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Effect of door-to-door distribution of HIV self-testing kits on HIV testing and antiretroviral therapy initiation: a cluster randomised trial in Malawi

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ABSTRACT

Introduction Reaching high coverage of HIV testing remains essential for HIV diagnosis, treatment and prevention. We evaluated the effectiveness and safety of door-to-door distribution of HIV self-testing (HIVST) kits in rural Malawi.

Methods This cluster randomised trial, conducted between September 2016 and January 2018, used restricted 1:1 randomisation to allocate 22 health facilities and their defined areas to door-to-door HIVST alongside the standard of care (SOC) or the SOC alone. The study population included residents (≥16 years). HIVST kits were provided door-to-door by community-based distribution agents (CBDAs) for at least 12 months. The primary outcome was recent HIV testing (in the last 12 months) measured through an endline survey. Secondary outcomes were lifetime HIV testing and cumulative 16-month antiretroviral therapy (ART) initiations, which were captured at health facilities. Social harms were reported through community reporting systems. Analysis compared cluster-level outcomes by arm.

Results Overall, 203 CBDAs distributed 273 729 HIVST kits. The endline survey included 2582 participants in 11 HIVST clusters and 2908 participants in 11 SOC clusters. Recent testing was higher in the HIVST arm (68.5%, 1768/2582) than the SOC arm (48.9%, 1422/2908), with adjusted risk difference (RD) of 16.1% (95% CI 6.5% to 25.7%). Lifetime testing was also higher in the HIVST arm (86.9%, 2243/2582) compared with the SOC arm (78.5%, 2283/2908; adjusted RD 6.3%, 95% CI 2.3% to 10.3%). Differences were most pronounced for adolescents aged 16–19 years (adjusted RD 18.6%, 95% CI 7.3% to 29.9%) and men (adjusted RD 10.2%, 95% CI 3.1% to 17.2%). Cumulative incidence of ART initiation was 1187.2 and 909.0 per 100 000 population in the HIVST and SOC arms, respectively (adjusted RD 309.1, 95% CI −95.5 to 713.7). Self-reported HIVST use was 42.5% (1097/2582), with minimal social harms reported.

Conclusion Door-to-door HIVST increased recent and lifetime testing at population level and showed high safety, underscoring potential for HIVST to contribute to HIV elimination goals in priority settings.

Trial registration number NCT02718274.

WHAT IS ALREADY KNOWN?

⇒ HIV self-testing (HIVST) can further extend coverage of HIV testing among underserved population subgroups.

⇒ Limited data were previously available on the effectiveness and safety of HIVST from rural, underserved populations in high HIV prevalence settings.

WHAT ARE THE NEW FINDINGS?

⇒ Door-to-door distribution of HIVST kits by community-based distribution agents increased recent HIV testing and lifetime HIV testing, with differences most pronounced among adolescents aged 16–19 years and men.

⇒ Cumulative incidence of antiretroviral therapy initiations was not shown to increase for the overall 16-month intervention period.

⇒ Self-reported HIVST use was 42.5%, with minimal social harms reported.

WHAT DO THE NEW FINDINGS IMPLY?

⇒ Door-to-door HIVST demonstrates significant potential to contribute to HIV elimination goals in priority settings.

INTRODUCTION

In 2016, an estimated 19.4 million people were living with HIV in southern and eastern Africa.[1] Despite expansion of HIV testing and treatment programmes, one-quarter of people living with HIV remained unaware of their HIV status. HIV testing gaps were highest in adolescents and men, including in Malawi.[1] In 2015–2016, the proportion of undiagnosed HIV was 46% among HIV-positive adolescents and young adults aged 15–24 years, the highest across age groups.[2] Of men with HIV, 28% were unaware of their status compared with 20% of women with HIV.[2] Reaching high coverage of HIV testing remains essential for

HIV diagnosis, treatment and prevention,[3] but access of facility-based HIV services can be limited by social, economic and health system barriers.[4–6]

Community-based HIV testing strategies can identify HIV-positive persons at earlier stages of infection and improve antiretroviral therapy (ART) initiation and retention when provided with universal treatment services.[7 8] Provision of HIV self-testing (HIVST) through community-based approaches can further extend coverage of HIV testing among underserved population subgroups.[9] In Malawi, urban community-based distribution of HIVST kits achieved high uptake, with offer of home-based HIV care further increasing demand for ART.[10 11] Introducing HIVST with door-to-door HIV testing services (HTS) by community health workers increased knowledge of HIV status among urban Zambians.[12] Community-based HIVST is therefore a promising approach for providing HIV testing, though lower literacy and healthcare access among rural populations could influence uptake of self-care technologies.[13] Limited data were previously available on the effectiveness and safety of HIVST from rural, underserved populations in high HIV prevalence settings.

In this study, we used a cluster randomised trial to evaluate the effectiveness and safety of door-to-door distribution of HIVST kits in rural Malawi. Specifically, we aimed to assess whether distribution of HIVST kits through community-based distribution agents (CBDAs) increased the proportion of the population who tested for HIV and were initiated on ART at cluster level. Our study is part of a multicountry evaluation of community-based distribution of HIVST kits under the Unitaid/Population Services International (PSI) HIV Self-Testing Africa (STAR) Initiative.

METHODS

Design, setting and participants

We conducted a parallel cluster randomised trial of door-to-door distribution of HIVST kits.[14] The study was based in 22 government primary health centres and their defined areas in four high HIV prevalence districts (Blantyre, Machinga, Mwanza, Neno). A cluster randomised design was adopted since the intervention was implemented at the health facility level. The study team enrolled health facilities providing HIV testing and ART services to rural communities in their catchment areas, with verbal consent obtained from facility representatives. Boundaries were drawn for: (1) the facility catchment area, and (2) the evaluation area within the facility catchment area. The intervention was delivered throughout the facility catchment area, while primary and secondary outcomes were measured among residents from the evaluation area. Specifically, the study population included residents aged 16 years and older from the evaluation area.

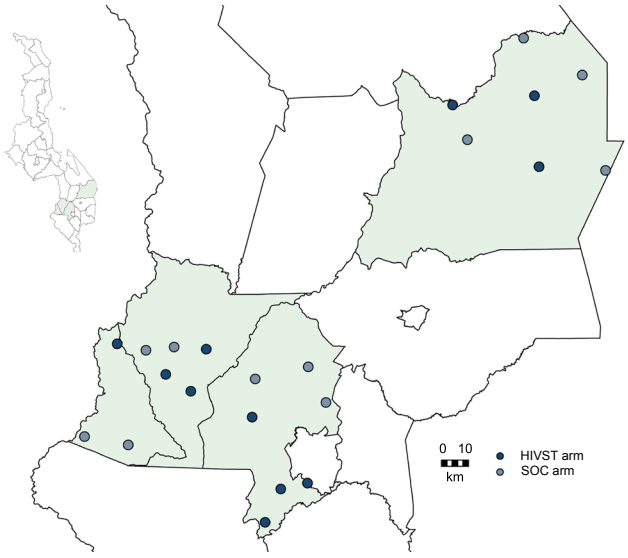

Figure 1 Map of trial clusters in Malawi. Map of Blantyre, Machinga, Mwanza and Neno district with government health facilities and their defined clusters. Malawi National Spatial Data Centre, http://www.masdap.mw/. HIVST, HIV self-testing; SOC, standard of care.

Randomisation

The 22 health facilities were randomised 1:1 to the HIVST intervention alongside the standard of care (SOC) or the SOC alone, which primarily consisted of facility-based HTS (figure 1). A computer-generated random sample was drawn by MN from 150 855 unique combinations of allocating health facilities to one of the two study arms, restricted by district, catchment population size, number of HTS clients and the proportion of clients testing HIV positive.[15] The final allocation was assigned at a public ceremony on 21 March 2016. Numbered balls were selected by community and government representatives from an opaque bag that corresponded to a unique allocation. Blinding of the implementation team and residents was not feasible due to the nature of the intervention, but masking was maintained where possible, including data collection, management and analysis without reference to the study arms.

A planned second randomisation of home-based HIV care in the HIVST arm was not implemented due to delays in initiating the intervention, leaving an insufficient interval for assessment.[14]

Procedures

The HIVST intervention was delivered for at least 12 months within the evaluation area of eligible health facilities before expanding to the rest of the facility catchment area. HIVST kits were distributed by existing CBDAs, who provided reproductive health products prior to HIVST distribution, and newly recruited CBDAs selected in consultation with village heads.

PSI Malawi conducted 1-week trainings based on an HIVST training curriculum developed in collaboration with the Ministry of Health. The training included basic information on HIV diagnosis and treatment; promoting

HIVST using social marketing; using kits and interpreting results; providing pretest and post-test information and support, including referral for confirmatory HIV testing and ART following a positive self-test; anticipating and managing social harms; storing kits; and collecting data. National HIV testing and counselling practices and principles on voluntariness, consent and protection of client privacy and confidentiality were also covered in the training.

CBDAs then provided the OraQuick HIV Self-Test (OraSure Technologies, Thailand), along with locally adapted instructions for use,[16] an opaque envelope for disposal and a self-referral card to facilitate linkage to routine HIV services at health facilities. In their respective areas, CBDAs distributed HIVST kits door-to-door or on request to residents aged 16 years and older, with their sociodemographic characteristics recorded in registers. Residents could self-test with CBDAs or in private. If residents elected to self-test privately, CBDAs followed up within 7 days of distribution to provide optional post-test support. Disclosure was not required, and HIVST results were not recorded in registers. Residents were also asked to place their used kits in envelopes to be returned to CBDAs or deposited in locked boxes located centrally in each village. PSI provided monthly supervision to verify data in CBDA registers, collect used kits and restock supplies. CBDAs were remunerated for each kit distributed (MWK100/US$0.15) and each kit distributed with linkage to HIV care (MWK150/USD$0.23).

The SOC in both arms included HIV testing and ART services under the Ministry of Health, offered primarily at health facilities. Standard HIV testing used blood-based rapid diagnostic testing algorithms, with ART initiated immediately following a confirmed HIV diagnosis.

Outcomes and measurement

The primary outcome compared between arms the proportion of individuals aged 16 years and older who self-reported recent testing for HIV (in the last 12 months), measured at cluster level using an endline survey. Secondary outcomes compared (1) self-reported lifetime HIV testing, and (2) cumulative 16-month incidence of ART initiations per 100 000 population, which was ascertained using ART clinic records during the intervention period.

HIV testing outcomes were measured through a cross-sectional survey administered at the end of the intervention period. In each evaluation area, two villages with a minimum of 250 residents aged 16 years and older were randomly selected, with one village surveyed at endline and one village surveyed at baseline. The baseline survey was conducted prior to the intervention to adjust for imbalance between arms in the primary outcome.

Households in the evaluation villages were enumerated and randomly selected to provide a sample of at least 250 participants per village. All individuals aged 16 years and older in selected households were eligible for the survey, with multiple visits for interviews attempted to maximise the response rate. Informed verbal consent or assent was obtained. Participants were then interviewed on household and sociodemographic characteristics and prior use of HIV testing, treatment and prevention services.

ART initiation data were extracted from registers at each of the health facilities for the 16-month intervention period and the 12-month period preceding the intervention. Eligibility criteria included ART patients aged 16 years and older from the evaluation area. Population estimates for the evaluation area, which were used as the denominator for the ART outcome, were obtained from facility and village registers.

