State-of-the-ART Care: Revolutionizing Medication Delivery in Rural Settings with a Person-Centered Care Approach

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Abstract

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Rural Settings with a Person-Centered Care Approach

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As of 2022, there were 7.8 million people living with HIV in South Africa. HIV prevalence in South Africa varies geographically, with the KwaZulu-Natal province continuing to have the highest HIV prevalence in the country and rural formal farming communities reporting a higher HIV prevalence than urban areas. It is important to identify strategies that can help close the remaining gaps in HIV treatment and care in South Africa. Until a cure for HIV is available, reliable access to antiretroviral therapy (ART) is needed to maintain HIV viral suppression for people living with HIV. The current standard-of-care in South Africa to refill ART supply is for individuals to go in-person to clinics, with the duration of ART refills limited to one to three months for most individuals.

Resupplying ART through community-based venues, such as home delivery, can effectively increase ART coverage and adherence compared to clinic-based care while decongesting clinics for attention to acute patients. Home-delivered ART and monitoring could

potentially offer cost savings compared to clinic-based care in terms of financial costs and environmental costs. I investigated the differential COVID-19 pandemic impact for home-delivery of ART compared to standard clinic-based care among people living with HIV in rural South Africa and compared the environmental and cost impacts of the two ART delivery models. In Chapter 1, I observed no difference in the self-reported number of missed ART doses by method of ART refill (home-delivered vs. at clinics) when comparing between or within time periods during the first COVID-19 wave in South Africa. In Chapter 2, I found that incremental CO_2 emissions were higher for participants receiving home-delivered vs. clinic-based ART refills in rural South Africa but could be offset by six- or 12-month refills (and reducing delivery frequency) and/or switching to electric delivery vehicles, decreasing the impact on the environment. In Chapter 3, I found that the average annual cost per client and average annual cost per client virally suppressed of implementing a home-delivered ART intervention was higher than the cost of clinic-based ART refills and care from the payer perspective in the as-observed scenario. Personnel costs were the largest cost for home-delivered refills while ART drug costs were the largest cost of clinic-based refills. When provided at scale, home-delivered ART in a rural setting not only offers clinical benefits for a hard-to-reach population but is also comparable in cost to the provincial standard of care. While fee for home delivery was demonstrated to be an effective ART refill method for achieving viral suppression compared to clinic-based refills in the Deliver Health Study, home-delivered ART was found to be more environmentally and financially costly compared to standard clinic-based refills in the as-observed scenario, and did not have a significant effect on the risk of missing ART doses during the first COVID-19 wave in South Africa. However, when home ART delivery is implemented at-scale and with multi-month refills, there are potential cost- and environmental savings relative

to the standard clinic-based care. This research provides novel insights to the financial costs and environmental impact associated with implementing home-delivered ART refills and monitoring in rural South Africa, a relatively new differentiated service delivery method which could be scaled up more widely in an effort to reduce physical access barriers for people living with HIV and to offer clients more resupply options that could better suit their lifestyle preferences.

Dedication

This dissertation is dedicated to my family.

To my grandparents, who worked hard to survive so that their descendants could thrive,

and who I have been so lucky to know, learn from, and be loved by.

To my parents, who raised me to never take anything for granted,

to always give grace to others and help however I can,

and let me feel like the world was my oyster.

To my uncle Gin-Weigh Wu, the first PhD in the family and

who believed every day should feel like Christmas

(and it always did in his presence).

And to my dear friend Melanie Woods,

who loved the following quote by Ruth Bader Ginsburg:

“Fight for the things that you care about,

but do it in a way that will lead others to join you.”

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Introduction

With scientific and technological advancements in healthcare, we have the ability to diagnose health conditions earlier on and can tailor disease screening for specific individuals based on genetic or lifestyle risk factors identified in past epidemiological studies. Although public health is greater equipped than ever before from a prevention standpoint, not all diseases are preventable (e.g., emerging infectious diseases, congenital anomalies) and not all cases of a preventable disease can be prevented (e.g., vaccine-preventable diseases like measles and polio). Upon diagnosis of a disease, medical professionals do their best to provide individuals with information on all available treatment options so that individuals can make an informed decision that best suits their own needs and preferences. While being diagnosed with a disease is not something an individual chooses, how they would like to treat or manage a disease is their choice. Unlike infectious diseases, most chronic health conditions will require consistent monitoring and use of medication to manage symptoms across the lifespan.

While transmission occurs from person-to-person, Human Immunodeficiency Virus (HIV) actually straddles the worlds between infectious and chronic diseases. Antiretroviral therapy (ART), the best treatment option for people living with HIV currently, has made it possible for people living with HIV to achieve almost complete suppression of viral replication and undetectable viral load.[1] ART has been scientifically shown to prevent HIV-associated morbidity, mortality, and transmission to sexual partners and from mother to baby[2–4] and to lead to nearly normal life expectancy for people with HIV.[5] Until a cure for HIV is available, reliable access to ART is needed to maintain HIV viral suppression for people living with HIV.

As of 2022, there were 7.8 million people living with HIV in South Africa.[6] Nearly at-target of meeting the 95-95-95 HIV goals set forth by the Joint United Nations Programme on

HIV/AIDS, 90% of South African adults aged 15 years and older were aware of their HIV status, 91% of those who knew their HIV status were on ART, and 94% of those on ART were virally suppressed.[6] HIV prevalence in South Africa varies geographically, with the KwaZulu-Natal province continuing to have the highest HIV prevalence in the country[6] and rural formal farming communities reporting a higher HIV prevalence than those living in urban areas (18% vs. 13%).[7] A study from 2018 identified the rural Greater Edendale and Vulindlela areas of uMgungundlovu district, KwaZulu-Natal as having the highest estimated HIV prevalence in South Africa of 36%, with 40% of people living with HIV on ART and 50% on ART virally suppressed.[8] With such disparities between urban and rural areas, it is important to identify strategies that can help close the remaining gaps in HIV treatment and care in South Africa.

The current standard-of-care in South Africa to refill ART supply is for individuals to go in-person to clinics, with the duration of ART refills limited to 1 to 3 months for most individuals.[9] The vast majority of ART in South Africa is dispensed through clinics, with up to 70% of a clinic's prescription load devoted to dispensing ART refills on any given day.[10] Public funding for HIV/AIDS programs in South Africa occurs through a conditional HIV, Tuberculosis, Malaria and Community Outreach Grant which transfers funds from the national to provincial governments. This dedicated funding stream has enabled an expansion of ART coverage across South Africa over the past decade,[11] but with an increased demand for free health services and funding levels that do not match the rate of demand, public health facilities experience increased wait times for clients, reduced staff morale, and pharmacy stock-outs.[12] Small primary clinics in resource-limited areas may additionally experience constraints such as limited staffing capacity and space shortages,[13] all of which make it difficult to serve the large volume of people living with HIV requiring continuous access to HIV treatment and care. From the client perspective, obstacles to

retention in HIV care and maintenance of viral suppression include long waiting times at clinics, transportation barriers (cost, time, and/or availability of transportation), and social stigma associated with living with HIV.[14–16]

Given the high HIV prevalence and importance of sustained HIV care, national scale-up of differentiated service delivery models for HIV treatment are being expanded in South Africa. Funded by the South African government, one differentiated service delivery model focused on the delivery of medications (including ART) outside the clinic is the Centralised Chronic Medicines Dispensing and Distribution (CCMDD) program.[17] Recent studies in South Africa have demonstrated how alternative dispensing mechanisms improved clients' adherence to taking their medications compared to the standard-of-care[18], and shown the feasibility and acceptability of home-delivered medications by community health workers[19,20] and as a fee-based delivery service[16,21]. Resupplying ART through community-based venues can effectively increase ART coverage and adherence compared to clinic-based care[22] while decongesting clinics for attention to acute patients. Currently, CCMDD delivery services to community-based venues exist predominantly in urban areas, thus a differentiated service delivery approach like home-delivered ART refills could cover the gap of CCMDD's services in rural settings.

In a real-world implementation example, during the COVID-19 pandemic, cancellation of health services due to government-imposed COVID-19 lockdowns was a major source of stress and anxiety for individuals with chronic conditions requiring consistent and frequent access to clinics.[23] As a response to country-wide COVID-19 lockdowns and associated service disruptions, home-delivery of medication was rapidly implemented for individuals with chronic conditions in South Africa.[24] Multi-month scripts for people living with HIV also enabled sustained ART provision[25,26] in South Africa during the pandemic. During large-scale disruptions

in health services, novel strategies for refilling ART (like home delivery) for people living with HIV can enable providers to continue to meet the needs of their patients without the patient barriers of physical commuting demands, long clinic wait times, and opportunity cost of missing work to refill prescriptions.

Beyond increasing coverage of ART in rural areas and decongesting public health clinics, home-delivered ART and monitoring could potentially offer savings compared to clinic-based care in terms of financial costs and environmental costs. Climate change is an ongoing global public health and environmental health emergency.[27] South Africa, an energy- and emissions-intensive middle-income developing country, has an existing energy crisis and experiences regular episodes of temporary power shutdowns,[28] and climate change is anticipated to only further exacerbate the country's energy crisis. As a signatory to the United Nations Framework Convention on Climate Change and to the Paris Agreement, South Africa is committing efforts to move towards net-zero carbon emissions by 2050.[29] The transportation sector contributes more than 10% of South Africa's national gross emissions, having emitted more than 55 megatonnes carbon dioxide (CO_2) emissions in 2017.[30] Recent studies have compared greenhouse gas emissions of traditional in-person shopping practices with the delivery of goods to clients' homes or nearby parcel lockers located in the community, successfully identifying opportunities to incorporate greener last mile delivery (e.g., by cargo bike or on foot with hand trucks) and collection (e.g., individuals biking or walking to community locations rather than drive) strategies.[31–33] As healthcare delivery moves closer to clients in the community to increase the proportion of people accessing treatment, the environmental impact of decentralized care requires evaluation to identify modifiable factors and limit consequences for global warming.

Therefore, the following questions are useful for improving our understanding of how home-delivered ART refills compares to the current standard-of-care in South Africa, clinic-based ART refills: Was there a difference in self-reported ART adherence under different COVID-19 alert levels during the first wave of COVID-19 in South Africa by method of ART refills? What is the environmental impact of home-delivered ART refills and how does it compare to the cumulative environmental impact of people living with HIV each commuting to clinics to refill their ART supply? How do the costs of implementing a home delivery of ART intervention compare to the cost of standard clinic-based refills in KwaZulu-Natal, South Africa?

In Chapter 1, I begin by estimating the effect of changing COVID-19 alert levels during the first COVID-19 wave in South Africa on self-reported missed ART doses for participants receiving home-delivered vs. clinic-based refills using the difference-in-differences technique. I additionally estimate the effect of changing COVID-19 alert levels on the occurrence of late clinic refill visits for people living with HIV receiving clinic-based refills only. In Chapter 2, I compare the difference in average cost in carbon dioxide emissions for each person virally suppressed between those receiving home-delivered vs. clinic-based ART refills as well as the incremental emissions and health differences from switching from one strategy to the other. In Chapter 3, I calculate the cost of implementing home-delivered ART for people living with HIV in KwaZulu-Natal South Africa and compare it to the cost of standard clinic ART resupply. I also identify cost drivers of home-delivered and clinic-based ART refill methods and assess how costs of home-delivered ART would change under different implementation scenarios.

This body of research investigates what the COVID-19 pandemic impact, environmental impact, and cost impact were for home-delivery of ART compared to standard clinic-based care among people living with HIV in rural South Africa. The ultimate goal of this research is to

inform South Africa NDoH strategies for increasing physical access to ART for people living with HIV and to offer clients a greater number of resupply options with the hopes that they can choose a method which best suits their needs and preferences to support long-term retention in HIV care.

Chapter 1: Estimating the Effect of COVID-19 Pandemic Restrictions on Self-reported Antiretroviral Therapy Use and Late Refill Visits Among People Living with HIV in Rural South Africa

ABSTRACT

People living with HIV require reliable access to and adequate supply of antiretroviral therapy (ART) for viral suppression. The Deliver Health Study, a randomized trial conducted during the COVID-19 pandemic, found that home-delivered ART significantly increased viral suppression compared to clinic-based care. The effect of changing COVID-19 alert levels on self-reported ART use has not been quantified. Adults living with HIV in KwaZulu-Natal, South Africa were followed in the Deliver Health Study during October 2019-December 2020. I used difference-in-differences (DiD) to estimate the effect of changing COVID-19 alert levels during three distinct periods on self-reported missed ART doses (missed 0 vs. ≥1 doses in past week) for participants receiving home-delivered vs. clinic-based refills. I additionally estimated the effect of changing COVID-19 alert levels on late clinic ART refill visits (late vs. on-time). I used relative risk regression for both binary outcomes. Of 155 participants, 46% were women and median age was 36 years. The mean number of missed weekly doses was 0.11, 0, and 0.12 in the home-delivery group and 0.09, 0.08, and 0.18 in the clinic group during periods 1, 2, and 3, respectively. There were no differences in relative risk (RR) of self-reported daily ART use between refill groups when comparing across periods ($DiD_{period\ 2\ vs.\ 1}$=1.05; 95% confidence interval [CI]: 0.97, 1.13 and $DiD_{period\ 3\ vs.\ 2}$=0.99; 95% CI: 0.91, 1.08). In the clinic group, the risk of late refill visits was significantly higher during COVID-19 restrictions (vs. before alert level 5 implementation) and even after the COVID-19 alert level was downgraded to level 1 ($RR_{period\ 2\ vs.}$

$_{1}$=1.83, 95% CI: 1.34, 2.51 and $RR_{period\ 3\ vs.\ 2}$=1.71; 95% CI: 1.43, 2.04). The COVID-19 pandemic did not differentially impact self-reported ART adherence by method of ART refills, but the risk of late clinic refill visits was significantly higher during COVID-19 restrictions and sustained after restrictions were loosened.

INTRODUCTION

While efforts to increase HIV status awareness through testing have been largely successful with 86% of people living with HIV globally knowing their HIV status at the end of 2022, the proportion of people living with HIV who were accessing treatment and who were virally suppressed was 76% and 71%, respectively.[34] In South Africa alone, nearly 8 million people are living with HIV, 74% of whom are on antiretroviral therapy (ART) and 65% are virally suppressed.[35] KwaZulu-Natal has the highest estimated HIV prevalence in South Africa at 27%.[7] Once diagnosed with HIV, all people living with HIV require a reliable ART supply for their lifetime or until a cure is available. Research in HIV care has centered around strengthening the HIV continuum, from HIV diagnosis, to ART initiation, and viral suppression for life.[36]

Given the high HIV prevalence and importance of sustained HIV care, national scale-up of differentiated service delivery (DSD) models for HIV treatment tailored to specific patient populations are being expanded. The current standard-of-care in South Africa to refill ART prescriptions is for individuals to go in-person to clinics, with duration of ART refills often limited to one to three months.[9] One DSD model in South Africa focused on the delivery of medications, including ART, outside the clinic is the Centralised Chronic Medicines Dispensing and Distribution (CCMDD) program.[17] Resupplying ART through community-based venues has effectively increased ART coverage and adherence compared to clinic-based care[22] while decongesting clinics for attention to acute patients. Currently, CCMDD delivery services to community-based venues exist predominantly in urban areas, thus a DSD approach like home-delivery of ART could cover the gap of CCMDD's services in rural settings.

During the COVID-19 pandemic, cancellation of health services due to government-imposed COVID-19 lockdowns were a major source of stress and anxiety for individuals with

chronic conditions requiring consistent and frequent access to clinics.[23] As a response to country-wide COVID-19 lockdowns and associated service disruptions, home-delivery of medication was rapidly implemented for individuals with chronic conditions in South Africa.[24] Multi-month scripts for people living with HIV also enabled sustained ART provision[25,26] in South Africa during the pandemic, with one study[37] demonstrating the success of 12-month ART scripts in KwaZulu-Natal for clinically-stable people living with HIV. Beyond during large-scale disruptions in health services, novel strategies for refilling ART (e.g., home-delivery) for people living with HIV can enable providers to continue to meet the needs of their patients without the patient barriers of physical commuting demands, long clinic wait times, and opportunity cost of missing work to refill prescriptions.

The Deliver Health Study found that home-delivered ART significantly increased viral suppression compared with clinic-based ART refills, including during COVID-19 lockdowns in rural South Africa (88% vs. 74%).[38] At each follow-up visit, Deliver Health Study participants were asked to self-report their number of missed ART doses. While viral suppression is the gold standard indicating treatment success for individuals living with HIV and is a composite measure of success for ART programs, frequent viral load measurements are not always feasible and alternative medication adherence measures are being researched. A recent study of a South African adolescent cohort found self-reported missed doses in the past week to be predictive of elevated viral load at 87% sensitivity and 19% specificity.[39] Ideally, self-reported daily ART use would provide a robust measure of ART delivery system resilience during times of social upheaval and during regular programming, allowing assessment of access to care. Interrupted time series analyses of the COVID-19 lockdown impact on HIV care in KwaZulu-Natal showed no marked changes in the number of ART refill visits[25] or HIV-related care clinic visits[40]

immediately after lockdown (COVID-19 alert level 5) vs. before the lockdown. Another study found limited evidence of the association between health care access and ART adherence during the lockdown.[41] However, the impact of the COVID-19 pandemic itself and changes in COVID-19 alert levels on self-reported missed ART doses among adults living with HIV who received their ART refills through a DSD approach like home-delivery vs. standard clinic care in rural South Africa is not known. Further, to our knowledge, the impact of COVID-19 restrictions on delayed ART refill visits at clinics in rural South Africa has not been characterized.

The primary aim of this study was to investigate the impact of the COVID-19 pandemic by estimating the effect of changing COVID-19 alert levels on self-reported daily ART use among people living with HIV receiving home-delivered vs. clinic-based ART refills in rural settings. I hypothesized that persons receiving home-delivered refills would report greater daily ART use than persons going to clinics to resupply due to uninterrupted access to refills via home-delivery. For people living with HIV in the clinic-based care group only, I also estimated the effect of changing COVID-19 alert levels on the occurrence of late clinic refill visits as a secondary aim, hypothesizing a greater risk of late refill visits during more restrictive COVID-19 alert levels.

METHODS

Data source

The Deliver Health Study (NIH R21MH115770; ClinicalTrials.gov ID: NCT04027153) was a pilot randomized controlled trial comparing fee for home delivery of ART to clinic-based ART refills in South Africa conducted from October 7, 2019 – December 31, 2020, during the COVID-19 pandemic. The objectives were to develop and test routing algorithms for mobile vans that deliver ART in rural, high prevalence HIV settings in South Africa and to evaluate the

impact of a fee for home-delivery of ART on viral suppression. A total of 162 individuals were enrolled in the Deliver Health Study. All participants were randomized to either receive their ART refills through home-delivery via mobile vans or at clinics. Data on participant demographics, previous HIV testing history, clinical history, use of health care services, and barriers to care were collected. Plasma specimens were collected from participants at enrollment and at the exit visit for HIV-1 viral load testing. Participants completed a questionnaire on self-reported missed doses at each ART resupply visit. All participants were followed for at least 9 months with follow-up refill visits at months 1, 3, 6, and 9. While only 6 months of follow-up were originally planned, a month 9 visit was added to mitigate movement restrictions under the higher COVID-19 alert levels until an in-person exit visit could be conducted for the home-delivery group. The full study procedures have been previously published.[38] With its unique timing capturing the full first wave of the COVID-19 pandemic in South Africa, the Deliver Health Study was a suitable data source to answer the research question in this study.

Study design

This study leveraged a natural experiment introduced by the COVID-19 pandemic. The South African government implemented five-level alert system during the COVID-19 pandemic to ease into lockdown (see Supplemental Figure 1.1 in Appendix A**,** summary of alert levels). Alert level 5 indicated high rates of COVID-19 infection with low health system readiness and had the most stringent lockdown measures, during which all non-essential and recreational travel were not permitted, schools and non-essential businesses were closed, public transportation was restricted, and individuals were required to stay at home unless to perform an essential service or seek emergency or chronic medical care.[42] The healthcare sector was considered an essential service with no restrictions placed on access to or delivery of healthcare services during

lockdown,[40] though this does not account for reduced clinic capacity due to COVID-19-associated measures. Alert level 1 indicated low rates of COVID-19 infection with high health system readiness, during which most normal activities were resumed. Supplemental Figure 1.2 is a visual timeline of alert level changes during the first COVID-19 wave in South Africa.

The exposures for the primary and secondary aims of the study were 1) the implementation of the COVID-19 alert level 5 (lockdown) on March 27, 2020 and 2) downgrading the COVID-19 alert level to level 1 on September 21, 2020. There were three time periods of interest within the observed time frame of the Deliver Health Study: *before* the first COVID-19 alert level 5 (lockdown) was implemented in South Africa from October 15, 2019-March 26, 2020 (period 1), *during* the first COVID-19 lockdown (alert levels 5, 4, 3, and 2) in South Africa from March 27-September 20, 2020 (period 2), and *after* the COVID-19 alert level was downgraded to level 1 in South Africa from September 21-December 31, 2020 (period 3). Periods 1 and 2 were the relevant time periods to quantify the effect of implementing alert level 5, and periods 2 and 3 were the relevant time periods to quantify of the effect of downgrading to alert level 1. Participants in the Deliver Health Study were enrolled between October 15, 2019 and January 30, 2020. Thus, participants had varying follow-up windows and total follow-up time varied from participant to participant. Some participants had visits only during period 1 and period 2, some participants had visits only during period 2 and period 3, and some participants had visits during periods 1, 2, and 3.

Study population and eligibility criteria

To be enrolled in the Deliver Health Study, individuals needed to meet the following criteria: ≥18 years old, test positive for HIV during study screening, reside in the study community for the duration of follow-up, be eligible for ART by national guidelines or currently

taking ART, willing to pay for home-delivery service, and able and willing to provide informed consent for study procedures. In addition to the inclusion criteria of the Deliver Health Study, for our analysis individuals needed to have completed the study (i.e., not lost to follow-up) and have a follow-up visit during at least one of the three time periods of interest.

Definition of outcomes

The primary outcome measure was the number of ART doses missed in the past week (7 days), self-reported by participants at each follow-up visit. I operationalized the outcome as a binary variable, comparing zero reported missed ART doses (100% adherence) to ≥1 missed ART doses in the past week. I ran a sensitivity analysis with one missed dose as the cutoff (i.e. 85% adherence) vs. ≥2 missed doses in the past week based on data from the literature on optimal adherence levels.[43] While HIV viral load is considered the gold standard for determining viral suppression, viral load measurements were only taken at study exit though participants were asked to self-report their number of missed doses at each follow-up visit. As a comparison, I examined if there was a difference in self-reported daily ART use and HIV viral suppression (undetectable HIV viral load), defined as having less than 20 copies per milliliter of blood, based on HIV plasma viral loads measured at study exit. I conducted a complete case analysis per time period, including individuals who had available data in the analytic dataset of each time period. For example, if an individual had outcome data available in periods 1 and 2 but not 3, they were still included as part of the analytic dataset in periods 1 and 2, but not for period 3. While it is not entirely plausible to assume that participants were missing self-reported data on missed ART doses completely at random, complete case analysis was a reasonable approach as there were only 8 out of 611 observations (1%) with missing data on the number of ART doses missed in the

past week, which would not have changed our results significantly if a single or multiple imputation approach was used to recover those eight observations.

For the clinic-based care group only, I had a secondary outcome measure of late vs. on-time ART refill visits to assess if participants in the clinic-based care group were able to refill their ART before their prior prescription ran out. The goal of including this secondary outcome was to help quantify the impact of changing COVID-19 alert levels in South Africa on delayed clinic visits among people living with HIV in rural areas.

Statistical analysis

To estimate the effect of changing COVID-19 alert levels on ART adherence of people living with HIV receiving home-delivered vs. clinic-based refills, I conducted two controlled differences-in-differences (DiD) analyses. First, to estimate the effect of COVID-19 alert level 5 being implemented, I compared the number of missed ART doses in the past week in the home-delivery group compared to the clinic-based ART refills group (the control) in period 1 vs. period 2. Second, to estimate the effect of downgrading to COVID-19 alert level 1, I compared the number of missed ART doses in the past week in the home-delivery group compared to the clinic-based ART refills group in period 2 vs. period 3. For the secondary aim, I compared the occurrence of late clinic ART refill visits in period 1 vs. period 2, and in period 2 vs. period 3.

For both primary and secondary aims, I used relative risk regression with sandwich estimators to obtain robust standard errors (generalized linear models with Poisson distribution and log link) because relative risks (RRs) were our quantity of interest and the prevalence of both zero missed ART doses and late ART refill visits were common in our study population (thus odds ratios estimated from logistic regression would not have approximated the RRs[44]). I reported differences in relative risks (RRs) with corresponding 95% confidence intervals (CIs)

for the primary aim, and RRs with 95% CIs for the secondary aim. I shifted the time periods of interest forward by 7 days to account for the time lag of the outcome asking participants to recall on their number of missed doses in the past week. Thus, period 1 was considered October 15, 2019-April 2, 2020; period 2 was April 3-September 30, 2020; and period 3 was October 1-December 31, 2020. I assumed the clinic-based care group was a good comparison group for the home-delivered refills group since it demonstrated what access to ART refills for people living with HIV would have been in South Africa in the absence of the home-delivery intervention. All analyses were conducted at the visit-level. I used Pearson's Chi-squared (two-sided) test at the $p<0.05$ level to determine if there was a significant association between self-reported missed ART doses and viral suppression. More detailed statistical analysis methods and model equations are reported in **Appendix A**.

