

Treat All Adoption Improves Rapid Treatment Initiation in Six Sub-Saharan Countries

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BACKGROUND

Implementation of the World Health Organization's 2015 recommendation of universal HIV treatment (Treat All) is accelerating in low- and middle-income countries. To date, there has not been a rigorous assessment of the real-world impact of Treat All on antiretroviral treatment (ART) uptake across different practice and implementation contexts.

METHODS

<u>Aim</u>: To (a) describe rapid ART initiation (within 30 days) rates under different country-level eligibility guidelines, (b) assess the impact of Treat All policies on rapid ART initiation, and (c) identify factors associated with failure to start treatment rapidly under Treat All.

<u>Data</u>: Longitudinal medical record data from 814,603 patients ≥16 years old, enrolled in HIV care in six sub-Saharan African countries (Rwanda, Kenya, Burundi, Malawi, Zambia, Uganda).

• Patients enrolling 30 days prior to the date of national Treat All adoption were excluded from regression discontinuity analyses to prevent overlap in outcome estimation windows.

<u>Outcome</u>: Rapid ART initiation — initiation of treatment within 30 days of enrollment in HIV care. <u>Analysis</u>:

Effect of ART eligibility expansion to Treat All on rapid ART initiation

• A regression discontinuity design was used, with the date of HIV care enrollment used as a continuous eligibility assignment variable, creating a quasi-experimental condition where the only systematic difference between patients enrolling before and after Treat All adoption is the probability of treatment eligibility.

Risk difference at Treat All adoption threshold (percentage points)^a 14.2 17.7 (2.2, 26.2) 95% Confidence Interval (6.5, 28. 41.7) p-value Imbens-Kalyanaraman bandwidth, days 405 376 N within bandwidth 1,163 2,189 Predicted outcomes at the Treat All threshold^a Enrollment just before Treat All adoption 55.7% 44.4% 73.4% Enrollment just after Treat All adoption 78.9% 80.7% Relative change after Treat All adoption 77.7% 31.8% 46.7% Slopes before and after Treat All adoption^b Percentage point change in rapid ART initiation per month before Treat All adoption 0.6 0.4 Percentage point change in rapid ART initiation per month after Treat All adoption 0.8 0.7 p-value for difference of slopes 0.105 0.619 0.006

Table 1. Effect of enrollment under Treat All on rapid ART initiation (within 30 days of enrollment), by country and pooled, and slopes before and after Treat All adoption

^a Risk difference and predicted outcomes at the Treat All threshold are from regression discontinuity analysis. Effects are calculated at the modified guideline expansion threshold of 31 days before versus one day after Treat All adoption.

^b Slope comparison is from separate linear regression models comparing the period before Treat All adoption (starting 90 days after ART eligibility expansion to CD4≤500) and after adoption.

di	Malawi	Zambia	Uganda
	12.5	0.4	-4.2
8.9)	(7.5, 17.5)	(-2.9, 3.8)	(-9.0, 0.7)
2	<0.001	0.804	0.090
	97	79	205
3	5 <i>,</i> 020	12,762	5,371
6	68.6%	62.4%	70.6%
6	81.1%	62.8%	66.4%
6	18.2%	0.6%	-5.9%
	0.1	0.2	0.4
	2.8	2.6	2.2
9	<0.001	<0.001	<0.001

METHODS (CONT.)

- with data-driven Imbens-Kalyanaraman bandwidths.
- Due to incomplete information about patient ART eligibility, this study is an intent-to-treat analysis using a "sharp" regression discontinuity design.

