Successful antiretroviral therapy delivery and retention in care among asymptomatic individuals with high CD4$^+$ T-cell counts above 350 cells/μl in rural Uganda

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Background: HIV antiretroviral therapy (ART) is being rapidly scaled up in sub-Saharan Africa, including recently patients with CD4$^+$ T-cell counts above 350 cells/μl. However, concerns persist about adherence and virologic suppression among these asymptomatic, high CD4$^+$ cell count individuals.

Objective: To determine the virologic efficacy and safety of ART among asymptomatic HIV-positive Ugandan adults with high CD4$^+$ cell counts above 350 cells/μl via a streamlined model of care.

Design: Prospective nonrandomized clinical study (EARLI Study: clinicaltrials.gov NCT#01479634).

Setting: Prototypic rural Ugandan HIV clinic.

Patients/participants: Asymptomatic, ART-naive adults (aged >18 years, $N = 197$) with CD4$^+$ at least 350 cells/μl, without pregnancy or WHO stage 3/4 illness.

Interventions: ART included tenofovir/emtricitabine/efavirenz, with ritonavir/lopinavir substitution for efavirenz available. Streamlined ART model included nurse-driven visits with physician back-up, basic safety laboratory monitoring with HIV viral load, clinician telephone contact, and defaulter tracking. No incentives were provided.

Outcomes: Undetectable viral load (≤400 copies/ml) at 24 and 48 weeks [intention to treat (ITT); missing = detectable), self-reported ART adherence, retention in care, and laboratory/clinical ART toxicities.

Results: Of the 197 patients with CD4$^+$ above 350 cells/μl, median CD4$^+$ cell count was 569 cells/μl (interquartile range 451–716). Undetectable viral load was achieved in 189 of 197 (95.9%, ITT) and 189 of 195 (96.9%, ITT) of participants at weeks 24 and 48, respectively. Self-reported adherence was 98% and 192 of 197 (97%) of the patients were retained at week 48. Laboratory adverse events and hospitalizations were rare.

Conclusions: We demonstrate high virologic suppression, retention, and safety among asymptomatic individuals with CD4$^+$ above 350 cells/μl in a prototypic Ugandan

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clinic. Our results challenge current concerns that individuals with high $CD4^+$ cell count lack motivation for ART, and may not achieve sustained virologic suppression.

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Introduction

HIV antiretroviral therapy (ART) access is being rapidly scaled up worldwide according to 2013 WHO guidelines [1,2], with over 9.7 million individuals now receiving ART [3]. However, in sub-Saharan Africa, ART is only recently being offered to patients with high $CD4^+$ T-cell counts (e.g. $\geq$350 cells/μl) [4]. The 2013 WHO guidelines on ART now recommend expanding ART eligibility to individuals with $CD4^+$ cell counts 350–500/μl, as well as to several special focus groups regardless of $CD4^+$ cell count including pregnant and breastfeeding women and individuals with HIV-negative (serodiscordant) sexual partners [1].

As countries adapt WHO recommendations into their existing treatment frameworks, one concern is that individuals with high $CD4^+$ cell count – who are healthier, often asymptomatic, and more frequently engaged in the workforce [5] – will have lower ART adherence, retention in care, and viral suppression. In a group of South African patients eligible for ART initiation, 'feeling healthy' was associated with declination of therapy [6]. In a south-western Ugandan clinic, virologic suppression following ART initiation was 80% in individuals with $CD4^+$ cell count 250–350 cells/μl, and 90% in individuals with $CD4^+$ cell count below 250 cells/μl [7], suggesting lower adherence in patients with higher $CD4^+$ cell count.

Within Malawi's national 'option B+' program – ART initiation for pregnant women regardless of $CD4^+$ cell count – a recent study reported higher rates of loss to follow-up of option B+ pregnant women compared to nonpregnant women initiating ART due to having $CD4^+$ cell count below 350 cells/μl [8]. Additionally, in a qualitative study of serodiscordant couples enrolled in a pre-exposure prophylaxis (PrEP) trial, many HIV-positive index individuals expressed negativity towards ART due to a perception that it portended imminent mortality [9].

