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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

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Summary

Background: Home delivery and monitoring of antiretroviral therapy (ART) is convenient, overcomes logistical barriers, and could increase individual ART adherence and viral suppression. With client payment and sufficient health benefits, this strategy could be scalable. The aim of the Deliver Health Study was to test the acceptability and efficacy of a user fee for home ART monitoring and delivery.

Methods: We conducted a randomised trial, the Deliver Health Study, of a fee for home delivery of ART compared with free clinic ART delivery in South Africa. People with HIV who were 18 years or older and clinically stable (including CD4 count >100 cells per µL and WHO HIV stage 1–3) were randomly assigned to: (1) fee for home delivery and monitoring of ART, including community ART initiation if needed; or (2) clinic-based ART (standard of care). The one-time fee for home delivery (ZAR 30, 60, and 90; equivalent to US$2, 4, 6) was tiered on the basis of participant income. The primary outcomes were recorded fee payment and acceptability assessed via questionnaire. The key virological secondary outcome was viral suppression with the difference between study groups assessed through robust Poisson regression including participants with viral load measured at exit (modified intention-to-treat analysis). This trial is registered on ClinicalTrials.gov (NCT04027153) and is complete, with analyses ongoing.

Findings: From Oct 7, 2019, to Jan 30, 2020, 162 participants were enrolled; 82 were randomly assigned to the fee for home delivery group and 80 to the clinic-based group, with similar characteristics at baseline. Overall, 87 (54%) participants were men, 101 (62%) were on ART, and 98 (60%) were unemployed. In the home delivery group, 40 (49%), 33 (40%), and nine (11%) participants qualified for the ZAR 30, 60, and 90 fee, respectively. Median follow-up was 47 weeks (IQR 43–50) with 96% retention. 80 (98%) participants paid the user fee, with high acceptability and willingness to pay. In the modified intention-to-treat analysis of 155 (96%) participants who completed follow-up, fee for home delivery and monitoring statistically significantly increased viral suppression from 74% to 88% overall (RR 1·21, 95% CI 1·02–1·42); and from 64% to 84% among men (1·31, 1·01–1·71).

Interpretation: Among South African adults with HIV, a fee for home delivery and monitoring of ART significantly increased viral suppression compared with clinic-based ART. Clients' paying a fee for home delivery and monitoring of ART was highly acceptable in the context of low income and high unemployment, and improved health outcomes as a result. Home ART delivery and monitoring, potentially with a user fee to offset costs, should be evaluated as a differentiated service delivery strategy to increase access to care.

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Introduction

In KwaZulu-Natal, South Africa, after an abrupt decline in the 1990s, life expectancy rebounded starting in 2004 with the introduction of antiretroviral therapy (ART).[1,2] The more than 10-year increase in lifespan was driven primarily by substantial access to effective, safe, well tolerated, once-daily, oral ART for treatment and prevention of HIV.[1] Effective and efficient ART delivery is key for increasing population coverage and maintaining suppression for life, the key indicator of treatment success. However, in South Africa, of the 7·8 million individuals with HIV, 72% are on ART, and only 66% are virally suppressed.[3] Men are less likely to be suppressed than women (58% compared with 72%, respectively),[3] due to masculine gender norms and barriers to care, including clinic bottle-necks in ART provision; men more often report that the time taken to access clinic-based care is a barrier.[4,5] Further, there are limited options for collection of medication outside the clinic setting in rural areas.[6] HIV-associated mortality continues to be high, particularly among priority populations who do not regularly visit the clinic on a sufficiently frequent schedule to maintain uninterrupted ART and viral suppression.[7,8] Over 4 years, a third of people living with HIV in South Africa are no

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Research in context

Evidence before this study

Antiretroviral therapy (ART) for HIV has prevented almost 10 million premature HIV-associated deaths globally. ART is safe, well tolerated, generally taken once daily, and widely available at low or no cost in many settings worldwide. However, coverage of ART, as measured by the gold standard of viral suppression among people with HIV, has fallen short of the 86% suppression target set by UNAIDS, with suppression higher among women compared with men. We searched PubMed on Jan 13, 2022, with no date or language restrictions, to identify studies evaluating community-based strategies to increase viral suppression, with these keywords: "HIV", "viral load", and "community-based". Before this study, Dave and colleagues conducted a systematic review and meta-analysis evaluating the effectiveness of community-based HIV initiatives. For the outcome of viral suppression, community health workers and peers increased the relative risk of viral suppression by 40% (pooled odds ratio 1·40, 95% CI 1·06–1·86). In a randomised trial of community-based ART initiation, monitoring, and resupply (the DO ART Study) viral suppression significantly increased overall from 63% to 74%. However, a quarter of individuals with HIV continued to have detectable viral loads. Client-centred, accessible services such as home ART delivery and monitoring have the potential to adapt to changing restrictions, overcome barriers, and increase viral suppression.

