WEB MATERIAL

One Pill, Once a Day: Simplified Treatment Regimens and Retention in HIV Care

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WEB APPENDIX

Two-Stage Least Squares Equations for Estimation of the Complier Average Causal Effect of Fixed-Dose Combination Treatment Relative to Multiple-Pill Treatment on Attrition

First stage:

$$E[T_i|Z_i] = \beta_0 + \beta_1(Z_i - c) + \beta_2\, 1[Z_i < c] + \beta_3(Z_i - c)*1[Z_i < c]$$

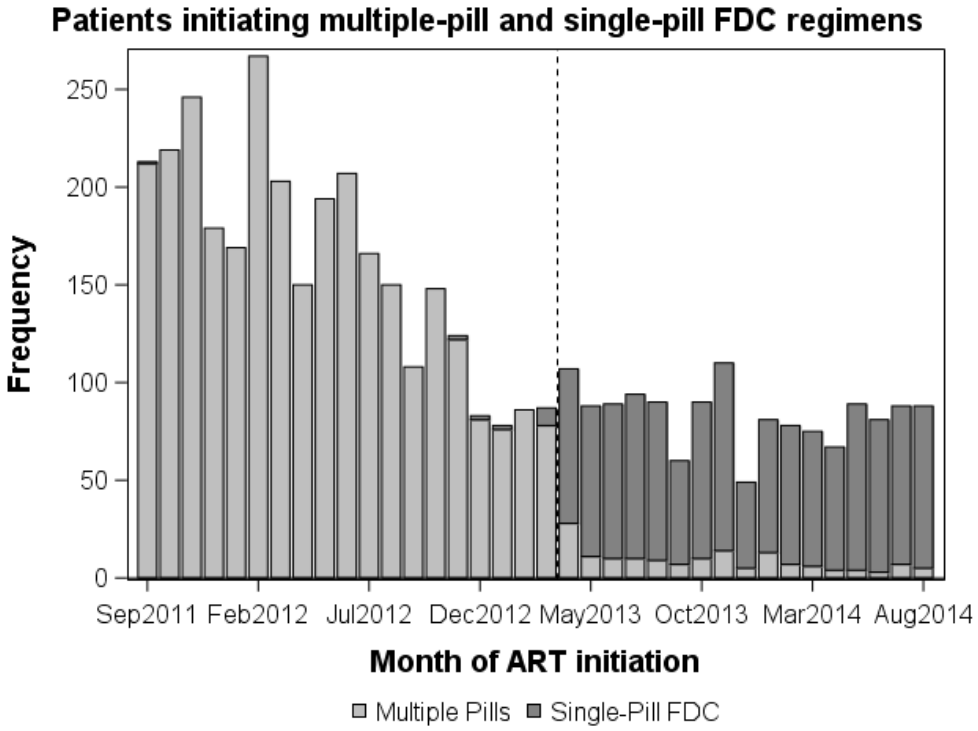
Second stage:

$$E[Y_i|\hat{T}_i] = \beta_0 + \beta_1(Z_i - c) + \beta_2(\hat{T}_i) + \beta_3(Z_i - c)*(\hat{T}_i)$$

where T_i represents treatment regimen, Z_i represents an individual's date of ART initiation, and c is a constant for April 1, 2013.

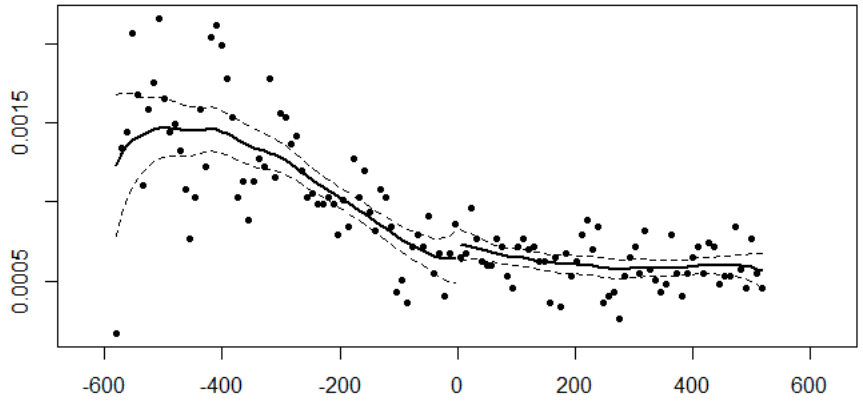
For the first stage of this two-stage least squares regression we fit local linear regression curves before and after the April 2013 threshold to estimate the probability of FDC treatment for each individual. We used this result as a predictor in a second-stage local linear regression model to estimate the risk of attrition according to each individual's probability of FDC treatment. The second-stage coefficient for the predicted probability of FDC variable is the Complier Average Causal Effect (CACE) of FDC treatment on attrition, specific to an unidentifiable population of "compliers" who would have been prescribed multiple-pill treatments had they initiated ART before the policy change, or FDCs had they initiated ART after the policy change. The CACE estimated by two-stage least squares is equal to the ITT effect divided by the change in probability of FDC treatment at the threshold.

