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# Cost-effectiveness of interventions targeting hard-to-reach populations living with HIV in Eastern and Southern Africa

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

By

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#### Abstract

In Eastern and Southern Africa, hard-to-reach populations (e.g., long distance truck drivers and female sex workers), defined as populations that are difficult to interact or engage with due to their unique behaviors and characteristics, are disproportionately affected by the HIV epidemic and are at high-risk of acquiring and transmitting HIV. Further, these populations have substantially low uptake of HIV testing services, and those that have been diagnosed with HIV and on antiretroviral therapy experience high loss-to-follow-up from treatment programs.

Hard-to-reach populations face unique barriers in accessing and utilizing routine HIV care such as provider stigmatization towards sex workers and highly mobile nature of their occupations. Innovative and targeted strategies, which may be resource-intensive, are required to improve their engagement and retention in care. Evidence on cost-effective strategies to improve HIV testing uptake and to reduce loss to follow-up from HIV treatment programs in hard-to-reach populations in Eastern and Southern Africa remains limited.

This dissertation is comprised of three papers examining the cost-effectiveness of HIV testing and loss to follow-up strategies among hard-to-reach populations in Eastern and Southern Africa, using female sex workers and long-distance truck drivers as case study populations and Kenya as a case study setting. In paper one, I conducted a trial-based cost-effective analysis of offering the choice to HIV self-test compared to provider-administered HIV testing among long-distance truck drivers in Kenya. Paper two extended the analysis for paper one by examining the costeffectiveness of a broad range of alternative HIV testing strategies among hard-to-reach populations in Eastern and Southern Africa using a lifetime Markov model. Seven strategies were examined: i) No testing, ii) voluntary counseling and testing, iii) provider-initiated and - administered testing, delivery of: iv) self-testing kits, v) self-testing coupons, and vi) HIV testing referral cards in the community using peer-educators, and vii) offering a choice of self-testing at the health facility. In paper three, I applied the same Markov model from paper two to examine strategies to prevent loss to follow-up among female sex workers on antiretroviral therapy in Eastern and Southern Africa. Strategies included: 1) No intervention; 2) Home ART delivery using community-health workers; 3) Home ART delivery using community-health workers; 3) Home ART delivery using community-health workers plus monthly nutrition supplement; 4) physical and phone-tracing of patients that miss an appointment plus transport refund to the health facility; 5) physical and phone-tracing with free medical care for opportunistic infections; 6) free medical care for opportunistic infections; 6) free medical care for paper one came from a randomized controlled trial (n=150, intervention; n=155, control), while data for paper two and three came from peer-reviewed and grey literature. All costs were reported in 2017 international dollars in paper one and 2017 US dollars for paper two and three.

Findings from these studies suggest that investing resources in strategies that offer choices in HIV testing approaches such self-testing at the health facility or in communities using peer educators would improve HIV testing uptake and reaching out to patients on treatment in their communities to deliver them ART drugs may improve retention in ART programs in Eastern and Southern Africa. In paper one, I found that offering a choice of HIV self-testing at the clinic was cost-effective compared to only the provider-administered HIV testing with an incremental cost-effectiveness ratio (ICER) equal to \$163. In paper two, delivery of HIV self-testing kits in the community using peer educators was cost-effective (ICER < \$600) in both truck drivers and female sex worker sub-populations. Finally, in paper three, delivery of antiretroviral therapy drugs to female sex workers in the community was cost-effective (ICER < \$500).

### **Chapter I: Introduction**

In Eastern and Southern Africa, hard-to-reach populations (e.g., long distance truck drivers and female sex workers), which are defined as populations that are difficult to interact or engage with due to their unique behaviors and characteristics,<sup>1</sup> are disproportionately affected by the HIV epidemic, with HIV prevalence of five times more than that in the general population.<sup>2–7</sup> Additionally, hard-to-reach populations are at high-risk of acquiring and transmitting HIV but have substantially low uptake of HIV testing services,<sup>2,5,8–10</sup> and those that have been diagnosed with HIV and on antiretroviral therapy (ART), experience higher (53%) loss to-follow-up (LTFU) from treatment programs<sup>11–18</sup> compared to people living with HIV (PLWH) in the overall population (14%).<sup>19</sup>

Awareness of HIV status has downstream implications for timely linkage to care, ART initiation, and viral suppression, which are critical for achieving the UNAIDS goal of ending the HIV epidemic by 2030.<sup>20</sup> However, hard-to-reach populations face unique barriers that impact their accessibility and utilization of care including HIV testing. For example, truck drivers are highly mobile with irregular work schedules and hours that are discordant with healthcare facility opening hours.<sup>3</sup> Evidence suggests that differentiated approaches such as oral self-administered HIV testing at healthcare facilities<sup>21</sup> and delivery of HIV self-testing kits to targeted populations in the communities<sup>22</sup> are effective at improving HIV testing uptake among hard-to-reach populations due to their acceptability, flexibility and privacy.<sup>23–26</sup> Although the effectiveness of these approaches particularly in hard-to-reach populations is still emerging, little is known about their value for money.

Hard-to-reach populations are not only hard-to-reach but among those able to be reached, diagnosed with HIV, and initiated on ART experience high LTFU from care—opting out of care for more than 180 days without being classified as either dead or transferred to another ART clinic or program.<sup>19</sup> For example, female sex workers are at high-risk of LTFU due to fear of being identified and to provider stigmatization, which may impact routine utilization of care and retention in HIV care among those living with HIV.<sup>27</sup> Identifying cost-effective strategies to reduce LTFU is critical for improving HIV-related morbidity and mortality, preventing new HIV transmission, and for efficiency in allocation of scarce resources. No strategies have been examined to reduce LTFU among hard-to-reach populations in Eastern and Southern Africa.

This dissertation focused on efficiency in allocation of resources for HIV response including HIV testing and reduction of LTFU for those on ART among hard-to-reach populations in Eastern and Southern Africa. HIV response programs in low- and middle-income countries are largely funded by global donors. Given the recent HIV funding constraints, with more than half of high-income countries reducing their funding for HIV response programs to low-income countries,<sup>28</sup> it is critical for local policy makers to allocate scarce resources efficiently by investing in cost-effective strategies.

The goal for this dissertation was to identify cost-effective strategies to diagnose hard-to-reach individuals living with HIV and retain them in HIV care. HIV testing is the first stage along the HIV care continuum, in papers one and two, I examined the cost-effectiveness of strategies to improve HIV testing uptake among those who are undiagnosed and to engage them in care. Once engaged in care and initiated on ART, it is important to retain people living with HIV in care. In

paper three, I examined the cost-effectiveness of strategies to reduce LTFU among those in HIV care and on ART.

#### Paper one

I conducted a trial-based cost-effectiveness analysis of offering the choice of HIV self-testing at the healthcare facility to increase HIV testing uptake among truck drivers compared to provider-administered HIV testing only, which is the standard of care. This study was based on a randomized controlled trial conducted in 2015 in Kenya among truck drivers at two roadside clinics. In the trial, participants (n=150) in the intervention arm were offered the choice to test for HIV using (1) the provider-administered HIV testing or (2) HIV self-testing under the supervision of a provider. Those who declined the two options were offered a third choice (3) HIV self-testing at home without supervision of a provider. Participants (n=155) in the control arm were offered the provider-administered HIV testing only. The primary outcome in the trial was HIV testing uptake, defined as a participant that accepts to be tested for HIV. Participants in the intervention (CHIVST) arm had significantly higher odds of testing for HIV compared to the control (SOC) arm (2.8, 95% Confidence Intervals [1.5, 5.4]).<sup>21</sup>

Effectiveness data came from a randomized-controlled trial of CHIVST versus provideradministered blood (finger-prick) testing only at a roadside wellness clinic in Kenya. Economic cost data came from the literature, reflecting a societal perspective. Generalized Poisson and linear gamma regression models were used to estimate the effectiveness and incremental costs (2017 I\$), respectively; incremental effectiveness was reported as the number needed to receive CHIVST for an additional HIV test uptake. I evaluated the performance of incremental costeffectiveness ratios (ICERs) using a willingness-to-pay threshold of 3xGDP per capita for Kenya and assessed uncertainty using deterministic sensitivity analyses and the cost-effectiveness acceptability curve.

HIV test uptake was 23% more likely for CHIVST versus SOC, with six individuals needed to receive CHIVST for an additional HIV test uptake. The mean cost per patient was over fourfold higher for CHIVST versus SOC (I\$35.59 vs I\$8.84). CHIVST was I\$ 163.77, 95% CI [151.57, 175.37] per additional HIV test uptake compared to SOC. Self-test kit and cell service were the main cost drivers of the ICER, with findings robust even in a worst-case scenario (highest possible costs). The probability of CHIVST being cost-effective approached one at willingness-to-pay of I\$250. CHIVST was cost-effective at a low willingness-to-pay threshold (\$163), suggesting that CHIVST is a highly efficient use of resources for improving HIV test uptake among high-risk sub-populations. Policies supporting CHIVST and similar sub-populations may expedite achievement of international targets.

#### Paper two

In paper two, I extended the analysis for the first paper and examined the cost-effectiveness of a broad range of alternative HIV testing strategies in hard-to-reach populations in Eastern and Southern Africa. Seven alternative HIV testing strategies were examined: i) No testing; ii) voluntary counseling and testing (VCT);<sup>29</sup> iii) provider-initiated and -administered testing and counseling (PITC);<sup>21</sup> delivery of: iv) self-testing kits, v) self-testing coupons, and vi) HIV testing referral cards in the community using peer-educators;<sup>22</sup> and vii) offering a choice of self-testing at the health facility in addition to provider-initiated and -administered testing.<sup>21</sup> I developed a lifetime Markov model to examine life years saved, disability adjusted life years (DALYs) averted, economic costs, and incremental cost-effectiveness ratios in a cohort of 30-year-old

high-risk and hard-to-reach men and women living with HIV. Economic costs were estimated from a societal perspective and reported in 2017 US dollars. The cost-effectiveness of strategies was determined according to the willingness to pay threshold equivalent to 3xGDP per capita for Kenya in 2017 (3x\$1,570 = \$4,710). Future costs and health benefits were discounted at an annual rate of 3%. Deterministic sensitivity analysis was performed to assess uncertainty in model parameter inputs.

I found that the Kit delivery strategy was cost-effective and had the highest cost and life expectancy at 30 years and lowest DALYs lost among female sex workers (FSWs) and truck drivers. Total costs ranged from \$1,400 to \$6,100 and \$1,400 to \$4,951 in the "No testing" and kit delivery strategies among FSWs and truck drivers, respectively. More DALYs were lost in the "No testing" strategy (21.93 and 22.11) compared to the Kit delivery strategy (12.70 and 14.77) among FSWs and truck drivers, respectively. The kit delivery strategy was cost-effective compared to alternative HIV testing strategies among both FSWs and truck drivers with an ICER of less than \$600 per DALY averted. The kit delivery strategy compared to No testing, cost more but averted 9.23 and 7.34 DALYs and saved 8.88 and 7.13 life years among FSWs and truck drivers, respectively. Delivery of self-testing kits in the community was cost-effective among FSW when 75% or more are reached. Variations in parameter inputs did not change the main findings among truck drivers. Using peer-educators to deliver HIV self-testing kits in the community is a cost-effective strategy to improve HIV test uptake in populations that are hard to reach and at high-risk of acquiring and transmitting HIV.

#### Paper three

In the third paper, I examined the cost-effectiveness of alternative strategies to reduce LTFU among female sex workers on ART in Eastern and Southern Africa. Using a similar Markov model from paper two, I projected costs and DALYs for six alternative strategies: 1) No intervention; 2) Home ART delivery using community-health workers; 3) Home ART delivery using community-health workers; 3) Home ART delivery using community-health workers; 3) Home ART delivery using community-health workers plus monthly nutrition supplement; 4) physical and phone-tracing of patients that miss an appointment plus transport refund to the health facility; 5) physical and phone-tracing with free medical care for opportunistic infections; 6) free medical care for opportunistic infections with transport refund to the health facility and free breakfast. The analysis was conducted from a payer perspective with future DALYs lost and costs discounted at 3%. Costs were valued in US dollars and inflation-adjusted to 2017 currency year. The ICER was used to assess the relative performance of the strategies, with the cost-effectiveness of a given strategy determined according to a threshold of 3x the GDP per capita for Kenya in 2017 (3x\$1,570 = \$4,710). Uncertainty in inputs was assessed using probabilistic sensitivity analysis.

In the base case analysis, total costs and DALYs lost per strategy ranged from \$2,994 to \$10,022 and 11.52 to 9.27 for No Intervention and ART delivery plus nutrition supplement, respectively. ART delivery was cost-effective compared to alternative strategies with an ICER of \$470 per DALY averted. Although ART delivery with nutrition supplement had lower DALYs lost (9.27), total costs were substantially higher compared to the next best alternative, ART delivery (\$10,022 vs \$5,173). Tracing with transport refund had higher costs (\$4,386 vs \$3,460) and DALYs lost (11.05 vs 10.55) compared to the next best alternative, ART delivery, and was absolutely dominated. Strategies: tracing with free medical care for opportunistic infections and

transport refund with free medical care for opportunistic infections plus breakfast had lower costs (\$4,606 and \$5,173) but higher DALYs lost (10.51 and 10.35) and were extendedly dominated by ART delivery with nutrition supplement that had higher costs (\$10,022) but with lower DALYs lost (9.27). FSWs remain disproportionately impacted by HIV with high rates of LTFU from ART programs among those on treatment. I found that delivering ART drugs to FSWs in their homes, places that they frequent, or community centers was a cost-effective strategy to reduce LTFU among patients in FSWs in ART programs in Eastern and Southern Africa **Chapter II:** Choice of Self-Administered Oral HIV Testing among Long Distance Truck Drivers in Kenya: A Trial-based Costeffectiveness Analysis

### Introduction

The HIV epidemic in sub-Saharan Africa remains a major global public health challenge, with over 1 million people living with HIV in the region unaware of their HIV status.<sup>30</sup> Early awareness of HIV status has downstream implications along the care continuum, including timely linkage to care, antiretroviral therapy (ART) initiation, and viral suppression, which are critical for achieving the international targets that can end the HIV epidemic.<sup>31</sup> However, uptake of HIV testing services is low, particularly in sub-populations that are disproportionately impacted by HIV and at high risk of transmission.<sup>2,5,8</sup> To improve and sustain high HIV awareness levels in these sub-populations, targeted, innovative HIV testing strategies are needed. These strategies may require more resources,<sup>32</sup> a significant challenge when HIV funding is limited.<sup>33</sup>

Long distance truck drivers in the region are at high risk of acquiring and transmitting HIV, but have relatively low HIV testing uptake.<sup>2,5,8</sup> For example, from 2013 to 2015, only 32% of 13,252 patients that visited the clinics utilized HIV-related services including HIV testing.<sup>8</sup> In 2018, the North Star Alliance—an organization providing healthcare services to mobile workers and people they interact with along truck routes—reported that only 34% of 289,078 services offered at wellness centers were HIV testing,<sup>34</sup> indicating that HIV testing uptake is still sub-optimal even when healthcare facilities are geographically close to places where truckers congregate such as truck stops.

This sub-population has unique characteristics contributing to their high HIV risk and low-test uptake. Truck drivers travel for many days away from their main partners, which provides opportunities to engage with other partners and commercial sex workers,<sup>35–37</sup> increasing their HIV risk.<sup>38</sup> Truck driver mobility coupled with irregular work schedules and discordance between work hours and healthcare facility opening hours limit the accessibility and utilization of healthcare services, including routine HIV testing.<sup>39</sup> Further, men are less likely to test for HIV and, given that majority of truck drivers are men, there is an additional gender barrier to HIV testing uptake.<sup>40</sup> Standard of care approaches for HIV testing, such as clinic-based, provider-administered testing, do not address these barriers.

Emerging evidence suggests that patient-centered care delivery, including self-administered oral HIV testing,<sup>41</sup> improves HIV test uptake among truck drivers.<sup>21,42</sup> One approach—selfadministered oral HIV testing—has generated considerable interest due to its acceptability, flexibility and user privacy.<sup>23–26</sup> The introduction of HIV self-testing to compliment the traditional standard of care—provider administered HIV testing—has improved uptake of HIV testing, both in the general population<sup>23,43</sup> and among high-risk sub-populations including truck drivers<sup>21,22,42</sup> and sex workers<sup>22,44</sup> in sub-Saharan Africa.

While HIV self-testing has been found to be effective,<sup>21</sup> evidence on cost<sup>32</sup> and costeffectiveness<sup>45–48</sup> is limited and no cost-effectiveness study exists among high-risk subpopulations including truck drivers. Examining cost-effectiveness is particularly pertinent in resource-limited settings where in-country resources are often insufficient to implement all HIV response programs and may potentially worsen since the global HIV funding in recent years has decreased or remained flat<sup>33,49</sup> and emerging external shocks (e.g., COVID-19) threaten the availability of ongoing donor support.<sup>50</sup> This funding shortfall and ongoing future financing challenges underscore the need to prioritize available resources for cost-effective interventions.

In Kenya, a recent randomized controlled trial found that offering truck drivers the choice of self-administered oral HIV-testing versus provider-administered testing at an easily accessible roadside wellness clinic resulted in HIV testing uptake nearly three times that of provider-administered testing only, suggesting HIV testing approaches that are tailored to individual need or preference in this sub-population are effective.<sup>21</sup> While this trial found the intervention effective, there is little knowledge of its value for money in this sub-population. This study examined the incremental cost-effectiveness of offering the choice of HIV self-testing (CHIVST) compared to provider-administered HIV testing, the standard of care (SOC) only, among truck drivers presenting for care at a roadside wellness clinic in Kenya. Two research questions are examined: 1) are economic costs of offering the CHIVST greater than the SOC? 2) is offering the CHIVST a cost-effective intervention compared to the SOC?

#### **Overview of the trial**

In 2015, a randomized controlled trial was conducted at two roadside wellness clinics in Kenya to compare HIV testing uptake among truck drivers offered the choice of self-administered rapid oral HIV-testing compared to uptake among those offered provider-administered rapid blood (finger-prick) HIV testing only, the standard of care (SOC).<sup>21</sup> In the intervention arm, truck drivers (n=150) were offered the choice to test for HIV using 1) the SOC HIV testing or 2) self-administered oral HIV-testing under the supervision of a provider. If the truck driver declined the two options, they were offered a third option; 3) self-administered oral HIV-testing outside the clinic (at home) without supervision of a provider but with phone-based support and post-test

counseling. In the control arm, truck drivers (n=155) were offered only the SOC HIV testing. The adjusted odds ratio (2.8, 95% CI [1.5, 5.4]) of HIV testing uptake in the intervention arm were significantly higher compared to the control arm.<sup>21</sup>

#### Methods

#### Overview

I conducted a trial-based incremental cost-effectiveness analysis of offering the CHIVST to increase HIV testing uptake among truck drivers in Kenya compared to the SOC. Data from the trial was used to estimate the effectiveness and incremental effectiveness of offering the CHIVST, with incremental effectiveness estimated as the number of participants needed to receive the CHIVST for an additional truck driver to test for HIV. Economic cost data were derived from the literature according to the societal perspective, which considers economic costs for both the payer and the patient. Incremental cost-effectiveness ratios were calculated, with the economic performance of the CHIVST intervention evaluated according to a threshold of 3 x gross domestic product (GDP) per capita in Kenya. I assessed uncertainty using deterministic sensitivity analyses and a cost effectiveness acceptability curve. This study was reviewed by the Virginia Commonwealth University Institutional Review Board and designated as exempt to regulations of human subject (Reference Number: HM20015160).

#### **Costing Approach**

Economic cost data came from the literature. Studies conducted in Kenya were prioritized, with data from studies conducted in lower-middle-income countries in sub-Saharan Africa also considered if they were contextually relevant to the trial. I restricted the search to studies with data collected less than 10 years from the year of the trial, since more recent cost data sources

reflect current healthcare delivery systems and utilization patterns, which tend to vary overtime. Costs were adjusted for inflation using the World Bank GDP deflator<sup>51</sup> to account for changes in costs over time and reported in 2017 international dollars (I\$),<sup>52</sup> which enables comparison of costs across multiple settings (countries) and captures differences in local currency purchasing power. Micro- and gross costing approaches were used to assign per-patient costs. Micro-costing enables more precise estimation of costs (medical, labor and patient time) for resources utilized<sup>53</sup> by multiplying the quantity of resources and the unit cost. Gross-costing aggregates costs (equipment, capital, cell phone service, overhead costs) for an intervention to estimate the per patient cost for resources that cannot be explicitly allocated at the patient level based on individual utilization.<sup>54</sup>

#### Data

Costs were estimated based on the HIV testing procedure (SOC or oral self-test) performed and/or the setting (clinic only or clinic and home). Medical costs included the cost of HIV testing kits (OraQuick for self-test, I\$ 15.52<sup>55</sup>; Colloidal Gold test for SOC, I\$ 1.43<sup>56</sup>) as well as medical supplies (self-test, I\$ 0.26; SOC, I\$ 0.42) used in the HIV testing process at the clinic,<sup>57</sup> which varied based on the HIV testing procedure. Medical supplies considered are listed in the supplementary material, Table S11. I emphasize that the cost of the SOC test kit was only considered in the sensitivity analysis, since SOC kits were provided to North Star Alliance by the Kenyan Ministry of Health and thus the trial did not incur the cost for these kits.<sup>55</sup> Labor costs included salaries for the nurse per-patient (self-test, I\$ 2.84; SOC, I\$ 2.27),<sup>55</sup> non-clinical healthcare facility staff (I\$ 1.10 per-patient that tested from the clinic only; I\$ 0.47 per-patient that visited the clinic but tested from home)<sup>32</sup> and one-time training (I\$ 0.09 per-patient in the intervention arm) for nurses on how to use the HIV self-testing kit.<sup>55</sup> Equipment (cell phone, I\$

2.47 per-patient in the intervention arm),<sup>55</sup> healthcare facility site (I\$ 1.72 per-patient that tested from the clinic only; I\$ 0.74 per-patient that visited the clinic but tested from home),<sup>32</sup> overhead (I\$ 4.24 per-patient that tested at the clinic only; \$I 2.26 per-patient that visited the clinic but tested from home)<sup>32</sup> and cell phone service (13.65 per-patient in the intervention arm)<sup>55</sup> costs were allocated using the gross-costing.<sup>54</sup> Patient time spent at the healthcare facility or home testing for HIV, including pre- and post-test counseling, was considered time lost that could have been alternatively used to economically benefit the patient; patient time (oral self-test, I\$ 3.13; SOC, I\$ 2.51) was calculated as the product of the time spent testing for HIV and the hourly wage of a truck driver, estimated based on income of participants in trial.<sup>21</sup> The HIV testing process took 40 and 50 minutes for participants that tested using the standard of care and oral self-administered test, respectively.<sup>55</sup>

#### Statistical analysis

I conducted analysis using two statistical models. A generalized linear Poisson regression model with a robust variance was used to estimate the effectiveness and incremental effectiveness of CHIVST and a generalized linear gamma regression model to estimate the incremental cost. Equation 1 below shows the generalized linear model for estimating effectiveness, incremental effectiveness, and incremental costs of the CHIVST.

$$Outcome_i = \beta_o + \beta_1 Choice_i + X_i B + u_i \tag{1}$$

where,  $Outcome_i$  represents HIV testing uptake or cost assigned to the  $i^{th}$  patient;  $Choice_i$  is a binary variable equal to 1 if a patient is assigned to CHIVST arm and equal to 0 if assigned to the SOC;  $\beta_1$  is the coefficient of interest—effect of CHIVST on the outcome.  $X_i$  and B are vectors and coefficients, respectively, of the control variables. I controlled for four variables that have

been found to impact HIV testing uptake<sup>40</sup> and/or are contextually applicable to the study. These include the healthcare facility (the trial was conducted at two facilities), age of the participant, whether the participant visited the clinic to purposely test for HIV, and whether they have paid of sex in the last 6-months prior to the date of the clinic visit.

#### **Effectiveness and Incremental Effectiveness**

I estimated the effectiveness of CHIVST as the relative risk of HIV test uptake in the CHIVST arm compared to the SOC arm. The incremental effectiveness was estimated as the Number Needed to Treat (NNT)<sup>58</sup> and interpreted as the number of truck drivers who need to be offered the CHIVST for an additional driver to get tested for HIV. The NNT approach was selected as an alternative to more traditional measures of incremental effectiveness such as the disability adjusted life years (DALYs) averted because the primary outcome (HIV test uptake) in the trial was an intermediate outcome and the trial time period (3 months) was too short to estimate DALYs. Using DALYs as a measure of health benefit would not have generated meaningful differences between trial arms and multiple assumptions would be required to estimate when considering a longer time horizon without developing a mathematical model.

NNT was derived in four steps:

- Step 1: Predict the absolute risk of HIV testing uptake per patient.
- Step 2: Calculate the mean per-patient absolute risk for HIV testing uptake per trial arm.
- Step 3: Estimate the mean per-patient absolute risk difference between trial arms
- Step 4: Take the reciprocal of the mean absolute risk difference to calculate NNT.

#### **Economic Costs and Incremental Costs**

Economic costs per-patient by trial arm were calculated by multiplying resources utilized at the individual level with unit costs and summarized using the mean with 95% confidence intervals (CIs), since decisions are made based on expected costs.<sup>59</sup> Incremental costs reflect the difference in mean per-patient costs between the CHIVST and SOC arms.

#### Incremental Cost-effectiveness Ratio (ICER)

The ICER was calculated as the product of the incremental cost and incremental effectiveness. Conventionally, the ICER is calculated by dividing the incremental cost ( $\Delta$ C) by incremental effectiveness ( $\Delta$ E) i.e.,  $ICER = \frac{\Delta C}{\Delta E}$ . When using the NNT approach, however, the incremental effectiveness (NNT) is calculated as the reciprocal of the mean per-patient absolute risk difference ( $\frac{1}{RD}$ ). Thus, the ICER is calculated as the product of  $\Delta$ C and NNT (ICER =  $\Delta$ C \*  $\frac{1}{RD}$  =  $\Delta$ C \* NNT). I calculated the 95% CI for the ICER using non-parametric bootstrapping method since the data (cost and effectiveness variables) were not normally distributed.<sup>59</sup>

A threshold of 3 x GDP per capita (2017) for Kenya was used to determine the cost-effectiveness of the CHIVST.<sup>60</sup> The threshold represents the maximum willingness-to-pay (WTP) value for the additional health benefit gained from the CHIVST and is used to determine whether CHIVST presents a good value for money. The willingness-to-pay threshold is used as guide for cost-effectiveness decision making, in addition to other factors including local competing priorities, intervention affordability, and feasibility of implementation, which are not accounted for in the willingness-to-pay threshold.<sup>61,62</sup> I also assessed a lower threshold (GDP per capita) to account for differences in affordability across settings given that the threshold of 3xGDP per capita may be too high for low-income countries with resource constraints and high opportunity cost.<sup>61–64</sup>

#### Missing data

In the analytic sample, only 9 (3%) participants were missing at least one data point. Using Little's test, I examined the randomness assumption about the missing data and found that the data were missing completely at random (MCR) across trial arms,<sup>65</sup> implying that the missing data were not systematically correlated with other variables across trial arms. Participants (9) with data MCR were then excluded from the analysis since they had no significant impact on the study outcomes.

