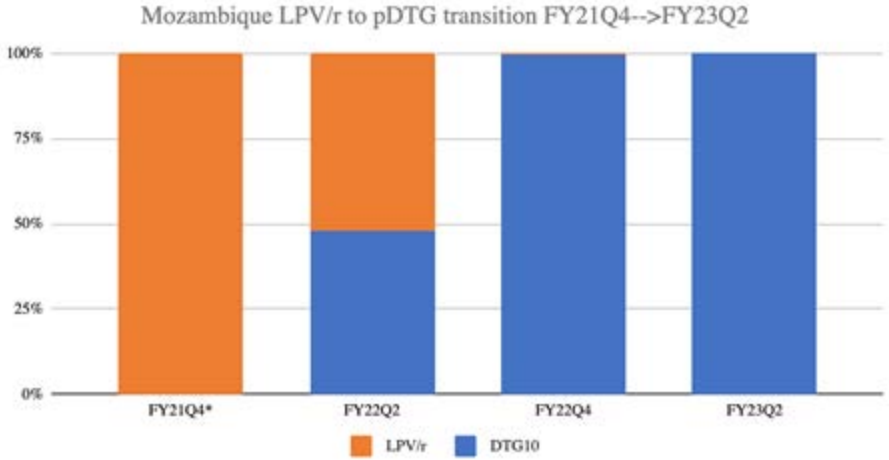


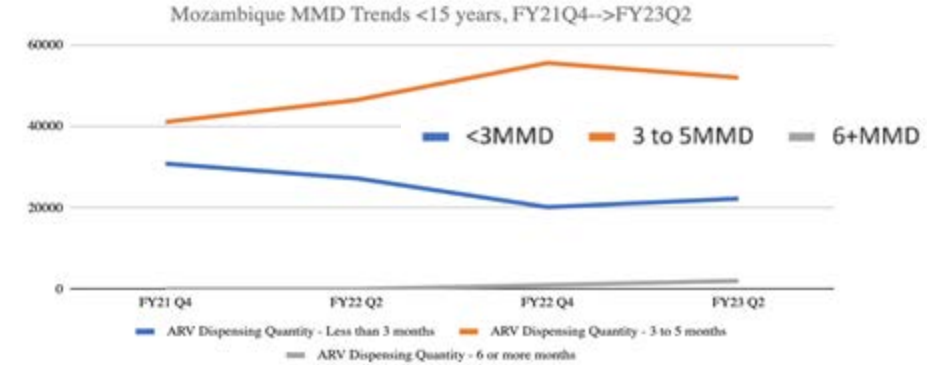


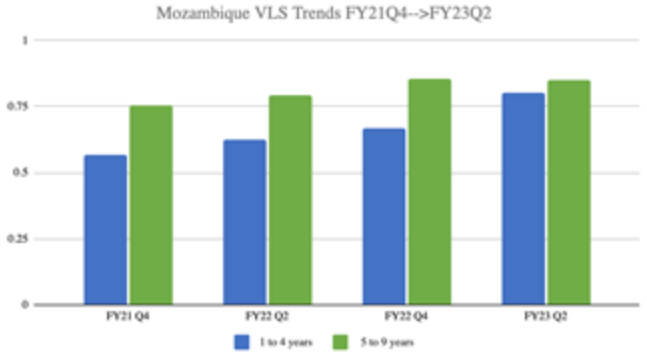
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

Mozambique



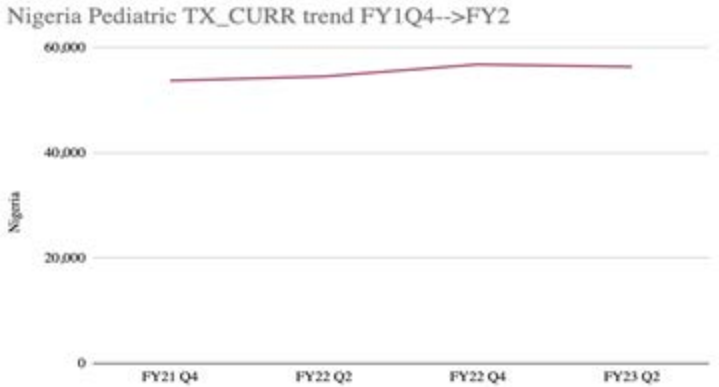


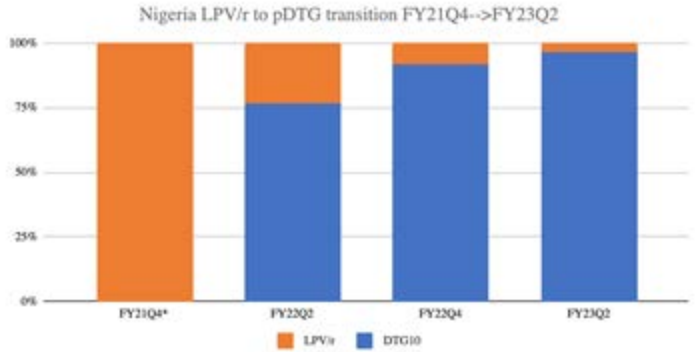


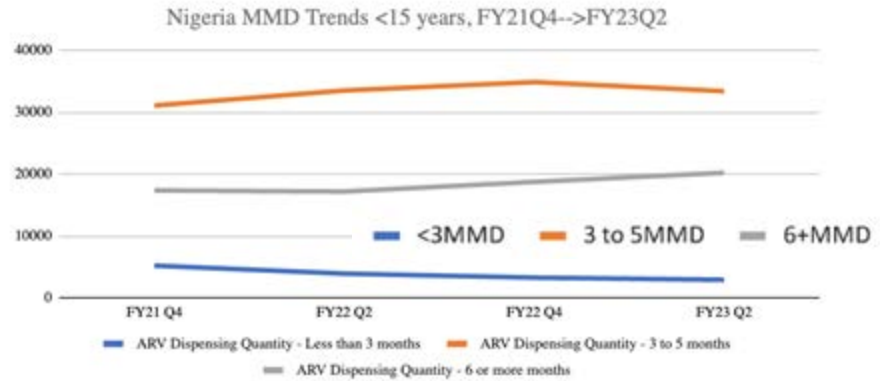


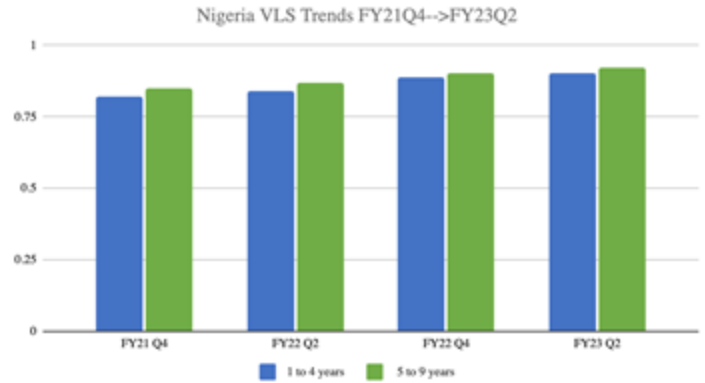
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