Web Figure 1. Monthly count of patients initiating antiretroviral therapy at Themba Lethu Clinic in Johannesburg, South Africa, according to type of regimen prescribed: multiple-pill versus single-pill.



FDC = fixed-dose combination; ART = antiretroviral therapy

Web Figure 2. McCrary density test for bunching of ART initiation at the April 1, 2013 policy change recommending fixed-dose combination treatment as standard first-line ART

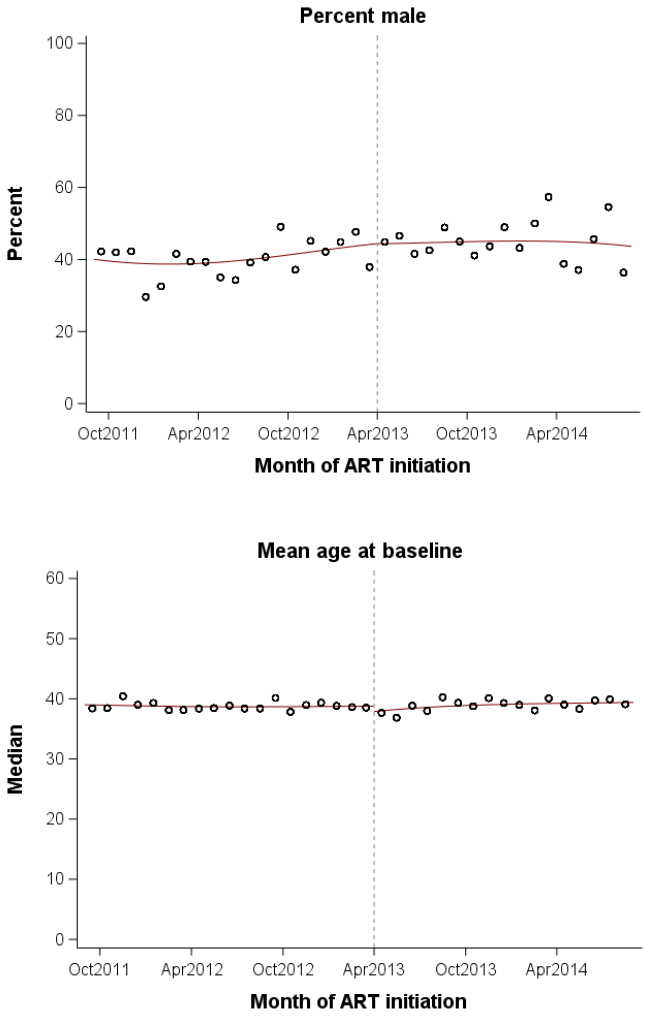


Bin size = 9 days; bandwidth = ±160 days

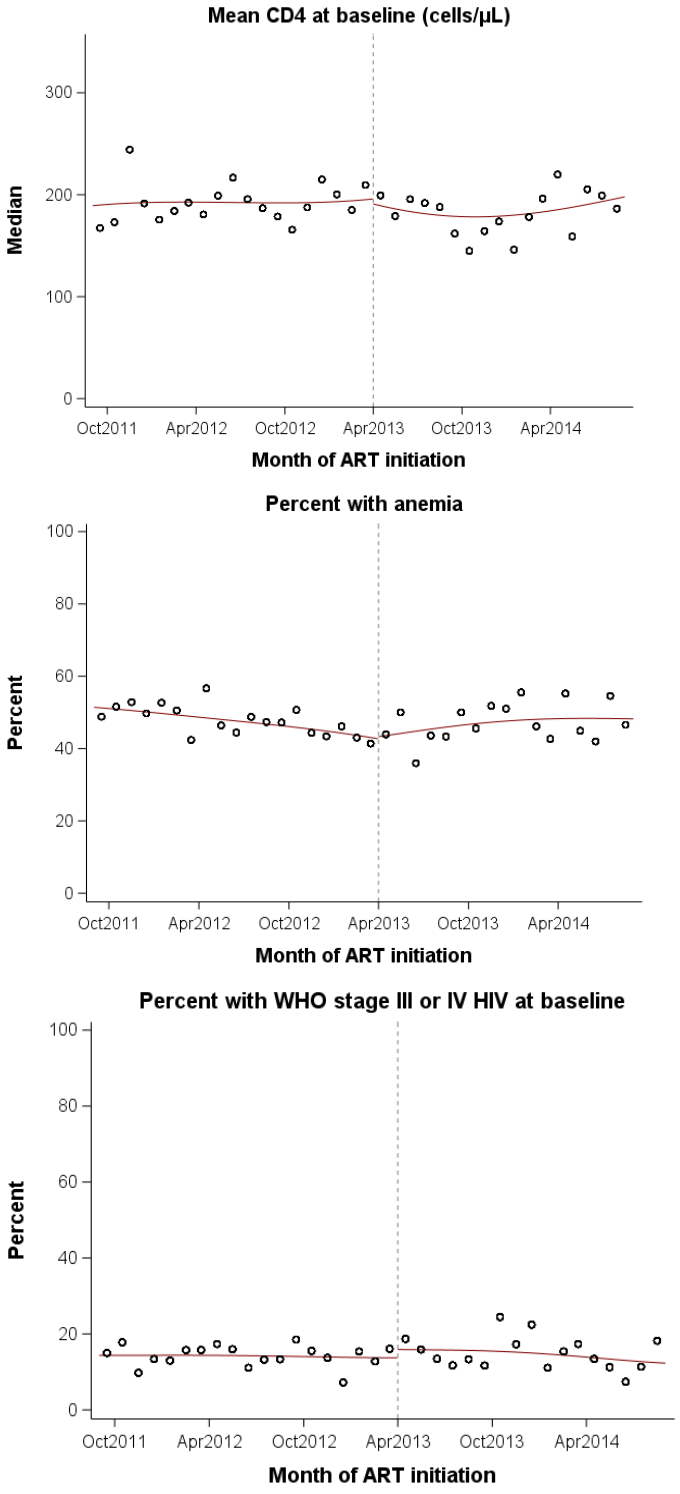
X axis value 0 = April 1, 2013

Risk difference = 0.11 (SE 0.14), p = 0.43

Web Figure 3. Evaluating the balance in baseline covariates at the date of the policy change, April 1, 2013. Plots show monthly mean covariate values according to date of antiretroviral therapy initiation for patients who initiated HIV treatment at Themba Lethu Clinic in Johannesburg, South Africa.