#### Uncertainty

I assessed the impact of variation in costs on the ICER using deterministic sensitivity analyses (one-way and multi-way sensitivity analysis)<sup>60</sup> and uncertainty in the base case ICER using the cost-effectiveness acceptability curve.<sup>66,67</sup> One-way sensitivity analysis identified the main cost drivers of variation in the ICER, with the results reported using a tornado diagram, which summarizes of the range of ICERs due to variation in unit cost estimates. Multi-way sensitivity analysis assessed the robustness of the study findings by varying unit costs considering the bestand worst-case scenarios. The worst-case scenario was defined according to the upper bound values, while the best-case scenario was defined as the lower bound values of each economic cost. Although these scenarios may be unrealistic in practice, they can provide insight into the policy impact of the most optimistic and pessimistic cases in cost variation. I assessed uncertainty in the base case ICER using the cost-effectiveness acceptability curve. The acceptability curve summarizes the probability an intervention is cost-effective at different willingness-to-pay thresholds. I generated the acceptability curve from a joint distribution of incremental costs and incremental effects, which was estimated using non-parametric bootstrapping.<sup>67</sup>

#### Results

#### Base case analysis

CHIVST significantly increased HIV testing uptake among truck drivers. More than 87% (130/149) of truck drivers in the CHIVST arm tested for HIV compared to 73% (114/156) in the SOC arm. Truck drivers in the CHIVST arm were 23% more likely to test for HIV relative to those in the SOC arm. The incremental effectiveness, measured as the NNT, was 6.25, 95% CI [5.00, 8.33], meaning that for every six truck drivers offered the CHIVST, one additional driver will test for HIV.

The mean cost per-patient (Table 1) was more than four times higher in the CHIVST (I\$ 35.59 vs SOC (I\$ 8.84) arm. Majority (>70%) of the mean per-patient cost in the CHIVST was attributed to the cell phone service (I\$ 12.03), price of HIV testing kit (I\$ 10.12) and overhead (I\$ 3.59), while in the SOC arm, it was attributed to the overhead (I\$ 3.06), patient time (I\$ 1.81) and nurse salary (I\$ 1.64). The incremental cost was I\$26.20, 95% CI [23.32, 29.09], representing the adjusted difference in the mean per-patient costs between the CHIVST and SOC arm. In the base case analysis, the ICER for offering the CHIVST was I\$163.77, 95% CI [151.57, 175.37], meaning that offering truck drivers the CHI

VST costs I\$163 per additional HIV test uptake compared to the SOC.

#### Uncertainty

Our findings were robust to variations in economic costs and effectiveness of CHIVST. The cost of cell phone service and HIV self-testing kit were the key cost drivers and had the largest impact on the ICER (Figure 1), although the upper bound of the ICERs for both sensitivity analyses fell well below traditional willingness-to-pay thresholds. I examined the potential impact the HIV self-testing kit price reduction to US \$2, based on the Bill and Melinda Gates Foundation agreement with manufactures and low-income countries.<sup>68</sup> With the reduced price, CHIVST was cost-effective at a much lower willingness-to-pay value (I\$ 119 vs I\$ 163). Offering the CHIVST was still cost-effective in both the best- and worst-case scenarios (results reported in the supplementary material).

CHIVST increases both costs and effectiveness but is cost-effective at low willingness-to-pay thresholds. The joint distribution shows (Figure 2) that all the data points on the cost-effectiveness plane are in the northeastern quadrant. This indicates that offering the CHIVST increases both costs and HIV testing uptake and that there is less uncertainty in the cost per additional HIV test performed since all the data points are clustered in the same quadrant. The probability of CHIVST being cost-effective compared to the SOC is almost equal to 1 when the willingness-to-pay value is greater than I\$ 250 (Figure 2), which is much lower than even the minimum willingness-to-pay threshold considered of I\$3,258 (1xGDP per capita).

#### Discussion

HIV status awareness remains low, particularly in high-risk sub-populations in sub-Saharan Africa, and improving HIV test uptake may require efficient, innovative, and targeted strategies. I examined the cost-effectiveness of offering the CHIVST to truck drivers at a roadside clinic in Kenya compared to the SOC. I found CHIVST was effective—increasing the probability of HIV testing uptake by 23%—and cost-effective when the decision maker is willing to pay I\$163 per additional truck driver tested for HIV per year.

CHIVST costs more, with the mean cost of an HIV test uptake more than four times higher, but it is cost-effective, compared to the SOC. Although participants in the trial did not pay for the testing kits, cost remains one of the main barriers to accessing healthcare services, including HIV testing, and truck drivers consider cost as the strongest factor for the choice of HIV test.<sup>69</sup> However, CHIVST was cost-effective compared to the SOC at willingness-to-pay of I\$163 for an additional HIV test uptake, which is substantially lower than the willingness-to-pay threshold used for Kenya (\$19,774), suggesting that although CHIVST costs more, it has a higher health benefit and offers good value for money. Our findings were robust to extreme scenarios when I considered higher bounds of all costs, which are driven primarily by the cost of the cell phone service and HIV self-test kit in the CHIVST arm. I also considered a scenario with a self-administered oral HIV test kit costing US \$2 based on Bill and Melinda Gates Foundation agreement with manufactures and low- and middle-income countries,<sup>68</sup> but it did not change the policy conclusion.

This study provides a novel contribution to emerging broader literature on the effectiveness and cost-effectiveness of HIV self-testing, which has largely focused on the overall population of people living with HIV.<sup>45–47</sup> While little has been done to examine the cost and cost-effectiveness of HIV self-testing among truck drivers, previous work conducted a costing analysis and found self-administered oral HIV testing per test costs more (double) than routine

facility-based testing (the standard of care),<sup>32</sup> which is consistent with the current study. However, previous work did not examine the cost-effectiveness, and costs were only estimated from a provider perspective.<sup>32</sup> To our knowledge, this is the first study to examine the costeffectiveness of offering the CHIVST compared to the SOC among truck drivers in this setting. In Zimbabwe<sup>47</sup> and Malawi,<sup>45</sup> HIV self-testing in the general population was cost-effective compared to the provider administered HIV testing. Similar to findings in this study, the cost of HIV self-testing kit was higher compared to the provider-administered HIV testing kit and was one of the key variables impacting the cost-effectiveness of HIV self-testing. In Zimbabwe, HIV self-testing was cost-effective when efficacy was at least 20%,<sup>47</sup> which is comparable to the effectiveness (23%) of CHIVST. Only one study from sub-Saharan Africa included a high-risk or hard-to-reach sub-population (female sex workers) and found HIV self-testing to be costeffective when targeting female sex workers and in settings with high prevalence of undiagnosed HIV.<sup>46</sup> Based on previous work, more than 80% of HIV-infected truck drivers were unaware of their HIV status in some settings,<sup>5</sup> suggesting a high likelihood of HIV self-testing being costeffective in this sub-population. Although our study findings are broadly comparable with the HIV self-testing literature, they should be interpreted with caution since I examined the costeffectiveness of offering a choice of HIV self-testing in addition to the SOC test and not of offering only HIV self-testing. A large proportion of truck drivers in the CHIVST arm still chose the standard of care test, suggesting that some truck drivers may choose not to test if offered only HIV self-testing. In addition, I considered a short time horizon (3 months) and different effectiveness measure compared to previous work done in the overall population of PLWH that used mathematical models and considered a 20-year time horizon and long-term measures of effectiveness (e.g., DALYs).<sup>45-47</sup>

Findings indicate that differentiated care—in this case, choice of self-administered oral HIV testing for high-risk sub-populations—is an effective and cost-effective strategy to improve HIV test uptake. In Eastern and Southern African, HIV testing uptake remains low despite healthcare services being geographically and temporally convenient.<sup>34</sup> For example, roadside wellness centers, such as those run by North Star Alliance, offer a broad menu of healthcare services, including HIV testing and treatment, close to truck stops where truck drivers, sex workers and roadside community residents congregate and interact and at off hours when these groups are more likely to have time to seek services, but test uptake is low.<sup>34</sup> CHIVST provides a cost-effective potential solution to some of the limitations (e.g., lack of flexibility and privacy) of the SOC HIV testing offered at the roadside wellness clinics.<sup>70</sup>

Our results contribute to a substantial gap in knowledge on efficient strategies to improve HIV status awareness among truck drivers and other high-risk or hard-to-reach sub-populations in the sub-Saharan Africa, a region with more than half of the world's HIV population. In Kenya and Uganda, along the trans-African highway, sexual interaction between transport workers and communities at truck stops was estimated to contribute up to 4,148 new HIV infections in a year.<sup>38</sup> International and local policy makers could implement efficient strategies such as CHIVST that improves HIV testing uptake as one strategy to reduce onward HIV transmission by diagnosing people early and engaging them in HIV care. HIV-positive individuals aware of their HIV status are likely to have fewer sexual partners and to use condoms compared to those unaware of their status,<sup>71</sup> thus reducing onward HIV transmissions. But, despite the increase in the number of countries (from 6 to 77 countries in 2015 and 2019, respectively) in support of HIV self-testing policies, implementation and integration of HIV self-testing in national HIV programs remains a challenge,<sup>41</sup> with less than 37% (28/77) of the countries at the

implementation stage.<sup>72</sup> Findings from this study provide supporting evidence to guide policy makers in their decision making and implementation of HIV self-testing, particularly in high-risk sub-populations.

This study had some limitations to consider in its interpretation. First, I did not account for future costs and health benefits beyond the intervention period (3 months). For example, cost of antiretroviral drugs and health benefits such as disability-adjusted life years averted that account for long-term health benefits for truck drivers who were diagnosed with HIV and initiated on ART. Additionally, the effectiveness and incremental effectiveness were estimated using an intermediate outcome (HIV testing uptake), which limits comparability with cost-effectiveness studies in literature that used traditional measures (e.g., disability adjusted life years). Although using a mathematical model with a longer time horizon would account for future consequences, a trial-based cost-effectiveness analysis provides evidence to inform policy decisions which are usually implemented on short term basis (e.g., 1 to 5 years). Second, CHIVST was offered in a healthcare facility setting among truck drivers already seeking care, who may have different healthcare utilization behaviors compared those not accessing the healthcare facility. However, the intervention is likely to be more effective in the outside setting. Third, economic costs data were derived from literature since I did not collect data on the exact costs incurred during the trial. However, I conducted sensitivity analyses to account for uncertainty in cost estimates and the findings were robust.

As countries aim to achieve UNAIDS targets with limited resources available, innovative, and targeted cost-effective strategies are imperative, particularly for sub-populations at high risk of acquiring and transmitting HIV. This study finds offering self-administered oral HIV testing as a

testing choice at roadside wellness clinics in Kenya to be a highly efficient use of resources compared to the SOC of offering provider-administered blood-based HIV testing only. Future studies should examine the cost-effectiveness of self-administered HIV testing outside the clinic setting among high-risk sub-populations and consider the long-term costs and health benefits of HIV testing.

# **Chapter III:** Cost-effectiveness of Alternative HIV Testing Strategies among Hard-to-Reach Populations in Eastern and Southern Africa

#### Introduction

HIV testing remains substantially low in populations that are hard-to-reach and at high-risk of transmitting HIV.<sup>2,5,8–10</sup> These populations that are difficult to interact or engage with due to their unique behaviors and characteristics, and as result, are hard to reach and engage in care.<sup>1</sup> Low HIV testing has downstream consequences for engagement in HIV care, new HIV infections<sup>73</sup> and may halt the global target of ending the HIV epidemic by 2030.<sup>20</sup>

Female sex workers (FSWs) and long-distance truck drivers (truck drivers), particularly in Eastern and Southern Africa, have been hard-to-reach and are disproportionately impacted by HIV, with prevalence more than five times that of the general population in some settings.<sup>2,5,7</sup> Traditional facility-based HIV testing approaches may not to reach these populations because of the unique barriers they face in accessing care.<sup>3,10</sup> For example, truck drivers are highly mobile due to their occupation and usual opening hours at healthcare facilities are unfavorable for routine health care utilization.<sup>74,75</sup> FSWs face various barriers including provider stigma and discrimination, which may negatively impact their willingness to seek HIV prevention services and care.<sup>76,77</sup>

Innovative strategies targeting high-risk and hard-to-reach populations have shown improved uptake of HIV testing but require more resources<sup>21,22</sup> and their cost-effectiveness remains unknown, despite the urgent need for efficient allocation of limited HIV funds. Globally, HIV funding has stagnated, and over the past decade, funding from high-income countries has

declined by more than \$1 billion and future funding remains uncertain.<sup>28</sup> This increases the burden on low-income countries to close the ongoing and increasing funding gap.<sup>78</sup> To ensure long-term sustainability of the HIV response programs, resources need to be allocated efficiently by investing in cost-effective strategies. In this study, I examined the cost-effectiveness of alternative HIV testing strategies among female sex workers and long-distance truck drivers in Eastern and Southern Africa.

#### Methods

#### Overview

I used a Markov model to examine the cost-effectiveness of seven HIV testing strategies in a hypothetical cohort of 30-year-old<sup>21,22</sup> undiagnosed truck drivers and FSWs living with HIV. The primary outcomes included economic costs, life expectancy, disability-adjusted life years (DALYs) lost and incremental cost-effectiveness ratios (ICERs). The analysis was conducted from the societal perspective over a lifetime time horizon, with future economic costs and DALYs discounted at 3%.<sup>60</sup> Economic costs were valued in US dollars (\$) and inflation-adjusted to 2017 currency year. The relative performance of the HIV testing strategies was assessed using the ICER (2017 \$/DALYs averted), and the cost-effectiveness determined based on the willingness to pay threshold equivalent to 3xGDP per capita for Kenya in 2017 (\$4,710),<sup>60</sup> although lower thresholds were also assessed to account for differences in affordability and willingness to pay across settings.<sup>61–64,79</sup> I assessed uncertainty in parameter inputs using deterministic sensitivity analysis.

## Strategies

Seven strategies were examined (Table 2): i) No testing; ii) voluntary counseling and testing (VCT);<sup>29</sup> iii) provider-initiated and -administered testing and counseling (PITC);<sup>21</sup> delivery of: iv) self-testing kits, v) self-testing coupons, and vi) HIV testing referral cards in the community using peer-educators;<sup>22</sup> and vii) offering a choice of self-testing at the health facility in addition to provider-initiated and -administered testing.<sup>21</sup> Strategies were classified (community, facility and combination of both facility and community) based on the setting of the initial contact with target population and setting for HIV test uptake. Community-based strategies had higher costs, probability of reaching the target population and HIV test uptake compared to facility-based strategies.

### **Model Structure**

I used a Markov model with mutually exclusive health states—a single state of health where one event occurs per time period—but with probabilities that collectively sum up to 1. Statetransition probabilities are exponentially distributed (constant) and conditional on current but not previous health states.<sup>80</sup> The model has 24 health states defined by HIV disease progression and engagement in clinical HIV care (Figure 3).<sup>81</sup> The clinical stages of HIV disease progression were defined as follows: Asymptomatic Early (corresponding with CD4 count >500 cells/µL); Asymptomatic Late (corresponding with CD4 count >350 - 500 cells/µL); Symptomatic (CD4 count >200-350 cells/µL); and AIDS (CD4 count  $\leq$ 200 cells/µL)). Disease stages defined based on CD4 stratification is consistent with current mathematical modeling literature and enables estimation of benefits and costs for diagnosis, linkage and ART initiation at early vs later stages of the disease.<sup>82,83</sup> The model did not include health states reflecting viral suppression due to data limitations among people living with HIV in these settings. Further, the differences in health benefits across strategies attributed to viral suppression in the long run would be minimal after discounting. I assumed that individuals who were consistently on ART (first or second line) achieved viral suppression. Engagement in HIV care was characterized as undiagnosed, diagnosed, linked to care, on first line ART, on second-line ART, lost from care, and death. Although current guidelines recommend test and treat, evidence shows delays in linkage and ART initiation in this setting.<sup>84</sup>

HIV diagnosis cascade (Figure 4) implemented in this study followed the HIV testing algorithm in Kenya.<sup>85</sup> The cohort undergoing HIV testing received an initial test and if the test was a reactive test, a confirmatory test was performed, with a tiebreaker test used when the initial test was reactive, but the confirmatory test had a negative result. Figure 4 shows pathways with fraction of the cohort moving from undiagnosed to diagnosed health states. The sensitivity of the initial HIV test was strategy specific, but the confirmatory test and tie-breaker test was the same across all strategies. Strategies (Kit Delivery, Coupon Delivery and HIVST Choice) that offered the oral self-administered test used the Oral Sure OraQuick test, with sensitivity (95% confidence interval) of 92% (66.0 – 99.0).<sup>86,87</sup> Strategies (Referral card, HIVST Choice, PITC, VCT) that offered the blood-based provider-administered test used KHB colloidal Gold test, sensitivity (95% CI) = 100.0% (97.4 – 100.0).<sup>85</sup> Sensitivity of the confirmatory (First Response 1-2.0) and tiebreaker (Uni-Gold) test were 100.0% (97.4 – 100.0) and 96.4% (91.8 – 98.8),<sup>85</sup> respectively. Consistent with the current HIV care guidelines in Kenya, those diagnosed with HIV were linked to care and initiated on treatment irrespective of the disease stage.<sup>88</sup> Death could occur in all health states due HIV- or non-HIV-related causes with variations in the probability of death based on disease stage, engagement in HIV care<sup>89</sup> and background mortality.<sup>90</sup> The model (Figure 3) was implemented in TreeAge Pro software version 2021.

I made the following key assumptions: 1) I assumed FSWs and truck drivers older than 49 years were not considered part of the high-risk and hard-to-reach populations and were comparable to the overall population of people living with HIV (PLWH). Based on previous research, a significant majority (>85%) of truck drivers and FSWs are below 50 years and I assumed they change occupations.<sup>8,42,70,91</sup> 2) HIV testing strategies that used peer-educators reached all the targeted population since they work in smaller groups and are likely to trace, follow-up and gain trust of their peers.<sup>92</sup> 3) All truck drivers and FSWs that got a reactive initial HIV test and a confirmatory test were linked to care and initiated treatment.

## **Parameter inputs**

Data for parameter inputs (Table 3): HIV test uptake, disease progression, engagement in HIV care and death came from published and grey literature, and were converted to monthly probabilities to reflect the model cycle length.<sup>93</sup> The initial distribution of 30 year-old, undiagnosed individuals living with HIV came from a cohort study of newly diagnosed HIV individuals in Kenya.<sup>94</sup> I varied this distribution in sensitivity analysis to reflect limited data on CD4 cell count distribution among truck drivers and FSWs living with HIV in sub-Saharan Africa.

HIV test uptake data came from two randomized controlled trials (RCT) conducted in Uganda and Kenya among FSWs (Intervention = 610; Control = 316)<sup>95</sup> and truck drivers (Intervention = 150; Control=155),<sup>21</sup> respectively, and two studies with evidence on HIV test uptake among truck drivers and FSWs for the VCT strategy (standard of care).<sup>21,96</sup> HIV test uptake varied based on setting, sex, age, HIV disease stage and, with community-based (vs facility-based) strategies reaching more people<sup>97,98</sup> and women testing more than men except in older adults above 50 years.<sup>99</sup> Further, those at AIDS stage were more likely to test since they tend to be sicker compared to those in non-AIDS stage.<sup>100</sup>

After the initial reactive test, a confirmatory test was required before linkage to HIV care and ART initiation. I assumed perfect (100%) receipt of a confirmatory test in facility-based testing and 90% for community-based testing with peer educators.<sup>92,101</sup> Data for timely (within 30 days of HIV diagnosis) linkage to care and ART initiation came from a longitudinal study on "test and treat" in sub-Saharan Africa.<sup>102</sup> Data for loss-to-follow-up (LTFU) came from a retrospective study among FSWs in Rwanda.<sup>14</sup> HIV natural history data came from a community-based HIV testing study in South Africa, which estimated disease progression by fitting data to a pooled-analysis of observational cohort studies in Africa.<sup>89</sup> I assumed mortality reduces by 58% among PLWH and on ART.<sup>103</sup> I accounted for age and sex specific background mortality using the World Health Organization (WHO) life tables.<sup>90</sup>

Disability weights, which represented the total disease burden, were assigned to each health state to project disability-adjusted life-years (DALYs) per strategy.<sup>104</sup> The sum of weights over the analytic time horizon reflected the total strategy specific DALYs lost. Monthly disability weights came from Eaton et al.,<sup>105</sup> derived from the global disease burden study.<sup>106</sup> Disability weights varied based on disease stage (asymptomatic, symptomatic and AIDS) and ART status (On ART and Not on ART). I assigned equal disability weights for all ART health states, irrespective of the disease stage, which is also consistent with other mathematical modeling studies.<sup>107–109</sup> Future DALYs were discounted at 3% per annum.

### Costs

Economic costs associated with each HIV testing strategy, linkage to care and ART drugs came from published and grey literature. Costs were valued US dollars for comparability with prior studies and inflation-adjusted to 2017 currency year using the GDP deflator.<sup>60</sup> Future costs were discounted at an annual rate of 3%.<sup>60</sup> HIV testing costs varied by strategy based on the setting (community-based vs healthcare facility-based), medical supplies (blood-based test vs oral selftest), personnel, and patient costs (patient time and transport to healthcare facility). Facilitybased strategies required patients to visit the healthcare facility and incurred transportation costs and more time associated with the HIV testing process. Community-based strategies reduced patient costs but incurred more costs to reach patients in the communities. Costs considered included medical (HIV test kits, ART drugs and medical supplies), personnel (salaries for the nurse, healthcare facility management and peer educators), capital (healthcare facility site), overhead, patient time and transport to the healthcare facility. Cost data for HIV self-test kits, personnel, overhead, capital, training and medical supplies costs came from the trial<sup>55</sup> and a costing analysis conducted among truck drivers in Kenya.<sup>32</sup> Costs for peer-educators came from the RCT in Uganda that used peer-educators to distribute HIV self-testing kit and coupons to FSWs.<sup>22</sup> Costs associated with delivery of HIV care among patients on Pre-ART and ART came from the ministry of health report on the cost of comprehensive HIV treatment in Kenya.<sup>110</sup> The cost of ART drugs (first line - TDF+3TC (FTC)+EFV; second line AZT+3TC+ATV/r)<sup>111</sup> came from the Médecins Sans Frontieres report on ART prices in low and middle income countries.<sup>112</sup>

## **Cost-effectiveness analysis**

The total cost and DALYs lost per HIV testing strategy over the time horizon were used to calculate the incremental cost, incremental effectiveness (DALYs averted) and the incremental

effectiveness ratio (ICER). The ICER represents the cost of averting a DALY lost for a given HIV testing strategy compared to the next least costly strategy. HIV testing strategies that cost more but have less health benefits (DALYs averted) compared to the next best alternative are strongly dominated (represented as "s domintaed"). Those with lower cost and lower health benefits compared to the next most costly strategy are considered weakly dominated (represented as "w dominated"). Performance of strategies was evaluated by comparing the ICER with the willingness pay threshold (3xGDP per capita for Kenya in 2017),<sup>60</sup> where a strategy is considered to be cost-effective when the ICER is less than the willingness to pay threshold. The threshold represents the willingness to pay value for the additional health benefit gained from a strategy compared to other competing interests. I considered lower thresholds (1-3xGDP per capita) to account for differences in affordability across settings<sup>61–64,79</sup> and examine the robustness of our findings considering at lower willingness to pay thresholds. Further, since many factors (e.g., data quality, the comparator, and sub-groups of the target population) can impact the cost-effectiveness of an intervention, using a fixed WTP threshold as the only criteria to guide decision-making may lead to a wrong decision.<sup>61</sup> There is an ongoing debate in literature about the true WTP threshold to determine the cost-effectiveness of a strategy, partly due to the multiple factors that inform decision making. By considering different WTP thresholds, I account for the uncertainty in the WTP threshold.

# Sensitivity analysis

I performed deterministic sensitivity analysis to identify parameter inputs that impact the ICER including the initial distribution given limited data on CD4 in undiagnosed high-risk populations in this setting. Given that our target population is hard to reach, I examined the threshold under which the probability of reaching the targeted population may impact the base case findings. I

first assumed equal probability of reaching the targeted in both community- and facility-based strategies and then examined the threshold for the probability of reaching the targeted population where the community-based strategy may not be cost-effective. In the base case analysis, I assumed that truck drivers and FSWs transition into other occupations by age 50 and were considered part of PLHW in non-high-risk populations. Therefore, I assumed that the probability of reaching the targeted population, HIV test uptake and LTFU varied between age <50 and  $\geq$ 50 years. I relaxed this assumption and considered truck drivers and FSWs to remain as high-risk sub-populations for the entire time horizon.

### Model validation

The model was validated by comparing the life expectancy at 30 years for truck drivers and FSWs living with HIV and on ART to overall population of PLWH in Rwanda on ART.<sup>113</sup> Life expectancy for truck drivers and FSWs in a given CD4 strata was estimated by assuming all (100%) the initial cohort in that CD4 strata and projecting life years over the lifetime horizon. The life expectancy increased based on the CD4 strata at the time of HIV diagnosis with truck drivers and FSWs diagnosed at AIDS stage and initiated on treatment having a life expectancy of nearly 20 years compared to 29 years among those diagnosed at asymptomatic early stage. Life expectancy (Figure 5) estimated in the model was comparable to data from the literature except for the cohort that were diagnosed with CD4>500 which had a lower life expectancy than that reported in the literature. However, this could be a result of high LTFU in hard-to-reach populations and delays in linking to care and initiating treatment. The average life expectancy at 30 years in the model for those diagnosed with CD4>500, CD4 >350 – 500, CD4 >200-350, and CD4 <200 was 27.9, 27.1, 25.0 and 19.7, respectively which was comparable with that (30.1, 27.3, 25.9 and 19.06) of people living with HIV in the overall population

# Results

#### **Base case analysis**

In the base case analysis (Table 4 & 5), among both FSWs and truck drivers, the Kit delivery strategy was cost-effective and had the highest cost and life expectancy at 30 years and lowest DALYs lost. The "No testing" strategy had the lowest cost and life expectancy at 30 years and highest DALYs lost. For undiscounted outcomes, total costs ranged from \$1,700 to \$10,100 and \$1,700 to \$7,500 in the "No testing" and "Kit delivery" strategies among FSWs and truck drivers, respectively. More DALYs were lost in the "No testing" strategy (45.36 and 45.6) compared to the "Kit delivery" strategy (29.31 and 33.78) among FSWs and truck drivers, respectively. Findings were consistent for the discounted outcomes. Costs ranged from \$1,400 to \$6,100 and \$1,400 to \$4,951; and DALYs lost from 21.93 to 12.70, and from 22.11 and 14.77 among FSWs and truck drivers, respectively. The "Kit delivery" strategy was cost-effective with an ICER of \$520 and \$480 among FSWs and Truck Drivers, respectively. For undiscounted estimates, all strategies were dominated by the "Kit delivery" strategy in FSWs and truck drivers. However discounted estimates, among FSWs, although the ICERs for the provider-initiated testing (\$500) and HIVST Choice (\$510) strategies were lower than the WTP and comparable to the ICER for the Kit delivery strategy, these strategies had more DALYs lost compared to the Kit delivery strategy.