Other data on specialized populations of patients with high $CD4^+$ cell count with $CD4^+$ cell count above350 cells/μl, however, present a distinctly different picture. HIV/tuberculosis (TB) coinfected patients with $CD4^+$ cell count above350 cells/μl had 86% virologic suppression at 6 months in a Ugandan trial of early vs. delayed ART [10]. Furthermore, in sero-discordant couples in the HPTN 052 study, 886 HIV-positive individuals with $CD4^+$ cell counts of 350–550 had above 89% virologic suppression throughout the median 2.1 years of follow-up [11,12].

Against this backdrop of emerging data, to increase understanding of ART outcomes in asymptomatic high $CD4^+$ cell count adults, we investigated ART efficacy and safety within a streamlined care model in a prototypic rural Ugandan HIV clinic.

Methods

Research/ethics approvals

The study was approved by institutional review boards at Makerere University, Kampala, Uganda, the University of California, San Francisco, the Uganda National Council for Science and Technology, and the Ugandan National Drug Authority. All participants provided written informed consent for participation.

Study design and setting

The Early Antiretroviral Therapy in Resource Limited Settings in Patients with High $CD4^+$ Cell Counts Study (EARLI) is a prospective, two-arm, nonrandomized study of open-label ART, evaluating the safety and efficacy of ART administration under a streamlined care delivery system. The participants were HIV-infected individuals with high $CD4^+$ cell counts ($CD4^+$ $\geq$250 cells/μl) in Mbarara District, Uganda. The study was conducted at Bwizibwera Health Center [a level IV government clinic 25 km from the Mbarara town, providing HIV care via the Makerere University Joint AIDS Program, a President's Emergency Program for AIDS Relief (PEPFAR)-sponsored implementing partner]. This study registered with ClinicalTrials.gov, #NCT01479634.

Participant screening and enrollment

Three methods were used for initial screening of the participants. First, a database of registered clinic patients was searched for individuals meeting four criteria: age at least 18 years, not receiving ART, latest $CD4^+$ cell count at least 250 cells/μl performed less than 6 months prior, and residence less than 30 km from the health center. Clinic charts were reviewed to verify the ART-naive status. The staff then invited the qualifying patients by

phone for screening. Second, HIV-positive individuals attending clinic visits during the screening period were invited for screening if they met the above criteria. Lastly, individuals referred to Bwizibwera Health Center after diagnosis with HIV during a community-wide HIV testing campaign in May 2011 [13] were also invited to screen if they met criteria as above.

Further inclusion criteria were: ability to give informed consent, documentation of HIV-1 infection in the medical chart or community health campaign results, and ability to swallow medications. Exclusion criteria were: intent to relocate more than 30 km from the clinic during the subsequent 3 years, receipt of ART for more than 7 days, except during pregnancy or for occupational exposure, an active WHO stage 3 or 4 illness on physical examination, and pregnancy by self-report or examination.

Eligible participants then underwent secondary laboratory screening; female participants also had a urine beta-human chorionic gonadotropin test for pregnancy. Laboratory exclusion criteria were: CD4$^+$ cell count below 250 cells/μl, absolute neutrophil count 500 cells/μl or less, hemoglobin 7.0 g/dl or less, platelets 50 000/μl or less, alanine aminotransferase (ALT) at least five times the upper normal range value, estimated glomerular filtration rate (eGFR) 60 ml/min or less determined by the Modification of Diet in Renal Disease (MDRD) formula, evidence of tuberculosis determined by a positive Cepheid Xpert MTB/RIF assay result, and positive urine pregnancy test. If eligibility criteria were met, consent for study participation was undertaken.