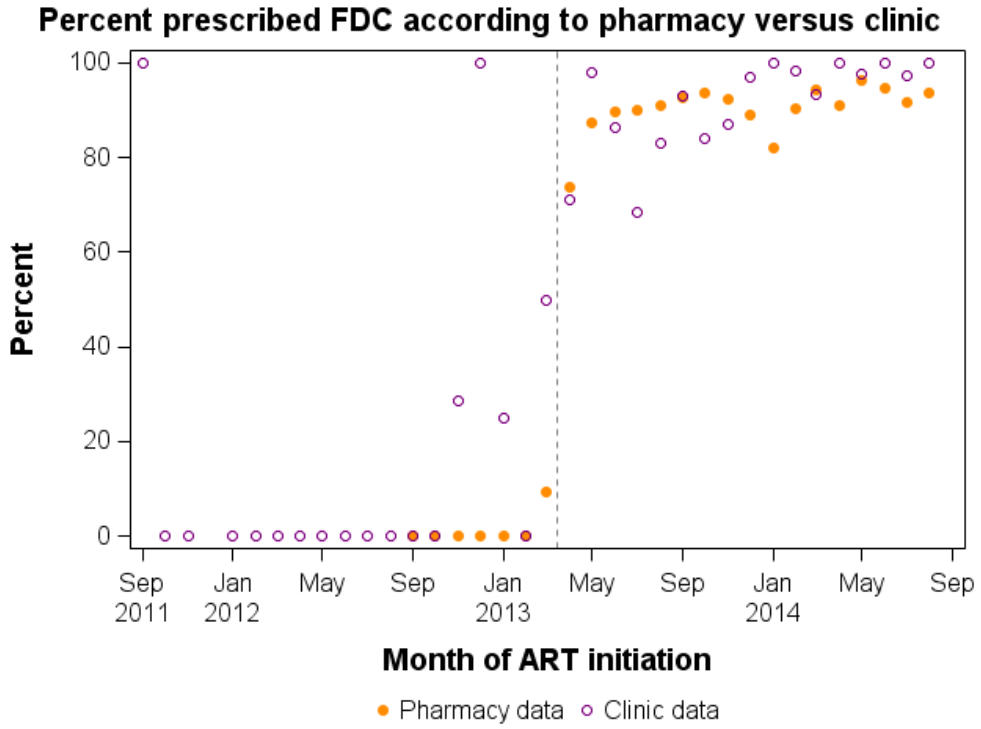


Web Figure 3, continued



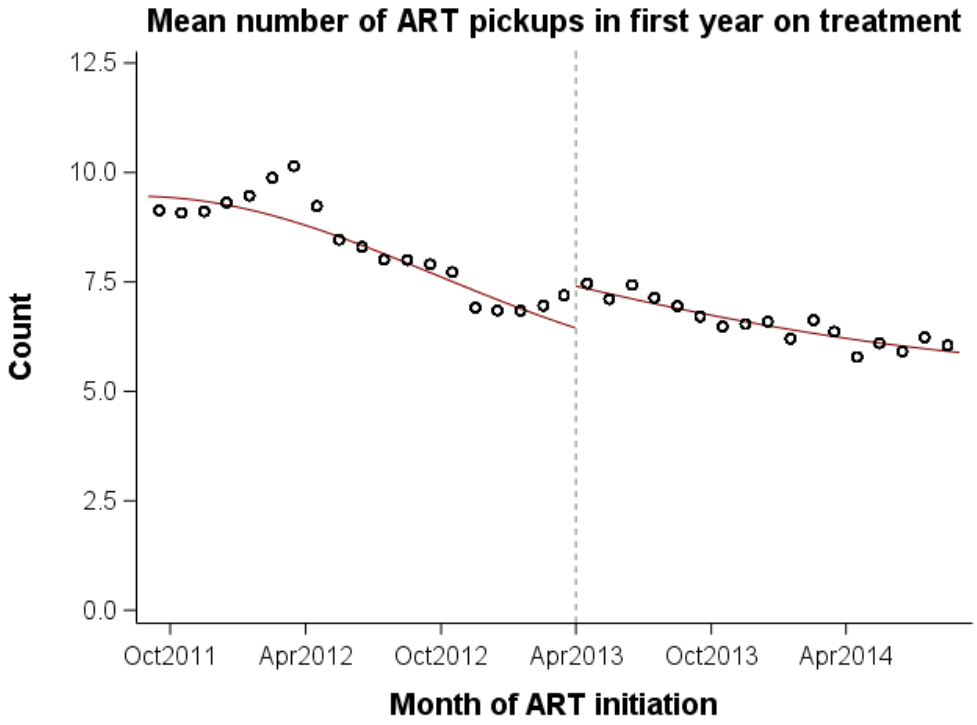
ART = antiretroviral therapy; WHO = World Health Organization

Web Figure 4. Sensitivity analysis: Comparing patterns in monthly percent of patients prescribed fixed-dose combination treatment in pharmacy versus clinic records in Themba Lethu Clinic, Johannesburg, South Africa.



FDC = fixed-dose combination; ART = antiretroviral therapy

Web Figure 5. Mean count of ART pickups per patient at the hospital pharmacy in the first year on HIV treatment at Themba Lethu Clinic in Johannesburg, South Africa.



ART = antiretroviral therapy

Web Table 1. (A) First stage (complier proportion), (B) Intention-to-treat, and (C) Complier average causal effect regression discontinuity results for all attrition outcomes, using bandwidth optimized for CACE analysis. Exposure for ITT is the April 1, 2013 policy change; exposure for CACE is FDC treatment compared to multiple-pill regimens.

Outcome	MSE-Optimal Bandwidth[a] (days)	(A) First Stage Risk Difference	(B) ITT Risk Difference	(C) CACE Risk Difference (95% CI)
≥4-month gap in care	±129.6	58.3	-12.6	-21.7 (-46.2; 2.8)
Absent from care at 1 year	±130.4	58.4	-11.6	-19.9 (-42.2; 2.4)
Long-term attrition by 1 year	±127.4	57.8	-12.5	-21.6 (-51.1; -0.1)
No 6-month viral load monitoring	±119.2	56.0	-15.5	-27.7 (-58.8; -0.7)

ITT = Intention-to-treat; CACE = Complier average causal effect; FDC = Fixed-dose combination; CI = confidence interval; ART = antiretroviral therapy

[a]Complier Average Causal Effect (CACE) is estimated using Stata's `rdrobust, fuzzy()` command, using a triangular kernel and the same MSE-optimal bandwidth for the first and second stage equations. Column (C) is equal to column (B) / column (A).

