ICAP Journal Club

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Article

Barnabas RV, Szpiro AA, Ntinga X, et al**. Fee for home delivery and monitoring of antiretroviral therapy for HIV infection compared with standard clinic-based services in South Africa: A randomised controlled trial**. *Lancet HIV*. 2022.
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Study Summary

This unblinded, randomized controlled trial evaluated the acceptability and efficacy of home-based antiretroviral (ART) service delivery with a fee, compared to standard clinic ART services in adults living with HIV.

Study Setting

- Rural and peri-urban areas in KwaZulu-Natal, South Africa.
- Population-level HIV prevalence of 36%, with communities characterized by high unemployment and low per capita income (below USD 2 per day).

Methods

- Adults (≥ 18 years) living with HIV were eligible to participate if they were a resident in the participating communities, willing to pay for home delivery of ART, and clinically stable, defined as CD4 count >100 cells/µL, World Health Organization (WHO) HIV stage 1–3, not pregnant, normal renal function, and no symptoms of active tuberculosis.
- Participants already on ART and newly initiating ART were recruited through HIV clinics and HIV testing at community locations.
- Individuals testing positive in the community received additional point-of-care testing to assess clinical eligibility for community-based ART initiation (CD4 cell count, WHO clinical HIV stage, pregnancy testing, creatinine testing, and symptom screening for tuberculosis).
- Eligible participants were randomized (1:1) to either 1) client payment of a fee for community ART initiation as indicated, monitoring, and ART resupply; or 2) standard clinic ART initiation as indicated, monitoring, and ART resupply.
- In the home ART delivery group:
    - The fee was determined based on participants' reported monthly income. For income ZAR <500, ZAR 500–3200, and ZAR >3200 the cost of delivery was ZAR 30, 60, and 90 (equivalent to USD 2, 4, and 6), respectively. This was paid in cash to the study team as a one-time fee, covering delivery for the study duration.

- Participants also completed a delivery preferences survey indicating suitable delivery times, confirming location at home or work, and updating contact details.
- Participants received same-day ART initiation if not already on ART, and 7 days after ART initiation, participants received a phone call to ask about symptoms, ART side effects, and adverse events.
- Using the preferred delivery times and locations, a custom scheduling algorithm optimized the timing and order for each week's deliveries, minimizing the total distance travelled while matching client availability, and ensuring that clients had an uninterrupted supply of ART. The algorithm also accounted for the average drive time at that time of day and the typical duration of the home monitoring and delivery visits.
- Deliveries took place 2–3 weeks prior to participants exhausting their ART supply; the algorithm accounted for remaining ART and included an option for urgent deliveries to avoid participants running out of medication.
- Participants received a text message to confirm the date and time of their delivery and could reschedule the visit by text message, request a vacation supply, and nominate someone else to collect their medication by contacting the study staff. The home delivery service was regularly available on evenings and on the weekends.
- If participants were not at home to receive the delivery, it was added to the following week's delivery algorithm.
- Following enrollment, participants received month 1 and then quarterly home visits for ART resupply, clinical monitoring, counseling, and ascertainment of adverse events and social harms. Trimethoprim-sulfamethoxazole prophylaxis and tuberculosis preventive treatment were also provided according to national guidelines.
- Staff used a phone-based application to conduct standardized monitoring that included counselling guidelines, and participants completed a questionnaire to screen for symptoms of side-effects associated with ART, tuberculosis, and other common opportunistic infections.
- Point-of-care creatinine testing was done to monitor renal function and participants who required additional clinical services were referred for care and followed up until they linked.
- Participants were administratively linked to a clinic and their files kept up-to-date.

- Participants in the clinic group were referred to established local ART clinics for ART initiation (if required), monitoring, and refills. They also received quarterly phone calls to document ART initiation and adverse events.
- Social harms and adverse events were assessed at every in-person visit and with every phone call.
- At the exit visit, plasma was collected for HIV viral load and participants completed a questionnaire regarding their experience in accessing care, acceptability of home ART

delivery, and barriers for not visiting the clinic in the clinic group. Participants receiving home ART delivery were then transferred to the clinic or a differentiated service delivery model as appropriate.

- The primary trial outcomes were the proportion of participants paying the delivery fee and the acceptability of home delivery.
- Secondary outcomes included achieving HIV viral suppression (<20 copies per mL) assessed at month 12 among all participants and among men, adverse events, social harm and miles travelled.
- The endpoint of viral suppression only included participants who had viral load assessed at exit, in a modified intention-to-treat analysis.

Study Population and Follow-up

- Between October 2019 and January 2020, 173 participants completed screening for study eligibility and 162 were randomized; 80 to the clinic group and 82 to the home ART group.
- Overall, 107 (66%) participants where already known to be living with HIV and of those 101 (94%) were on ART.
- Participants had a median age of 36 years (interquartile range [IQR] 31–43), 54% were men, all were Black race and 60% were unemployed.
- Based on reported income, 54% qualified for the ZAR 30 fee tier, 38% for the ZAR 60 fee, and 8% for the ZAR 90 fee.
- At baseline, 96% of participants were WHO clinical stage 1 and 81% had a CD4 count ≥ 350 cells/µL.
- Seven participants were lost to follow-up; six in the clinic group and one in the home ART group.
- At least 96% of participants completed each visit (months 1, 3, 6 and 9) in the home ART delivery group and median follow-up was 47 weeks (IQR 43–50).
- Data for 155 (96%) participants were included for the fee payment and viral load endpoints analyses.