RESULTS

After excluding 7 participants who were lost to follow up, there were 155 participants in our study. Of those lost to follow-up, 6 participants were in the clinic-based care group, 43% were women, median age was 37 years, and all except one participant completed their month 6 follow-up visit but did not have an exit visit or viral load measurement. Of the 155 participants included in our study, 46% were women and the median age was 36 years (Table 1.1). The majority of participants (67%) knew their HIV status at baseline, of whom 95% were currently taking ART. One-third of participants did not know their HIV status prior to study screening and newly-intiated ART. All study participants were taking the Tenofovir/Emtricitabine/Efavirenz (TDF/FTC/EFV) ART regimen. Eighty-one participants received ART refills through home-delivery compared to 74 participants who received standard clinic-based care. Most participants (n=120; 82%) reported taking 100% of daily ART doses in the past week the entire duration of

the study. Twenty-two participants (14%) reported 75% adherence across the study period, one participant (1%) reported 67% adherence, and five participants (3%) reported ≤50% adherence. Of those receiving home-delivered refills, 80% (65/81) reported taking 100% of daily ART doses in the past week compared to 84% (62/74) of those receiving clinic-based refills.

The 155 participants accrued a total of 603 ART refill visits over the study period, after excluding eight visits missing data on the number of ART doses missed in the past week. The total number of ART refill visits included in the period 1, period 2, and period 3 datasets were 291 visits (across 150 participants), 180 visits (across 139 participants), and 132 visits (across 132 participants), respectively. For persons receiving home-delivered refills, the mean number of missed weekly doses was 0.11, 0, and 0.12 during periods 1, 2, and 3, respectively; with clinic-based refills, the mean number of missed doses was 0.09, 0.08, and 0.18 during periods 1, 2, and 3, respectively (Table 1.2). In the clinic group, the mean number of late refill visits over the study period was 2.32 (range: 1-3). Self-reported missed doses was not associated with viral suppression at exit at the 100% adherence level (Pearson's χ^2 = 0.14; p-value = 0.71) or at the ≥85% level (Pearson's χ^2 = 0.03; p-value = 0.85).

Difference-in-differences of missing ART doses between home-delivered vs. clinic refills

The RR of missing ART doses in a given week among participants receiving home-delivered ART refills was 1.05 times the RR among participants refilling ART at clinics in period 2 vs. period 1, but was not statistically significant (95% CI: 0.97, 1.13) (Table 1.3). Comparing period 3 to period 2, the RR of missing ART doses in a given week among participants receiving home-delivered ART refills was 0.99 times the RR among participants refilling ART at clinics, though was also not statistically significant (95% CI: 0.91, 1.08). When lowering the adherence

cutoff from 100% to ≥85%, the results for both time period comparisons were unchanged ($DiD_{period\ 2\ vs.\ 1}$ = 1.01; 95% CI: 0.98, 1.06 and $DiD_{period\ 3\ vs.\ 2}$ = 0.98, 95% CI: 0.90, 1.06).

Relative risk of late clinic refill visits between different periods

Among participants refilling their ART at clinics, the risk of late ART refill visits during period 2 was 1.83 times (95% CI: 1.34, 2.51) the risk of late ART refill visits during period 1 (Table 1.4). The risk of late ART refill visits during period 3 was 1.71 times (95% CI: 1.43, 2.04) the risk of late ART refill visits during period 2.

Additional results are reported in Appendix A.

DISCUSSION

In this study, I was able to quantify the effect of changing COVID-19 alert levels throughout the first COVID-19 wave in South Africa on self-reported ART daily dosing among people living with HIV receiving home-delivered or clinic-based refills by segmenting the study period to correspond to the dates of COVID-19 alert level changes. I was also able to assess the impact of changing COVID-19 alert levels on occurrence of late refill visits for those refilling ART at clinics only. While I did not observe significant differences in the RR of missing ART doses for people living with HIV receiving home-delivered vs. clinic-based ART refills between the different periods of changing COVID-19 alert levels as hypothesized, I did find that self-reported ART adherence was high during all three periods regardless of the ART refill method. Further, participants in the clinic-based care group had a significantly greater risk of late ART refill visits in both time period comparisons.

While the home-delivery group of the Deliver Health Study was not affected by the COVID-19 pandemic lockdown in terms of access to ART refills, participants in the clinic-based refills group did experience disruptions to their care such as delayed clinic visits due to limited

healthcare capacity or inability to commute to clinics because of reduced public transportation services during COVID-19 restrictions. However, I did not find significant differences in self-reported daily ART dosing between people living with HIV receiving ART refills from home-delivery vs. at clinics during or between each period in our study, suggesting limited evidence of the association between method of ART access and ART adherence during COVID-19, consistent with the literature on health services access and ART adherence.[41] A potential explanation for our finding is that the study staff in the Deliver Health Study made phone calls to each participant to monitor their ART initiation and care, regardless of which study arm they were randomized to. Thus, since all participants received ART monitoring, it is a reasonable finding that there were no differences in self-reported daily dosing between people living with HIV receiving home-delivered or clinic-based ART refills. Among those enrolled in a randomized cluster trial in Cape Town testing different community health worker interventions to improve ART adherence that was interrupted by COVID-19, 70% of participants stated they missed their community health worker's support in their HIV care during COVID-19 lockdowns.[41] The Deliver Health Study staff who made phone calls to participants for each follow-up visit could be viewed as a similar function as community health workers meeting with people living with HIV regularly to promote ART adherence and retention in care.

An advantage of scaling up home-delivery of medication for people living with chronic conditions is that deliveries can be scheduled ahead of time, ensuring that clients receive their next medication refill prior to their existing refill running out. In contrast, needing to go in-person to refill one's ART supply requires taking personal time to commute to the clinic and waiting a long time to see a health care provider alongside patients with acute health conditions, among other potential barriers to care. The COVID-19 pandemic, particularly early on in 2020,

created additional barriers to accessing care at clinics with movement and capacity restrictions implemented by the government and personal fears of COVID-19 infection before vaccines were available. This was reflected in our study findings as all participants in the clinic group had at least one late refill visit across the study period. To quantify the COVID-19 pandemic's impact on health care disruptions, I examined timeliness of ART refill visits for participants in the clinic arm only and found that participants refilling their ART at clinics had a significantly greater risk of late ART refill visits during period 2 (when varying levels of lockdown measures were in place) compared to before COVID-19 alert level 5 was implemented, which is consistent with what I would have expected due to lockdown restrictions on non-urgent care and reduced clinic capacities. There was also a significantly greater risk of late clinic refill visits after the COVID-19 alert level was downgraded to level 1 (period 3) compared to during period 2. A potential explanation for this observed trend is that individuals had greater competing interests (e.g., return to work, errands) after lockdown restrictions were loosened, decreasing their availability to go to clinics for scheduled refill appointments compared to during period 2 with likely fewer competing interests. Another possible explanation is the development of concerns related to the COVID-19 pandemic that persisted even after the COVID-19 alert level was downgraded to level 1 in December 2020 and it was deemed "safe" to resume to regular activities. A study of telephone interviews with people living with HIV in KwaZulu-Natal during COVID-19 identified new concerns about picking up ART going forward, including COVID-19 infection risk, transportation availability, safety concerns, concern or knowledge that pick-up point is closed/no staff present, long queues, delay in being attending to, transportation cost, illness in self or family, and busy with work or family.[45]

In our study, self-reported daily ART dosing was high among people living with HIV before, during, and after COVID-19 lockdowns, regardless of ART refill method, but did not correlate with viral suppression. While not correlated with viral suppression in our study, medication adherence is a self-monitored task by patients which should be emphasized during HIV counseling services. In fact, a recent systematic review found that high levels of patient self-efficacy and physician-supported patient control over disease management (i.e., a joint empowerment approach) promoted greater patient empowerment and medication adherence.[46] Even though there was a significant difference in the proportion of people living with HIV who were virally suppressed at exit in home-delivery vs. clinic-based care groups in the Deliver Health Study,[38] I did not observe a significant difference based on the self-reported measure of missed ART doses. While there was likely social desirability bias in the self-reported outcome measure, this reporting bias likely occurred in both groups of participants who received home-delivered and clinic-based refills (i.e., non-differential misclassification) which would not have resulted in a biased effect estimate. With a retrospective study design, the measure of self-reported missed ART doses at each refill visit was the best variable that I could utilize as a proxy for adherence in this study. Future studies should consider using objective medication adherence measures in the design stage to minimize potential measurement bias, whether that is continued use of dried blood spots[47] or alternatives such as hair samples[48], electronic adherence monitors[49], and ingestible sensors[50].

Limitations of this study included a small sample size resulting in limited statistical power, very specific time periods corresponding to changing COVID-19 alert levels during the first COVID-19 wave in South Africa resulting in limited generalizability, and self-reported ART adherence resulting in measurement error (internal validity) concerns. Strengths of our study

included use of data from a clinical trial which previously found that there was a significant increase in the proportion of people living with HIV who were virally suppressed for those receiving home-delivered vs. clinic-based ART refills, and the unique insights drawn about the impacts of changing COVID-19 alert levels on access to medication and HIV care for people living with HIV in rural settings.

Home-delivery of ART allowed for uninterrupted access to refills during the COVID-19 pandemic when there were greater barriers to accessing in-person clinic-based care in rural South Africa. While home-delivered refills can reduce an individual's uncertainty about physically accessing ART resupply, I did not find a difference in the self-reported number of missed ART doses by method of ART refill (home-delivered vs. at clinic) when comparing between or within time periods during the first COVID-19 wave in South Africa. All participants in the clinic-based refills group had at least one delayed refill visit during the first COVID-19 wave, and were more likely to have a late clinic refill visit after the COVID-19 alert level 5 was implemented (vs. before COVID-19 lockdowns) and even after the COVID-19 alert level was downgraded to level 1 (vs. during COVID-19 alert levels 5, 4, 3, and 2). In rural South Africa, people living with HIV in standard clinic-based care experienced disruptions to ART refill access during the COVID-19 pandemic while home-delivery proved to be a reliable method of sustained ART provision. DSD approaches like home-delivered ART is promising and could address current physical access or stigma barriers faced by people living with HIV, and could potentially be bundled with the delivery of other medications with for people living with multiple chronic conditions.

TABLES & FIGURES

Table 1.1. Characteristics of people living with HIV from the Deliver Health Study by antiretroviral therapy (ART) refill method, 2019-2020

Characteristic	ART Refill Method		Total (N=155)
	Home delivery (N=81)	Clinic-based (N=74)	
	Median (IQR) or n (%)		
Age at baseline (years)	38.00 (10.00)	34.00 (10.00)	36.00 (12.00)
Gender			
Women	36 (44.4)	35 (47.3)	71 (45.8)
Men	45 (55.6)	39 (52.7)	84 (54.2)
Marital status at baseline			
Divorced or widowed	5 (6.2)	4 (5.4)	9 (5.8)
Member of an unmarried couple	30 (37.0)	32 (43.2)	62 (40.0)
Single	40 (49.4)	38 (51.4)	78 (50.3)
Married	6 (7.4)	0 (0)	6 (3.9)
Educational attainment at baseline			
Primary	16 (19.8)	24 (32.4)	40 (25.8)
Secondary	57 (70.4)	40 (54.1)	97 (62.6)
Tertiary and above	8 (9.9)	10 (13.5)	18 (11.6)
Employment status at baseline			
Employed	33 (40.7)	27 (36.5)	60 (38.7)
Unemployed	48 (59.3)	47 (63.5)	95 (61.3)
Knowledge of HIV status at baseline			
Yes, I knew my status	53 (65.4)	51 (68.9)	104 (67.1)
No, I found out today	28 (34.6)	23 (31.1)	51 (32.9)
ART use at baseline (among those who knew their HIV status, n=104)			
Yes, currently on ART	51 (96.2)	48 (94.1)	99 (95.2)
I have taken in the past but I have stopped taking them	1 (1.9)	2 (3.9)	3 (2.9)
Never taken ART	1 (1.9)	1 (2.0)	2 (1.9)
WHO clinical HIV status at baseline			
Stage 1	78 (96.3)	71 (95.9)	149 (96.1)

Characteristic	ART Refill Method		Total (N=155)
	Home delivery (N=81)	**Clinic-based (N=74)**	
	Median (IQR) or n (%)		
Stage 2	3 (3.7)	3 (4.1)	6 (3.9)
Stage 3	0 (0)	0 (0)	0 (0)
Stage 4	0 (0)	0 (0)	0 (0)
Taking other medications besides ART or TPT	5 (6.2)	3 (4.1)	8 (5.2)
Virally suppressed at study exit (<20 copies per mL)	71 (87.7)	55 (74.3)	126 (81.3)

Abbreviations: TPT = tuberculosis preventive treatment; WHO = World Health Organization.

Table 1.2. Antiretroviral therapy (ART) adherence[1] self-reported by people living with HIV at each ART refill visit during different time periods of varying COVID-19 alert levels throughout the first COVID-19 wave in South Africa, 2019–2020 (N=603 refill visits)

	Period 1: Before Implementation of COVID-19 Alert Level 5[2] October 15, 2019-March 26, 2020			**Period 2: During COVID-19 Alert Levels 5, 4, 3, and 2[3]** March 27-September 20, 2020			**Period 3: After Downgrading to COVID-19 Alert Level 1[4]** September 21-December 31, 2020		
ART Refill Method	Mean number of missed doses in past 7 days[5]	Refill visits with ≥ 1 doses missed in past 7 days reported *n (%)*	Refill visits with ≥ 2 doses missed in past 7 days reported *n (%)*	Mean number of missed doses in past 7 days[5]	Refill visits with ≥ 1 doses missed in past 7 days reported *n (%)*	Refill visits with ≥ 2 doses missed in past 7 days reported *n (%)*	Mean number of missed doses in past 7 days[5]	Refill visits with ≥ 1 doses missed in past 7 days reported *n (%)*	Refill visits with ≥ 2 doses missed in past 7 days reported *n (%)*
Home delivery	0.11	16 (9.5)	10 (5.9)	0	0 (0)	0 (0)	0.12	3 (5.2)	4 (6.9)
Clinic	0.09	9 (7.4)	8 (6.6)	0.08	1 (1.1)	0 (0)	0.18	4 (5.4)	7 (9.5)

[1]The number of missed ART doses in the past 7 days was self-reported by participants at each study follow-up visit (months 1, 3, 6, and 9).

[2]Alert level 5 was equivalent to a full lockdown during which all non-essential activities and services were restricted. The total number of ART refill visits included in period 1 was 291 across 150 participants. There were 169 visits accrued by 81 participants in the home delivery group and 122 visits accrued by 69 participants in the clinic group during period 1.

[3]The total number of ART refill visits included in period 2 was 180 across 139 participants. There were 89 visits accrued by 65 participants in the home delivery group and 91 visits accrued by 74 participants in the clinic group during period 2.

[4]The total number of ART refill visits included in period 3 was 132 across 132 participants. There were 58 visits accrued by 58 participants in the home delivery group and 74 visits accrued by 74 participants in the clinic group during period 3.

[5]The ART regimen was one daily dose. The possible range of missed doses in the past 7 days was 0 to 7.

Table 1.3. Difference-in-difference estimates of optimal medication adherence (100% and ≥85%) comparing people living with HIV receiving home-delivered vs. clinic-based antiretroviral therapy (ART) refills between time periods during the first COVID-19 wave in KwaZulu-Natal, South Africa

Time Period Comparison	Optimal ART Adherence (in the past 7 days)	Difference in Relative Risk Ratio	95% Confidence Interval[1]
Period 2[3] vs. Period 1[2]	100% adherence: 0 missed doses vs. ≥1 missed doses	1.05	0.97, 1.13
	≥85% adherence: ≤1 missed doses vs. ≥2 missed doses	1.01	0.98, 1.06
Period 3[4] vs. Period 2[3]	100% adherence: 0 missed doses vs. ≥1 missed doses	0.99	0.91, 1.08
	≥85% adherence: ≤1 missed doses vs. ≥2 missed doses	0.98	0.90, 1.06

[1]Robust standard errors were estimated using the 'sandwich' and 'lmtest' packages in R.
[2]Period 1 = Before implementation of COVID-19 alert level 5 (lockdown). The total number of ART refill visits included in period 1 was 291 across 150 participants. There were 169 visits accrued by 81 participants in the home delivery group and 122 visits accrued by 69 participants in the clinic group during period 1.
[3]Period 2 = During COVID-19 alert levels 5, 4, 3, and 2. The total number of ART refill visits included in period 2 was 180 across 139 participants. There were 89 visits accrued by 65 participants in the home delivery group and 91 visits accrued by 74 participants in the clinic group during period 2.
[4]Period 3 = After downgrading to COVID-19 alert level 1. The total number of ART refill visits included in period 3 was 132 across 132 participants. There were 58 visits accrued by 58 participants in the home delivery group and 74 visits accrued by 74 participants in the clinic group during period 3.

Table 1.4. Difference in late antiretroviral therapy (ART) refill visits between time periods during the first COVID-19 wave for people living with HIV refilling ART supply at clinics in KwaZulu-Natal, South Africa

Time Period Comparison	Relative Risk Ratio	95% Confidence Interval[1]
Period 2[3] vs. Period 1[2]	1.83	1.34, 2.51
Period 3[4] vs. Period 2[3]	1.71	1.43, 2.04

[1]Robust standard errors were estimated using the 'sandwich' and 'lmtest' packages in R.
[2]Period 1 = Before implementation of COVID-19 alert level 5 (lockdown). There were 122 visits accrued by 69 participants in the clinic group during period 1.
[3]Period 2 = During COVID-19 alert levels 5, 4, 3, and 2. There were 91 visits accrued by 74 participants in the clinic group during period 2.
[4]Period 3 = After downgrading to COVID-19 alert level 1. There were 74 visits accrued by 74 participants in the clinic group during period 3.

Chapter 2: Comparing the Environmental Costs of Home-Delivered vs. Standard Clinic-Based Antiretroviral Therapy Refills for People Living with HIV in Rural South Africa

ABSTRACT

With the increased use of home delivery and antiretroviral therapy (ART) monitoring, measuring and mitigating the change in greenhouse gas emissions by ART delivery method could support a carbon-neutral approach for community-based HIV care. Deliver Health Study (ClinicalTrials.gov Identifier: NCT04027153) participants in KwaZulu-Natal, South Africa, were randomized to receive three-month ART refills and monitoring at home or standard clinic-based care over 12 months. The study demonstrated increased viral suppression with home delivery and ART monitoring compared to clinic-based services. I estimated carbon dioxide (CO_2) emissions with quarterly refills for each ART refill method to compare their environmental impacts using incremental environmental cost-effectiveness ratio and comparative cost-effectiveness outcomes. Six- and 12-month refill scenarios were also evaluated. I used delivery log data to compute distances from participants' homes/workplaces to clinics and to generate home delivery routes. Distances were multiplied by estimated per-km CO_2 emissions of the transport mode (clinic: walking [55%], transit [42%], driving [2%], cycling [1%]; home delivery: Ford Ranger delivery vehicles [100%]) to estimate cumulative CO_2 emissions. Of 154 participants, 81 (53%) received home-ART delivery and monitoring. Average cumulative carbon emissions in the home-delivery group were 7.25 kgCO_2 per person compared to 0.70 kgCO_2 in the clinic group. The incremental carbon-cost was 47.87, 23.94, and 11.97 kgCO_2 per additional person virally suppressed through home-delivery, equivalent to driving 259, 129, and 65 extra km in the delivery vehicle for 3-, 6-,

and 12-month resupply scenarios, respectively. Compared to the clinic group, home-delivery cost an extra 7.32, 3.66, and 1.83 kgCO_2 emissions per person virally suppressed for 3-, 6-, and 12-month scenarios, respectively. In rural South Africa, incremental CO_2 emissions were higher for participants receiving home-delivered vs. clinic-based ART refills, primarily since a majority of participants walked to obtain clinic-based refills, but could be offset by 6- or 12-month refills and/or changing delivery vehicle types.

INTRODUCTION

Climate change is an ongoing global public health and environmental health emergency.[27] South Africa, an energy- and emissions-intensive middle-income developing country, has an existing energy crisis and experiences regular episodes of temporary power shutdowns,[28] and climate change is anticipated to only further exacerbate the country's energy crisis. As a signatory to the United Nations Framework Convention on Climate Change and to the Paris Agreement, South Africa is committing efforts to move towards net-zero carbon emissions by 2050.[29]

The transportation sector contributes more than 10% of South Africa's national gross emissions, having emitted more than 55 megatonnes carbon dioxide (CO_2) emissions in 2017.[30] Recent studies have compared greenhouse gas emissions of traditional in-person shopping practices with the delivery of goods to clients' homes or nearby parcel lockers located in the community, successfully identifying opportunities to incorporate greener last mile delivery (e.g., by cargo bike or on foot with hand trucks) and collection (e.g., individuals biking or walking to community locations rather than drive) strategies.[31–33] As health care delivery moves closer to clients in the community to increase the proportion of people accessing treatment, the environmental impact of decentralized care requires evaluation to identifiable modifiable factors and limit consequences for global warming.

The Deliver Health Study, a pilot randomized controlled trial conducted in 2019-2020, tested clients' willingness to pay a small fee for medication home delivery to increase coverage for decentralized ART delivery in rural South Africa for people living with HIV, increase retention in care through strengthened patient implementation intentions and commitment to care, and increase overall funds for HIV care since the small fees paid by the client could offset

costs of home delivery. In this investigation I further test the environmental cost-effectiveness of the pilot delivery program.

Specifically, I sought to estimate the difference in average cost in CO_2 emissions for each person virally suppressed between those receiving home-delivered vs. clinic-based ART refills as well as the incremental emissions and health differences from switching from one strategy to the other.

METHODS

Study design

The Deliver Health Study (U.S. NIH R21MH115770; ClinicalTrials.gov Identifier: NCT04027153), a randomized controlled trial, was conducted from October 7, 2019 – December 31, 2020 to test a fee for home delivery service for ART delivery vs. clinic-based ART refills for people living with HIV in rural communities of KwaZulu-Natal, South Africa. Deliver Health Study participants were randomized to receive either 3-month ART refills and monitoring at home or standard clinic-based care over a 6-month follow-up period, which was extended to up to 12 months due to the COVID-19 pandemic with limited in-person visits.

Ethics statement

The Human Sciences Research Council Research Ethics Committee in South Africa (REC 1/21/11/18) and the University of Washington Institutional Review Board in Seattle, Washington, U.S. approved this study (STUDY00005739). All study participants provided written informed consent per local Institutional Review Board requirements.

Study procedures

Full study procedures have been previously published.[38] Participants randomized to the home-delivery group were asked about their delivery preferences, which included their preferred

delivery location (home, work, or other location), day of the week, and time of day. These preferences were used as inputs for the delivery algorithm described in greater detail below. Participants needed to be physically present at the time of delivery for the study team to dispense the ART refill and conduct a study follow-up questionnaire. The ART was initially dispensed with 1-month supply, followed by a 2-month refill, and then 3-month refills thereafter in the home-delivery group. After enrollment, home-delivery group participants had their first home visit after 1 month, then quarterly visits, during which ART was dispensed, clinical monitoring and counselling were done, and adverse events and social harms were documented. It should be noted that while the intervention group is designated as "home delivery," participants could have opted to have the ART delivered to their workplace or another prespecified location. The reason for this delivery option is to 1) respect participants' privacy in situations in which the people whom they reside with do not know about their HIV status or they do not want their neighbors potentially finding out their status and 2) acknowledge that participants could be working long hours or spend most of their time at a location that is not their home, so they are unable to be physically present at home at the provided delivery days and times. I will use "home-delivery" group throughout this chapter to include all locations chosen by intervention group participants.

Deliver Health Study participants randomized to the standard clinic-based care group received refills at the public health clinic of their choice from 11 available options within the study region (specifically Pata, Azalea, and Dambuza communities in uMgungundlovu District, KwaZulu-Natal, South Africa). Participants in the clinic-based care group received quarterly phone calls from study staff to ascertain adverse events and social harms, and study staff went to the public health clinics to perform chart abstractions for participants in the clinic group.

At the study exit visit, HIV plasma viral load was measured and a questionnaire about their experience in accessing HIV care was administered for all participants. Participants in the home-delivery group were additionally asked about their acceptability of home ART delivery and referred to a public health clinic or DSD (e.g., the South Africa Department of Health's Central Chronic Medicines Dispensing and Distribution program) for continuation of their HIV care.

Study population and eligibility criteria

To be enrolled in the Deliver Health Study, individuals needed to be 18 years or older, test positive for HIV during study screening (if HIV status was unknown) or complete a clinic verification form (if known to be living with HIV), reside in the study community for the duration of follow-up, be eligible for ART by national guidelines (if newly diagnosed or not in care) or currently taking ART, willing to pay for the home delivery service based on a sliding fee scale, and provide informed consent for study procedures. In addition to the inclusion criteria of the Deliver Health Study, individuals included in this environmental assessment needed to have completed the study, have viral load measurements at exit, and have sufficient data to estimate their CO_2 emissions to be included in our study.

Delivery routing algorithm

A data-driven delivery algorithm was developed in collaboration with Amazon data scientists to generate optimized driving routes for home delivery of ART.[38] The algorithm optimized the order and timing of each week's home deliveries, accounting for participant delivery preferences, minimizing the total distance travelled, and prioritizing deliveries to participants who would exhaust their ART supply in the next 2-3 weeks to ensure uninterrupted access to ART refills. The algorithm was written in MATLAB R2019a and used the Distance Matrix API from

Google. The output of the algorithm was a GPS Exchange Format (GPX) file containing waypoints and routes disseminated on a weekly basis which the delivery team used on Google Maps.

Estimating carbon dioxide emissions for the clinic-based refills group

For the clinic group, since I did not have recorded GPS routes to and from every ART refill visit for each participant, I mapped the roundtrip distance between their provided home, work, or other location to the public health clinic they visited using the exact home/work and clinic coordinates in Google Maps. Ascribed distances from participant home or work location to clinic (in km) were multiplied by the estimated average emissions of the transport method listed for the refill visit (in kg of CO_2 per km [$kgCO_2/km$]) to obtain the $kgCO_2$ emissions per visit.[51] For those who took public transit (a minibus) to their refill visit, the estimated emissions were divided by 10 to account for the South Africa COVID-19 protocol which allowed 15-seater minibus vehicles to take a maximum of 10 passengers.[52] Then, the $kgCO_2$ emissions for month 1, 3, 6, and 12 visits were summed up to obtain the per person cumulative CO_2 emissions. I assumed that all participants commuted from their homes or workplaces to clinics for their refill visits, ignoring any stops that they could have made in between or the possibility that their start point for a given refill visit was not their provided home, work, or other locations.