Added value of this study

This study presents new evidence from a randomised clinical trial in South Africa on the effectiveness of home-based ART delivery and monitoring to achieve higher viral suppression, particularly among men, and meet the UNAIDS goal for 86% viral suppression. Importantly, despite high unemployment, 98% of participants paid a fee that could offset some of the delivery costs and serve as an incentive for daily adherence, with high reported satisfaction with the service and willingness to pay for home ART delivery. The automated delivery algorithm increased flexibility of the service by accounting for client preferences for delivery times, remaining medication supply, and need for clinical monitoring.

Implications of all the available evidence

We demonstrated that home ART delivery and monitoring is an effective strategy and could be scaled up to address the gap in viral suppression overall and for men. While this client-centred approach will require adaptation of current services including expanding to new delivery platforms, cost might not be a limiting factor. These findings add to the growing literature supporting decentralised delivery and monitoring of ART as a mechanism to increase HIV viral suppression at the population level by increasing access to HIV care.

longer retained in care.[9] Clinically stable individuals (ie, without advanced HIV) can safely and effectively receive ART and monitoring in the community.[10,11] In South Africa, medication delivery outside the clinic is available through the Centralised Chronic Medicines Dispensing and Distribution (CCMDD), supported by Project Last Mile, which packages and delivers medication to external pick-up points across the country and to clinic-based pick-up points; services outside the clinic are primarily available in urban areas.[12] Home delivery could offer an alternative to CCMDD, particularly in rural settings, and incorporating clinical screening could reduce clinic visits. Gaps in data exist on the efficacy of home ART delivery and acceptability of a fee for a home delivery service in a rural setting. A fee for home delivery has the potential to offset programmatic staffing and transportation costs. Innovations in efficient service delivery—including expanding community ART initiation, monitoring, and refill delivery—are needed for people living with HIV, particularly men, among whom the largest gap in viral suppression is seen, to achieve the UNAIDS 95-95-95 goal leading to 85% viral suppression among all people living with HIV.[3,13]

Community-based ART services—ie, ART initiation and refills outside the clinic—increase viral suppression by removing logistical barriers to clinic access and engaging people living with HIV in care.[10,14] However, gaps in service provision and access persist. Routing science—ie, the scheduling of the route or itinerary of people or goods—uses data-driven algorithms (eg, the travelling salesman algorithm) to match client delivery preferences and identify efficient delivery routes to ensure on-time delivery of the right goods to the right person. Leveraging the experience and expertise of routing science, home ART delivery could address gaps in access, meet client preferences, improve individual health, minimise carbon emissions through combined deliveries, and increase viral suppression over time. Further, since minimal financial resources are available (the South African National Department of Health pays a relatively small fee per refill distributed), delivery optimisation, a standard component of routing algorithms, is essential. Few data from randomised trials directly compare the efficacy of data-driven home ART delivery and monitoring with clinic services.

We conducted a randomised trial to evaluate the efficacy of client payment of a fee for community ART initiation as indicated, monitoring, and ART resupply, compared with standard clinic ART initiation as indicated, monitoring, and ART resupply for adults with HIV in KwaZulu-Natal, South Africa. The objectives were to evaluate client payment of the fee for home delivery; acceptability of the delivery service; and the relative efficacy of a client fee for home delivery versus clinic-based ART with regard to the proportion of people with HIV who were virally suppressed at 1 year.

Methods

Study design

We conducted an unblinded, individually randomised trial of home ART delivery (including ART initiation if the participant had not yet initiated ART), monitoring, and ART resupply compared with standard clinic ART services among South African adults living with HIV. We hypothesised that a data-driven ART delivery algorithm would match efficient supply with client preferences, clients would pay a fee for the service, and home delivery would overcome logistical barriers and increase viral suppression. Further, we hypothesised that paying a fee for delivery and requesting a specific time for ART delivery and monitoring would increase engagement in care and implementation intention (ie, a strategy that automates action control, in this case receiving medication delivery which could increase adherence[15]). Finally, we hypothesised that home ART delivery and monitoring would increase viral suppression, especially among men, who have a lower rate of viral suppression in part due to work and other opportunity costs,[16] and address disparities in viral suppression by gender.

