

*Temporal Changes in Pediatric and Adolescent HIV Outcomes across the Care Continuum in Zambia: an interrupted time-series analysis*

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## **ADDITIONAL METHODOLOGIC DETAILS**

### Study Setting

Zambia updated its HIV treatment guidelines on February 1, 2014 and then again on January 1, 2017. In 2010, universal ART was adopted for children less than 2 years old. Efavirenz- or nevirapine-based regimens were considered first-line regimens for all age groups. In 2014, universal ART was adopted as policy for children between 2 and 15 years old and any pregnant or breastfeeding woman (i.e., Option B+); additionally, the CD4 eligibility threshold for everyone else was increased from less than 350 cell/ $\mu$ l to less than 500 cells/ $\mu$ l. Additionally, for children less than 5 years old, lopinavir-based regimens became first-line recommendations, and for children greater than 5 years old, efavirenz-based regimen became first-line (as opposed to either efavirenz- or nevirapine-based regimens). Lastly, in 2017, Zambia transitioned to universal ART treatment for all people living with HIV. These guidelines also considered a provision to consider same-day ART initiation if appropriate. Of note, dolutegravir-based regimens were introduced in Zambia in mid-2018. age groups in supplemental analysis as it was only introduced in mid-2018 in Zambia. ART eligibility criteria and first-line regimens for different age groups during each of these periods is summarized in the Table S1 (appendix p 6).

Once new guidelines were adopted, the Ministry of Health—in collaboration with implementing partners such as CIDRZ—updated training packages to include new guidance. CIDRZ also developed standard operating procedures and conducted healthcare working trainings and mentorship to assist in implementation of guidelines. This orientation process took approximately 6 months for all CIDRZ-supported sites.

Children and adolescents not eligible for ART at the time of enrollment were followed up with clinical evaluations and CD4 counts every 6 months until becoming eligible for ART.

### Measurements

Sociodemographic, clinical, facility-level, and visit history measurements were obtained from the national EHR and laboratory systems used in routine HIV care in Zambia. To populate the EHR, providers first complete standardized paper clinical forms during routine patient encounters, and then data clerks enter this information into the electronic database. At CIDRZ-supported sites, data entry was supported by trained data technicians on a continuous basis. These efforts included routine monthly data audits, quality checks, and data cleaning that were also enhanced by targeted chart review. These procedures thus helped to ensure relatively high-quality data.

We queried this database for all data from individuals meeting eligibility criteria from the 102 included facilities in our cohort. We used patient sociodemographic characteristics (e.g., age, sex, facility), clinical characteristics (e.g., CD4 counts, WHO Stage, anthropometrics, ART regimen), and longitudinal visit history (e.g., follow-up visits, ART pick-ups, enrollment date, date of ART initiation) for our analyses. Of note, race/ethnicity was not available in this database as 100% of clients are expected to be Black.

This data capture process provided us with individual-level data for all individuals in the cohort. Among those eligible for our cohort, no individuals were excluded for having missing data. Data capture extended through December 31, 2019 to ensure all individuals had adequate time to observe the retention outcome.

### Statistical Analysis

We used an interrupted time-series design to examine how outcomes among newly enrolling CALHIV have changed over time in relation to the 2014 and 2017 guidelines changes<sup>1</sup>. Among all newly enrolling children and adolescents living with HIV, we examined ART initiation within 3 months of enrollment, time from enrollment to ART initiation, and retention in care on ART at 6 months (defined as having initiated ART and making at least one visit between 3- and 9- months post-enrollment after). Among those individuals who initiated ART, we also examined the proportion initiated on either an efavirenz-, nevirapine-, or lopinavir/ritonavir-based regimen. We also examine

scale-up of dolutegravir-based regimens across age groups in supplemental analysis as it was only introduced in mid-2018 in Zambia. All outcomes were generated using longitudinal data from the EHR at the individual-level.

Statistically, we modelled these individual-level patient outcomes as a function of their date of enrollment using linear splines, stratifying by age group. We considered that the implementation of new guidelines would be associated with an initial rapid (but not immediate) effect on patient outcomes during the first 90 days after guidelines were rolled out, followed by a return to a new baseline secular trend after the 90-day transition period up until the next treatment guidelines were implemented. Thus, we modelled the impact of new guidelines on patient outcomes as a change of slope during the first 90 days after guidelines were implemented in 2014 and 2017 (i.e., to account for the rapid transition period where guidelines were being fully implemented) followed by another change of slope after transition period to establish the new baseline secular trend during the remainder of the guideline period<sup>1</sup>. We only modelled a slope change and no jump at the time of guideline implementation since we did not consider that guidelines to have an immediate impact (i.e., within one day).

To model binary outcomes (i.e., ART initiation within 3 months, retention on ART at 6 months, and ART regimens), we applied established methods<sup>2,3</sup> using Poisson regression with robust variances. We performed sensitivity analyses using logistic regression to ensure results remained consistent. For time to ART initiation, we used median regression (i.e., quantile regression estimating the 50<sup>th</sup> percentile) to estimate the median time to ART initiation among all newly enrolling CALHIV. This approach using median regression to estimate the median allowed us to include and account for individuals who never initiated ART without affecting estimates of the median. To accomplish this for those who did not initiate ART, we set the value for time to ART initiation higher than all other recorded values (i.e., 5000 days). This approach is in contrast to using linear regression to estimate the mean, which would have required us to restrict the analysis to only those who had initiated ART.