In terms of missing data, I opted to do a complete case analysis: for each participant, only their follow-up visit records with the clinic name and transport method used for their ART refill visit were included as part of calculating their total distance travelled and estimating total CO_2 emissions over the study period.

Sensitivity analysis

I conducted sensitivity analyses to compare estimated participant-level cumulative CO_2 emissions with imputed clinic and transportation mode information. If a participant in the clinic-

based care group was missing the clinic name in any of their ART refill visit records, then I imputed the missing field with the named clinic on their last visit record (or next visit record if they were missing the clinic name for their month 1 follow-up visit). This imputation strategy was based on an assumption that the participants in the clinic-based care group consistently went to the same public health clinic located in the study community to seek care and obtain refills. Similarly, if participants in the clinic group were missing the mode of transportation on any of their ART refill visit records, then I imputed that missing field with the transportation mode indicated on their last (or next, as explained above) ART refill visit, and compared the estimated cumulative CO_2 emissions to if I did not impute this information (i.e., complete case analysis).

Estimating carbon dioxide emissions for the home delivery group

For the home delivery group, the total km driven over the entire delivery day was multiplied by 0.185 $kgCO_2/km$, the estimated CO_2 emissions of the study delivery vehicles (2016 Ford Ranger 2.2L Diesel Double Cab 4x4) to obtain the total $kgCO_2$ emissions (Table 2.1). Then, the total $kgCO_2$ emissions was divided by the number of home delivery stops made on that delivery trip to yield the per person cumulative CO_2 emissions.

Incremental cost-effectiveness ratio

In order to determine the incremental cost-effectiveness (with 'cost' referring to CO_2 emissions or carbon costs) of shifting from quarterly clinic-based ART refills to quarterly home-delivered refills for people living with HIV over a 12-month period, I calculated an incremental cost-effectiveness ratio (ICER). The ICER was calculated as the change in CO_2 emissions divided by the change in the number of people virally suppressed. For equations and sample calculations, please see Appendix B.

Sensitivity analysis

As a sensitivity analysis, I modelled the ICER for offering 6-month refills of ART (equivalent to two ART refills visit per person over 12 months) and offering 12-month refills of ART (equivalent to one ART refill visit per person over 12 months), assuming no difference in viral suppression from quarterly (3-month) deliveries.

Comparative cost-effectiveness

I additionally estimated the comparative cost-effectiveness (CCE), or the difference in carbon cost per virally suppressed person, in order to identify which ART refill method (home-delivery or clinic) was more cost-effective (in terms of CO_2 emissions) on average than the other. I also modelled the CCE for 6- and 12-month resupply scenarios, just as described above for the ICER sensitivity analysis. Please refer to Appendix B for the CCE equation and sample calculations.

RESULTS

Descriptive statistics and average CO_2 emissions calculations

After excluding 7 participants lost to follow-up (6 of whom were in the clinic-based care group) and one participant with insufficient data for estimating CO_2 emissions, our study sample consisted of 154 participants. Of 154 participants, 83 (54%) were men, the mean age was 37 years, and 95 (62%) were not employed at baseline (Table 2.2). Of those who knew their HIV status at baseline (n=104), most (95%) participants self-reported currently taking ART and 10 participants (10%) had taken a break from taking ART at some point in the past. Reasons for discontinued ART use included long clinic waiting times and clinics being located too far away. Eighty-one (53%) participants were assigned to home-ART delivery and monitoring, and the proportion of participants in the home delivery group who were virally suppressed at exit was

significantly greater than the proportion in the clinic group (88% vs. 74%, respectively; p-value = 0.04975).

The 154 participants accrued a total of 603 ART refill visits over the study period. After excluding 85 refill visits with missing CO_2 emissions data due to missing either clinic name (and therefore clinic location), mode of transport used to attend the refill visit, or home location (coordinates), there were 518 observed refill visits included (316 refill visits for the home delivery group and 202 refill visits in the clinic-based care group) in the calculations for estimating CO_2 emissions. All 85 refill visits with missing CO_2 emissions data were from participants in the clinic-based care group. Of the 85 visits excluded from the complete case analysis, 79 were missing both the clinic name and transport mode, two were missing the clinic name only, one was missing the transport mode only, and three visits were missing home coordinates. After imputing missing clinic names based on the information provided for the follow-up visit prior, there were a total of 523 refill visits across 154 participants. After imputing missing clinic names and transport mode based on the information provided for the follow-up visit prior, 82 visits were recovered and there was a total of 600 refill visits across 154 participants. One participant was missing home coordinates for all their refill visits in addition to the clinic name and transport mode for each visit, so the distance travelled could not be computed and all three of their refill visits were excluded.

The overall average CO_2 emissions across all 521 ART refill visits was 1.23 kg (standard deviation [SD] = 2.90), and overall average cumulative CO_2 emissions per participant over study follow-up was 4.14 kg (SD = 6.81) (Table 2.3).

Of 202 total ART refill visits in the clinic group, walking was the most common (n=112; 55%) mode of transportation to clinics, followed by minibus (n=85; 42%), then driving (n=4;

2%). One participant reported commuting via bicycle to one of their refill visits. Across all transportation methods, the average roundtrip distance travelled to clinics for a refill visit was 18.06 km (SD = 31.61). The average roundtrip distance travelled among those who walked to their visits was 20.17 km (SD = 35.31). After imputing clinic names, the average roundtrip distance travelled to clinics for a refill visit across all transportation methods was 18.68 km (SD = 33.11). After imputing both clinic names and transport mode, the average roundtrip distance travelled to clinics for a refill visit across all transportation methods was 19.27 km (SD = 33.70). The average CO_2 emissions in the clinic-based group across all 205 refill visits was 0.25 kgCO_2 (SD = 0.67), and average cumulative CO_2 emissions per participant over the duration of study follow-up was 0.70 kgCO_2 (SD = 1.09) (Table 2.3). The average cumulative CO_2 emissions per participant over the duration of study follow-up increased to 0.72 kgCO_2 with imputed clinic names and to 0.89 kgCO_2 with imputed clinic names and transport mode.

There were 91 total home delivery trips made in the study, each of which involved multiple ART deliveries at an average of four refill deliveries made to participants and an average of 35.10 km driven total per trip. The average distance driven per refill delivered was 12.00 km (SD = 23.68). Of 316 total ART refill visits in the home delivery group, the average CO_2 emissions per refill visit via home delivery was 1.86 kgCO_2 (SD = 3.53), and average cumulative CO_2 emissions per participant across the study duration was 7.25 kgCO_2 (SD = 8.19).

Incremental cost-effectiveness ratio

The incremental carbon cost between the home-delivery and clinic-based refills group was $(7.25\ \text{kgCO}_2 - 0.70\ \text{kgCO}_2) = 6.55\ \text{kgCO}_2$. The incremental viral suppression effect between the home-delivery and clinic-based refills group was $\left(\frac{71\ \text{virally suppressed persons}}{81\ \text{persons in home delivery group}} - \frac{54\ \text{virally suppressed persons}}{73\ \text{persons in clinic group}}\right) = 0.1368$. Thus, the incremental carbon-cost was 47.87 kgCO_2 per

additional person virally suppressed through home delivery over 12 months, equivalent to driving 259 extra km in the delivery vehicle (Table 2.4).

With imputed clinic names only, the incremental carbon cost between the home-delivery and clinic-based refills group was 6.53 kgCO_2, changing the incremental carbon-cost from 47.87 to 47.73 kg of CO_2 per additional person virally suppressed through home delivery, equivalent to driving 258 extra km in the delivery vehicle. With imputed clinic names as well as transport mode, the incremental carbon cost between the home-delivery and clinic-based refills group was 6.36 kgCO_2, reducing the incremental carbon-cost to 46.49 kg of CO_2 per additional person virally suppressed through home delivery, equivalent to driving 251 extra km in the delivery vehicle.

Modelling 6- and 12-month refill scenarios

If 6- or 12-month refills were provided instead, and assuming the same viral suppression results for 6- or 12-month refills as with quarterly delivery, incremental emissions for home-delivered ART could be 23.94 and 11.97 kgCO_2, equivalent to 129 and 65 km driven, respectively (Table 2.4). With imputed clinic names only, the incremental emissions for home-delivered ART could be 23.86 and 11.93 kg of CO_2, equivalent to 129 and 64 km driven, respectively. With imputed clinic names as well as transport mode, incremental emissions for home-delivered ART could be 23.24 and 11.62 kg of CO_2, equivalent to 126 and 63 km driven, respectively.

Comparative cost-effectiveness

The cost per virally suppressed person living with HIV receiving home-delivered ART refills was $\left(\frac{7.25\ \text{kgCO}_2 * 81\ \text{persons in home delivery group}}{71\ \text{virally suppressed persons}}\right) = 8.27\ \text{kgCO}_2$ per person virally suppressed. The cost per virally suppressed person living with HIV receiving clinic-based ART

refills was $\left(\frac{0.70\ \text{kgCO}_2 * 73\ \text{persons in clinic group}}{54\ \text{virally suppressed persons}}\right) = 0.95\ \text{kgCO}_2$ per person virally suppressed. Compared to the clinic group, home delivery cost an extra 7.32 $kgCO_2$ emissions on average per person virally suppressed for quarterly (3-month) ART refills (Table 2.4).

With imputed clinic names, the cost per virally suppressed person living with HIV receiving clinic-based ART refills was 0.97 $kgCO_2$ per person virally suppressed, meaning home delivery cost an estimated extra 7.30 kg of CO_2 emissions on average per person virally suppressed compared to the clinic group. After imputing both clinic names and transport mode, the cost per virally suppressed person living with HIV receiving clinic-based ART refills was 1.20 $kgCO_2$ per person virally suppressed, computing to an estimated extra 7.07 $kgCO_2$ emissions per person virally suppressed through home delivery compared to clinic refills.

Modelling 6- and 12-month refill scenarios

For 6- and 12-month resupply scenarios, home-delivery of ART cost an extra 3.66 and 1.83 $kgCO_2$ emissions per person virally suppressed, respectively, compared to clinic-based refills in the complete case analysis. Compared to clinic-based refills, home delivery cost an extra 3.65 and 3.53 $kgCO_2$ per person virally suppressed if 6-month refills were dispensed instead with imputed clinic names only and imputed clinic names and transport mode, respectively. If 12-month refills were dispensed, home delivery would cost an extra 1.82 and 1.77 $kgCO_2$ per person virally suppressed compared to clinic-based refills with imputed clinic names only and imputed clinic names and transport mode, respectively. A summary table of all modelled scenarios and sensitivity analyses is contained in Appendix B, Supplemental Table 2.1.

DISCUSSION

In this study, I found that refilling ART at clinics was more cost-effective than home-delivered ART refills in terms of carbon costs (CO_2 emissions) for adults living with HIV in rural

South Africa by both ICER and CCE metrics, primarily due to the fact that the majority of participants walked to obtain clinic-based refills. While our finding is unexpected and in tension with our prior findings of increased viral suppression rates of home-delivered vs. clinic-based ART refills for people living with HIV, the results are not entirely surprising when considering the local cultural context. Further, by applying health economic and logistics optimization concepts outside of their traditional scopes, I demonstrated one way in which climate change impacts can be quantified and integrated in the evaluation of public health interventions, including in clinical trials.

On average, participants in the home-delivered ART refill group contributed greater cumulative CO_2 emissions than those in the clinic-based refills group (7.25 kg and 0.70 kg, respectively). This was true when comparing average CO_2 emissions per refill visit as well. This difference is primarily attributable to participants in the clinic-based refills group walking to their refill visits the majority of the time, and thereby contributing zero CO_2 emissions, despite needing to walk an average of 20.17 km roundtrip. In the Pata, Azalea, and Dambuza communities of uMgungundlovu District, transit options are limited to minibus taxis, which are 15-seater vans that do not subscribe to a regimented pick-up and drop-off schedule. Thus, uncertainty around the timeliness of minibuses or the fact that most South African households in the lowest income quintile spend more than 20% of their monthly income on public transport[53] could be reasons why individuals tended to walk to their destination. A 2021 report by Statistics South Africa on the National Household Travel Survey in South Africa found that South Africans indeed take most of their trips by foot.[54] In terms of the distance commuted, on average participants in the clinic group lived 18.06 km to their closest public health clinic, in comparison to the average 35.10 km driven per home delivery trip and average 12.00 km driven per refill

delivered. While multiple ART refill deliveries were made per home delivery trip, the starting point for each home delivery trip was the Human Sciences Research Council office in Sweetwaters, KwaZulu-Natal, South Africa. Further, opting to do a complete case analysis likely underestimated the CO_2 emissions that the participants in the clinic group contributed, inflating the difference in emissions that I observed between the home-delivery and clinic groups. To reconcile the potential underestimation concerns from complete case analysis and to recover the excluded refill visits from participants in the clinic-based care group, I imputed the missing information and conducted a sensitivity analysis. The results from both imputing clinic name alone and from imputing both clinic name and transport mode were similar to that of the complete case analysis.

Estimates in the literature of the average CO_2 emissions contributed per person by transportation method taken are limited. A 2013 study that asked participants to recall their travel in the past week estimated the average CO_2 emissions per person in the United Kingdom to be 35.1 $kgCO_2$ weekly or 1.6 tonnes CO_2 (tCO_2) annually,[51] while Climate Watch estimated the annual per capita emissions to be 7.3 tCO_2 in 2013 and 4.8 tCO_2 in 2020.[55] In comparison, Climate Watch estimated the annual per capita emissions in South Africa to be 8.3 tCO_2 in 2013 and 6.7 tCO_2 in 2020, roughly equivalent to 177 $kgCO_2$ weekly and 143 $kgCO_2$ weekly.[55] Thus, our ICER estimate of 47.87 $kgCO_2$ per additional person virally suppressed through quarterly home-delivered ART refills and CCE estimate of 7.32 $kgCO_2$ over 12 months are reasonable in terms of per capita CO_2 emissions estimates for South Africa. Home-delivered ART may be worth scaling up when coupling our study findings with the positive intervention effectiveness for higher proportion of virally suppressed persons and high client acceptability of the service.[38]

Similar to other chronic conditions, there is no cure yet available for HIV, but it is a condition that can be managed with ART. People living with HIV require access to ART across their lifetime to maintain viral suppression and sustaining engagement in care remains a challenge.[56,57] Offering different ART resupply options is one way to shift the focus to patient-centered care for people living with HIV. Home-delivered ART can remove the physical access barrier of commuting to clinics or another community-based venue for people living with HIV, especially if the reason for not wanting to go to clinics is a long commute, long waiting times, negative experiences with facility staff, or fear of being recognized by someone in their community and unintentionally disclosing their HIV status. A complementary strategy for increasing engagement in HIV care is by increasing the ART supply dispensed at each refill visit, reducing the possibility of missed ART doses due to refill challenges. Multi-month dispensing of ART has been shown to be effective for clinically-stable people living with HIV in other contexts.[58,59] I modelled 6- and 12-month scenarios in our study, showing that reducing the refill frequency (i.e., increasing the supply dispensed at each visit) would reduce the incremental CO_2 emissions per person virally suppressed between home-delivered and clinic-based ART refills and the CCE. Offering multi-month ART supply has the potential to reduce CO_2 emissions and barriers to care, ultimately increasing engagement in HIV care.

Limitations of our study include a relatively small sample size, differential missing data, and a conservative assumption that all participants commuted from their homes or workplaces to clinics for their refill visits. The Deliver Health Study was a pilot study to test acceptability and feasibility of home-delivered ART in KwaZulu-Natal, the findings of which informed an ongoing clinical trial, the sequential multiple assignment randomized controlled trial of scalable interventions for ART delivery (the SMART ART Study) (ClinicalTrials.gov Identifier:

NCT05090150).[60] In the ongoing SMART ART Study, the team is also quantifying the environmental health impacts of home-delivered ART vs. clinic-based ART refills for people living with HIV in rural South Africa. Having developed a method to estimate carbon costs in a clinical trial in this study, the team will have the ability to apply this method to the SMART ART Study with a larger sample size after trial completion. While missing data can never fully be recovered, I attempted to address it by conducting sensitivity analyses and did not find major differences in our results. It was an important feature of the Deliver Health Study to mimic real-world conditions as much as possible since it tested out a new public health intervention. Therefore, collecting detailed information for each participant about any stops they made en route to their clinic ART refill visit was not feasible. Thus, I ignored any stops that participants in the clinic group could have made in between and the possibility that their start point was not their provided home or work locations, both of which likely resulted in underestimations of the total distance travelled and the CO_2 emissions contributed. Further, there is uncertainty around whether the proportion of those virally suppressed would remain the same when modelling 6- and 12-month refill scenarios. Lastly, our calculations for modelling 6- and 12-month refill scenarios abstract from any delivery route re-optimization for less frequent deliveries, which could contribute either more or less miles driven altogether. Amazon has been building their capacity for delivery to rural areas in South Africa and supported the Deliver Health Study in adapting their vehicle routing algorithms[61–63] to determine the placement and driving routes of mobile vans for home delivery of ART refills in rural South African communities. Beyond its traditional uses in the private sector, routing science-guided delivery has the potential to increase efficiency and coverage of ART resupply and monitoring, reduce logistics barriers for clients, and improve the cost efficiency to the health system. A major strength of our study is the creation

of a novel approach to incorporate environmental costing into a clinical trial, striving to identify strategies in which both climate change adaptation efforts and improving access to care for people living with HIV in rural, high prevalence settings can be addressed.

In rural South Africa, incremental CO_2 emissions were higher for participants receiving home-delivered vs. clinic-based ART refills but could be offset by 6- or 12-month refills (and reducing delivery frequency) and/or switching to electric delivery vehicles, decreasing the impact on the environment. The environmental costing methods developed in this study can be applied to analyzing the data currently being collected in the SMART ART Study and potentially other studies interested in estimating the environmental impact of a public health intervention. Further, a traditional cost-effectiveness analysis of home-delivered vs. clinic-based ART refills for people living with HIV in rural South Africa would also be informative in weighing the findings of this environmental-effectiveness finding. Beyond the scope of our study, if carbon costs were to become quantified in either health effects (e.g., disability-adjusted life years) or in monetary terms (e.g., cost of lost productivity), then they could theoretically be included in a cost-effectiveness analysis from the societal perspective in any health economic study.

TABLES & FIGURES

Table 2.1. Estimated carbon dioxide (CO_2) emissions by transport method to antiretroviral therapy (ART) refill visits

ART Refill Method	Transport Method	Estimated CO_2 Emissions ($kgCO_2/km$)
Home delivery	Delivery vehicle (2016 Ford Ranger 2.2L Diesel Double Cab 4x4)	0.185[a,64]
Clinic-based	Walking	0
	Bicycling	0
	Driving (personal vehicle)	0.148 [65]
	Public Transit/Taxi (Toyota Quantum Sesfikile bus)	0.339[b,66]

[a]For each home delivery trip, the total estimated $kgCO_2$ emissions was divided by the number of home delivery stops made to yield the per person cumulative CO_2 emissions.
[b]For participants who took public transit/taxis (i.e., minibuses), their CO_2 emissions were divided by 10 to account for the shared transit method. The COVID-19 protocol in South Africa allowed 15-seater minibuses, the standard minibus vehicle, to take a maximum of 10 passengers.[52]

Table 2.2. Sociodemographic characteristics of people living with HIV by study arm (N=154)

Characteristic	ART Refill Method		Total (N=154)
	Home delivery (N=81)	Clinic-based (N=73)	
	Mean (SD) or n (%)		
Age (years)	38.8 (9.28)	35.6 (8.51)	37.3 (9.04)
Gender			
Women	36 (44.4)	35 (47.9)	71 (46.1)
Men	45 (55.6)	38 (52.1)	83 (53.9)
Relationship status			
Single	40 (49.4)	38 (52.1)	78 (50.6)
Member of an unmarried couple	30 (37.0)	31 (42.5)	61 (39.6)
Married	6 (7.4)	0 (0)	6 (3.9)
Divorced or widowed	5 (6.2)	4 (5.5)	9 (5.8)
Education			
Primary	16 (19.8)	23 (31.5)	39 (25.3)
Secondary	57 (70.4)	40 (54.8)	97 (63.0)
Tertiary and above	8 (9.9)	10 (13.7)	18 (11.7)
Employment status			
Employed	33 (40.7)	26 (35.6)	59 (38.3)
Not Employed	48 (59.3)	47 (64.4)	95 (61.7)
Baseline knowledge of HIV status			
Individuals known to be living with HIV	53 (65.4)	51 (69.9)	104 (67.5)
Individuals newly identified as living with HIV	28 (34.6)	22 (30.1)	50 (32.5)
Baseline ART use (among individuals known to be living with HIV; n=104)			
Currently on ART	51 (96.2)	48 (94.1)	99 (95.2)
Taken ART in the past and stopped	1 (1.9)	2 (3.9)	3 (2.9)
Never taken ART	1 (1.9)	1 (2.0)	2 (1.9)
Ever took a break from taking ART that was longer than one month (among individuals known to be living with HIV; n=104)			
Yes	6 (11.3)	4 (7.8)	10 (9.6)
No	44 (83.0)	44 (86.3)	88 (84.6)

Characteristic	ART Refill Method		Total (N=154)
	Home delivery (N=81)	Clinic-based (N=73)	
	Mean (SD) or n (%)		
Refused	1 (1.9)	0 (0)	1 (1.0)
Missing	2 (3.8)	3 (5.9)	5 (4.8)
Viral suppression status at month 12 endline			
Virally suppressed (<20 copies per mL)	71 (87.7)	54 (74.0)	125 (81.2)
Not virally suppressed (≥20 copies per mL)	10 (12.3)	19 (26.0)	29 (18.8)

Abbreviations: ART = antiretroviral therapy, HIV = Human Immunodeficiency Virus, SD = standard deviation.

Table 2.3. Overall average distance travelled and CO_2 emissions by ART refill group

	Home delivery (n=316)	**Clinic-based (n=202)**	**Overall (N=518)**
		Mean (SD)	
Average total distance travelled (km) per participant	12.00 (23.68)	18.06 (31.61)	13.17 (25.02)
Average $kgCO_2$ emissions across all ART refills	1.86 (3.53)	0.25 (0.67)	1.23 (2.90)
Average cumulative $kgCO_2$ emissions per participant over study period	7.25 (8.19)	0.70 (1.09)	4.14 (6.81)

Abbreviations: ART = antiretroviral therapy, SD = standard deviation.

Table 2.4. Home delivery vs. clinic-based care incremental cost-effectiveness ratio (ICER) and comparative cost-effectiveness (CCE) results for 3-, 6-, and 12-month antiretroviral therapy (ART) resupply scenarios, under complete case analysis

Outcome Measure	**ART Resupply Scenario**		
	3-month	6-month	12-month
ICER $kgCO_2$ per additional person virally suppressed through home delivery vs. clinic-based care	47.87	23.94	11.97
ICER converted to extra distance driven km	259	129	65
CCE $kgCO_2$ extra emissions per additional person virally suppressed through home delivery vs. clinic-based care	7.32	3.66	1.83

Chapter 3: Costs of home-delivered antiretroviral therapy refills for persons living with HIV: evidence from a pilot randomized controlled trial in KwaZulu-Natal, South Africa

ABSTRACT

Antiretroviral therapy (ART) is needed across the lifetime to maintain viral suppression for people living with HIV. In South Africa, obstacles to reliable access to ART persist and are magnified in rural areas, where HIV services are also typically costlier to deliver. A recent pilot randomized study (the Deliver Health Study) found that home-delivered ART refills, provided at a low user fee, effectively overcame logistical barriers to access and improved clinical outcomes in rural South Africa. In the present costing study using the payer perspective, we conducted retrospective activity-based micro-costing of home-delivered ART within the Deliver Health Study and when provided at-scale (in a rural setting), and compared to facility-based costs using provincial expenditure data (covering both rural and urban settings). Within the context of the pilot Deliver Health Study which had an average of three deliveries per day for three days a week, home-delivered ART cost (in 2022 USD) $794 in the first year and $714 for subsequent years per client after subtracting client fees, compared with $167 per client in provincial clinic-based care. We estimated that home-delivered ART can reasonably be scaled up to 12 home deliveries per day for five days per week in the rural setting. When delivered at scale, home-delivered ART cost $267 in the first year and $183 for subsequent years per client. Average costs of home delivery further decreased when increasing the duration of refills from three-months to six- and 12-month scripts (from $183 to $177 and $135 per client, respectively). Personnel costs were the largest cost for home-delivered refills while ART drug costs were the largest cost of

clinic-based refills. When provided at scale, home-delivered ART in a rural setting not only offers clinical benefits for a hard-to-reach population but is also comparable in cost to the provincial standard of care.

INTRODUCTION

Until a cure for HIV is available, reliable access to antiretroviral therapy (ART) is needed across the lifetime to maintain viral suppression. South Africa has one of the highest burdens of HIV worldwide with an HIV prevalence of 16% among adults aged 15 and older and a total of 7.8 million people with HIV who require lifetime ART.[6] In the past two decades, the South African government has invested heavily in their HIV programme, and has made great progress towards achieving the UNAIDS 95-95-95 treatment targets: as of 2022, 90% of South African adults with HIV knew their status, 91% of adults who knew their status were on ART, and 94% of people on ART were virally suppressed.[6] However, the status of HIV control varies considerably across the nation, with KwaZulu-Natal province continuing to have the highest HIV prevalence in the country (22%)[6] and rural farming communities reporting higher HIV prevalence than urban areas (18% vs. 13%).[7] Access to HIV care is further constrained by slowing government funding which has not matched the level of demand,[12] particularly in rural areas where the cost of successfully treating HIV is higher due to logistical barriers, supply chain considerations, and staffing challenges.[67] In light of these rural/urban disparities in HIV outcomes and costs, novel and low-cost strategies to address gaps in HIV care in rural South Africa are critically needed.

