Health Economics and Epidemiology Research Office
HE²RO
Wits Health Consortium
University of the Witwatersrand

HE²RO Policy Brief

Number 11 · June 2016

This policy brief is drawn from: Rosen S, Maskew M, Fox MP, Nyoni C, Mongwenyana C, Malete G, et al. (2016) Initiating Antiretroviral Therapy for HIV at a Patient's First Clinic Visit: The RapIT Randomized Controlled Trial. PLoS Med 13(5): e1002015.
http://dx.doi.org/10.1371/journal.pmed.1002015 (CC BY 4.0)

INITIATING ANTIRETROVIRAL THERAPY AT A PATIENT'S FIRST CLINIC VISIT: THE RAPIT STUDY

Background

One of the most persistent operational challenges facing South Africa's antiretroviral therapy (ART) programme is late presentation of patients for care and high rates of attrition from care between HIV testing and ART initiation. Even among those who have been diagnosed and found to be treatment-eligible, loss to care before starting ART has consistently been estimated at a third to a quarter of patients[1,2].

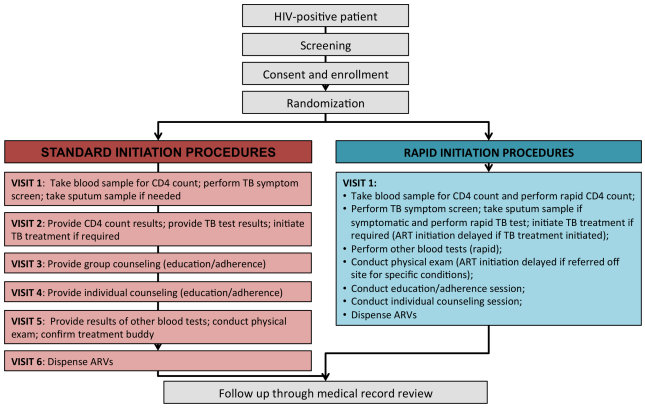
There are multiple causes of loss to care before treatment initiation, but one reason is that starting ART is a lengthy and burdensome process, imposing long waits and multiple clinic visits on the patient. The process typically includes an HIV test (visit 1); determination of treatment eligibility (visit 2); adherence education and counseling and baseline blood tests (visits 3, 4, and 5), and physical examination and dispensing of ARVs (visit 6). Many patients do not make it all the way through this process from beginning to end.

If patients are deterred from starting treatment by the complexity of the process, then one strategy for reducing losses of patients prior to ART initiation and encouraging earlier treatment initiation may be to shorten the time period, reduce the number of visits, and simplify the steps required before medications are dispensed. There have not yet been any rigorous, controlled evaluations of an integrated, rapid HIV treatment initiation algorithm incorporating clinic procedural changes and point-of-care (POC) laboratory tests for adult, non-pregnant patients. We therefore conducted a randomized controlled trial of rapid ART initiation that allowed patients to have treatment eligibility determined, all treatment preparation steps performed, and ARV medications dispensed on the day of their first HIV-related clinic visit.

Methods

The RapIT study was conducted from 2013 to 2015 at two clinics in Johannesburg. One was a primary health clinic and the other a hospital-based HIV clinic. Adult, non-pregnant patients who had come to the clinics either to have an HIV test or to get the results of their first CD4 count and were eligible for ART (CD4 count ≤ 350 cells/mm^3 or a Stage 3 or 4 condition) were randomized to either rapid or standard ART initiation (Figure 1). The standard group followed the usual schedule for starting treatment, which required 3-5 more clinic visits. The rapid group received a POC CD4 count if a CD4 count had not already been done; those ART-eligible received a POC TB test if symptomatic, POC blood tests, physical exam, education, counseling, and ARV dispensing all at that same clinic visit.

Figure 1. Study procedures for each group



After the first visit, we followed patients through their medical records. The primary outcome of the study was viral suppression, defined as initiated, retained in care, and suppressed (≤400 copies/ml) within 10 months of study enrollment. Secondary outcomes included initiation of ART within 90 days of study enrollment, retention in care at 10 months after study enrolment, and time to ART initiation.

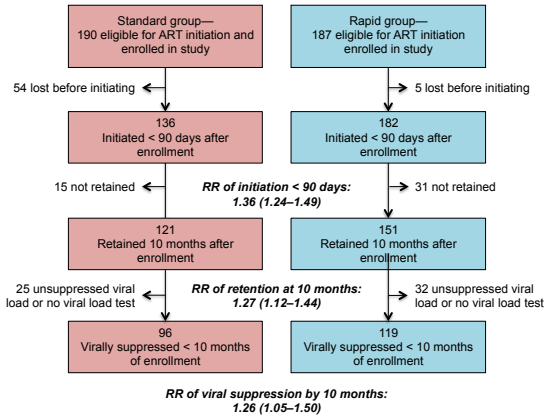
Results

We enrolled 187 in the rapid group and 190 patients in the standard group (n=377 total). Results are illustrated in Figure 2. The primary trial outcome was viral suppression within 10 months of study enrollment; 64% of patients in the rapid group and 51% in the standard group achieved this outcome, equating to a risk difference of 13% and a crude relative risk of 1.26. The key programmatic outcome was ART initiation within 90 days of study enrollment; 97% of patients in the rapid group and 72% of patients in the standard group started ART within 90 days, for a risk difference of 25% and a crude relative risk of 1.36.