Nigeria



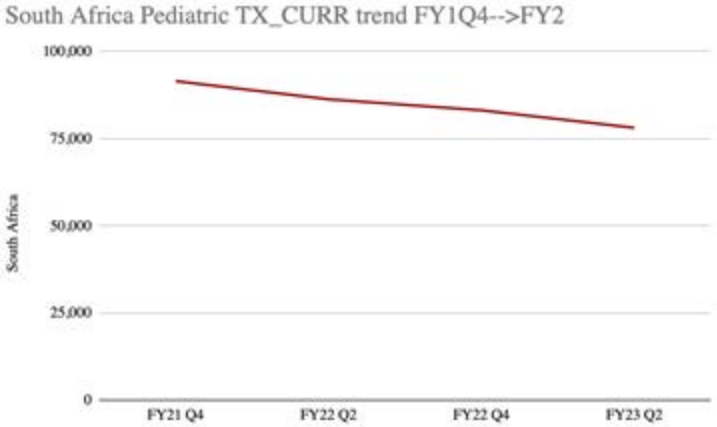


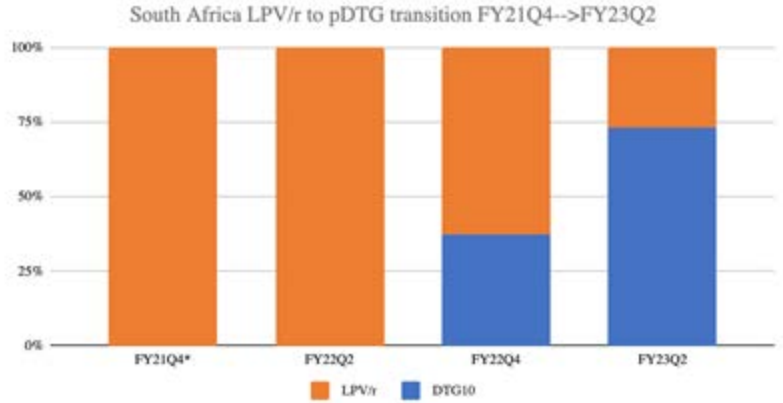


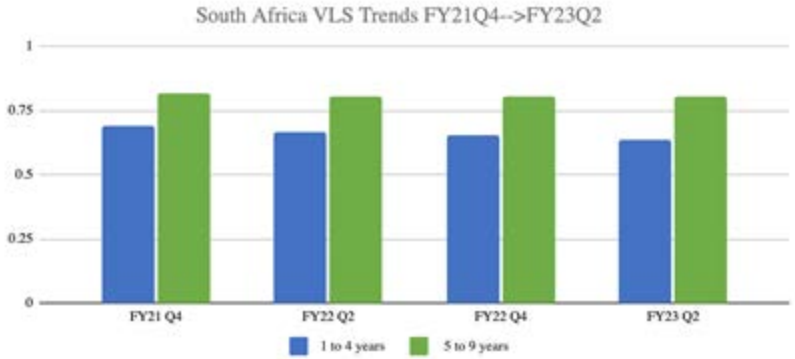


Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

South Africa



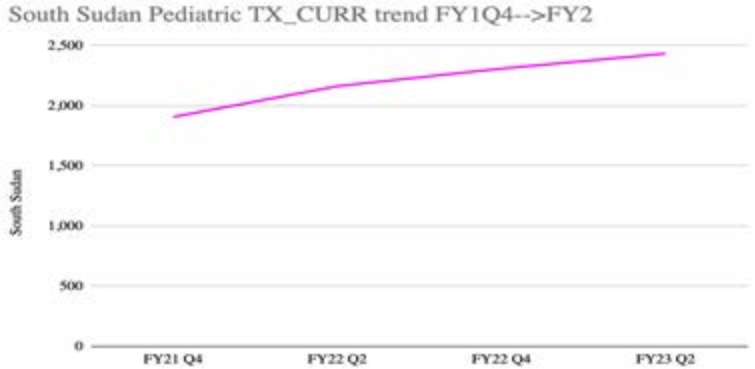


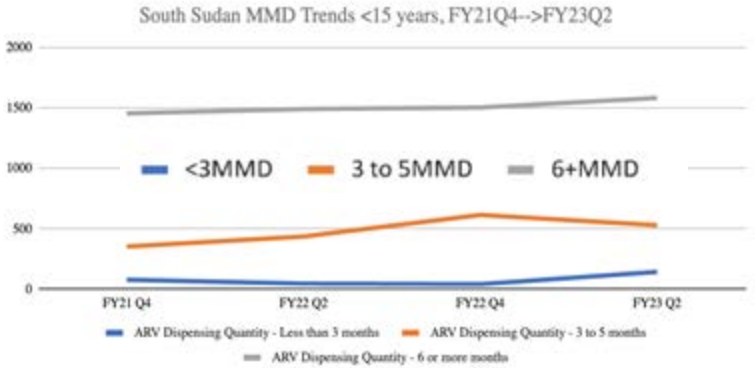


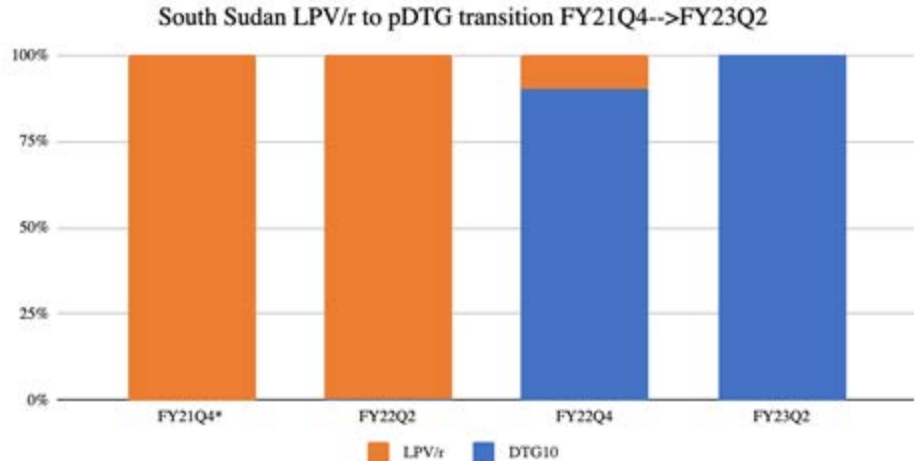
No MMD data

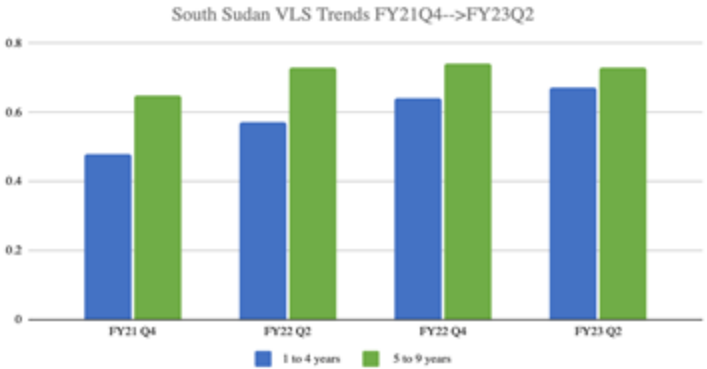
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