The study was conducted in rural and peri-urban areas of high HIV prevalence in South Africa; Pata, Azalea, and Dambuza communities in uMgungundlovu District, KwaZulu-Natal, South Africa. Population HIV prevalence in KwaZulu-Natal was 36%,[17] representing high-prevalence settings in southern Africa. Public clinics in South Africa offer access to ART at no cost. These communities are characterised by high unemployment, low per capita income (below US$2 per day), and income inequality.

The Human Sciences Research Council Research Ethics Committee in South Africa, and the University of Washington Institutional Review Board in Seattle, WA, USA, approved this study.

Participants

Following community mobilisation, which included discussing the proposed study with the Community Advisory Board, community stakeholders, and the local Department of Health, participants were recruited through HIV clinics and HIV testing at community locations. At community-based HIV testing and counselling service points in high traffic areas, such as transportation depots, and at clinics, information about the study was provided to potential participants.

Trained nurses and supervised lay counsellors conducted study activities. Staff received standardised national nurse-initiated and managed ART (NIMART) training in nurse-led HIV testing and counselling; clinical evaluation for ART initiation; ART initiation, monitoring, and adverse effects; and national algorithms for HIV care. A nurse was responsible for clinical oversight, prescriptions, and blood draws. Participants completed an interview during which staff electronically collected preferences for delivery, demographics, and HIV exposure via the REDCap Mobile App.[18] Lay counsellors conducted HIV testing with standardised pre-test and post-test counselling. Individuals living with HIV received additional point-of-care testing to stage their HIV and assess clinical eligibility for community-based ART initiation: CD4 cell count, WHO clinical HIV stage, pregnancy testing, creatinine testing to assess renal function, and symptom screening for tuberculosis. A dried blood spot was collected to assess HIV viral load at baseline.

People living with HIV were eligible for randomisation if they were able to provide informed consent, were 18 years or older, a resident in the participating communities, clinically stable (CD4 count >100 cells per μL, WHO HIV stage 1–3, not pregnant, normal renal function, and had no symptoms on a standardised symptom screen for active tuberculosis), and willing to pay for home delivery of ART. Clinic records were reviewed to facilitate transfer of participants on ART to the study. ART was initiated at enrolment for participants who reported not being on ART and for whom no clinic records were found; a clinic file was started for those participants. As the participants were clinic patients, their medications were available from a central pharmacy and were packaged into 3 months' supply for the purposes of the study. Participants who were not eligible for randomisation for clinical reasons or pregnancy were referred to care and followed until they linked to clinic-based services. We chose a CD4 threshold of more than 100 cells per μL to facilitate clinic care for individuals with advanced HIV/AIDS who were at risk for opportunistic infections. Before enrolment, all participants provided written informed consent, which included counselling about randomisation, procedures in each study group, and their rights as research participants.

Randomisation and masking

The study analyst (TTS) generated the randomisation allocation using randomly selected blocks of size 2, 4, or 6. The randomisation allocation was performed using codes in sequentially numbered, sealed, opaque envelopes. Participants were randomised in a 1:1 ratio to (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. Due to the infeasibility of masking the study team and study participants to ART delivery method, the study was unblinded; however, the laboratory staff, who assessed the outcome of plasma HIV viral load, were masked to the allocation of participants, as were the study investigators.

Procedures

Participants reported their monthly income, which was used to determine the cost of ART delivery in the home ART delivery group. For income less than ZAR 500, ZAR 500–3200, and more than ZAR 3200 the cost of

delivery was ZAR 30, 60, and 90 (equivalent to US$2, 4, and 6), respectively, with a one-time fee covering the cost of delivery for the duration of the study analogous to an annual fee. The fee was paid in cash to the study team, who recorded payment and monitored payment receipt. 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, including standardised counselling and the national HIV programme's first line ART regimen at that time of efavirenz, tenofovir, and emtricitabine. 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 provided by participants, a custom scheduling algorithm solved the "travelling salesman problem" (ie, mathematical optimisation function) to optimise the timing and order for each week's deliveries, minimising the total distance travelled while matching client availability, and ensuring that clients had an uninterrupted supply of ART. The final driving route was determined using a commercially available route planning smartphone app. Deliveries took place 2–3 weeks prior to participants exhausting their ART supply; the algorithm accounted for remaining ART and also included an option for urgent deliveries to avoid participants running out of medication. 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. 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. Missed deliveries, if participants were not at home to receive the delivery, were added to the following week's delivery algorithm. The study team members received a weekly delivery memo including the order of participants receiving ART on each day and the driving directions.