A number of strategies have been proposed to improve HIV outcomes and reduce the burden of care associated with one to three-month ART refill visits for both clients and health systems.[9] In particular, the World Health Organization now recommends DSD for HIV care, which involves tailoring programs to accommodate client needs to improve HIV treatment outcomes and reduce health system burden.[68] Various client-centered DSD mechanisms are being proposed to increase viral suppression by overcoming barriers to accessing HIV care including long wait times at clinics, transportation barriers, and social stigma.[14–16] As a result, alternative ART dispensing

mechanisms which reduce clinic burden including home delivery of medications are being explored and have had demonstrated feasibility and success in improving client adherence in South Africa.[9,19,24,69]

The recent Deliver Health Study found that home-delivered ART and monitoring for a small user fee increased viral suppression by 21% compared to standard facility-based care among 162 participants in rural KwaZulu-Natal[21]; however, the costs of this program have not previously been quantified. The objective of the present study was to estimate the cost of home-delivered ART for adults living with HIV in rural South Africa (1) within the context of the pilot study and (2) when provided at-scale, compared to standard clinic-based ART resupply. A secondary objective was to identify cost drivers for each mode of ART delivery. In a sensitivity analysis, I also estimated cost savings when home-delivered ART used multi-month refill scripts. This study aims to inform the South African National Department of Health's (NDoH) strategy to improve HIV treatment outcomes and reduce health system burden in rural South Africa.

METHODS

Deliver Health Study

The Deliver Health Study (United States NIH R21MH115770; ClinicalTrials.gov Identifier: NCT04027153) was a pilot randomized trial of home ART delivery, monitoring, and ART resupply conducted in three rural and peri-urban communities in uMgungundlovu District, KwaZulu-Natal from October 2019 to December 2020. The detailed study procedures have been previously published,[38] and are also summarized in the Supplemental Figure 3.1 flow map in Appendix C. Briefly, 162 ART-eligible[70] adults aged 18 or over with HIV were identified through home and mobile van HIV testing and counselling and at HIV clinics. Following the enrollment and ART initiation visit, clients were randomized to receive either home delivery of HIV care

which was provided for a small user fee of 30–90 South African Rand (ZAR) (2–7 United States Dollars [USD]), or standard clinic-based ART follow-up care at a health center of choice within the study catchment area. Home delivery of HIV care was provided leveraging an optimized delivery algorithm to reduce travel times and associated costs, described further in Appendix C. For the home delivery arm of the pilot study, study staff made deliveries three days per week, spent an average of 26 minutes per home delivery of ART (including transportation time), and made an average of three deliveries a day. Home delivery was at first implemented by a team of three (nurse, driver, data collector), but staffing was later reduced to just the nurse due to pandemic social distancing restrictions (Appendix C). All Deliver Health Study participants received the TDF/FTC/EFV ART regimen for the treatment of HIV.

Ethical approval was granted by the review committees at the Human Sciences Research Council in South Africa and the University of Washington.

Study population

Deliver Health Study participant demographics

A total of 155 adults living with HIV completed follow-up in the Deliver Health Study, 81 (52%) of whom received home-delivered ART refills and monitoring and 74 (48%) of whom received clinic-based care. The median age of participants was 38 years (interquartile range: 12), and 72 (47%) were women. Seventy-one (88%) people living with HIV in the home-delivery group were virally suppressed at study exit compared to 55 (74%) people living with HIV in the clinic-based care group. The average monthly salary of participants randomized to the home delivery group, self-reported at baseline, was 1376 ZAR (108 USD) per individual with a standard deviation of 2247 ZAR (176 USD).

Study setting

KwaZulu-Natal was the province in South Africa with the highest estimated HIV prevalence of 22% among adults aged 15 years and older in 2022,[6] totaling approximately 1.9 million adults.[71] An estimated 52% of the population in KwaZulu-Natal resided in rural areas,[72] and rural districts of KwaZulu-Natal had the highest estimated HIV prevalence in South Africa of greater than 28%.[73] At the end of 2022, 31% of 15-64 year olds residing in KwaZulu-Natal were unemployed[74] and the average monthly earnings of employees in the formal non-agricultural sector was 26,032 ZAR across South Africa.[75]

Cost estimation

Our primary analysis compared the cost of quarterly home delivery of ART (the pilot Deliver Health Study intervention) with the Standard of Care (SOC), i.e., clinic-based care with three-month refill scripts, in KwaZulu-Natal province. Due to limited capacity for costing during the trial (which was conducted during the COVID-19 pandemic), costs were collected retrospectively, and the home-delivery and SOC costs relied on different data sources representing different regions of KwaZulu-Natal, described further below. All costs were estimated from the payer perspective to inform the South African NDoH's financial planning and strategy. To quantify resource use,[76] I first outlined program activities in a detailed Narrative Summary for the Deliver Health Study (Appendix C) which further informed our assumptions regarding programmatic implementation (Appendix C). Our primary outcomes of interest were:

1) <u>Average annual cost per client</u>: the average annual cost per person living with HIV in the Deliver Health Study or in KwaZulu-Natal
2) <u>Average annual cost per client virally suppressed</u>: the average annual cost per person living with HIV who was virally suppressed in the Deliver Health Study or in KwaZulu-Natal.

In our secondary objective, costs for each mode of service delivery were disaggregated by cost categories (personnel, vehicles and fuel, drugs, etc.) to understand the main cost drivers (detailed methods in Appendix C).

Costs were reported in 2022 USD. For costs originally reported in ZAR, I used the World Bank GDP implicit deflator for South Africa[77] and the average ZAR-to-USD exchange rate in 2022.[78] I deflated costs reported in USD using the US annual average Consumer Price Index.[79] Capital items and other costs with a useful life of more than one year were discounted 3%. Full details of these adjustments are provided in Appendix C.

Costing of home delivery of ART and monitoring

For home-delivered refills, I conducted activity-based micro-costing for home-delivered ART and monitoring in the Deliver Health Study in rural uMgungundlovu District of KwaZulu-Natal. I excluded costs for research-specific procedures (e.g., data collection, research-related personnel costs). Personnel salaries were obtained from the Deliver Health Study and South Africa Department of Public Service and Administration.[80] To estimate personnel time, vehicle costs, and fuel, I used recorded travel logs for the home delivery trips. I assumed the home-delivery intervention was delivered by a team of a nurse, a driver, and a community outreach worker. Full cost assumptions including staff time and vehicle costs are detailed in Appendix C.

Costing of clinic-based ART refills and care

To estimate costs for clinic-based care, I used provincial government expenditure data for the full province of KwaZulu-Natal and scaled it to ART-specific care. I obtained actual HIV/AIDS spending (i.e., the rectified budget) for financial years 2019 and 2020 from the South African National Treasury.[81] I then estimated the proportion of the HIV program budget used for ART using a 2020 government HIV/AIDS spending report[11] and applied this proportion to the total 12-month

HIV program budget. Full details for these calculations are in Appendix C. Of note, clinic expenditure data covered both rural as well as urban areas in KwaZulu-Natal (e.g., the major cities of Durban and Newcastle), where ART costs may be lower than in rural regions.[67]

Scenarios

For the home-delivered ART intervention, I modelled two sets of scenarios over a 12-month time horizon: programmatic and at-scale. Our baseline estimation assumed three-month (quarterly) refills; in a sensitivity analysis I also estimated the costs of home delivery for six- and 12-month ART refill scripts starting after the first quarter. Costs of home-delivered ART for all scenarios were compared to the SOC, i.e., clinic-based care with three-month ART refill scripts. Full details of the estimation for all scenarios are in Appendix C.

Programmatic cost estimation

The primary cost was the programmatic scenario for home-delivered ART, which I estimated to reflect the resource requirements if home-delivered ART were implemented by the South African NDoH. Accordingly, I substituted staff salaries paid under the Deliver Health Study with corresponding salaries reported by the South African government.[80] The programmatic scenario assumed that ART was delivered by a team of two (nurse and driver) who spent approximately 3.5 hours a day for 3 days a week making home deliveries to support 81 clients in the Deliver Health Study, and that the program was also supported by a community outreach worker and other operational staff (Appendix C). In a sensitivity analysis, I also estimated a second programmatic "as-observed" scenario using staff salaries from within the Deliver Health Study.

At-scale cost estimation

Given the low client volume within the pilot Deliver Health Study, I estimated a scenario where home delivery of ART was scaled up to accommodate a larger client volume. Granted that

within the Deliver Health Study, the maximum number of deliveries made in a given day was 16 visits and the average time per visit was 26 minutes (including driving), I estimated that the same team could reasonably make 12 home deliveries a day for five days per week, spending approximately six hours of their working day making home deliveries to clients and about two hours to load and unload the delivery vehicle at the central office. This estimation assumed a 40-hour work week and 214 workdays a year (excluding weekends, holidays, and other leave). In addition, I assumed an ART initiation visit (which includes HIV counselling) would take three times as long as an ART refill visit, which was qualitatively informed by time-and-motion observations conducted during January–February 2023 for an ongoing follow-up trial to the Deliver Health Study (Appendix C).

RESULTS

Programmatic scenarios

For the 81 clients receiving home-delivered ART in the Deliver Health Study, cost of home delivery was substantially higher than provincial estimates for annual per-client facility-based ART costs. Specifically, I estimated that in the context of the pilot study the average annual cost per client receiving home-delivered ART refills was $794 per client and $907 per client virally suppressed in the first year of intervention and $714 per client and $815 per client virally suppressed for subsequent years, after subtracting paid client fees (Tables 3.1 and 3.2). In comparison, the SOC was estimated to cost an average of $167 annually per client and $254 per client virally suppressed. “As-observed” costs for home-delivered ART in the Deliver Health Study were somewhat higher the primary programmatic scenario due to differences in assumptions around staff salaries ($819 per client and $935 per client virally suppressed for quarterly refills in

the first year of intervention). Multi-month scripting scenarios (with six- and 12-monthly refills) further reduced the cost of home-delivered ART, as shown in Table 3.2.

For home-delivered ART, the largest cost categories were personnel costs (33%), buildings and overhead (17%), and vehicles and fuel (11%) for the first year of implementation (Fig 3.1a). These proportions remained relatively stable for subsequent years (Fig 3.1b). For the SOC, the largest costs were ART drugs (42%), personnel costs (35%), and materials and supplies (20%) for each year of implementation (Fig 3.1a). Total annual costs by cost category are reported in Appendix C.

At-scale scenarios

I estimated that if the home delivery team was working full-time (using the parameters described in the methods), the team could feasibly make 12 home delivery stops per working day and accommodate a client volume of 367 newly diagnosed people with HIV in the first year and up to 642 clients in subsequent years. I estimated that this at-scale programmatic cost of home delivery would be $267 annually per client for home-delivered ART refills and monitoring in the first year and $183 in subsequent years (Table 3.3), in comparison to $167 for clinic-based refills. The average annual cost per client virally suppressed receiving home-delivered ART refills would be $303 in the first year and $208 in subsequent years (Table 3.3) vs. $254 for clients receiving clinic-based care.

Multi-month scripting further reduced the cost of home-delivered ART so that it was comparable or even lower in cost than SOC. With six-month ART refill scripts, the annual cost per client would be $225 for home-delivered refills in the first year and $177 for subsequent years, (compared to $167 for the SOC), and the average cost per client virally suppressed would be $255 in the first year and $201 in subsequent years (vs. $254 for the SOC). At-scale 12-month ART

refills would be cost-saving after the first year: the annual cost per client would be $135 in subsequent years (compared to $167 for the SOC) (Table 3.3).

For three-month at-scale home delivered ART, the largest first-year costs were ART drugs (26%), personnel costs (22%), materials and supplies (17%), and buildings and overheads (12%) (Figure 3.2a). The rankings of cost categories remained the same for subsequent years (Figure 3.2b). Average client costs per cost category for the six-month refill programmatic and at-scale scenarios are reported in Appendix C, along with additional cost driver figures.

DISCUSSION

In this costing study of home-delivered ART refills in a high-prevalence rural setting in South Africa, I estimate that when delivered at scale, home delivery costs in a rural setting are comparable to the SOC of clinic-based refills administered across both rural and urban settings. Specifically, assuming a reasonable client volume of 12 home deliveries per day, I estimate that the annual per-client cost of home-delivered ART is $267 in the first year and $183 in subsequent years, as compared to the province-level average of $167 for clinic-based refills; this corresponds to a per-client incremental cost of $100 in the first year and $16 in subsequent years (Table 3.3). These incremental costs were predominantly driven by differences in personnel requirements (Figure 3.1). Importantly, this comparison covers a rural setting for home-delivered ART and a combined rural/urban setting for the SOC – the difference in setting may contribute to an increase in observed incremental costs given prior literature from South Africa which suggests that the cost of delivering ART is on average 7% more costly in rural areas than in urban areas.[67] Multi-month scripting (six- and 12-months) even further reduced costs of home delivery compared with standard clinic-based refills, and were either comparable (six-months) or cost-saving (12-months) when provided at-scale after the first year (Table 3.3). The published Deliver Health Study results

demonstrated clinical effectiveness of home-delivered ART,[38] and the present costing study suggests that home-delivered ART can be feasibly scaled up in a high prevalence rural setting in South Africa at modest incremental cost.

Our estimates somewhat differ from other costing studies for DSD and ART delivery in South Africa. Importantly, our estimates for the SOC using KwaZulu-Natal's provincial budget data ($167 per client annually) are substantially lower than the estimates from the South African HIV investment case, which estimated that the average cost (in 2022 USD) for providing ART per client annually across South Africa was $290.[82] Using a lower comparator means that our estimates of the incremental cost of home-delivered care are higher than would be if I compared to the South African HIV investment case. Our estimated at-scale annual per-client costs of ART with quarterly refills were higher than those observed in the DO ART Study, a study of community-based ART conducted in the same region of rural South Africa ($183 in this study, compared with $287 in the DO ART Study for subsequent years after adjusting for inflation as shown in Appendix C).[83] While it is expected that home delivery costs might be higher than community-based delivery of ART due to increased personnel and fuel costs; however, an approach like home delivery would remove the physical access barrier for the client, which could result in better retention in care and ART adherence. Finally, in line with other studies on multi-month scripting from Southern Africa which have also found comparable clinical outcomes,[37,84–86] I found that that increasing the duration of ART scripts to six- and 12-months further reduced costs due to the fewer follow-up visits.

Interestingly, the largest cost category for home-delivered ART was personnel wages and benefits (33% in the baseline scenario) and not vehicle and fuel costs (11%). Personnel was the largest cost for a number of reasons. First, within the Deliver Health Study, staff coordinated and made individual home deliveries based on client delivery preferences. In addition, the protocol

required that clients were physically present at the time of delivery (vs. dropping off refills at their front door). Thus, planning of delivery trips and routes driven were not always optimized. With a greater volume of clients, optimized delivery algorithms adapted from routing science-guided delivery in the private sector[61–63] could be useful in managing client delivery preferences and delivery personnel time, and may ultimately lower programmatic costs. This point is evidenced by our findings in the at-scale scenarios, in which ART drugs contributed the largest costs to the home-delivery intervention in both three- and six-month refill scenarios. Second, I assumed that programmatic implementation of home-delivered ART included a full-time professional nurse at grade 2 and a driver. These programmatic nurse salaries were in fact higher than the nurse staff salaries from the Deliver Health Study, which is generally not consistent with the literature.[83,87] Alternative team configurations with task shifting to lower cadre health workers (e.g., lower grade nurses or community health workers) could be tested in future work to determine effectiveness and efficiency. Finally, vehicles did not contribute a substantial portion of total estimated costs due to low diesel and vehicle costs relative to personnel costs.

In the Deliver Health Study, clients paid a one-time fee, tiered based on individuals' income (US $2, $4, or $6), for a six-month ART home delivery service (which was extended due to COVID-19). User fees in general were well accepted: in the Deliver Health Study, 98% of clients paid the full user fee for the home-delivery ART service and 100% reported willingness to continue to pay a fee for the service due to its perceived convenience and flexibility.[16] Notably, these client fees for the home delivery service did not substantially offset delivery costs (personnel, vehicle, and fuel) in either the as-observed or at-scale scenarios. Moreover, the fee in the Deliver Health Study covered home ART delivery service for six months, thus an annual service fee per client would likely be higher (e.g., double that of the six-month service) in implementation. However,

the user fees still contributed to a modest reduction in programmatic costs and may additionally have contributed to program effectiveness.[88,89]

Our study had a number of limitations. First, as discussed above, our costing of home-delivered ART covered a rural setting while the SOC covered a rural and urban setting, likely leading to an overestimate of incremental costs.[90] In a related point, I did not obtain all costing inputs from a single source; however, I relied on either peer-reviewed studies or published data from the South African government. Third, our study included a low client volume from pilot randomized controlled trial leading to higher costs per person. To account for the small sample size, I modelled at-scale scenarios to accommodate a higher client volume; these findings were more in line with estimates from the literature. Fourth, I estimated costs for TDF/FTC/EFV (the regimen prescribed for Deliver Health Study participants); however, as of 2023 South Africa recommends ART regimens containing DTG for greater adherence and viral suppression[70,91 92,93] – future costing studies should note this change in clinical guidelines. Fifth, while our study was conducted from the payer perspective to reflect the stakeholder of interest, a societal perspective could better capture benefits to clients (e.g., transportation costs, lost wages due to time spent on clinic visits, childcare[16]). Sixth, this study uses the SOC as the comparison, but does not compare to costs of other DSD models for HIV, such as the use of community package lockers (smart lockers) being tested in an ongoing trial throughout rural KwaZulu-Natal.[60] Finally, while the present study does not incorporate health outcomes, the estimates generated in this study can be leveraged for future cost-effectiveness analysis.

National scale-up of DSD models for HIV treatment, tailored to specific patient populations and geographies, are needed in South Africa. A number of alternative ART dispensing mechanisms have demonstrated improved medication adherence and retention compared to clinic

care, including home delivery service, community package lockers, and automated pharmacy dispensing units.[18] These methods, particularly when clients can flexibly choose the most convenient option, can strengthen individuals' commitment to care.[94,95] Additionally, community-based ART resupply can increase coverage in rural areas[22] and reduce clinic congestion.[96] At scale, home-delivered ART could be optimized using a centralized warehouse to fulfill and dispatch delivery trucks that synchronize deliveries to neighboring locations, similar to what is used in the private sector by Amazon.[97] These warehouses could even be used for other chronic medications as part of the Centralised Chronic Medicine Dispensing and Distribution,[10] freeing up clinics and pharmacies to focus on clients with health care needs other than refills. Drone delivery, which has successfully been tested in other African countries including Uganda (for ART) and Malawi (for transportation of lab samples), offers a promising cost-effective solution for rural areas.[98,99] In fact, Amazon has recently begun implementing home delivery of medications via drones in the US.[100] These innovative methods hold promise for addressing the hard-to-reach and high prevalence populations in rural South Africa, where interventions increasing early adoption of and adherence to ART can be highly cost-effective (increases cost-effectiveness relative to the base-case by 23% in a rural areas of South Africa, compared to 1.1% in urban areas).[67] Future research should explore the costs and outcomes of various innovative approaches compared to traditional clinic-based care.

Conclusion

Our costing study is a novel evaluation to quantify the costs associated with implementing home-delivered ART and monitoring in rural South Africa. Implementing home-delivered ART and monitoring costs more on average annually per client and per client virally suppressed compared to standard three-month clinic-based ART refills in KwaZulu-Natal, but incremental costs were reduced when home delivery was scaled to a larger client volume and potentially even

cost-saving when using home-delivery and six- and 12-month refill scripts. The findings of this study could help inform the South African NDoH's strategy to meet the 95-95-95 targets by focusing on the scale-up of novel DSD methods, such as home-delivered ART, to promote long-term retention in HIV care while reducing patient load at public health clinics.

TABLES & FIGURES

Table 3.1. Average annual cost per client and average annual cost per virally suppressed client by refill method within the context of the Deliver Health Study, under the programmatic scenario with 3-month ART refill scripts

Cost category	Average annual cost per client						Average annual cost per client virally suppressed					
	Home delivery[a]				**Clinic**[c,d] N=1,925,698		**Home delivery**[e]				**Clinic**[c,d] N=1,270,961	
	First year[b] N=81		Subsequent years N=81				First year[b] N=71		Subsequent years N=71			
	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD
	Cost (% of total cost)											
ART drugs	1,150 (9)	70 (9)	1150 (10)	70 (10)	1150 (42)	70 (42)	1,312 (9)	80 (9)	1,312 (10)	80 (10)	1,743 (42)	106 (42)
Buildings and administrative overhead	2,189 (17)	134 (17)	2,091 (18)	128 (18)	58 (2)	4 (2)	2,497 (17)	152 (17)	2,386 (18)	146 (18)	88 (2)	5 (2)
Communication	1,269 (10)	78 (10)	1,269 (11)	78 (11)	6 (0.22)	0.36 (0.22)	1,448 (10)	88 (10)	1,448 (11)	88 (11)	9 (0.22)	0.55 (0.22)
Equipment	1,200 (9)	73 (9)	150 (1)	9 (1)	2 (0.06)	0.11 (0.06)	1,369 (9)	84 (9)	172 (1)	10 (1)	3 (0.06)	0.16 (0.06)
Hiring and training	657 (5)	40 (5)	657 (6)	40 (6)	2 (0.09)	0.15 (0.09)	749 (5)	46 (5)	749 (6)	46 (6)	4 (0.09)	0.22 (0.09)
Materials and supplies	753 (6)	46 (6)	590 (5)	36 (5)	561 (20)	34 (20)	859 (6)	52 (6)	674 (5)	41 (5)	850 (20)	52 (20)
Personnel wages and benefits	4,354 (33)	266 (33)	4,354 (37)	266 (37)	960 (35)	59 (35)	4,968 (33)	303 (33)	4,968 (37)	303 (37)	1454 (35)	89 (35)
Vehicles and fuel	1,491 (11)	91 (11)	1,489 (13)	91 (13)	0.26 (0.01)	0.02 (0.01)	1,701 (11)	104 (11)	1,699 (13)	104 (13)	0.40 (0.01)	0.02 (0.01)
Total[f]	13,006	794	11,694	714	2,740	167	14,846	907	13,349	815	4,151	254

Abbreviations: ART = antiretroviral therapy, ZAR = South African Rand, USD = United States Dollars, HIV = Human Immunodeficiency Virus, UNAIDS = Joint United Nations Programme on HIV/AIDS.
[a]There were 81 people living with HIV on ART in the home-delivered ART refills group of the Deliver Health Study.
[b]Includes startup costs.
[c]The standard-of-care in South Africa is 3-month ART refills at clinics.
[d]The total number of adults (aged 15 years and older) living with HIV in KwaZulu-Natal in September 2022 was 1,925,698 people. Source: UNAIDS HIV sub-national estimates viewer.
[e]There were 71 people living with HIV on ART who were virally suppressed at study exit in the home-delivered ART refills group of the Deliver Health Study.
[f]The average fee for home delivery service, about 4 USD, paid by clients in the home delivery intervention of the Deliver Health Study was subtracted from the programmatic costs of implementing home delivery.

Table 3.2. Estimated cost implications of multi-month home-delivered and standard clinic-based ART refills and monitoring as-observed by the South African National Department of Health with South African government salaries, under the programmatic scenario with 3-, 6-, and 12-month ART refill scripts

Scenario	Average annual cost per client						Average annual cost per client virally suppressed					
	Home delivery				Clinic[b] N=1,925,698		Home delivery				Clinic[b] N=1,270,961	
	First year[a] N=81		Subsequent years N=81				First year[a] N=71		Subsequent years N=71			
	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD
Programmatic costs with 3-month refills	13,006	794	11,694	714	2,740	167	14,846	907	13,349	815	4,151	254
Programmatic costs with 6-month refills	10,014	612	9,337	570			11,424	698	10,652	651		
Programmatic costs with 12-month refills	8,261	504	7,521	459			9,424	576	8,581	524		

Abbreviations: ART = antiretroviral therapy, ZAR = South African Rand, USD = United States Dollars, HIV = Human Immunodeficiency Virus, UNAIDS = Joint United Nations Programme on HIV/AIDS.
[a]Includes startup costs.
[b]The standard-of-care in South Africa is 3-month ART refills at clinics.

Table 3.3. Estimated cost implications of multi-month home-delivered and standard clinic-based ART refills and monitoring provided at-scale by the South African National Department of Health with South African government salaries, with 3-, 6-, and 12-month ART refill scripts

Scenario	Average annual cost per client						Average annual cost per client virally suppressed					
	Home delivery				Clinic N=1,925,698		Home delivery				Clinic N=1,270,961	
	First year[b] N=367		Subsequent years N=642				First year[b] N=323		Subsequent years N=565			
	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD
At-scale programmatic costs with 3-month refills[a]	4,367	267	2,996	183	2,740	167	4,963	303	3,405	208	4,151	254
At-scale programmatic costs with 6-month refills	3,681	225	2,900	177			4,183	255	3,296	201		
At-scale programmatic costs with 12-month refills	3,921	239	2,214	135			4,455	272	2,516	154		

Abbreviations: ART = antiretroviral therapy, ZAR = South African Rand, USD = United States Dollars, HIV = Human Immunodeficiency Virus, UNAIDS = Joint United Nations Programme on HIV/AIDS.

[a]The standard-of-care in South Africa is 3-month ART refills.

[b]Includes startup costs.

Figure 3.1. Average annual cost per client (2022 USD) for home-delivered 3-month ART refills vs. clinic-based 3-month ART refills (standard-of-care) by cost category in the programmatic NDoH-implemented scenario. The NDoH scenario assumes fixed costs as implemented in the Deliver Health Study and public sector clinical staff salaries instead of study salaries.