After running these regression models, we used the *margins* post-estimation command in *Stata version 17.0* to use the fitted models to generate marginal estimates (i.e., absolute percentages of ART initiation/retention or median time to ART) with 95% confidence intervals. We also used them to estimate the change in outcomes from a baseline immediately prior to 2014 and 2017 guideline rollout compared to 90, 180, 365, and 730 days after guideline rollout. We chose to use the time of guideline rollout as the baseline value for comparisons as we did not think that the traditional assumption for ITS study designs—that the pre-guideline trend would continue indefinitely if new guidelines had not been implemented—was plausible<sup>1</sup>.

Lastly, we performed multivariable mixed-effects Poisson regression with robust variances to identify patient, facility, and temporal factors associated with ART initiation by 3 months and being retained on ART at 6 months. When used with binary outcomes, Poisson regression with robust variances yields estimates of risk ratios with valid confidence intervals<sup>2,3</sup>. We stratified models by age category and included sex, whether an enrollment CD4 was performed, facility size, province, and secular time; health facility was included as a random effect. We modelled secular time using the same specifications as in the ITS model. We also estimated the intraclass correlation for facility, which represents the percent of the total variability attributable to the facility at which an individual enrolled. Of note, we did not include enrollment CD4 counts/percentages, WHO Stage, and weight/BMI-for-age z-scores in regression models due to high levels of missingness for these variables (Table S2, appendix p 7).

All analyses were conducted using Stata MP version 17.0.

### Citations

1. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol* 2017; **46**(1): 348-55.
2. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004; **159**(7): 702-6.
3. Zou GY, Donner A. Extension of the modified Poisson regression model to prospective studies with correlated binary data. *Stat Methods Med Res* 2013; **22**(6): 661-70.

<b>Table S1. Zambian HIV Treatment guidelines from 2010 to 2019</b>			
<b>Guidelines</b>	2010 Guideline Period (Sep 9, 2010 - Jan 31, 2014)	2014 Guideline Period (Feb 1, 2014 - Dec 31, 2016)	2017 Guideline Period (Jan 1, 2017 – Dec 31, 2018)
<b>Age Groups</b>			
<b>&lt;2 years</b>	<ul style="list-style-type: none"> <li>• Universal treatment</li> <li>• EFV- or NVP-based regimen</li> </ul>	<ul style="list-style-type: none"> <li>• Universal treatment</li> <li>• LPV-based regimen</li> </ul>	<ul style="list-style-type: none"> <li>• Universal treatment</li> <li>• Consider rapid ART initiation (i.e., less than 7 days)</li> <li>• LPV-based regimen</li> </ul>
<b>2 to &lt;5 years</b>	<ul style="list-style-type: none"> <li>• WHO Stage 3 or 4</li> <li>• CD4 ≤ 750</li> <li>• CD4% &lt;25</li> <li>• EFV- or NVP-based regimen</li> </ul>		
<b>5 to &lt;15 years</b>	<ul style="list-style-type: none"> <li>• WHO Stage 3 or 4</li> <li>• CD4 ≤ 350</li> <li>• EFV- or NVP-based regimen</li> </ul>	<ul style="list-style-type: none"> <li>• Universal treatment</li> <li>• EFV-based regimen</li> </ul>	<ul style="list-style-type: none"> <li>• Universal treatment</li> <li>• Consider rapid ART initiation (i.e., less than 7 days)</li> <li>• EFV-based regimen</li> </ul>
<b>15 to 19 years</b>	<ul style="list-style-type: none"> <li>• WHO Stage 3 or 4</li> <li>• CD4 ≤ 350</li> <li>• EFV- or NVP-based regimen</li> </ul>		

Abbreviations: EFV – Efavirenz, NVP – Nevirapine, LPV – ritonavir-boosted lopinavir

	<b>&lt;2 years</b>			<b>2 - &lt;5 years</b>			<b>5 - &lt;15 years</b>			<b>15-19 years</b>		
	<b>2010 Guidelines (n = 1533)</b>	<b>2014 Guidelines (n = 1325)</b>	<b>2017 Guidelines (n = 1376)</b>	<b>2010 Guidelines (n = 1119)</b>	<b>2014 Guidelines (n = 883)</b>	<b>2017 Guidelines (n = 1036)</b>	<b>2010 Guidelines (n = 2886)</b>	<b>2014 Guidelines (n = 2412)</b>	<b>2017 Guidelines (n = 2830)</b>	<b>2010 Guidelines (n = 3058)</b>	<b>2014 Guidelines (n = 3478)</b>	<b>2017 Guidelines (n = 4278)</b>
Sex, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Age, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
CD4 count at enrollment, n (%)	1305 (85.1)	915 (69.1)	1191 (86.6)	885 (79.1)	474 (53.7)	797 (76.9)	2188 (75.8)	1143 (47.4)	1979 (69.9)	2430 (79.5)	1837 (52.8)	3151 (73.7)
CD4 percent at enrollment, n (%)	1313 (85.6)	930 (70.2)	1194 (86.8)	890 (79.5)	498 (56.4)	808 (78.0)	2203 (76.3)	1203 (49.9)	2040 (72.1)	2453 (80.2)	1955 (56.2)	3208 (75.0)
WHO stage, n (%)	1415 (92.3)	1209 (91.2)	1341 (97.5)	1040 (92.9)	820 (92.9)	1012 (97.7)	2540 (88.0)	2212 (91.7)	2715 (95.9)	624 (20.4)	799 (23.0)	1147 (26.8)
Weight/BMI-for-Age z-score at enrollment, n (%)	395 (25.8)	391 (29.5)	369 (26.8)	214 (19.1)	191 (21.6)	259 (25.0)	631 (21.9)	588 (24.4)	958 (33.9)	1509 (49.3)	1889 (54.3)	2500 (58.4)
Province, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
CD4 count at ART initiation*, n (%)	769 (78.3)	691 (66.7)	1044 (88.9)	611 (74.4)	409 (55.3)	696 (77.8)	1515 (69.7)	1010 (49.1)	1806 (70.2)	1504 (73.4)	1572 (52.6)	2897 (73.7)
CD4 percent at ART initiation*, n (%)	779 (79.3)	707 (68.2)	1047 (89.1)	613 (74.7)	433 (58.6)	707 (79.0)	1527 (70.2)	1072 (52.2)	1865 (72.5)	1530 (74.7)	1683 (56.3)	2709 (71.9)
ART at 3 months, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Days to ART Initiation*, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
In Care on ART at 6 months, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
First ART Regimen, n (%)	1 (0.1)	0 (0)	1 (0.1)	4 (0.5)	1 (0.1)	0 (0.0)	18 (0.8)	16 (0.8)	40 (1.6)	129 (6.3)	282 (9.4)	353 (9.0)