Antiretroviral therapy

In participants with CD4$^+$ cell count above 350 cells/μl, ART consisted of Truvada [co-formulated tenofovir (TDF) 300 mg/emtricitabine (FTC) 200 mg, one tablet daily administered as a fixed-dose combination] with efavirenz (EFV) 600 mg (one tablet daily). Participants could initiate Aluvia [coformulated ritonavir (RTV) 50 mg/lopinavir (LPV) 200 mg, two tablets twice per day administered as a fixed-dose combination] instead of EFV if they had concerns about becoming pregnant while on EFV. For suspected toxicity related to Truvada, drug substitutions with another approved ART medication or medications were allowed at the discretion of study clinicians. TDF was discontinued if eGFR was 50 ml/min or less. Participants could continue FTC and/or EFV if desired, and could restart TDF or Truvada, at clinicians' discretion. For suspected Aluvia (RTV/LPV) toxicity, alternate ART medications were offered at clinicians' discretion. Participants with CD4$^+$ cell count 250–350 cells/μl received standard first-line ART in line with 2009 Uganda National Guidelines [14].

Streamlined care

In our streamlined care model, nurses conducted rapid-throughput routine visits unless symptom screening indicated that physician evaluation was needed. Baseline, week 24 and week 48 viral load results were discussed with patients. Participants were asked if they had questions about their viral load results, and were given encouragement when viral load was undetectable. Phlebotomy was done on site, and 1-month ART refills (for visits at weeks 0, 4, and 8) or 3-month ART refills (for visits at weeks 12, 24, 36, and 48) were provided at an on-site pharmacy window. Participants were informed at enrollment that they could access the clinic medical officer by telephone or text messaging, and could present to the clinic outside of the regular visit schedule for any urgent care complaints. Participants were tracked if they missed visits. No incentives were provided for study participation.

Streamlined care assessments

Participants were assessed at week 0 (enrollment) and week 4 by a medical officer, and at weeks 8, 12, 24, 36, and 48 by a nurse. Upon enrollment, participants completed a multiple-choice questionnaire regarding their motivations for participation and expectations about the impact of ART.

Screening for toxicities and adverse events

At all visits, clinic staff screened participants for clinical symptoms or problems. At enrollment and week 4 visits, the medical officer evaluated patients for adverse events. During nurse visits (weeks 8–48), positive responses triggered conversion of the visit to the medical officer who evaluated participants for an adverse event. All grade 3 and 4 adverse events, as well as serious adverse events [as defined by the National Institutes of Health, Division of AIDS (DAIDS) scale] were tabulated and reported to review boards.

Adherence

At all visits, a 3-day recall test was performed, asking participants how many medication doses they had taken 1, 2, and 3 days before. Visits in which all ART medications were reported taken on all 3 days were considered adherent. Visits with any missed dose reported were considered nonadherent.

Laboratory evaluations

Sodium, potassium, chloride, bicarbonate and glucose were measured at enrollment and week 48. Blood urea nitrogen and creatinine were assessed at weeks 8 and 48. Complete blood count and liver function tests (aspartate aminotransferase, ALT, total and direct bilirubin, and alkaline phosphatase) were assessed at weeks 12 and 48. Viral load was assessed at enrollment and weeks 24 and 48. CD4$^+$ cell count was assessed at enrollment and week 24.

Pregnancy testing

Female participants were asked during each visit if they might have become pregnant since their prior visit. Positive responses triggered urine pregnancy testing. The

date of last menses was also sought; participants reporting menses at least 6 weeks prior also underwent urine pregnancy testing.

Retention in care and participant tracking

Upon completing each visit, participants were given a target return date for their next visit. Visits were considered made 'on schedule' if they occurred from 7 days prior to 7 days after the target date. If a participant failed to appear on the target date, study staff attempted to contact them via telephone. If a participant did not appear by 1 week after the target visit date, the visit was considered 'missed', and the tracker attempted to visit the participant at his/her residence to encourage them to return to clinic. The medical officer handled all visits following a missed visit. Participants were withdrawn from the study if they missed three consecutive visits, and transitioned to routine care at the health center without ART interruption.