The proportion of lifetime HIVST use and the number of HIVST kits distributed were evaluated using the endline survey and CBDA registers. Adverse events related to HIVST were also measured using the endline survey in addition to a community reporting system established in evaluation villages to identify and manage potential adverse events.[17] Community stakeholders, including village heads, community health workers, religious leaders and police officers, documented, investigated and managed social harms related to HIV testing and self-testing. Adverse events were reported to the study team and assessed, categorised by severity and followed up as appropriate.[17]

Sample size

With 11 clusters per arm and 250 participants per cluster, we had at least 80% power at a 5% significance level to detect a 30% relative increase in the primary outcome of recent HIV testing in the HIVST arm, assuming 25%–40% coverage in the SOC arm.[18] The study was also powered to identify a 45% relative increase in lifetime HIV testing in the HIVST arm, assuming 42%–60% coverage in the SOC arm. The sample size was calculated using a coefficient of variation (k) in clusters of 0.25.[15]

Statistical analysis

We conducted an intention-to-treat analysis based on cluster assignment to study arms and used methods appropriate for cluster randomised trials.[15] The risk difference (RD) and risk ratio were calculated respectively from cluster-level risks and log risks, which were compared by arm using a t-test. For HIV testing outcomes, we adjusted for imbalances in individual-level covariates based on a two-stage approach.[15] The first stage used logistic regression with individual-level covariates to obtain predicted values, which were summed at the cluster level and applied to calculate the difference and ratio of observed and predicted values. The second stage used linear regression of covariate-adjusted residuals obtained from the first stage and included the study arm. To adjust for imbalance in the primary outcome prior to the intervention, the cluster-level baseline covariate of recent HIV testing was also included in the regression model. The ART initiation outcome adjusted for ART uptake in the 12-month preintervention period.

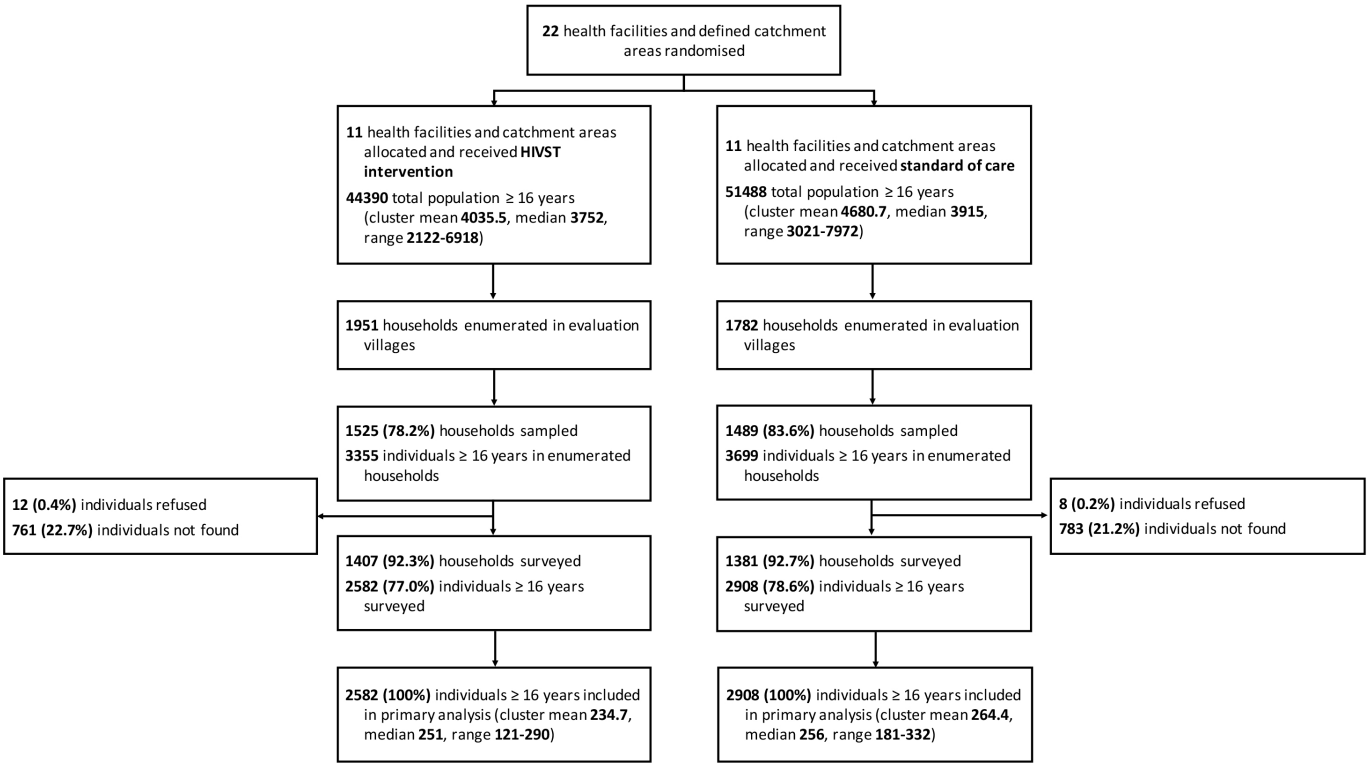

Figure 2 Trial flow diagram. Flow diagram of the cluster randomised trial. HIVST, HIV self-testing.

For recent HIV testing, a priori subgroup analyses were specified by sex, age group (16–19 years, 20 years and older) and socioeconomic status (lowest, middle, highest strata). Post hoc analysis used alternative categories of age group (16–19 years, 20–39 years, 40 years and older). Further, subgroup analyses were conducted for lifetime HIV testing by sex, age group and socioeconomic status, and for ART initiations by intervention period (0–5, 6–11, 12–16 months). Statistical analysis used Stata V.14.0.

RESULTS

Implementation of the intervention was staggered, starting from September to December 2016, and continuing until January 2018. Overall, 203 CBDAs (cluster mean 18.5) distributed 273 729 HIVST kits (cluster mean 24 884.45) throughout the catchment area of health facilities, including evaluation and non-evaluation areas (online supplemental table 1). The volume of kits distributed was similar by sex, with 50.2% (n=137 433) of kits delivered to men.

The population in the evaluation area included 44 390 residents in 11 clusters in the HIVST arm and 51 488 residents in 11 clusters in the SOC arm. Participants were recruited for the endline survey between October 2017 and January 2018. The trial flow diagram is reported in figure 2. The endline survey included 77.0% (2582/3355) of enumerated residents in the HIVST arm and 78.6% (2908/3699) of enumerated residents in the SOC arm, with few eligible residents refusing to participate (10/7054).

Population characteristics for the endline survey are summarised in table 1. The proportion of men was 42.6% (2339/5490) and the median age was 31 years old. The majority of participants did not have beyond primary-level education (84.9%, 4661/5490). Most characteristics were well balanced by arm. Differences were observed for marital status, with 69.5% (1795/2582) married in the HIVST arm and 63.2% (1838/2908) married in the SOC arm.

The baseline survey was administered between May and August 2016. Of listed individuals, 78.5% (2809/3577) and 74.7% (2664/3567) were surveyed in the HIVST and SOC arms, respectively (online supplemental tables 2 and 3). Baseline coverage of HIV testing in the last 12 months was higher in the HIVST arm (56.0%, 1574/2809) than the SOC arm (48.4%, 1289/2664; table 1). We therefore adjusted for baseline differences in analysis of primary and secondary outcomes. Self-reported lifetime use of HIVST at baseline was limited (7/5473).

Primary outcome

At endline, recent HIV testing (in the last 12 months) was higher in the HIVST arm (68.5%, 1768/2582) compared with the SOC arm (48.9%, 1422/2908), with adjusted RD of 16.1% (95% CI 6.5% to 25.7%; table 2; online supplemental figure 1). In subgroup analysis, the intervention had a more pronounced effect among adolescents aged 16–19 years (adjusted RD 26.1%, 95% CI 12.9% to 39.2%) than adults aged 20 years and older (adjusted RD 14.7%, 95% CI 4.8% to 24.6%), though data were consistent with no interaction effect (p value for interaction=0.18). Post

Table 1 Comparison of endline population characteristics by study arm

	HIVST	SOC
	n (%)	n (%)
Baseline		
Individual characteristics	**(n=2809)**	**(n=2664)**
Ever tested	82.2% (2308)	77.1% (2054)
Tested in the last 12 months	56.0% (1574)	48.4% (1289)
Endline		
Household characteristics	**(n=1407)**	**(n=1381)**
Adults (median/range)	2 (1–7)	2 (1–9)
Children (median/range)	2 (0–8)	2 (0–9)
Household wealth index*		
Lowest	434 (32%)	468 (35.7%)
Middle	456 (33.6%)	422 (32.2%)
Highest	466 (34.4%)	421 (32.1%)
Individual characteristics	**(n=2582)**	**(n=2908)**
Male	1075 (41.6%)	1264 (43.5%)
Age (median/range)	31 (16–97)	31 (16–91)
Age group (years)		
16–19	366 (14.2%)	439 (15.1%)
20–24	469 (18.2%)	558 (19.2%)
25–39	931 (36.1%)	998 (34.3%)
≥40	816 (31.6%)	913 (31.4%)
Marital status		
Married or living together	1795 (69.5%)	1838 (63.2%)
Separated, divorced or widowed	405 (15.7%)	438 (15.1%)
Never married	382 (14.8%)	632 (21.7%)
Educational attainment		
None	463 (17.9%)	555 (19.1%)
Primary	1745 (67.6%)	1898 (65.3%)
Secondary or higher	374 (14.5%)	455 (15.6%)
Literate	1639 (63.5%)	1907 (65.6%)
Resident in last 12 months	2429 (94.1%)	2748 (94.5%)
Self-rated health status†		
Very good	662 (25.7%)	996 (34.3%)
Good	1470 (57.0%)	1429 (49.1%)
Fair	319 (12.4%)	320 (11.0%)
Poor	128 (5.0%)	163 (5.6%)

Samples for the baseline and endline survey include different individuals.
*51 missing values in the HIVST arm and 70 missing values in the SOC arm.
†3 missing values in the HIVST arm.
HIVST, HIV self-testing; SOC, standard of care.

hoc analysis found similar differences among adults aged 20–39 years and adults 40 years and older (online supplemental table 4). While the difference in the proportion of recent testing was also higher for men (adjusted RD 20.6%, 95% CI 7.1% to 34.0%) compared with women (adjusted RD 12.8%, 95% CI 4.0% to 21.6%), there was weak evidence for interaction (p=0.07). In terms of socioeconomic status, the effect of the intervention was greater among participants in the highest strata (adjusted RD 20.2%, 95% CI 8.3% to 32.1%) than the lowest strata (adjusted RD 13.0%, 95% CI 1.1% to 24.8%). However, there was no evidence for interaction (highest vs lowest strata: p value for interaction=0.18).