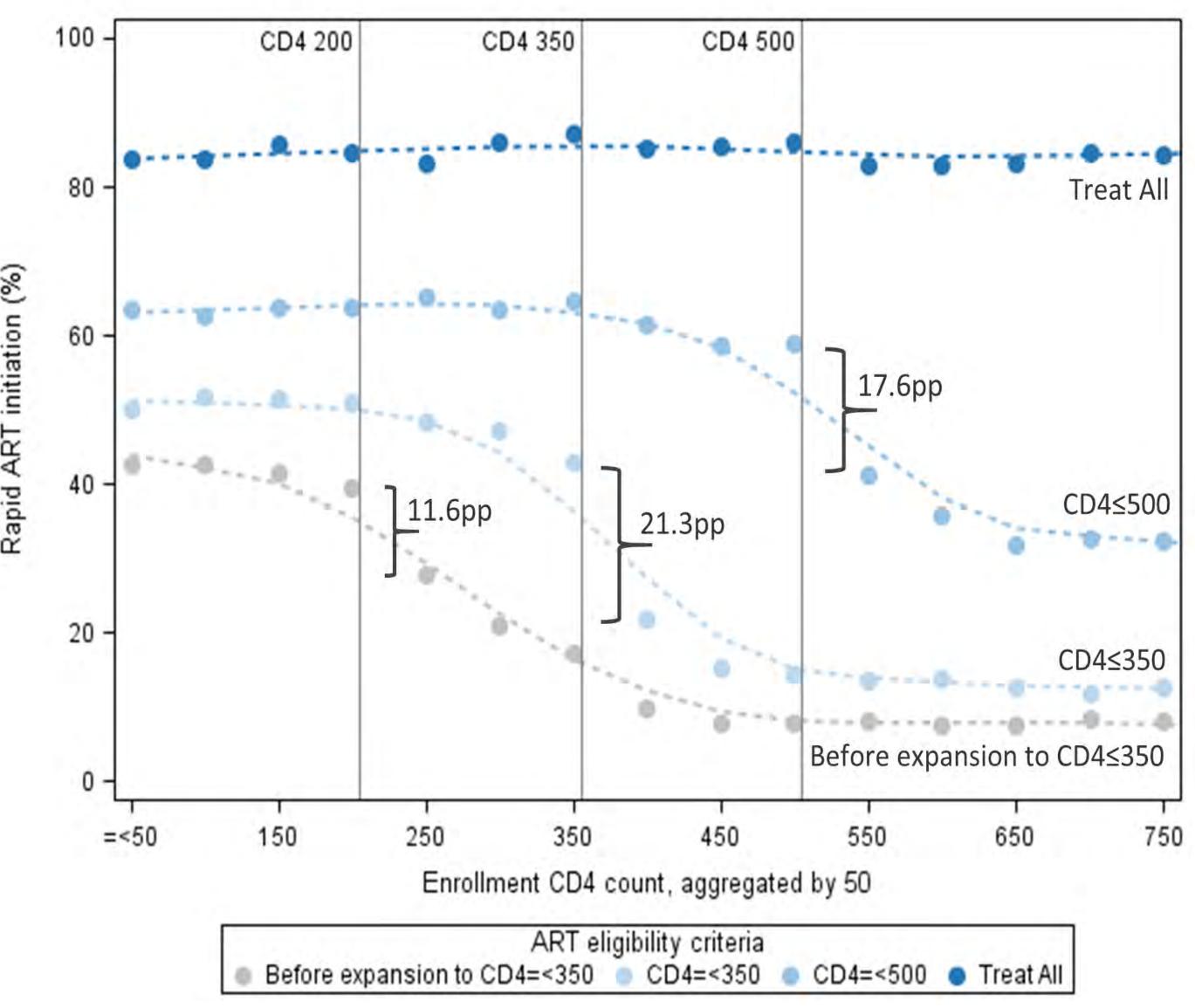
Trends in rapid ART initiation before and after Treat All adoption

Factors associated with failure

FINDINGS

- Across the six countries, 81.6% of patients enrolling under Treat All initiated treatment rapidly.
- Rapid ART initiation under Treat All was highest in Malawi (88.9%) and Rwanda (86.9%), and lowest in Burundi (77.9%).
- Large increases in rapid ART initiation were observed at every enrollment CD4 count level after each CD4-based ART eligibility expansion prior to national adoption of Treat All. However, there was little difference in rapid ART initiation across enrollment CD4 count levels under Treat All (Fig 1).
- There were statistically significant increases in rapid ART initiation following national adoption of Treat All in Rwanda, Kenya, Burundi, and Malawi (Table 1).
- The greatest increases in rapid ART initiation immediately after Treat All adoption were observed in Cl: 6.5 to 28.9pp) (Fig 2).





• Predicted outcomes and risk differences at the Treat All threshold date were estimated using local linear regressions

• Slopes from linear regression models for the period before (starting 90 days after eligibility expansion to CD4 \geq 500) and after the Treat All adoption date, expressed as percentage point (pp) change in rapid ART initiation per month.