### Sensitivity analysis

Base case results were mainly sensitive to the cost of ART although policy conclusions did not change. Results of the one-way sensitivity analysis were reported in tornado diagrams, Figure 6 and 7 for FSWs and truck drivers, respectively. Given that our target population was hard to reach, I assessed how the probability of being reached would impact the base case results. When

I assumed equal reach between facility- and community-based strategies, the Kit delivery strategy was still cost-effective (ICER = \$498/DALY averted) among truck drivers but among FSWs, the HIVST choice strategy was cost-effective (ICER = \$516/DALY averted). In addition, I found that when the probability of reach is below 75%, the kit delivery strategy ceases to be cost-effective among FSWs but not truck drivers. Results were also sensitive to the probability of disclosing test results and seeking a confirmatory test. I found that when the probability of discloser is less than 60%, the Referral card strategy is cost-effective (ICER = \$520/DALY averted) among FSWs but not in truck drivers. When I considered truck drivers and FSWs to remain as high-risk for the entire time horizon, base case findings didn't change substantially, with HIVST kit delivery remaining cost-effective among both truck drivers and FSWs.

# Discussion

HIV testing and counseling remains substantially low in high-risk and hard-to-reach populations, but little is known about cost-effective strategies to improve HIV test uptake in these populations, particularly in Eastern and Southern Africa. I developed a Markov model to examine the cost-effectiveness of six alternative HIV testing strategies in hard-to-reach populations (truck drivers and FSWs). I found that the delivery of HIVST kits to the targeted population in the community using peer-educators is a cost-effective strategy in both truck drivers and FSWs with an ICER of \$480 and \$520, respectively. The findings were largely robust to parameter variations in sensitivity analysis but delivery of HIVST kits in the community was not cost-effective among FSWs when the probability of reaching the undiagnosed FWSs or disclosing test results was less than 75% and 60%, respectively.

The findings were broadly consistent with the literature although limited evidence exists on costeffective HIV testing strategies among high-risk and hard-to-reach populations. Previous studies evaluating the cost-effectiveness of HIV testing have largely focused on the general population, and among high-risk populations, few have included FSWs but not truck drivers. Comparable to this study findings, previous work has shown that community-based strategies, including community-based HIV self-testing, were cost-effective compared to facility-based strategies, particularly in high prevalence areas such Eastern and Southern Africa. For example, in Uganda and South Africa, home-based testing was cost-effective compared to facility-based with an ICER of \$3.5 per patient tested<sup>114</sup> and \$2,960 per HIV infection averted,<sup>115</sup> respectively. Homebased HIV testing was more cost-effective when targeting high HIV prevalence (32%) areas, with linkage to care and ART initiation expanded to individuals with CD4 cell count >350.<sup>115</sup> Although evidence is limited and emerging, HIVST seems to be cost-effective compared to blood-based provider administered HIV testing. For example, community-based HIVST was cost-effective when uptake of HIV testing increased by at least 20% with the cost of HIVST kit less than \$3<sup>47</sup> and when more individuals were diagnosed at early stages of the disease and immediately enrolled on ART.<sup>45</sup> one study that included FSWs as part of the sub-populations in the model, found the community-based HIVST to be cost-effective when the prevalence of undiagnosed FSWs was above 5.5% and the cost per patient equal to \$5.61.46

Hard-to-reach and high-risk populations have high HIV prevalence and a substantial proportion remain undiagnosed until late stages of the disease. With community-based HIV testing<sup>116–118</sup> such as home-based HIV testing, more undiagnosed individuals may be reached. Home-based VCT and mobile HIV testing have substantially higher (83% and 98%) HIV testing uptake compared to facility-based approaches.<sup>119</sup> Further, community-based approaches reach

undiagnosed individuals at earlier stages of the disease, which can potentially avert new HIV infections and reduce mobility and mortality through early linkage to care and initiation of ART. But despite having high HIV test uptake, community-based approaches have low rates (15-35%) of linkage to care<sup>120</sup> although this can improved (97%) with facilitated linkage to care programs.<sup>119</sup> With facilitated linkage to care programs, the Delivery of HIVST kits at truck stops may be cost-effective.

This is the first study to examine the cost-effectiveness of HIV testing strategies including HIV self-testing and the use of peer-educators with a focus on both truck drivers and FSWs. There is strong evidence supporting use of peer-educators to promote HIV prevention, particularly in high-risk and hard-to-reach populations.<sup>92</sup> I found the HIVST kit delivery strategy using peereducators cost-effective in both truck drivers and FSWs. Peer-educators usually operate in smaller groups and are able to gain access and trust to populations that are hard to reach with the usual standard of care practices. For example, among FSW, the kit delivery strategy overcomes the limitation of provider stigma faced by FSWs when seeking health care services, particularly in countries where sex work is illegal. Truck drivers are hard to reach due to the unique characteristics of their occupation-highly mobile-that may impact utilization of routine health care services. Using peer-educators may be a suitable strategy to reach those that do not routinely visit the health facility. Previous work on truck drivers has shown that even when drivers are aware of HIV testing services at the healthcare facility that is geographically accessible (e.g., roadside wellness clinic along the truck routes), they were not willing to visit to the health facility.<sup>42</sup> The HIVST kit delivery strategy may improve HIV testing uptake within this population through delivery of kits at truck stops. Although community-based strategies such as the HIVST kit delivery tend to have lower rates of linkage to care compared to facility-based

strategies, using peer-educators may also improve linkage to care and ART initiation by motivating those that test positive for HIV to seek medical care. The kit delivery strategy may also be more attractive to payers since it has high rates of HIV test uptake and requires low skilled labor as compared to provider-administered facility-based testing. But there is a potential problem of high turnover which may negatively impact continuity of the strategy when implemented and overall effectiveness and costs incurred in frequent hiring and training.

This study had several limitations: 1) I did not account for HIV prevalence, which impacts the percentage of individuals diagnosed, total strategy costs and DALYs. When the HIV prevalence is high, more individuals are identified, linked to care, and initiated on treatment increases the costs for the strategy through antiretroviral drugs but lowers the DALYs. By not accounting for HIV prevalence, I am unable to determine thresholds at which strategies are cost-effective based on HIV prevalence in the cohort. However, prior evidence shows HIV testing strategies have been consistently cost-effective even in low prevalence settings of less than 1%.<sup>46,121–123</sup> Both truck drivers and FSWs have relatively high HIV prevalence (>10%),<sup>2–7</sup> thus, considering HIV prevalence will not change the study's overall policy conclusions. For example, in one study HIV prevalence was varied from 0.01% to 20% and was found to be cost-effective in all cases.<sup>123</sup> At 0.01% HIV prevalence, the incremental cost-effectiveness ratio was \$451 per quality adjusted life years gained, which is much lower than the GDP per-capita threshold for most of lowincome countries.<sup>124</sup> In a community-based self-testing study, HIV testing was found to be costeffective with HIV prevalence of undiagnosed individuals at 3%.<sup>46</sup> Given that HIV prevalence is high among hard-to-reach populations,<sup>125</sup> HIV testing strategies are likely to be cost-effective at all levels of HIV prevalence. 2) Due to data limitations, I did not include viral suppression in the model and assumed that all fractions of the cohort in ART health states achieved viral

suppression. This assumption may have overestimated the benefits of ART by not accounting for those that did not achieve viral suppression. Those on ART were assigned lower disability weights and by including those that haven't achieved viral suppression, I may have increased the effectiveness of the strategy and the incremental effectiveness, and as a result, the ICER may be lower than the true value leading to wrong decision making. However, the ICERs were substantially lower (<\$700) than the WTP threshold (\$4700) and thus, we do not anticipate would materially impact the final policy recommendation. 3) Some of the HIV testing strategies were only implemented in one sub-population (e.g., FSWs) but I assumed the same level of efficacy applies to both sub-populations (truck drivers and FSWs). For example, HIVST kit delivery, coupon delivery and VCT referral card were implemented among FSWs although I assumed similar effectiveness among truck drivers and the HIVST choice was only implemented among truck drivers. Although both truck drivers and FSWs are hard-to-reach, the efficacy of these strategies may vary given that HIV testing varies based on gender.

Low uptake of HIV testing, particularly for high-risk and hard-to-reach populations significantly impacts achievement of country and global UNIADS targets. Using peer-educators to deliver HIV self-testing kits in the community is a cost-effective strategy to improve HIV test uptake in populations that are hard to reach and at high-risk of acquiring and transmitting HIV. Future studies should account viral suppression and HIV prevalence.

**Chapter IV:** Cost-Effectiveness of Alternative Strategies to Reduce Loss to Follow-up after Antiretroviral Therapy Initiation among Female Sex Workers in Eastern and Southern Africa

# Introduction

Female sex workers (FSWs) living with HIV, particularly in Eastern and Southern Africa, are at high risk of loss to follow up (LTFU) from antiretroviral therapy (ART) programs.<sup>126,127</sup> However, little evidence exists on strategies to reduce LTFU and their cost-effectiveness. Consistent ART is beneficial for reducing HIV-related morbidity and mortality,<sup>128</sup> and preventing onward HIV transmissions when people living with HIV (PLWH) achieve viral suppression.<sup>129</sup> PLWH are considered LTFU if they miss their last three consecutive visits to the health facility and are not classified as either dead or transferred-out to another healthcare facility.<sup>130</sup>

FSWs are disproportionately impacted by HIV with 30 times higher risk of acquiring HIV compared to the general population.<sup>131</sup> In addition, they are hard-to-reach and face unique barriers that impact their engagement in care.<sup>27</sup> For example, FSWs are unlikely to self-identify as sex workers due to fear of societal violence and provider stigmatization, particularly in countries where sex work is illegal,<sup>27</sup> which impacts their willingness to seek routine care and retention in HIV care for those living with HIV.<sup>27</sup> In fact, among those in HIV care and on ART, up to 53% are LTFU after initiation of ART within 36 months,<sup>11–18</sup> compared to 14% reported for the overall population of PLWH.<sup>19</sup> Given that nearly 1 in 5 of new HIV infections in sub-Saharan Africa is attributed to FSWs,<sup>132</sup> retaining them in care and on ART is critical for

improving HIV-related morbidity and mortality among those living with HIV and preventing onward HIV transmissions.

This study examined the cost-effectiveness of strategies to reduce LTFU among FSWs after initiating ART. Studies conducted in overall population of PLWH suggest home ART delivery,<sup>133</sup> home ART delivery with nutrition supplement,<sup>134</sup> tracing patients who miss appointment plus transport reimbursement<sup>135</sup> and offering free medical care for opportunistic infections and lab tests<sup>136</sup> are effective in reducing LTFU. In West Africa, offering free medical care for opportunistic infections, transport reimbursement and breakfast<sup>137</sup> for PLWH was costeffective with a baseline LTFU  $\geq$ 18% and risk reduction  $\geq$ 41%.<sup>137</sup> However, evidence on costeffective LTFU strategies is limited, and none exists among FSWs or other high-risk and hardto-reach populations.

To contextualize the contribution of this study, I discuss the evidence on the cost-effectiveness of LTFU strategies in the overall PLWH. Strategies to reduce LTFU have been shown to be cost-effective when the percentage of people living with HIV and on ART that are LTFU from ART programs was at least 12%.<sup>133,137,138</sup> Community support programs such as delivery of ART in the community and supporting adolescents to adhere to treatment in South Africa reduced LTFU by 40% compared to the standard of care (no community-based support) and was cost-effective.<sup>133</sup> One study examined the cost-effectiveness of three hypothetical strategies: 1) Risk Reduction (40%), lower likelihood of disengaging from care, 2) Outreach (60%), patients with missed ART appointments are traced and re-linked to care, and 3) a combination of both Risk Reduction and Outreach strategies.<sup>138</sup> Compared to the standard of care (no intervention), a combination of Risk Reduction and Outreach was a cost-effective with increase in life

expectancy by 5.2 years, 2.4 Quality adjusted life years (QALYs) gained and an incremental cost-effectiveness ratio of \$4700/QALY gained.<sup>138</sup> However, these strategies were hypothetical and their efficacy has not been examined in a real world setting. In West Africa, four strategies to reduce LTFU: 1) elimination of ART co-payments; 2) #1 plus treatment costs for opportunistic infections; 3) #2 plus increased training for health workers; and 4) #3 plus reimbursing transportation costs and providing breakfast for patients attending scheduled visits were examined.<sup>137</sup> With a baseline annual LTFU reduction of 40% (from 18% to 11%), and efficacy range (10% to 75%), a given strategy was be cost-effective if it costs between US \$22 - \$77 per person-year with efficacy of at least 12 - 41%, respectively.<sup>137</sup> These studies provide baseline for examining strategies in other populations such as FSWs at high risk of LTFU but with limited evidence on strategies to prevent LDTU. Further, identifying efficient strategies to reduce LTFU is critical for guiding resource allocation, particularly in the current climate with constraints in international funding for HIV response programs.<sup>28</sup>

## Methods

#### **Overview**

I used a Markov model to examine costs and disability-adjusted life years (DALYs) lost of six LTFU strategies in a cohort of FSWs living with HIV and receiving ART. The analysis was conducted from a payer perspective with future DALYs lost and costs discounted at 3%.<sup>60</sup> Each health state was assigned a disability weight to reflect the disease burden. Costs were valued in US dollars and inflation-adjusted to 2017 currency year. The primary outcomes were costs, DALYs averted, and incremental cost-effectiveness ratios (ICERs). The ICER was used to assess the relative performance of the strategies, with the cost-effectiveness of a given strategy determined according to a threshold of 3x the GDP per capita for Kenya in 2017 (\$4,710),<sup>60</sup> although lower thresholds were also assessed to account for differences in affordability and willingness to pay across settings.<sup>61–64,79</sup> Uncertainty in inputs was assessed using probabilistic sensitivity analysis.

## Strategies

Six alternative strategies (Table 6) were examined: 1) No intervention; 2) Home ART delivery using community-health workers<sup>133</sup>; 3) Home ART delivery using community-health workers plus monthly nutrition supplement<sup>134</sup>; 4) physical and phone-tracing of patients that miss an appointment plus transport refund to the health facility<sup>135</sup>; 5) physical and phone-tracing with free medical care for opportunistic infections<sup>136</sup>; 6) free medical care for opportunistic infections with transport refund to the health facility and free breakfast.<sup>137</sup>

LTFU strategies came from studies conducted among the overall population of PLWH. I assumed that the effectiveness of these interventions is comparable when implemented in a highrisk and hard-to-reach population such as FSWs. I justified this assumption using the case of HIV pre-exposure prophylaxis (PrEP) since PrEP interventions implemented in both the general population and hard-to-reach population have been similar and have shown comparable effectiveness, with overlap in 95% confidence intervals implying effectiveness across the two populations is not statistically different.

I relied on PrEP interventions, versus other interventions at other steps along the HIV care continuum, to justify this assumption for the following reasons: 1) PrEP interventions implemented in the general population are also routinely implemented among hard-to-reach populations, which enables comparison of their efficacy or effectiveness. 2) There is no evidence

that different PrEP interventions are implemented for the general population and hard-to-reach populations. 3) PrEP interventions are implemented over a longer time period (>1 year), require longer-term adherence and compliance to treatment, and report HIV incidence, which can be used as a proxy measure for adherence and patient behavior outcomes. Adherence is a key factor associated with the likelihood of LTFU among people living with HIV.<sup>139</sup> 4) There is no evidence that different interventions are implemented for the general population and hard-toreach populations at some additional key steps along the HIV care continuum, including linkage and retention in care. Indeed, no evidence exists for any intervention to promote linkage or retention in care among hard-to-reach populations of people living with HIV. Importantly, however, interventions to improve HIV testing uptake-for which there is variation in implementation across populations<sup>10,22,140–143</sup>—were not considered. This is because, these interventions are implemented for a relatively short period of time<sup>22,144</sup> (compared to PrEP interventions),<sup>145,146</sup> potentially at discrete intervals, and may not adequately capture patient behavior (e.g., visiting the clinic regularly for drug refills), in terms of adherence to a longer term prescribed regimen, over a period of time.

I focused in particular on a particular aspect of PrEP: patient behavior. I relied on patient behavior—defined here in terms of adherence to ART or PrEP continuously and over a longer time horizon—to justify the assumption that LTFU reduction strategies are similarly effective among hard-to-reach populations living with HIV and on ART and among the overall population of PLWH since the behavior that results in PrEP adherence parallels similar behaviors required to remain in HIV care. This parallel is particularly relevant in sub-Saharan Africa where people diagnosed with HIV not only take daily medication but must visit the clinic more regularly (monthly or every two months) for drug refills.<sup>147</sup> When examining adherence to PrEP, I found

comparable adherence to PrEP among hard-to-reach populations and the general population for a given intervention. For example, adherence to PrEP among female sex workers in South Africa ranged from 70% at nine months and 95% at eighteen months<sup>13</sup> compared to HIV discordant couples with average adherence of  $\geq$ 85% within a similar time period,<sup>148</sup> which is within the range for adherence to PrEP in FSWs.<sup>13</sup> Notably, there is precedent in the mathematical modeling literature to assume that intervention efficacy is similar across different populations. For example, Anderson et al. assumed the efficacy of PrEP to be identical not only across different sub-populations, including FSWs, but also for the general population.<sup>149</sup>

While there are differences in the measures of central tendency for PrEP effectiveness among the general population and hard-to-reach populations, PrEP interventions among the general population report comparable effectiveness among hard-to-reach populations, suggesting that they are not statistically different across the two populations. I drew from this evidence to assume that LTFU interventions are as effective in hard-to-reach populations as in the general population.

## **Model structure**

I used the Markov model in paper 2 (Figure 8) of the dissertation but restricted the initial cohort distribution to health states prior to first-line ART. The model projected lifetime economic costs and DALYs lost associated with each strategy in a hypothetical cohort of FSWs on ART, with a mean age of 30 years. Model health states represented HIV disease clinical stages based on CD4 cell count to account for differences in the probability of LFTU across CD4 cell count strata.<sup>150–152</sup> On-ART disease progression (i.e., changes in CD4 count due to ART) is not modeled, given evidence that LTFU is associated with baseline CD4 count at ART initiation; however, disease

progression is modeled in the absence of ART, with differences in the probability of LTFU and death according to disease progression.<sup>153,154</sup> The initial cohort was followed over a lifetime time horizon with transitions and outcomes updating monthly to reflect the average frequency of visits to the clinic for drug refills in Eastern and Southern African countries.<sup>155–157</sup> To project lifetime DALYs lost and economic costs, each health state was assigned a disability weight and monthly cost with the sum of DALYs and costs over the analytic time horizon to reflect total strategy-specific DALYs lost and costs.<sup>104</sup>

## Data

Data for parameter inputs (Table 7) came from the literature. The initial distribution of FSWs on ART came from a cohort study of newly diagnosed HIV individuals in Kenya,<sup>94</sup> although I assessed other distributions in sensitivity analysis given the limited CD4 data in this setting.<sup>158</sup> Probabilities of disease progression and switching to second-line ART came from a prospective study among PLWH in South Africa<sup>83</sup> and a retrospective study on rates of switching to second-line ART in Uganda,<sup>159</sup> respectively. Monthly disability weights came from Eaton et al.,<sup>105</sup> derived from the global disease burden study.<sup>106</sup> I assumed equivalent disability weights for asymptomatic health states (not on ART). Similarly, all health states indicating patients on ART have equal disability weights irrespective of CD4 cell count given the clinical benefits of ART, comparable to other mathematical modeling studies.<sup>107–109</sup>

Data for LTFU came from a retrospective study that examined retention in care among FSWs on ART in sub-Saharan Africa.<sup>14</sup> Data for LTFU risk reduction came from different studies conducted among PLWH and on ART in sub-Saharan Africa: 1) a retrospective study among young adults on ART in South Africa who received community-based ART delivery<sup>133</sup>; 2) a

prospective community-based support program in Rwanda which provided home ART delivery with nutrition support for PLWH and on ART<sup>134</sup>; 3) a retrospective study among PLWH in Eastern Africa who were LTFU and traced to reengage them in HIV care<sup>135</sup>; 4) a prospective study among adults on ART who received free medical care for opportunistic infections and lab tests with a primary care physician and case manager to monitor the patients' health<sup>136</sup>; 5) a mathematical modeling study that examined hypothetical strategies to reduce LTFU including offering free ART plus medical care for opportunistic infections, transport refund and breakfast.<sup>137</sup>

## Costs

Economic costs associated with each strategy came from the literature and reflected a payer perspective.<sup>60</sup> Costs were valued and reported in US dollars (\$) and adjusted for inflation to 2017 currency year using the GDP deflator.<sup>60</sup> Costs varied based on the strategy including medical (ART drugs, opportunistic infections drugs and laboratory costs); labor (salaries for healthcare workers including community health care workers, non-clinical healthcare facility staff, physician, and lab technician); capital (health facility and equipment), overhead costs and patient transport refund. Data for ART drugs, labor, capital and overhead costs came from the Ministry of Health costing analysis report for treating PLWH in Kenya.<sup>110</sup> The cost of patient transport to the health facility came from a costing analysis report of PLWH in Uganda.<sup>160</sup> Costs associated with community-based ART delivery including training, salaries, management, equipment and overhead came from a retrospective study among young adults on ART in South Africa.<sup>133</sup> The cost for nutrition supplement was estimated at approximately a \$1 per day.<sup>161</sup>

### **Cost-effectiveness Analysis**

Performance of alternative strategies to reduce LTFU was determined based on the willingness to pay (WTP) threshold of 1-3xGDP per capita of Kenya in 2017.<sup>60</sup> We used Kenya as a representative country in Eastern and Southern Africa since it has a large number of truck drivers, routes and truck stops where drivers engage with FSWs.<sup>162</sup> The WTP threshold represents a country's willingness to pay for an additional health benefit, measured as DALYs averted in this study. The GDP per-capita is used as a WTP threshold because the health benefit gained from the intervention would increase an individual's productivity which is measured by an increase the GDP per-capita. While I use a 3xGDP per capita threshold, I take in account the ongoing debate regarding the true threshold for evaluating cost-effectiveness. This debate centers on a criticism that the 1-3xGDP per capita threshold is too high for resource-limited settings, given other competing priorities.<sup>61–64,79</sup> To attend to this concern, I also evaluated costeffectiveness using a more conservative threshold of 1x GDP per capita for Kenya. Although multiple factors are considered in the decision-making process, the WTP threshold provides a monetary value with which to compare alternative strategies. Strategies with higher costs and lower health benefits than the next most costly alternative were considered "strongly dominated;" strategies with a higher ICER than the next most costly non-dominated alternative strategy were eliminated as "weakly dominated" because they provide less health benefit per additional cost unit.

#### Sensitivity analysis

One-way, multi-way and probabilistic sensitivity analysis were used to assess uncertainty in parameter inputs. In one-way sensitivity analysis I identified the main cost drivers of variation in the ICER, with the results reported using a tornado diagram, which summarizes the range of

ICERs due to variation in unit cost estimates. For multi-way sensitivity analysis, I considered extreme values (lower and upper bound) of parameter inputs to examine the impact of simultaneous variation of parameters given that in a real-world setting multiple values change concurrently. I conducted a probabilistic sensitivity analysis to assess the impact of random variation in parameter inputs on the cost-effectiveness of the strategies. I assumed a beta and gamma distribution for probability and cost variables, respectively. The beta distribution bounds probability between 0-1 and the gamma accounts for skewness of cost data.<sup>163</sup> Ten thousand Monte Carlo simulations were performed with values sampled randomly within the parameter input range, with ICERs calculated for each simulation. Results from simulations were reported using a cost-effectiveness acceptability curve.<sup>66,67</sup> The acceptability curve summarizes the probability a strategy is cost-effective at different WTP thresholds. I accounted for misclassification of LTFU given prior evidence from sub-Saharan Africa suggests that some patients recorded as LTFU had died or transferred to another clinic.<sup>19,130,164–166</sup> I applied a probability weight of 0.43, derived from 1 - proportion LTFU who die (0.208) - proportion LTFU who self-transfer from site (0.359). These estimates were based on evidence among patients in ART programs in sub-Saharan Africa that suggested 20.8% and 35.9% of patients recorded as LTFU had died or self-transferred to another ART clinic.<sup>19</sup> In the base case analysis I assumed that all strategies are implemented over the cohort's lifetime, which may not be the case in the real-world setting since programs are implemented for shorter time periods such as 5 and 10 years. In particular, "ART delivery + nutrition supplement" was the most effective but costly strategy with nutrition supplement contributing a larger (65%) percentage of the cost. In the sensitivity analysis, I examined the cost-effectiveness of the strategies with nutrition supplement only offered for 5 and 10 years. Further, since "ART delivery + nutrition supplement" was not

cost-effective in the base case, I examined the cost of nutrition supplement at which the strategy would be cost-effective if it is offered throughout the cohort's lifetime.

## Results

#### **Base case analysis**

In the base case analysis (Tables 8 and 9), ART delivery was cost-effective compared to alternative LTFU strategies. Undiscounted costs ranged from \$4,664 to \$16,292 and DALYs lost from 28.41 to 23.40 in "No Intervention" and "ART delivery + nutrition supplement", respectively; discounted estimates ranged from \$2,994 to \$10,022 and 11.52 to 9.27, respectively. ART delivery was cost-effective compared to alternative strategies with an ICER of \$470 per DALY averted. ART delivery with nutrition supplement had lower DALYs lost (9.27) but cost substantially more compared to the next best alternative, ART delivery (\$10,022 vs \$5,173). This resulted in an ICER of \$5,100 per DALY averted and was not cost-effective at a willingness to pay threshold of \$4,710.

### Sensitivity analysis

In one-way sensitivity analysis (Figure 9), we compared the impact of individual parameters on the cost-effectiveness of the "ART delivery" strategy compared to "No Intervention". ART drugs had the largest impact on ICER, in particular, second line ART, and the relative reduction in LTFU by the ART delivery. However, regardless of the variation in the ICER, the study conclusions did not change, ART delivery remained cost-effective compared to No intervention. In the multi-way sensitivity analysis (Tables 10 and 11), the ART delivery + Nutrition supplement strategy was cost-effective when lower bound costs were considered while the "Medical care + Transport + Breakfast" strategy was cost-effective for the upper bound costs. I examined the impacted of adjustment for LTFU misclassification, but the findings (Table 12 and 13) remained consistent with the base case analysis—ART Delivery remained cost-effective compared to the No Intervention strategy, with an ICER of \$500 per DALY averted. When I reduced the time frame when the nutrition supplements were offered to 5 and 10 years (supplementary material, Tables S21 and S22), the "ART delivery + Nutrition" supplement was cost-effective in 5 years (ICER = \$4,300) but not in 10 years (ICER = \$6,880).

Results for the probabilistic sensitivity analysis are shown in the cost-effectiveness acceptability curve (Figure 10). The probability of cost-effectiveness of a given strategy (No Intervention, ART Delivery and ART Delivery + Nutrition Supplement) varied based on the WTP threshold. When the WTP was <\$500, No Intervention had the highest probability of cost-effectiveness; \$500-\$4,600 ART Delivery was more likely to be cost-effective; and >\$460 the ART Delivery + Nutrition Supplement had a higher probability of cost-effectiveness. In the cost-effectiveness plane (Figure 11), majority of the data points for incremental costs and incremental effectiveness fall eastern quadrants of the plane, indicating that ART delivery averted DALYs but may also be cost-saving.

## Discussion

I used a Markov model to estimate costs and DALYs averted by strategies aimed at reducing LTFU among FSWs living with HIV and on ART in Eastern and Southern Africa. Home ART delivery using community-health workers was cost-effective at a willingness to pay threshold of \$ 470 per DALY averted. I estimated 0.98 DALYs could be averted at an additional cost of \$ 466. Taking an example of Rwanda with approximately 12,278 FSWs, of which 6,237 (50.8%)

are living with HIV, these per patient estimates would translate to 6,112 DALYs averted at an additional cost of \$2.9m.