Secondary outcomes

Lifetime HIV testing was higher in the HIVST arm (86.9%, 2243/2582) than the SOC arm (78.5%, 2283/2908; adjusted RD 6.3%, 95% CI 2.3% to 10.3%; table 2; online supplemental figure 1). In exploratory analysis, the effect of the intervention was larger for adolescents aged 16–19 years (adjusted RD 18.6%, 95% CI 7.3% to 29.9%) than adults aged 20 years and older (adjusted RD 4.4%, 95% CI 0.5% to 8.2%; p value for interaction=0.02), and for men (adjusted RD 10.2%, 95% CI 3.1% to 17.2%) than women (adjusted RD 3.4%, 95% CI −0.9% to 7.7%; p value for interaction=0.07; online supplemental table 4). The intervention effect on lifetime testing was similar in the lowest and highest socioeconomic strata and close to zero for the middle strata.

Cumulative incidence of ART initiation captured at health facilities during the 16-month intervention period was 1187.2 and 909.0 per 100 000 population in the HIVST and SOC arms, respectively (adjusted RD 309.1, 95% CI −95.5 to 713.7; table 2; online supplemental figure 1). Stratified by time period since study initiation, the adjusted RD for periods of 0–5, 6–11 and 12–16 months was 142.6 (95% CI −81.5 to 366.7), 194.8 (95% CI 31.4 to 358.1) and 28.3 (95% CI −186.5 to 129.9), respectively. There was no evidence for statistical differences measured (6–11 months vs 0–5 months: p value for interaction=0.51; 12–16 months vs 0–5 months: p value for interaction=0.42; online supplemental table 4).

Process outcomes

Consistent with the high number of HIVST kits distributed, there were large differences between arms in awareness and use of HIVST at endline. The proportion of participants who had heard of HIVST at endline was 88.8% (2294/2582) in the HIVST arm and 31.5% (917/2908) in the SOC arm (table 3). Self-reported lifetime HIVST use was respectively 42.5% (1097/2582) in the HIVST arm, with uptake highest in young men aged 20–24 years (58%) and adolescent boys (49.0%; online supplemental figure 2). Similar coverage was reported for HIVST use in the last 12 months. HIVST use was 8.3% (240/2908) in the SOC arm, with one cluster exposed to an external community-based HIVST programme in 2017. Among participants who recently self-tested in the HIVST arm (n=794), most received HIVST kits from the CBDA (97.9%, n=777) and collected their kits at home (76.7%, n=609). Further, 0.8% (n=6) reported a new HIV-positive result and 2.0% (n=16) reported a

Table 2 Primary and secondary outcomes by study arm

	HIVST		SOC		Risk difference (95% CI)	Adjusted risk difference (95% CI)	Risk ratio (95% CI)	Adjusted risk ratio (95% CI)	
	n/N (%)	GM	n/N (%)	GM	P value	P value	P value	P value	k
Primary outcome									
HIV testing in the last 12 months	1768/2582 (68.5%)	68.1%	1422/2908 (48.9%)	48.1%	19.2% (10.1% to 28.3%) <0.001	16.1% (6.5% to 25.7%) 0.002	1.42 (1.2 to 1.66) <0.001	1.33 (1.13 to 1.58) 0.002	0.17
Stratified by age group*									
16–19 years	252/366 (68.9%)	69.5%	185/439 (42.1%)	39.2%	27.5% (13.4% to 41.5%) <0.001	26.1% (12.9% to 39.2%) <0.001	1.77 (1.31 to 2.41) <0.001	1.78 (1.33 to 2.38) <0.001	
≥20 years	1516/2216 (68.4%)	68.0%	1237/2469 (50.1%)	49.5%	17.6% (8.1% to 27.0%) <0.001	14.7% (4.8% to 24.6%) 0.006	1.37 (1.16 to 1.63) <0.001	1.3 (1.09 to 1.55) 0.006	
Stratified by sex†									
Male	699/1075 (65.0%)	64.1%	529/1264 (41.9%)	41.2%	22.3% (10.1% to 34.5%) 0.001	20.6% (7.1% to 34.0%) 0.01	1.55 (1.25 to 1.94) <0.001	1.51 (1.18 to 1.93) 0.002	
Female	1069/1507 (70.9%)	70.9%	893/1644 (54.3%)	53.1%	16.9% (8.4% to 25.4%) <0.001	12.8% (4.0% to 21.6%) 0.007	1.33 (1.14 to 1.56) <0.001	1.24 (1.06 to 1.45) 0.01	
Stratified by household wealth index‡									
Lowest	463/723 (64.0%)	60.6%	427/902 (47.3%)	46.0%	14.5% (3.1% to 25.9%) 0.02	13.0% (1.1% to 24.8%) 0.03	1.32 (1.06 to 1.64) 0.02	1.28 (1.02 to 1.61) 0.04	
Middle	590/829 (71.2%)	70.8%	454/868 (52.3%)	51.6%	18.2% (8.7% to 27.6%) <0.001	13.8% (3.7% to 23.8%) 0.01	1.37 (1.17 to 1.61) <0.001	1.27 (1.07 to 1.5) 0.008	
Highest	660/961 (68.7%)	70.2%	477/1013 (47.1%)	46.4%	22.8% (11.5% to 34.2%) <0.001	20.2% (8.3% to 32.1%) 0.002	1.51 (1.24 to 1.86) <0.001	1.45 (1.17 to 1.79) 0.002	
Secondary outcomes									
Lifetime HIV testing	2243/2582 (86.9%)	87.1%	2283/2908 (78.5%)	78.6%	8.6% (4.7% to 12.5%) <0.001	6.3% (2.3% to 10.3%) 0.004	1.11 (1.06 to 1.16) <0.001	1.08 (1.03 to 1.13) 0.004	0.04
ART initiation per 100 000 population across intervention period§	527/44 390 (1187.2)	1159.1	468/51 488 (909.0)	810.6	366.9 (–90.1 to 823.8) 0.11	309.1 (–95.5 to 713.7) 0.13	1.43 (0.91 to 2.24) 0.11	1.34 (0.92 to 1.96) 0.12	0.46

HIV testing outcomes adjusted for cluster-level baseline outcomes (testing in the last 12 months) and individual-level covariates (age, sex, marital status). Subgroup analysis by age group adjusts for the same covariates except for age group. Subgroup analysis by sex adjusts for the same covariates except for sex. ART initiation outcome adjusted for cumulative incidence of ART initiations in 12-month preintervention period.
Post hoc analysis with one SOC cluster dropped due to exposure to separate community-based HIVST implementation. For HIV testing in the last 12 months, HIVST: 1768/2582 (68.5%), SOC: 1230/2665 (46.2%); adjusted RD: 19.0% (11.5%–26.5%), p<0.001. For lifetime HIV testing, HIVST: 2243/2582 (86.9%), SOC: 2074/2665 (77.8%); adjusted RD: 6.9% (3.0%–10.8%), p<0.001.
*P value for interaction, p=0.18.
†P value for interaction, p=0.07.
‡P value for interaction (middle vs lowest), p=0.74. P value for interaction (highest vs lowest), p=0.18.
§Denominator for ART initiations is the estimated population of adults ≥16 years in the evaluation area, which was estimated using village and health facility registers.
ART, antiretroviral therapy; GM, geometric mean (of cluster-level proportions); HIVST, HIV self-testing; k, coefficient of variation in health facility-defined clusters; RD, risk difference; SOC, standard of care.

Table 3 Fidelity to HIV self-testing intervention

	HIVST	SOC
	n (%)	n (%)
	(n=2582)	(n=2908)
Heard of self-testing*	2294 (88.8)	917 (31.5)
Ever self-tested†	1097 (42.5)	240 (8.3)
Self-tested in the last 12 months‡	974 (37.7)	211 (7.3)
If self-tested in most recent test:	(n=794)	
Self-test distributor		
CBDA	777 (97.9)	
Other distributor	17 (2.1)	
Self-test collection location		
Home	609 (76.7)	
Other location	185 (23.3)	
Self-test result§		
New positive	6 (0.8)	
Repeat positive	16 (2.0)	
Negative	771 (97.2)	
Linked to confirmatory HIV testing (n=22)	7 (31.8)	
Initiated on ART (n=22)	6 (27.3)	
Forced to self-test or disclose self-test result	4 (0.5)	

*1 missing value in the HIVST arm.
†1 missing value in the HIVST arm.
‡2 missing values in the HIVST arm.
§1 missing value in the HIVST arm.
ART, antiretroviral therapy; CBDA, community-based distribution agent; HIVST, HIV self-testing; SOC, standard of care.

repeat positive result, of whom 31.8% (7/22) linked to confirmatory HIV testing and 27.3% (6/22) initiated on ART.

Safety outcomes

At endline, 0.5% (4/794) of participants reported being forced to self-test or disclose their self-test results (table 3). Three events of social harm related to HIVST were reported, managed and resolved through the community reporting system: one case involved discrimination from household members for collecting an HIVST kit; two cases involved temporary separation between couples, with one event from self-testing and one event due to newly identified serodiscordancy within the couple. In an additional event reported to implementers in non-evaluation areas, a perinatally infected adolescent under the eligible age acquired an HIVST kit and suffered a highly stigmatising response following self-testing with her friends. These events have been described in detail elsewhere.[17]

DISCUSSION

The main findings from this cluster randomised trial were that door-to-door distribution of HIVST kits by CBDAs increased recent and lifetime HIV testing at population level in rural Malawi. Our primary outcome of recent testing increased by 16.1%. Lifetime testing increased by 6.3%, with differences between arms most pronounced among priority subgroups: adolescents aged 16–19 years and men. The HIVST intervention did not show an effect on cumulative incidence of ART initiations at health facilities for the overall 16-month intervention period. HIVST use was reported by 42.5% of participants in the HIVST arm, with uptake highest among young men aged 20–24 years and adolescent boys. Few serious adverse events were reported. Our results therefore support door-to-door HIVST as an effective and safe strategy that can be used to meet HIV testing needs in underserved rural populations.

Our study is one of three community-based randomised trials from rural settings in southern Africa that were implemented as part of STAR.[14 19 20] Affordable, convenient and safe HIV testing strategies are important for rural populations, who often have more pronounced barriers to accessing healthcare.[13] The STAR trials had critical differences that can be used to guide policy and future research priorities. Our results showed increased recent and lifetime HIV testing from door-to-door HIVST, consistent with a separate Zambian trial, which added HIVST to an intensive community-based HIV programme.[12] High coverage of lifetime testing (88.7%) and lifetime HIVST use (50.2%) was reported for both arms of the STAR Zimbabwe trial, which compared the impact of remuneration strategies under campaign-style distribution by CBDAs on linkage to HIV care.[19] Our study, along with the Zimbabwe trial, implemented door-to-door distribution. In contrast, provision of HIVST kits at home, high-density community sites and health facilities under the STAR Zambia trial resulted in lower HIVST use (26.3%) and no measurable increase in lifetime or recent testing.[20] Process outcomes, such as HIVST awareness, were also lower in Zambia than in Malawi and Zimbabwe, suggesting that door-to-door distribution can lead to higher penetration than broader community-based models.[19 20]

We showed encouraging uptake of HIVST, with minimal social harms reported. Uptake was highest among young men aged 20–24 years followed by adolescent boys aged 16–19 years. Our study also reported increased lifetime HIV testing among adolescents and men. HIVST can bypass barriers that prevent uptake of standard HTS by these priority subgroups,[10 21] with HIVST valued for the convenience and confidentiality afforded.[5 22] However, our results demonstrated lower uptake compared with the STAR Zimbabwe trial, which evaluated more intensive distribution across a shorter period of time.[19] Similarly, a previous study in urban Malawi reported 84% uptake from distribution of HIVST kits by community volunteers, which may indicate higher acceptability

among urban counterparts.[10] Understanding remaining demand-side barriers may allow for further optimisation of community-based HIVST strategies to maximise coverage and impact among underserved subgroups. Alternative HIVST strategies should also be considered. In Malawi, facility-based provision of HIVST kits among outpatients increased coverage of HIV testing, especially among adolescents.[23] Another study in Malawi found that secondary distribution to male partners of pregnant women extended testing coverage.[21]