\*Missing values for CD4 count/percentage at ART initiation, Days to ART initiation, and First ART Regimen only represented among individuals known to have initiated ART.

<b>Table S3. Interrupted-Time-Series Estimates of Patient Outcomes at Timepoints since Guideline Implementation</b>								
	<b>&lt;2 years</b>		<b>2 to &lt;5 years</b>		<b>5 to &lt;15 years</b>		<b>15 to 19 years</b>	
	Percent (95% CI)	Change from Baseline (95% CI)	Percent (95% CI)	Change from Baseline (95% CI)	Percent (95% CI)	Change from Baseline (95% CI)	Percent (95% CI)	Change from Baseline (95% CI)
<b>ART Initiation Within 3 months</b>								
<u>Days after 2014 Guideline implementation</u>								
0	42.4 (37.6 - 47.2)	0 (REF)	39.3 (34.1 - 44.4)	0 (REF)	49.2 (45.7 - 52.7)	0 (REF)	52.4 (48.9 - 55.9)	0 (REF)
90	56.5 (51.7 - 61.2)	14.1 (7.2 - 21.0)	59.5 (53.7 - 65.2)	20.2 (12.3 - 28.2)	63.1 (59.7 - 66.5)	13.9 (9.0 - 18.9)	67.8 (64.9 - 70.6)	15.4 (10.7 - 20.0)
180	58.1 (53.8 - 62.4)	15.7 (9.1 - 22.3)	61.4 (56.2 - 66.7)	22.2 (14.7 - 29.7)	64.7 (61.7 - 67.8)	15.5 (10.8 - 20.2)	68.9 (66.4 - 71.5)	16.5 (12.1 - 21.0)
365	61.5 (58.1 - 64.9)	19.1 (13.1 - 25.1)	65.7 (61.6 - 69.8)	26.4 (19.7 - 33.1)	68.1 (65.7 - 70.5)	18.9 (14.6 - 23.2)	71.4 (69.4 - 73.3)	19.0 (14.9 - 23.1)
730	68.8 (66.2 - 71.5)	26.4 (20.9 - 32.0)	74.9 (71.7 - 78.0)	35.6 (29.5 - 41.7)	75.3 (73.5 - 77.2)	26.1 (22.2 - 30.1)	76.5 (75.0 - 78.0)	24.1 (20.2 - 27.9)
<u>Days after 2017 Guideline implementation</u>								
0	76.3 (71.5 - 81.2)	0 (REF)	84.5 (78.4 - 90.5)	0 (REF)	82.6 (79.3 - 86.0)	0 (REF)	81.4 (78.8 - 84.1)	0 (REF)
90	75.4 (71.1 - 79.8)	-0.9 (-7.6 - 5.9)	79.2 (74.2 - 84.1)	-5.3 (-13.4 - 2.7)	83.8 (81.1 - 86.5)	1.2 (-3.3 - 5.6)	92.0 (90.1 - 93.9)	10.6 (7.2 - 13.9)
180	76.3 (72.6 - 79.9)	-0.1 (-6.3 - 6.2)	79.7 (75.6 - 83.7)	-4.8 (-12.3 - 2.7)	84.2 (82.0 - 86.4)	1.6 (-2.6 - 5.7)	91.2 (89.7 - 92.7)	9.7 (6.6 - 12.9)
365	78.0 (75.6 - 80.5)	1.7 (-3.9 - 7.2)	80.7 (78.0 - 83.4)	-3.8 (-10.5 - 3.0)	85.0 (83.5 - 86.5)	2.3 (-1.4 - 6.1)	89.5 (88.4 - 90.5)	8.0 (5.1 - 10.9)
730	81.6 (77.9 - 85.2)	5.2 (-0.8 - 11.2)	82.8 (78.9 - 86.6)	-1.7 (-8.8 - 5.4)	86.6 (84.3 - 88.8)	3.9 (0.0 - 7.8)	86.2 (84.5 - 87.9)	4.8 (1.7 - 7.9)
	Median Days (95% CI)	Change from Baseline (95% CI)	Median Days (95% CI)	Change from Baseline (95% CI)	Median Days (95% CI)	Change from Baseline (95% CI)	Median Days (95% CI)	Change from Baseline (95% CI)
<b>Time to ART Initiation</b>								
<u>Days after 2014 Guideline implementation</u>								
0	95 (28 - 161)	0 (REF)	208 (166 - 249)	0 (REF)	68 (38 - 97)	0 (REF)	22 (-16 - 60)	0 (REF)
90	38 (-35 - 110)	-57 (-157 - 44)	32 (-18 - 81)	-176 (-242 - 109)	36 (3 - 70)	-31 (-77 - 14)	23 (-15 - 61)	1 (-54 - 56)
180	34 (-29 - 98)	-60 (-154 - 34)	29 (-14 - 72)	-179 (-240 - 117)	33 (4 - 62)	-35 (-77 - 8)	21 (-12 - 54)	-1 (-53 - 50)
365	27 (-20 - 74)	-67 (-150 - 16)	23 (-9 - 54)	-185 (-238 - 131)	26 (4 - 48)	-42 (-79 - -4)	16 (-8 - 41)	-6 (-52 - 40)
730	13 (-29 - 55)	-81 (-161 - -2)	11 (-18 - 40)	-197 (-248 - 146)	12 (-7 - 32)	-55 (-91 - -20)	8 (-13 - 29)	-14 (-58 - 29)
<u>Days after 2017 Guideline implementation</u>								
0	0 (0 - 71)	0 (REF)	0 (0 - 50)	0 (REF)	0 (0 - 33)	0 (REF)	0 (0 - 36)	0 (REF)
90	0 (0 - 75)	0 (-106 - 106)	0 (0 - 48)	0 (-72 - 72)	0 (0 - 32)	0 (-48 - 48)	0 (0 - 35)	0 (-52 - 52)