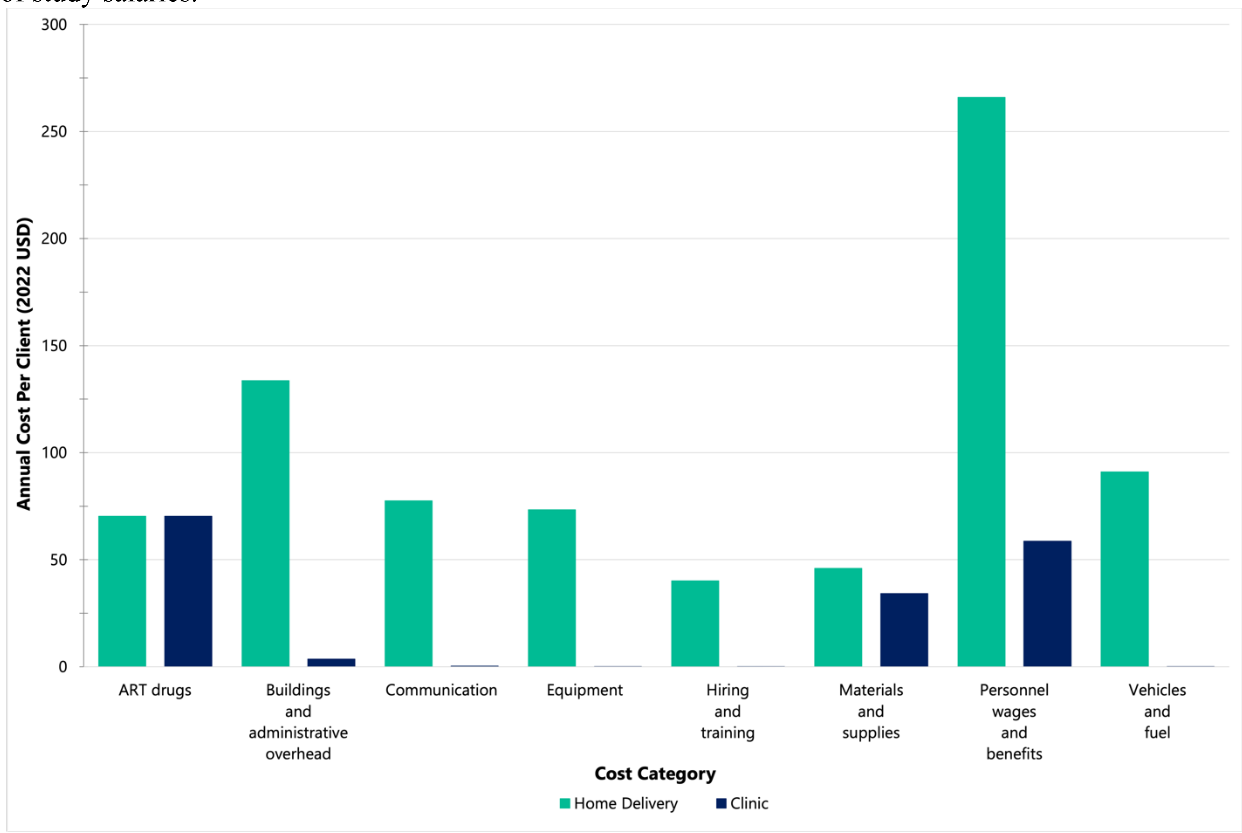

Figure 3.1a. Home-delivered ART intervention (first year costs) vs. clinic-based ART refills

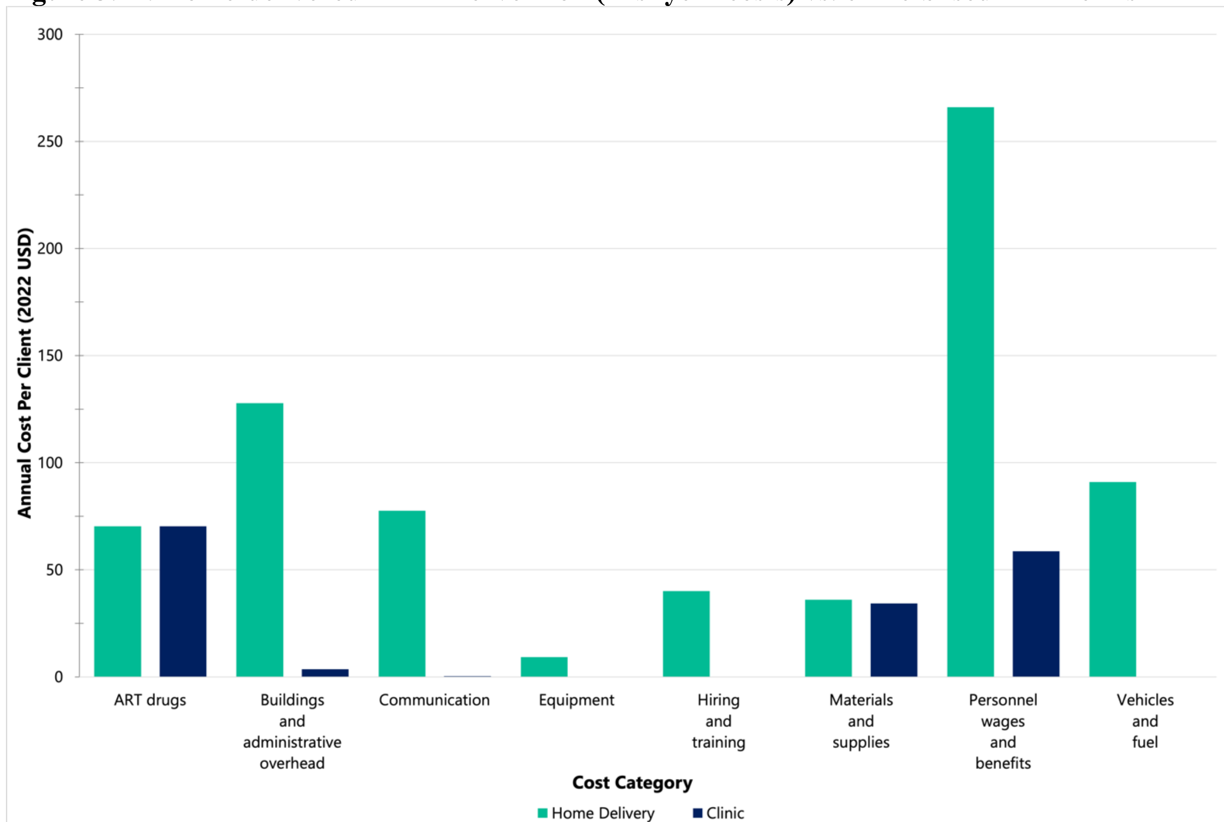

Figure 3.1b. Home-delivered ART intervention (subsequent year costs) vs. clinic-based ART refills

Figure 3.2. At-scale average annual cost per client (2022 USD) for home-delivered 3-month ART refills vs. clinic-based 3-month ART refills (standard-of-care) by cost category in the programmatic NDoH-implemented scenario. The NDoH scenario assumes fixed costs as implemented in the Deliver Health Study and public sector clinical staff salaries instead of study salaries.

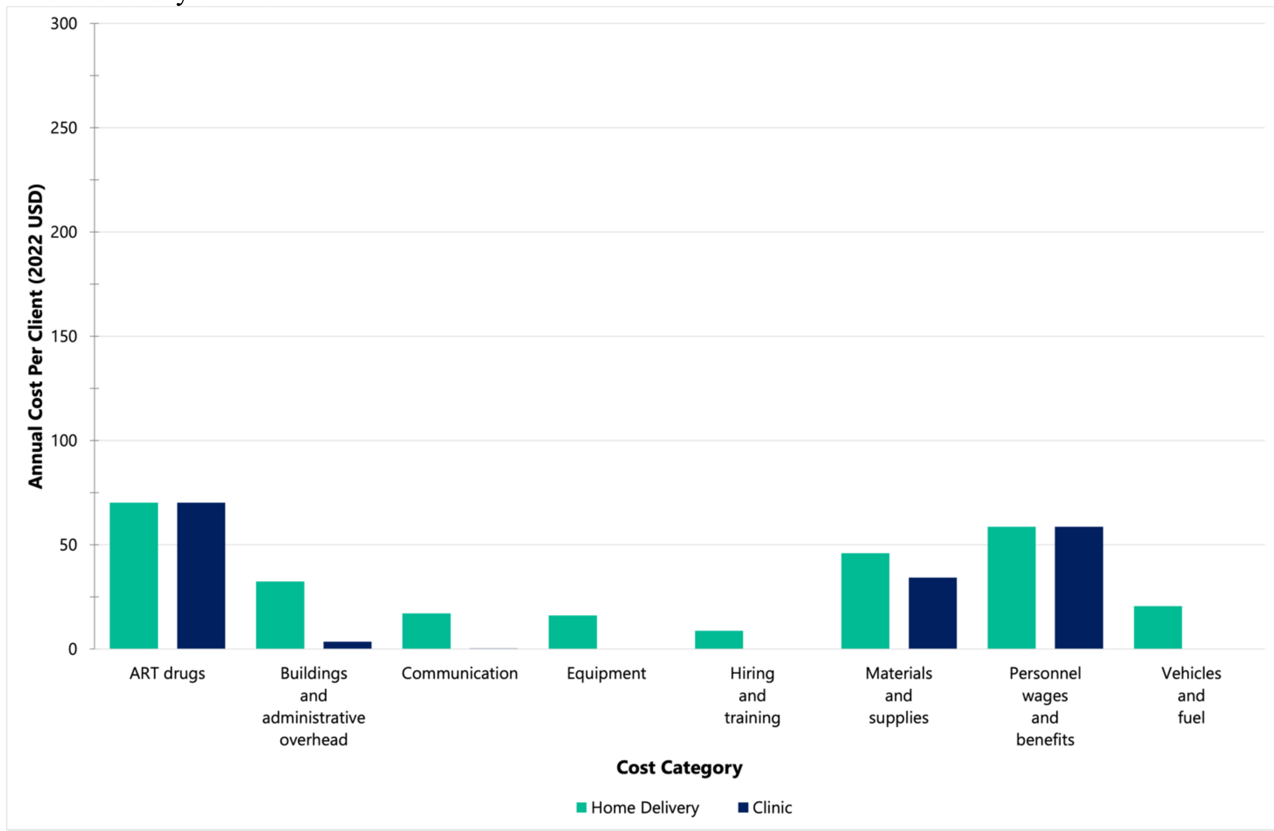

Figure 3.2a. Home-delivered ART intervention (first year costs) vs. clinic-based ART refills

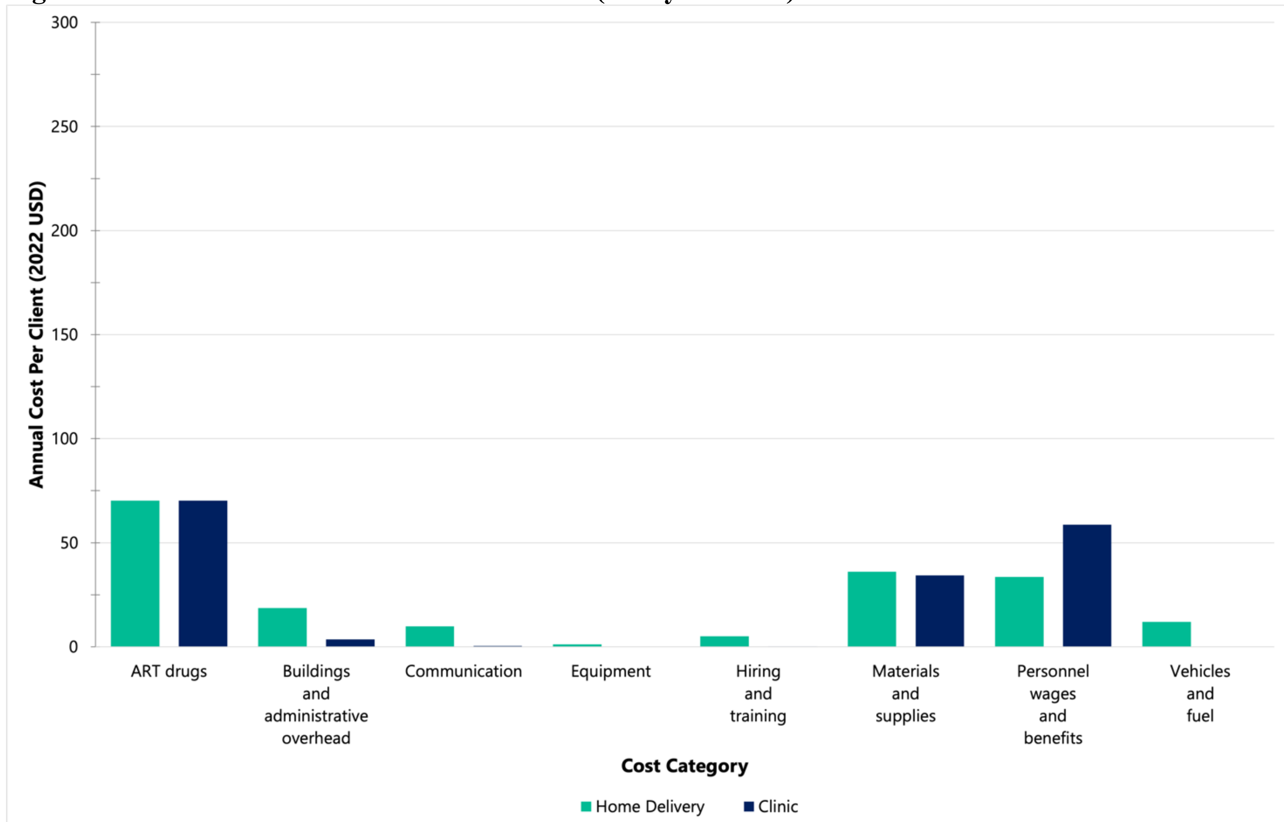

Figure 3.2b. Home-delivered ART intervention (subsequent year costs) vs. clinic-based ART refills

Conclusion

While fee for home delivery was demonstrated to be an effective ART refill method for achieving viral suppression compared to clinic-based refills in the Deliver Health Study, home-delivered ART was found to be more environmentally and financially costly compared to standard clinic-based refills, and did not have a significant effect on the risk of missing ART doses during the first COVID-19 wave in South Africa. However, when home ART delivery is implemented at-scale and with multi-month refills, there are potential cost- and environmental savings relative to the standard clinic-based care.

In Chapter 1, I observed no difference in the self-reported number of missed ART doses by method of ART refill (home-delivered vs. at clinics) when comparing between or within time periods during the first COVID-19 wave in South Africa. In Chapter 2, I found that incremental CO_2 emissions were higher for participants receiving home-delivered vs. clinic-based ART refills in rural South Africa but could be offset by 6- or 12-month refills (and reducing delivery frequency) and/or switching to electric delivery vehicles, decreasing the impact on the environment. In Chapter 3, I found that the average annual cost per client and average annual cost per client virally suppressed of implementing a home-delivered ART intervention was higher than the cost of clinic-based ART refills and care from the payer perspective in the as-observed scenario. Personnel costs were the largest cost for home-delivered refills while ART drug costs were the largest cost of clinic-based refills. When provided at scale, home-delivered ART in a rural setting not only offers clinical benefits for a hard-to-reach population but is also comparable in cost to the provincial standard of care.

This research provides novel insights into the financial costs and environmental impact associated with implementing home-delivered ART refills and monitoring in rural South Africa, a

relatively new DSD method which could be scaled up more widely in an effort to reduce physical access barriers for people living with HIV and to offer clients more resupply options that could better suit their lifestyle preferences. While my analyses were limited by a small sample size resulting in limited statistical power, I used data from a randomized controlled trial which previously found that there was a significant increase in the proportion of people living with HIV who were virally suppressed for those receiving home-delivered vs. clinic-based ART refills, the primary clinical outcome used in HIV treatment. Further, I strengthened my findings by conducting sensitivity analyses and modeling different implementation scenarios. There are several key takeaways from this dissertation.

First, multi-month dispensing showed potential cost-savings in terms of environmental and financial costs for the home delivery of ART intervention. In Chapter 2, I modelled 6- and 12-month scenarios in my study, showing that reducing the refill frequency (i.e., increasing the supply dispensed at each visit) would reduce the incremental CO_2 emissions per person virally suppressed between home-delivered and clinic-based ART refills and the CCE. A complementary strategy for increasing engagement in HIV care is by increasing the ART supply dispensed at each refill visit, reducing the possibility of missed ART doses due to refill challenges. Multi-month dispensing of ART has been shown to be effective for clinically-stable people living with HIV in other contexts.[58,59] Offering multi-month ART supply has the potential to reduce CO_2 emissions and barriers to care, ultimately increasing engagement in HIV care. In Chapter 3, I found that increasing the duration of ART scripts from 3-months to 6- and 12-months reduced costs due to the fewer follow-up visits. Home delivery of ART cost less than clinic-based ART refills at-scale in subsequent years in the 12-month script scenario for the average annual cost per client and for 3-, 6-, and 12-month script scenarios for average annual cost per client virally

suppressed. My findings were in line with other studies on multi-month scripting from Southern Africa which have also found comparable clinical outcomes.[37,84–86] In addition to national scale-up of DSD models for HIV treatment with greater durations of ART refills, future research should explore the costs and outcomes of various innovative approaches, such as centralized warehouses or drone delivery for home delivery ART resupply fulfillment, compared to traditional clinic-based care.

Second, home delivery of medication can remove barriers to care experienced by people living with HIV. In Chapter 1, I observed that home delivery of ART allowed for uninterrupted access to refills during the COVID-19 pandemic when there were greater barriers to accessing in-person clinic-based care in rural South Africa. During the COVID-19 pandemic, cancellation of health services due to government-imposed COVID-19 lockdowns were a major source of stress and anxiety for individuals with chronic conditions requiring consistent and frequent access to clinics.[23] As a response to country-wide COVID-19 lockdowns and associated service disruptions, home-delivery of medication was rapidly implemented for individuals with chronic conditions in South Africa.[24] While home-delivered refills can reduce an individual's uncertainty about physically accessing ART resupply, I did not find a difference in the self-reported number of missed ART doses by method of ART refill (home-delivered vs. at clinic) when comparing between or within time periods during the first COVID-19 wave in South Africa. In rural South Africa, people living with HIV in standard clinic-based care experienced delays in ART refill access during the COVID-19 pandemic. A qualitative study of Deliver Health Study participants provided further evidence for the high acceptability and willingness to continue to pay a fee for the home-delivered ART service due to its perceived convenience and flexibility, and how the home delivery service alleviates barriers to HIV care experienced by people living with HIV in

rural South Africa.[16] DSD approaches like home-delivered ART is promising and could address current physical access or stigma barriers faced by people living with HIV, and could potentially be bundled with the delivery of other medications with for people living with multiple chronic conditions.

Third, as often stated in the business field, "you cannot improve what you do not measure." This body of work demonstrates ways in which existing methods can be used outside their traditional scopes (e.g., routing science for healthcare delivery, health economics approaches for estimating environmental costs), and also adds evidence to the literature about home-delivered medication interventions specific to South Africa. While I did not find that home-delivered ART offered financial or environmental cost-savings relative to the standard clinic-based care as-observed in the Deliver Health Study, I hope that my analytic approach can be replicated and applied to other studies in the future to further add to the evidence for potential scale-up of home delivery. The environmental costing methods developed in Chapter 2 can be applied to analyzing the data currently being collected in the SMART ART Study[60] and potentially other studies interested in estimating the environmental impact of a public health intervention. While not traditionally estimated as part of clinical trials or epidemiologic studies, I believe it is important to estimate the environmental health impact of any public health intervention due to the pressing nature of climate change. South Africa has an ongoing energy crisis in addition to the existing global climate crisis, and has nearly 8 million people living with HIV requiring consistent access to refills and monitoring but limited healthcare capacity (one that could be even further limited by large-scale events like the COVID-19 pandemic). If home-delivery of medications could reduce overall CO_2 emissions and environmental impact, then investments should be made to scale up home delivery for the purpose of climate change

remediation efforts. The cost estimates associated with home-delivered ART refills and monitoring in rural South Africa in Chapter 3 could be useful for South Africa's NDoH planning as home delivery is a relatively new DSD method which could be implemented more widely in an effort to reduce physical access barriers for people living with HIV and to offer clients more resupply options that could better suit their lifestyle preferences. A traditional cost-effectiveness analysis of home-delivered vs. clinic-based ART refills for people living with HIV in rural South Africa would also be informative in weighing the findings of our environmental-effectiveness and costing studies. Further, if carbon costs were to become quantified in either health effects (e.g., disability-adjusted life years) or in monetary terms (e.g., cost of lost productivity), then they could theoretically be included in a cost-effectiveness analysis from the societal perspective in any health economic study.

Alternative ART dispensing mechanisms such as fee for home delivery service, package lockers in a community location, and automated pharmacy dispensing units have been found to increase medication adherence and retention in HIV care compared to standard clinic-based care,[18] potentially through strengthened individual implementation intentions and commitment to care when giving clients the opportunity to choose a method that works for them.[94,95] Further, investing in resupplying ART through community-based venues can effectively increase ART coverage,[22] particularly in rural areas, and decongest clinics for attention to acute patients.[96] The findings of this dissertation could help inform the South Africa NDoH's strategy to meet the 95-95-95 targets by focusing on the scale-up of novel DSD methods, such as home-delivered ART, to promote long-term retention in HIV care while reducing patient load at public health clinics.

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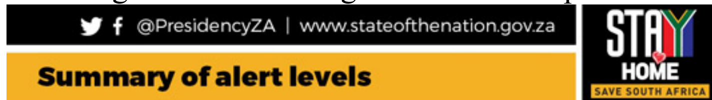
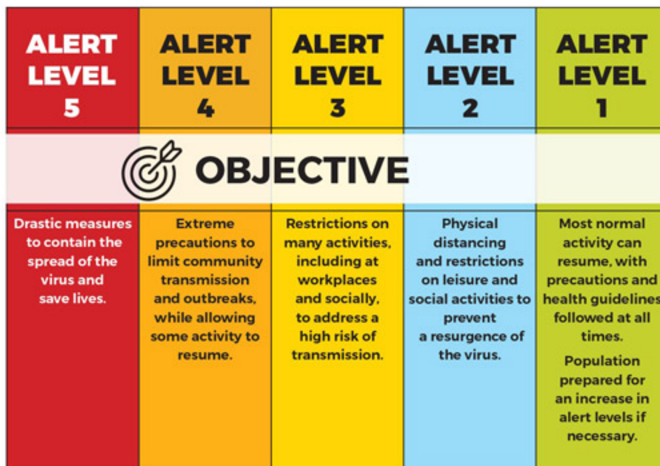
Appendices

APPENDIX A: Methodology and Supplemental Materials for Chapter 1

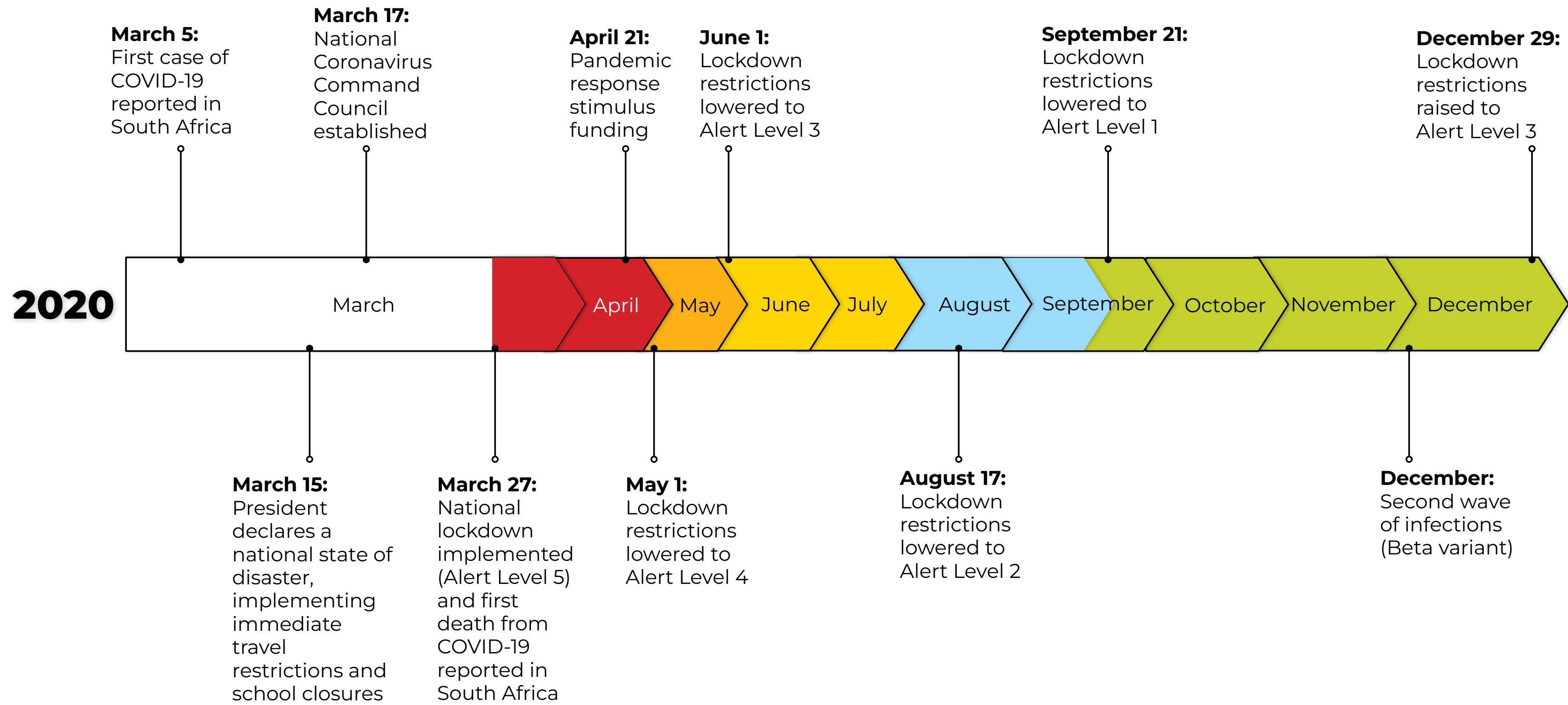
i. Context of the first COVID-19 pandemic wave in South Africa

Supplemental Figure 1.1. Summary of the five-level alert system implemented by the South African government during the COVID-19 pandemic to ease into lockdown