LTFU remains a major public health problem that negatively impacts the success of ART programs, particularly in low-income settings.<sup>126,167</sup> Previous studies indicate that LTFU from ART programs increases the risk of treatment failure, drug resistance, viral load rebound and mortality.<sup>128,167,168</sup> A number of factors can contribute to LTFU from ART programs including stigma to visit an HIV clinic, failure to remember getting treatment, distance to the health facility, lack of transport to the clinic and being too sick to visit the clinic.<sup>169</sup> These factors are enhanced particularly among vulnerable populations such as FSWs, leading to higher rates of LTFU.<sup>11–18</sup> For example, in Côte d'ivoire, 53% of 376 female and 38 male sex workers were LTFU of within a follow-up period of 36 months.<sup>14</sup> In South African FSWs, 30% were LTFU within 12 months, which is higher than what is reported (8.5%) in general population considering the same time period.<sup>13</sup>

Strategies to reduce LTFU among FSWs living with HIV may cost more than in the overall HIV population. Previous studies have shown that ART programs that work with members of the community to follow up with patients to support them in adherence to treatment, report improved retention in HIV care,<sup>170</sup> but no study has examined the cost-effectiveness of this strategy. In this study, I found ART delivery in the community was cost-effective in reducing LTFU suggesting that reaching to patients in areas where they live and delivering ART drugs could be an efficient way of retaining them on HIV treatment. Using peer-educators may be suitable for reach the FSWs since some may not be easily identified by community health workers in the general population and this may require me resources. A substantially body of literature has shown

tracing (at home or by phone) patients that miss appointments at the clinic effective in reducing LTFU<sup>171</sup> however, I didn't find tracing cost-effective in this study. This may potentially result from higher costs of tracing a hard-to-reach population such as female sex workers. The costs of tracing FSWs may be higher given that majority are less likely to disclose their physical address for tracing, particularly in countries where sex work is illegal.

ART delivery + nutrition supplement (nutrition offered over a lifetime period) was the most effective strategy but not cost-effective at a willingness to pay threshold of 3xGPD per capita of Kenya (\$4,710). Previous work has shown that the nutrition supplement may improve adherence to treatment, retention in HIV care and reduce the mortality rate among patients on HIV treatment since ART drugs affect their metabolism and good nutrition is vital is reducing the side effects of the drugs.<sup>172</sup> In this study, if the reduction in mortality rate was considered, the ART delivery + nutrition supplement strategy may have been more effective with lower total number of DALYs lost over the time horizon and potentially be cost-effective. Previous work found that nutrition supplement was cost-effective when targeting HIV patients who start ART with low body mass index and mulnarished.<sup>173</sup> In sensitivity analysis, I found that offering nutrition supplement for 5 years and reducing the amount of money from \$30 to \$15 per month would result in ART delivery with nutrition supplement being cost-effective. This suggests that nutrition supplement is a potentially cost-effective intervention when offered for a shorter time period and targeting patients with food insecurity. Although nutrition supplement may be effective in reducing LTFU and improving overall health of PLWH, there may be potential unintended consequences such as FSWs getting HIV so that they can benefit from the nutrition program.<sup>174</sup>

The findings are novel yet comparable to the limited evidence on cost-effectiveness of LTFU strategies in the overall population of PLWH.<sup>133,137,138</sup> In South Africa, a community-based ART support program for adolescents living with HIV was implemented for 2 years and reduced LTFU by 40% compared to the standard of care (no community-based support) and was cost-effective with an incremental cost-effectiveness ratio of US \$600 per averted patient LTFU.<sup>133</sup> Adolescents also require targets strategies since to engage in care and the findings<sup>133</sup> support this study conclusion that delivering ART in the communities is a cost-effective approach. In côte d'ivoire, an intervention that offered free ART drugs, treatment costs for opportunistic infections, increased training for health workers, reimbursing transportation costs and provided breakfast for patients attending scheduled visits was found to be cost-effective in reducing LTFU when costs ranged between \$22 and \$77 per person-year with efficacy of at least 12% to 41%.<sup>137</sup> Although I did not examine this identical strategy, offering free medical care, transport reimbursement and breakfast was not a cost-effective strategy compared to alternative strategies.

This study has several limitations. First, strategies to reduce LTFU that were examined in this study came from previous work done in PLWH on ART in the overall HIV population, which is not representative of a hard-to-reach population. However, despite the differences in study populations, these strategies can be applied to hard-to-reach populations given that similar strategies have been implemented in both hard-to-reach and overall HIV population to improve adherence to PrEP and the effectiveness of those strategies was comparable. Second, this study focuses on FSWs in the Eastern and Southern Africa region, but model parameters were largely derived from Kenya, which I use as a case study country. Although Kenya is a good representative of countries in this setting, estimates may not be generalizable to countries such as South Africa where the cost of living and income classification is higher. Nevertheless, the

findings make contribution to this topic and population that is under studied. Third, potential benefits of nutrition supplement were not accounted for such as reduction in mortality rate which could have increase the effectiveness of the ART delivery + nutrition supplement strategy and potentially the cost-effectiveness. Finally, viral suppression was not included in the model due to limitations of data to inform parameter inputs. Thus, I assumed that all patients on ART achieved viral suppression. This assumption may have overestimated the benefits of ART and underestimated the cost-effectiveness thresholds of the strategies. Although we found ART delivery cost-effective at a low WTP threshold, results need to be interpreted with caution due to potential overestimation of the effectiveness of the strategy from this assumption.

To achieve the global goal of ending the HIV epidemic, its critical to reach all PLWH, link, and retain them on ART. Hard-to-reach populations including FSWs remain disproportionately impacted by HIV with high rates of LTFU from ART programs. This study found that delivering ART drugs to FSWs in their homes, places that they frequent, or community centers is a cost-effective strategy to reduce LTFU among FSWs in ART programs in Eastern and Southern Africa. Despite the lack of RCTs or observations studies examining the effectiveness of LTFU strategies in FSWs or similar hard-to-reach populations, these findings provide insights on efficient interventions to be considered by policy makers.

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# **Tables and Figures**

## Paper one

Cost component	CHIVS	Γ (Intervention)*	SOC (C	'ontrol)†	Р-
_	Mean	95% CI	Mean	95% CI	value‡
HIV test Kit	10.12	[8.85 - 11.38]	$0.00^{\$}$	[0.00 - 0.00]	< 0.001
Medical Supplies	0.25	[0.22 - 0.27]	0.30	[0.27 - 0.33]	< 0.001
Labor					
Nurse	2.37	[2.22 - 2.53]	1.64	[1.47 - 1.80]	< 0.001
Health facility staff	0.92	[0.86 - 0.99]	0.79	[0.71 - 0.87]	0.037
Training	0.08	[0.07 - 0.08]	0.00	[0.00 - 0.00]	< 0.001
Capital costs					
Health facility	1.44	[1.34 - 1.54]	1.24	[1.11 - 1.37]	0.037
Equipment	2.18	[2.04 - 2.31]	0.00	[0.00 - 0.00]	< 0.001
Overhead	3.59	[3.35 - 3.83]	3.06	[2.75 - 3.37]	0.037
Cell phone service	12.03	[11.28 - 12.79]	0.00	[0.00 - 0.00]	< 0.001
Patient time	2.67	[2.45 - 2.79]	1.81	[1.63 – 1.99]	< 0.001
Cost per patient	35.59	[33.08 - 38.09]	8.84	[7.96 – 9.73]	< 0.001

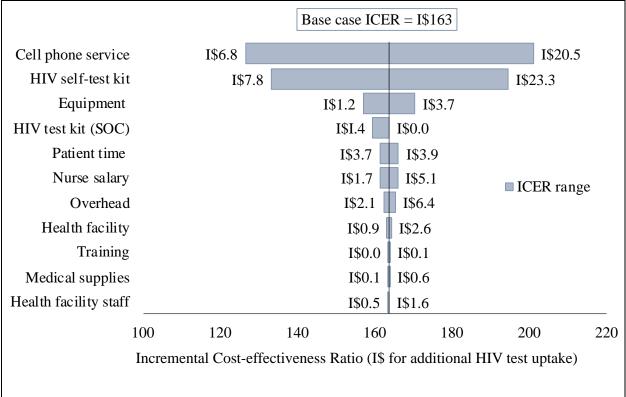
### Table 1: Mean costs per patient, by cost component and trial arm, reported in 2017 I\$

Abbreviations: CHIVST=Choice of Self-Administered Oral HIV Testing; SOC = Standard of care

\* Participants were offered the choice to test for HIV using 1) the provider-administered HIV testing or 2) self-administered oral HIV-testing under the supervision of a provider. If the truck driver declined the two options, they were offered a third option; 3) self-administered oral HIV-testing outside the clinic (at home) without supervision of a provider.

† Participants were offered on the provider-administered HIV testing.

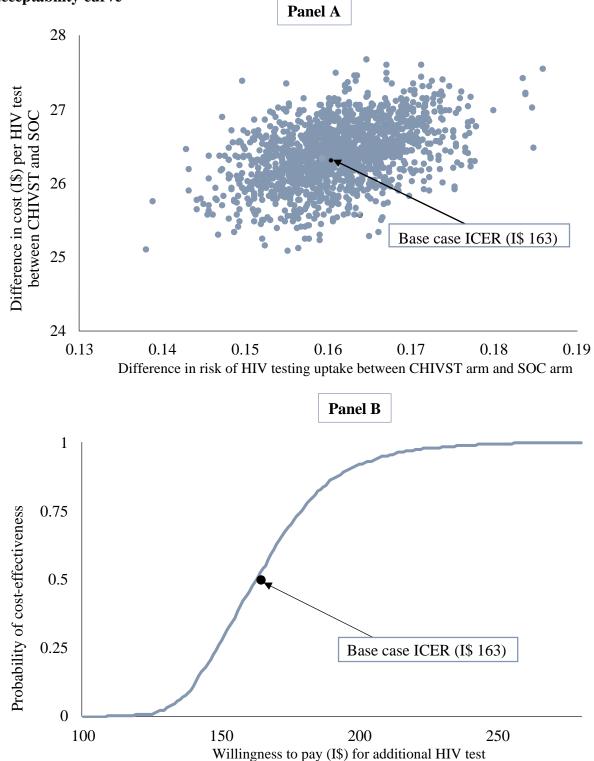
‡ The p-values are from the Wilcoxon rank sum test for differences in median costs by trial arm. § The cost of the SOC HIV test kit was I\$0.00 because SOC kits were provided by the Kenyan Ministry of Health at the clinic. However, I consider a scenario where the kits are not subsidized by alternative sources in sensitivity analysis.

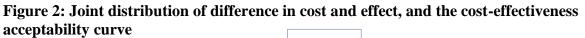


### Figure 1: One-way sensitivity analysis of unit costs

Figure 1 shows the incremental cost-effectiveness ratios (ICERs) corresponding to variations in cost variables based on upper and lower bound values. The x-axis shows the ICER and y-axis the cost variables considered in the study. The vertical line indicates the ICER (I\$163) when costs are considered at base line values. The costs of cell phone service and of the HIV self-testing kit were the key drivers of costs and had the largest impact on the ICER followed by equipment (cell phones), and economic cost of the SOC HIV test kit and patient time spent at the clinic for the HIV testing process. Other cost variables have little impact on the ICER.

Figure 2, Panel A shows the joint distribution of the difference in cost (y-axis) and the difference in risk of HIV testing uptake (x-axis) across trial arms from 1500 bootstrap samples. All the data points on the cost-effectiveness plane are in the northeastern quadrant. This implies that offering the CHIVST increases both costs and risk of HIV testing uptake and there is less uncertainty in the cost per additional per HIV test performed since all the data points are clustered in the same quadrant. Panel B shows the probability (y-axis) of CHIVST being cost-effective compared to the SOC is almost equal to 1 when the willingness to pay value (x-axis) is greater than I\$ 250. The willingness-to-pay of I\$ 250 is much lower than to the cost-effectiveness threshold of I\$ 9,774 (3xGDP per capita of Kenya in 2017), which shows that CHIVST is cost-effective compared to the SOC even at very low willingness to pay thresholds. The black dot indicates the base case willingness to pay (I\$ 163) with the probability of cost-effectiveness at 0.5.





### Paper two

		Truck Driver	S	Female Sex W	Vorkers		
Category*	Strategy†	Reach‡	Test uptake	Reach‡	Test uptake	Cost (\$ 2017)	Source
	No testing						
Facility	VCT	0.037	0.022	0.063	0.042	\$ 6.77	29,32,56
	PITC	0.037	0.103	0.063	0.175	\$ 6.77	21,32,56
Community	Kit Delivery	0.319	0.198	0.319	0.198	\$ 18.73	22,32,56,95
Combination	Coupon Delivery	0.319	0.040	0.319	0.115	\$ 20.87	22,32,56,95
	Referral card	0.319	0.035	0.319	0.093	\$ 14.74	22,32,56,95
	HIVST Choice	0.037	0.158	0.063	0.221	\$ 13.11	21,32,56

Table 2: HIV testing strategies with associated probability of reaching the target population, test-uptake, and cost per HIV test

Abbreviations: HIVST=HIV self-testing; VCT=Voluntary Counseling and Testing; PITC=Provider-initiated counseling and testing \*Strategies are classified based on the setting where the target population was reached and HIV testing. The combination category includes both the health facility and the community setting.

†Strategies are defined as follow: 1) No Testing – I assumed that there is no HIV testing and all FSWs and Truck Drivers living with HIV remained undiagnosed. 2) VCT – FSWs and Truck Drivers voluntarily visit the clinic and request an HIV test which is blood-based and provider-administered. 3) PITC – A health provider at the health facility initiates the discussion with the patient to have an HIV test and when the patient agrees the provider administers the blood-based HIV test. 4) Kit Delivery – HIV self-testing kits are delivered in communities to FSWs and Truck Drivers by peer-educators. 5) Coupon Delivery – HIV self-testing coupons are delivered in the communities to FSWs and Truck Drivers by peer-educators to exchange for a free-of-charge HIV self-test kit at the health facility. 6) – Referral cards are delivered in the community by peer-educators to exchange for a free-of-charge HIV self-test kit at the health facility. 6) – Referral cards are delivered in the community by peer-educators to exchange for a free-of-charge provider-administered blood-based HIV test. 7) HIVST Choice – FSWs and Truck Drivers who visit the clinic to seek care are offered a choice of provider-administered blood-based rapid test OR oral HIV self-testing at the clinic OR, if either testing refused, oral HIV self-testing at home.
‡Reach is defined as the probability of getting in contact with the Truck Drivers and FSWs living with HIV and hard-to-reach.