Following enrolment, in the home-delivery group, participants received month 1 and then quarterly home visits for ART resupply, clinical monitoring, counselling, and ascertainment of adverse events and social harms. ART was dispensed with 1 month supply, 2 months, and then every 3 months thereafter. Trimethoprim–sulfamethoxazole prophylaxis was dispensed according to country guidelines and tuberculosis preventive therapy (isoniazid) was provided. Participants received appointments for their home visits. Participants who missed visits were contacted and their visit rescheduled. The home delivery service was regularly available on evenings and on the weekends. Staff used a phone-based application to conduct standardised monitoring that included counselling guidelines. For HIV and ART monitoring, participants completed a clinical 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. HIV plasma viral load was assessed at exit for treatment success and the results provided to participants to guide adherence counselling. Participants who required additional clinical services were referred for care and followed up until they linked. Participants in the home delivery group were administratively linked to the 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. Participants in the clinic group attended the clinic of their choice from the 11 available. They received quarterly phone calls to document ART initiation and adverse events.

Social harms (eg, whether participants experienced stigma associated with HIV) and adverse events were assessed at every in-person visit and with every phone call. Participants were asked about adverse events, including serious adverse events; we included hospitalisations related to HIV and ART among serious adverse events. Chart abstraction was planned for all participants to capture additional clinical events and test results.

At the exit visit, planned for month 6, all home ART delivery group procedures were conducted as outlined above, with the addition of collection of plasma for measurement of HIV viral load. In addition, all 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 differentiated service delivery (eg, decentralised medication dispensing) as appropriate.

The trial was fully enrolled in January, 2020, before the COVID-19 pandemic. During the course of the pandemic, the local Department of Health requested that the study continue to limit the number of participants waiting at the clinic to collect refills as a mitigation strategy for COVID-19 transmission. Deliveries halted for 2 weeks in March, 2020, and then home delivery continued as no-contact deliveries with clinical assessments via telemedicine from March, 2020, until guidance from the Department of Health allowed in person visits for research to restart in September, 2020, which increased follow-up time from the planned 6 months to 12 months for both study groups. In the clinic group, the Department of Health increased access to fast-track ART collection as a COVID-19 transmission mitigation strategy. Participants in both groups received a standard 3-month resupply of ART per visit during the COVID-19 pandemic.

Rapid HIV testing was conducted according to national guidelines: Determine HIV 1-2 (Abbott Diagnostics, Tokyo, Japan) and First Response HIV 1-2-0 Card Test (Prima Medical, Kachigam, India), with SD BIOLINE

HIV-1/2 Rapid (G-Ocean, Hong Kong) as a tie-breaker. Creatinine testing was done using point-of-care StatSensor Xpress (Nova Biomedical, Waltham, MA, USA). Point-of-care CD4 cell count testing (Pima; Abbott Rapid Diagnostics, Cologne, Germany) was conducted using a finger-stick specimen. Plasma HIV viral load was assessed by branched DNA (NucliSENS easyMAG; bioMérieux, Marcy-l'Etoile, France), with a limit of detection of 20 copies per mL, at Global Laboratories in Durban, South Africa.

Outcomes

The primary trial outcomes were the proportion of participants paying the delivery fee and the acceptability of home delivery. The key secondary outcome was achieving HIV viral suppression (<20 copies per mL) assessed at month 12 among all participants and among men; plasma viral load testing was conducted by an accredited laboratory. Other secondary outcomes reported here are safety, clinical adverse events, and social harm, assessed through adverse event reporting, total miles travelled, and CO_2 production. Secondary outcomes that will be reported elsewhere in a planned analysis include: proportion of deliveries made on time; self-reported adherence; and incremental cost of using the routing algorithm.

Statistical analysis

For the primary outcome, we reported the proportion paying the fee, and we did not conduct a power calculation. To estimate power for the secondary outcome of viral suppression, we assumed a total sample size of 120 participants, randomised 1:1. We assumed that viral suppression among participants in the standard of care group would be 75%. With an estimated 5% loss to follow-up and 57 participants retained per group, the power was more than 80% to see a 20% difference (75% *vs* 95%) in viral suppression. The sample size calculation did not account for correlation of viral suppression within the clinic; the effect of within-clinic correlation was explored in sensitivity and exploratory analyses.