180	0 (0 - 61)	0 (-97 - 97)	0 (0 - 40)	0 (-66 - 66)	0 (0 - 27)	0 (-44 - 44)	0 (0 - 29)	0 (-48 - 48)
365	0 (0 - 41)	0 (-83 - 83)	0 (0 - 26)	0 (-58 - 58)	0 (0 - 18)	0 (-39 - 39)	0 (0 - 19)	0 (-42 - 42)
730	0 (0 - 65)	0 (-95 - 95)	0 (0 - 39)	0 (-62 - 63)	0 (0 - 28)	0 (-43 - 43)	0 (0 - 29)	0 (-46 - 46)
	Percent (95% CI)	Change from Baseline (95% CI)	Percent (95% CI)	Change from Baseline (95% CI)	Percent (95% CI)	Change from Baseline (95% CI)	Percent (95% CI)	Change from Baseline (95% CI)
<b>In Care on ART at 6 months</b>								
<u>Days after 2014 Guideline implementation</u>								
0	35.4 (30.5 - 40.3)	0 (REF)	40.2 (34.4 - 45.9)	0 (REF)	46.7 (43.0 - 50.4)	0 (REF)	40.1 (36.5 - 43.7)	0 (REF)
90	42.6 (37.6 - 47.6)	7.2 (0.1 - 14.3)	41.0 (35.3 - 46.8)	0.9 (-7.4 - 9.2)	55.4 (51.7 - 59.1)	8.7 (3.4 - 14.1)	46.9 (43.7 - 50.1)	6.8 (1.8 - 11.8)
180	43.3 (38.9 - 47.8)	8.0 (1.2 - 14.7)	42.8 (37.6 - 48.1)	2.7 (-5.3 - 10.6)	56.0 (52.7 - 59.3)	9.3 (4.3 - 14.4)	47.4 (44.6 - 50.3)	7.3 (2.6 - 12.0)
365	44.9 (41.5 - 48.3)	9.6 (3.5 - 15.6)	46.8 (42.6 - 51.0)	6.6 (-0.7 - 13.9)	57.3 (54.8 - 59.8)	10.6 (6.1 - 15.1)	48.4 (46.3 - 50.6)	8.3 (4.0 - 12.6)
730	48.2 (45.3 - 51.2)	12.8 (7.1 - 18.6)	55.7 (52.1 - 59.3)	15.5 (8.7 - 22.4)	59.9 (57.7 - 62.0)	13.2 (8.9 - 17.5)	50.5 (48.7 - 52.3)	10.4 (6.3 - 14.4)
<u>Days after 2017 Guideline implementation</u>								
0	51.4 (46.1 - 56.8)	0 (REF)	65.4 (58.2 - 72.5)	0 (REF)	62.3 (58.6 - 66.1)	0 (REF)	52.5 (49.3 - 55.7)	0 (REF)
90	46.6 (41.4 - 51.9)	-4.8 (-12.5 - 2.9)	57.1 (50.8 - 63.4)	-8.2 (-18.1 - 1.7)	69.0 (65.4 - 72.5)	6.6 (1.2 - 12.0)	57.1 (54.0 - 60.2)	4.6 (0.0 - 9.2)
180	47.3 (43.0 - 51.7)	-4.1 (-11.2 - 3.0)	56.8 (51.6 - 61.9)	-8.6 (-17.7 - .5)	68.2 (65.3 - 71.0)	5.8 (0.9 - 10.7)	56.5 (53.9 - 59.0)	4.0 (-0.2 - 8.2)
365	48.9 (45.9 - 51.8)	-2.6 (-8.8 - 3.6)	56.0 (52.6 - 59.3)	-9.4 (-17.5 - - 1.3)	66.5 (64.6 - 68.4)	4.2 (-0.2 - 8.5)	55.2 (53.5 - 56.8)	2.7 (-1.0 - 6.4)
730	52.0 (47.3 - 56.7)	0.6 (-6.4 - 7.6)	54.4 (49.4 - 59.4)	-10.9 (-19.6 - -2.3)	63.4 (60.4 - 66.4)	1.1 (-3.7 - 5.8)	52.7 (50.3 - 55.2)	0.3 (-3.7 - 4.3)