# **Table 3: Monthly Parameter Inputs**

		Baseline (ra	nge), [95% CI]	
Parameter*		Truck drivers	Female sex workers	Source
Initial distribution (%)				94
	Asymptomatic Early	28.8		
	Asymptomatic Late	19.6		
	Symptomatic	19.7		
	AIDS	31.9		
Disease progression				
1 0	Asymptomatic Late	0.013 (0.007 - 0.020)		83
	Symptomatic	0.029(0.014 - 0.043)		
	AIDS	0.023(0.012 - 0.035)		
Reaching undiagnosed individuals				74,98,175,176
30-49 years: Non-AIDS stage	Community-based <sup>†</sup>	0.088(0.045 - 0.129)	0.088(0.045 - 0.129)	
	Facility-based <sup>‡</sup>	0.037(0.018 - 0.054)	0.063(0.032 - 0.093)	
30-49 years: AIDS stage	Community-based <sup>†</sup>	0.129(0.067 - 0.188)	0.129 (0.067 - 0.188)	
	Facility-based <sup>‡</sup>	0.054(0.028 - 0.080)	0.093(0.047 - 0.135)	
50+ years: Non-AIDS stage		0.319 (0.175 – 0.438)	0.319 (0.175 - 0.438)	
50+ years: AIDS stage		0.438(0.250 - 0.578)	0.438(0.250 - 0.578)	
·				
HIV Testing				21,22,29,91,177-18
30-49 years: Non-AIDS stage	HIVST Kit Delivery	0.198 (0.104 - 0.282)	0.198 (0.104 - 0.282)	
	HIVST Coupon Delivery	0.040(0.020 - 0.059)	0.115(0.059 - 0.167)	
	VCT Referral card	0.035 (0.017 - 0.052)	0.093 (0.047 - 0.136)	
	HIVST Choice	0.158(0.082 - 0.227)	0.221 (0.117 - 0.312)	
	PITC	0.103 (0.053 - 0.151)	0.175 (0.091 - 0.250)	
	VCT	0.042 (0.021 - 0.063)	0.022 (0.011 - 0.033)	
			``````	
30-49 years: AIDS stage	HIVST Kit Delivery	0.282 (0.152 - 0.391)	0.282 (0.152 - 0.391)	
	HIVST Coupon Delivery	0.059(0.030 - 0.087)	0.167(0.087 - 0.240)	
	VCT Referral card	0.052(0.026 - 0.076)	0.136(0.070 - 0.197)	

	HIVST Choice	0.227 (0.121 - 0.321)	0.312 (0.171 – 0.430)	
	PITC	0.151 (0.078 - 0.217)	0.250 (0.134 – 0.351)	
	VCT	0.063 (0.032 - 0.093)	0.033 (0.017 - 0.049)	
50+ years: Non-AIDS stage		0.019 (0.009 - 0.028)	0.010 (0.005 - 0.015)	
50+ years: AIDS stage		0.028 (0.014 - 0.042)	0.015 (0.008 - 0.023)	
HIV Test Sensitivity (%)				85–87
Initial Test	OraQuick	92.00 [66.00 - 99.00]		
	KHB colloidal Gold	100.00 (97.40 - 100.00)		
Confirmatory test	First Response 1-2.0	100.00 (97.40 - 100.00)		
Tie-breaker test	Uni-Gold	96.40 [91.8 – 98.8]		
Receive confirmatory test				
-	Community-based <sup>†</sup>	0.900(0.750 - 1.00)		21,181,182
	Facility-based <sup>‡</sup>	1.000(0.500 - 1.000)		Assumption
Linkage to care	· ·	``````````````````````````````````````		1
C	Non-AIDS	0.641 (0.401 - 0.785)		22
	AIDS	0.785(0.536 - 0.900)		
ART initiation				102
	Non-AIDS	0.830(0.588 - 0.930)		
	AIDS	0.930(0.735 - 0.981)		
Switch to second Line ART				
	Non-AIDS	0.004(0.003 - 0.006)		159
	AIDS	0.006(0.005 - 0.008)		
Loss to follow up (LTFU)				14,183–185
Pre-ART				
30-49 years	Asymptomatic	0.029(0.015 - 0.044)	0.025 (0.012 - 0.037)	
-	Symptomatic	0.040(0.020 - 0.059)	0.033 (0.017 - 0.049)	
	AIDS	0.043(0.022 - 0.059)	0.036 (0.018 - 0.054)	
50+ years		0.025(0.012 - 0.037)	0.022 (0.011 - 0.033)	
On ÅRT			· · · · · · · · · · · · · · · · · · ·	
30-49 years	Asymptomatic	0.015(0.007 - 0.022)	0.012 (0.006 - 0.018)	
-	Symptomatic	0.020(0.010 - 0.030)	0.017(0.008 - 0.025)	

Asymptomatic Symptomatic AIDS Kit Delivery Coupon Delivery	0.012 (0.006 - 0.019) 0.004 (0.002 - 0.007) 0.023 (0.011 - 0.034) 0.049 (0.024 - 0.073) 0.004 (0.002 - 0.007) 18.73 (9.37 - 28.10) 20.87 (10.44 - 31.31)	0.012 (0.006 – 0.018)	105,106 32,95,186
Symptomatic AIDS Kit Delivery	0.023 (0.011 - 0.034) 0.049 (0.024 - 0.073) 0.004 (0.002 - 0.007) 18.73 (9.37 - 28.10)		32,95,186
Symptomatic AIDS Kit Delivery	0.023 (0.011 - 0.034) 0.049 (0.024 - 0.073) 0.004 (0.002 - 0.007) 18.73 (9.37 - 28.10)		32,95,186
AIDS Kit Delivery	0.049 (0.024 - 0.073) 0.004 (0.002 - 0.007) 18.73 (9.37 - 28.10)		32,95,186
Kit Delivery	0.004 (0.002 - 0.007) 18.73 (9.37 - 28.10)		32,95,186
•			32,95,186
•			32,95,186
•			32,95,186
•			
Coupon Delivery	20.87(10.44 - 21.21)		
	20.67(10.44 - 51.51)		
Referral card	14.74 (7.37 – 22.12)		
HIVST Choice	13.11 (6.55 – 19.66)		
PITC	6.77 (3.39 – 10.16)		
VCT	6.77(3.39 - 10.16)		
	6.75 (3.37 – 10.12)		186
	7.74 (3.87 – 11.62)		186
	23.13 (10.80 - 43.33)		110
	33.01 (19.24 - 59.03)		110
	49.02 (23.06 - 82.59)		110
	1,692.62 (483.61 – 2,901	1.63)	187
	PITC VCT d life-years; HIVST = HIV	PITC $6.77 (3.39 - 10.16)$ VCT $6.77 (3.39 - 10.16)$ 6.77 (3.39 - 10.16) 6.75 (3.37 - 10.12) 7.74 (3.87 - 11.62) 23.13 (10.80 - 43.33) 33.01 (19.24 - 59.03) 49.02 (23.06 - 82.59) 1,692.62 (483.61 - 2,901) d life-years; HIVST = HIV self-testing; VCT = volunt	PITC $6.77 (3.39 - 10.16)$ VCT $6.77 (3.39 - 10.16)$ 6.75 (3.37 - 10.12) 7.74 (3.87 - 11.62) 23.13 (10.80 - 43.33) 33.01 (19.24 - 59.03)

\*Parameters reflect monthly probabilities, costs and disability weights unless specified otherwise

<sup>†</sup>PLWH are reached in the community for HIV testing

‡PLWH are visit the health facility for HIV testing

§Cost is applied per test uptake

¶Costs included are in Appendix

¥Funeral costs incurred by the family

Domain*	HIV Testing Strategy	Costs (\$)	Incremental Cost (\$)	DALYs Lost	<b>DALYs Averted</b>	<b>ICER</b> <sup>†</sup>
Female sex wor	kers					
Health facility	No Testing	\$ 1,693		45.36		
	Voluntary testing	\$ 2,909		43.07		w_dominated
	Provider-initiated testing	\$ 7,101		35.09		w_dominated
Combination	HIVST Choice	\$ 7,561		34.09		w_dominated
	HIV testing referral card	\$ 9,143		31.18		w_dominated
	HIVST coupon delivery	\$ 9,192		31.10		w_dominated
Community	HIVST kit delivery	\$ 10,110	\$ 8,418	29.31	16.05	\$ 520
<b>T 1 1 1</b>						
Long distance tr	ruck drivers					
Health facility	No testing	\$ 1,693		45.61		
	Voluntary testing	\$ 2,580		43.86		w_dominated
	Provider-initiated testing	\$ 3,520		41.99		w_dominated
Combination	HIVST Choice	\$ 4,073		40.89		w_dominated
	HIVST coupon delivery	\$ 5,021		38.99		w_dominated
	HIV testing referral card	\$ 5,123		38.78		w_dominated
Community	HIVST kit delivery	\$ 7,549	\$ 5,856	33.81	11.80	\$ 500

#### Table 4: Undiscounted base case cost-effectiveness results¶

Abbreviations: HIVST = HIV self-testing, DALYs = Disability Adjusted Life Years, ICER = Incremental cost effectiveness ratio;

w\_dominated = weakly dominated

\*Strategies are classified by setting including health facility only, community only and a combination of both the health facility and the community setting.

<sup>†</sup>ICER is expressed as incremental cost/DALYs averted.

‡Life expectancy at 30 years.

§Compared to "No testing" strategy.

Costs and health benefits are undiscounted

Domain*	HIV Testing Strategy	Costs (\$)	Incrementa	ll Cost (\$) DALYs Lost	<b>DALYs Averted</b>	ICER <sup>†</sup>
Female sex wor	kers					
Health facility	No Testing	\$ 1,404		21.93		
	Voluntary testing	\$ 2,028		20.70		w_dominated
	Provider-initiated testing	\$ 4,301	\$ 2,896	16.20	5.73	\$ 500
Combination	HIVST Choice	\$ 4,565	\$ 264	15.69	0.51	\$ 510
	HIV testing referral card	\$ 5,502		13.88		w_dominated
	HIVST coupon delivery	\$ 5,535		13.83		w_dominated
Community	HIVST kit delivery	\$ 6,107	\$ 1,541	12.70	2.98	\$ 520
Long distance the	ruck drivers					
Health facility	No testing	\$ 1,425		22.11		
•	Voluntary testing	\$ 1,911		21.11		w_dominated
	Provider-initiated testing	\$ 2,447		19.99		w_dominated
Combination	HIVST Choice	\$ 2,769		19.32		w_dominated
	HIVST coupon delivery	\$ 3,332		18.18		w_dominated
	HIV testing referral card	\$ 3,392		18.04		w_dominated
Community	HIVST kit delivery	\$ 4,951	\$ 3,526	14.77	7.34	\$ 480

#### Table 5: Discounted base case cost-effectiveness results<sup>¶</sup>

Abbreviations: HIVST = HIV self-testing, DALYs = Disability Adjusted Life Years, ICER = Incremental cost effectiveness ratio,

w\_dominated = weakly dominated

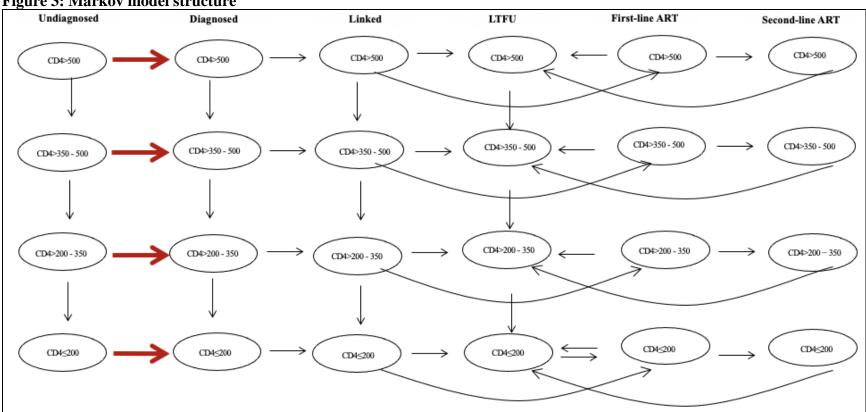
\*Strategies are classified by setting including health facility only, community only and a combination of both the health facility and the community setting.

<sup>†</sup>ICER is expressed as incremental cost/DALYs averted.

‡Life expectancy at 30 years.

§Compared to "No testing" strategy.

¶Costs (2017 \$) and health benefits are discounted at 3% per annual.

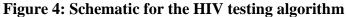


#### Figure 3: Markov model structure

Abbreviations: LTFU = Loss to follow up; ART = Antiretroviral therapy

Figure 3 shows the model structure with clinical stages of HIV disease progression defined as follows: Asymptomatic Early (corresponding with CD4 count >500 cells/ $\mu$ L); Asymptomatic Late (corresponding with CD4 count >350 - 500 cells/ $\mu$ L); Symptomatic (CD4 count 200-350 cells/ $\mu$ L); and AIDS (CD4 count 200 cells/ $\mu$ L)). Engagement in HIV care was characterized as undiagnosed, diagnosed, linked to care, on first line ART, on second-line ART, lost from care, and death (not shown). The cohort starts at undiagnosed stages transitions through the health states using probabilities at a monthly cycle. HIV testing strategies impact the probability of being diagnosed.

→ Represents the probability of a FSW or truck driver getting diagnosed and the probability varied across strategies



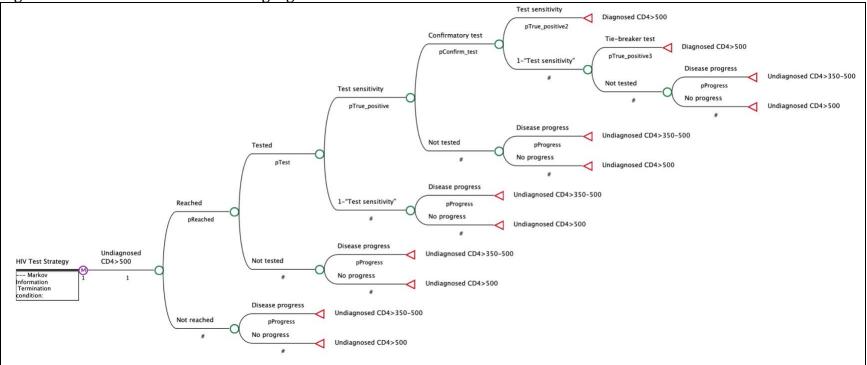


Figure 4 illustrates the possible pathways for HIV testing algorithm used in this study. For example, an initial cohort of undiagnosed truck drivers with CD4>500, a fraction of the cohort can be reached by an HIV testing strategy and among those that are reached, an initial HIV test is offered and if the test is reactive, they perform a confirmatory test or a tiebreaker in a case of inconsistency between the initial test and the confirmatory test. Since all the initial cohort included people living with HIV, fractions of the cohort that are not reached, refused the test, or got a false negative remain undiagnosed.

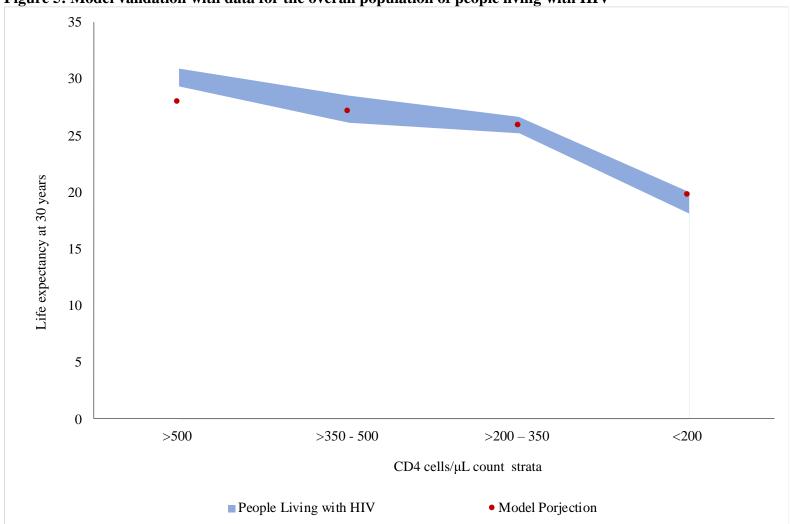
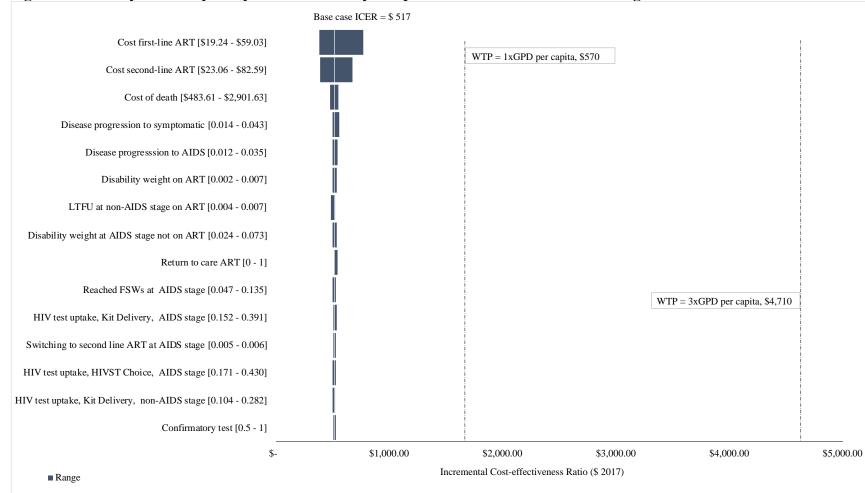


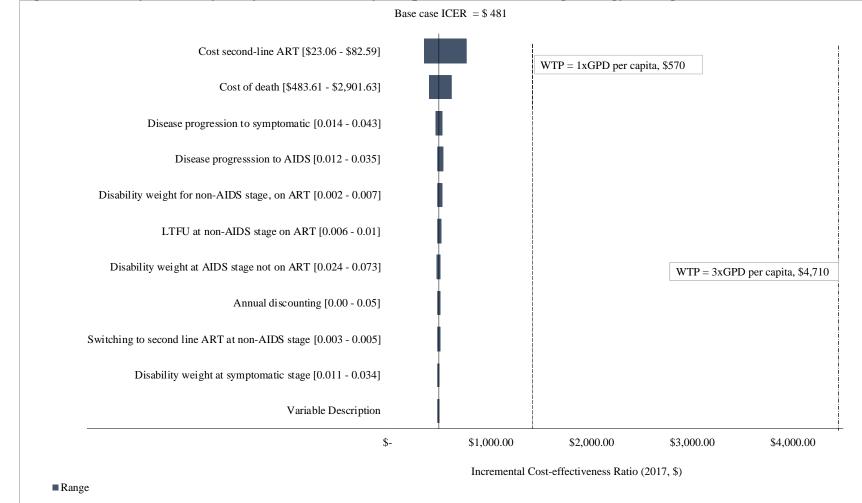
Figure 5: Model validation with data for the overall population of people living with HIV

Figure 5 shows results for the model validation. I validated the model by corroborating the life expectancy at 30 years for truck drivers and FSWs living with HIV to data on overall population of PLWH in Rwanda. The blue trend band shows the confidence intervals of life-expectancy for people living with HIV in Rwanda who are diagnosed at 32 years of age.<sup>113</sup> Overall, based on clinical stage at the time of HIV diagnosis, The life expectancy in the model was comparable to the data from Rwanda.



#### Figure 6: One-way sensitivity analysis of Kit delivery compared to the HIVST Choice among female sex workers

Abbreviations: ART = Antiretroviral Therapy, LTFU = Loss to follow-up, HIVST = HIV self-testing; ICER = Incremental Cost Effectiveness Ratio, WTP = willingness to pay



### Figure 7: One-way sensitivity analysis of Kit delivery compared to the No testing strategy among truck drivers

Abbreviations: ART = Antiretroviral Therapy, LTFU = Loss to follow-up, HIVST = HIV self-testing; ICER = Incremental Cost Effectiveness Ratio, WTP = willingness to pay

# Paper three

Strategy	Description	LTFU RRR	Cost, 2017	' USD (range)	Source
		% (range)	First-line ART	Second-line ART	
No Intervention	Standard of care that offers only free ART at the health facility		17.38 (8.69 – 26.07)	32.88 (16.44 -49.32)	14
ART Delivery	Home free ART delivery by community health workers	40 (29 – 49)	16.62 (8.31 – 24.93)	32.12 (16.06 – 48.18)	133
ART Delivery + Nutrition	Home free ART delivery by community health workers plus nutrition supplement	71 (53 – 88)	46.62 (23.31 – 69.93)	62.12 (31.06 – 93.18)	134
Tracing + Transport	Free ART, tracing patients that miss appointments with transport reimbursement.	22 (7–36)	24.71 (12.36 – 37.07)	40.21 (20.11 – 60.32)	135
Tracing + Medical Care	Free ART, tracing patients that miss appointments with free medical care for opportunistic infections	46 (22 - 63)	26.14 (13.07 – 39.21)	41.64 (20.82 – 62.46)	136
Medical Care + Transport + Breakfast	Free ART, treatment for opportunistic infections, transport cost reimbursement, and breakfast.	41 (12 – 75)	23.51 (11.76 – 35.27)	39.01 (19.51 – 58.52)	137

Abbreviations: ART = Antiretroviral therapy; RRR = Relative Risk Reduction; LTFU = Loss to follow up

 Table 7: Monthly parameter inputs

Parameter*		Baseline (range)	Distribution	Source
Initial distribution, %			Beta	94,158
	Asymptomatic Early	28.8 [41.8]	Deta	
	Asymptomatic Late	19.6 [25.3]		
	Symptomatic	19.7 [21.1]		
	AIDS	31.9 [11.6]		
Disease progression			Beta	83
progression	Asymptomatic Late	0.013 (0.007 - 0.020)	Deta	
	Symptomatic	0.029(0.014 - 0.043)		
	AIDS	0.023 (0.012 - 0.035)		
Switch to second line ART			Beta	159
	Non-AIDS	0.004 (0.003 - 0.006)		
	AIDS	0.006(0.005 - 0.008)		
LTFU		· · · · · · · · · · · · · · · · · · ·	Beta	
30-49 years: non-AIDS	No Intervention	0.011 (0.008 - 0.013)		14
	ART delivery	0.006(0.005 - 0.007)		133
	ART delivery + Nutrition	0.003(0.001 - 0.005)		134
	Tracing + Transport	0.008(0.007 - 0.010)		135
	Tracing + Medical care	0.006(0.004 - 0.008)		136
	Medical care + Transport + Breakfast	0.006 (0.003 - 0.009)		137
80-49 years: AIDS	No Intervention	0.021 (0.016 - 0.027)		14
-	ART delivery	0.013 (0.011 - 0.015)		133
	ART delivery + Nutrition	0.006(0.002 - 0.010)		134
	Tracing + Transport	0.016 (0.013 - 0.019)		135
	Tracing + Medical care	0.011 (0.008 - 0.016)		136
	Medical care + Transport + Breakfast	0.012 (0.005 - 0.018)		137
50+ years	No Intervention	0.004 (0.003 - 0.005)		14
-	ART delivery	0.002(0.001 - 0.003)		133
	ART delivery + Nutrition	0.001(0.001 - 0.002)		134

	Tracing + Transport	0.003 (0.002 - 0.003)		135
	Tracing + Medical care	0.002 (0.001 - 0.003)		136
	Medical care + Transport + Breakfast	0.002 (0.001 - 0.003)		137
Costs (US \$, 2017)		,	Gamma	
FWS on first-line ART	No Intervention	17.38 (8.69 – 26.07)		110
	ART delivery	16.62 (8.31 – 24.93)		110,133
	ART delivery + Nutrition	46.62 (23.31 – 69.93)		110,133,161
	Tracing + Transport	24.71 (12.36 - 37.07)		110,160
	Tracing + Medical care	26.14 (13.07 – 39.21)		110,160,188
	Medical care + Transport + Breakfast	23.51(11.76 - 35.27)		110,137,160,188
FWS on second-line ART	No Intervention	32.88 (16.44 - 49.32)		110
	ART delivery	32.12 (16.06 - 48.18)		110,133
	ART delivery + Nutrition	62.12 (31.06 - 93.18)		110,133,161
	Tracing + Transport	40.21(20.11 - 60.32)		110,160
	Tracing + Medical care	41.64 (20.82 - 62.46)		110,160,188
	Medical care + Transport + Breakfast	39.01 (19.51 - 58.52)		110,137,160,188

Abbreviations: ART = Antiretroviral drugs; LTFU = Loss to follow up; FSW = Female sex workers \*Parameters reflect monthly probabilities, costs and disability weights unless specified otherwise

Strategy	C	ost	Inc	remental cost	DALYs Lost	<b>DALYs</b> Averted	ICER
No Intervention	\$	4,664.02			28.41		
ART delivery	\$	5,533.25	\$	869.23	26.36	2.05	\$ 400
Tracing + Transport	\$	6,842.64			27.44		s_dominated
Medical care + Transport + Breakfast	\$	7,299.20			26.29		w_dominated
Tracing + Medical care	\$	8,218.37			25.92		w_dominated
ART delivery + Nutrition	\$	16,292.13	\$ 10	),758.88	23.40	2.96	\$ 3,200

Table 8: Undiscounted base case results for strategies to reduce LTFU from ART programs among female sex workers

Strategy	Cost	<b>Incremental cost</b>	DALYs Lost	DALYs Averted	ICER
No Intervention	\$ 2,994.56		11.52		
ART delivery	\$ 3,460.73	\$ 466.17	10.55	0.98	\$ 470
Tracing + Transport	\$ 4,386.60		11.05		s_dominated
Medical care + Transport + Breakfast	\$ 4,606.21		10.51		w_dominated
Tracing + Medical care	\$ 5,173.28		10.35		w_dominated
ART delivery + Nutrition	\$ 10,022.73	\$ 6,561.99	9.27	1.28	\$ 5,100

Table 9: Discounted base case results for strategies to reduce LTFU from ART programs among female sex workers

Strategy	Co	ost	In	cremental cost	DALYs Lost	<b>DALYs</b> Averted	ICER
No Intervention	\$	1,497.28			10.94		
ART delivery	\$	1,632.37	\$	135.00	10.30	0.64	\$ 210.00
Tracing + Transport	\$	2,020.06			10.70		s. dominated
Medical care + Transport + Breakfast	\$	2,069.35			10.80		s. dominated
Tracing + Medical care	\$	2,302.64			10.47		s. dominated
ART delivery + Nutrition	\$	4,461.36	\$	2,829.00	9.54	0.76	\$ 3,720.00

Table 10: Multi-way sensitivity analysis of LTFU strategies with low bound parameter values considered

Strategy	Cost	<b>Incremental cost</b>	DALYs Lost	<b>DALYs</b> Averted	ICER
No Intervention	\$ 4,491.84		12.23		
ART delivery	\$ 5,479.14	\$ 987.29	10.94	1.28	\$ 770
Tracing + Transport	\$ 7,018.73		11.37		s. dominated
Medical care + Transport + Breakfast	\$ 8,637.60	\$ 3,217.41	10.37	1.19	\$ 2,670
Tracing + Medical care	\$ 8,696.55		9.74		s. dominated
ART delivery + Nutrition	\$ 17,298.98	\$ 8,602.43	8.88	0.86	\$ 9,950

Table 11: Multi-way sensitivity analysis of LTFU strategies with upper bound parameter values considered

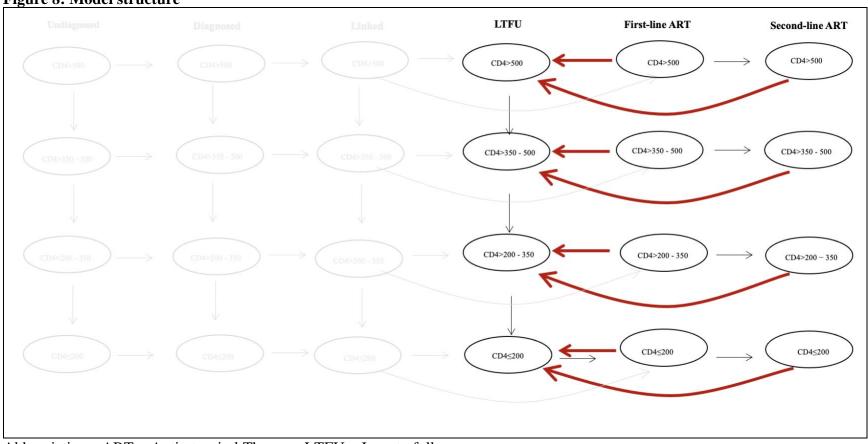
Strategy	C	ost	Inc	cremental cost	DALYs Lost	<b>DALYs Averted</b>	ICER
No Intervention	\$	6,500.45			24.97		
ART delivery	\$	7,431.96	\$	931.51	22.97	2.00	\$ 460
Tracing + Transport	\$	9,231.43			23.96		s_dominated
Medical care + Transport + Breakfast	\$	9,625.14			22.91		w_dominated
Tracing + Medical care	\$	10,684.33			22.60		w_dominated
ART delivery + Nutrition	\$	19,338.22	\$1	1,906.26	20.80	2.18	\$ 5,400

Table 12: Undiscounted cost-effectiveness of LTFU strategies after adjusted for misclassification of patients

Strategy	Cost	<b>Incremental cost</b>	DALYs Lost	<b>DALYs</b> Averted	ICER
No Intervention	\$ 3,987.28		9.93		
ART delivery	\$ 4,414.55	\$ 427.27	9.09	0.84	\$ 500
Tracing + Transport	\$ 5,638.55		9.50		s_dominated
Medical care + Transport + Breakfast	\$ 5,780.22		9.06		w_dominated
Tracing + Medical care	\$ 6,407.93		8.94		w_dominated
ART delivery + Nutrition	\$ 11,482.61	\$ 7,068.06	8.21	0.88	\$ 8,000

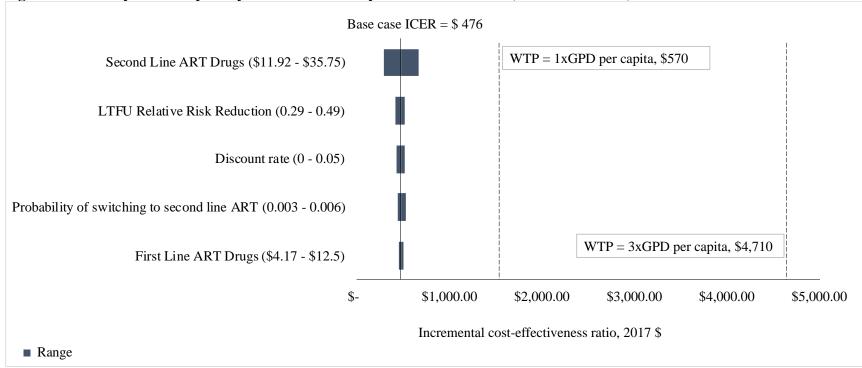
Table 13: Discounted cost-effectiveness of LTFU strategies after adjusted for misclassification of patients

Tables 12 and 13 show cost-effectiveness results after adjusting for LTFU misclassification. I applied a probability weight of 0.43, derived from 1 - proportion LTFU who die - proportion LTFU who self-transfer from site. In sub-Saharan Africa its estimated that 20.8% and 35.9% of patients recorded as LTFU have died or self-transferred to another ART clinic.<sup>19</sup>



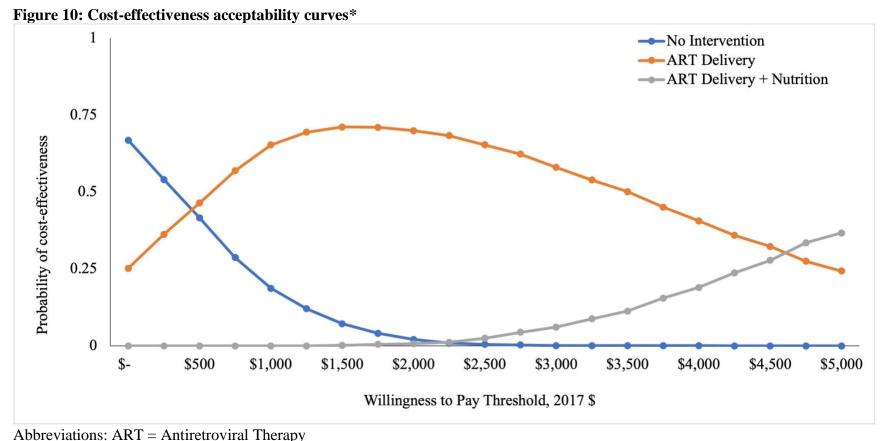
#### **Figure 8: Model structure**

Abbreviations: ART = Antiretroviral Therapy; LTFU = Loss to follow up Represents the probability of LTFU, which varies across strategies



#### Figure 9: One-way sensitivity analysis of ART delivery vs No intervention (standard of care)

Abbreviations: ART = Antiretroviral Therapy; LTFU = Loss to follow up; ICER = Incremental Cost-effectiveness Ratio, WTP = willingness to pay



\*Cost-effectiveness acceptability curves of other strategies were not included because their probabilities of cost-effectiveness were always lower than the three strategies indicated in the figure. However, I included the plot in the supplementary material (Figure S6).

Figure 10 shows cost-effectiveness acceptability curve generated from the probabilistic sensitivity analysis. When the WTP was <\$500, No Intervention had the highest probability of cost-effectiveness; \$500-\$4,600 ART Delivery was more likely to be costeffective; and >\$460 the ART Delivery + Nutrition Supplement had a higher probability of cost-effectiveness.

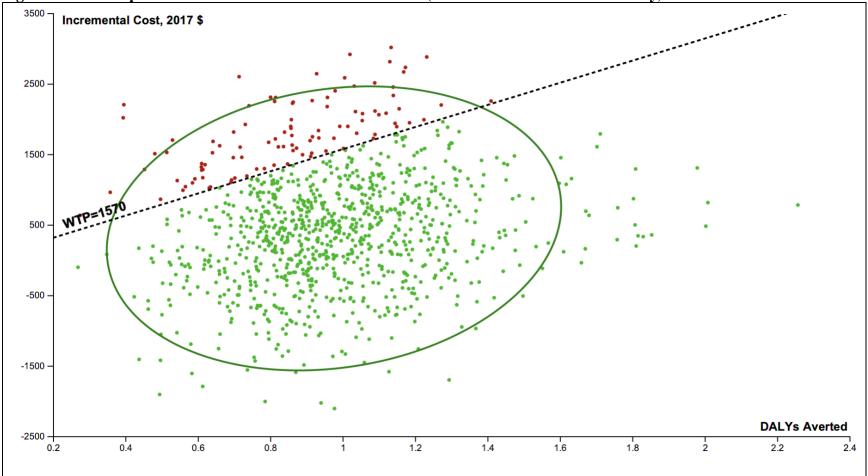


Figure 11: Scatter plot for incremental costs and effectiveness (No Intervention vs ART Delivery)

Abbreviations: ART = Antiretroviral Therapy; DALYs = Disability Adjusted Life Years; WTP = Willingness to Pay

Figure 11 shows the cost-effectiveness plane with majority of the data points for the joint distribution of incremental costs and incremental effectiveness fall in the Northeastern and Southeastern quadrants of the plane, indicating that the ART delivery strategy averted DALYs and may also be cost-saving.

# Supplementary material

This document contains supplemental information including the justification for analytical decisions, analyses, and results.

# **Supplementary materials for paper one**

Analytical Decision	Recommendation
Study perspective	The WHO recommends conducting cost-effectiveness
	studies from a societal perspective, which takes into
This study was conducted based on a societal perspective	account direct health (e.g., clinical services) and non-health
	(e.g., patient time) related costs of a health intervention for
	a society as a whole regardless of who is paying. <sup>1</sup>
Inflation adjustment	The WHO recommends the Gross Domestic Product
	deflator to be used for inflation adjustment of health
The GDP deflator was used for inflation adjustment because it is the	sector costs because it takes into account changes in prices
only available and recommended index inflation adjustment in low-	in the whole economy. <sup>1</sup>
income settings such as Kenya. The Gross Domestic Product (GDP)	
deflator is a price index which measures the annual change in prices for	
a quantity goods and services produced in the economy including those	
exported to other countries. The index is more comprehensive as it	
takes into account government and household consumption and	
international trade.	
Currencies used for measuring and reporting costs	The WHO recommends that costs are valued in
	international dollars to enable comparison of results
We reported costs in international dollars to facilitate comparison of	across countries/settings. For interventions that are
cost-effectiveness results across other countries in the region. An	specifically local, and all prices are collected in local
international dollar is a hypothetical currency, which has the same	currency, WHO recommends using the local currency
value as the US dollar and has the same purchasing power in every	since it is more practical and useful to local policy
country. The international dollar is used in cost-effectiveness analysis	makers. <sup>1</sup>
because it enables cross-country comparisons of costs easier and	
interventions easier. The purchasing power of 1 I\$ is the same in all	
countries. Costs reported in local currency are converted to	
international dollars using the purchasing power parity (PPP) exchange	
rate, which takes into account the country's standards of living.	

#### Table S1: Summary of justifications for analytical decisions

Statistical model for estimating effectiveness The Poisson regression model with a robust variance was used to estimate the effectiveness of CHIVST. The Poisson regression model is part of the generalized linear models and uses the log-link function.	There is no gold standard statistical model that is recommended for estimating relative risks for cohort studies. However, the log-binomial model is recommended in literature since it generates more reliable confidence intervals. But, given the challenges of
Poisson regression model with a robust variance has been shown in	convergence of the log-binominal model, the Poisson
literature to generate similar results as the log-binomial model. <sup>2</sup> We use	model with robust-variance is recommended as an alternative model.
a robust variance because the Poisson regression model does not impose any restrictions to the estimated parameter and hence is likely to overestimates the bounds of the estimate. <sup>3</sup>	
Statistical model for estimating incremental costs	In literature, there is no consensus on a single model to use for estimating mean costs per trial arm. However, the
The generalized linear gamma model was used to estimate the	generalized linear gamma model is commonly
incremental costs. A review on regression models for analyzing cost data found that the gamma GLM is preferred estimating costs. <sup>4</sup> The	recommended because it produces unbiased mean costs.
gamma model does not assume equal variance across datasets and is	
not affected by skewed distribution of the data.	

Method	Description	Advantages	Disadvantages	Recommendations and	Source
				Decision	
The	The CPI is a statistical	1 - Most	1 – CPI depends only on a	WHO:	1,5
consumer	estimate that reflects the	frequently used	fixed basket of consumer	Recommends the Gross	
price index	change in prices of a fixed	method to	goods and services selected,	Domestic Product	
(CPI)	basket of consumer goods	account for	which may not reflect all	deflator to be used for	
	and services. The goods	general inflation	the health care related costs.	inflation adjustment of	
	and services considered for	and easy to	For example, CPI takes into	health sector costs	
	the index are representative	understand.	account only out-of-pocket	because it takes into	
	of the usual consumer		but not all medical	account changes in prices	
	expenditures. The CPI is	2 - CPI can be	expenditures.	in the whole economy.	
	calculated on a monthly	generated for			
	basis and weights are used	specific	2 - CPI may not be	US Panel:	
	to generate the aggregated	commodities. For	appropriate if the rate in	Recommends inflation	
	annual CPI.	example, the	change of price for a	adjustment to be done	
		Medical CPI can	specific resource is not the	using the Personal Health	
	The CPI uses the Laspeyres	be computed for	same as the general price	Care expenditure deflator	
	price index—an arithmetic	only medical	inflation.	because it accurately	
	mean for a fixed basket of	costs (drugs,		reflects the changes in	
	goods and services and	physician, and	3 - The index does not take	prices in the medical	
	adjusted periodically to	nurse salaries)	into account the substitution	sectors as compared to	
	take into account changes		effect where consumers are	the Consumer Price Index	
	in consumption and		more likely to substitute	or Personal Consumption	
	production of goods and		goods and services that are	Expenditure. In case the	
	services.		pricy for cheaper goods,	Personal Health Care is	
			hence overestimating the	not available for the	