Outcome measures

The primary outcome was the proportion of participants with an undetectable plasma HIV-1 RNA level (viral load $\leq$400 copies/ml) at 48 weeks. Secondary outcomes were: proportion of participants with undetectable viral load at 24 weeks, retention in care at 24 and 48 weeks, self-reported rates of adherence at each study visit, and prevalence of grade 3/4 toxicities and adverse events occurring during the first 48 weeks of ART.

Streamlined care measurements: medical officer utilization

To assess the need for medical officer evaluations outside of the standard visit schedule (i.e. enrollment and week 4), we tabulated visits including: visits converted by the nurse to the medical officer due to a suspected clinical issue or adverse event, unscheduled 'drop-in' visits (all of which were seen by medical officer), follow-up visits that were scheduled by the medical officer (e.g. to re-evaluate a laboratory abnormality), visits following a missed visit, or other.

Participant time and motion study

To assess the impact of our streamlined care intervention on study visit duration and waiting times, the lengths of participants' study visits were measured in a time and motion study spanning 3 months, consisting of clinic visit observations from week 8 to 48. During this period, the staff were informed that visits were being timed. A tracker recorded participants' time of entry into the clinic waiting room, and the staff noted the start and finish time for the portions of the visit conducted by the nurse, medical officer, phlebotomist, and pharmacist, respectively. Final exit time from the pharmacy window was also recorded. Total entry-to-exit time, as well as the fraction of total time spent waiting, was calculated.

Results

From October 2011 to May 2012, 300 patients were screened for the EARLI study entry; 200 individuals enrolled in the $CD4^+$ above 350 cells/μl arm and 49 enrolled in the $CD4^+$ 250–350 arm (Fig. 1). Enrollment in the $CD4^+$ 250–350 arm was affected by the 2011 change in Uganda ART initiation guidelines from a $CD4^+$ cell count threshold of 250–350 cells/μl [15]. Many patients with $CD4^+$ cell counts 250–350 cells/μl had ART initiated through standard clinic operations and were not available for recruitment; this study arm was thus closed to accrual, having insufficient follow-up for analyses.

Reasons for study enrollment and antiretroviral therapy initiation

At enrollment, top reasons for participation cited by participants with $CD4^+$ cell count above 350 cells/μl included preserving individual health and work productivity, as well as minimizing HIV transmission to others (Fig. 2). A small fraction reported being motivated by current illness.

Demographics, baseline clinical characteristics, and antiretroviral therapy regimens

Among participants with $CD4^+$ above 350 cells/μl, 65% were women, median age was 35 years [interquartile range (IQR) 29–41], and agriculture was the predominant occupation, consistent with previously reported demographics in south-western Uganda (Table 1) [16,17]. $CD4^+$ cell counts were high: the median was 564 cells/μl, and 25% of the participants had $CD4^+$ above 712 cells/μl. Median baseline viral load was 22 400 copies/ml. In the $CD4^+$ above 350 arm, all participants initiated TDF/FTC + EFV, except for three participants who initiated TDF/FTC + RTV/LPV.

Retention in care

Of the 200 participants originally enrolled in the $CD4^+$ above 350 arm, three were withdrawn after baseline viral load testing showed an undetectable plasma RNA level, and subsequent testing confirmed HIV-negative serostatus. After 24 weeks, 194 of 197 participants remained in the study (98%). Two patients died between week 24 and 48; thus overall retention at week 48 was 192 of 197 (97%) (Table 2).

Virologic efficacy of antiretroviral therapy

In the $CD4^+$ above 350 arm, 189 of 197 (95.9%) of participants achieved an undetectable HIV-1 plasma RNA level at week 24 by intention-to-treat (ITT) analysis that treated missing values as detectable. At week 48, 189 of 195 participants were undetectable (96.9%, ITT; Table 2).