South Sudan



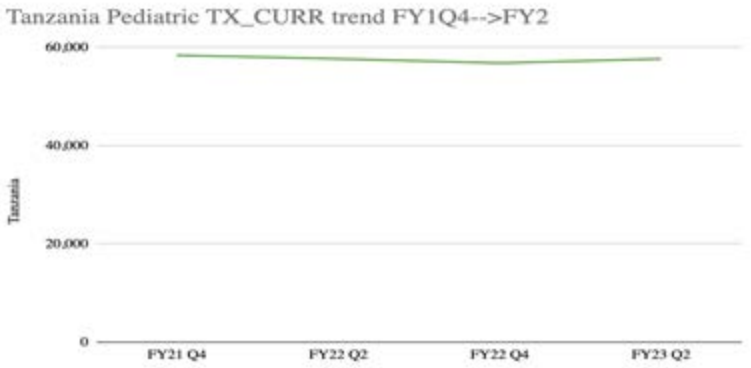


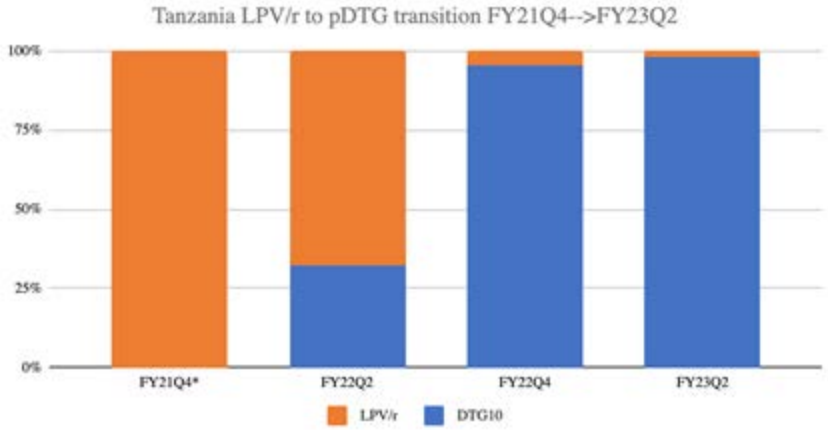


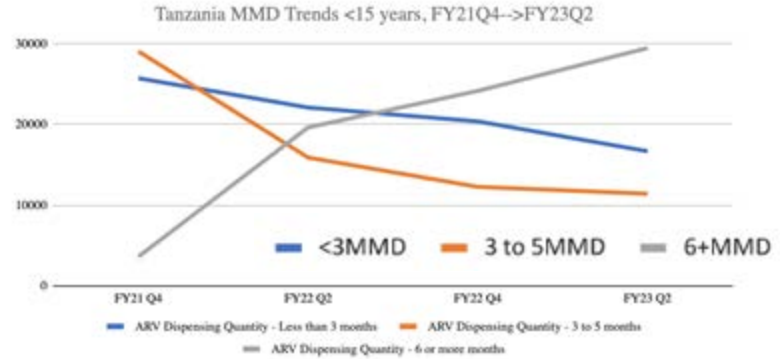


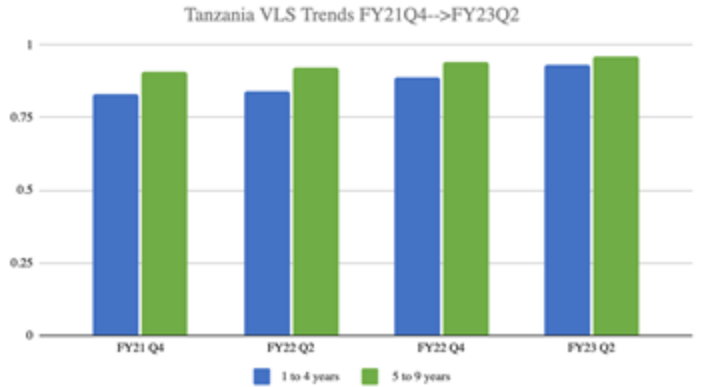
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