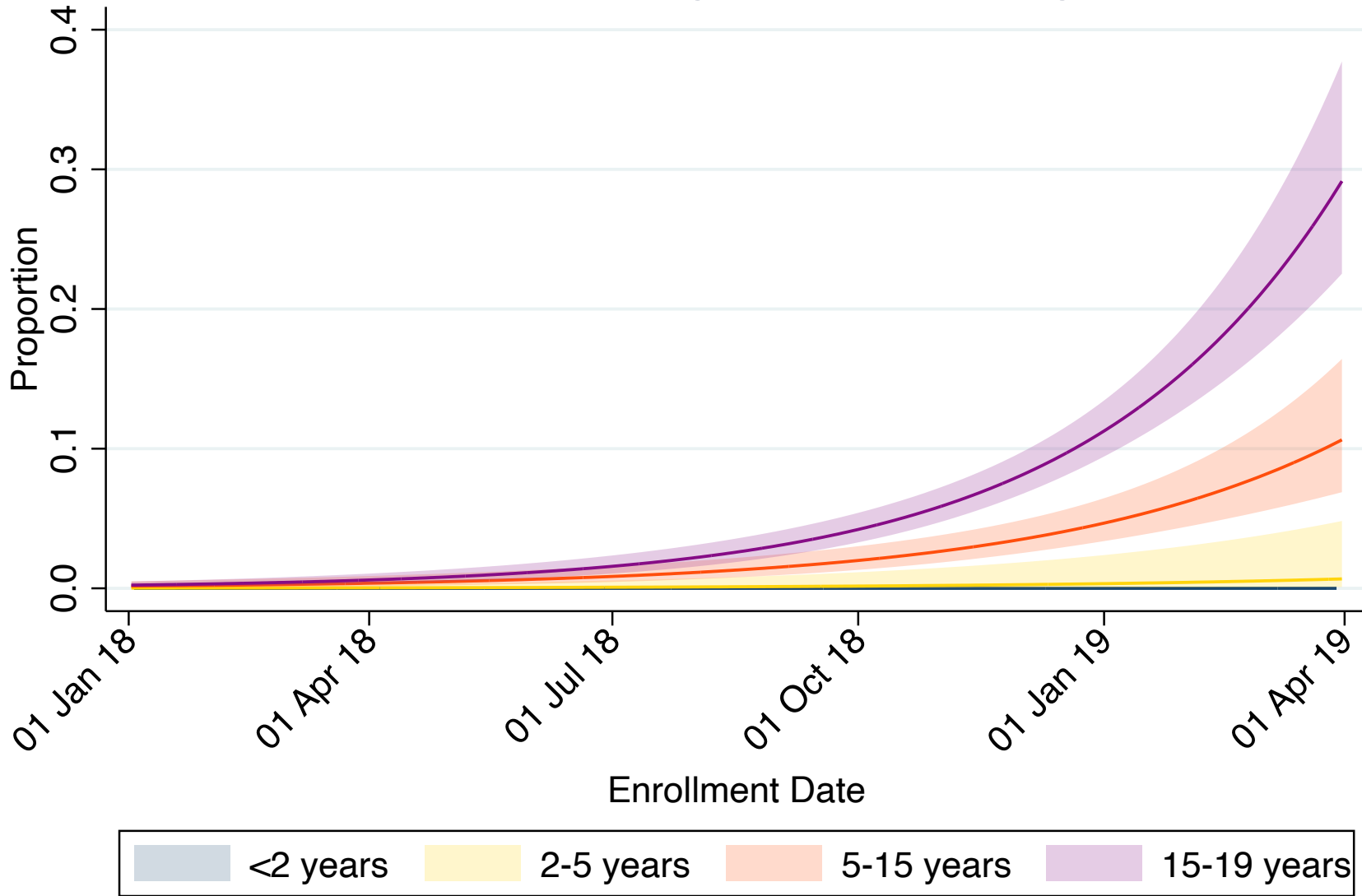
\*Table contains outcome estimates with 95% confidence intervals from interrupted-time-series models at 0, 90, 180, 365, and 730 days since the 2014 and 2017 guidelines were implemented. For ART initiation by 3 months and In Care on ART at 6 months, we present absolute percentages at each timepoint (with corresponding confidence intervals) and the change since the guideline were implemented (i.e., risk difference relative to the day guidelines were implemented). For Time to ART Initiation, we present median time to ART initiation (in days) and change to the median since guidelines were implemented.