	The CPI has a medical		inflation.	current year, the panel	
	component, which takes			recommends using the	
	into account differences in		4 – The CPI medical	Personal Health Care up	
	prices for medical sector.		component has been	to the most recent year	
			reported to have	and then use the Personal	
			measurement errors but also		

### Table S2: Methods and recommendations for inflation adjustment

			it is not available in many countries including Kenya.	Consumption Expenditure. <sup>5</sup>	1.5
The Gross Domestic Product (GDP) deflator	The GDP deflator is a price index which measures the annual change in prices for a quantity goods and services produced in the economy including those exported to other countries. The index is more comprehensive as it takes into account government and household consumption and international trade. The GDP uses the Fisher's index—geometric mean of prices of goods and services in the base year and current year. Since the index takes into account	<ul> <li>1 – GPD deflator takes into the substitution effect.</li> <li>2 – GDP deflator measures the annual price change and incorporates the whole aspect of the economy.</li> </ul>	1 – The GDP deflator regarded as the best option among all methods, but it also does not take into account the quality of the goods and services and may be cumbersome to calculate all the prices and quantities in the economy.	World Bank: No recommendations Decision: The GDP deflator is used because it is the only available and recommended index inflation adjustment in low-income settings such as Kenya.	1,5
Personal	prices in the base and current, it reduces the substitution bias—clients substitute cheaper goods for expensive goods. The PCE price index	1 - The PCE	1 - The PCE index does not		5,6
Consumption Expenditure (PCE) price index	(Fisher's index) is used to reflect all personal expenditures including medical, education and other services as compared	includes more expenditures including those paid by the third party (not	include government investments and expenditures.		

Personal Health Care (PHC) expenditure deflator	to the CPI that only accounts for consumption items. The PHC index is a more specific and includes personal health expenditures (out-of-pocket and third-party payments). This index is built on the CPI-medical component, but the PHC also includes the third-party	government), which makes it a better estimate than the CPI. 2 - More appropriate when adjusting for changes in the purchasing power for personal consumption. 1 – The PHC index is more specific and appropriate for medical related expenditures compared to the general PCE or CPI.	1 – The PHC is not available in many countries and in the United States, the index is estimated after a 2- year lag.	5,6
The rate of wage inflation	expenditures. This approach only measures the average increase in the wages in the whole economy or a given sector in the economy.	1 – The rate of wage inflation is more specific and may be more accurate and appropriate for wage adjustment.	1 – The rate of wage inflation is too narrow to apply as the general inflation index.	1
The rate of inflation for	This approach in applicable to a specific industry or sector. Some countries	1 – The method is more specific	2 – The index does not cover all potential costs to	1

specific	produce the index for the	and may be more	be applied broadly as the	
products	health sector (goods and	accurate.	general inflation index.	
	services).			
			3 - The index is also not	
			readily available in most of	
			the countries especially	
			developing countries such	
			as Kenya.	
WHO = Wor	ld Health Organization guide to	Cost-effectiveness	analysis	
	he US Panel on Cost-effectiven		•	
World Bank -	- Cost-effectiveness recommend	dation for disease co	ontrol priorities	

Method	Description	Advantages	Disadvantages	Recommendations and Decision	Source
International dollar (I\$)	An international dollar is a hypothetical currency, which has the same value as the US dollar and has the same purchasing power in every country. The international dollar is used in cost-effectiveness analysis because it enables easier cross-country comparisons of costs and interventions. The purchasing power of 1 I\$ is the same in all countries. Costs reported in local currency are converted to international dollars using the purchasing power parity (PPP) exchange rate, which takes into account the country's standards of living.	1 - The international dollar enables cross- country comparison of costs and interventions especially when costs are collected from multiple sources and reported in different currencies.	<ul> <li>1 - A large body of cost- effectiveness studies use market exchange rates and report costs in US dollars, which makes comparison with studies that use international dollars a challenge.</li> <li>3 - Some regions don't have PPP exchange rates, which may limit the use of international dollars</li> <li>2 - The international dollar is a hypothetical currency and costs in real life are measured in US dollars.</li> </ul>	<ul> <li>WHO: Recommends that costs are valued in international dollars to enable comparison of results across countries/settings. For interventions that are specifically local, and all prices are collected in local currency, WHO recommends using the local currency since it is more practical and useful to local policy makers.</li> <li>US Panel: No recommendations</li> <li>World Bank: Recommends using the international dollar and</li> </ul>	1,7
US dollar (US \$)	The US dollar is used in many cost-effectiveness studies given because most goods and services on international markets are traded in US dollars.	1 – The US dollar is more relatable given that prices of most of commodities on the international	1 – The US dollar does not account for differences in costs of goods that are not traded on international markets such as labor. Salaries vary across countries, and it is not	they base their recommendation on the WHO recommendation. Decision: I decided to report costs in international dollars to	1,7

Table S3: Currencies used for measuring and reporting costs.

		market are traded in US dollars. 2 – The US dollar is appropriate to if all costs are coming from one country and there's no need for comparison of costs also multiple countries.	possible to assign a US dollar value that would represent the cost of labor in all countries.	facilitate comparison of cost-effectiveness results across other countries in the region. Truck drivers are a mobile population in the region and hence this intervention could be applied to another country in East and Southern Africa.			
Local currency (Kenyan Shilling)	Cost-effectiveness studies have used local currencies especially when the intervention is locally funded, and prices are all valued in local currency.	1 – Use of local currency is useful and practical to local policy makers given that budgets are done in local currency.	<ul> <li>1 – Local currency is only practical to use when all costs are collected and reported in local currencies.</li> <li>2 – The cost-effectiveness results are less likely to be generalizable and compared to other similar interventions in other setting when costs are reported in local currency.</li> </ul>		1		
US Panel – T	WHO = World Health Organization guidelines to Cost-effectiveness analysis US Panel – The US Panel on Cost-effectiveness in Health and Medicine World Bank – Cost-effectiveness recommendation for disease control priorities						

Method	Description	Advantages	Disadvantages	Recommendations and Decision	Source
logistic	The ordinary logistic regression	1 – The logistic	1 - The method for	There is no gold	8-10
regression	model is the most commonly used	regression model is	converting odds ratios	standard statistical	
model	model to estimate a binary	easy, widely	generated by the logistic	model that is	
	outcome, but it produces only	acceptable, and able	regression model is	recommended for	
	odds ratios instead of risk ratios	to estimate relative	likely to generate wide	estimating relative	
	(relative risk). Odds ratios are	risks in situations	confidence intervals and	risks for cohort	
	generated using a logit link	where more	has been found to be	studies. However, the	
	function—logarithm of the ratio	advanced models	inconsistent.9	log-binomial model is	
	between success and failure of an	are not required.		recommended in	
	intended outcome. The link		2 - The converted	literature since it	
	function connects the model's		relative risk	generates more reliable	
	outcome to its predictors.		overestimates the risk	confidence intervals.	
			ratio when the incidence	But, given the	
	A method was developed by Jun		of the outcome is more	challenges of	
	Zhang to convert odds ratios		common (>10 percent) <sup>10</sup>	convergence of the	
	generated by the logistic			log-binominal model,	
	regression model to risk ratios			the Poisson model with	
	(relative risk), <sup>8</sup> which has been			robust-variance is	
	widely used in medical and public			recommended as an	
	health studies.			alternative model.	
log-	The log-binomial regression	1 - The log-binomial	1 - The drawback of the		
binomial	model is part of the Generalized	regression estimates	log-binomial model is	The Poisson model	
regression	Linear Models that assumes a	the relative risks,	that in some situations it	overcomes the	
model	linear relationship between the	which we need for	does not converge to	problem of failure to	
	outcome and the predictors using	estimating the	produce the estimates. <sup>3</sup>	converge because it	
	the log link function. Since the	incremental	The issue of	does not impose any	
	outcome in this study is binary,	effectiveness of the	convergence occurs	restriction on the	
	the relationship between the	intervention.	because the log-binomial	estimated parameters.	
	outcome and the predictors is non-		model imposes	We use a robust	

# Table S4: Statistical models used in the literature to estimate the relative risk of binary outcomes in non-clustered randomized controlled trials

Poisson Similar to t	or a unit change in the	which makes our study comparable with other studies.	to find/generate the MLE estimate. Some studies have developed alternative methods to overcome the issue of convergence. For example, modifying the data so that the MLE estimate is within the parameter space (COPY method). <sup>12,13</sup> The COPY method uses multiple simulations to replicate the original data and estimate the relative risks. However, alternative models have been recommended than using the COPY method.	the binary dependent outcome with the linear predictors. In this case, the log link function exponentiates the linear predictors to generate relative risk estimates per linear predictor. <sup>11</sup>	2,14
regression the Poissor	n regression model is generalized linear	regression model generates	model is more preferred when the prevalence of		

with a	models and uses the log-link	comparable relative	the outcome is low but in	
robust	function. Poisson regression	risk estimates to the	our study the preference	
variance	model with a robust variance has	log-binomial model	is high. However, the	
	been shown in literature to	and is recommended	model is still able to	
	generate comparable results as the	in literature as the	generate correct	
	log-binomial model. <sup>2</sup> The robust	ideal substitute	estimates in high	
	variance is used because the	when the log-	prevalence outcomes.	
	Poisson regression model does not	binomial fails to		
	impose any restrictions to the	converge.		
	estimated parameter and hence is			
	likely to overestimate the bounds			
	of the parameter estimate. <sup>3</sup>			

Method	Description	Advantages	Disadvantages	Recommendations	Source
				and Decision	
Arithmetic	This method includes the	1 - This	1 - The arithmetic method does	In literature, there	15
mean	summing up of total costs per	method is	not take into account the	is no consensus on	
	trial arm and calculating the	simple and	distribution of the costs and the	a single model to	
	mean per trial arm. The	easy to	average my not be presentative	use for estimating	
	means are compared to	implement	of the true average cost per	mean costs per trial	
	determine the difference		participant. This is particularly	arm. However, the	
	between the two arms.		true if there are differences in	generalized linear	
			baseline characteristics between	gamma model is	
			subjects in the trial arms. <sup>15</sup>	commonly	
The ordinary	The OLS regression model is	1 - The OLS	1 – OLS has a limitation of	recommended	16
least squares	one of the commonly used	model	failure to take into account the	because it produces	
(OLS)	multivariate models for	estimates	skewed distribution of costs and	unbiased mean	
regression	estimating mean costs	mean costs	since OLS is sensitive to	costs.	
	between the 2 trials arms. The	difference	outliers (extreme costs), the		
	OLS model is simple to	between trial	estimates may be innacurate. <sup>16</sup>		
	implement and takes in to	arms and			
	account the individual	accounts for	2 – OLS assumes equal		
	characteristics of the	variations	variance across arms, which		
	participants.	across	may not be always true.		
		participants.			
	OLS model assumes equal		This limitation of extreme costs		
	variance of costs across trial		can be overcome by taking the		
	arms and the predicted mean		log of costs but in some		
	is a linear combination of		situations log of costs can does		
	coefficients and control		not wotk. <sup>17</sup> Such situations		
	variables.		include: 1) when observations		
			include zero costs; 2) when the		
			distribution of log of costs is		
l			not normal; and 3) when there		

			are differences in the variance	
<u> </u>		4 571	of log of costs across trial arms.	4,18–20
Generalized	The generalized linear models	1 - The	1 - The GML models have a	4,10-20
linear	are used to overcome the	gamma model	limitation of failure to identify	
(gamma)	limitations of OLS models	does not	the correct link function to use	
models	(does not assume constant	assume equal	prior to estimating the model.	
(GLM)	variance and linear	variance and	However, the log-link function	
	combination of coefficients	is not affected	has been shown to be the most	
	and control variables).	by skewed	applicable. Further, a number of	
		distribution of	diagnostic tests can be	
	GLM (gamma) model uses a	the data.	conducted to identify the	
	log link function which		correct link function These	
	characterizes the relationship		include: Pregibon link test, <sup>19</sup>	
	between the linear		which evaluates the linearity	
	combination of coefficients		response of the estimation and	
	and control variables with the		the Hosmer-Lewshow test,	
	predicted outcome. Unlike the		which estimates the bias in the	
	OLS that models the log of		estimates. <sup>20</sup>	
	the mean cost, the gamma			
	models the mean of log cost,			
	which overcomes the			
	limitations OLS. To generate			
	the arithmetic, we exponential			
	the log of mean cost.			
	GLM distributions includes			
	Normal, Bernoulli, Binomial,			
	Poisson, Gamma and Inverse			
	Normal. <sup>18</sup> A review on			
	regression models for			
	analyzing cost data found that			
	the gamma GLM is preferred			
	estimating costs. <sup>4</sup>			
	commaning costs.			

**Descriptive statistics:** Table S6 shows descriptive statistics for key variables by trial arm (CHIVST and SOC). We performed the chisquare test for categorical variables, Mann-Whitney U test for differences in Medians, and Fisher's exact test for small samples to test for differences between CHIVST and SOC arm. The descriptive statistics show that participants are not statistically different across trial arms.

Variable	Total, n (column %)	SOC Arm, n (row %)	CHIVST Arm, n (row %)	P-value, chi- square test
Total	305	155 (50.8%)	150 (49.2%)	
Clinic where recruited				0.787
Clinic 1	144 (47.2%)	72 (46.5%)	72 (48.0%)	
Clinic 2	161 (52.8%)	83 (53.5%)	78 (52.0%)	
Age in years				$0.989^{1}$
Mean (SD)	37.0 (7.9)	36.9 (8.0)	37. 2 (7.8)	
Median (Range)	36.0 (21.0 - 62.0)	35.0 (21.0 - 60.0)	37.0 (24.0 - 62.0)	
High school graduate				0.417
No	196 (64.3%)	103 (66.5%)	93 (62.0%)	
Yes	109 (35.7%)	52 (33.5%)	57 (38.0%)	
Mean trucking income per month (Kenyan Shillings)				0.074*
8,000–15,999 KES	15 (5.2%)	12 (8.1%)	3 (2.1%)	
16,000–23,999 KES	65 (22.6%)	33 (22.3%)	32 (22.9%)	
24,000–55,000 KES	208 (72.2%)	103 (69.6%)	105 (75.0%)	
Number of years worked as truck driver				$0.650^{1}$
Mean (SD)	8.7 (7.1)	9.0 (7.8)	8.4 (6.3)	
Median (range)	6.7 (1.0 – 38.9)	6.7 (1.0 – 38.9)	6.7 (1.0 – 37.0)	
Clinic is on usual trucking route				0.573
No	51 (16.8%)	24 (15.6%)	27 (18.0%)	
Yes	253 (83.2%)	130 (84.4%)	123 (82.0%)	
Number of nights away from home in the past 30 days				0.495 <sup>1</sup>
Mean (SD)	21.6 (5.6)	21.3 (5.9)	21.8 (5.3)	

#### Table S6: Descriptive statistics for the sample overall and by randomization arm

Median (range)	22.5 (0.0 - 30.0)	22.0 (0.0 - 30.0)	23 (2.0 - 30.0)	
Came to the clinic specifically for HIV testing				0.365
No	173 (56.7%)	84 (54.2%)	89 (59.3%)	
Yes	132 (43.3%)	71 (45.8%)	61 (40.7%)	
Sexually active in the past 6 months				0.116 <sup>2</sup>
No	6 (2.0%)	1 (0.7%)	5 (3.4%)	
Yes	295 (98.0%)	152 (99.3%)	143 (96.6%)	
Married (legal or common law)				0.998
No	51 (16.9%)	26 (16.9%)	25 (16.9%)	
Yes	251 (83.1%)	128 (83.1%)	123 (83.1%)	
Has other regular partner(s) on the trucking route				0.619
No	163 (53.4%)	85 (54.8%)	78 (52.0%)	
Yes	142 (46.6%)	70 (45.2%)	72 (48.0%)	
Paid for sex in the past 6 months				0.789
No	126 (44.1%)	65 (43.3%)	61 (44.9%)	
Yes	160 (55.9%)	85 (56.7%)	75 (55.1%)	
Always used condoms when had sex in the past 6				0.358
months (among those that had sex)				
No	250 (85.9%)	127 (84.1%)	123 (87.9%)	
Yes	41 (14.1%)	24 (15.9%)	17 (12.1%)	
Ever tested for HIV before				0.259
No	25 (8.2%)	10 (6.5%)	15 (10.0%)	
yes	280 (91.8%)	145 (93.5%)	135 (90.0%)	
Number of years since last HIV test among those tested				$0.934^{1}$
Mean (SD)	1.1 (1.6)	1.0 (1.4)	1.1 (1.9)	
Median (range)	0.5 (0.1 – 12.0)	0.5 (0.1 – 7.4)	0.5 (0.1 – 12.0)	
Ever self-tested for HIV among those who ever tested				$0.171^{2}$
No	276 (99.3%)	142 (98.6%)	134 (100.0%)	
Yes	2 (0.7%)	2 (1.4%)	0 (0.0%)	

\*\*\* p<0.01, \*\* p<0.05, \* p<0.1 <sup>1</sup>Mann-Whitney U test <sup>2</sup>Fisher's exact test

#### Missing data

Table S7 shows the total number of participants in the sample and the missing data in each variable in the total sample and per trial arm. The percentage of patients missing data in all the variables is less than 10%. There is no consensus in literature on the minimum percentage of missing data that could bias the results. Missing data can be accounted for in 2 ways: 1) deleting observations with missing data or 2) imputing the missing data. Deleting observations with missing data may bias the results if the data is not missing completely at random, which means that patients that have missing data could be different from those that have data, and this may bias the results. Missing data may be imputed if it is not missing completely at random.

Variable	Total Sample	Total Missing, n (%)	Choice Arm	SOC Arm
Choice arm	305			
Clinic visited	305			
Age	305			
Education level	305			
Income	288	17 (5.57%)	10	7
Years worked as a truck driver	302	3 (0.98%)		3
Clinic is on usual track route	304	1 (0.32%)		1
Number of nights away from home in the last 30 days	297	8 (2.6%)	4	4
Visited clinic to test for HIV	305			
Had sex in the last six months	301	4 (1.31%)	2	2
Married	302	3 (0.98%)	2	1
Has partner(s) on the trucking route	305			
Paid for sex in the past 6 months*	286	9 (3.05%)	7	2
Always used condoms when had sex in the past 6 months*	291	4 (1.36%)	3	1
Ever tested for HIV before	305			
Number of years since last HIV test among those tested	276	29 (9.51%)	18	11
Ever self-tested	278	27 (8.85%)	16	11

Table S7: Missing data in the total sample and across trial arms

\* The question was asked among those that reported to have had sex in the last 6 months.

#### Examining missing data in the analytical sample

Before accounting for the missing data, we first identified variables to include in our study. Explanatory variables (Table S8) were considered based on theoretical and contextual significance to HIV testing uptake and this study. Among the four explanatory variables, only one variable (payment for sex in the last six months) had missing data—9 (3%) participants were missing data of which 7 were in the CHIVST arm and 2 in the SOC arm. We examined the missing data and found the data were missing completely at random across trial arms. Considering that data was missing completely at random, we did not impute the missing data and patients with missing data were excluded from the analysis.

Variable	Justification for inclusion
Clinic visited	We included the clinic where participants tested because randomization was done at the clinic. There is a
	possibility of differences across clinics that are not accounted for in the data that could impact the outcome. For
	example, the staff at the clinic may treat patients differently.
Visited the clinic	We controlled for the reason a participant visited the clinic to account for those that may have tested for HIV
to test for HIV	regardless of the intervention.
Paid for sex in	Payment for sex is a high-risk behavior that is associated with increased risk of acquiring HIV. In literature, men
last 6 month	who perceived to have a high risk of acquiring HIV were more likely to test for HIV compared to those that perceived lower risk. <sup>21</sup>
Age	Age is associated with HIV testing uptake with more older individuals likely to test for HIV compared to the young, but the evidence is mixed. In some studies, adults compared to adolescents have shown more uptake of HIV testing services, <sup>22</sup> while others have shown more uptake among adolescents <sup>21,23</sup> and age having no effect on HIV testing. <sup>24</sup> The variation in association of age with HIV testing uptake across studies could be attributed to different age groups compared and study settings.

#### Table S8: Justification for the variables included in the regression model

#### Univariate analysis

We conducted a univariate analysis to determine the individual effect of the variables on the uptake of HIV testing services. Table S9 shows that only four variables are statistically significant. Four variables (trial arm, clinic visited, if a patient visited the clinic to test for HIV and payment for sex in the last 6 months) were statistically significant.

Table S9: U	nivariate	analysis on	the HIV	testing uptake
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Variable	Sample Size	<b>Odds Ratio</b>	95% CI
Choice arm	305	2.56***	[1.40 - 4.66]
Clinic visited	305	0.10***	[0.04 - 0.23]
Age	305	1.00	[0.97 - 1.04]
Visited clinic to test for HIV	305	8.01***	[3.54 – 18.5]
Paid for sex in the past 6 months	286	2.51***	[1.38-4.54]

\*\*\* p<0.01, \*\* p<0.05

#### Economic costs data sources

Economic cost data (Table S10) came from peer-reviewed and grey literature. Costs incurred in the trial were first identified by reviewing the report that summarized the implementation and findings from the trial.<sup>25</sup> Costs including SOC HIV test kit, HIV self-testing kit, nurse salary, training, cell phone service, equipment (mobile phone) and patient time came from the trial report.<sup>25</sup> Costs for health facility, health facility staff and overhead came from a costing analysis study within the same setting and study population.<sup>26</sup> Since SOC HIV test kits were offered for free at the clinic, we identified the cost of SOC HIV test in Kenya<sup>27</sup> to examine the impact of SOC HIV test kit cost variation in the sensitivity analysis. Finally, the cost of medical supplies (Table S11) came from an HIV testing study in Kenya.<sup>28</sup>

Cost component	Country	Year of the data	Currency	<b>Reported Unit</b>	Baseline [Range]	Source
SOC HIV test kit	Kenya	2015	USD	Per test kit	0.00	25
	Kenya	2012	USD	Per test kit	0.79*	27
HIV self-testing kit	Kenya	2015	USD	Per test kit	7.54	25
Medical supplies	Kenya	2014	USD	Per HIV test	0.14 [0.07 – 0.21] †	28
	Kenya	2014	USD	Per HIV test	0.23 [0.12 – 0.35]	28
Nurse salary	Kenya	2015	USD	Per hour	1.50	25
One-time training	Kenya	2015	USD	Per patient	0.04	25
Health facility staff	Kenya	2016	USD	Per HIV test	0.51	26
Health facility	Kenya	2016	USD	Per HIV test	0.83	26
Overhead	Kenya	2016	USD	Per HIV test	2.05	26
	Kenya	2016	USD	Per patient	1.08‡	26
Cell phone service	Kenya	2015	USD	Per HIV test	6.60	25
Equipment (mobile phone)	Kenya	2015	USD	Per patient	1.20	25
Patient time	Kenya	2015	KES	Per hour	165.72 [160.99 - 170.46]	Trial data

 Table S10: Selected data sources for HIV testing costs, derived from literature

\* Applicable only in the one-way sensitivity analysis

<sup>†</sup>Applicable to patients that tested using self-administered oral HIV testing at the clinic.

‡ Applicable to patients that tested using self-administered oral HIV testing at home.

 Table S11: Cost of medical supplies

Type of cost performed	Medical supplies	Unit	Cost (USD 2014)
SOC	Dual safe powdered gloves	per person tested	\$ 0.06
	Capillary tubes	per person tested	\$ 0.04
	Medimax cotton wool	per person tested	\$ 0.01
	Hand sanitizer	per person tested	\$ 0.06
	Alcohol swabs	per person tested	\$ 0.03
	Biohazard bags	per person tested	\$ 0.02
	lancets	per person tested	\$ 0.01
	Sum	per person tested	\$ 0.23
CHIVST (HIV self-test at the	Dual safe powdered gloves	per person tested	\$ 0.06
clinic)	Hand sanitizer	per person tested	\$ 0.06
	Biohazard bags	per person tested	\$ 0.02