As Figure 2 indicates, overall retention in care was 81% in the rapid group and 64% in the standard group. Of the patients in the rapid group who were not retained, most (86%) were lost from care after ART initiation. In

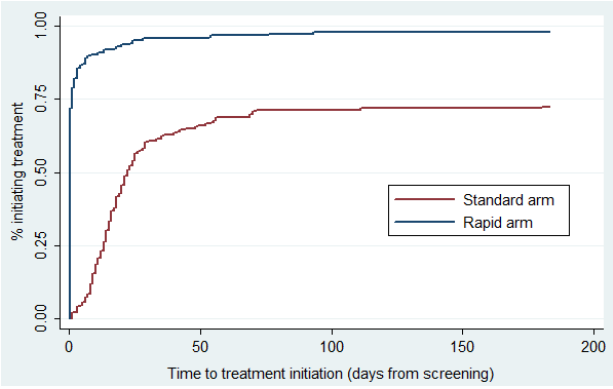
contrast, of the patients in the standard group who were not retained, most (78%) were lost before initiation. The higher loss to follow up after initiation in the rapid group was more than offset by the higher loss before initiation in the standard group, resulting in an overall increase in retention in care of 17%. Among the patients lost to care after initiation (15 in the standard group and 31 in the rapid group), a large majority either never came back after their initiation visit or came back just once, suggesting that most of these patients were never "established" on ART.

Figure 2. Study results



In the rapid group, 72% of patients started ART on the same day as study enrollment. An additional 7% started on the next day, and 96% of the group started within 1 month. In the standard group, 58% of patients initiated within one month. In the standard group, the median time to initiation in the standard arm for the subset who did initiate within 90 days was 17 days. Figure 3 illustrates time to treatment initiation in each group.

Figure 3. Time to treatment initiation



In the rapid group, from provision of informed consent (study enrollment) to dispensing of the first supply of ARV medications, rapid initiation took a median of 2.4 (IQR 2.1–2.8) hours for those who initiated on the same day as study enrollment.

To see if there were differences in study results between the two study sites or by age or sex, we also conducted a stratified analysis. We observed differences in effect sizes for the primary outcome (viral suppression at 10 months) by sex, age group, and study site. We found a larger effect among men under age 35 (risk difference 34%, 95% CI 12%–55%), while little effect was seen among men or women over 35 (5%, 9%–19%). The effect size was also greater at the primary health clinic (21%, 8%–34%), while little effect was seen at the hospital-based HIV clinic (2%, -12%–17%). The study was not powered to detect differences among subgroups, however, and these differences in effect size were not statistically significant.

Policy Relevance

Although it took place at only two clinics, both in urban areas in a single province, the RapIT trial showed that it is possible to start nearly all patients on HIV treatment in a much shorter time frame than previously required, and that offering patients the chance to start ART during their first HIV-related clinic visit can be an effective strategy for improving health outcomes. Primary health clinics, where we saw a larger effect of the intervention, have fewer resources than hospital-based clinics but treat 85% of HIV patients in South Africa. PHCs may struggle more with loss to follow-up before treatment initiation than do hospital-based clinics, creating a greater opportunity for a service delivery intervention like RapIT to be effective. The potential for reaching younger men, who have been among the least likely to access ART in the past, is another important potential benefit of rapid initiation.

In May 2016, the National Department of Health announced that by September 2016, ART will be offered to all patients with HIV, regardless of CD4 count[3]. The removal of a CD4 count threshold for ART eligibility will simplify ART initiation in one of the ways suggested by RapIT. Several other recent studies using different approaches than RapIT, but with the same goal of simplifying and speeding up the process of treatment initiation, have also shown promising results, in countries ranging from Uganda[4] to China[5] to the United States[6]. Accelerating treatment initiation may thus offer an effective way to achieve treatment for all.

References

1. Plazy M, Dray-Spira R, Orne-Gliemann J, Dabis F, Newell M-L. Continuum in HIV care from entry to ART initiation in rural KwaZulu-Natal, South Africa. *Trop Med Int Health* 2014; 19: 680–9.
2. Clouse K, Pettifor AE, Maskew M, et al. Patient retention from HIV diagnosis through one year on antiretroviral therapy at a primary health care clinic in Johannesburg , South Africa. *J Acquir Immune Defic Syndr* 2013; 62: 39–46.
3. UNAIDS. South Africa takes bold step to provide HIV treatment for all. Geneva: UNAIDS, 2016.
4. Amanyire G, Semitala FC, Namusobya J, et al. Streamlining antiretroviral therapy uptake: a stepped-wedge cluster randomized trial. Boston: CROI 2016.
5. Wu Z, Zhao Y, Ge X, et al. Simplified HIV testing and treatment in China: analysis of mortality rates before and after a structural intervention. *PLOS Med* 2015; 12: e1001874.
6. Highleyman L. Same-day start to antiretroviral treatment leads to faster HIV suppression in San Francisco. *AIDSMap News*, 2015.