Supplemental Figure 1.2. A visual timeline of alert level changes during the first COVID-19 wave in South Africa



ii. About the measure of self-reported missed ART doses

For the primary analysis, participants could have reported missing 0 to 7 doses of ART in a given week. All study participants were taking the Tenofovir/Emtricitabine/Efavirenz (TDF/FTC/EFV) ART regimen. Each daily "dose" was a combination of three different HIV medicines and included multiple pills as part of the daily HIV treatment regimen.

iii. Model equation for difference-in-differences (DiD) of home-delivered vs. clinic-based ART refills in period 2 vs. period 1

$$\log(E[Y_{it}]) = \beta_0 + \beta_1 HOME_i + \beta_2 INT1_{it} + \beta_3 HOME_{it} * INT1_{it}$$

Where:

$Y_{it} = \text{self} - \text{reported daily adherence in the past week for individual } i \text{ at time } t$

$$= \begin{cases} 0 = \text{one or more doses missed} \\ 1 = 100\% \text{ adherence (zero doses missed)} \end{cases}$$

$HOME_{it} = \text{ART refill method for individual } i \text{ at time } t = \begin{cases} 0 = \text{clinic} - \text{based} \\ 1 = \text{home delivery} \end{cases}$

$INT1_{it} = \text{time period for individual } i \text{ at time } t$

$= \begin{cases} 0 = \text{before COVID} - 19 \text{ alert level 5 (lockdown) was implemented (period 1)} \\ 1 = \text{during COVID} - 19 \text{ alert levels } 5, 4, 3, 2 \text{ (period 2)} \end{cases}$

$\beta_3 = \log(\text{DID estimate})$

$= \log$ (difference in relative risk of Y_{it} of home delivery group in period 2 vs. period 1 and relative risk of Y_{it} of clinic group in period 2 vs. period 1)

iv. Model equation for difference-in-differences of home-delivered vs. clinic-based ART refills in period 3 vs. period 2

$$\log(E[Y_{it}]) = \beta_0 + \beta_1 HOME_i + \beta_2 INT2_{it} + \beta_3 HOME_{it} * INT2_{it}$$

Where:

$Y_{it} = \text{self} - \text{reported daily adherence in the past week for individual } i \text{ at time } t$

$$= \begin{cases} 0 = \text{one or more doses missed} \\ 1 = 100\% \text{ adherence (zero doses missed)} \end{cases}$$

$HOME_{it} = \text{ART refill method for individual } i \text{ at time } t = \begin{cases} 0 = \text{clinic} - \text{based} \\ 1 = \text{home delivery} \end{cases}$

$INT2_i = \text{time period for individual } i \text{ at time } t$

$$= \begin{cases} 0 = \text{during COVID} - 19 \text{ alert levels } 5, 4, 3, 2 \text{ (period 2)} \\ 1 = \text{after COVID} - 19 \text{ alert level was downgraded to level 1 (period 3)} \end{cases}$$

$\beta_3 = \log(\text{DID estimate})$

$= \log$ (difference in relative risk of Y_{it} of home delivery group in period 3 vs. period 2 and relative risk of Y_{it} of clinic group in period 3 vs. period 2)

v. About the measure of delayed ART refill visits

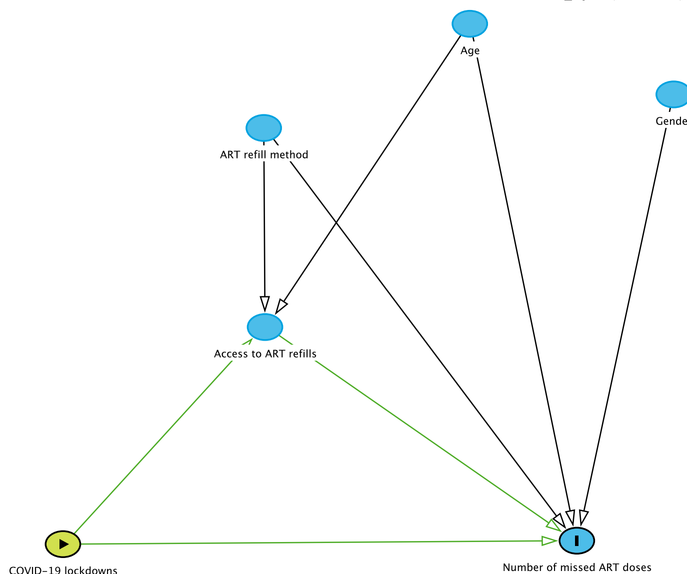
For the secondary analysis, to calculate the binary outcome of occurrence of late ART refill visits, I compared the ART refill visit date noted on each participant's study records and the last date they would have needed to pick up their ART refill based on their prior visit date and created a binary variable indicating '1' if the ART refill visit was after their last prescription ran out and '0' if the ART refill visit was before their last prescription ran out. For example, if the last date a participant would have needed to pick up their ART refill before running out of their

prior prescription was January 27 and they picked up their refill on February 1, then they would have an affirmative response (1) for the binary variable, indicating that they had a late refill visit.

vi. Comparison group and consideration of confounders justification

Had the individuals who were randomized to the home-delivered ART group not been randomized to the home-delivery group, they would have received their ART refills at clinics, the current standard-of-care. Since participants in the Deliver Health Study were randomized to each study group, I assumed that the distribution of individual-level confounders was equal across groups and the two groups were comparable. I also created a causal diagram to conceptualize the relationship of variables such as gender and age with the exposure of COVID-19 lockdowns and outcome of self-reported missed ART doses, further confirming that no observed variables needed to be adjusted for as potential confounders (Supplemental Figure 1.3). The green circle with the triangle indicates the exposure and the blue circle with the vertical bar indicates the outcome. Blue circles are ancestors of the outcome. The diagram was created using DAGitty (Johannes Textor, Benito van der Zander, Mark K. Gilthorpe, Maciej Liskiewicz, George T.H. Ellison. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. International Journal of Epidemiology 45(6):1887-1894, 2016). Daggity suggests a sufficient minimum set of confounders.

Supplemental Figure 1.3. Causal diagram for the association between COVID-19 lockdowns and the number of missed antiretroviral therapy (ART) doses



vii. Supplemental Results

I additionally determined if there were any differences in ART adherence between home delivery and clinic groups during each time period of the first COVID-19 wave in South Africa. To assess this, I compared the number of missed ART doses in the past week of participants in the home-delivered ART refills group to that of participants in the clinic-based ART refills group in each time period (period 1, 2, and 3).

During period 1, the risk of missed ART doses in the past week among persons receiving home-delivered refills was 0.98 times the risk of missed ART doses in the past week among those refilling ART at clinics (95% confidence interval [CI]: 0.91, 1.05). During period 2, the risk of missed ART doses in the past week among persons receiving home-delivered refills was 1.01 (95% CI: 0.99, 1.03) the risk for persons refilling from clinics. The results for period 3 were similar to that of period 2 (Supplemental Table 1.1). There were no statistically significant differences in self-reported ART adherence between refill groups during any of the time periods. I found similar results when lowering the adherence cutoff from 100% to ≥85% ART adherence, with the relative risk changing slightly for periods 1 and 3.

Supplemental Table 1.1. Difference in optimal medication adherence (100% and ≥85%) to antiretroviral therapy (ART) comparing people living with HIV receiving home-delivered vs. clinic-based ART refills within each time period during the first COVID-19 wave in KwaZulu-Natal, South Africa

Time Period	Optimal ART Adherence (in the past 7 days)	Relative Risk Ratio	95% Confidence Interval[1]
Period 1: Before Implementation of COVID-19 Alert Level 5[2]	100% adherence: 0 missed doses vs. ≥1 missed doses	0.98	0.91, 1.05
	≥85% adherence: ≤1 missed doses vs. ≥2 missed doses	1.00	0.97, 1.03
Period 2: During COVID-19 Alert Levels 5, 4, 3, and 2[3]	100% adherence: 0 missed doses vs. ≥1 missed doses	1.01	0.99, 1.03
	≥85% adherence: ≤1 missed doses vs. ≥2 missed doses	1.01	0.99, 1.03
Period 3: After Downgrading to COVID-19 Alert Level 1[4]	100% adherence: 0 missed doses vs. ≥1 missed doses	1.00	0.92, 1.09
	≥85% adherence: ≤1 missed doses vs. ≥2 missed doses	0.99	0.92, 1.07

[1]Robust standard errors were estimated using the 'sandwich' and 'lmtest' packages in R.
[2]Alert level 5 was equivalent to a full lockdown during which all non-essential activities and services were restricted. The total number of ART refill visits included in period 1 was 291 across 150 participants. There were 169 visits accrued by 81 participants in the home delivery group and 122 visits accrued by 69 participants in the clinic group during period 1.
[3]The total number of ART refill visits included in period 2 was 180 across 139 participants. There were 89 visits accrued by 65 participants in the home delivery group and 91 visits accrued by 74 participants in the clinic group during period 2.
[4]The total number of ART refill visits included in period 3 was 132 across 132 participants. There were 58 visits accrued by 58 participants in the home delivery group and 74 visits accrued by 74 participants in the clinic group during period 3.
[5]The ART regimen was one daily dose. The possible range of missed doses in the past 7 days was 0 to 7.

APPENDIX B: Methodology and Supplemental Materials for Chapter 2

i. Estimating carbon dioxide emissions for the clinic-based refills group
For the clinic group, the per person cumulative carbon dioxide (CO_2) emissions were calculated as follows:

Step 1: Calculate the CO_2 emissions per ART refill visit

$$(\text{mapped distances from participant home or work location to clinic in km}) * (\text{estimated average emissions of the transport method listed for the refill visit in kgCO}_2\text{/km}) = \text{kgCO}_2 \text{ emissions per visit}$$

Example: Participant walks from their home to X clinic for ART refill at months 1, 3, and 6 → $5\ km * 0\ kgCO_2/km = 0\ gCO_2$ *for their month 1 visit. Same participant takes a minibus from their home to X clinic for ART refill at month 12 →* $5\ km * 0.339\ kgCO_2/km = 1.695\ kgCO_2$ *for their month 12 visit.*

Step 2: For each participant, sum up the CO_2 emissions (per ART refill visit) across all their refill visits to estimate their cumulative CO_2 emissions over the study period

$$(\text{kgCO}_2 \text{ emissions for month 1 visit}) + (\text{kgCO}_2 \text{ emissions for month 3 visit}) + (\text{kgCO}_2 \text{ emissions for month 6 visit}) + (\text{kgCO}_2 \text{ emissions for month 12 visit}) = \text{cumulative kgCO}_2 \text{ emissions per person}$$

Example: (0 $kgCO_2$) + (0 $kgCO_2$) + (0 $kgCO_2$) + (1.695 $kgCO_2$) = 1.695 $kgCO_2$ cumulative emissions for this participant over the study period.

ii. Estimating carbon dioxide emissions for the home delivery group
For the home delivery group, the per person cumulative CO_2 emissions were calculated as follows:

$$\frac{(\text{total km driven over the entire delivery day}) * (0.185\ \text{kgCO}_2/\text{km})}{(\text{number of home delivery stops made on the delivery trip})}$$

iii. Incremental cost-effectiveness ratio (ICER)
In order to determine the incremental cost-effectiveness of shifting to the more expensive strategy in terms of CO_2 emissions, I calculated an incremental cost-effectiveness ratio (ICER). The ICER was calculated as the change in CO_2 emissions divided by the change in the number of people virally suppressed.

Modelling 3-month refills:

$$\text{ICER}_{3mo} = \frac{(\text{Avg. total CO}_2 \text{ emissions of home delivery group}) - (\text{Avg. total CO}_2 \text{ emissions of clinic group})}{\left(\frac{\#\ \text{virally suppressed home delivery group}}{\#\ \text{of people in home delivery group}}\right) - \left(\frac{\#\ \text{virally suppressed in clinic group}}{\#\ \text{of people in clinic group}}\right)}$$

$$= \frac{(7.25 - 0.70)}{\left(\frac{71}{81} - \frac{54}{73}\right)}$$

$= 47.87$ kg extra emissions of CO_2 per additional person virally suppressed, comparing home-delivery to clinic group

47.87 kg extra CO_2 emissions per additional person virally suppressed is equivalent to driving $\frac{47.87\ \text{kgCO}_2}{0.185\ \text{kgCO}_2/\text{km}} = 259$ extra kilometers in the delivery vehicle.

Modelling 6-month refills:

Offering a 12-month refills of ART would be equivalent to two ART refill visits per person.

$$\text{ICER}_{6\text{mo}} = \frac{(\text{Avg. total CO}_2 \text{ emissions of home delivery group}) - (\text{Avg. total CO}_2 \text{ emissions of clinic group})}{\left(\frac{\#\text{ virally suppressed home delivery group}}{\#\text{ of people in home delivery group}}\right) - \left(\frac{\#\text{ virally suppressed in clinic group}}{\#\text{ of people in clinic group}}\right)}$$

$$= \frac{\left(\left(\frac{7.25}{4} * 2\right) - \left(\frac{0.70}{4} * 2\right)\right)}{\left(\frac{71}{81} - \frac{54}{73}\right)}$$

$= 23.94$ kg extra emissions of CO_2 per additional person virally suppressed, comparing home-delivery to clinic group

23.94 kg extra CO_2 emissions per additional person virally suppressed is equivalent to driving $\frac{23.94\ \text{kgCO}_2}{0.185\ \text{kgCO}_2/\text{km}} = 129$ extra kilometers in the delivery vehicle.

Modelling 12-month refills:

Offering a 12-month refills of ART would be equivalent to one ART refill visit per person.

$$\text{ICER}_{12\text{mo}} = \frac{(\text{Avg. total CO}_2 \text{ emissions of home delivery group}) - (\text{Avg. total CO}_2 \text{ emissions of clinic group})}{\left(\frac{\#\text{ virally suppressed home delivery group}}{\#\text{ of people in home delivery group}}\right) - \left(\frac{\#\text{ virally suppressed in clinic group}}{\#\text{ of people in clinic group}}\right)}$$

$$= \frac{\left(\left(\frac{7.25}{4} * 1\right) - \left(\frac{0.70}{4} * 1\right)\right)}{\left(\frac{71}{81} - \frac{54}{73}\right)}$$

$= 11.97$ kg extra emissions of CO_2 per additional person virally suppressed, comparing home-delivery to clinic group

11.97 kg extra CO_2 emissions per additional person virally suppressed is equivalent to driving $\frac{11.97\ \text{kgCO}_2}{0.185\ \text{kgCO}_2/\text{km}} = 65$ extra kilometers in the delivery vehicle.

iv. Comparative cost-effectiveness (CCE)

I additionally estimated the comparative cost-effectiveness, or the difference in carbon cost per virally suppressed person, in order to identify which approach is more cost-effective (in terms of CO_2 emissions) than the other.

Modelling 3-month refills:

$\text{CCE}_{3\text{mo}} =$

$$\left(\frac{\text{Avg. total } CO_2 \text{ emissions of home delivery group } * \text{ \# of people in home delivery group}}{\text{\# virally suppressed home delivery group}}\right) - \left(\frac{\text{Avg. total } CO_2 \text{ emissions of clinic group } * \text{ \# of people in clinic group}}{\text{\# virally suppressed in clinic group}}\right)$$

$$= \left(\frac{7.25 * 81}{71}\right) - \left(\frac{0.70 * 73}{54}\right)$$

= 7.32 kg extra CO_2 emissions per additional person virally suppressed between home delivery and clinic groups

<u>Modeling 6-month refills:</u>

$$CCE_{6mo} = \left(\frac{\text{Avg. total } CO_2 \text{ emissions of home delivery group } * \text{ \# of people in home delivery group}}{\text{\# virally suppressed home delivery group}}\right) - \left(\frac{\text{Avg. total } CO_2 \text{ emissions of clinic group } * \text{ \# of people in clinic group}}{\text{\# virally suppressed in clinic group}}\right)$$

$$= \left(\frac{\left(\frac{7.25}{4} * 2\right) * 81}{71}\right) - \left(\frac{\left(\frac{0.70}{4} * 2\right) * 73}{54}\right)$$

= 3.66 kg extra CO_2 emissions per additional person virally suppressed between home delivery and clinic groups

<u>Modeling 12-month refills:</u>

$$CCE_{12mo} = \left(\frac{\text{Avg. total } CO_2 \text{ emissions of home delivery group } * \text{ \# of people in home delivery group}}{\text{\# virally suppressed home delivery group}}\right) - \left(\frac{\text{Avg. total } CO_2 \text{ emissions of clinic group } * \text{ \# of people in clinic group}}{\text{\# virally suppressed in clinic group}}\right)$$

$$= \left(\frac{\left(\frac{7.25}{4} * 1\right) * 81}{71}\right) - \left(\frac{\left(\frac{0.70}{4} * 1\right) * 73}{54}\right)$$

= 1.83 kg extra CO_2 emissions per additional person virally suppressed between home delivery and clinic groups

v. Additional results

Supplemental Table 2.1. Incremental cost-effectiveness ratio (ICER) and comparative cost-effectiveness (CCE) results for 3-, 6-, and 12-month antiretroviral therapy (ART) resupply scenarios by analytic method for missing data

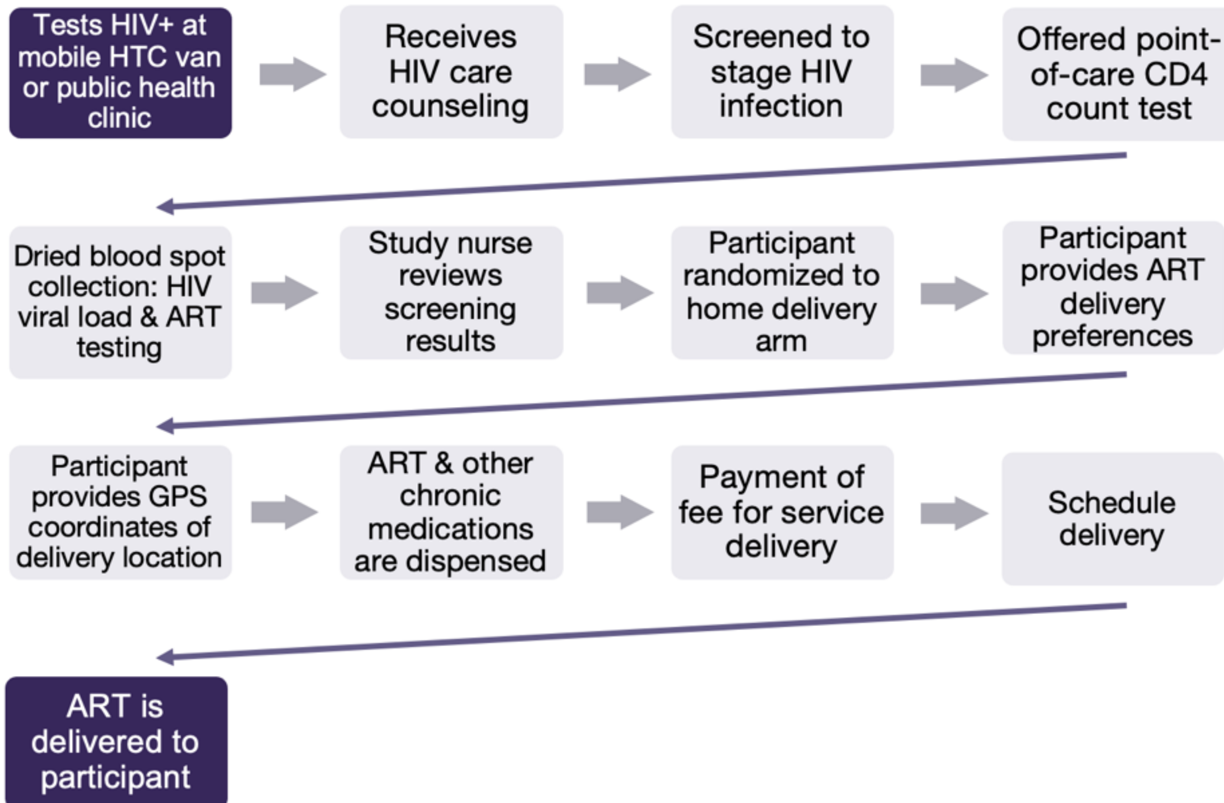
Analytic method for missing data	**Number of ART refill visits included in analysis**	**3-month**			**6-month**			**12-month**		
		ICER	ICER in extra distance driven	CCE	ICER	ICER in extra distance driven	CCE	ICER	ICER in extra distance driven	CCE
Complete case analysis	518	47.87	259	7.32	23.94	129	3.66	11.97	65	1.83
Imputing clinic names	523	47.73	258	7.30	23.86	129	3.65	11.93	64	1.82
Imputing clinic names + transport mode	600	46.49	251	7.07	23.24	126	3.53	11.62	63	1.77

Note: The ICER is reported in $kgCO_2$ per additional person virally suppressed through home delivery. The CCE is reported in $kgCO_2$ extra emissions per additional person virally suppressed through home delivery.

APPENDIX C: Methodology and Supplemental Materials for Chapter 3

i. Narrative summary of Deliver Health Study activities

The Deliver Health Study was conducted between October 2019 and December 2020. This narrative summary of activities was compiled by Ashley Tseng and Xolani Ntinga, and used to guide the costing work.



Supplemental Figure 3.1. Flow map of home-delivered ART resupply steps in the Deliver Health Study

Supplemental Table 3.1. Narrative description of Deliver Health Study antiretroviral therapy (ART) refill activities administered through the Human Sciences Research Council (HSRC) in Sweetwaters, KwaZulu-Natal, South Africa

Study activity	Deliver Health Study ART refill method	
	Home delivery	**Clinic-based**
Supply chain	HSRC has a memorandum of understanding with the South Africa National Department of Health (NDOH) where they provide HSRC with HIV test kits and ART. The Deliver Health Study purchased all supplies for point-of-care tests including PIMA machines and PIMA cartridges (to measure CD4 cell counts) and blood collection tubes (to measure HIV viral load and determine viral suppression). The study had two dedicated HSRC fleet vehicles: a fleet bus (mobile clinic) and a Ford Ranger or similar vehicle (if only home delivery was needed).	The South Africa NDOH provided all public health facilities with ART and other medications, and all the resources the clinics used (e.g., computers, supplies).
Community sensitization and study recruitment	The Deliver Health Study worked with local HIV clinics to establish procedures for registration of ART clients, ART supply procurement, and clinic referrals when needed for the community-based participants.[1] Recruitment at HIV clinics: Outreach for recruitment was conducted by study staff at five public health clinics to identify people living with HIV and who may be engaged in care. If individuals were interested in participating in the study, then they were given the Deliver Health Study phone number to send a "please call me" request. Upon receiving the request, a study staff member would call the individual to provide more information about the study. Recruitment at community-based venues: The Deliver Health Study team conducted community mobilization talks with groups of community members to encourage HIV testing through discussions around HIV and HIV testing at taxi ranks, taverns, and other community hotspots.	
Training	All study staff were trained in all study activities. Over the course of one work week, the Deliver Health Study data manager and research coordinator administered trainings at HSRC on data collection (e.g., how to use REDCap, how to complete case report forms in REDCap, how to set up REDCap on a mobile device, how to use the GPS devices for home delivery) and on the following study activities: • Home HIV testing and counseling • Mobile HIV testing and counseling • CD4 testing • Dried blood spot card collection • Blood tube collection • Interpretation of screening tests In implementation, the study nurse primarily focused on clinical activities.	
Enrollment	Participants who were HIV-positive and ART-eligible according to national guidelines (2023 ART Clinical Guidelines for the Management of HIV in Adults, Pregnancy and Breastfeeding, Adolescents, Children, Infants and Neonates) were eligible to continue with enrollment. Each potential study participant provided written informed consent to the study. Participants were provided with a unique identifier to enable tracking of participants through each stage of the continuum of care (testing, visiting a clinic, initiating ART, monitoring, and collecting ART refills).	

