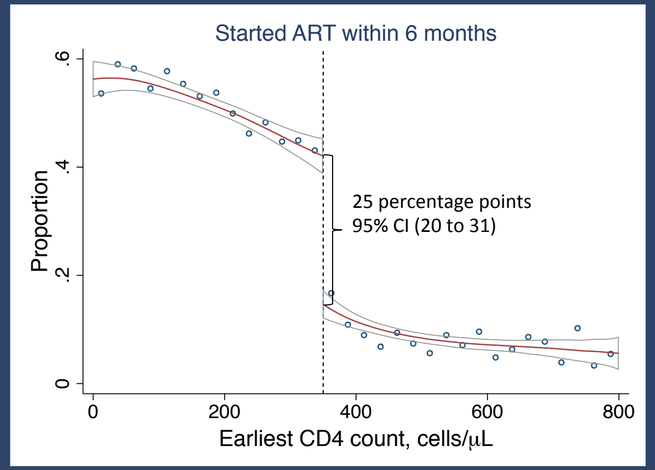
The real world impact of CD4-eligibility criteria on retention in HIV care

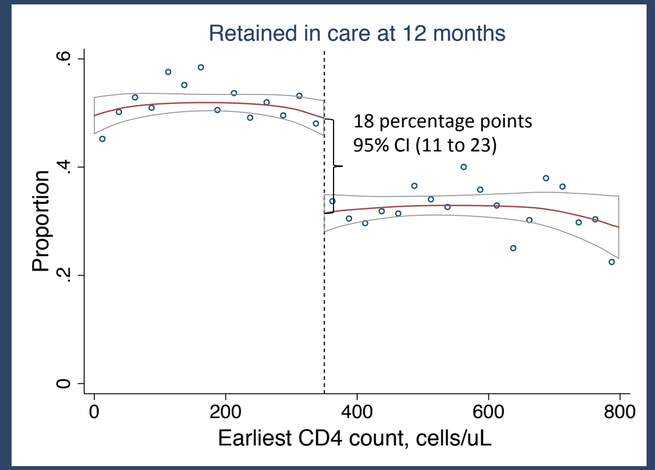
Jacob Bor,[1,2,3,*] Matthew P. Fox,[3,4] Sydney Rosen,[1,3] Atheendar Venkataramani,[5] Frank Tanser,[2] Deenan Pillay,[2,6] Till Bärnighausen[2,7]

[1]Department of Global Health, Boston University School of Public Health, Boston, MA, USA, [2]Africa Centre for Population Health, Mtubatuba, South Africa, [3]Health Economics & Epidemiology Research Office, University of Witwatersrand, Johannesburg, South Africa, [4]Department of Epidemiology, Boston University School of Public Health, Boston, MA, [5]Massachusetts General Hospital, Boston, [6]Faculty of Medical Sciences, University College London, London, UK, [7]Department of Global Health and Population, Harvard T. H. Chan School of Public Health, *jbor@bu.edu

BACKGROUND

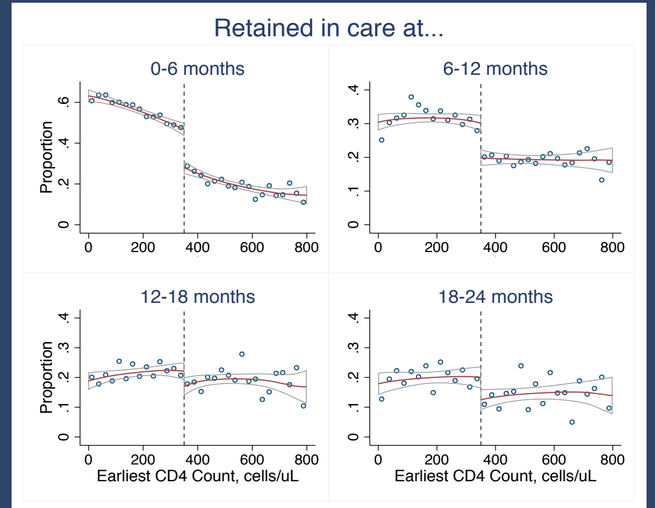
- The START[1] and TEMPRANO[2] trials found significant health benefits to early ART. But absolute effects were relatively modest due to low underlying risk in both treated and controls.
- **Trials may underestimate benefits of early ART** due to efforts to limit attrition in control group. In TEMPRANO, retention was 97% in both arms.
- Immediate vs. deferred ART eligibility may have different consequences in real world settings, where clinical retention is not tightly monitored.
- We assess the real world impact of immediate (v. deferred) ART eligibility on retention in care.[3]





METHODS

- **Data and study population** We analyzed data on all patients (n = 11,307) presenting in the Hlabisa HIV Treatment and Care Programme (Hlabisa Cohort)[4] with a first CD4 count August 2011 - December 2012.
- **Study Design** Regression discontinuity design, exploiting the quasi-random assignment of ART eligibility for patients with first CD4 counts close to the eligibility threshold. Patients presenting just above and just below the 350-cell threshold are similar on both observable *and unobservable* characteristics, similar to an RCT.[5,6]
- **Intervention** Immediate vs. deferred ART eligibility, as determined by a CD4 count < 350 cells/μL. Patients not yet eligible for ART were instructed to return every six months for CD4 monitoring or sooner if they felt sick.
- **Main outcome measure** Retention in HIV care at 12 months, as measured by the presence of a clinic visit, lab test, or ART start date in the interval 6 to 18 months.
- **Statistical analysis** We estimated local linear regression models with a data-driven bandwidth.[7] Our models were of the form: $E[Y|CD4] = b_0 + b_1(CD4-350) + b_2\ 1[CD4<350] + b_3\ 1[CD4<350]*(CD4-350)$. We allowed for separate slopes on either side of 350 and a intercept shift at 350 (b_2), which is the effect of treatment eligibility. We estimated the intention-to-treat effect of ART eligibility on uptake of ART within six months, on 12-month retention, and on patient retention within six month intervals 0-6, 6-12, 12-18, and 18-24 months. We also estimated the complier average causal effect, i.e. the effect of starting ART immediately vs. deferred ART on 12-mo retention among those patients whose treatment decision was made based on CD4 count. Finally, we calculated 12-mo retention probabilities for both treated and control compliers.



RESULTS

Intention-to-treat effects

- Having an ART-eligible CD4 count increased 12-month retention from 32% to 50% (difference: 18 percentage points; 95%CI 11-23; p < 0.001).
- An eligible CD4 increased the probability of starting ART within six months from 18% to 43% (difference: 25 percentage pts; 95%CI 20-31; p < 0.001).
- Evidence of significantly lower retention in care even at 18-24 months.

Complier average causal effects

- Among patients whose uptake of ART was determined by the value of their CD4 count, starting ART increased 12-month retention from 21% to 91% (difference: 70 percentage points; 95%CI 42-98; p < 0.001).

Percent Retained	TEMPRANO Trial	Hlabisa Cohort
Early ART	97%	91%
Deferred ART	97%	21%

CONCLUSIONS

- **Immediate ART eligibility has a large positive effect on retention in care.**
- It has been widely observed that pre-ART retention is lower than retention on ART.[3] We show that this relationship is causal.
- **Immediate ART has both biological[1,2] and behavioral consequences.**
- Behavioral effects are not captured in clinical trials.
- For patients willing to start, **benefits to immediate ART may be larger than previously thought.**
- Quasi-experimental designs enable inference on real world effects.[8]

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