Antiretroviral therapy adherence

Self-reported adherence was very high by 3-day recall interview: in the $CD4^+$ above 350 arm, participants

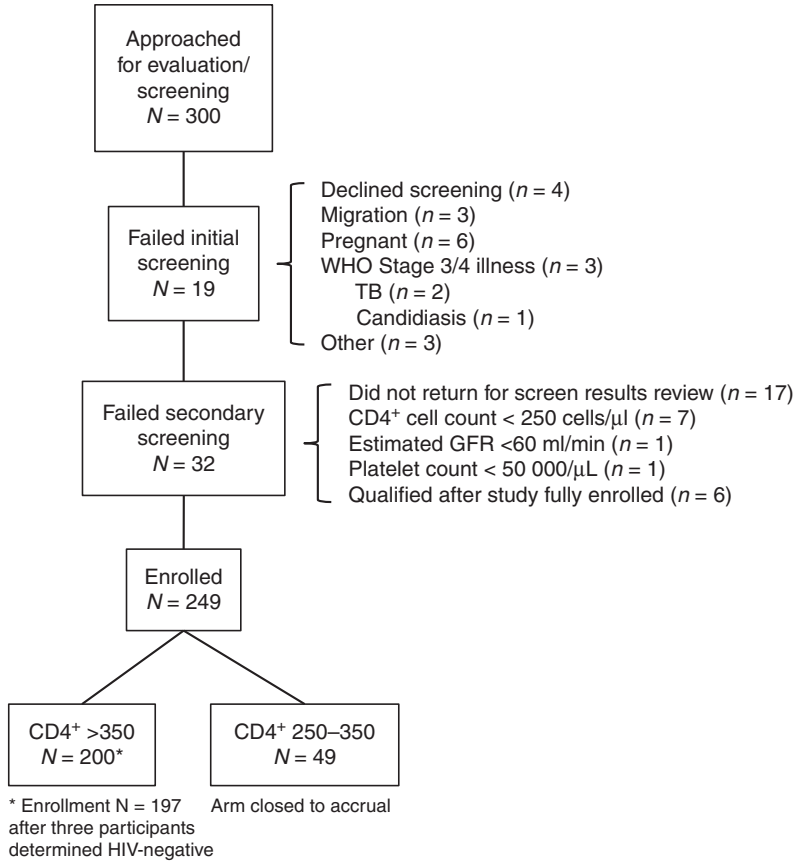

Fig. 1. Study screening and enrollment characteristics. Of the 300 individuals approached and evaluated for screening and study participation, 249 enrolled: 200 in the CD4$^+$ above 350 cells/μl arm, and 49 in the CD4$^+$ 250–350 cells/μl arm prior to close of accrual. GFR, glomerular filtration rate; TB, tuberculosis.

reported taking ART on all three days prior at 97.9% of the study visits (Table 2).

Adverse events

The overall rate of adverse laboratory events, as well as hospitalizations and deaths was low (Table 2). Among CD4$^+$ above 350 cells/μl patients, a total of 22 grade 3 or grade 4 laboratory adverse events occurred across 18 participants. The most common was asymptomatic neutropenia ($n = 11$). Creatinine elevations occurred in two participants, both of whom interrupted Truvada, but subsequently resumed it after creatinine normalization.