Primary Outcomes

- In the home ART delivery group, 98% (95% confidence interval [CI] 92–99) paid the full user fee; 100% (95% CI 70–100) in the ZAR 90 group, 94% (95% CI 80–98) in the ZAR 60 group, and 100% (95% CI 91–100) in the ZAR 30 group.
- Acceptability was high, with 100% of participants reporting willingness to continue to pay a fee, reporting that the fee was reasonable, and that they would recommend participation to others.

Secondary Outcomes

- Overall, home ART delivery and monitoring increased viral suppression at 47 weeks compared with the clinic group (88% vs 74%; relative risk [RR] 1.21, 95% CI 1.02–1.42).

- The home ART delivery strategy significantly increased viral suppression among men compared with standard of care (84% vs 64%; RR 1.31, 95% CI 1.01–1.71).
- Viral suppression for women was higher in the home ART delivery group (92%), compared with women in the clinic group (86%), but this difference was not statistically significant.
- No serious adverse events or social harms related to study participation were reported.
- Comparison of medication dispensation and transportation logs indicated good correlation between travel and successful ART delivery, with 426 successful medication dispensation visits.
- An estimated 18 km (11 miles) was driven per successful stop, with it taking an average of 35 min per dispensation including driving, monitoring, ART dispensing, multiple dispensations at a single stop, and unsuccessful stops.

Critical Analysis

This unblinded, randomized controlled trial found that home delivery of ART services with a client-paid fee was highly acceptable and increased viral suppression among adults with HIV, particularly among men, compared with standard clinic-based services. The study also demonstrated how home-based ART services could be optimized using automated, data-driven delivery algorithms to provide more person-centered services.

The following points should be considered when interpreting the study findings:

- The study design meant the study team and participants were not blinded to ART delivery method. However, the laboratory staff who assessed the viral load outcome and the study investigators were masked to group allocation.
- The study initially planned for 6 months of follow-up and was fully enrolled in January 2020, before the COVID-19 pandemic. The pandemic impacted the study in a number of ways:
    - Home visits had to be no-contact deliveries with clinical assessments via telemedicine from March to September 2020. This increased follow-up time to 12 months for both study groups.
    - The standard of clinic care changed to increase access to fast-track ART and multi-month refills as a COVID-19 mitigation strategy, which may have improved viral suppression in the clinic group.
    - Movement restrictions during COVID-19 might have increased the impact and efficiency of home-based ART services, since participants were more likely to be at home.
- Home-based ART initiation was facilitated by the availability of point-of-care tests to determine eligibility (CD4 count, creatinine and pregnancy status). These resources may not be available in other settings, but only a small number of individuals were determined to be ineligible for the study using these tests (six had a CD4 count <100 cells/µL and one was pregnant).
- In addition to home ART delivery and point-of-care tests, participants received a comprehensive pack of services, including follow-up phone calls, availability of services during the evenings and on weekends, a buffer supply of medications and the ability to reschedule deliveries via text. This package would likely be cost prohibitive in many real-

world settings. Furthermore, the fee for delivery of ART was relatively low and would only partially offset the cost of the services. Formal costing and cost-effectiveness analyses have not been conducted to date.

- All of the participants who paid the fee reported that the fee helped them remember to take their medication, which was one of the investigators' hypotheses. However, this comparison was not randomized and the impact of the fee on adherence cannot be disentangled from that of ART home delivery.
- This study was conducted in settings with medium and high HIV prevalence and might not be generalizable to settings with lower prevalence, because a sufficient number of clients within a geographical radius is required for home ART delivery and monitoring to be cost-efficient.
- The study did not include participants lost to follow-up in the viral load analysis. However, if it was assumed they were not virally suppressed, that would have strengthened the study outcome.
- Clinical care was provided by nurses, and the use of a mobile application helped to standardized care and facilitate task shifting. This approach may not be possible in more resource-limited settings.
- Rates of viral suppression were not statistically different in the two groups among women. However, the study was not powered to detect a difference in viral suppression among women.

Implications

This unblinded, randomized controlled trial provides evidence that home-based ART delivery and monitoring can achieve better viral suppression than clinic-based services, particularly among men. Despite high unemployment and poverty, acceptability was high for home-based ART delivery supported by a client-paid fee. The use of an automated delivery algorithm increased flexibility of the service by accounting for client preferences for delivery time and remaining medication supply. This model of service delivery is a promising approach to providing more person-centered ART services that overcome barriers to care faced by people living with HIV.

This article synopsis was written by Dr. Cassia Wells. Share your thoughts on this article or suggest an article for Journal Club by emailing her at caw2208@columbia.edu.