Tanzania



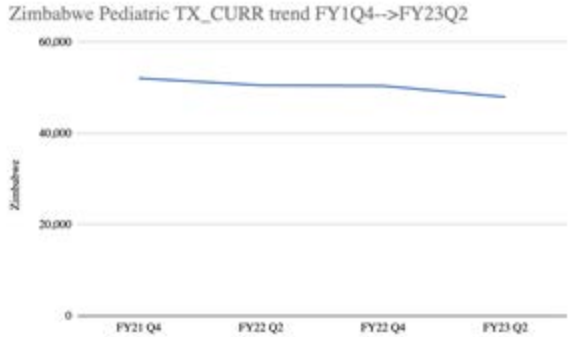


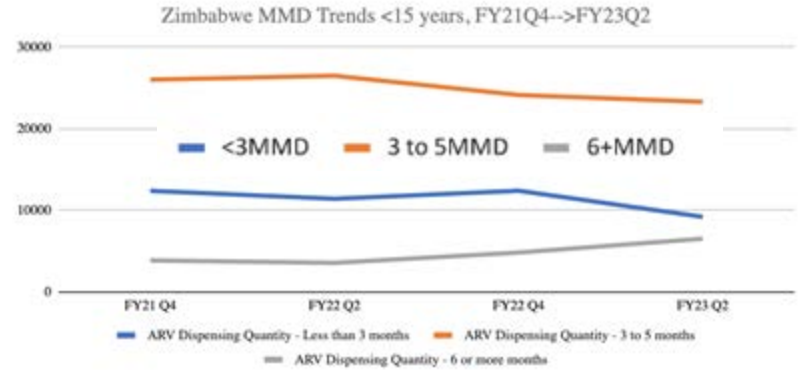


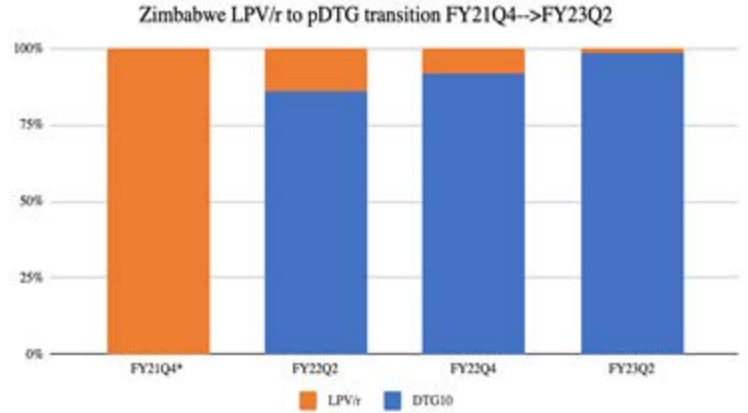


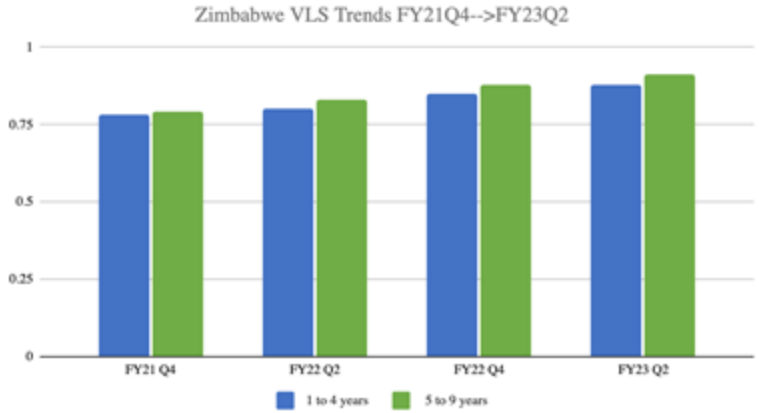
Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

Zimbabwe









Data from USAID Pediatric workbook in Tableau FY23Q3 workbook

Pediatric ABC/3TC/DTG (pALD) 60/30/5 mg, #180

pALD approved for CLHIV Aug/Sep 2023 ~ $15 per bottle of 180 tabs
Starting at 6kg and 3months

Policy Brief available in English, French, Portuguese, Spanish, Swahili

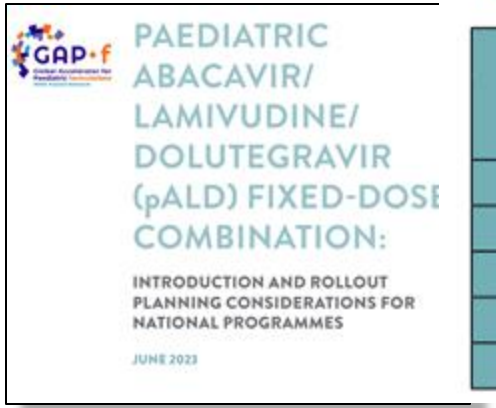
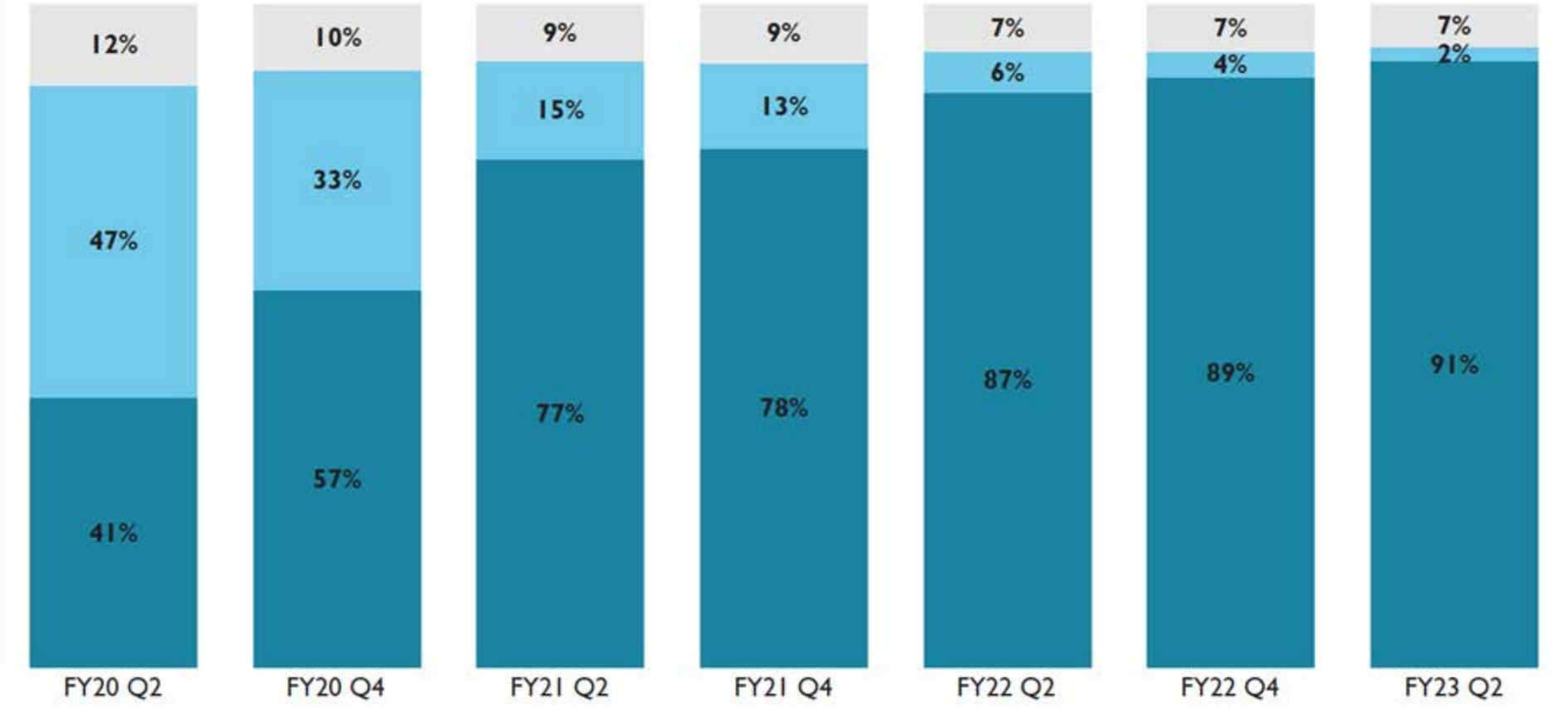