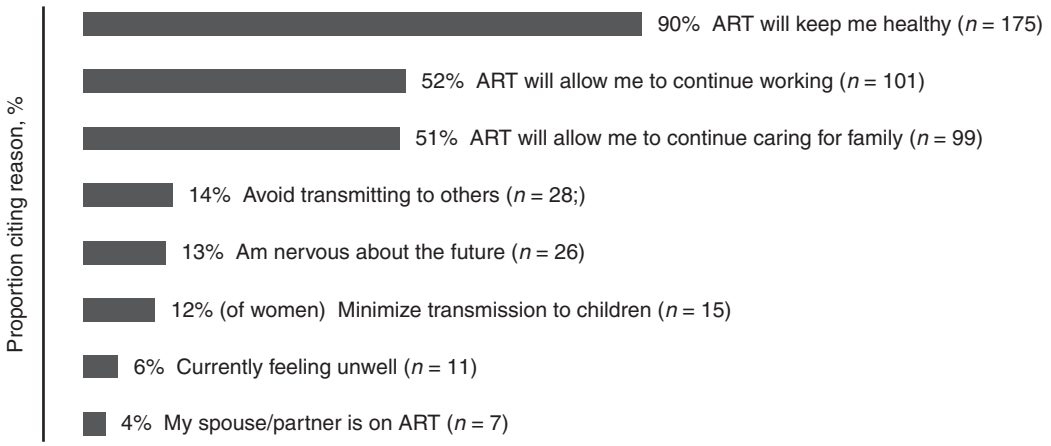

Fig. 2. Reasons for study participation and antiretroviral therapy initiation. Motivations for enrolling in study and initiating ART are displayed for 195 individuals with CD4$^+$ T-cell count above 350 cells/μl surveyed upon study entry. Participants could indicate one or more motivations. ART, antiretroviral therapy.

Table 1. Demographic and baseline characteristics.

Variable	$CD4^+$ >350/μl participants ($n=197$)
Age, median (IQR)	36 (29–41)
Sex, % female	64.5%
$CD4^+$, median (IQR) (cells/μl)	569 (451–716)
HIV RNA, median (IQR) (c/ml)	23200 (4170–88194)
[0,1-2]Occupation	
Agriculture – animal or farm	136
Trader/shop worker	16
Business owner	15
Domestic/house work (maid, etc.)	8
Construction worker	4
Restaurant/bar worker	3
Other	15[a]

IQR, interquartile range.
[a]Carpenter/metal worker ($n=4$); driver/transportation ($n=3$); mechanic, civil servant ($n=2$ each); teacher, factory worker, nurse ($n=1$ each); N/A ($n=1$).

Hospitalizations were rare, occurring in 4% (8/200) of participants overall. The most common reason was community-acquired pneumonia. Two patients died before week 48: one from postoperative complications following cholecystectomy, and one from inoperable gastric carcinoma. Both participants had an undetectable week 24 viral load prior to their deaths.

Streamlined care measurements

Nonroutine medical officer utilization outside of the standard visit schedule was modest (Table 3). In addition to the 1743 routine study visits (249 participants × 7 visits), 384 nonroutine medical officer visits occurred (average 1.5 visits/participant by week 48). Overall, 51% of these nonroutine visits represented unscheduled drop-in visits; the majority were for minor dermatologic conditions, respiratory complaints (e.g. cough or rhinitis), or mild gastrointestinal symptoms (e.g. dyspepsia or diarrhea). Only 24% of the nonroutine visits were visit conversions from the nurse to the medical officer. Many of these occurred per study protocol, for example, when pregnancy was suspected. Lastly, 17% of the nonroutine visits occurred because a participant had missed a prior visit; protocol mandated physician evaluation in such cases.

Table 2. Antiretroviral treatment outcomes in participants with $CD4^+$ above 350/μl.

Parameter	Study visit	Outcome
Virologic efficacy	Week 24	189/197 (96.4%, ITT)
	Week 48	189/195 (96.9%, ITT)
ART adherence	Week 4	94.4% (186/197)
	Week 8	97.8% (182/186)
	Week 12	99.4% (183/184)
	Week 24	98.9% (188/190)
	Week 36	98.3% (176/179)
	Week 48	98.9% (178/180)
	Total	97.9% (1093/1116)
Retention in care	Week 24	194/197 (98%)
	Week 48	192/197 (97%)
Adverse events	Grade 3 or 4 laboratory adverse event	22[a]
	Elevated creatinine	2
	Hospitalization	8[b] (4%)
	Death	2[c]

ITT, intention to treat: considered missing viral load values detectable.
[a]Events occurred in 18 participants of the 197 total participants. Events included neutropenia ($n=11$), creatinine elevation ($n=2$), thrombocytopenia ($n=2$), hyponatremia ($n=2$), and ALT elevation ($n=1$).
[b]Causes included: community acquired pneumonia ($n=3$), sepsis/renal failure, tuberculosis, altered mental status, malaria, and gastric carcinoma ($n=1$ each).
[c]Causes included: postoperative complications following cholecystectomy ($n=1$) and inoperable gastric carcinoma ($n=1$).