<b>Table S4. Interrupted-Time-Series Estimates of First ART Regimens at Timepoints since Guideline Implementation</b>								
	<b>&lt;2 years</b>		<b>2 to &lt;5 years</b>		<b>5 to &lt;15 years</b>		<b>15 to 19 years</b>	
	Percent (95% CI)	Risk Difference (95% CI)	Percent (95% CI)	Risk Difference (95% CI)	Percent (95% CI)	Risk Difference (95% CI)	Percent (95% CI)	Risk Difference (95% CI)
<b>Efavirenz-based Regimen</b>								
<u>Days after 2014 Guideline implementation</u>								
0	8.2 (4.5 - 11.9)	0 (REF)	13.4 (9.2 - 17.7)	0 (REF)	40.1 (35.9 - 44.2)	0 (REF)	83.6 (79.6 - 87.5)	0 (REF)
90	11.8 (7.6 - 16.0)	3.6 (-2.1 - 9.4)	18.9 (13.0 - 24.8)	5.4 (-2.1 - 12.9)	46.1 (42.4 - 49.7)	6.0 (0.4 - 11.6)	92.6 (90.6 - 94.5)	9.0 (4.4 - 13.5)
180	11.2 (7.8 - 14.7)	3.1 (-2.1 - 8.2)	18.9 (13.8 - 24.1)	5.5 (-1.4 - 12.4)	48.6 (45.2 - 52.0)	8.5 (3.1 - 14)	92.9 (91.2 - 94.7)	9.4 (4.9 - 13.8)
365	10.1 (7.8 - 12.4)	1.9 (-2.5 - 6.4)	19.0 (15.3 - 22.8)	5.6 (-0.2 - 11.4)	54.2 (51.4 - 57.0)	14.1 (9.0 - 19.2)	93.7 (92.5 - 95.0)	10.1 (5.9 - 14.4)
730	8.2 (6.3 - 10.2)	0.1 (-4.1 - 4.3)	19.2 (16.0 - 22.5)	5.8 (0.4 - 11.2)	67.2 (65.1 - 69.3)	27.1 (22.5 - 31.8)	95.3 (94.5 - 96.1)	11.7 (7.7 - 15.8)
<u>Days after 2017 Guideline implementation</u>								
0	6.8 (4.1 - 9.6)	0 (REF)	19.4 (13.6 - 25.2)	0 (REF)	81.8 (77.7 - 86.0)	0 (REF)	96.7 (95.3 - 98.2)	0 (REF)
90	7.3 (4.0 - 10.7)	0.5 (-4.1 - 5.1)	22.4 (16.5 - 28.4)	3.0 (-5.6 - 11.6)	75.3 (71.7 - 78.9)	-6.6 (-12.3 - -0.9)	100 (98.4 - 100)	3.4 (1 - 5.7)
180	6.4 (4.0 - 8.8)	-0.4 (-4.3 - 3.5)	21.6 (16.9 - 26.3)	2.2 (-5.5 - 9.9)	73.7 (70.8 - 76.5)	-8.2 (-13.4 - -3.0)	98.1 (96.8 - 99.3)	1.3 (-0.7 - 3.4)
365	4.9 (3.6 - 6.3)	-1.9 (-5.0 - 1.3)	20.1 (17.1 - 23.0)	0.7 (-5.9 - 7.3)	70.5 (68.6 - 72.4)	-11.4 (-16.0 - -6.7)	94.0 (93.2 - 94.8)	-2.8 (-4.5 - -1.0)
730	2.9 (1.5 - 4.4)	-3.9 (-6.9 - -0.8)	17.3 (13.3 - 21.4)	-2.1 (-9.0 - 4.9)	64.6 (61.4 - 67.7)	-17.3 (-22.4 - -12.2)	86.4 (84.5 - 88.4)	-10.3 (-12.7 - -7.9)
<b>Nevirapine-based Regimen</b>								
<u>Days after 2014 Guideline implementation</u>								
0	65.0 (59.7 - 70.2)	0 (REF)	72.6 (67.0 - 78.2)	0 (REF)	50.9 (47.4 - 54.5)	0 (REF)	14.7 (12.4 - 17.0)	0 (REF)
90	57.1 (48.8 - 65.4)	-7.9 (-17.9 - 2.2)	61.8 (52.3 - 71.3)	-10.8 (-22.2 - 0.6)	52.5 (46.9 - 58.1)	1.6 (-5.3 - 8.4)	4.6 (2.6 - 6.5)	-10.2 (-13.2 - -7.1)
180	48.5 (42.5 - 54.4)	-16.5 (-24.6 - -8.4)	53.2 (46.3 - 60.1)	-19.4 (-28.6 - -10.2)	45.3 (41.2 - 49.4)	-5.6 (-11.2 - 0.0)	4.0 (2.5 - 5.4)	-10.8 (-13.5 - -8.0)
365	34.6 (31.3 - 37.9)	-30.4 (-36.7 - -24.1)	39.0 (35.0 - 43.1)	-33.5 (-40.6 - -26.5)	33.5 (31.1 - 35.9)	-17.4 (-21.8 - -13.1)	3.0 (2.2 - 3.8)	-11.7 (-14.2 - -9.3)
730	17.8 (15.0 - 20.5)	-47.2 (-53.1 - -41.3)	21.2 (17.7 - 24.8)	-51.3 (-57.9 - -44.7)	18.5 (16.5 - 20.5)	-32.5 (-36.6 - -28.4)	1.7 (1.1 - 2.3)	-13.0 (-15.4 - -10.7)
<u>Days after 2017 Guideline implementation</u>								
0	9.7 (7.1 - 12.2)	0 (REF)	12.1 (8.7 - 15.6)	0 (REF)	10.7 (8.7 - 12.6)	0 (REF)	1.0 (0.4 - 1.7)	0 (REF)
90	5.3 (2.6 - 7.9)	-4.4 (-8.0 - -0.7)	9.3 (5.1 - 13.5)	-2.9 (-8.4 - 2.7)	7.5 (5.5 - 9.5)	-3.2 (-6.1 - -0.3)	1.0 (0.3 - 1.7)	0.0 (-1.0 - 0.9)
180	4.7 (2.8 - 6.7)	-4.9 (-8.1 - -1.7)	7.9 (4.9 - 10.8)	-4.3 (-8.8 - 0.3)	7.0 (5.5 - 8.6)	-3.7 (-6.2 - -1.1)	1.0 (0.4 - 1.5)	-0.1 (-0.9 - 0.8)
365	3.8 (2.6 - 4.9)	-5.9 (-8.7 - -3.1)	5.6 (4.0 - 7.2)	-6.5 (-10.3 -	6.1 (5.1 - 7.1)	-4.6 (-6.8 - -2.3)	0.9 (0.6 - 1.2)	-0.2 (-0.9 - 0.6)