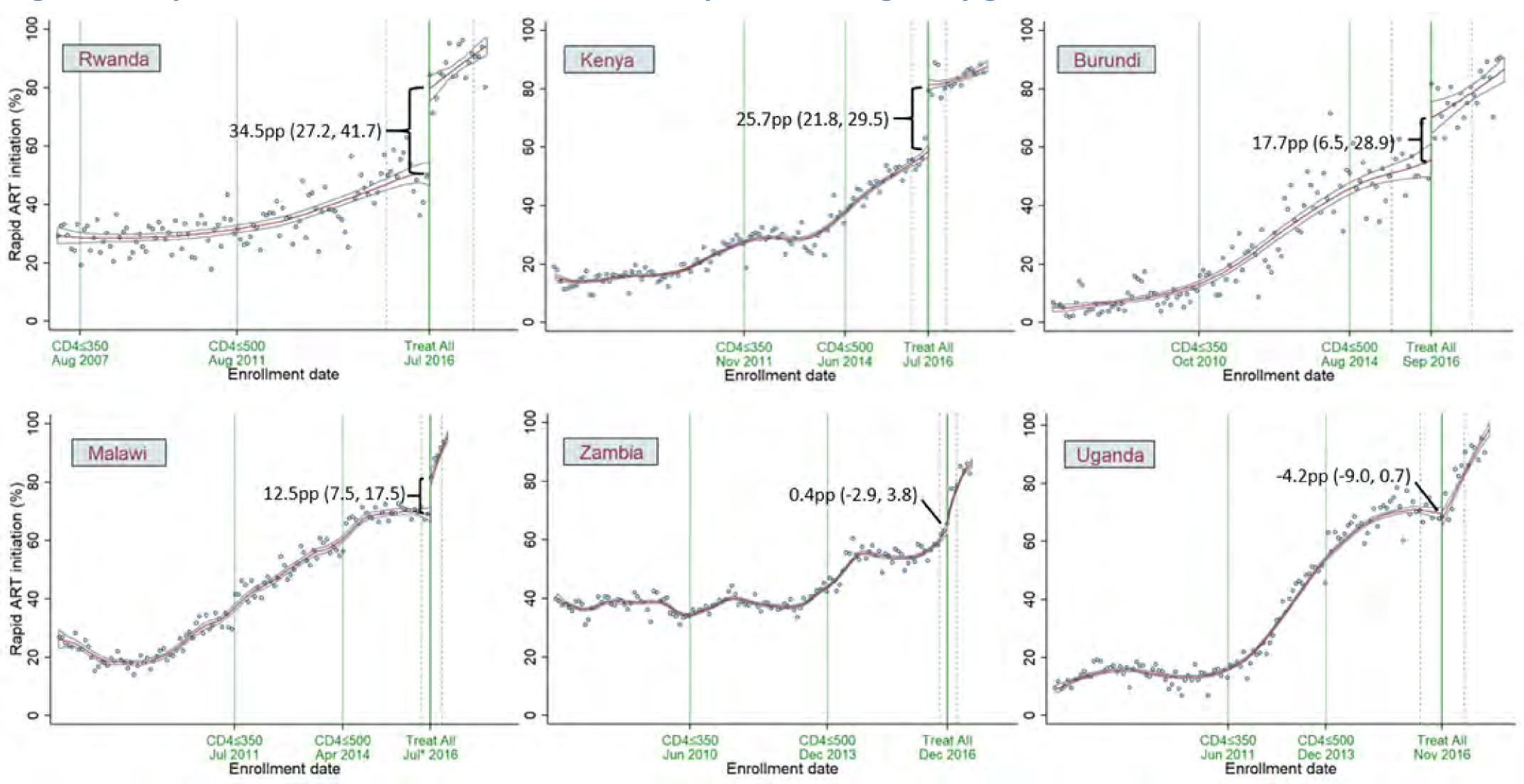
• A modified multivariable Poisson model was fitted for all six countries, with age group (16-24, ≥25 years), sex, country, and time between Treat All adoption and enrollment (0-<3 mos., 3-<6 mos., 6-<12 mos., and ≥12 mos.) as covariates.

• For all countries, national adoption of Treat All was associated with large increases in rapid ART initiation.

Figure 1. Rapid ART initiation under different ART eligibility guidelines and enrollment CD4 counts

Rwanda (34.5 pp; 95% CI: 27.2-41.7 pp), Kenya (25.7pp, 95% CI: 21.8 to 29.5pp), and Burundi (17.7pp, 95%

FINDINGS (CONT.)



in the regression discontinuity analyses

CONCLUSION

Our study demonstrates a strong and sustained effect of national-level adoption of Treat All policies on rapid ART initiation in diverse, largely public-sector, service-delivery settings across six sub-Saharan African countries. We found no evidence that the most immunosuppressed patients are being "crowded out" by patients with less advanced disease under Treat All, nor were there appreciable differences in rates of rapid ART initiation across different enrollment CD4 counts. Adoption and implementation of Treat All policies should be accelerated, with particular care to identify and address possible barriers to treatment by subgroups at higher risk of not rapidly initiating treatment following diagnosis and care enrollment (e.g., young adults and males).

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• After Treat All adoption, the rate of rapid ART initiation increased most in Malawi (from 0.1 to 2.8pp/ mo.), Zambia (from 0.2 to 2.6pp), and Uganda (from 0.4 to 2.2pp) (all p<0.001).

• Among patients enrolling under Treat All, persons ages 16-24 years had an 18% greater risk of not starting ART rapidly compared to those ≥25 years old (adjusted risk ratio [aRR]=1.18, 95% CI: 1.12 to 1.24), and males had a 12% higher risk than females (aRR=1.12, 95% CI: 1.07 to 1.17).

Figure 2. Rapid ART initiation under Treat All and prior ART eligibility guidelines, 2007-2018^a

elays. Labels include effect sizes (percentage point change in the proportion of patients rapidly initiating ART) and 95% confidence intervals from nalysis across the Treat All adoption date threshold. Dotted lines on either side of the Treat All date represent the width of the Imbens-Kalyanaraman bandwidth used