Randomization	Randomization was stratified by community or clinic and blocked to ensure balance. The randomization sequence was designed at the University of Washington International Clinical Research Center (ICRC) and programmed into the mobile phone for each participant/household enrolled. The randomization arm was not determined until the participant had completed all screening procedures. For participants who were already engaged in HIV care at a public health clinic, study staff informed the clinic that the participant was not lost to follow-up but would be working with HSRC for the Deliver Health Study. Participants in the fee for delivery arm received tailored ART delivery to their location of choice (home, work, etc.). At the randomization visit, the following procedures took place: • Participant completed the detailed delivery preferences questionnaire • Staff collected GPS coordinates of the delivery location • Nurse dispensed ART and other chronic medications • Staff collected payment of the fee for service delivery* • Scheduled delivery for 1 month follow-up visit *Nominal fee on a tiered system based on socio-economic status (ZAR 20-150 = USD 0.75-12). An invoice was provided to each participant. Cash received was logged and stored in a secure lock box. If delivery fees were not paid by month 5, then a 20-day notice was given and the participant was transferred back to ART collection at the clinic.	Randomization was stratified by community or clinic and blocked to ensure balance. The randomization sequence was designed at the University of Washington ICRC and programmed into the mobile phone for each participant/household enrolled. The randomization arm was not determined until the participant had completed all screening procedures. At randomization, for participants who were not currently taking ART, the study nurse followed local guidelines on 'test and treat' for HIV and supplied ART and a referral to the clinic. If the participant was currently taking ART, the study nurse documented the clinic the participant was receiving care from.
ART dispensation	Study nurses dispensed ART (TDF/FTC/EFV: Tenofovir/Emtricitabine/Efavirenz [Atripla/FDC]) and any other chronic medications the participants were taking. For participants who were already engaged in HIV care at baseline, the study nurse went to the clinics to verify active participant engagement in care and check what other medications they were on, then dispensed all medications at HSRC and loaded onto the home delivery vehicle.	The pharmacist at each public health clinic dispensed ART and any other medications.
ART refill visits at months 1, 3, 6, and exit	Participants in the fee for delivery arm had visits at 1 month and 3 months after enrollment to deliver their medication. At each follow up visit, the following procedures took place: • Completed health questionnaire • Dispensed medication (ART and other chronic medications) • Blood draw for HIV viral load testing • Took dried blood spots	Participants received an optimized ART linkage package, including a clinic referral card to support linkage to ART. At months 1 and 3, participants randomized to the clinic arm received a phone call to record if the participant had visited the clinic, initiated ART (if not already on ART at

<table>
<tr><td></td><td>Measured CD4 counts with PIMA cartridges and PIMA machine
Scheduled following visit
The Deliver Health Study home-delivery team comprised of 3 staff members: 1 nurse, 1 driver/data collector, and 1 data collector. Later in the study (during the first COVID-19 wave in South Africa), the home-delivery team was reduced to a team of 1 due to COVID-19 restrictions – the nurse also became a driver and data collector.[2] The team made home deliveries 3 days per week.</td><td>enrollment), and if they had picked up their refills while at the clinic.</td></tr>
<tr><td>Chart abstractions</td><td>The study team reviewed participant medical records at clinics to record any visits to the clinic and the reason.</td><td>Clinic chart abstractions included the following information: patient name, date of birth, next ART pickup dates, what medication they were on.</td></tr>
<tr><td>Study exit</td><td>At the in-person exit visit, either at a community location in the mobile van or at the participant's home, the following procedures took place:
Completed health questionnaire (uptake of HIV care, clinic visits, ART initiation, ART adherence barriers to care)
Completed acceptability questionnaire on home delivery
Dispensed medication (ART and other chronic medications)
Blood draw for HIV viral load testing (up to 6mL), the results of which was provided to participants to support their HIV care
Referral to a public health clinic
For people living with HIV who were <u>newly diagnosed</u> in the study: after the study concluded, study staff referred these individuals to a public health clinic and notified the clinics of new diagnoses, providing the selected clinic with study clinical records
For people living with HIV who <u>already knew their HIV status</u> at baseline: these individuals "exited" their clinic care during participation in the study and resumed standard clinic care after the study ended, providing clinics with study clinical records</td><td>At the in-person exit visit, either at a community location in the mobile van or at the participant's home, the following procedures took place:
Health questionnaire (uptake of HIV care, clinic visits, ART initiation, ART adherence barriers to care)
Blood draw for HIV viral load testing (up to 6mL), the results of which was provided to participants to support their HIV care</td></tr>
</table>

ii. Optimized home delivery algorithm

Clients randomized to the home-delivered ART and monitoring arm provided their delivery preferences and paid a one-time fee for the home delivery service at the baseline visit (or a following visit if the client was unable to pay at baseline). A novel feature of the Deliver Health Study was that an algorithm was developed in collaboration with Amazon data scientists to generate optimized driving routes for the home delivery of ART [38]. The algorithm solved the "travelling salesman problem" [101] to optimize the weekly deliveries and considered the following parameters: participants who will run out of ART in the next month, participant locator information (address or geographic coordinates of their pre-specified delivery location, usually the home), and participant availability. Delivery preferences were based on pre-specified days and time windows during which the study team planned for home deliveries, specifically on Tuesdays and Thursdays between 10:00 AM and 7:00 PM and Saturdays between 8:00 AM and 4:00 PM. The nominal service fee for home delivery was determined through community engagement and based on a tiered system proportional to the client's income level, self-reported at study enrollment. If delivery fees were not paid by month 5, then a 20 days' notice was given, and the client was transferred to ART collection at a public health clinic. All participants received follow-up calls and reminders from the study staff.

iii. Detailed methods for costing of clinic-based ART refills and care

To estimate costs for clinic-based care, I obtained actual spending values for KwaZulu-Natal province for financial years 2019 and 2020 from the South African National Treasury [81]. In South Africa, the financial year period occurs from April 1 to March 31 in the following year. In order to mirror the 15-month period of implementation in the Deliver Health Study for a more accurate cost comparison, I estimated clinic financial year 2019 costs for the 6-month period of October 1, 2019-March 31, 2020 and financial year 2020 costs for the 9-month period of April 1-December 31, 2020. I multiplied the 15-month total estimate by 0.8 to scale to a 12-month (annual) estimate.

For training, vehicles, equipment, building, utilities, personnel, drugs, laboratory and clinical supplies, and miscellaneous costs, I used the 2020 HIV/AIDS Component of the HIV, TB, Malaria and Community Outreach Grant report [11] to obtain the proportion of comprehensive HIV/AIDS program that was spent on ART-related care and applied that proportion to the value of each costing category. Spending on ART care in KwaZulu-Natal for 2019-2020 was estimated to be ZAR 4,206,397 and spending on the comprehensive HIV/AIDS program in KwaZulu-Natal for 2019-20 was approximately ZAR 5,206,664, thus the proportion of ART care of the comprehensive HIV/AIDS program in KwaZulu-Natal for 2019-2020 was ZAR $\frac{4{,}206{,}397}{5{,}206{,}664} = 0.8079$.

iv. Detailed methods for costing of clinic-based ART refills and care

To estimate costs for clinic-based care, I obtained actual spending values for KwaZulu-Natal province for financial years 2019 and 2020 from the South African National Treasury.[81] In

South Africa, the financial year period occurs from April 1 to March 31 in the following year. In order to mirror the 15-month period of implementation in the Deliver Health Study for a more accurate cost comparison, I estimated clinic financial year 2019 costs for the 6-month period of October 1, 2019-March 31, 2020 and financial year 2020 costs for the 9-month period of April 1-December 31, 2020. I multiplied the 15-month total estimate by 0.8 to scale to a 12-month (annual) estimate.

For training, vehicles, equipment, building, utilities, personnel, drugs, laboratory and clinical supplies, and miscellaneous costs, I used the 2020 HIV/AIDS Component of the HIV, TB, Malaria and Community Outreach Grant report[11] to obtain the proportion of comprehensive HIV/AIDS program that was spent on ART-related care and applied that proportion to the value of each costing category. Spending on ART care in KwaZulu-Natal for 2019-2020 was estimated to be ZAR 4,206,397 and spending on the comprehensive HIV/AIDS program in KwaZulu-Natal for 2019-20 was approximately ZAR 5,206,664, thus the proportion of ART care of the comprehensive HIV/AIDS program in KwaZulu-Natal for 2019-2020 was ZAR $\frac{4,206,397}{5,206,664} = 0.8079$.

v. Detailed description of outcomes

In the Deliver Health Study, when a client was first diagnosed with HIV and initiated in care, they were prescribed a one-month supply of ART and had a follow-up visit 1 month after their initiation visit. At the month 1 follow-up visit, they received HIV care counseling and were prescribed a two-month supply of ART, and had their next follow-up visit two months later. At the month 3 follow-up visit, they were prescribed a 3-month supply of ART and had follow-up refill visits every 3 months thereafter. Thus, the first-year costs of home delivery comprised the initiation visit, month 1, month 3, month 6, and month 9 refill visits. The cost of home-delivered ART refills and monitoring in subsequent years were estimated based on ART refill visits every 3 months for a total of 4 follow-up visits per year. Costs in the first year (start-up costs) and subsequent years were reported for the home delivery intervention, while annual costs were reported for standard clinic-based care since I did not have data on the start-up costs from clinics. The total sum of fees paid by clients for the home delivery service were subtracted from the total programmatic cost.

vi. Costing categories and sources

Supplemental Table 3.2. Home-delivered ART refills and monitoring costing categories and sources

Type of cost	Cost category name	Data year	Data source	Notes
Fixed costs	Hiring	2017	DO ART Study[83]	Discount rate of 3% - assumed hiring was a process that needs to be repeated every few years.
	Training	2017	DO ART Study[83]	Discount rate of 3% - assumed training was a process that needs to be repeated every few years.
	Community outreach/ mobilization	2017	DO ART Study[83]	
	Vehicles	2014, 2015, and 2017	DO ART Study[83]	• Ford Ranger purchased June 15, 2015: annuity factor calculated with a discount rate of 3% and 10 years of useful life. 50% for intervention because only one team (of 3 study staff) that was traveling in one vehicle. • HSRC fleet bus (mobile clinic) purchased June 15, 2014: annuity factor calculated with a discount rate of 3% and 10 years of useful life. 50% for intervention because only one team (of 3 study staff) that was traveling in one vehicle. • Maintenance in 2017 costs: annuity factor calculated with a discount rate of 3% and 1 year of useful life
	Equipment	2016, 2019	DO ART Study[83]; Deliver Health Study[38]	Discount rate of 3%. Assumed the same equipment costs for Deliver Health Study as the DO ART Study. Specific costs from the Deliver Health Study: • Smartphones (Android) • Laptops • GPS trackers
	Building	2016	Human Sciences Research Council (obtained in DO ART Study[83])	Assumed the same building (Human Sciences Research Council) costs for Deliver Health Study as the DO ART Study. Office rental was included at 100% and central office at 10%.
	Utilities	2015	Human Sciences Research Council (obtained in DO ART Study[83])	Data usage was included in this category at 100%; all other cost items are included at 10%.
	Personnel	2017, 2019, 2020	*See notes*	As implemented in Deliver Health Study[38]: • Salaries from Deliver Health Study budget (2019)[38]: Primary Investigator, Study Implementation, Study Coordinator, Driver, Research Assistant, Data Collector • All other salaries from DO ART Study (2017)[83]: Study Nurse, Community Outreach Worker, Data Specialist, Study Logistics, Human Resources, Accountant As implemented by the South African National Department of Health: • Professional Nurse Grade 2 (General Nursing) salary (notch 4, full-time) from FY2019 SA DPSA salary data[80]: ZAR 342,033

				• All other salaries from DO ART Study (2017)[83]: Senior Program Manager, Team Leader, Community Outreach Worker, Human Resources, Accountant, Driver, Data Specialist *Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
Variable costs	Drugs	2024	South African National Department of Health Master Health Product List January 2024[102]	All participants in the Deliver Health Study were on the TDF/FTC/EFV (Tenofovir/Emtricitabine/Efavirenz or Atripla/FDC) ART regimen which is one tablet taken once orally daily[103] The cost of ART drugs is negotiated through a tender process with the South African National Department of Health and are fixed for a number of years, thus I did not adjust the ART costs for inflation.[82] This was the only item for which did not adjust for inflation. *Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Labs	2016	DO ART Study[83]	Assumed the same lab consumables costs for Deliver Health Study as the DO ART Study. *Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Materials and clinical supplies	2016	DO ART Study[83]	Assumed the same clinical supplies costs for Deliver Health Study as the DO ART Study. *Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Fuel	2019	*See notes*	• Distance calculations using data from the Deliver Health Study[38] • Diesel prices from November 2019[104] • Estimated fuel efficiency of Ford Ranger (km/L)[64] *Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Administrative overhead	2019	Deliver Health Study[38]	8% of all costs except for ART.
Fees	Fee for home delivery service	2019	Deliver Health Study[38]	Clients in the home delivery arm paid a one-time fee for the home delivery service at the baseline/randomization visit. The fee was determined based on a sliding scale proportional to the client's income (self-reported at study enrollment). The total sum of fees paid by clients and subtract that from the total programmatic cost (before dividing by the # of clients and # of virally suppressed clients).

Cost estimation steps for home-delivered ART refills and monitoring:

1. For all costs reported in ZAR (except for ART drugs), they were first inflation-adjusted using the World Bank GDP implicit deflator for South Africa[77] from the year the data were collected to 2022 ZAR, then converted to 2022 USD based on the average ZAR to USD exchange rate in 2022.[78] For costs reported in USD, they were inflation-adjusted to 2022 USD using the United States annual average Consumer Price Index.[79]
2. Calculating average annual costs:
    a. Cost per client: I divided the total cost by the number of participants in the home-delivery group of the Deliver Health Study with successful follow-up (81 participants)
        i. Note: The total sum of fees paid by clients in the home-delivery group of the Deliver Health Study (ZAR 4686 or US $286) was deducted from the sum of fixed and variable costs to obtain the total cost
    b. Cost per client virally suppressed: I divided the total cost by the number of participants in the home-delivery group of the Deliver Health Study with successful follow-up and who were virally suppressed at study exit (71 participants)
        i. Note: The total sum of fees paid by clients in the home-delivery group of the Deliver Health Study (ZAR 4686 or US $286) was deducted from the sum of fixed and variable costs to obtain the total cost

Supplemental Table 3.3. Clinic-based ART refills and care costing categories and sources

Type of cost	Cost category name	Data year	Data source	Notes
Fixed costs	Hiring			Assuming that hiring costs were included in "Training and development"
	Training	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Training and development
	Community outreach/ mobilization	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Advertising • Communication (G&S)
	Vehicles	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Fleet services (including government motor transport) • Rental and hiring • Transport provided: Departmental activity
	Equipment	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Other machinery and equipment • Minor assets • *Transport equipment (ZAR 0 for 2019/2020)*
	Building	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Operating leases • Property payments • *Venues and facilities (ZAR 0 for 2019/2020)*
	Utilities	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Operating payments
	Personnel	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Salaries and wages • Social contributions • Agency and support / outsourced services • Contractors • *Consultants and professional services: Business and advisory services (ZAR 0 for 2019/2020)*

Variable costs	Drugs	2024	South African National Department of Health Master Health Product List January 2024[102]	I assumed the only ART regimen being used was TDF/FTC/EFV to properly estimate costs relative to the Deliver Health Study (all participants in the Deliver Health Study were on the TDF/FTC/EFV regimen). I had the cost of TDF/FTC/EFV from the South African National Department of Health Master Product List from January 2024, which was ZAR 287.57 for 84 tablets. The cost of ART drugs is negotiated through a tender process with the South African National Department of Health and are fixed for a number of years, thus I did not adjust the ART costs for inflation (Meyer-Rath et al., 2019). This was the only item for which did not adjust for inflation. All other costs were inflated to 2022 ZAR, then converted from 2022 ZAR to 2022 USD. Notes: The spreadsheet downloaded from Vulekamali included an "Inventory: Medicine" expense category under the HIV/AIDS program, but I opted to use the cost of TDF/FTC/EFV from the NDOH because the "Inventory: Medicine" category could have included other HIV-related non-ART medicines (e.g., PrEP) which would overestimate the cost of ART intervention only. For the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Labs	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Laboratory services *Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Materials and clinical supplies	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Consumable supplies • Consumable: Stationery, printing and office supplies • Inventory: Clothing material and accessories • Inventory: Materials and supplies • Inventory: Medical supplies • Inventory: Other supplies *Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Administrative overhead	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Administrative fees *Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Miscellaneous	April 1, 2019-March 31, 2020	South African Department of Treasury (Vulekamali)[a,81]	Includes: • Catering: Departmental activities • Travel and subsistence

				*Note: for the 6-month and 12-month refill scenarios, the annual values were divided by 2 and 4, respectively, to account for a reduction in visits from 4 visits per year (for the standard 3-month refill scenario) to 2 visits and 1 visit per year, respectively.
	Fuel			Assuming that fuel costs were included in the "Vehicles" category

[a]Extracted value for HIV/AIDS program in KwaZulu-Natal for 2019 and 2020 from the "Budgeted and Actual Provincial Expenditure" spreadsheet downloaded from Vulekamali. The period of coverage for the 2019 financial year is April 1, 2019-March 31, 2020. The period of coverage for the 2020 financial year is April 1, 2020-March 31, 2021. Vulekamali pulls data from the Estimates of Provincial Revenue and Expenditure (EPRE) tables published on the South African National Treasury website.

Cost estimation steps for clinic-based ART refills and care:

1. For training, vehicles, equipment, building, utilities, personnel, drugs, labs, clinical supplies, and miscellaneous costs, I used the 2020 HIV/AIDS programme spending report[11] to obtain proportion of comprehensive HIV/AIDS program that was spent on ART-related care, and applied that proportion to the value of each costing category:
    a. Spending on ART care in KZN for 2019-20: ZAR 4,206,397
    b. Spending on the comprehensive HIV/AIDS program in KZN for 2019-20: ZAR 5,206,664
    → Proportion of ART care of the comprehensive HIV/AIDS program in KZN for 2019-20: ZAR $\frac{4,206,397}{5,206,664} = 0.8079$
2. For all costs except for ART drugs, they were first inflation-adjusted using the World Bank GDP implicit deflator for South Africa[77] from the year the data were collected to 2022 ZAR, then converted to 2022 USD based on the average ZAR to USD exchange rate in 2022[78]
3. Calculating average annual costs:
    a. Cost per client: I divided the total cost by the number of adults (aged 15 years and older) living with HIV in KwaZulu-Natal
        i. Total number of adults (aged 15 years and older) living with HIV in KwaZulu-Natal in September 2022[71]: 1,925,698 people
    b. Cost per client virally suppressed: I divided the total cost by the number of adults (aged 15 years and older) living with HIV with suppressed viral load in KwaZulu-Natal
        i. I multiplied the estimated proportion of adults (15+) living with HIV with suppressed viral load in South Africa in 2020 (0.66)[105] by the total number of adults (15+) living with HIV in KwaZulu-Natal (1,925,698 people)[71] to obtain the number of adults (15+) living HIV in KwaZulu-Natal estimated to be virally suppressed in 2022: 1,270,961 people

vii. Duration of ART initiation and ART refill visits based on time-and-motion study

As a follow-up to the pilot Deliver Health Study, the SMART ART Study is an ongoing clinical trial in the same study area trialing home delivery of ART and community-based pick-up of ART, in comparison to standard clinic-based refills.[60] A time-and-motion study was conducted in January–February 2023 as part of the SMART ART Study at four public health clinics in the study area and of home delivery refill visits. For our study, I used the SMART ART Study time-and-motion results to inform the duration of ART initiation vs. refill visits. In the time-and-motion study, there were only two home delivery visits observed and both were ART resupply visits, thus I did not have an initiation visit to estimate staff time for. There were 14 clinic observations, 13 of which were ART resupply visits and one was an initiation visit. In terms of total staff time, the one initiation visit took 1 hour 19 minutes, compared to an average of 24 minutes and 42 seconds across the 13 refill visits at clinics. Therefore, I assumed an ART initiation visit (which includes HIV counselling) would take 3 times as long as an ART refill visit.

viii. As-observed scenario summary

In the Deliver Health Study, the team made home deliveries 3 days per week and the average time spent driving per delivery trip was 91.07 minutes. The start/end location was the Human Sciences Research Council (HSRC) office in Sweetwaters, KwaZulu-Natal, South Africa. The Deliver Health Study home-delivery team comprised of 3 staff members: 1 nurse, 1 driver/data collector, and 1 data collector. The data collectors and study nurse recruited participants in the Deliver Health Study. There were no community outreach workers working on participant recruitment for the study outside of the data collectors and study nurse who were already hired with the Deliver Health Study team. Later in the study (during the first COVID-19 wave in South Africa), the home-delivery team was reduced to a team of 1 due to COVID-19 restrictions – the nurse also became a driver and data collector. The team made home deliveries 3 days per week.

ix. Programmatic scenario of home-delivery intervention assumptions

In the programmatic scenario of the home-delivery intervention, I assumed the following:

- No data collector in programmatic implementation (since it is a research-specific role)
- Dedicated community outreach worker to recruit people living with HIV
- Home-delivery team of 2 individuals: 1 nurse and 1 driver
- 40-hour work weeks (8 hours per day, 5 days per week)
    - 6 hours for home deliveries
    - 1 hour to prepare/load delivery vehicle
    - 1 hour to unload delivery vehicle after

Supplemental Table 3.4. Percent of staff time spent on the home delivery of antiretroviral therapy intervention in the Deliver Health Study

Deliver Health Study position title	Equivalent position title based on South Africa National Department of Health salaries	Number of staff	% of total working hours spent on home delivery intervention	Assumptions
Study Nurse	Professional Nurse (Grade 2, General Nursing, notch 4)	1	27%	Calculation: $(91.07\ \text{minutes}/60) * 3\ \text{days per week}) + ((1\ \text{hour pre} - \text{home deliveries} + 1\ \text{hour post} - \text{home deliveries}) * 3\ \text{days per week})) / (40\ \text{hours per week}) = 27\%$
Driver	Driver	1	27%	Calculation: $(91.07\ \text{minutes}/60) * 3\ \text{days per week}) + ((1\ \text{hour pre} - \text{home deliveries} + 1\ \text{hour post} - \text{home deliveries}) * 3\ \text{days per week})) / (40\ \text{hours per week}) = 27\%$
Community Outreach Worker	Community Outreach Worker	1	25%	Works for HSRC to help with participant recruitment into the Deliver Health Study. Assumed 25% of their total working hours were spent on participant recruitment for the Deliver Health Study.
Study Coordinator	Team Leader	1	25%	Assumed 25% of total working hours on the Deliver Health Study were spent directly on managing the home deliveries.
Human Resources	Human Resources	1	5%	Works for HSRC to help with hiring of study staff (e.g., advertising position, compiling paperwork, etc.)
Accountant	Accountant	1	5%	Works for HSRC to help with ordering study supplies, manage budgets, etc.

x. Converted cost estimates from the literature to 2022 USD

Cost estimates from the literature were inflation-adjusted to 2022 USD using the United States annual average Consumer Price Index[79] for comparability to our study estimates.

Supplemental Table 3.5. Barnabas et al. 2020 DO ART Study estimates of South Africa[83]

Cost estimate	Original Cost (reported in 2018 USD)	GDP Inflator from 2018 to 2022 USD	Total Cost in 2022 USD
Midlands KZN annual cost per client (first year), community-based ART, steady-state (programmatic) scenario	523.00	1.17	610
Midlands KZN annual cost per client (subsequent years), community-based ART, steady-state (programmatic) scenario	427.00	1.17	498
Midlands KZN annual cost per client virally suppressed (first year), community-based ART, steady-state (programmatic) scenario	759.00	1.17	885
Midlands KZN annual cost per client virally suppressed (subsequent years), community-based ART, steady-state (programmatic) scenario	678.00	1.17	790
Midlands KZN annual cost per client (subsequent years), facility-based ART, efficient at-scale scenario	249.00	1.17	290
Midlands KZN annual cost per client virally suppressed (subsequent years), facility-based ART, efficient at-scale scenario	422.00	1.17	492
Midlands KZN annual cost per client (first year), community-based ART, efficient at-scale scenario	312.00	1.17	364
Midlands KZN annual cost per client (subsequent years), community-based ART, efficient at-scale scenario	246.00	1.17	287
Midlands KZN annual cost per client virally suppressed (first year), community-based ART, efficient at-scale scenario	452.00	1.17	527
Midlands KZN annual cost per client virally suppressed (subsequent years), community-based ART, efficient at-scale scenario	390.00	1.17	455

Supplemental Table 3.6. Meyer-Rath et al. 2019 estimates of South Africa[82]

Annual cost per client	Original Cost (reported in 2018 USD)	GDP Inflator from 2018 to 2022 USD	Total Cost in 2022 USD
Midlands KZN (first year)	249.00	1.17	290

Supplemental Table 3.7. Guthrie et al. 2022 estimates of Uganda[106]

Cost estimate	Original Cost (reported in 2018 USD)	GDP Inflator from 2018 to 2022 USD	Total Cost in 2022 USD
SOC Facility-based individual management (FBIM) annual cost per client (first year)	157.93	1.17	184
SOC Facility-based individual management (FBIM) annual cost per client (second year)	152.49	1.17	178
Community drug distribution points (CDDP) annual cost per client virally suppressed (first year)	166.85	1.17	194
Community drug distribution points (CDDP) annual cost per client virally suppressed (second year)	146.42	1.17	171

Supplemental Table 3.8. Prust et al. 2017 estimates of Malawi[107]

Total ART costs per patient	Original Cost (reported in 2016 USD)	GDP Inflator from 2016 to 2022 USD	Total Cost in 2022 USD
Facility-based multi-month scripting (MMS): 3-month scripts	121.41	1.22	148

Supplemental Table 3.9. Benade et al. 2023 estimates of Zimbabwe[84]

Total average annual cost of HIV treatment per patient	Original Cost (reported in 2020 USD)	GDP Inflator from 2020 to 2022 USD	Total Cost in 2022 USD
Community ART refill groups with 3-month dispensing	178.00	1.13	201
Community ART refill groups with 6-month dispensing	167.00	1.13	189

Supplemental Table 3.10. Nichols et al. 2021 estimates of Lesotho[85]

Average total annual cost of providing HIV care and treatment per patient	Original Cost (reported in 2018 USD)	GDP Inflator from 2018 to 2022 USD	Total Cost in 2022 USD
3-month facility-based arm	122.28	1.17	143
3-month community adherence groups	114.20	1.17	133
6-month community ART distribution	112.58	1.17	131

xi. Total annual cost of home-delivered ART under different scenarios

I estimated annual total programmatic cost based on National Department of Health costs and varied the salary sources and refill scripts. The total annual programmatic with 3-month refills was $103,486 (**Supplemental Table 3.11**). In the 6-month refill script scenario with NDoH staff salaries, the total annual cost decreased to $69,113. In the 12-month refill script scenario with NDoH staff salaries, the total annual cost further decreased to $59,652. Scaling up the home delivery intervention increased total costs to $136,992 with 3-month refills, to $118,866 annually with 6-month refills, and to $121,467 annually with 12-month refills.

Supplemental Table 3.11. Estimated total annual cost of home-delivered ART under different programmatic scenarios

Programmatic Scenario	**Total annual cost**	
	2022 ZAR	2022 USD
Programmatic costs with 3-month refills[a]	1,053,454	64,336
Programmatic costs with 6-month refills	811,139	49,538
Programmatic costs with 12-month refills	669,115	40,864
At-scale programmatic costs with 3-month refills[a]	1,602,080	97,842
At-scale programmatic costs with 6-month refills	1,350,519	82,478
At-scale programmatic costs with 12-month refills	1,438,355	87,843

[a]The standard-of-care in South Africa is 3-month ART refills at clinics.

xii. Average annual per-client costs of home-delivered ART under different scenarios

The average annual Deliver Health Study costs per client and per client virally suppressed for quarterly refills in the first year of intervention are shown in **Supplemental Table 3.12**. Using staff salaries from the Deliver Health Study, the average annual cost per client and per client virally suppressed of home-delivered ART was $1,260 and $1,437, respectively, compared to $1,240 and $1,415, respectively, when substituting study expenses for NDoH costs.