Our study did not observe an increase in ART initiations for the overall 16-month intervention period but in subgroup analysis for the 6–11 months' postintervention period. Further, 0.8% of participants reported a new positive result from HIVST, with frequent repeat testing among participants already known to be HIV positive. Impact on ART uptake varied across STAR trials.[24] A non-randomised evaluation accompanying the Zimbabwe trial estimated a 27% increase in ART initiation rates,[19] while no difference was observed in Zambia.[20] Linkage to HIV care is practically difficult to capture, with potential for measurement errors.[24] True impact on ART demand from HIVST will depend on the prevalence of untreated HIV, which has been declining in southern and eastern Africa.[2] The intensity and reach of HIVST distribution strategies will also influence population-level impact. Additionally, interventions to encourage timely linkage to health facilities may be required, such as provision of home-based HIV care or more substantial financial incentives.[11 21]

The benefits of community-based HTS are well established, with the main barrier to implementation including high cost per test and cost per new diagnosis, especially as countries reach the 'First 90' targets.[25] Economic analysis of our intervention is reported separately.[26] CBDA distribution showed average cost of 2017 US$8.15 per HIVST kit distributed, with the main cost contributors including personnel and HIVST kits.[26] Unit cost of community-based HIVST was higher than the average cost of facility-based HTS (2016 US$4.92) and facility-based HIVST (US$4.99) in Malawi.[23 27] While community-based HIVST is likely to maintain higher levels of knowledge of recent HIV status than standard HTS alone, sustainable provision will require further reductions in costs and optimisation of linkage to HIV treatment and prevention. For example, providing periodic campaigns is likely to be less costly than maintaining a continuous programme, especially if targeted to high-prevalence populations or underserved subgroups with ongoing HIV risk. Alternatively, a community-led approach for delivering HIVST has potential to further reduce costs.[28]

The main strength of this study is the use of a robust cluster randomised design to report on the effectiveness and safety of large-scale implementation of community-based HIVST. Further, CBDAs are commonly used to distribute health commodities in Malawi, with our findings potentially generalisable to settings in sub-Saharan Africa with similar community health cadres. We also add to the body of evidence on effective strategies for expanding HIV testing coverage in rural, HIV-prevalent populations and among population subgroups with substantial undiagnosed HIV.

Limitations included HIV testing outcomes that were self-reported and therefore susceptible to misreporting. ART initiations may be underestimated if study residents accessed non-study health facilities, which we aimed to minimise with our inclusion criteria of health facilities. Non-participation in the endline survey could result in ascertainment bias, with response rates lower among men than women. We did not account for household-level clustering, though this was unlikely to have altered our findings.[29] We discontinued second randomisation of home-based HIV care in the HIVST arm; however, the outcomes reported in this study were not affected. Data on social harms were passively collected through community reporting systems, potentially under-reporting the number of adverse events. Finally, our findings are limited to our intervention design, which included door-to-door implementation through remunerated CBDAs.

CONCLUSION

Door-to-door distribution of HIVST kits by CBDAs increased recent and lifetime HIV testing in rural, underserved populations, including among adolescents 16–19 years and men. ART initiations showed no differences between arms for the overall 16-month intervention period. HIVST was very acceptable and safe, with uptake highest among young men and adolescent boys. Door-to-door HIVST demonstrates significant potential to contribute to HIV elimination goals in priority settings. Further, as countries approach the 'First 90' targets, this approach could be adapted for periodic implementation to meet the ongoing need for HTS in settings with high undiagnosed HIV.

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Contributors ELC conceptualised the study. PPI, KF, RC, ND, KH and ELC contributed to the study design. PPI, MK, RC and RNz supervised the implementation of the study, including the intervention and data collection. PPI, MN and KF conducted the statistical analysis. PI, KF, RNy, CCJ, MT, ND, KH and ELC critically interpreted the results. PPI wrote the first draft of the manuscript. All authors reviewed and approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The trial is registered with ClinicalTrials.gov. The trial protocol (https://hivstar.lshtm.ac.uk/protocols/) was approved by the University of Malawi College of Medicine (ref: P.01/16/1861) and the London School of Hygiene & Tropical Medicine (ref: 10566).

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Supporting information

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Table 1. Cluster-level fidelity to HIV self-testing intervention

					Endline survey		
	Population N	**CBDAs N**	**HIVST kits distributed N**	**N**	**Heard of self-testing n (%)**	**Ever self-tested n (%)**	**Self-tested in the last 12 months n (%)**
HIVST							
Chifunga	3933	9	7357	251	233 (92.8%)	87 (34.7%)	76 (30.3%)
Chikowa	6918	24	22697	251	224 (89.2%)	70 (27.9%)	64 (25.5%)
Chikweo	6471	51	90582	265	239 (90.2%)	115 (43.4%)	106 (40.0%)
Kunenekude	2947	15	14145	254	223 (87.8%)	92 (36.2%)	82 (32.3%)
Luwani	2638	8	5769	188	147 (78.2%)	71 (37.8%)	54 (28.7%)
Madziabango	2434	13	10579	228	211 (92.5%)	105 (46.1%)	100 (43.9%)
Magareta	3544	9	11864	233	218 (93.6%)	131 (56.2%)	114 (48.9%)
Mangamba	3752	21	20159	290	236 (81.4%)	75 (25.9%)	69 (23.8%)
Mpemba	5801	18	19994	229	192 (83.8%)	104 (45.4%)	96 (41.9%)
Namanja	2122	22	53402	272	258 (94.9%)	185 (68.0%)	160 (58.8%)
Soche Maternity	3830	13	17181	121	113 (93.4%)	62 (51.2%)	53 (43.8%)
Total	44390	203	273729	2582	2294 (88.8%)	1097 (42.5%)	974 (37.7%)
SOC							
Dziwe	6244			232	60 (25.9%)	3 (1.3%)	2 (0.9%)
Ligowe	6649			300	60 (20.0%)	2 (0.7%)	2 (0.7%)
Lirangwe	7972			252	29 (11.5%)	3 (1.2%)	1 (0.4%)
Makata	3283			267	38 (14.2%)	2 (0.7%)	1 (0.4%)
Mbonechera	3526			181	40 (22.1%)	1 (0.6%)	1 (0.6%)
Mkwepere	3021			243	186 (76.5%)	112 (46.1%)	105 (43.2%)
Nayuchi	3298			332	255 (76.8%)	69 (20.8%)	63 (19.0%)
Ngokwe	4914			256	146 (57.0%)	43 (16.8%)	33 (12.9%)
Pensulo	5532			250	46 (18.4%)	4 (1.6%)	3 (1.2%)
Thambani	3915			288	24 (8.3%)	1 (0.3%)	0 (0.0%)
Tulonkhondo	3134			307	33 (10.7%)	0 (0.0%)	0 (0.0%)
Total	51488			2908	917 (31.5%)	240 (8.3%)	211 (7.3%)

CBDA, community-based distribution agents; HIVST, HIV self-testing; SOC, standard of care.

Table 2. Household and individual response rates at baseline and endline

	Households enumerated N	Households sampled n/N (%)	Individuals in sampled households N	Individuals ≥ 18 years surveyed and included in primary analysis		
				Overall n/N (%)	Males n/N (%)	Females n/N (%)
Baseline						
HIVST	2286	1633/2286 (71.4%)	3577	2809/3577 (78.5%)	1170/1676 (69.8%)	1639/1901 (86.2%)
SOC	2349	1643/2349 (69.9%)	3567	2664/3567 (74.7%)	1085/1617 (67.1%)	1579/1950 (81.0%)
Endline						
HIVST	1951	1525/1951 (78.2%)	3355	2582/3355 (77%)	1075/1546 (69.5%)	1507/1809 (83.3%)
SOC	1782	1489/1782 (83.6%)	3699	2908/3699 (78.6%)	1264/1746 (72.4%)	1644/1953 (84.2%)

HIVST, HIV self-testing; SOC, standard of care.

Table 3. Comparison of baseline population characteristics by study arm

	HIVST n (%)	SOC n (%)
Household characteristics	(N=1467)	(N=1426)
Adults (median/range) *	2 (1-8)	2 (1-7)
Children (median/range) *	2 (0-8)	2 (0-10)
Household wealth index †		
Lowest	590 (40.4%)	717 (50.3%)
Middle	382 (26.1%)	332 (23.3%)
Highest	489 (33.5%)	376 (26.4%)
Individual characteristics	(N=2809)	(N=2664)
Age (median/range)	31 (16-96)	31 (16-96)
Male	1170 (41.7%)	1085 (40.7%)
Age group		
16-19 years	445 (15.8%)	407 (15.3%)
20-24 years	507 (18.0%)	476 (17.9%)
25-39 years	971 (34.6%)	934 (35.1%)
≥ 40 years	886 (31.5%)	847 (31.8%)
Marital status ‡		
Married or living together	1938 (69.0%)	1744 (65.5%)
Separated, divorced or widowed	382 (13.6%)	461 (17.3%)
Never married	488 (17.4%)	458 (17.2%)
Educational attainment §		
None	602 (21.4%)	665 (25.0%)
Primary	1740 (62.0%)	1661 (62.4%)
Secondary or higher	465 (16.6%)	337 (12.7%)
Literate ‖	1864 (66.4%)	1660 (62.3%)
Resident in last 12 months	2736 (97.4%)	2612 (98.0%)
Self-rated health status		
Very good	814 (29.0%)	699 (26.2%)
Good	1163 (41.4%)	1191 (44.7%)
Fair	627 (22.3%)	617 (23.2%)
Poor	204 (7.3%)	157 (5.9%)

HIVST, HIV self-testing; SOC, standard of care.
* 3 missing values in the HIVST arm and 1 missing value in the SOC arm.
† 6 missing values in the HIVST arm and 1 missing value in the SOC arm.
‡ 1 missing values in the HIVST arm and 1 missing value in the SOC arm.
§ 2 missing values in the HIVST arm and 1 missing value in the SOC arm.
‖ 1 missing value in the HIVST arm and 1 missing value in the SOC arm.
¶ 1 missing value in the HIVST arm.