730	2.4 (1.0 - 3.7)	-7.3 (-10.1 – -4.4)	2.9 (1.4 - 4.4)	-2.7 -9.3 (-13.0 – -5.5)	4.7 (3.4 - 6.0)	-6.0 (-8.3 – -3.7)	0.7 (0.2 - 1.2)	-0.3 (-1.1 - 0.5)
<b>Lopinavir-based Regimen</b>								
<u>Days after 2014 Guideline implementation</u>								
0	14.0 (9.1 - 18.9)	0 (REF)	3.6 (0.9 - 6.2)	0 (REF)	1.5 (0.5 - 2.4)	0 (REF)	1.1 (0.2 - 2.0)	0 (REF)
90	34.8 (30.0 - 39.5)	20.7 (13.7 - 27.7)	19.1 (15.0 - 23.2)	15.5 (10.5 - 20.5)	2.4 (1.3 - 3.4)	0.9 (-0.5 - 2.3)	2.7 (1.2 - 4.3)	1.6 (-0.3 - 3.5)
180	37.5 (33.0 - 42.0)	23.5 (16.6 - 30.3)	21.6 (17.4 - 25.7)	18.0 (12.9 - 23.0)	2.6 (1.6 - 3.7)	1.2 (-0.3 - 2.6)	2.3 (1.2 - 3.4)	1.2 (-0.3 - 2.7)
365	43.8 (39.9 - 47.8)	29.8 (23.4 - 36.3)	27.7 (23.7 - 31.6)	24.1 (19.2 - 29.0)	3.3 (2.3 - 4.2)	1.8 (0.4 - 3.2)	1.6 (1.0 - 2.2)	0.5 (-0.6 - 1.6)
730	59.7 (56.6 - 62.7)	45.6 (39.8 - 51.5)	45.2 (41.4 - 49.1)	41.7 (36.9 - 46.4)	5.0 (4.0 - 6.0)	3.6 (2.2 - 5.0)	0.8 (0.4 - 1.2)	-0.3 (-1.3 - 0.7)
<u>Days after 2017 Guideline implementation</u>								
0	79.1 (7.03 - 85.3)	0 (REF)	71.1 (62.2 - 79.9)	0 (REF)	7.5 (5.2 - 9.8)	0 (REF)	0.4 (0.1 - 0.8)	0 (REF)
90	76.0 (71.2 - 80.8)	-3.1 (-11.2 - 5.0)	59.1 (52.8 - 65.4)	-12.0 (-23.3 – -0.7)	11.9 (9.5 - 14.2)	4.4 (0.9 - 7.8)	1.6 (0.7 - 2.5)	1.2 (0.2 - 2.1)
180	76.8 (72.8 - 80.7)	-2.4 (-10.0 - 5.2)	60.3 (55.0 - 65.7)	-10.7 (-21.4 – -0.1)	12.5 (10.5 - 14.6)	5.0 (1.8 - 8.3)	1.6 (0.9 - 2.3)	1.2 (0.4 - 2.0)
365	78.3 (75.6 - 80.9)	-0.9 (-7.7 - 6.0)	63.0 (59.3 - 66.6)	-8.1 (-17.9 - 1.7)	14.0 (12.4 - 15.5)	6.5 (3.6 - 9.4)	1.6 (1.1 - 2.0)	1.2 (0.6 - 1.7)
730	81.4 (77.5 - 85.4)	2.3 (-5.0 - 9.5)	68.5 (63.3 - 73.7)	-2.6 (-12.7 - 7.6)	17.4 (14.8 - 20.0)	9.9 (6.5 - 13.3)	1.5 (0.8 - 2.3)	1.1 (0.3 - 2.0)

\*Table contains outcome estimates with 95% confidence intervals from interrupted-time-series models at 0, 90, 180, 365, and 730 days since the 2014 and 2017 guidelines were implemented. We present absolute percentages at each timepoint (with corresponding confidence intervals) and also the change since the guideline were implemented (i.e., risk difference relative to the day guidelines were implemented).

# Scale-Up of Dolutegravir-Based Regimens



**Figure S5: Scale-Up of Dolutegravir-Based Regimens.** Lines with shaded regions represent descriptive estimates with 95% confidence intervals of the proportion of individuals who were first started on a dolutegravir-based regimen based on their date of enrollment, stratified by age group.