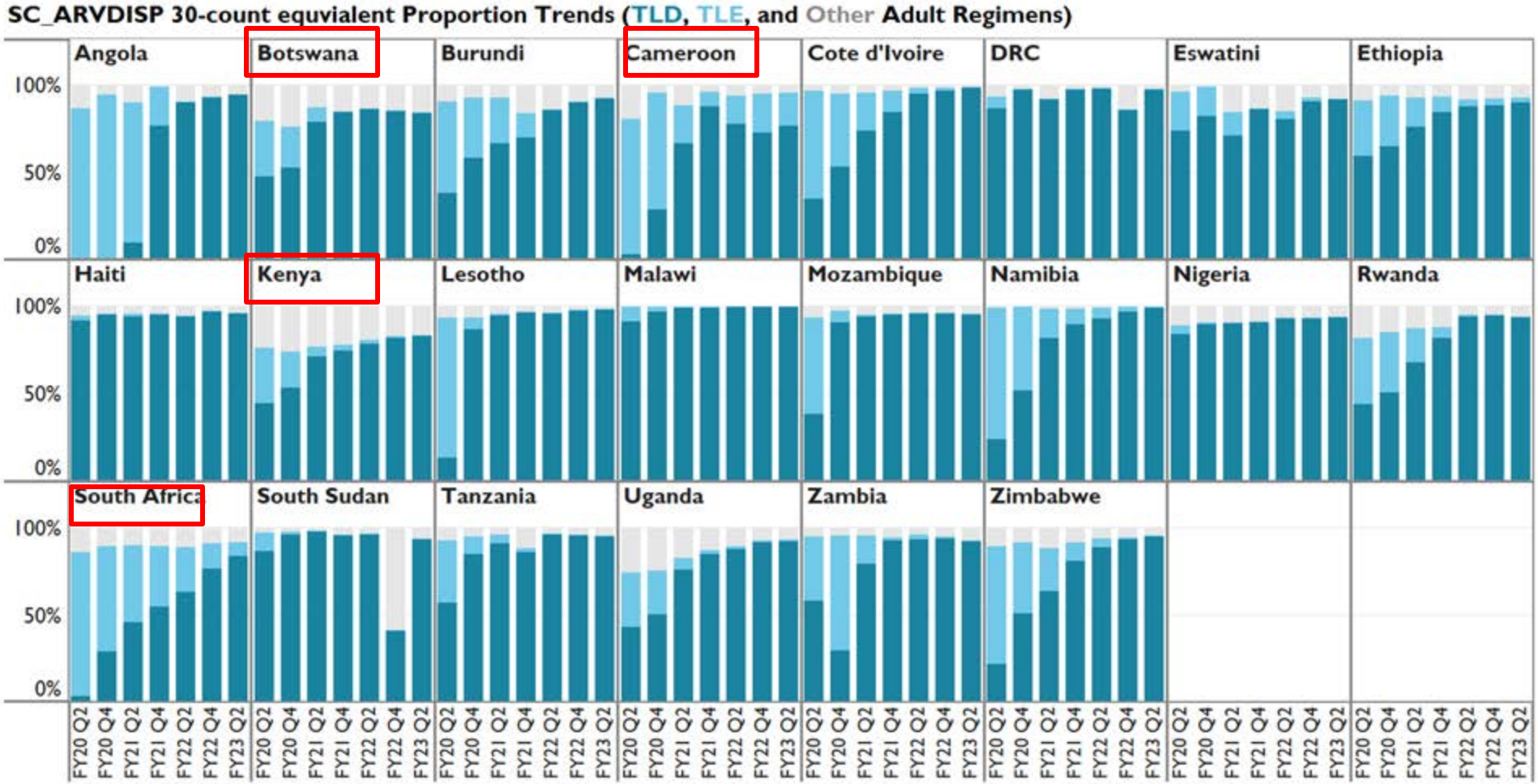
Table 2. Weight-based Dosing Comparisons Between Various DTG-based Regimens

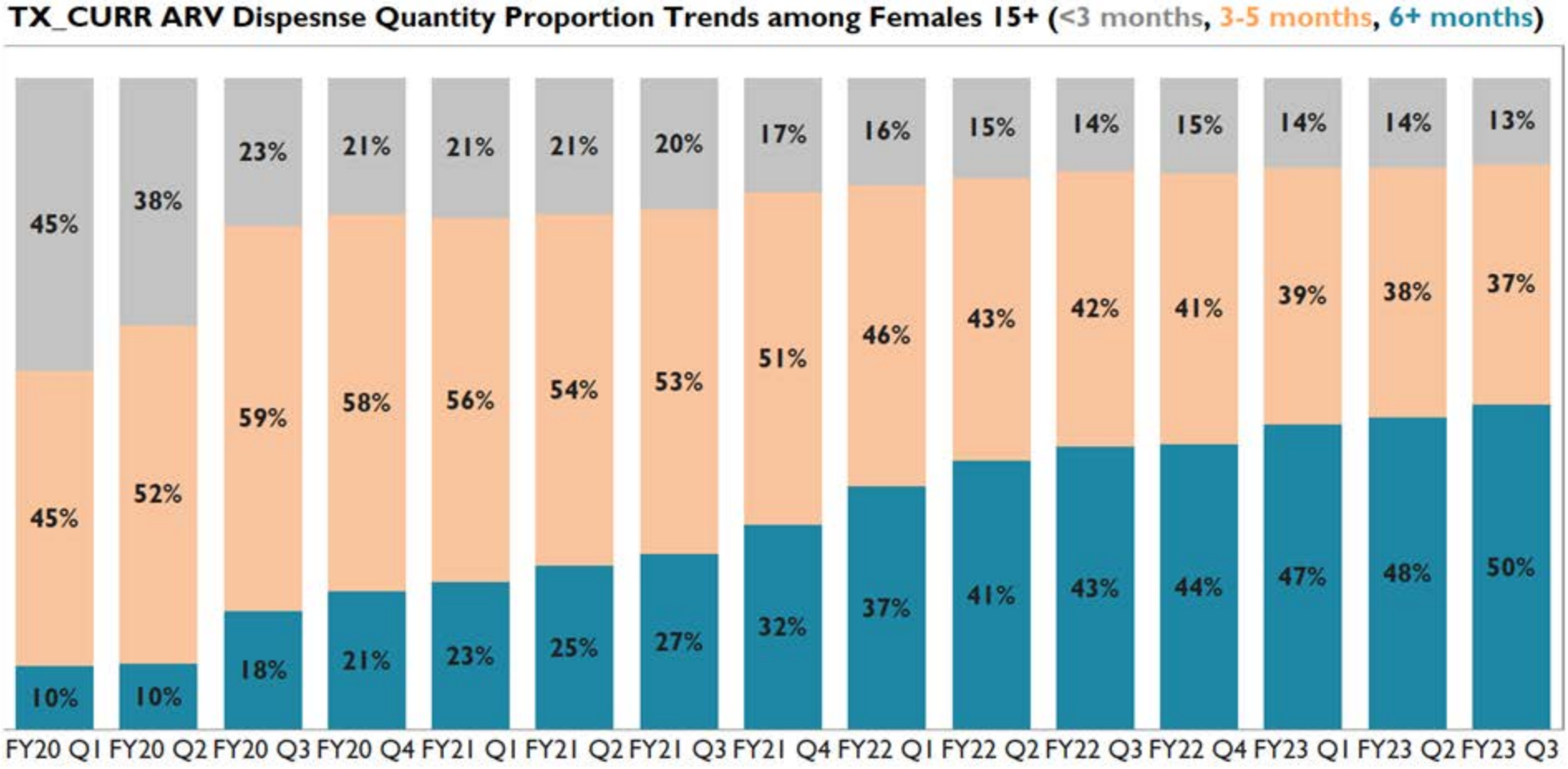
Weight Band	Number of Tablets Per Day	
	pABC/3TC 120/60 mg + pDTG 10 mg	pALD: ABC/3TC/DTG 60/30/5 mg
3 to 5.9 kg	1 + 0.5	N/A – use separate products
6 to 9.9 kg	1.5 + 1.5	3
10 to 13.9 kg	2 + 2	4
14 to 19.9 kg	2.5 + 2.5	5
20 to 24.9 kg	3+ 1 DTG (50 mg) tablet	6