All available exit assessments from participants contributed to assignment of whether the participant

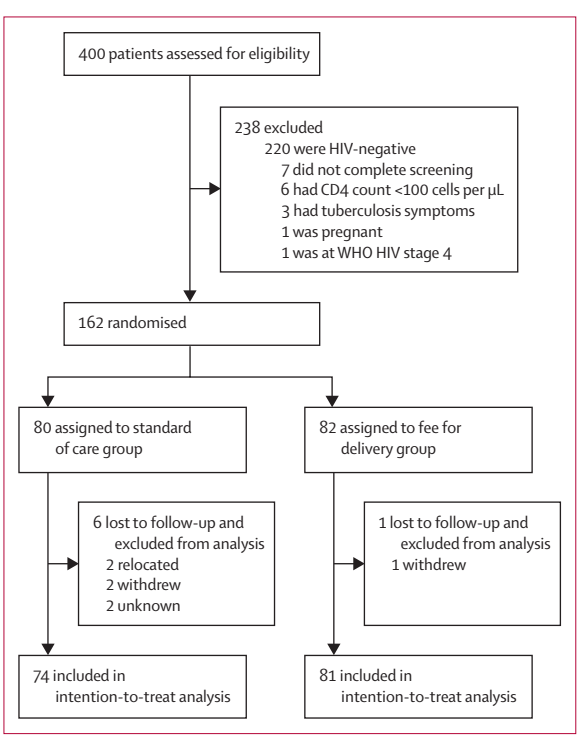

Figure 1: **Trial profile**

	Clinic group (n=80)	Fee for delivery group (n=82)	Total (n = 162)
Gender			
Women	37 (46%)	38 (46%)	75 (46%)
Men	43 (54%)	44 (54%)	87 (54%)
Age, years			
18–29	23 (29%)	12 (15%)	35 (22%)
30–49	49 (61%)	59 (72%)	108 (67%)
≥50	8 (10%)	11 (13%)	19 (12%)
Education			
Primary	26 (32%)	16 (20%)	42 (26%)
Secondary	44 (55%)	58 (71%)	102 (63%)
Tertiary and above	10 (12%)	8 (10%)	18 (11%)
Employed	31 (39%)	33 (40%)	64 (40%)
Knowledge of HIV status			
Individuals known to be living with HIV	53 (66%)	54 (66%)	107 (66%)
Individuals newly identified as living with HIV	27 (34%)	28 (34%)	55 (34%)
Past ART use (among individuals known to be living with HIV)			
Currently on ART	50/53 (94%)	51/54 (94%)	101/107 (94%)
Taken ART in the past	2/53 (4%)	1/54 (2%)	3/107 (3%)
Never taken ART	1/53 (2%)	2/54 (4%)	3/107 (3%)
WHO clinical HIV stage			
Stage 1	77 (96%)	79 (96%)	156 (96%)
Stage 2	3 (4%)	3 (4%)	6 (4%)
Stage 3 or 4	0	0	0
CD4 count, cells per µL			
100–349	13 (16%)	17 (21%)	30 (19%)
≥350	67 (84%)	65 (79%)	132 (81%)
Creatinine, µmol/L	82 (76–97)	86 (77–98)	83 (75–97)
Fee tier*			
30 ZAR	47 (59%)	40 (49%)	87 (54%)
60 ZAR	29 (36%)	33 (40%)	62 (38%)
90 ZAR	4 (5%)	9 (11%)	13 (8%)

Data are n (%), n/N (%), or median (IQR). *Fee tier for the clinic group is the tier in which they would have been placed, based on their monthly income, had they been randomised to the fee for delivery group.

Table 1: **Baseline characteristics by randomisation group**

was virally suppressed. Acceptability was assessed through an exit questionnaire that reviewed willingness to continue to pay a fee for home ART delivery and monitoring,

We calculated the proportion of participants who paid the fee, who answered affirmatively to the acceptability questions (appendix p 2), and the rates of viral suppression (95% CIs were calculated using the Wilson score method). The endpoint of viral suppression was assessed among participants who had viral load assessed at exit (the modified intention-to-treat cohort). Effects of the randomisation groups on viral suppression were estimated as relative risks (RRs) and risk differences (RDs) produced with robust Poisson regression.[19] Models were adjusted a priori for gender and age younger than 30 years, which are known covariates of viral suppression. Tests for superiority of the intervention group compared with the clinic group were based on two-sided Wald p values <0·05. This regression analysis was repeated separately for men. To account for correlation within the clinic and cluster variation between clinics, in a sensitivity analysis, we estimated the RRs and RDs using generalised estimating equations with exchangeable correlation structure. In an exploratory analysis, we also evaluated the effects of randomisation groups on viral suppression using an independence correlation structure.

See Online for appendix

Delivery vehicles were equipped with GPS devices to monitor the distance driven and logs were kept separately to record stops and medication dispensation. These data were evaluated to estimate the total distance driven, miles driven per successful ART dispensation and monitoring visit, time taken per visit, and to calculate the carbon emissions and equivalent carbon offset from driving a delivery vehicle with a combustion engine. We did all analyses with R version 4.1.