<b>Table S6. Mixed-Effects Poisson Regression of Factors Associated with ART Initiation and Retention in Care</b>								
	<b>&lt;2 years</b>		<b>2 to &lt;5 years</b>		<b>5 to &lt;15 years</b>		<b>15 to 19 years</b>	
	<b>Risk Ratio (95% CI)</b>	<b>p-value</b>	<b>RR (95% CI)</b>	<b>p-value</b>	<b>RR (95% CI)</b>	<b>p-value</b>	<b>RR (95% CI)</b>	<b>p-value</b>
<b>ART Initiation Within 3 months</b>								
Male Sex	1.03 (0.99-1.08)	0.18	1.05 (1.00-1.10)	0.036	1.02 (0.99-1.05)	0.19	1.02 (0.99-1.06)	0.25
CD4 Performed at Enrollment	1.11 (1.04-1.19)	0.0011	1.03 (0.97-1.08)	0.31	1.04 (0.99-1.08)	0.098	1.00 (0.97-1.03)	0.95
Facility Size, per 50 patient increase	0.99 (0.96-1.02)	0.49	0.99 (0.97-1.02)	0.59	0.99 (0.97-1.01)	0.46	1.00 (0.99-1.00)	0.62
Province								
Lusaka	1 (REF)	0.27	1 (REF)	0.93	1 (REF)	0.93	1 (REF)	0.19
Western	1.14 (0.91-1.42)		0.99 (0.80-1.23)		0.99 (0.86-1.15)		1.04 (0.98-1.12)	
Time Period, per 30 day increase during period								
2010 Guidelines	1.00 (1.00-1.01)	0.39	1.00 (0.99-1.00)	0.26	1.01 (1.00-1.01)	0.017	1.01 (1.00-1.01)	<0.0001
2014 Guidelines – First 90 days	1.08 (1.02-1.14)	0.0094	1.15 (1.07-1.22)	<0.0001	1.08 (1.03-1.13)	0.0011	1.09 (1.04-1.14)	0.0004
2014 Guidelines – After 90 days	1.01 (1.00-1.02)	0.0010	1.01 (1.00-1.01)	0.0017	1.01 (1.00-1.01)	<0.0001	1.01 (1.00-1.01)	0.0092
2017 Guidelines – First 90 days	1.01 (0.98-1.04)	0.53	1.00 (0.97-1.02)	0.92	1.00 (0.98-1.02)	0.72	1.04 (1.02-1.06)	0.0003
2017 Guidelines – After 90 days	1.00 (0.99-1.01)	0.95	1.00 (1.00-1.00)	0.51	1.00 (1.00-1.00)	0.48	1.00 (0.99-1.00)	0.31
Facility – Intraclass Correlation	0.23 (0.16-0.32)		0.22 (0.15-0.32)		0.17 (0.12-0.24)		0.05 (0.03-0.08)	

\*Weight-for-age z-score calculated for those <5 years old, BMI-for-age z-score calculated for those 5-19 years old

**Table S6 (cont). Mixed-Effects Poisson Regression of Factors Associated with ART Initiation and Retention in Care**

	<b>&lt;2 years</b>		<b>2 - &lt;5 years</b>		<b>5 - &lt;15 years</b>		<b>15-19 years</b>	
	<b>Risk Ratio (95% CI)</b>	<b>p-value</b>	<b>RR (95% CI)</b>	<b>p-value</b>	<b>RR (95% CI)</b>	<b>p-value</b>	<b>RR (95% CI)</b>	<b>p-value</b>
<b>In Care on ART at 6 months</b>								
Male Sex	1.01 (0.93-1.10)	0.77	1.05 (0.97-1.14)	0.21	1.03 (0.99-1.06)	0.15	1.14 (1.06-1.22)	0.0004
CD4 Performed at Enrollment	1.35 (1.20-1.50)	<0.0001	1.16 (1.05-1.27)	0.0026	1.16 (1.10-1.22)	<0.0001	1.26 (1.18-1.34)	<0.0001
Facility Size, per 50 patient increase	0.99 (0.97-1.02)	0.60	0.99 (0.97-1.02)	0.70	1.00 (0.97-1.02)	0.79	1.00 (0.99-1.00)	0.53
Province								
Lusaka	1 (REF)	0.082	1 (REF)	0.089	1 (REF)	0.066 0.063	1 (REF)	0.027
Western	0.76 (0.56-1.04)		0.76 (0.56-1.04)		0.76 (0.57-1.02)		0.81 (0.67-0.98)	
Time Period, per 30 day increase during period								
2010 Guidelines	1.01 (1.00-1.01)	0.052	1.01 (1.00-1.02)	0.020	1.01 (1.00-1.02)	0.0034	1.01 (1.01-1.02)	0.0003
2014 Guidelines – First 90 days	1.04 (0.98-1.10)	0.18	1.02 (0.95-1.09)	0.56	1.06 (0.99-1.12)	0.080	1.05 (1.00-1.11)	0.053
2014 Guidelines – After 90 days	1.01 (1.00-1.02)	0.0079	1.01 (1.00-1.02)	0.0051	1.00 (1.00-1.01)	0.13	1.01 (1.00-1.01)	0.052
2017 Guidelines – First 90 days	0.97 (0.92-1.03)	0.31	0.98 (0.92-1.05)	0.60	1.04 (1.01-1.07)	0.0033	1.03 (0.99-1.06)	0.13
2017 Guidelines – After 90 days	1.00 (0.99-1.01)	0.56	0.99 (0.98-1.00)	0.31	1.00 (0.99-1.00)	0.15	1.00 (0.99-1.01)	0.56
Facility – Intraclass Correlation	0.12 (0.08-0.18)		0.14 (0.09-0.22)		0.19 (0.13-0.27)		0.03 (0.02-0.06)	

\*Weight-for-age z-score calculated for those <5 years old, BMI-for-age z-score calculated for those 5-25 years old