Table 4. Post-hoc outcomes by study arm

	HIVST n/N (%)	HIVST GM	SOC n/N (%)	SOC GM	Risk difference (95% CI) p-value	Adjusted risk difference (95% CI) p-value	Risk ratio (95% CI) p-value	Adjusted risk ratio (95% CI) p-value
HIV testing in the last 12 months								
Stratified by age group *								
16-19 years	252/366 (68.9%)	69.5%	185/439 (42.1%)	39.2%	27.5% (13.4-41.5%) <0.001	26.1% (12.9-39.2%) <0.001	1.77 (1.31-2.41) <0.001	1.78 (1.33-2.38) <0.001
20-39 years	1062/1400 (75.9%)	75.8%	897/1556 (57.6%)	56.3%	18.6% (8.7-28.6%) <0.001	15.0% (4.7-25.3%) 0.007	1.35 (1.14-1.59) 0.001	1.27 (1.06-1.51) 0.01
≥ 40 years	454/816 (55.6%)	54.0%	340/913 (37.2%)	37.4%	15.2% (4.5-25.9%) 0.008	13.9% (2.0-25.7%) 0.03	1.44 (1.14-1.83) 0.005	1.38 (1.06-1.8) 0.02
Lifetime HIV testing								
Stratified by age group †								
16-19 years	280/366 (76.5%)	77.0%	239/439 (54.4%)	53.5%	21.7% (9.5-33.8%) 0.001	18.6% (7.3-29.9%) 0.003	1.44 (1.16-1.78) 0.002	1.38 (1.13-1.7) 0.004
≥ 20 years	1963/2216 (88.6%)	88.9%	2044/2469 (82.8%)	82.8%	6.1% (2.5-9.7%) 0.002	4.4% (0.5-8.2%) 0.03	1.07 (1.03-1.12) 0.002	1.05 (1.01-1.1) 0.03
Stratified by sex ‡								
Male	898/1075 (83.5%)	83.7%	908/1264 (71.8%)	72.2%	11.6% (5.3-18.0%) 0.001	10.2% (3.1-17.2%) 0.007	1.16 (1.07-1.26) 0.001	1.14 (1.04-1.25) 0.007
Female	1345/1507 (89.3%)	89.8%	1375/1644 (83.6%)	83.5%	6.4% (2.4-10.4%) 0.004	3.4% (-0.9-7.7%) 0.12	1.08 (1.03-1.13) 0.004	1.04 (0.99-1.09) 0.13
Stratified by household wealth index								
Lowest	612/723 (84.6%)	84.5%	669/902 (74.2%)	73.8%	10.8% (4.5-17.1%) 0.002	9.2% (3.0-15.4%) 0.006	1.15 (1.06-1.24) 0.002	1.12 (1.04-1.21) 0.005
Middle	721/829 (87.0%)	87.2%	717/868 (82.6%)	82.60%	4.7% (0.6-8.9%) 0.03	1.6% (-3.2-6.3%) 0.49	1.06 (1.01-1.11) 0.03	1.02 (0.96-1.08) 0.53
Highest	846/961 (88.0%)	89.2%	801/1013 (79.1%)	79.5%	9.5% (3.7-15.3%) 0.003	7.9% (3.2-12.5%) 0.002	1.12 (1.05-1.2) 0.003	1.1 (1.04-1.17) 0.002
ART initiation per 100,000 population across intervention period ‖								

Stratified by period ¶								
0-5 months	214/44390 (482.1)	439.2	185/51488 (359.3)	282.1	173.8 (-77.6-425.2) 0.17	142.6 (-81.5-366.7) 0.20	1.56 (0.79-3.05) 0.19	1.42 (0.8-2.52) 0.22
6-11 months	198/44390 (446.0)	448.1	147/51488 (285.5)	241.9	211.0 (39.8-382.2) 0.02	194.8 (31.4-358.1) 0.02	1.85 (1.1-3.13) 0.02	1.75 (1.08-2.82) 0.03
12-16 months	115/44390 (259.1)	221.4	136/51488 (264.1)	199.6	-17.9 (-176.4-140.6) 0.82	-28.3 (-186.5-129.9) 0.72	1.11 (0.59-2.09) 0.74	1.07 (0.57-2.01) 0.84

ART, antiretroviral therapy; GM, geometric mean (of cluster-level proportions); HIVST, HIV self-testing; k, coefficient of variation in health facility-defined clusters; SOC, standard of care.

HIV testing outcomes adjusted for cluster-level baseline outcomes (testing in the last 12 months) and individual-level covariates (age, sex, marital status). Sub-group analysis by age group adjusts for the same covariates except for age group. Sub-group analysis by sex adjusts for the same covariates except for sex. ART initiation outcome adjusted for cumulative incidence of ART initiations in 12-month pre-intervention period.

* P-value for interaction (20-39 years versus 16-19 years), p=0.13. P-value for interaction (≥ 40 years versus 16-19 years), p=0.40.

† P-value for interaction, p=0.02.

‡ P-value for interaction, p=0.07.

§ P-value for interaction (middle versus lowest), p=0.005. P-value for interaction (highest versus lowest), p=0.51.

|| Denominator for ART initiations is the estimated cluster population of adults ≥16 years, which was estimated using village and health facility registers.

¶ P-value for interaction (6-11 months versus 0-5 months), p=0.38. P-value for interaction (12-16 months versus 0-5 months), p=0.42.

Figure 1. Cluster risks for primary and secondary HIV testing outcomes

ART, antiretroviral therapy; HIVST, HIV self-testing; SOC, standard of care. Comparison of cluster risks for primary and secondary outcomes by study arm, with blue circles indicating cluster risks and red triangles indicating geometric means of cluster risks.

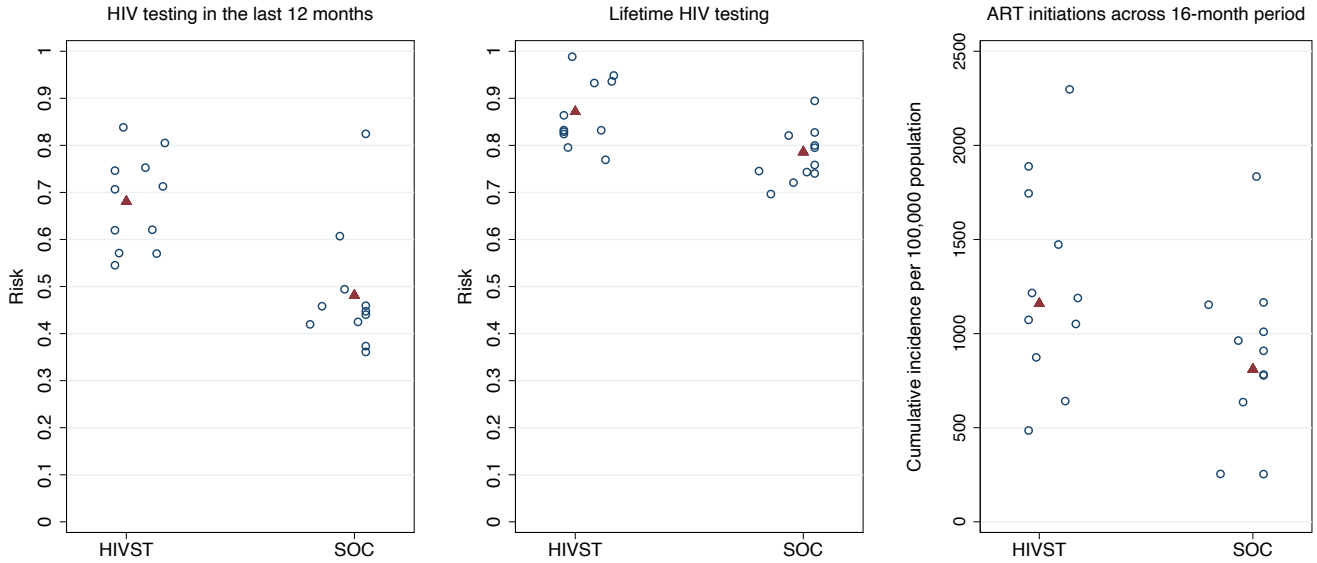

Figure 2. Fidelity to HIV self-testing intervention by sex and age group

HIVST, HIV self-testing; SOC, standard of care. The proportion ever self-testing and 95% CI adjusted for clustering following the HIVST intervention. Data are stratified by study arm, sex and age group.

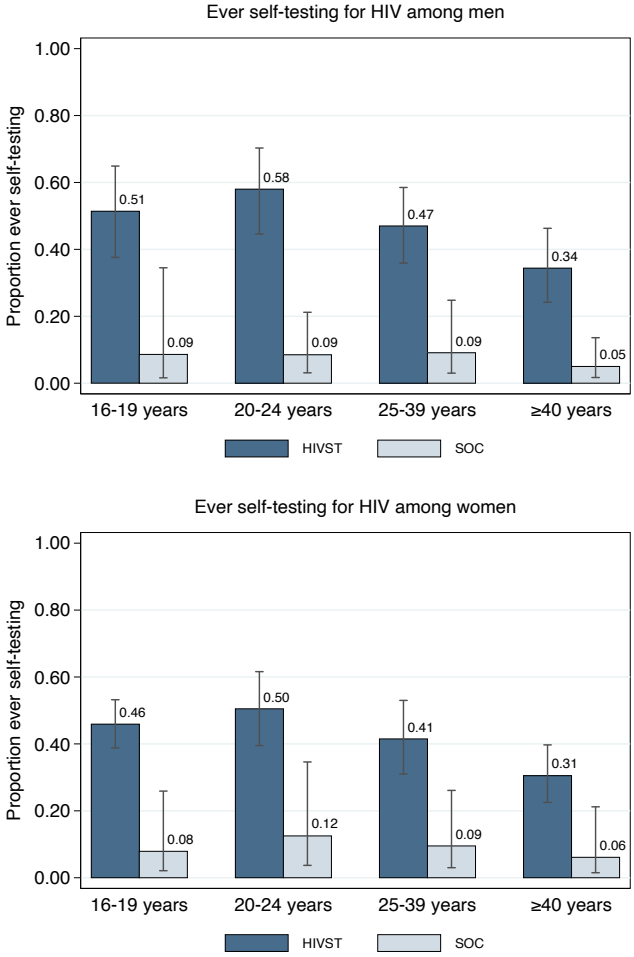

Table 1. CONSORT 2010 checklist of information to include when reporting a cluster randomised trial

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No *
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	Title page
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[1,2]	See table 2	Abstract
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	Introduction; Methods – Design, setting, and participants
	2b	Specific objectives or hypotheses	Whether objectives pertain to the cluster level, the individual participant level or both	Introduction ¶3
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	Methods – Design, setting, and participants; Methods – Randomisation ¶1
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		Methods – Randomisation ¶2
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	Methods – Design, setting, and participants; Methods – Procedures ¶3; Methods – Outcomes and measurement ¶3-4

	4b	Settings and locations where the data were collected		Methods – Design, setting, and participants; Figure 1
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	Methods – Procedures
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Whether outcome measures pertain to the cluster level, the individual participant level or both	Methods – Outcomes and measurement
	6b	Any changes to trial outcomes after the trial commenced, with reasons		N/A
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	Methods – Sample size
	7b	When applicable, explanation of any interim analyses and stopping guidelines		N/A
Randomisation:				
Sequence generation	8a	Method used to generate the random allocation sequence		Methods – Randomisation ¶1
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	Methods – Randomisation ¶1
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the	Methods – Randomisation ¶1

		steps taken to conceal the sequence until interventions were assigned	individual participant level or both	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	N/A
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	Methods – Design, setting, and participants; Methods – Randomisation ¶1
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)	Methods – Outcomes and measurement ¶2-4
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	Methods – Design, setting, and participants; Methods – Outcomes and measurement ¶3
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		Methods – Randomisation ¶1
	11b	If relevant, description of the similarity of interventions		N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	Methods – Statistical analysis ¶1
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		Methods – Statistical analysis

Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	Results ¶2, 4; Figure 2; Online supplementary Table 2
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	Results ¶2, 4; Figure 2; Online supplementary Table 2
Recruitment	14a	Dates defining the periods of recruitment and follow-up		Results ¶1-2, 4
	14b	Why the trial ended or was stopped		N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	Results ¶3-4; Table 1; Online supplementary Table 3
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	Results; Table 1-3; Online supplementary Table 1-4
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	Results – Primary outcome; Results – Secondary outcome; Table 2; Online supplementary Table 4
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		Results – Primary outcome; Results – Secondary outcome; Table 2; Online

				supplementary Table 4
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		Results – Primary outcome; Results – Secondary outcome; Table 2; Online supplementary Table 4
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[3])		Results – Safety outcomes; Table 3
Discussion				
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		Discussion ¶7
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	Discussion
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		Discussion
Other information				
Registration	23	Registration number and name of trial registry		Methods – Ethical considerations
Protocol	24	Where the full trial protocol can be accessed, if available		Methods – Ethical considerations
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		Funding

* *Note: page numbers optional depending on journal requirements*

Table 2. Extension of CONSORT for abstracts to reports of cluster randomised trials

Item	Standard Checklist item	Extension for cluster trials
Title	Identification of study as randomised	**Identification of study as cluster randomised**
Trial design	Description of the trial design (e.g. parallel, cluster, non-inferiority)	
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	**Eligibility criteria for clusters**
Interventions	Interventions intended for each group	
Objective	Specific objective or hypothesis	**Whether objective or hypothesis pertains to the cluster level, the individual participant level or both**
Outcome	Clearly defined primary outcome for this report	**Whether the primary outcome pertains to the cluster level, the individual participant level or both**
Randomization	How participants were allocated to interventions	**How clusters were allocated to interventions**
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	
Results		
Numbers randomized	Number of participants randomized to each group	**Number of clusters randomized to each group**
Recruitment	Trial status[1]	
Numbers analysed	Number of participants analysed in each group	**Number of clusters analysed in each group**
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	**Results at the cluster or individual participant level as applicable for each primary outcome**
Harms	Important adverse events or side effects	
Conclusions	General interpretation of the results	
Trial registration	Registration number and name of trial register	
Funding	Source of funding	

[1] Relevant to Conference Abstracts

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1 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet* 2008, 371:281-283

2 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG at al (2008) CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med* 5(1): e20

3 Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; 141(10):781-788.

HIV Self-Testing AfRica (STAR) Malawi: A cluster randomised trial of community-based distribution of HIV self-testing kits to improve testing rates and promote ART initiation in rural, Malawi

Statistical analysis plan

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Version 5, 31 Jan 2018

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Indravudh PP, *et al. BMJ Global Health* 2021; 6:e004269. doi: 10.1136/bmjgh-2020-004269

1. INTRODUCTION

In Malawi, adult HIV prevalence remains high, with pronounced social and economic inequity in HIV testing and linkage to HIV services. Self-testing for HIV (HIVST) is becoming an established option for providing highly accurate results when used by lay individuals. However, more research is needed to establish the potential role of HIVST in rural Africa, where coverage of HIV testing services is especially low. This project aims to investigate the feasibility, affordability, and health and social impact of introducing HIVST to rural communities through existing community-based distribution agents (CBDA).

The HIV STAR Malawi General Population study includes a cluster-randomized trial investigating the effects of introducing HIVST through CBDAs in 4 districts in Malawi's Southern region. This research protocol is nested within the UNITAID/Population Services International (PSI) HIV Self-Testing Africa (STAR) project. PSI is leading the implementation of this project, with the evaluation conducted by the Malawi-Liverpool-Wellcome Trust (MLW) and the London School of Hygiene and Tropical Medicine (LSHTM).

This document outlines the plan for primary analysis of the STAR Malawi cluster randomized trial for the publication of primary results. Only the randomization of clinics to the HIVST intervention is discussed below; the planned second randomization of CBDAs to home-based ART initiation was not implemented due to delays in study initiation.

2. TRIAL DESIGN

2.1 Research objectives

The primary objectives of this trial are to: estimate the impact of introducing HIVST through CBDAs on i) coverage of recent testing (within the last 12 months) and lifetime testing among residents ages 16 years and older and ii) cumulative incidence of ART initiation per 100,000 population in primary care clinics.

2.2 Trial arms, randomization, and blinding

This study will be conducted in rural settings in Malawi's Southern region. The study was originally designed with two randomization stages, but only one was completed. We refer to outcomes for the first randomization only.

Stage 1 randomization. The first randomization was conducted at the clinic (cluster) level, because the intervention is administered at this level. Primary care clinics offering ART services (22 total) and their catchment areas were randomized to either HIVST or standard of care (SOC) arms.

- **Arm A (11 clinics). HIVST**. All CBDAs working within the catchment area of clinics in the HIVST arm were trained by PSI to provide HIVST (OraQuick HIV Self-Test). Some CBDAs had been working with PSI before the study to distribute reproductive health products, while others were hired and trained for the study. CBDAs provide i) brief pre-test information; ii) a self-referral form with all kits to facilitate linkage into HIV care and prevention services; iii) generic or results-based post-test advice, depending on disclosure of results to CBDAs.
- **Arm B (11 clinics). SOC.** In the SOC arm, no kits will be provided to CBDAs working with PSI, and no additional CBDAs were trained to distribute reproductive health products.

Allocation was completed using restricted randomization, with allocation options restricted to ensure balance by geography; proportion of positive tests in each clinic; total number of tests

conducted in each clinic; and catchment population. To ensure that intervention and control clinics were distributed geographically across the study area, we applied the following restrictions.

(1) **Blantyre district**: 8 clinics were located in Blantyre. Of these, at least 3 and no more than 5 were assigned to the intervention. 4 clinics (Madziabango Health Centre, Mpemba Health Centre, Pensulo Health Centre, and Soche Maternity) were located south of Blantyre. Of these, at least 1 and no more than 3 were assigned to the intervention. 4 clinics (Chikowa Health Centre, Dziwe Health Centre, Lirangwe Health Centre, and Makata Heath Centre) were located north of Blantyre. Of these, at least 1 and no more than 3 were assigned to the intervention.
(2) **Machinga district**: 7 clinics were located in Machinga. Of these, at least 3 and no more than 4 were assigned to the intervention.
(3) **Mwanza district**: 3 clinics were located in Mwanza. Of these, at least 1 and no more than 2 were allocated to the intervention.
(4) **Neno district**: 4 clinics were located in Neno. Of these, at least 1 and no more than 3 were allocated to the intervention.

The following additional criteria were used to ensure balance across arms by clinic characteristics:

- **Number of testers:** We calculated the total number of testers in clinics in each arm and removed randomization options having the largest difference between the two arms (10% greatest positive difference between intervention and control and 10% greatest negative difference between intervention and control).
- **Proportion positive tests:** We calculated the average proportion of HIV tests that were positive across each arm and removed randomization options having arms with the greatest difference (10% greatest positive difference between intervention and control and 10% greatest negative difference between intervention and control).
- **Clinic catchment population:** We calculated the total catchment population in each arm and removed randomization options having the largest difference between the two arms (10% greatest positive difference between intervention and control and 10% greatest negative difference between intervention and control).

An analyst based at LSHTM (MN) generated a list of 1,000 randomization options falling within the restriction parameters described above. The final randomization scheme was selected at a public ceremony on 21 March 2016.

Blinding. Because of the nature of the intervention, implementers cannot be blinded to the allocation of the clinic. However, analyses will be conducted on data with arm identification removed, and the analyst will be un-blinded only after results have been finalized.

2.3 Duration of intervention and timing of baseline and endline surveys

The HIVST intervention will be evaluated after at least 12 months of implementation. The interventions will be implemented across all areas in September 2016.

The baseline household survey was conducted between May-August 2016, and the household endline survey is expected to begin in September 2017 and end in December 2017-January 2018. Clusters will be surveyed in the same order for the baseline and endline surveys.

2.2 Study population and informed consent

Selection of clinics and evaluation areas. The population included in the impact evaluation are all residents ages 16 and older living in selected evaluation villages and areas located in 4 districts.

22 clinics were selected from rural areas within these districts for inclusion in the study. We identified clinics in areas where PSI had existing CBDAs of reproductive health services and that offered ART initiation. 23 clinics met these criteria, and the clinic with the lowest HIV prevalence was removed.

While HIVST distribution will occur across the entire catchment area of randomly selected clinics, evaluation data collection, including both household survey data collection and clinic data extraction, will be conducted only within selected areas. Evaluation villages represent villages selected for inclusion in the household survey. Evaluation areas represent the area of residence for clients whose data will be captured at the clinic.

Two villages in each cluster served as evaluation villages, with one village randomly receiving the baseline survey and the other receiving the endline survey. Eligibility requirement for the evaluation villages include:

- Location within the catchment area of an eligible ART clinic, with the clinic acting as the most dominant source of ARTs for the village.
- Presence of at least one active PSI CBDA.
- Population of at least 250 residents (ages 16 years and older) per village.
- Road access for most/all of the year.
- Sufficient distance and separation from administrative boundaries and other intended evaluation villages to minimise 1) 'contamination' between HIVST and control villages, and 2) missed linkage to events from seeking HIV care at a remote clinic not included in the evaluation.
- Villages delineated by natural boundaries (e.g., rivers, roads, forests, etc.) will be preferentially selected.

Selection of respondents for baseline and endline surveys. Within evaluation villages, all households were enumerated and a variable fraction were selected to ensure that at least 250 residents (16 years and older) within households were surveyed. Within selected households, all eligible household members were interviewed with the basic questionnaire, and 20% of surveyed individuals received an extended questionnaire. All residents (ages 16 years and older) living in households within the intervention area are eligible to receive HIVST from CBDAs.

Participants provided verbal consent to participate in the baseline and endline surveys. Written informed consent (for residents ages 18 years and older) or assent with parental consent (for residents ages 16-17 years) was required to participate in the extended household survey and midline survey. Children ages 15 years and younger and those unable or unwilling to provide informed consent were excluded from the extended household survey.

3. OUTCOME EVALUATION AND DATA DESCRIPTION

3.1. PRIMARY OUTCOME AND SAMPLE SIZE CALCULATION

The primary outcome is the proportion of residents (16 years and older) who tested for HIV within the 12 months prior to the endline survey, which will begin at least 12 months after initiation of the HIVST intervention.

Outcome data (numerators and denominators) will be collected during the endline survey.

The survey sample size was estimated to ensure sufficient power to identify a difference in the primary outcome between those receiving the HIVST intervention and those receiving the SOC, and accounted for clustering by incorporating the cluster coefficient of variation (*k*) using methods outlined in Hayes and Moulton (2009). The average cluster size was estimated to be 250-500 residents (16 years and older), which is the average size of a rural village based on from previous experience in Malawi. We estimated that the cluster coefficient of variation (*k*) was 0.25. Using 2010 DHS data, the proportion of individuals testing in the last 12 months is estimated to be 25% to 40% and ever tested at 42% to 60% in the SOC arm. Using these assumptions, we have 80% power to detect a 30% relative difference in recent HIV testing and a 45% relative difference in lifetime HIV testing in the HIVST arm with α=0.05.

3.2. SECONDARY OUTCOME

There are two secondary outcomes for the HIVST intervention. First, we will compare between arms the proportion of residents (16 years and older) who tested for HIV in their lifetime. Outcome data (numerators and denominators) will be collected during the endline survey.