Transit time through clinic

Average start-to-finish visit durations ranged from 25 to 54 min, with most visits being conducted in approximately 30 min (Table 3). Average waiting time during visits ranged from 13 to 28 min, and for most visit types represented approximately one-half of the total visit duration.

Discussion

We report here virologic suppression rates exceeding 95%, excellent retention in care, and low toxicity during the first year of a clinical study of asymptomatic patients with $CD4^+$ cell counts above 350 cells/μl receiving ART and HIV care via a streamlined care delivery model in a prototypical HIV clinic in rural Uganda. Our results challenge current concerns that individuals with high $CD4^+$ cell count may not desire or adhere well to ART, or be able to achieve robust virologic suppression.

Prior literature has focused on individuals with $CD4^+$ cell counts below 350 cells/μl [6,7,9], since this is the $CD4^+$ threshold that has largely defined ART eligibility since the start of the ART scale-up in sub-Saharan Africa. In addition, prior studies have focused on potential reasons why healthy asymptomatic patients may decline ART when eligible, or adhere suboptimally after initiating ART. However, it is possible that patient attitudes to ART in previous years were, in part, shaped by clinical messaging to high $CD4^+$ cell count patients that ART was not indicated and its benefits were uncertain.

By contrast, our results from patients with high $CD4^+$ cell count (>350 cells/μl) provide data on current motivations for ART among asymptomatic individuals. Our participants cited a desire to preserve health and productivity, as well as reduce the risk of transmission. These attitudes may reflect a growing knowledge among patients that ART initiation at higher $CD4^+$ cell counts can reduce clinical events [12] and dramatically reduce transmission to partners [11]. These factors should continue to be incorporated into health education

Table 3. Streamlined care outcomes (physician utilization and mean transit time for clinic visits).

Physician utilization outside standard visit schedule

Reason for visit	Converted from RN	Unscheduled	Scheduled by MD	Missed last visit	Other
No. of visits (% of total nonroutine physician visits, $N = 384$)	92 (24%)	193 (51%)	28 (7%)	65 (17%)	6 (2%)

Mean participant transit time during clinic visits

Visit week	Week 8	Week 12	Week 24	Week 36	Week 48	Unscheduled
Visit duration (min)	35	32	35	25	54	30
Waiting time (min)	15	14	19	13	28	11

MD, study physician; RN, study nurse.

around HIV care and updated to share accumulating clinical evidence on the benefits of earlier ART.

Several additional factors may have contributed to our strong clinical results. First, the streamlined nurse-driven system of care may have helped patients complete study visits with less disruption to their work and other routines. Strong evidence demonstrates the effectiveness of nurse-driven care models [18–21]; our study expands this evidence base with time and motion data indicating that visits can be effectively shortened to 30 min or less while retaining good outcomes. Visit durations in our study were far shorter than mean visit lengths of 183–270 min that have been reported in other HIV clinics in Mbarara District [22,23]; these previously reported longer times may have been partially driven by mandatory counseling and education sessions offered at patient visits.

Our short study visits were primarily focused on simple screening for ART toxicities and clinical problems. Because toxicities were infrequent in these largely asymptomatic patients, screening was rapid, with participants directly proceeding to phlebotomy and/or to the pharmacy. Streamlined pharmacy visits dispensed a 3-month supply of antiretroviral drugs rather than a more typical 2-month supply, a strategy that has been investigated previously in Uganda [24,25]. Patients nonetheless still spent almost 50% of their visit duration waiting, suggesting that further streamlining of visits is possible.