This trial is registered on ClinicalTrials.gov (NCT04027153).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Oct 7, 2019, and Jan 30, 2020, 400 participants were identified for study screening; 180 participants were identified as living with HIV, of which 173 (96%) completed screening for study eligibility (figure 1). Of the 11 who were ineligible for randomisation, six (55%) had a CD4 count of less than 100 cells per µL, three (27%) screened positive using the symptomatic tuberculosis screening questionnaire, one (9%) screened positive in the clinical assessment for WHO stage 4 disease, and one (9%) was pregnant. A total of 162 participants were randomised: 80 to the clinic group, and 82 to the home ART group. Seven participants were lost to follow-up: six in the clinic group and one in the home ART group; of the seven, three withdrew, two moved out of the study area, and two were lost for an unknown reason. At least 96% of participants completed each visit (months 1, 3, and 6 visits; and a month 9 visit that was added to mitigate the COVID-19 movement restrictions until exit visits could be conducted in person) in the home ART delivery group. Data for 155 (96%) of the 162 participants were included for the fee payment and viral load endpoints analyses (modified intention-to-treat analysis).

The baseline characteristics for the 162 participants are shown in table 1, of whom 87 (54%) were men and all of whom were Black race and non-Hispanic. Participants had a median age of 36 years (IQR 31–43). 120 (74%) participants had completed secondary education and 98 (60%) reported that they were not employed. 87 (54%) participants qualified for the ZAR 30 fee tier, 62 (38%) for the ZAR 60 fee, and 13 (8%) for the ZAR 90 fee. Most participants were asymptomatic and clinically stable: 156 (96%) were WHO clinical stage 1, 132 (81%) had a CD4 count of 350 cells per µL or higher, and median creatinine was 83 µmol/L.

Median follow-up was 47 weeks (IQR 43–50). In the fee payment group, 80 (98%, 95% CI 92–99) of 82 participants paid the full user fee; nine (100%, 70–100) of nine in the

	Rate of viral suppression				Adjusted* RR of viral suppression, fee for delivery group *vs* clinic group		Adjusted* RD of viral suppression, fee for delivery group *vs* clinic group	
	Clinic group (n=80)		Fee for delivery group (n=82)					
	n/N	%	n/N	%	RR (95% CI)	p value	RD (95% CI)	p value
Overall	55/74	74%	71/81	88%	1·21 (1·02 to 1·42)	0·026	16% (3 to 29)	0·016
Men	25/39	64%	37/44	84%	1·31 (1·01 to 1·71)	0·045	21% (2 to 39)	0·030
Women	30/35	86%	34/37	92%	1·08 (0·88 to 1·33)	0·449	7% (–10 to 25)	0·420

RR=relative risk. RD=risk difference. *Adjusted for gender and age younger than 30 years.

Table 2: **Rates, relative risks, and risk differences of viral suppression, overall and by gender**

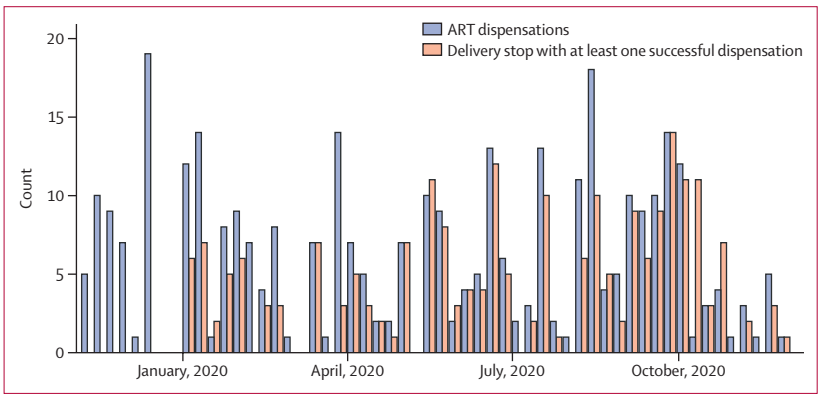

Figure 2: **Transport log compared with ART dispensation**
The transport log was a data entry form completed by the delivery driver and reported the odometer readings at the start and end of each delivery, whether the delivery was successful, and if unexpected stops were made. Transport logs were not collected before Jan 4, 2020. Deliveries were halted for 2 weeks in March, 2020, as a result of the COVID-19 pandemic. ART=antiretroviral therapy.

ZAR 90 group, 31 (94%, 80–98) of 33 in the ZAR 60 group, and 40 (100%, 91–100) of 40 in the ZAR 30 group. Acceptability was high, with 81 (100%) of 81 participants reporting willingness to continue to pay a fee, reporting that the fee was reasonable, and that they would recommend participation to others (appendix p 2). 79 (100%) of 79 participants who paid the fee also reported that the fee helped them remember to take their medication.