DTG for PREGNANT & LACTATING PEOPLE

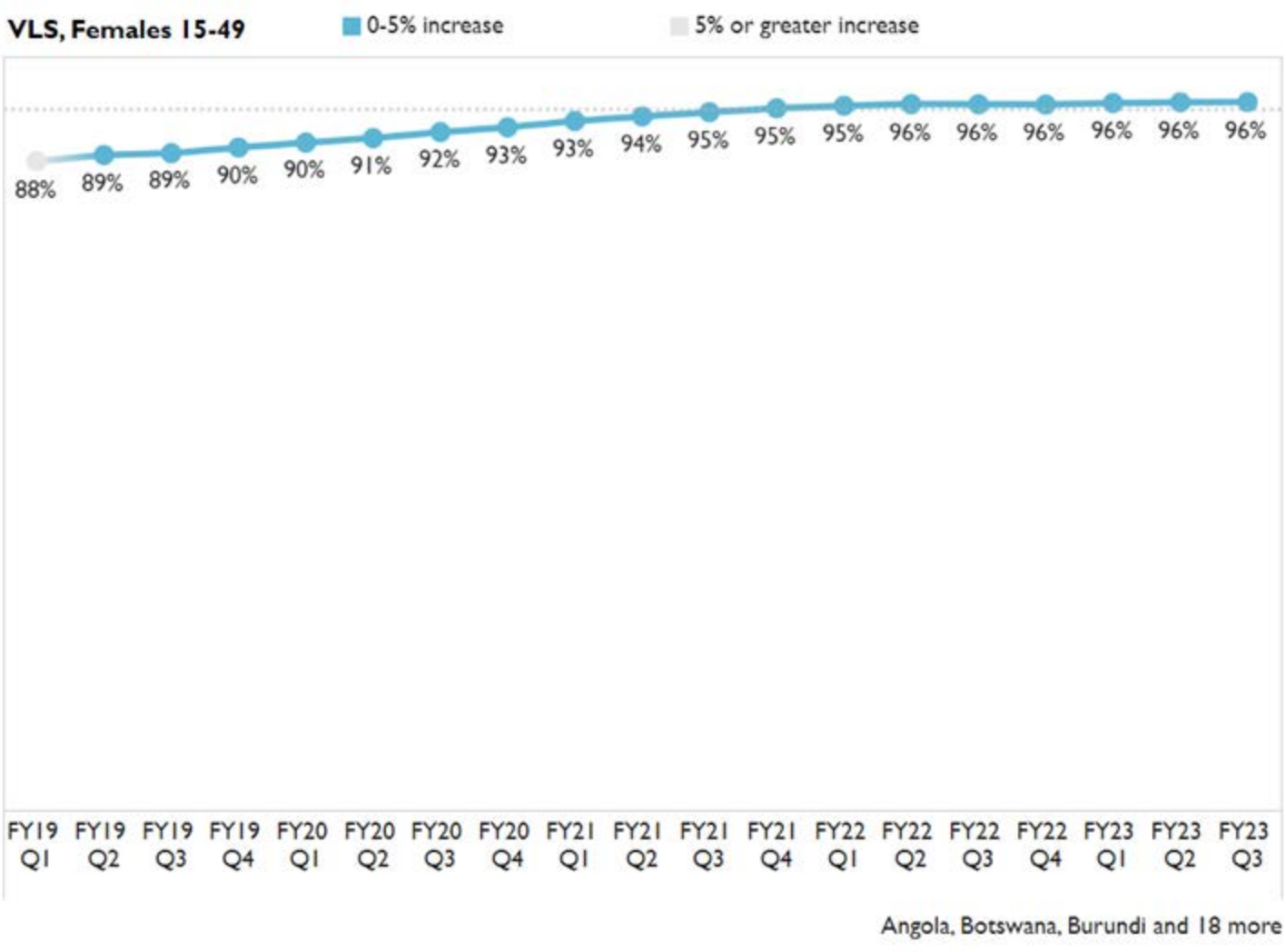
SC_ARVDISP 30-count equivalent proportion trend (TLD, TLE, and Other Adult Regimens)




SC_ARVDISP 30-count equvialent Proportion Trends (TLD, TLE, and Other Adult Regimens)
Angola
Botswana
Burundi
Cameroon
Cote d'Ivoire
DRC
Eswatini
Ethiopia
Haiti
Kenya
Lesotho
Malawi
Mozambique
Namibia
Nigeria
Rwanda
South Africa
South Sudan
Tanzania
Uganda
Zambia
Zimbabwe
100%
50%
0%
FY20 Q2
FY20 Q4
FY21 Q2
FY21 Q4
FY22 Q2
FY22 Q4
FY23 Q2