A second likely factor contributing to our strong clinical results was the provision of a clinician mobile phone number to all patients in the study. Whereas prior studies have demonstrated a positive impact of mobile phone reminders on ART adherence [26–28], and on staff members' ability to obtain clinical advice on HIV management from experts [29], the impact of patient access to clinicians via mobile phone is less well explored. The ability of our participants to contact the study clinician allowed triage of complaints and action-oriented recommendations, for example, to present for an outpatient clinic evaluation, to proceed to the hospital for a more serious problem, or simply to present for the next scheduled visit. With ready telephone access, basic ART questions (e.g. on side effects or dosing schedules), as well as appointment dates, were easily resolved. These may have prevented missed ART doses, and helped to avert missed visits (which can lower the chance of exhaustion of an individual's ART supply). All of these factors may have helped promote eventual virologic suppression. Most importantly, the telephone link may have provided patients with a greater sense of connectedness, mutual respect and trust, fostering both adherence and retention [30].

A third possible explanation for our results was our performance of viral load testing at 24 and 48 weeks, and the in-person review of these results with participants at subsequent clinic visits. Apart from certain national programs, for example, in South Africa, viral load testing is not currently widely performed, although it is recommended in the 2013 WHO guidelines on ART administration [1]. In our study, participants anecdotally demonstrated strong interest in their numerical viral load results at baseline, and at 24 and 48 weeks. We believe that the ability of the staff to demonstrate an undetectable viral load allowed reassurance about medication efficacy, encouraged patients to remain adherent, and afforded positive reinforcement of self-efficacy – namely, that patient effort was yielding positive results.

Our study has certain limitations. First, we did not randomize high CD4$^+$ cell count individuals to our streamlined care intervention versus standard clinical care; as such, the precise impact of our streamlined care model is hard to separate from our patients' generally positive health. Second, participants were not selected purely at random from the overall population of high CD4$^+$ cell count individuals in the clinic or in the geographic region. Some participants were already registered clinic patients; as such, they may have had a higher propensity to be retained in care due to their demonstrated retention in 'pre-ART' care. However, we did recruit from amongst these individuals randomly, and simultaneously enrolled participants who were new registrants to the clinic, including newly diagnosed adults identified during mobile HIV testing at a large scale, community-wide

health campaign [13]. Thus, the overall impact of this phenomenon is unclear. Additionally, we did not specifically recruit participants from marginalized populations (e.g. sex workers, MSM, intravenous drug utilizing individuals); as such, our results may be less generalizable to these groups. Third, we utilized only one measure of self-reported adherence to ART, which is limited in capture of true adherence. Finally, our results encompass 1 year of observation; longer-term data which we are collecting over the next 2 years will help to confirm the durability of the clinical success we report here.

In summary, we report excellent ART outcomes in Ugandan patients with $CD4^+$ cell counts above 350 cells/μl using a nurse-driven model of care that allows patients to spend a relatively short time conducting clinic visits. Current assumptions and concerns about low adherence and worse outcomes among healthier, higher $CD4^+$ cell count patients may not fully account for patients' actual motivations and updated knowledge of the health and productivity-preserving benefits of ART, or for improvements in the tolerability of ART medications. Furthermore, measuring viral load and sharing results with patients in real time (now universally recommended in sub-Saharan Africa [1]) may add motivation and encouragement – benefits beyond the established HIV monitoring function it clearly fulfills. Further research will be needed to demonstrate the long-term durability of streamlined care models for high $CD4^+$ cell count populations who are expected to preserve health and high $CD4^+$ cell counts during long-term therapy.

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Author contributions: V.J. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: V.J., D.M.B., G.A., M.R.K., D.V.H.

Acquisition of data: V.J., D.M.B., D.B., G.A.

Analysis and interpretation of data: V.J., D.M.B., G.A., D.B., M.R.K., D.V.H.

Drafting of the manuscript: V.J., D.M.B., M.R.K., D.V.H.

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Conflicts of interest

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