Supplemental Table 3.12. Estimated average annual costs of home-delivered ART under different implementation scenarios for quarterly refills in the first year of implementation

Scenario	**Average annual cost per client**		**Average annual cost per client virally suppressed**	
	2022 ZAR	2022 USD	2022 ZAR	2022 USD
With Deliver Health Study costs[a]	13,414	819	15,303	935
With NDOH costs + staff salaries from the Deliver Health Study[a]	13,087	799	14,930	912

[a]The standard-of-care in South Africa is 3-month ART refills at clinics.

xiii. Total annual programmatic cost

The total annual cost of home delivery was $103,486 for the first year of intervention and $96,996 for subsequent years (**Supplemental Table 3.13**). In comparison, standard clinic-based ART refills and care was estimated to cost a total of $322,205,262 annually across KwaZulu-Natal.

Supplemental Table 3.13. Total annual cost by ART refill method

Cost category	**Total annual cost**					
	Home delivery[a]				**Clinic**[c,d]	
	First year[b]		Subsequent years			
	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD
ART drugs	93,173	5,690	93,173	5,690	2,215,091,895	135,279,397
Buildings and administrative overhead	177,270	10,826	169,399	10,345	111,898,308	6,833,818
Communication	102,798	6,278	102,798	6,278	11,480,557	701,137
Equipment	97,189	5,936	12,181	744	3,402,951	207,824
Hiring and training	53,179	3,248	53,179	3,248	4,662,669	284,757
Materials and supplies	61,017	3,726	47,819	2,920	1,080,307,255	65,976,185
Personnel wages and benefits	352,713	21,541	352,713	21,541	1,848,506,990	112,891,438
Vehicles and fuel	120,799	7,377	120,609	7,366	502,772	30,705
Total	1,053,454	64,336	947,185	57,846	5,275,853,397	322,205,262

[a]There were 81 people living with HIV on ART in the home-delivered ART refills group of the Deliver Health Study.
[b]Includes startup costs.
[c]The standard-of-care in South Africa is 3-month ART refills at clinics.
[d]The total number of adults (aged 15 years and older) living with HIV in KwaZulu-Natal in September 2022 was 1,925,698 people. Source: UNAIDS HIV sub-national estimates viewer.

xiv. Cost drivers for the programmatic, 6-month refill scenario

Increasing the ART refill scripts from 3- to 6-month refills, the ordering of top largest costs were unchanged with personnel wages and benefits still the largest cost, followed buildings and administrative overhead and vehicles and fuel (**Supplemental Table 3.14**).

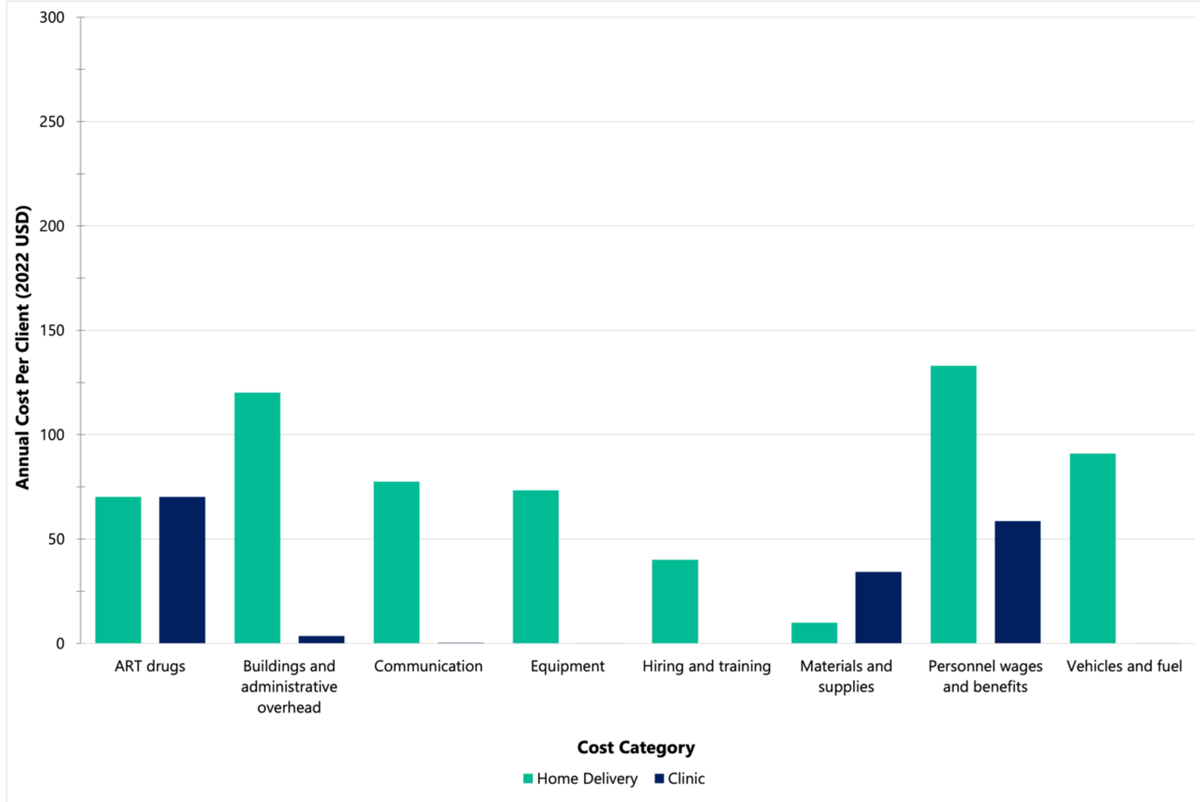
Supplemental Table 3.14. Average annual cost per client and per client virally suppressed for home-delivered and clinic-based ART refills under the programmatic 6-month refills scenario

Cost category	Average annual cost per client						Average annual cost per client virally suppressed					
	Home delivery[a]				Clinic[c,d] N=1,925,698		Home delivery[e]				Clinic[c,d] N=1,270,961	
	First year[b] N=81		Subsequent years N=81				First year[b] N=71		Subsequent years N=71			
	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD
	Cost (% of total cost)											
ART drugs	1,150 (11)	70 (11)	1,150 (12)	70 (12)	1,150 (42)	70 (42)	1,312 (18)	80 (18)	1,312 (20)	80 (20)	1,743 (42)	106 (42)
Buildings and administrative overhead	1,967 (20)	120 (20)	1,917 (21)	117 (21)	58 (2)	4 (2)	2,244 (30)	137 (30)	2,187 (33)	134 (33)	88 (2)	5 (2)
Communication	1,269 (13)	78 (13)	1,269 (14)	78 (14)	6 (0.22)	0.36 (0.22)	1,448 (20)	88 (20)	1,448 (22)	88 (22)	9 (0.22)	0.55 (0.22)
Equipment	1,200 (12)	73 (12)	150 (2)	9 (2)	2 (0.06)	0.11 (0.06)	1,369 (19)	84 (19)	172 (3)	10 (3)	3 (0.06)	0.16 (0.06)
Hiring and training	657 (7)	40 (7)	657 (7)	40 (7)	2 (0.09)	0.15 (0.09)	749 (10)	46 (10)	749 (11)	46 (11)	4 (0.09)	0.22 (0.09)
Materials and supplies	163 (2)	10 (2)	590 (6)	36 (6)	561 (20)	34 (20)	186 (3)	11 (3)	674 (10)	41 (10)	850 (20)	52 (20)
Personnel wages and benefits	2,177 (22)	133 (22)	2,177 (23)	133 (23)	960 (35)	59 (35)	2,484 (34)	152 (34)	2,484 (38)	152 (38)	1,454 (35)	89 (35)
Vehicles and fuel	1,489 (15)	91 (15)	1,484 (16)	91 (16)	0.26 (0.01)	0.02 (0.01)	1,699 (23)	104 (23)	1,693 (26)	103 (26)	0.40 (0.01)	0.02 (0.01)
Total[f]	10,014	612	9,337	570	2,740	167	7,383	451	6,611	404	4,151	254

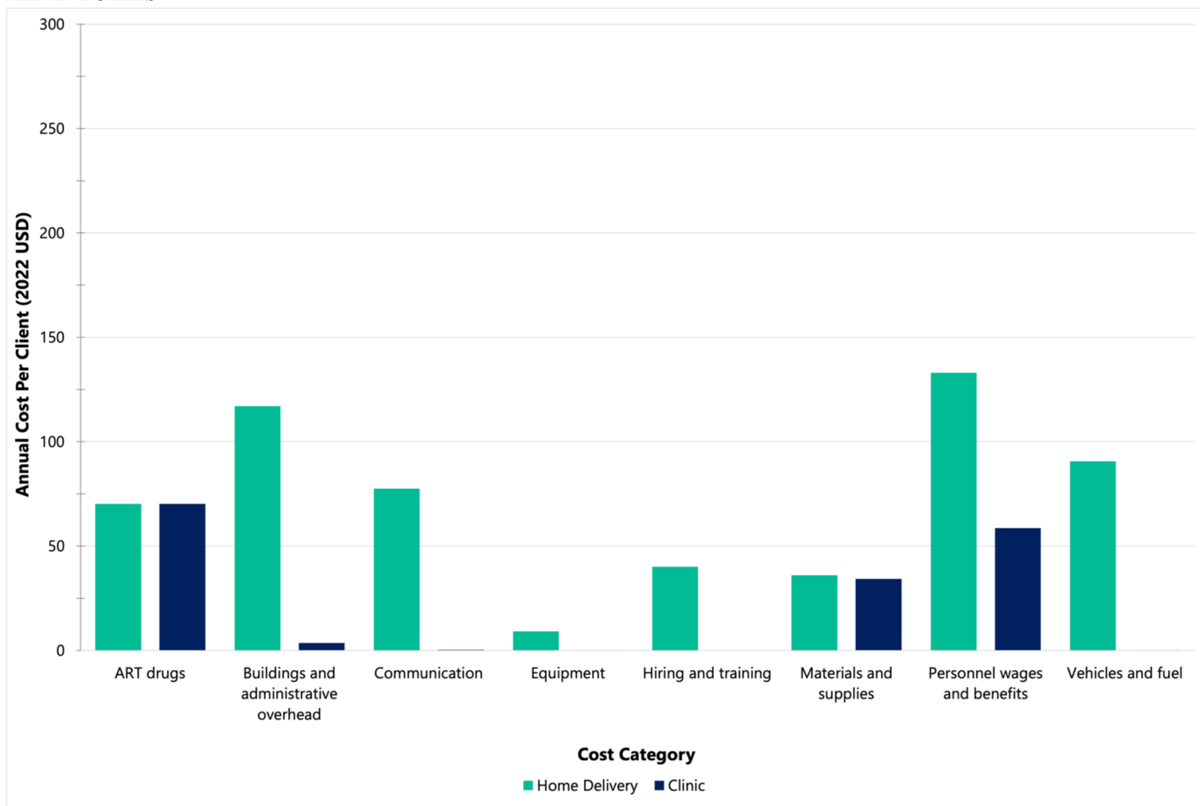
Abbreviations: ART = antiretroviral therapy, ZAR = South African Rand, USD = United States Dollars, HIV = Human Immunodeficiency Virus, UNAIDS = Joint United Nations Programme on HIV/AIDS.
[a]There were 81 people living with HIV on ART in the home-delivered ART refills group of the Deliver Health Study.
[b]Includes startup costs.
[c]The standard-of-care in South Africa is 3-month ART refills at clinics.
[d]The total number of adults (aged 15 years and older) living with HIV in KwaZulu-Natal in September 2022 was 1,925,698 people. Source: UNAIDS HIV sub-national estimates viewer.
[e]There were 71 people living with HIV on ART who were virally suppressed at study exit in the home-delivered ART refills group of the Deliver Health Study.

[f]The average fee for home delivery service, about 4 USD, paid by clients in the home delivery intervention of the Deliver Health Study was subtracted from the programmatic costs of implementing home delivery.

Supplemental Figure 3.2. Average annual cost per client (2022 USD) for 6-month ART refills by cost category in the programmatic NDoH-implemented scenario. The NDoH scenario assumes fixed costs as implemented in the Deliver Health Study and public sector clinical staff salaries instead of study salaries.



Supplemental Figure 3.2.a. Home-delivered ART intervention (first year costs) vs. clinic-based ART refills



Supplemental Figure 3.2.b. Home-delivered ART intervention (subsequent year costs) vs. clinic-based ART refills

xv. Cost drivers for the at-scale 3- and 6-month refill scenarios

When providing home-delivered 3-month ART refills at-scale, personnel wages and benefits were still the greatest cost driver at 37% (**Supplemental Table 3.15**). However, the ordering of the next few costs of the intervention were different than the programmatic scenario. ART drugs were the next largest cost of home delivery at 29%. Notice how the cost proportion of vehicles and fuel is reduced relative to other categories when home delivery is at-scale. The cost of all categories decreased when I increased the number of clients served by home-delivered ART refills.

Supplemental Table 3.15. Average annual cost per client and per client virally suppressed for home-delivered and clinic-based ART refills under the at-scale 3-month refills scenario

Cost category	**Average annual cost per client**						**Average annual cost per client virally suppressed**					
	Home delivery[a]				**Clinic**[c,d] N=1,925,698		**Home delivery**[e]				**Clinic**[c,d] N=1,270,961	
	First year[b] N=367		Subsequent years N=642				First year[b] N=323		Subsequent years N=565			
	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD
	Cost (% of total cost)											
ART drugs	1,150 (26)	70 (26)	1,150 (38)	70 (38)	1,150 (42)	70 (42)	1,307 (26)	80 (26)	1,307 (38)	80 (38)	1,743 (42)	106 (42)
Buildings and administrative overhead	531 (12)	32 (12)	306 (10)	19 (10)	58 (2)	4 (2)	603 (12)	37 (12)	347 (10)	21 (10)	88 (2)	5 (2)
Communication	280 (6)	17 (6)	160 (5)	10 (5)	6 (0.22)	0.36 (0.22)	318 (6)	19 (6)	182 (5)	11 (5)	9 (0.22)	0.55 (0.22)
Equipment	265 (6)	16 (6)	19 (0.63)	1 (0.63)	2 (0.06)	0.11 (0.06)	301 (6)	18 (6)	22 (0.63)	1 (0.63)	3 (0.06)	0.16 (0.06)
Hiring and training	145 (3)	9 (3)	83 (3)	5 (3)	2 (0.09)	0.15 (0.09)	165 (3)	10 (3)	94 (3)	6 (3)	4 (0.09)	0.22 (0.09)
Materials and supplies	753 (17)	46 (17)	590 (20)	36 (20)	561 (20)	34 (20)	856 (17)	52 (17)	671 (20)	41 (20)	850 (20)	52 (20)
Personnel wages and benefits	961 (22)	59 (22)	549 (18)	34 (18)	960 (35)	59 (35)	1,093 (22)	67 (22)	624 (18)	38 (18)	1,454 (35)	89 (35)
Vehicles and fuel	338 (8)	21 (8)	196 (7)	12 (7)	0.26 (0.01)	0.02 (0.01)	385 (8)	23 (8)	223 (7)	14 (7)	0.40 (0.01)	0.02 (0.01)
Total[f]	4,367	267	2,996	183	2,740	167	4,963	303	3,405	208	4,151	254

Abbreviations: ART = antiretroviral therapy, ZAR = South African Rand, USD = United States Dollars, HIV = Human Immunodeficiency Virus, UNAIDS = Joint United Nations Programme on HIV/AIDS.

[a]There were 81 people living with HIV on ART in the home-delivered ART refills group of the Deliver Health Study.

[b]Includes startup costs.

[c]The standard-of-care in South Africa is 3-month ART refills at clinics.

[d]The total number of adults (aged 15 years and older) living with HIV in KwaZulu-Natal in September 2022 was 1,925,698 people. Source: UNAIDS HIV sub-national estimates viewer.
[e]There were 71 people living with HIV on ART who were virally suppressed at study exit in the home-delivered ART refills group of the Deliver Health Study.
[f]The average fee for home delivery service, about 4 USD, paid by clients in the home delivery intervention of the Deliver Health Study was subtracted from the programmatic costs of implementing home delivery.

Supplemental Table 3.16. Average annual cost per client and per client virally suppressed for home-delivered and clinic-based ART refills under the at-scale 6-month refills scenario

Cost category	Average annual cost per client						Average annual cost per client virally suppressed					
	Home delivery[a]				**Clinic**[c,d] N=1,925,698		**Home delivery**[e]				**Clinic**[c,d] N=1,270,961	
	First year[b] N=367		Subsequent years N=642				First year[b] N=323		Subsequent years N=565			
	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD	2022 ZAR	2022 USD
	Cost (% of total cost)											
ART drugs	1,150 (31)	70 (31)	1,150 (40)	70 (40)	1,150 (42)	70 (42)	1,307 (31)	80 (31)	1,307 (40)	80 (40)	1,743 (42)	106 (42)
Buildings and administrative overhead	480 (13)	29 (13)	299 (10)	18 (10)	58 (2)	4 (2)	546 (13)	33 (13)	339 (10)	21 (10)	88 (2)	5 (2)
Communication	280 (8)	17 (8)	160 (6)	10 (6)	6 (0.22)	0.36 (0.22)	318 (8)	19 (8)	182 (6)	11 (6)	9 (0.22)	0.55 (0.22)
Equipment	265 (7)	16 (7)	19 (1)	1 (1)	2 (0.06)	0.11 (0.06)	301 (7)	18 (7)	22 (1)	1 (1)	3 (0.06)	0.16 (0.06)
Hiring and training	145 (4)	9 (4)	83 (3)	5 (3)	2 (0.09)	0.15 (0.09)	165 (4)	10 (4)	94 (3)	6 (3)	4 (0.09)	0.22 (0.09)
Materials and supplies	163 (4)	10 (4)	590 (20)	36 (20)	561 (20)	34 (20)	185 (4)	11 (4)	671 (20)	41 (20)	850 (20)	52 (20)
Personnel wages and benefits	919 (25)	56 (25)	465 (16)	28 (16)	960 (35)	59 (35)	1,045 (25)	64 (25)	528 (16)	32 (16)	1,454 (35)	89 (35)
Vehicles and fuel	336 (9)	21 (9)	191 (7)	12 (7)	0.26 (0.01)	0.02 (0.01)	382 (9)	23 (9)	217 (7)	13 (7)	0.40 (0.01)	0.02 (0.01)
Total[f]	3,681	225	2,900	177	2,740	167	4,183	255	3,296	201	4,151	254

Abbreviations: ART = antiretroviral therapy, ZAR = South African Rand, USD = United States Dollars, HIV = Human Immunodeficiency Virus, UNAIDS = Joint United Nations Programme on HIV/AIDS.
[a]There were 81 people living with HIV on ART in the home-delivered ART refills group of the Deliver Health Study.
[b]Includes startup costs.
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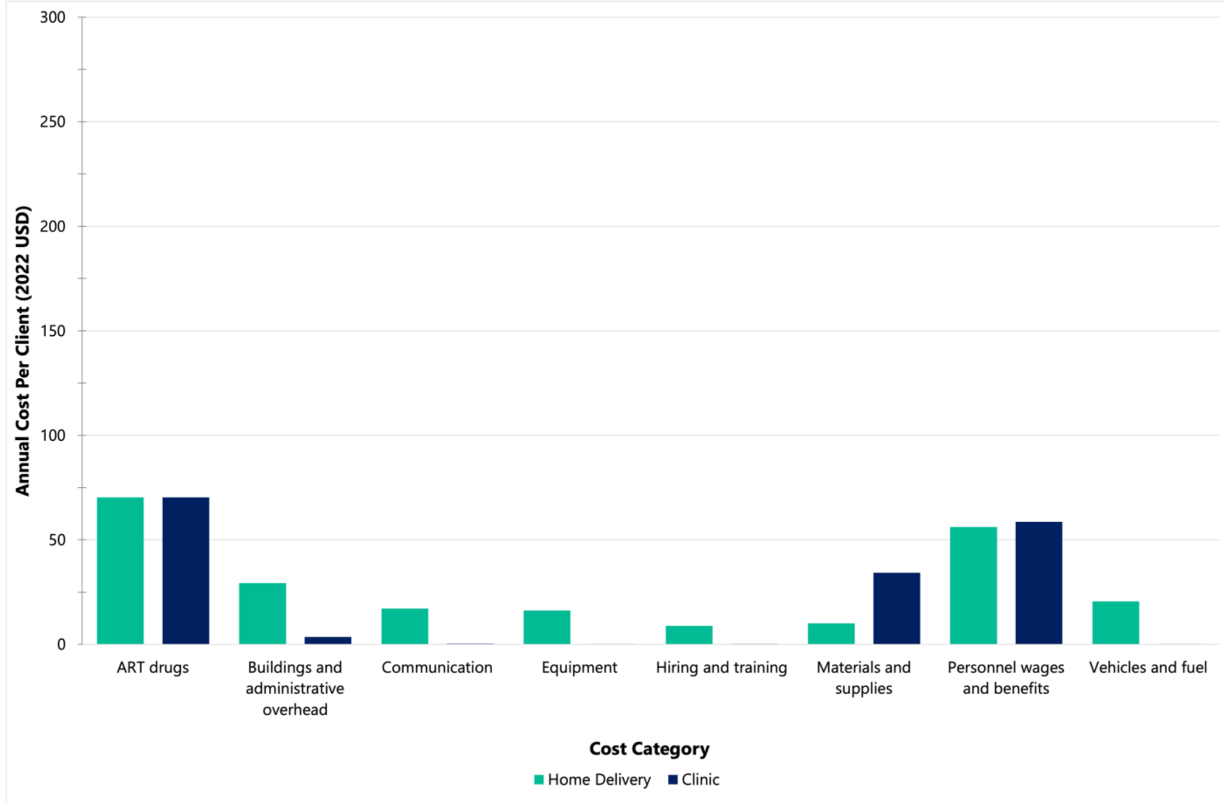
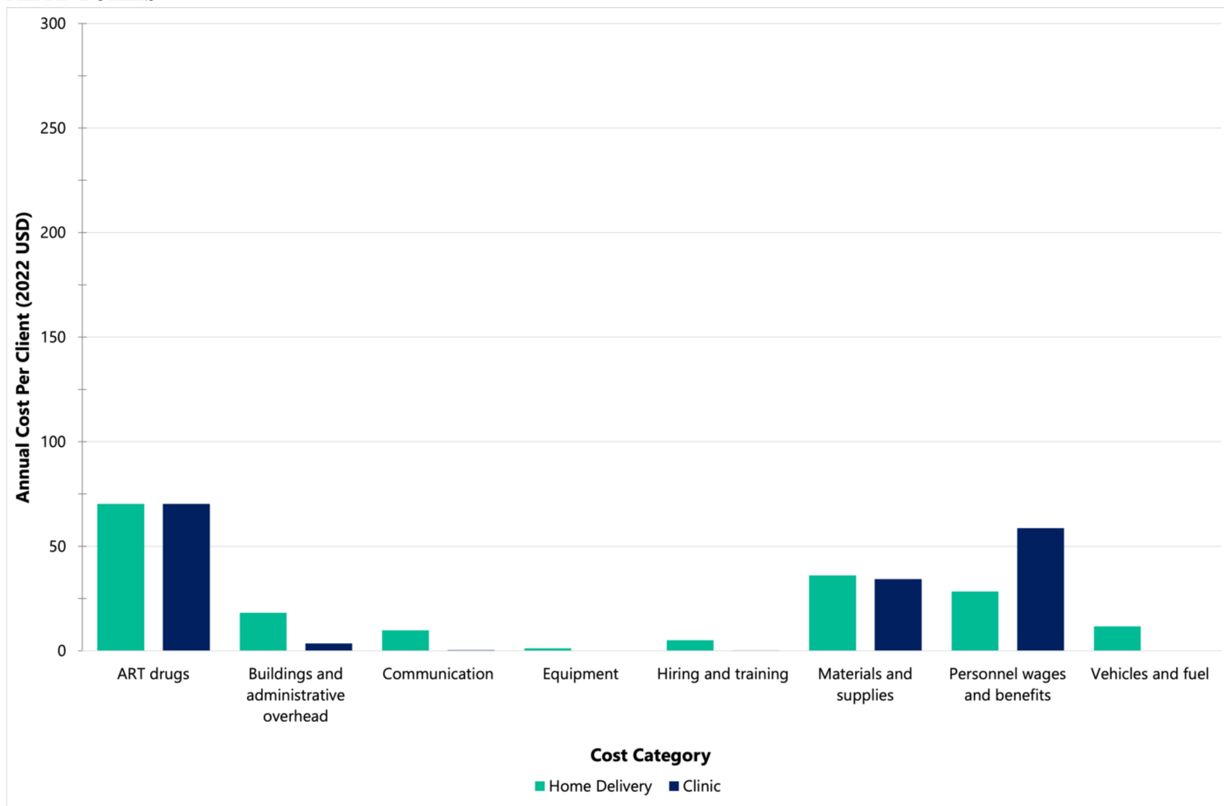
[d]The total number of adults (aged 15 years and older) living with HIV in KwaZulu-Natal in September 2022 was 1,925,698 people. Source: UNAIDS HIV sub-national estimates viewer.
[e]There were 71 people living with HIV on ART who were virally suppressed at study exit in the home-delivered ART refills group of the Deliver Health Study.
[f]The average fee for home delivery service, about 4 USD, paid by clients in the home delivery intervention of the Deliver Health Study was subtracted from the programmatic costs of implementing home delivery

Supplemental Figure 3.3. At-scale average annual cost per client (2022 USD) for 6-month ART refills by cost category in the programmatic NDoH-implemented scenario. The NDoH scenario assumes fixed costs as implemented in the Deliver Health Study and public sector clinical staff salaries instead of study salaries.



Supplemental Figure 3.3.a. Home-delivered ART intervention (first year costs) vs. clinic-based ART refills



Supplemental Figure 3.3.b. Home-delivered ART intervention (subsequent year costs) vs. clinic-based ART