Web Table 2. Testing robustness of RDD CACE estimate to different bandwidths.

Outcome	MSE-Optimal bandwidth[a] (days)	(A) CACE using MSE-optimal bandwidth Risk Diff. (95% CI)	(B) CACE using 0.5x MSE-optimal bandwidth Risk Diff. (95% CI)	(C) CACE using 2x MSE-optimal bandwidth Risk Diff. (95% CI)
≥4-month gap in care	±129.6	-21.7 (-46.2; 2.8)	-50.4 (-130.3; 17.8)	-11.5 (-40.7; 0.4)
Absent from care at 1 year	±130.4	-19.9 (-42.2; 2.4)	-42.1 (-129.5; -8.5)	-10.5 (-38.9; -1.4)
Long-term attrition by 1 year	±119.3	-21.6 (-51.1; -0.1)	-45.9 (-139.8; -18.9)	-12.4 (-41.3; -4.6)
No 6-month viral load monitoring	±103.5	-27.7 (-58.8; -0.7)	-68.0 (-183.6; -18.8)	-22.7 (-47.4; -5.7)

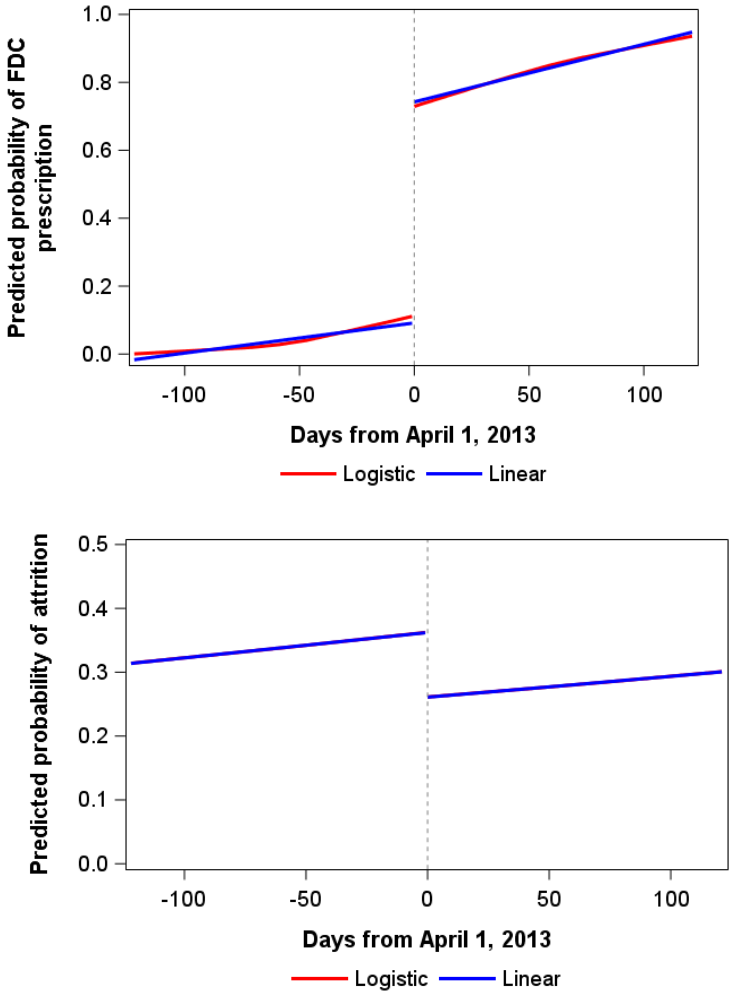
CACE = Complier average causal effect

[a]MSE- based on a triangular kernel, as implemented in Stata's `rdrobust` command [41].

[b]95% CI's are robust, bias-adjusted CI's implemented using Stata's `rdrobust` command.

[c]MSE-optimal bandwidth for CACE is estimated using Stata's `rdrobust, fuzzy()` command, using the same bandwidth for the first and second stage equations.

Web Figure 6. Comparison of linear versus logistic regression for first stage and ITT models.



ART = antiretroviral therapy; ITT = intention-to-treat; FDC = fixed-dose combination.