Overall home ART delivery and monitoring increased viral suppression at 47 weeks compared with the clinic group (88% *vs* 74%; RR 1·21, 95% CI 1·02–1·42; table 2). Viral suppression was high for men (84%) and women (92%) in the home ART delivery group, compared with 64% for men and 86% for women in the clinic group. 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). Rates of viral suppression were similar in the two groups among women; the study was not powered to detect a difference in viral suppression among women. The absolute increase in viral suppression, the RD, was 21% (95% CI 2–39) for men in the home ART group compared with the clinic group (table 2). When accounting for clustering among participants at clinics, the results were consistent with the primary findings (overall RR 1·16, 95% CI 1·06–1·27, and among men 1·22, 1·03–1·45; appendix pp 3–6). The intracluster correlation coefficient was 0·025 overall and –0·005 among men. No serious adverse events were reported and no social harms related to study participation were reported.

From January, 2020, onwards, in the home ART delivery and monitoring group, medication dispensation logs compared well with transportation logs, visually indicating good correlation between travel and successful ART delivery and monitoring (figure 2). 426 successful medication dispensations were conducted. Extrapolating data from 289 dispensations with routing logs, a distance of 3956 km (2458 miles) was driven, which was 18 km (11 miles) 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. We estimated that this would produce 25 kg of CO_2 per year for every ten people in the programme. To offset the annual carbon footprint for ART delivery and home monitoring, one tree would need to be planted for every ten participants in the programme.[20]

Discussion

This randomised trial conducted in a high HIV prevalence setting in South Africa during the global COVID-19 pandemic and consequent movement restrictions provides evidence that home delivery of ART, including same-day ART initiation as needed, monitoring, and ART resupply, increases viral suppression among people with HIV, particularly among men, compared with standard clinic-based services. The adaptation to no-contact delivery and clinical assessments via telemedicine also demonstrates the resilience of home delivery to COVID-19 movement restrictions. Further, the use of routing algorithms that prioritise client preferences and optimise delivery logistics can be leveraged to automate care provision and also meet the requirements of clinical protocols and constraints of medication supply. Client-centred services that overcome barriers to care might increase the proportion of people living with HIV who start ART, achieve viral suppression, and sustain engagement in care.

The COVID-19 pandemic has accelerated the adoption of differentiated service delivery (DSD) services for HIV care, such as multi-month dispensing, fast-track ART,[11] and additional pick-up points for medications, with more than 800 points available in KwaZulu-Natal. DSD has helped maintain rates of viral suppression but new HIV diagnoses were delayed.[21,22] However, current viral suppression levels fall short of the UNAIDS goal of overall 86%; interventions are needed to identify and link people with HIV to ART and achieve sustained viral suppression.[23] Further, a gap in evidence exists regarding how to achieve high levels of viral suppression, including among men for their own health benefits and to lower HIV incidence among women.[24,25] Using standard vehicle routing algorithms that match client preferences for ART delivery with existing ART supply, we demonstrated high levels of viral suppression that met the UNAIDS goals and eliminated gender disparities. Finally, even though 60% of participants reported being unemployed, payment of the delivery fee was high (98%), indicating the prioritisation of accessible services within the context of constrained client resources.

We hypothesised that home HIV delivery and monitoring would increase the proportion of people with HIV who achieve viral suppression, based on evidence that community-based HIV interventions increased suppression,[26] by overcoming barriers to care, including standard work hours, stigma, unfavourable perceptions of clinics and staff, cost of transport, and lost wages, and, more recently, the risk of COVID-19 acquisition.[8,27,28] Further, people in informal employment might need to choose between visiting the clinic or earning daily wages,[5] limiting their use of clinic-based services.[5,29] The use of delivery algorithms that account for client preferences increases flexibility and access for clients. We also hypothesised that payment of the fee by the client would increase treatment intention and adherence, which participants reported in their survey; however, this comparison was not randomised. To assess this, the home ART delivery service would need to be tested with and without a fee to determine whether the fee payment by the client increased their adherence. Offering convenient home ART delivery and monitoring including times outside of normal business hours and on weekends, being flexible to meet travel and mobility

needs, offering quarterly refills, and streamlining monitoring and resupply had better viral suppression outcomes, especially for men. Real-world equivalent services for home-delivery include private pharmacies that deliver medications, delivery services that use pre-packaged items, and delivery algorithms that are available through standard computing tools. These could be adapted for implementation of home ART delivery and monitoring. While the study collected plasma for viral load testing for the study, dried blood spots perform equally well for measuring viral load and could be incorporated into a home ART delivery service with collection of the dried blood spots for viral load testing.[30]

There were no serious and severe adverse events across the two study groups, indicating that home ART delivery is likely to be as safe as clinic-based ART. However, the proportion of participants achieving viral suppression was higher through home ART delivery, which could increase health gains over time. Lastly, for scale-up, implementation might need a mix of behavioural and social interventions to see the same (or larger) effect size across heterogeneous settings.