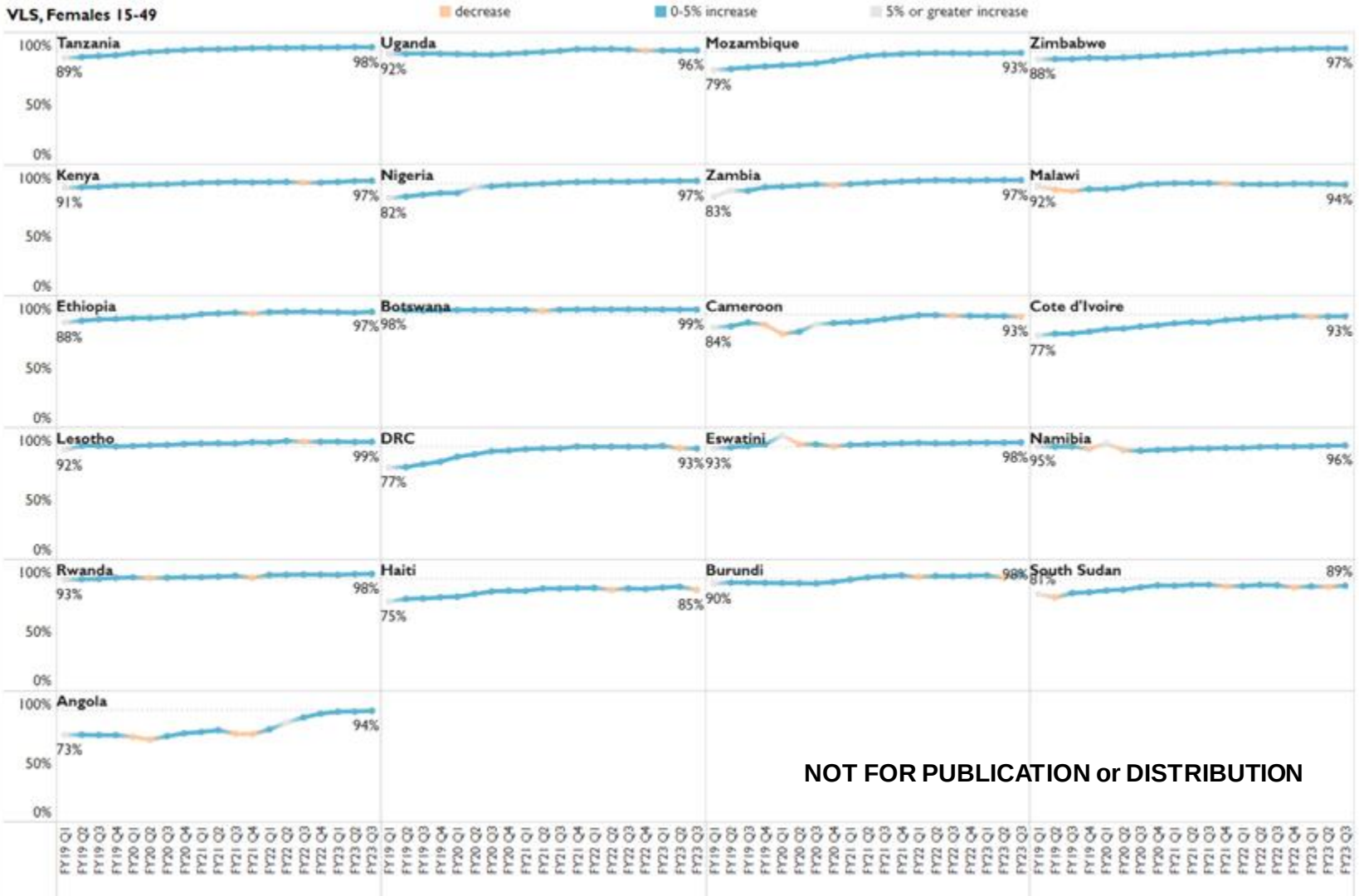
N.B.: UNABLE TO DISAGGREGRATE MMD DATA FOR ONLY PLP



- [ ] (All)
- [x] Angola
- [ ] Asia Region
- [x] Botswana
- [x] Burundi
- [x] Cameroon
- [x] Cote d'Ivoire
- [ ] Dominican Republic
- [x] DRC
- [x] Eswatini
- [x] Ethiopia
- [x] Haiti
- [x] Kenya
- [x] Lesotho
- [x] Malawi
- [x] Mozambique
- [x] Namibia
- [x] Nigeria
- [x] Rwanda
- [ ] South Africa
- [x] South Sudan
- [x] Tanzania
- [x] Uganda
- [ ] Vietnam
- [ ] West Africa Region
- [ ] Western Hemisphere Region
- [x] Zambia
- [x] Zimbabwe

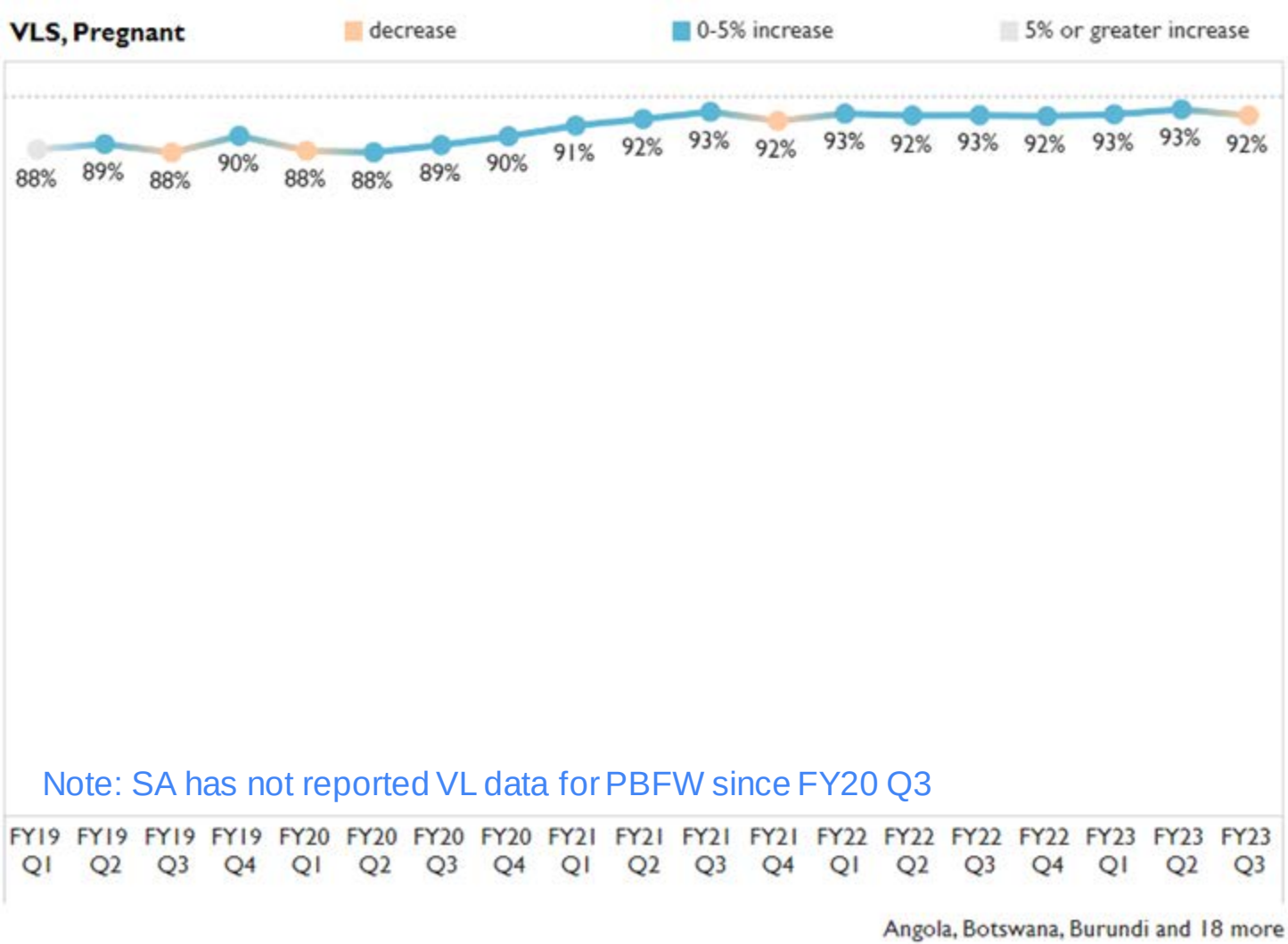
Legend represents % increase from previous quarter