We will also compare between arms cumulative incidence of ART initiation per 100,000 population for residents (16 years and older) during the intervention period, with ART clinic records used for this assessment. Data to measure ART initiation will be extracted from clinic records at three-month intervals for clients initiating ART from evaluation areas. The denominator will be the population (16 years and older) of evaluation areas, with data collected from village heads. We will cross-reference the population from village heads and baseline survey enumeration and ensure that differences between the two data sources are similar in the HIVST and SOC arm.

3.3. ADDITIONAL ITEMS IN BASELINE AND ENDLINE SURVEY

In addition to the primary and pre-specified testing outcomes, the following data were collected from all respondents in the baseline and endline survey.

- **Questions on HIV testing and self-testing**, including partner testing and acceptability of HIVST.
- **Socioeconomic status and educational attainment** at household and individual level. Socioeconomic status was ascertained at the household level using an assets index and the household food insecurity assessment scale (HFIAS). All individuals were asked about salaried employment status and educational attainment.
- **Sexual behaviour**
- **Circumcision status and intention to access VMMC** (men only)

The extended survey was given to a 20% sub-sample of respondents, chosen at random using a random number generated in the electronic data capture tool. The extended survey included all elements from the baseline survey, as well as:

- **Detailed questions on previous three HIV tests,** including mode of testing, harms or regrets experienced after testing
- **Household decision-making** questions from Malawi Demographic and Health Survey 2010 (National Statistical Office (NSO) and ICF Macro, 2011, Bossuyt et al., 2015)
- **Conformity of masculine norms inventory** (Mahalik et al., 2003)
- **HIV care** (HIV-positive respondents only)
- **Stigma,** including anticipated stigma and knowledge of treatment effectiveness

- **Intimate Partner Violence** questions adapted from a measure used in the WHO Multi-Country Study on Women's Health and Domestic Violence (women only) (Garcia-Moreno et al., 2006)
- **Discrete choice experiments and costs of HIV testing**

4. STATISTICAL METHODS

All analyses will be completed in Stata version 14, on an intention-to-treat basis, and will use methods appropriate for cluster randomized trials with a small number of clusters. Reporting will conform to the 2010 Consort statement (Campbell et al., 2012).

4.1. RECRUITMENT AND REPRESENTATIVENESS OF SAMPLE

The trial flow chart will show the process of recruitment of study participants.

4.2. BASELINE AND ENDLINE SURVEY RESPONSE RATES

Baseline and endline survey response rates at the household and individual level will be calculated by cluster for the total population, as well as separately for women and men and adolescents ages 16-17 years and adults 18 years and older.

4.3. BASELINE COMPARABILITY OF ARMS (STAGE 1 RANDOMIZATION - HIVST INTERVENTION)

Following baseline data collection, we will summarize baseline data by arm by the following characteristics:

- Age
- Sex
- Marital status
- Educational attainment and socioeconomic status measured using assets variables.
- HIV status, previous HIV testing and self-reported ART use

Baseline analyses will be completed before the endline data collection period begins. The study team will identify substantial differences between arms in terms of the above factors (excluding HIV status and self-reported ART use) and adjust for endline measures of these baseline differences in the outcome analysis (see below). This assessment will not be completed using statistical tests, and p-values will not be shown, as any difference will be due to chance if the randomisation was correctly performed.

4.4. UNADJUSTED ANALYSIS

This analysis will give each cluster equal weight. The overall risk for each cluster will be calculated, and a log transformation will be applied to the summary value for each cluster if necessary. For binary outcomes where there are clusters with no events, one event will be added to all clusters so that the log transformation can be conducted. The mean of these log risks will be used to obtain the geometric mean (GM).

The risk difference, 95% CI and p-value will be estimated using a t-test of the risk by arm, based on 20 degrees of freedom. The risk ratio, 95% CIand p-value will similarly be estimated using a t-test of the log risk.

4.5. ADJUSTED ANALYSIS

Factors for adjustment will be determined as stated above. If there are substantial baseline differences in recent testing across arms, we will adjust for baseline differences using cluster-level

summaries of baseline values. To adjust for other imbalances across arms, we will use endline measurements of these factors for adjustment, and will assume that there will be no substantial changes in these in the months between the baseline and endline surveys. The adjusted analysis will be the primary analysis.

The following covariates will be assessed as potential adjustors:

- Age
- Sex
- Marital status
- Educational attainment
- Assets index (in tertiles)

Logistic regression will be used to adjust for confounding bias at the individual level, adopting a two-stage approach as outlined in Hayes and Moulton (2009). In the adjusted analysis, the regression model will include terms for the individual-level adjustment factors, but not study arm. The fitted model will be used to obtain the difference and ratio of observed and expected events for each cluster. The ratio will be log-transformed as appropriate. A t-test will be used to estimate the risk difference and risk ratio and their respective 95% CIs and p-values. If adjustment for cluster level factors is considered necessary, this will be conducted at the second stage using linear regression, with appropriate adjustment for the degrees of freedom.

Because restricted randomization was used to allocate clinics, we will also report p-value and 95% confidence interval from a permutation test incorporating the restriction parameters described above (Li et al., 2016).

4.6. METHODS FOR ADDRESSING MISSING DATA

Missing data will be examined for each variable and for each cluster or participant. A systematic assessment of missingness will be conducted to ascertain the reason and possible mechanism for missing data by identifying the quantity of missing data and patterns within the data. Missingness will be particularly examined by cluster and between study arms to assess for systematic biases. Sensitivity analysis for the primary outcome of recent HIV testing will be carried out – comparing complete case analysis results with those where missing outcome status are re-classified as yes and no. Multiple imputation will be considered in the analysis as appropriate.

4.7. PLANNED SUBGROUP ANALYSES

In addition to the main analyses, we will conduct analyses to assess differences in the effect of the HIVST intervention on the primary outcome by sex and age (adolescents ages 16-19 years versus adults ages 20 years and older). We will also estimate the differential impact of the HIVST intervention by socioeconomic status using the assets index.

For the HIVST intervention, analyses of effect modification will be conducted using the method for testing for interaction in community randomized trials developed by Cheung el al. (2008). This method estimates the difference between intervention and control outcomes within each subgroup, then tests the hypothesis that the subgroups have the same intervention effect using a two-sample t-test.

5. PROCESS EVALUATION

Together with the main trial analysis, we will provide quantitative process data summarizing the strength and reach of the intervention, as well as a summary of harms reported in the household survey tabulated by respondent gender and allocation.

A full process evaluation, including both quantitative and qualitative data analysis, will be published separately.

6. OTHER ANALYSES

6.1. ECONOMIC ANALYSES

Economic analyses, including discrete choice analysis and cost-effectiveness analyses, are described separately.

6.2. MIDLINE ANALYSIS

A midline round of surveys and analysis will be conducted 4-6 months after the intervention begins to assess implementation. Midline data collection will occur within intervention clusters only, and will include a subset of questions asked at baseline about the following items.

- Sociodemographic data on age, sex, educational attainment, literacy
- Any HIV testing: location and mode of most recent test,
- Experiences with HIVST: familiarity with HIVST, where kit was obtained, care obtained after self-testing, harms or regrets experienced after self-testing

We propose a sample size of 550 individuals across 11 clusters (50/cluster) to detect a prevalence of 55% recent testing (as reported in the baseline survey) with 15% precision and ρ=0.03 (calculated using baseline data).

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HIV Self-Testing AfRica (STAR) Malawi: General Population V5

A cluster randomised trial of providing HIV self-testing kits through community-based distribution agents

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Abbreviations

ANC	Antenatal Care
ART	Antiretroviral Therapy
CBDAs	Community-Based Distribution Agents
CBO	Community Based Organisation
CD4	Cluster of Differentiation 4
COMREC	College of Medicine Research Ethics Committee
DALY	Disability-Adjusted Life Years
DBS	Dried Blood Spot
DCE	Discrete Choice Experiments
DHO	District Health Office
DHS	Demographic and Health Surveys
ELISA	Enzyme-Linked Immunosorbent Assay
FSW	Female Sex Workers
FBO	Faith-Based Organisation
FGD	Focus Group Discussion
GBV	Gender-Based Violence
GPS	Global Positioning System
HIV	Human Immunodeficiency Virus
HIVOFT	HIV Oral Fluid Tests
HIVRDT	HIV Rapid Diagnostic Tests
HIVST	HIV Self-Testing
HTC	HIV Testing and Counselling
ID	Identification
IDI	In-Depth Interview
IEC	Information, Education and Communication
IFU	Instructions-for-Use
KII	Key Informant Interview
Km	Kilometres
LSHTM	London School of Hygiene and Tropical Medicine
LSTM	Liverpool School of Tropical Medicine
M&E	Monitoring and Evaluation
MLW	Malawi Wellcome Trust Clinical Research Programme
MoH	Ministry of Health
MSM	Men who have Sex with Men
NGO	Non-Governmental Organization
PLHIV	People Living with HIV
PSI	Population Services International

SCQ	Self-Completed Questionnaire
SES	Socio-Economic Status
SOP	Standard Operating Procedures
STAR	Self-Testing Africa
TAG	Technical Advisory Group
TB	Tuberculosis
UCL	University College London
US	United States
USD	US Dollar
VCT	Voluntary Counselling and Testing
VMMC	Voluntary Medical Male Circumcision
WHO	World Health Organization

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1. Executive summary

1.1 Research problem

In Malawi, adult HIV prevalence remains high, with pronounced social and economic inequity in HIV testing and linkage to onward services. Self-testing for HIV (HIVST) is becoming an established option for providing highly accurate results when used by lay clients. However, more research is needed to establish the potential role of HIVST in rural Africa, where coverage of HTC services is especially low. This project aims to investigate feasibility, affordability as well as the health and social impact of introducing HIVST to rural communities through existing community-based volunteer services.

1.2 Research description

The HIV STAR Malawi General Population (HIV STAR Malawi GP) study consists of a cluster-randomised trial investigating the effects of introducing HIVST to the remit of volunteers providing reproductive health services to villages in up to 5 Southern Region Districts. This research protocol is nested into the UNITAID/PSI HIV Self-Testing Africa (HIV STAR) project, which is funded to provide 34,068 episodes of HIVST in Malawi during 2016/17 with potential extension to 2018/19.

The trial population will be the catchment population (~62,500 adults) of 20 Rural Primary health clinics that have a) ART services and b) support the activities of reproductive health community-based distribution agents (CBDAs). CBDAs are lay volunteers trained and supervised by PSI to socially market reproductive health products in the rural areas.

1.3 Research aims and objectives

Broadly, to investigate the incremental costs and health benefits of adding HIVST to the remit of existing cadres of community volunteers in the general population in Malawi.

Specific objects are to:

1. Validate the use of the OraQuick HIVST product in rural settings, establish preferences and social harms reporting systems, and conduct baseline surveys.
2. Carry out a pragmatic cluster-randomised trial with ART clinics and their catchment populations, including CBDAs, as the unit of randomisation.
3. Evaluate the impact of adding HIVST into the remit of VMMC mobilisers on demand for VMMC
4. Establish the expected costs and benefits of introducing HIVST to Malawi through economic and mathematical modelling.
5. Conduct interviews with policy-makers to prepare for national scale-up of HIVST and support the market introduction of quality-assured HIVST products.