	Sum	per person tested	\$ 0.14

Steps for converting costs from original currency to 2017 international dollars

- 1. Covert all costs to a common unit; per-patient cost
- 2. Covert cost estimate to Kenya currency using the exchange rate indicated in the data source
- 3. Adjust the costs for inflation to 2017 Kenyan currency year
- 4. Covert costs to 2017 international dollar currency year

Cost component*	Unit	SOC arm [Range]	CHIVST arm [Range]			Source
			SOC	Self-test (clinic)	Self-test (home)	
SOC HIV test kit	Per patient	$0.00 \ [0.00 - 0.00]$	0.00 [0.00 - 0.00]			25
	Per patient	1.43	1.43			27
HIV self-testing kit	Per patient		—	15.52 [7.76–23.28]	15.52 [7.76–23.28]	25
Medical supplies	Per patient	0.42 [0.21 – 0.63]	0.42 [0.21 – 0.63]	0.26 [0.13 – 0.38]		28
Nurse	Per patient	2.27 [1.13 – 3.40]	2.27 [1.13 – 3.40]	2.84 [1.42 - 3.40]	2.84 [1.42 - 3.40]	25
One-time training	Per patient	—	0.09 [0.05 - 0.14]	0.09 [0.05 - 0.14]	0.09 [0.05 - 0.14]	25
Health facility staff	Per patient	1.10 [0.55 – 1.65]	1.10 [0.55 – 1.65]	1.10 [0.55 – 1.65]	0.47 [0.24 – 0.71]	26
Health facility	Per patient	1.72 [0.86 – 2.57]	1.72 [0.86 – 2.57]	1.72 [0.86 – 2.57]	0.74 [0.37 – 1.12]	26
Equipment (Phone)	Per patient		2.47 [1.23 – 3.70]	2.47 [1.23 – 3.70]	2.47 [1.23 – 3.70]	25
Cell phone service	Per patient		13.65 [6.82 - 20.47]	13.65 [6.82-20.47]	13.65 [6.82-20.47]	25
Overhead	Per patient	4.24 [2.12 - 6.36]	4.24 [2.12 – 6.36]	4.24 [2.12 - 6.36]	2.26 [1.13 – 3.38]	26
Patient time*	Per patient	2.51 [2.43 - 2.58]	2.51 [2.43 - 2.58]	3.13 [3.04 – 3.22]	3.13 [3.04 - 3.22]	25

Table S12: Economic costs (2017 I\$) considered in this study

\*Patient time cost was estimated based on average income (trial data) lost for the time spent at the time during the HIV testing process which took 40, 50, and 50 minutes for participants that used the provider-administered test, self-testing at the clinic and self-testing at home, respectively. Using data from the trial, we estimated the mean wages per hour, assuming a 40-hour week schedule and multiplied it with the time spent at the clinic to calculate the patient time cost. The time spent at the clinic for HIV testing was significantly different across trial arms. The cost of pre- and post-test counseling was estimated at 20 minutes and the actual HIV testing process was also estimated at 20 minutes, for participants in both the CHIVST and SOC arm, totaling to 40 minutes per patient.<sup>25</sup> Participants that opted for HIV self-testing had an additional time of 6.5 minutes to watch the demonstration video on how to use the HIV self-testing kit. After watching the demonstration video, participants had questions regarding the HIV self-testing, and the total time was estimated at 10 minutes, including watching the video.<sup>25</sup> We assumed that participants who tested from home used the same time (20 minutes) for the actual HIV testing as those that tested from the clinic using the HIV self-testing. In summary, the HIV testing process took 40, 50, and 50 minutes for participants in the standard of care, HIV self-testing at the clinic and at home, respectively. We tested for the difference in mean time across trial arms using the "t-test" and the difference was statistically significant.

<sup>†</sup>All cost boundaries, apart from patient time where we had access to personal level data from the trial, were estimated as 0.5 and 1.5 of baseline value for the lower and upper bound, respectively because data sources did not report ranges or confidence intervals.

Domain	Scenario*	Estimate	95% CI
Incremental Effectiveness (NNT)	N/A	6.25	[5.00 - 8.33]
Incremental Cost			
	Base case	26.20	[23.32 - 29.09]
	Best case	13.47	[11.89 - 15.05]
	Worst case	38.94	[34.74 - 43.13]
Incremental cost-effectiveness ratio			
	Base case	163.77	[151.57 – 175.37]
	Best case	84.19	[77.95-90.12]
	Worst case	243.36	[225.15 - 260.57]

Table S13: Results from the multi-way sensitivity analysis

Abbreviations: NNT = Number Needed to Treat; N/A = Not Applicable

\*The base case considers costs at baseline value; best case considers only low bound costs; and worst case considers only the upper bound costs for each cost component.

## Supplementary materials for paper two

#### **Analytical decisions**

**Methodological approach:** We used a mathematical model (a single cohort state transition model) due to its ability to examine alternative strategies and project future costs and health benefits using multiple data sources. This methodology has been implemented in literature to examine HIV prevention and treatment strategies,<sup>29,30</sup> especially when observational data from one source is unavailable to perform statistical analysis. Although the single cohort state transition model does not capture individual heterogeneity that reflects the real world, it provides an insight in the potential cost-effectiveness of the strategies when data is unavailable to apply more advanced methods such as micro-simulation.<sup>31</sup>

**Model structure:** The model has 24 health states (including death) based on natural history disease progression stratified based on CD4 cell count disease stages and engagement in clinical HIV care. The clinical stages of HIV natural disease progression are defined based four CD4 cell count strata: Asymptomatic Early (corresponding with CD4 count >500 cells/µL); Asymptomatic Late (>350 - 500 cells/µL); Symptomatic (>200 - 350 cells/µL); and AIDS ( $\leq$ 200 cells/µL)). The 4 CD4 strata enables estimation of health benefits and economic costs for early diagnosis and engagement in care vs engagement in care at later stage of the disease.<sup>30,32</sup> Patients diagnosed in early stages of the disease and immediately initiated on ART experience lower risk of morbidity and mortality compared to those that are diagnosed at late stages of the disease.<sup>33,34</sup> However, CD4 stratification assumes similar behavior for the whole fraction of the cohort within the stratum, which may not be the case. We include six stages of engagement in HIV care (undiagnosed, diagnosed, liked to care, First-line ART, Second-line ART and lost from care). HIV diagnosis and linkage to care are modeled as separate health states to account for lower rates of linkage to care among community-based HIV testing approaches compared to facility-based approaches.<sup>35</sup> As test and treat policy implementation improves in sub-Saharan Africa, separating HIV diagnosis and linkage may underestimate the benefits of people starting ART on the same day. First- and second-line ART are modeled separately to account for more costly second-line ART costly.<sup>36</sup>

**Time horizon.** We examined costs and health benefits using a lifetime horizon. A number of cost-effectiveness analysis studies in literature using a Markov model have considered a lifetime time horizon while assessing efficiency of HIV prevention strategies.<sup>37–40</sup>

**Cycle length:** We used a monthly cycle length to account for timely linkage to care and ART initiation. The recommended time for linkage to care and ART initiation after being diagnosed with HIV is 30 days. Although test and treat has been implemented in East and Southern Africa,<sup>41,42</sup> linkage to care is still low among hard-to-reach population and the cycle length of one month will account for the timely linkage to care.<sup>43</sup>

**Discount rate:** We discounted future economic costs and health benefits at 3% to convert future values to present values.<sup>1</sup> People usually value things more in the present than in future so by discounting we account for that time preference. Although the discount rate of 3% is recommended by the WHO, there is less agreement on the true discount rate.<sup>1</sup> The application of a uniform discount rate overtime may not be true given that other variables change overtime including preferences.<sup>44</sup> In sensitivity analysis, we assess the impact of the discount rate on the incremental cost-effectiveness ratio by varying the discount rate between 0 and 5%.

**Measure of effectiveness:** Health benefits were measured as disability-adjusted life years (DALYs) averted. DALYs lost are the recommended measure of health benefits in cost-effectiveness analysis conducted in low-income countries as they estimate the overall burden of the disease (healthy life years lost due to both premature mortality and living with disability).<sup>1</sup>

DALYs is a standard measure of the burden of disease and can be compared across multiple conditions and cost-effectiveness analysis (CEA) studies. Monthly disability weights came from Eaton et al.,<sup>29</sup> and were derived from the global disease burden study.<sup>45</sup> Disability weights were applied to each health state based on the disease stage. All ART health states had the same disability weight regardless of the disease stage to account for ART health benefits.

**Study perspective:** This study was conducted from a societal perspective. The World Health Organization recommends conducting cost-effectiveness studies from a societal perspective, which takes into account direct health (e.g., clinical services and medications) and non-health (e.g., patient time and transport cost to the healthcare facility) related costs of a health intervention for a society as a whole regardless of who is paying.<sup>1</sup> In this study, I included patient time spent at the healthcare facility to seek care and transport costs.

#### **Parameter inputs**

**Initial distribution:** An initial hypothetical cohort, 30-year-old, undiagnosed, individuals living with HIV is based on the CD4 distribution of newly diagnosed HIV individuals in Kenya.<sup>46</sup> To our knowledge, no study has reported CD4 cell count distribution for newly diagnosed female sex workers (FSWs) and truck drivers in Eastern and Southern Africa. We assumed the CD4 distribution stratification in the general population would be comparable to that of FSWs and truck drivers.

**Probability of disease progression:** Data for disease progression came from a study conducted in south Africa that examined community-based strategies to improve HIV care with parameter inputs derived from observational data.<sup>30</sup> In our model, we assumed that fractions of the cohort that experience disease progression are in undiagnosed, diagnosed, linked and lost health states. Those in ART health states don't experience disease progression due to the benefits of ART. Although fluctuations on CD4 cell count occur among patients on ART, data to inform the parameters inputs were unavailable.

**Probability of death:** Data for the probability of death among people living with HIV (PLWH) who are not on treatment came from a longitudinal study in South Africa.<sup>47</sup> Due to lack of CD4 cell count specific data in high-risk populations, we used data from PLWH in the general population.<sup>47</sup> For PLWH and on antiretroviral therapy (ART), we assume their mortality rate reduces by 58% compared to those not on ART.<sup>48</sup> Previous studies have shown that the impact of ART on population level mortality rate ranging from 25%<sup>49</sup> - 90%.<sup>50</sup> Although gender variations in mortality rate in PLWH exist,<sup>51</sup> we assumed that this variation is already accounted for in the background mortality adjustment, thus ART is assumed to have an equal impact on men and women. In addition, the mortality rate was assumed to be same for patients on first-line ART and second-line ART.<sup>52</sup> We accounted for age and gender specific background mortality using lifetables from the World Health Organization (WHO).<sup>53</sup> The adjustment and calculation of monthly probability of death is done in three steps:

- 1. Add the annual HIV mortality rate to the age-specific background annual mortality rate from the WHO.
- 2. Calculate the monthly mortality rate by dividing by 12
- 3. We convert the monthly mortality rate to probability of death.

The relationship between a rate and probability is expressed as:  $Rate = \frac{-\ln(1-p)}{t}$ , where r = rate, p = probability, t = time period.

**Probability of being reached for HIV testing:** The probability of being reached varied by the type of strategy (facility-based vs community-based), gender (women vs men) and disease stage. Based on evidence from the general population, community-based strategies are likely to reach more people including men, particularly those that are less likely to visit health-facilities for care (e.g., HIV testing).<sup>54</sup> We assume that truck drivers, whom the significant majority are men, are less likely to access care or be reached by facility-based strategies compared to female sex workers who are women.<sup>55</sup> For facility-based strategies, one study that interviewed truck drivers at truck stops reported that only 36% of truck drivers used roadside wellness clinics for the past year, with 64% reporting either not using the clinics or unaware of the roadside wellness clinics.<sup>56</sup> We assume female sex workers are 50% more likely as truck drivers and female sex workers have the same likelihood of being reached. Based on a meta-analysis, 67% reported to have met or been reached by a peer educator with a period of 12 months.<sup>57</sup> Based on previous work done on truck drivers and female sex workers,<sup>58–61</sup> a significant majority are below 50 years. We assume that these individuals (50+ years) comparable access to care as people in the general population and are likely to visit the health facility at least once a year due to multiple conditions that are prevalent within this age group.<sup>62,63</sup>

**Probability of testing:** This probability of testing varies based on the strategy, gender (men vs women), age and disease stage. Since all truck drivers are men and female sex workers are women, we considered differences in their health care seeking behaviors are compared to men and women in the general population. Probability of HIV testing by will vary age as strategies targeting high-risk populations will only be applicable to 49 years and below those 50+ years old considered as part of the PLWH in general population

and use the standard of care and are 50% less likely to test for HIV compared to those less than 50 years.<sup>64</sup> We assume that HIV testing is offered ounce a year per strategy. We examined six alternative strategies including: 1) voluntary counseling and testing (VCT),<sup>65</sup> 2) provider-initiated and -administered HIV testing and counseling (PITC),<sup>66</sup> 3) peer educator direct delivery of HIV self-testing kits in the community (HIVST Kit Delivery),<sup>67</sup> 4) peer educator delivery of coupons in community to exchange for an HIV self-test kit at the healthcare facility (HIVST Coupon Delivery),<sup>67</sup> 5) peer educator referral to facility-based for a provider-administered HIV test (VCT Referral),<sup>67</sup> 6) provider-initiated offer of oral HIV self-testing or provider-administered HIV testing (HIVST Choice).<sup>66</sup> The HIVST Choice and PITC are based on a randomized controlled trial conducted among 305 truck drivers in Kenya in 2015 that offered the choice of provider-administered HIV testing or HIV self-testing at the clinic, or home vs only the provider-administered HIV testing.<sup>66</sup> Three other strategies (HIVST Kit Delivery, HIVST Coupon delivery, and VCT Referral) are based on a randomized controlled trial conducted among FSWs in Uganda in 2017 that examined the effectiveness of HIV testing delivery strategies.<sup>67</sup> The sixth strategy, VCT, is the standard of care.<sup>65</sup>

- Probability of testing among truck drivers
  - Kit Delivery: The probability of HIV testing for the Kit Delivery strategy is based on an RCT conducted among FSWs where 92.9% tested for HIV.<sup>67</sup> Since self-testing is equally acceptable among men,<sup>54,68,69</sup> we assume equal probability of HIV testing among truck drivers. Although no study has been done among truck drivers, previous work done among men who have sex with men (MSM) —a high-HIV-risk group— suggests that using peer-educators to distribute kits for HIV self-testing at the healthcare facility is effective (95% uptake) at improving HIV testing.<sup>70</sup>
  - Coupon Delivery: The probability of HIV testing for the Coupon Delivery strategy is also based on an RCT conducted among FSWs where 76.8% tested for HIV.<sup>67</sup> Although coupons are delivered in the community, individuals have to visit the health facility to pick HIV self-test kits. For truck drivers, we assume that coupons are delivered to drivers at truck stops and the probability of testing will be half (38.4%) of that of FSWs since men are less likely to visit the healthcare facility to seek care as compared to women.
  - VCT Referral: The probability of HIV testing for the Referral strategy is also based on an RCT conducted among FSWs where 68.9% tested for HIV.<sup>67</sup> Similar to the HIVST coupon delivery strategy, we assume that the probability for truck drivers testing for HIV will be half (34.5%) of that of FSWs since it requires visiting the clinic to get tested for HIV.
  - HIVST Choice: The probability of HIV testing is based on an RCT where truck drivers in the intervention were offered the choice of provider-administered HIV testing or HIV self-testing at the clinic, or home vs only the provider-administered HIV testing.<sup>66</sup> In the intervention, 87.3% of drivers tested for HIV.
  - Provider-initiated and -administered: Similar to the HIVST Choice strategy, we use the control arm of the RCT<sup>66</sup> to estimate the probability of truck drivers testing for HIV when the provider only offers the provider-administered test. In the control arm, 72.9% of drivers tested for HIV.

- VCT: Based on data from the RCT<sup>66</sup>, 40.5% of truck drivers who visited the clinic and agreed to participate in the study, had specifically come to test for HIV and actually tested for HIV.
- Probability of testing among female sex workers
  - The probability of testing for HIV for the HIVST kit delivery; HIVST coupon delivery and VCT referral was based on an RCT conducted among FSWs in Uganda where 92.9%, 76.8% and 68.9% tested for HIV, respectively.<sup>67</sup>
  - HIV self-testing Choice: Although no study has been conducted to offer a choice of self-testing in addition to the standard of care among FSWs at the healthcare facility, previous work has shown high (95%) acceptability of oral self-testing among FSWs.<sup>71,72</sup> We assume that FSWs will likely have a high uptake of HIV testing when offered the choice of HIVST compared to truck drivers.
  - PITC: The probability of HIV testing among FSWs in this strategy was 90% based on previous work that has shown high acceptability<sup>73–75</sup> of HIV testing in FSWs at the healthcare facility, ranging from 74%<sup>74</sup> to 100%<sup>75</sup>.
  - VCT: This is the standard of care strategy and the probability of HIV test uptake is 23.4%.<sup>60</sup> The probability of VCT testing for FSWs is lower than for truck drivers. This is counterintuitive given that women are more likely to use healthcare services compared to men. Although FSWs are likely to visit the healthcare facility, they tend to seek care for other health conditions but less for HIV prevention or HIV cares services.<sup>60</sup> A potential examination for this case could be that many FSWs fear the stigma from the community being aware of their HIV status and health provider discrimination. Alternatively, FSWs may be receiving HIV testing through during antenatal visits and also there are many programs focusing on HIV testing and care for female sex workers compared to truck drivers.<sup>76</sup>

**HIV test sensitivity:** The sensitivity of the first HIV test is strategy specific, but the confirmatory test and tiebreaker test are the same across all strategies. Strategies (HIVST Kit Delivery, HIVST Coupon Delivery and HIVST Choice) that offered the oral self-administered test used the Oral Sure OraQuick test, sensitivity (95% confidence interval) = 92% (66.0 - 99.0).<sup>77,78</sup> Strategies (VCT Referral, HIVST Choice, PITC, VCT) that offered the blood-based provider-administered test used KHB colloidal Gold test, sensitivity (95% CI) = 100.0% (97.4 - 100.0).<sup>79</sup> The Self-testing Choice uses both the Oral Sure OraQuick and KHB colloidal Gold test for individuals that tested using the self-administered test and provider-administered respectively. The sensitivity of the Self-testing Choice strategy is a pooled estimate based on the percentage of individuals that tested using the self-administered (73%) and provider-administered test (27%).<sup>66</sup> The HIV test algorithm in Kenya includes a confirmatory (First Response 1-2.0) and tiebreaker (Uni-Gold) test, which have a sensitivity (95% CI) of 100.0% (97.4 - 100.0) and 96.4% (91.8 - 98.8).<sup>79</sup>

**Probability of test results discloser and receipt of a confirmatory test:** The probability of disclosing test results after taking an HIV test varies based on the strategy setting (community-based vs facility-based). We assume that all (100%) individuals who test from the health-facility and have a reactive test will disclose their results to the healthcare provider and also get a confirmatory test as recommended in the HIV testing algorithm in Kenya.<sup>66,79</sup> Previous studies conducted in the general population have reported wide

variations on estimates for confirmatory test uptake. In Kenya, 60% of individuals were willing to get a confirmatory after an HIV self-test.<sup>80</sup> One study that examined partner testing through distribution of self-tests suggested that more than 50% of those that tested positive received a confirmatory test.<sup>81</sup> In another study, only 25% (2 of 8 that tested positive) of individuals that tested positive received a confirmatory test but the study couldn't confirm if the other individuals received HIV care from another health facility.<sup>82</sup> In Malawi, 56% of individuals that self-tested received a timely confirmatory test.<sup>83</sup> Little has been done in high-risk populations. In Kenya, willingness to receive a confirmatory test was 40% and 75% among MSM and female sex workers, respectively.<sup>80</sup> In another study, 44%, 24% and 64% of female sex workers that had a positive reactive test in the kit delivery, coupon delivery and VCT visited the clinic for HIV care.<sup>67</sup> Among the community-based strategies examined in our study, they use peer-educators who followed up on the individuals getting a confirmatory test after a reactive test. We assume that 90% of those that test outside the healthcare facility will seek timely care given that peer educators follow-up with nudge HIV positive individuals to seek care. The probability of discloser of test results and receipt of a confirmatory test for the HIVST Choice strategy is a pooled estimate based on the percentage of individuals that tested at health facility (91.5%) and home (8.5%).<sup>66</sup>

**Probability of linkage to care:** The probability of timely linkage to care<sup>67</sup> was the same across all strategies but varies by disease stage. All individuals, irrespective of the strategy, have to visit the health facility to get a confirmatory test before they considered diagnosed of HIV.

**Probability of ART initiation:** The probability of ART initiation was the same across all strategies and doesn't vary by disease stage since based on the current guidelines of treat all.<sup>84</sup> In Kenya, 83% of initiate ART within 30 days.<sup>85</sup>

**Lost from care:** The probability of loss from care varied by engagement in care (pre-ART and on ART), gender and risk.<sup>86–88</sup> Although studies have found advanced HIV disease stage (AIDS vs non-AIDS) has higher loss to follow up, the differences between AIDS vs non-AIDS haven't been statistically significant.<sup>86,88</sup> Further, the higher loss to follow up in advanced disease stages may be a misclassification of death as loss to follow-up.<sup>89–93</sup> Evidence from people living with HIV in the general population shows that Pre-ART patients have higher LTFU compared to ART patients, with Pre-ART patients nearly twice as likely as ART patients to be lost from care.<sup>87</sup> Since no study has examined differences in loss to follow up among high-risk populations, we base on general population evidence<sup>87,94</sup> to assume that Pre-ART patients are twice as likely as ART patients to be lost from care. Men are 1.5 times more likely to be LTFU compared to women.<sup>86</sup> Patients 50+ years old have a lower risk of LTFU compared to 49 years and below.<sup>95</sup>

Costs: HIV testing costs (Table A1) include fixed costs (healthcare facility, equipment such as phones); medical costs (HIV test kit<sup>43,96–</sup> <sup>99</sup> and medical supplies); personnel (medical and non-medical healthcare facility staff, and peer-educators), training, overhead costs, and patient costs (patient time and transport to the health facility). The cost of a confirmatory and tiebreaker test were considered as an

independent HIV test at a healthcare facility with all cost components of a standard HIV testing and counseling process applicable.<sup>27,79</sup> The costs for the initial test in Kit delivery, Coupon delivery and VCT referral strategy came from the randomized controlled trial report.<sup>43</sup> Costs VCT and PITC came from a costing study on HIV testing in Kenya.<sup>99</sup> Cost for patients in pre-ART and ART care came from a report on costing analysis of compressive HIV care by the ministry of health in Kenya.<sup>100</sup> All costs were estimated in three steps:

- 1. Convert costs from their original currency and year to Kenyan shillings
- 2. Convert costs to 2017 Kenyan shillings using the GDP deflator
- 3. Convert costs to 2017 international dollars

Analytical decision	Advantages	Disadvantages
Using a mathematical model methodology	<ul> <li>Mathematical models enable the analyst to examine scenarios that would be more complex in the real-world setting. For example, I am able to examine alternative strategies that were implemented in different settings at different time points, which would have been impossible to implement in the real-world.</li> <li>Mathematical models enable the analyst to better understand the impact of various degrees of variable on an outcome that would be hard to change in the real-world setting.</li> <li>Mathematical models enable the analyst to project future outcomes for various interventions. For example, in paper 2 and 3, I am able to project outcomes over a lifetime time horizon.</li> </ul>	based on certain assumptions that may not be realistic in a real-world setting.
Using a single cohort state transition model.	<ul> <li>State-transition models provide the flexibility of examining economic costs and health benefits of alternative strategies, which may be costly or unethical to implement in the real world.</li> <li>State-transition models can evaluate hypothetical scenarios to provide insight on outcomes of potential interventions if implemented in the real world.</li> <li>State-transition models provide the flexibility to examine outcomes of strategies beyond the time period of the existing data.</li> <li>State-transition models are straightforward to debug thus minimizing potential coding error</li> </ul>	<ul> <li>the probabilities are not dependent on history (e.g., previous states or time spent in a state), which is not always the case.</li> <li>The single cohort state transition model does not capture individual</li> </ul>
Model structure: Natural history disease progression as four CD4 strata	<ul> <li>The clinical stages of HIV natural disease progression are defined based 4 CD4 cell count strata: Asymptomatic Early (corresponding with CD4 count &gt;500 cells/µL); Asymptomatic Late (&gt;350 - 500 cells/µL); Symptomatic (&gt;200 - 350 cells/µL); and AIDS (≤200 cells/µL)).</li> <li>The 4 CD4 strata enables estimation of health benefits and economic costs for early diagnosis and engagement in care vs engagement in care at later stage of the disease.<sup>30,32</sup> Patients diagnosed in early stages and immediately initiate ART</li> </ul>	similar behavior for the whole fraction of the cohort within the stratum, which may not be the case.

Table S14: Advantages and disadvantages for the analytical decisions

	experience lower risk of morbidity and mortality compared to those that are diagnosed at late stages of the disease. <sup>33,34</sup>	
Model structure: six-stage engagement in HIV care	<ul> <li>HIV diagnosis and linkage to care are modeled as separate health states to account for lower rates of linkage to care among community-based HIV testing approaches compared to facility-based approaches.<sup>35</sup></li> <li>First- and second-line ART are modeled separately to account for more costly second-line ART costs.<sup>36</sup></li> </ul>	• As test and treat policy implementation improves in sub-Saharan Africa, separating HIV diagnosis and linkage may underestimate the number of people starting ART on time.
Health benefits: disability adjusted life years (DALYs) lost	<ul> <li>DALYs lost are the recommended measure of health benefits in cost-effectiveness analysis conducted in low-income countries as they estimate the overall burden of the disease (healthy life years lost due to both premature mortality and living with disability).<sup>1</sup></li> <li>DALYs is a standard measure of the burden of disease and can be compared across multiple conditions and CEA studies using DALYs.</li> </ul>	<ul> <li>DALYs only measure the health benefit of an individual without accounting for the societal impact of the disease. For example, it's impact on education and future employment.<sup>101</sup></li> <li>The application of disability weights in DALYs has been questioned due lack of a valid standard measure including the ethical aspect of allocating statistical value on someone's life.<sup>101</sup></li> </ul>
Lifetime analytic time horizon	<ul> <li>The lifetime horizon enables the analyst to capture future costs and health benefits of a strategy.</li> <li>Cost-effectiveness analysis studies on this topic have generally considered a lifetime time horizon. By implementing a similar time horizon, our findings will be comparable to literature.<sup>37-40</sup></li> </ul>	• Although a lifetime time horizon is suitable for examining the impact of strategies for chronic conditions such as HIV, in the real world, policy and other decision makers typically have relatively short time horizons for programmatic planning and implementation goals (e.g., 5, 10 or 20 years).
Monthly cycle length	• Although test and treat has been implemented in East and Southern Africa, <sup>41,42</sup> linkage to care is still low among hard-to-reach population and the cycle length of one month will account for the timely linkage to care. <sup>43</sup>	• In the era of test and treat, there is a possibility of more than one event (linkage to care and ART initiation)

		occurring within a one-month cycle. <sup>43</sup>
Discount rate of 3 percent	• I discount future economic costs and health benefits to convert future values to present values. <sup>1</sup> People usually value things more in the present than in future so by discounting I account for that time preference.	recommended by WHO, there is less

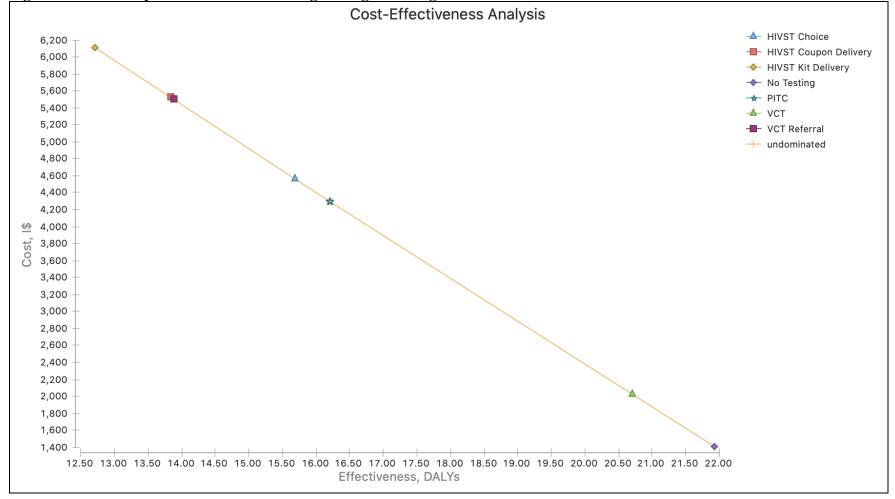


Figure S1: Efficiency frontier for HIV testing strategies among female sex workers

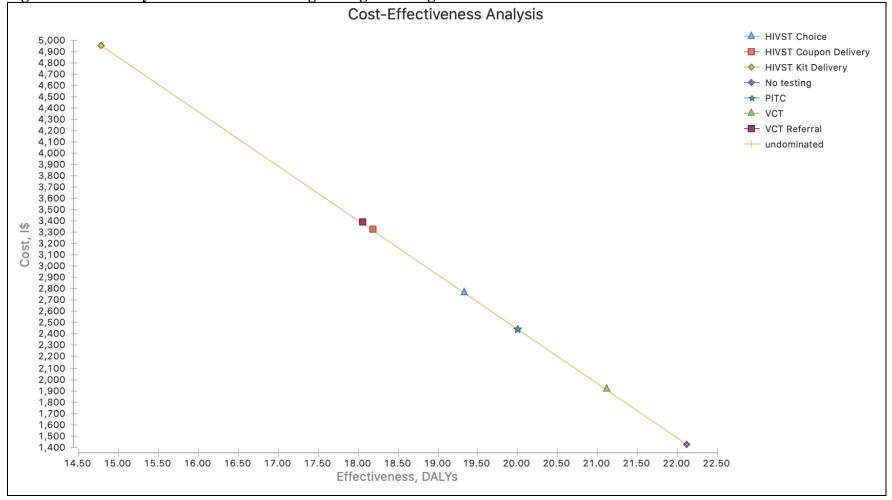


Figure S2: Efficiency frontier for HIV testing strategies among truck drivers

### Cost-effectiveness results for the base case analysis considering a payer perspective

Domain*	HIV Testing Strategy	Costs (\$)	Incremental Cost (\$)	DALYs Lost	DALYs Averted	ICER <sup>†</sup>
		Female Se	ex Workers			
Health facility	No Testing	\$ 1,405		21.93		
	Voluntary testing	\$ 1,854		20.70		
	Provider-initiated testing	\$ 3,491	\$ 2,086	16.20	5.73	\$ 364
Combination	HIVST Choice	\$ 3,682	\$ 191	15.69	0.51	\$ 373
	HIV testing referral card	\$ 4,359		13.88		
	HIVST coupon delivery	\$ 4,385		13.83		
Community	HIVST kit delivery	\$ 4,797	\$ 1,114	12.70	2.98	\$ 374
		Truck	Drivers			
Health facility	No testing	\$ 1,425		22.11		
	Voluntary testing	\$ 1,711		21.11		
	Provider-initiated testing	\$ 2,152		19.99		
Combination	HIVST Choice	\$ 2,381		19.32		
	HIVST coupon delivery	\$ 2,784		18.18		
	HIV testing referral card	\$ 2,825		18.04		
Community	HIVST kit delivery	\$ 3,934	\$ 2,509	14.77	7.34	\$ 342

### Table S15: Discounted base case cost-effectiveness results<sup>¶</sup>

Abbreviations: HIVST = HIV self-testing, DALYs = Disability Adjusted Life Years, ICER = Incremental cost effectiveness ratio \*Strategies are classified by setting including health facility only, community only and a combination of both the health facility and the community setting.

†ICER is expressed as incremental cost/DALYs averted.

§Compared to "No testing" strategy.

¶Costs (2017 \$) and health benefits are discounted at 3% per annual.

			Incremental	DALYs	DALYs	
Domain*	HIV Testing Strategy	Costs (\$)	Cost (\$)	Lost	Averted	<b>ICER</b> <sup>†</sup>
		Female Se	ex Workers			
Health facility	No Testing	\$ 1,405		21.93		
	Voluntary testing	\$ 3,442		17.93		
	HIV testing referral card	\$ 5,503	\$ 4,749	13.88	9.34	\$ 508
Combination	HIVST coupon delivery	\$ 5,535		13.83		
	HIVST kit delivery	\$ 6,107		12.70		
	Provider-initiated testing	\$ 6,154		12.59		
Community	HIVST Choice	\$ 6,297	\$ 143	12.32	0.98	\$ 530
		Truck	Drivers			
Health facility	No testing	\$ 1,425		22.11		
	HIVST coupon delivery	\$ 3,331		19.82		
	HIV testing referral card	\$ 3,391		18.19		
Combination	Voluntary testing	\$ 3,598		17.97		
	Provider-initiated testing	\$ 4,553		18.05		
	HIVST Choice	\$ 4,870	\$ 3,445	17.11	7.18	\$ 480
Community	HIVST kit delivery	\$ 4,948	\$ 78	14.78	0.15	\$ 516

### Scenario analysis: Assuming a FSW or truck driver will visit the health facility once a year

Abbreviations: HIVST = HIV self-testing, DALYs = Disability Adjusted Life Years, ICER = Incremental cost effectiveness ratio \*Strategies are classified by setting including health facility only, community only and a combination of both the health facility and the community setting.

†ICER is expressed as incremental cost/DALYs averted.

§Compared to "No testing" strategy.

¶Costs (2017 \$) and health benefits are discounted at 3% per annual.

# Supplementary materials for paper three

Intervention	Hard to reach population		General population	
	Intervention description	Outcome, [range] (95% CI)	Intervention description	Outcome, [range] (95% CI)
PrEP	Population: Female sex workers Country: Benin	HIV incidence = 0.8 (0.3-1.9) per	Population: General population (Serodiscordant Couples)	HIV incidence = 0.2 (0.0-0.9) per
(Prospective study design)	Design: Prospective cohort Sample size: 256	100 person years	Country: Kenya and Uganda Design: Prospective cohort	100-person years
	Year: 2018 Follow up time: 24 months Primary outcome: HIV incidence Secondary outcome: Adherence (self-reported) Study aim: To examine the impact of PrEP (emtricitabine/tenofovir disoproxil fumarate) on new HIV infections. <sup>102</sup>	Adherence = [57—78%]	Sample size: 1013 couples Year: 2012 Follow up time: 21 months Primary outcome: HIV incidence Secondary outcome: Adherence (monthly drug count). Study aim: To examine the impact of PrEP (emtricitabine/tenofovir disoproxil fumarate) on new HIV infections. <sup>103</sup>	Adherence >85%
	Population: Female sex workers Country: South Africa Design: Prospective cohort Sample size: 219 Year: 2017 Follow up time: 12 months Primary outcome: HIV incidence Secondary outcome: Adherence (self-reported) Study aim: To examine the impact of PreP (Truvada) on HIV incidence in HIV negative FSWs. <sup>104</sup>	No new infections Adherence [70—85%]		

 Table S17: Summary of the literature on PrEP effectiveness among hard-to-reach and general HIV populations

PrEP	Population: MSM	HIV incidence:	Population: General population	HIV incidence:
	Country: Peru, Ecuador, South	1.08 vs 1.93 per	Country: Kenya and Uganda	1.99 vs 0.65 vs 0.5
(RCT study	Africa, Brazil, Thailand, and US*	100 person years	Design: RCT	per 100 person-
design)	Design: RCT	in the intervention	Sample size: 4,747 (1,584 in	years for placebo,
	Sample size: 2,499 (1,224 in	and control	tenofovir; 1,579 in tenofovir-	Tenofovir and
	intervention and 1,217 in control)	respectively.	emtricitabine and 1,584 in the	tenofovir-
	Year: 2010		placebo group)	emtricitabine,
	Follow up time: 34 months	Efficacy	Year: 2012	respectively.
	Primary outcome: HIV incidence	(Tenofovir-	Follow up time: 36 months	
	Secondary outcome: Adherence	emtricitabine)	Primary outcome: HIV incidence	Efficacy
	(self-reported)	44% (15 – 63)	Secondary outcome: Adherence	(Tenofovir)
	HIV negative MSM were recruited		(monthly drug count).	67% (44 – 81)
	to examine the impact of daily	Adherence=95%		
	emtricitabine and tenofovir	(Not different	The aim of the study was to	Adherence $= 92\%$
	disoproxil fumarate on preventing	across groups)	examine the impact of PrEP on new	(Not different
	new HIV infections. <sup>105</sup>		infections. <sup>106</sup>	across groups)
	Population: Injection drug users	HIV incidence:	Population: General population	HIV incidence:
	Country: Thailand		Country: Botswana	Tenofovir-
	Design: RCT	Tenofovir	Design: RCT	emtricitabine - 1.2
	Sample size: 2,413 (1,204 in	0.35 (0.21-0.56)	Sample size: 1,219 (611 in	Vs placebo – 3.1
	tenofovir &1,209 in placebo	Vs Placebo	tenofovir-emtricitabine and 608	per 100 person
	group)	0.69 (0.47 – 0.96)	placebo group)	years.
	Year: 2013	per 100 person	Year: 2012	
	Follow up time: 84 months	years	Follow up time: 45 months	Efficacy
	Primary outcome: HIV incidence		Primary outcome: HIV incidence	(Tenofovir-
	Secondary outcome: Adherence	Efficacy	Secondary outcome: Adherence	emtricitabine)
	(drug dairies)	(Tenofovir)	(drug count).	62% (21 – 84)
	An RCT among injection drug	48% (10 – 72)		
	users examined impact of	Adherence=84%	The study aim was to examine the	Adherence=84.1%
	(tenofovir) on the risk of getting	(Not different	impact of PrEP on new HIV	(Not different
<u>بر المعامة الم</u>	HIV compared a placebo. <sup>107</sup>	across groups)	infections. <sup>108</sup>	across groups)

\*The number of participants from the US was less than 10%.

Table S18 show supporting evidence that adherence on ART and PrEP are comparable to further justify the decision to use PreP as a proxy measure of behavior for individuals on ART.

ART adherence		PrEP adherence		
Study description	Adherence estimate (95% CI), [Range]	Study description	Adherence estimate (95% CI), [Range]	
Design: Meta-analysis and systematic	72.6% (Pooled	Design: Meta-analysis and systematic	Range (66-81%)	
review	average adherence	review		
Sample size: 146 studies	across studies)	Sample size: 7 studies		
Year published: 2016		Year published: 2016		
Outcome: Adherence		Outcome: Adherence		
Study aim: To examine determinants		Study aim: To examine the efficiency of		
of adherence to antiretroviral therapy		PreP in preventing HIV-1 infection among		
in sub-Saharan Africa. <sup>109</sup>		women. <sup>110</sup>		
Design: Meta-analysis and systematic	84% (79–89) (Pooled	Design: Meta-analysis and systematic	Range (51-82%)	
review	average adherence	review		
Sample size: 50 studies	across studies)	Sample size: 13 studies		
Year published: 2014		Year published: 2017		
Outcome: Adherence		Outcome: Adherence		
Study aim: To examine levels of		Study aim: To examine the efficiency of		
adherence to antiretroviral therapy		PreP in preventing HIV-1 infection among		
among adolescents. <sup>111</sup>		adolescents. <sup>112</sup>		
Design: Meta-analysis and systematic	75% [48-79] (Median	Design: RCT*	Adherence varied	
review	adherence across	Population: MSM and Female sex	based on	
Sample size: 14 studies	studies)	workers	measurement method.	
Year published: 2019		Year published: 2012		
Outcome: Adherence		Outcome: Adherence	Daily medication	
Study aim: To examine impact of		Study aim: To examine adherence and	event monitoring	
antiretroviral therapy adherence		safety of PrEP among MSM and female	system for daily	
interventions among women living		sex workers in Arica. <sup>114</sup>	dosing - 83% [IQR:	
with HIV. <sup>113</sup>			63–92]	

Table S18: Systematic reviews and meta-analyses examining adherence to ART vs adherence to PrEP

Design: Meta-analysis and systematic	Older adults - 72%	Design: systematic review	Range (67-83%)
review	Young adults - 68%	Sample size: 13 studies	
Sample size: 20 studies		Year published: 2016	
Year published: 2019	(Pooled average	Outcome: Adherence	
Outcome: Adherence	adherence across	Study aim: To examine the efficiency of	
Study aim: To examine differences in	studies)	PreP in preventing HIV-1 infection in	
antiretroviral therapy adherence		women. <sup>116</sup>	
between older adults with younger			
adults in Africa. <sup>115</sup>			

\*This study was considered because it only focused on high-risk populations (MSM and FSW) and there is no meta-analysis that only considered these populations.

Cost Component	Country	Year of	Currency	Unit costs	Original estimate	Source
		data			(range)	
Community health	Uganda	2007	USD	Per month	35.00 (2.00 - 75.00)	117
worker salary	South Africa	2012	USD	Per patient month	(1.88 - 3.43)	118
	Sub-Saharan Africa	2012	USD	Per month	63.00 (2.00 – 294.00)	119
	Malawi	2014	USD	Per month	100.00	120
	Ethiopia	2014	USD	Per month	46.00	
	Kenya	2014	USD	Per month	23.00	
	Mozambique	2014	USD	Per month	40.00	
One-time training for community health worker	South Africa	2012	USD	Per patient year	5.97	121
Community health worker transport	Uganda	2007	USD	Daily	3.00	117
Clothing for community health worker	South Africa	2012	US	Per patient year	0.15	121
Management and administration for community health workers	South Africa	2012	USD	Per patient year	0.48	121
Monitoring and evaluation for community health workers program	South Africa	2012	USD	Per patient year	0.10	121
Salary for tracker –	South Africa	2010	USD	Per patient month	3.70	122
tracing patients	South Africa	2010	USD	Per patient month	2.14	122
Expenses for tracing patients	South Africa	2010	USD	Per patient month	0.57	122
Expenses for tracing patients	South Africa	2010	USD	Per patient month	0.57	122

 Table S19: Potential candidate cost data for LTFU strategies and ART-related costs to inform economic unit costs

Nutrition support to	Rwanda	2006	USD	Per patient year	128.00	123
patients	Uganda	2010	USD	Per patient year	538.00	124
	Senegal	2017	USD	Per patient day	0.99	125
	Mozambique	2009	USD	Per patient 3months	140.26	126
Breakfast	Côte d'Ivoire	2006	USD	Per patient month	1.00	127
ART-related costs sou					- 1	
Health Facility staff	South Africa	2012	USD	Per patient year	0.48	121
	Uganda	2012	USD	Per patient year	65.54	128
	Uganda	2010	UGX	Per patient year	55,000	129
	Uganda	2016	USD	Per patient year	51.08	130
	Kenya	2011	USD	Per patient year	38.44	100
Overhead costs	South Africa	2012	USD	Per patient year	0.99	121
	Uganda	2012	USD	Per patient year	47.09	128
	Uganda	2010	UGX	Per patient year	85,000	129
	Uganda	2016	USD	Per patient year	5.33	130
	Kenya	2011	USD	Per patient year	17.63	100
Health Facility and	South Africa	2012	USD	Per patient year	0.02	121
Equipment	Uganda	2016	USD	Per patient year	6.57	130
	Kenya	2011	USD	Per patient year	9.08	100
Laboratory costs	Uganda	2012	USD	Per patient year	20.94	128
•	Rwanda	2012	USD	Per patient year	15.00	131
	Malawi	2012	USD	Per patient year	5.00	131
	Ethiopia	2012	USD	Per patient year	16.00	131
	Zambia	2012	USD	Per patient year	13.00	131
	Zambia	2010	USD	Per patient year	69.94	132
	Uganda	2010	UGX	Per patient year	111,000.00	129
	Kenya	2011	USD	Per patient year	19.30	100
Opportunistic	Uganda	2012	USD	Per patient year	42.85	128
infections	Burkina Faso	2008	USD	Per patient month	0.60	133
	South Africa	2009	USD	Per patient year	96.00	134
	Ghana	2012	USD	Per patient year	(9.94 – 39.86)	135

	Kenya	2011	USD	Per patient year	8.51	100
	Uganda	2010	UGX	Per patient year	11,000.00	129
Opportunity cost of	Ghana	2009	USD	Per patient month	2.74	136
time for seeking care	South Africa	2010	USD	Per patient month	12.04	137
	Côte d'Ivoire	2014	USD	Per patient month	9.38	138
	Kenya	2011	USD	Per patient month	2.83	100
Transport to the clinic	South Africa	2009	USD	Per patient month	6.00	122
	South Africa	2017	USD	Per patient month	2.80	139
	Uganda	2010	UGX	Per patient year	7,069.00	129
	Uganda	2007	USD	Per patient month	(1.75 – 11.50)	140
	Uganda	2015	USD	Per patient month	1.89	141
	Kenya	2011	USD	Per patient year	33.80	100
First line ART						
TDF/3TC/EFV	LIC	2017	USD	Per patient year	90.00	36
	LIC	2016	USD	Per patient year	100.00	142
TDF/FTC/EFV	LIC	2017	USD	Per patient year	90.00	36
	LIC	2016	USD	Per patient year	106.00	142
AZT/3TC/EFV	LIC	2016	USD	Per patient year	164.00	142
Second Line ART						
AZT+3TC+ATV/r	LIC	2017	USD	Per patient year	233.00	36
	LIC	2016	USD	Per patient year	286.00	142

Abbreviations: LIC = Low-income countries; CHAI = Clinton Health Access Initiative; MSF = Medecins Sans Frontieres

<b>Initial Distribution</b>	Strategy	Cost	<b>Incremental cost</b>	DALYs Lost	<b>DALYs Averted</b>	ICER
	No Intervention	\$ 2,449.59		9.98		
	ART delivery	\$ 3,087.43	\$ 637.83	9.02	0.96	\$ 660
	Tracing + Transport	\$ 3,732.24		9.53		
	Medical care + Transport + Breakfast	\$ 4,110.88		8.99		
All cohort with	Tracing + Medical care	\$ 4,681.14		8.81		
CD4>500	ART delivery + Nutrition	\$ 9,849.08	\$ 6,761.65	7.60	1.42	\$ 4,700
	No Intervention	\$ 2,859.77		10.69		
	ART delivery	\$ 3,437.80	\$ 578.02	9.55	1.15	\$ 500
All cohort with	Tracing + Transport	\$ 4,258.12		10.15		
CD4 500 - >350	Medical care + Transport + Breakfast	\$ 4,571.81		9.51		
	Tracing + Medical care	\$ 5,167.03		9.30		
	ART delivery + Nutrition	\$ 10,418.27	\$ 6,980.47	7.92	1.63	\$ 4,300
	No Intervention	\$ 3,409.62		11.68		
	ART delivery	\$ 3,919.99	\$ 510.37	10.28	1.40	\$ 360
All cohort with	Tracing + Transport	\$ 4,976.13		11.00		
CD4 >350 - <200	Medical care + Transport + Breakfast	\$ 5,208.80		10.23		
	Tracing + Medical care	\$5,841.41		9.99		
	ART delivery + Nutrition	\$ 11,221.68	\$ 7,301.70	8.37	1.91	\$ 3,800
	No Intervention	\$ 3,323.55		13.40		
	ART delivery	\$ 3,528.45	\$ 204.90	12.78	0.62	\$ 330
	Tracing + Transport	\$ 4,701.29		13.07		
	Medical care + Transport + Breakfast	\$ 4,702.99		12.77		
All cohort with	Tracing + Medical care	\$ 5,206.65		12.69		
CD4 ≤200	ART delivery + Nutrition	\$ 9,156.46	\$ 5,628.00	12.27	0.51	\$ 10,900
>500 = 0.42	No Intervention	\$ 3,018.00		11.77		
500 - >350 = 0.25	ART delivery	\$ 3,446.14	\$ 428.15	10.86	0.91	\$ 470
>350 - <200 = 0.21	Tracing + Transport	\$ 4,398.94		11.32		
$\leq 200 = 0.12$	Medical care + Transport + Breakfast	\$ 4,588.11		10.83		
	Tracing + Medical care	\$ 5,143.12		10.68		
	ART delivery + Nutrition	\$ 9,842.42	\$ 6,396.28	9.72	1.14	\$ 4,800
A11 · /·					1	

Table S20: Cost-effectiveness results associated with different initial distributions

Abbreviations: ART = Antiretroviral Therapy; DALYs = Disability Adjusted Life Years; ICER = Incremental cost-effectiveness ratio

Table S20 shows results for the variation of the initial distribution. Results were consistent with the baseline findings. ART Delivery was cost-effective with an ICER less than \$700 compared to No Intervention when all the initial cohort was assumed to start at CD4 strata >500, 500 - >350, <350 - >200 and  $\leq$ 200. Further, ART Delivery with nutrition supplement was cost-effective at a WTP threshold of 3xGDP of Kenya (\$4,700), when all the initial cohort started at CD4 strata >500, 500 - >350 and <350 - >200 but not  $\leq$ 200. This suggests that ART Delivery with nutrition supplement maybe cost-effective in reducing LTFU if FSWs living with HIV are on treatment at early stages of HIV.

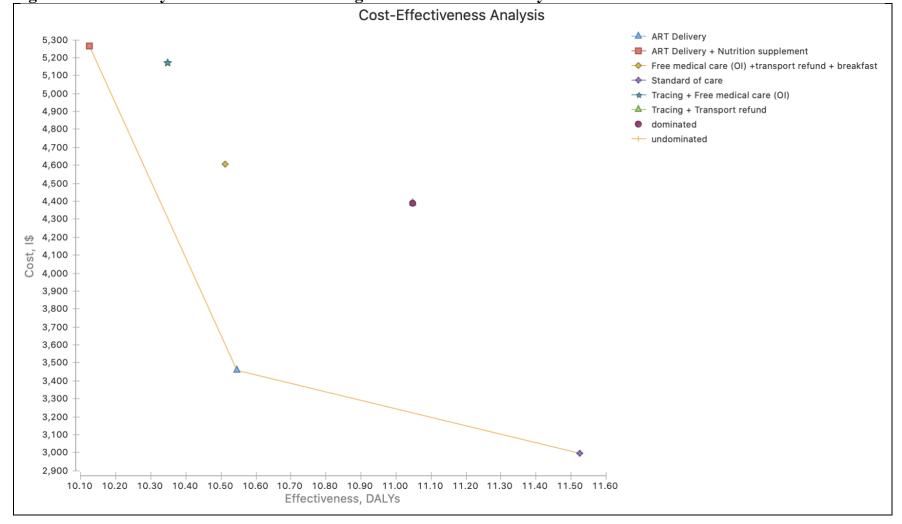


Figure S3: Efficiency frontier for LTFU strategies in the base case analysis

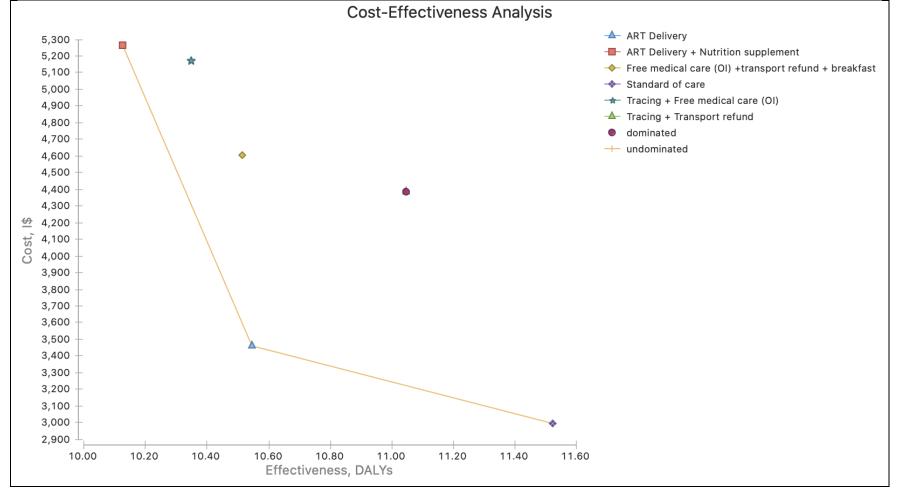


Figure S4: Cost-effectiveness results when we assume nutrition supplement is offered for only 5 years

			In	cremental	DALYs	DALYs			
Strategy	Cost		cost		Lost	Averted	ICER		
No Intervention	\$	2,994.56			11.52				
ART delivery	\$	3,460.73	\$	466.17	10.55	0.98	\$	470	
Tracing + Transport	\$	4,386.60			11.05				abs. dominated
Medical care + Transport + Breakfast	\$	4,606.21			10.51				ext. dominated
Tracing + Medical care	\$	5,173.28			10.35				ext. dominated
ART delivery + Nutrition	\$	5,263.00	\$	1,802.00	10.12	0.42	\$	4,300	

Table S21: Cost-effectiveness results when we assume nutrition supplement is offered for only 5 years

Abbreviations: ART = Antiretroviral Therapy; DALYs = Disability Adjusted Life Years; ICER = Incremental cost-effectiveness ratio

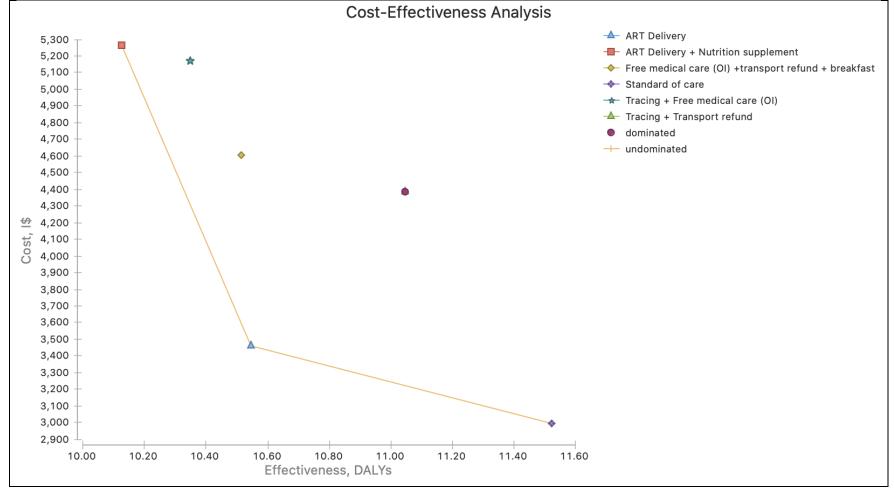


Figure S5: Cost-effectiveness results when we assume nutrition supplement is offered for only 10 years

			In	cremental	DALYs	DALYs			
Strategy	Cost		cost		Lost	Averted	ICER		
No Intervention	\$	2,994.56			11.52				
ART delivery	\$	3,460.73	\$	466.17	10.55	0.98	\$	470	
Tracing + Transport	\$	4,386.60			11.05				abs. dominated
Medical care + Transport + Breakfast	\$	4,606.21			10.51				ext. dominated
Tracing + Medical care	\$	5,173.28			10.35				ext. dominated
ART delivery + Nutrition	\$	6,354.00	\$	2,893.00	10.12	0.42	\$	6,880	

Table S22: Cost-effectiveness results when we assume nutrition supplement is offered for only 10 years

Abbreviations: ART = Antiretroviral Therapy; DALYs = Disability Adjusted Life Years; ICER = Incremental cost-effectiveness ratio

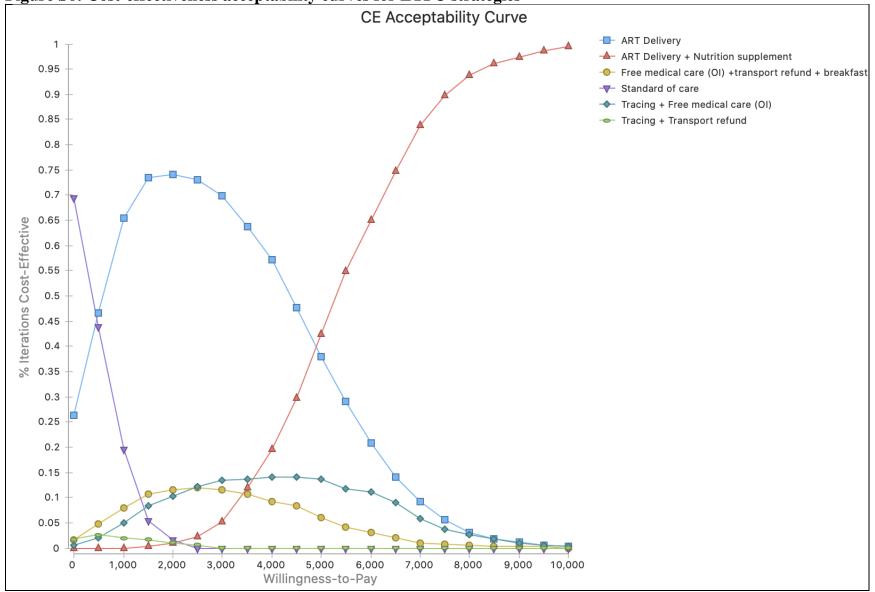


Figure S6: Cost-effectiveness acceptability curves for LTFU strategies

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## Vita

Deo Mujwara was born on June 16, 1986, in Fort Portal, Uganda. He received his Bachelors of science in Quantitative Economics from Makerere University (Kampala, Uganda) in 2011 and worked for Uganda Bureau of Statistics and Stanbic Bank Uganda before enrolling for his Masters of Arts in Economics at Georgia State University (Atlanta, Georgia) in 2013. After completing his Masters in 2015, Deo worked for Dekalb County Housing Authority as a research assistant for a year. In 2016, he joined the Healthcare Policy and Research Ph.D. program in the Department of Health Behavior and Policy at Virginia Commonwealth University School of Medicine. During the Ph.D. program, he conducted research under the supervision of Dr. April D. Kimmel focusing on access to HIV care and application of mathematical modeling techniques to inform efficient policy decisions. Through collaborations with faculty and fellow students, he worked on various manuscripts and presented his research at peer-reviewed conferences. He currently works as a health economist at Allelica, a company committed to reducing the impact of chronic diseases through genomic medicine. As a health economist, he develops mathematical models to examine the cost-effectiveness of polygenic risk scores in disease prevention.

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