Note: SA does not report VL for PBFW, but they DO report VLS for W 15-49. We excluded SA here to make it comparable with the PBFW VLS slide, but SA can always be added back here.



Legend represents % increase from previous quarter

NOT FOR PUBLICATION or DISTRIBUTION



Note: SA has not reported VL data for PBFW since FY20 Q3

- [ ] (All)
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- [ ] Asia Region
- [x] Botswana
- [x] Burundi
- [x] Cameroon
- [x] Cote d'Ivoire
- [ ] Dominican Republic
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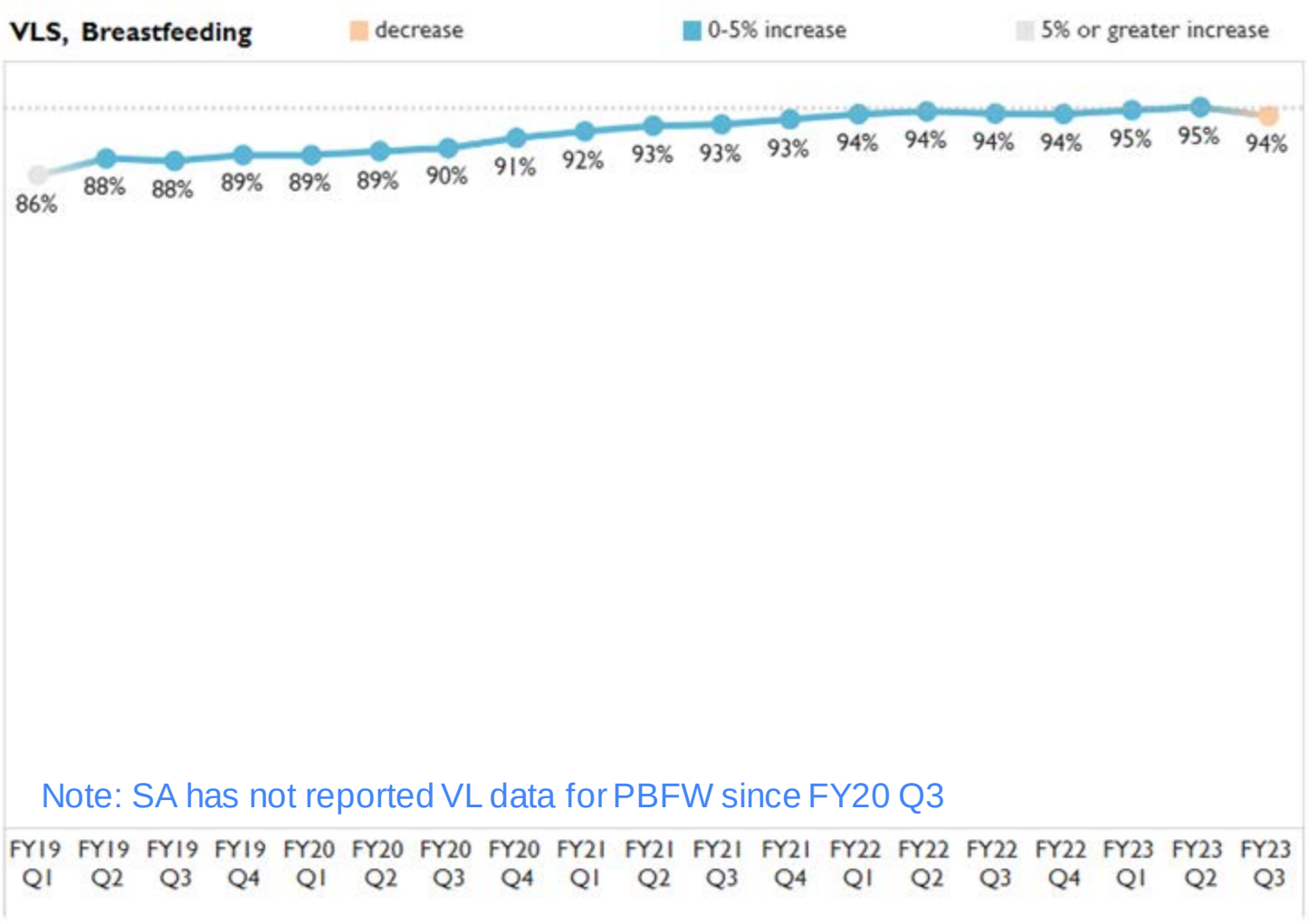

Note: SA has not reported VL data for PBFW since FY20 Q3

- [ ] (All)
- [x] Angola
- [ ] Asia Region
- [x] Botswana
- [x] Burundi
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- [x] Namibia
- [x] Nigeria
- [x] Rwanda
- [ ] South Africa
- [x] South Sudan
- [x] Tanzania
- [x] Uganda
- [ ] Vietnam
- [ ] West Africa Region
- [ ] Western Hemisphere Region
- [x] Zambia
- [x] Zimbabwe

DTG uptake CONCLUSIONS - and what comes next?

- Remarkable success in rapid, global scale-up of DTG for children
  - Accompanied by more convenient care (MMD) & rising VLS
- Rising and high (>90%) VLS among Pregnant & Lactating People
  - As DTG and MMD coverage for all adults rapidly scaled
- What's still needed? What's next?
  - pALD uptake
  - Closing gaps in some countries for TLD for women
    - Reluctance to transition second-line PI and other NRTI backbones could be mitigated by WHO guideline updates (NADIA & Kenya 2SD trials)
  - Confirmation that continuing ABC in transition to DTG from failing (NNRTI or PI) regimen will have high rates of VLS
  - Targeted INSTI resistance (surveillance, patient mgmt)
  - BIG: Case-finding for undiagnosed children & Addressing HIV and veritcal transmission prevention in women outside of ANC/PMTCT programs

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THANK YOU!!
Special thanks to:
ANOUK AMZEL
ALEXANDRA VRAZO
NASHIVA MCDAVID
For Data Summaries & Slide Development
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