We acknowledge several limitations of the study. The standard of clinic care changed during the COVID-19 pandemic to increase access to fast-track ART and multi-month refills;[11] both are evidence-based DSD strategies to maintain viral suppression. More than three-quarters of participants achieved viral suppression at the clinic and it is likely the changes to the standard of care at the clinic improved viral suppression in the clinic-based group, although the COVID-19 pandemic might have also limited clinic access. Movement restrictions during COVID-19 might have increased the impact of a home ART delivery and monitoring service, since participants were more likely to be at home. However, while clinic-based DSD services increased viral suppression overall, disparities in viral suppression by gender persisted in clinic-based services but were eliminated in the home ART delivery group, which had overall significantly higher viral suppression. The client fee for delivery of ART was relatively low (ZAR 30, 60 or 90), although it is higher than the ZAR 10 the Department of Health pays for CCMDD ART delivery to external pick-up points such as pharmacies. The cost of fuel per successful dispensation in South Africa is approximately ZAR 25 (for driving 14·2 km); thus, the fee could offset some of the costs of delivery. A formal costing and cost-effectiveness analysis have not been conducted to date. Our study was limited to settings with medium and high HIV prevalence and might not be generalisable 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 was limited to adults since the ability to pay a fee was a requirement for enrolment. However, adolescents and children are a priority group and should be included in future evaluations, including home ART delivery paid for by the health-care service. We did not include participants lost to follow-up in the analysis; however, if we assumed that they were not virally suppressed, that would have strengthened the study outcome. Lastly, a relatively small number of participants were ART-naive at enrolment and further studies should evaluate efficacy and safety among people initiating ART for the first time who might require additional counselling.

The strengths of the study include the randomised design, the use of a routing algorithm to meet client delivery preferences, successful enrolment of men (54% of the study population), and high retention across the randomised groups. The study primary aims were fee payment and acceptability so that the viral suppression outcome could be considered in the context of client fee payment, acceptability, and willingness to continue to pay a fee for service. Using a mobile app, standardised care was provided following clinical algorithms, thus limiting medical errors and facilitating task shifting.

The next steps for client-centred ART delivery and monitoring are to test a menu of strategies to match the services provided to client preferences and to allow for those to change over time and be responsive to external circumstances such as the COVID-19 pandemic. Also, evaluating the health impact and cost at scale in high HIV prevalence settings with a baseline gender gap in suppression would provide evidence for generalisability. Although home ART achieved viral suppression among almost 90% of women and men living with HIV, additional services are needed to reach the remaining 10%. Specifically, expanded home delivery services to address barriers to care and long-acting injectable antiretroviral therapy might overcome remaining logistical and other barriers. Future research directions should focus on scalable, client-centred strategies to deliver ART.

Contributors

RVB, AvH, AB, MLK, and AAS designed the trial. TZ programmed the delivery algorithm to schedule deliveries. TTS and AAS performed the data analyses and accessed and verified the data. All authors contributed equally to results interpretation. RVB wrote the first draft of the manuscript. All authors contributed equally to the execution of the trial and critically reviewed and approved the finalised manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

RVB reports grants from the Bill & Melinda Gates Foundation and grants from the US National Institutes of Health (NIH), during the conduct of the study; and conference abstract and manuscript writing support from Regeneron Pharmaceuticals, outside the submitted work. JMB reports grants from the Bill & Melinda Gates Foundation during the conduct of the study; grants from the Bill & Melinda Gates Foundation, US Centers for Disease Control and Prevention, NIH, and USAID; and is an employee at Gilead Sciences, outside the submitted work. CC reports grants from the Bill & Melinda Gates Foundation, during the conduct of the study; and personal fees from Gilead Sciences and personal fees from Merck, outside the submitted work. All other authors declare no competing interests.

Data sharing

A complete de-identified patient dataset sufficient to reproduce the study findings will be made available approximately 1 year after completion of the trial (NCT02929992), following approval of a concept sheet summarising the analyses to be done. Further enquiries can be directed to the Deliver Health Scientific Committee at lnakatsuka@partners.org.

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