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1.4 Methodology

A population-based CRT with associated mixed methods sub-studies. The intervention will be delivered through CBDAs, trained by PSI to provide HIVST in their rural villages. 20 ART Clinics and their catchment populations will be randomised to either HIVST or standard of care (SOC) arms. The ~200 CBDAs in the HIVST arm will be trained to provide HIVST (OraQuick ADVANCE HIV I/II test kits, packaged for self-use) along with reproductive health products. CBDAs will provide brief pre-test information and a self-referral form with all kits to facilitated linkage into HIV care and prevention services. Post-test advice will be provided for all who confide positive HIVST results.

Outcomes will be captured at 12 months through:

1. Household level surveys (~5,000 adults) at baseline and after 12 months of intervention .These will include questions on recent HIV testing through any modality (**Primary Outcome)**.
2. ART clinic records to investigate whether or not population-level demand for ART has increased (**Secondary Outcome)**.

A second stage randomisation of HIVST CBDAs will further explore the role of home-based HIV care assessment for encouraging disclose of positive HIVST results and ART initiation. This is an implementation research study, and no biological specimens will be required for research other than for pilot accuracy evaluation.

The study will be preceded by pilot studies to test the ability to interpret pictorial instructions and accurately use and interpret HIVST kits (packaged with instructions in Chichewa). The trial will be accompanied by economic evaluations. Interviews with key informants will be used to explore the policy and regulatory landscape for HIVST. Tools developed for the main study will be evaluated in other community volunteer cadres, notably voluntary medical male circumcision mobilisers.

1.5 Research findings and dissemination

Early evidence in Malawi points to substantial willingness to self-test and the potential of HIVST products to provide affordable community-based HTC and improve linkages to HIV services. The results of this research will be used to guide the introduction of self-testing into community-based HTC models and the formation of national and international policies around HIVST. Results will be disseminated to the Ministry of Health (MoH) HIV Unit, College of Medicine Research and Ethics Committee (COMREC) and UNITAID. Findings will also be distributed internationally to global health policy makers, nationally to the Malawian government, and regionally to District and Council Health Offices.

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2. Background

Malawi has a high HIV prevalence, with an estimated 10.2% of adults living with HIV. Of those who are HIV positive, 46% are on Antiretroviral Therapy (ART) (UNAIDS 2014). In key populations, HIV prevalence is substantially higher than in the general population, with estimated prevalence of 21.4% among Men who have Sex with Men (MSM) and 70.7% among Female Sex Workers (FSWs) (Wirtz, et al. 2014) (Baral, et al. 2009).

Major factors driving new HIV infections in Malawi include lack of knowledge on partner HIV status in serodiscordant relationships, high rates of transactional sex, and low uptake of HIV prevention services including consistent condom use and Voluntary Medical Male Circumcision (VMMC) (UNAIDS 2014). According to the 2010 Demographic and Health Survey (DHS), 9.7% of male respondents had paid for sex at least once, with low condom use (60.7%) during transactional sex (National Statistical Office and ICF Macro 2011). Uptake of VMMC in Malawi was estimated as 2% in December 2012 (UNAIDS 2014).

Reaching the Joint United Nations Programme on AIDS (UNAIDS) 90-90-90 targets (90% of all HIV-positive individuals aware of their status, of whom 90% are retained in ART programmes, of whom 90% have viral load suppression) will require substantial scale-up of HIV testing services with new approaches that more effectively reach marginalised populations who are not well served by current approaches. Notable gaps in HIV Testing and Counselling (HTC) coverage exist for men, adolescents (age 16 to 19 years), rural Malawians and the poorest members of society (National Statistical Office and ICF Macro 2011).

A further challenge is that linkage into HIV treatment and VMMC services following HTC remains suboptimal. In Blantyre, only 50.7% of newly diagnosed People Living with HIV (PLHIV) at routine facilities had successfully completed eligibility assessments and were retained into care 6 months after testing positive (MacPherson, et al. 2012).

Barriers to HTC and ART initiation include long distance and congestion of health facilities, concerns about lack of confidentiality and privacy, and high out-of-pocket costs (MacPherson, et al. 2012, Morin, et al. 2006, Angotti, et al. 2009). These barriers are particularly significant among certain demographics, including men, young people, impoverished rural residents (Weinreb and Stecklov 2009) and key populations (i.e., SWs, MSM) (Govindasamy, Ford and Kranzer 2012). Therefore, current HTC strategies, which are predicated on clinic-based service delivery, need to be complemented by affordable community-based services that allow better coverage, particularly for key populations and rural populations in Malawi.

Based on previous work in Malawi, proactive and accountable distribution of HIV Self-Testing (HIVST) products offers the promise of providing a safe and accurate form of HIV testing and facilitating acceptable rates of linkage into HIV care.

2.1 HIV self-testing

The development of HIV Rapid Diagnostic Tests (HIVRDT) has enabled highly accurate results from HIVST when carried out by untrained lay clients (Choko, et al. 2015). On a societal level, HIVST requires lower human resource demands and could provide more cost-effective community-based HTC in comparison to current community-based models (Cambiano, Mavedzenge and Phillips 2014).

HIVST kits are already available for purchase over-the-counter in several countries, including the United States, United Kingdom, and Kenya. However, the availability of quality-assured HIVST products will remain limited in resource-poor settings until the purchase of HIVST kits using donor funds is possible and national HIV programmes have adapted policy and programme documents, including algorithms and training materials, to fully accommodate HIVST (Ministry of Health Kenya 2009).

To be put on approved donor purchase lists, HIVST products need to be suitably low cost and be supported by:

1. Product approval by the World Health Organisation (WHO) Prequalification Department. An application is currently underway for OraQuick ADVANCE Rapid HIV-1/2 Antibody Test – the HIVST product to be used under the HIV STAR Malawi study – and has already received approval from the United States Food and Drug Administration (FDA).
2. WHO guidelines to support the use of HIVST in defined populations, such as rural and urban adults living in high HIV prevalence settings, adolescents, and key populations.

WHO and UNAIDS have already issued Technical Updates that are supportive of HIVST, but the development of full guidelines requires results from implementation research to evaluate the public health risks and benefits from introducing HIVST into a range of settings. Key considerations include user ability to conduct HIVST and interpret results, user ability to cope with and act upon positive HIVST results in the absence of face-to-face counselling, the accuracy of test results particularly among low literacy populations, and the potential for unwanted social harms such as coercive testing and gender-based violence (GBV) (Napierala Mavedzenge and Corbett 2009, Wright and Katz 2006, Pant-Pai and Klein 2008, Frith 2007).

Though evidence to date has been reassuring, more data is needed from implementation studies in representative African populations (Napierala Mavedzenge and Corbett 2009, Wright and Katz 2006, Pant-Pai and Klein 2008, Frith 2007, Gaydos, et al. 2009, Project Masiluleke 2010)

2.2 HIV self-testing in Malawi

Malawi has assumed a leadership position in HIVST research, with the only large-scale implementation project to date. From 2012-2015, a HIVST study was conducted in Blantyre in collaboration with the National HIV department (Choko, et al. 2015) and has produced results that have been highly influential in moving forward international policy regarding HIVST.

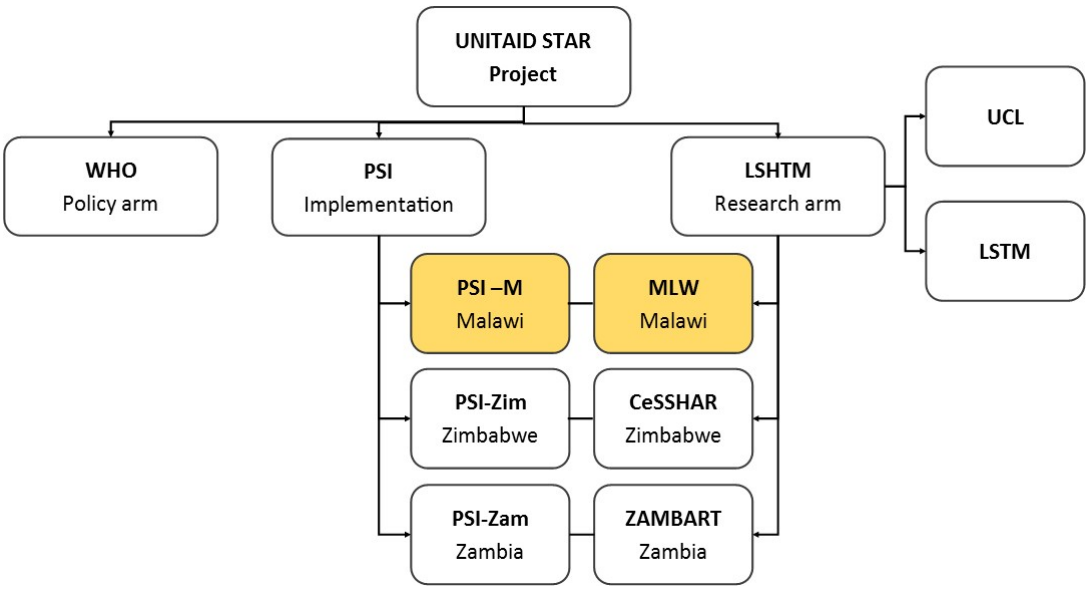
Choko, et al. demonstrated that there was high readiness for HIVST, with pronounced user preference for HIVST over facility-based services, and high accuracy of results. Acceptability was even high among men and adolescents, who have been difficult to reach with standard HTC services. Acceptable rates of linkage to confirmatory testing and HIV care services were also obtained through the promotion of HIVST by briefly trained local volunteers and provision of home-based ART eligibility assessments (MacPherson, et al. 2014). This resulted in a significant increase in demand for ART services at population level.

Additionally, national HIV policies and strategic frameworks (e.g., 2016-25 National HIV and AIDS Strategic Plan, 2015-20 HIV Prevention Strategy), have started to mention HIVST, but have yet to include adapted HIV testing algorithms and HTC materials and standard operating procedures and guidelines for how HIVST should complement current HTC models.

2.3 UNITAID/PSI HIV STAR project

The UNITAID/PSI HIV STAR project will conduct HIVST implementation research to generate the evidence base required for WHO guidelines in Malawi, Zambia and Zimbabwe. The project has a dual focus on marginalised sections of the general population (defined by poor coverage of HTC under current strategies) and key populations (i.e., FSWs, MSM).

Figure 1. HIV STAR Project Organogram



Collaborators include WHO, Population Services International (PSI), London School of Hygiene and Tropical Medicine (LSHTM), Liverpool School of Tropical Medicine (LSTM), and University College London (UCL).

PSI is responsible for HIVST implementation, while LSHTM, in conjunction with local partners (the Malawi-Liverpool-Wellcome Trust Clinical Research Programme (MLW) in Malawi) is responsible for implementation research. WHO will lead the development of policy and regulatory guidelines around HIVST.

The funding body for the UNITAID/PSI HIV STAR project is UNITAID, a United Nations organisation housed within WHO that supports the development and optimisation of robust, high-quality and low-cost products specifically intended to meet the diagnostic and pharmaceutical needs of HIV, tuberculosis (TB) and malaria programmes in low-resource countries.

2.3.1 Overall project goal

The UNITAID/PSI HIV STAR project aims to catalyse the HIVST market regionally by testing innovative interventions and strengthening the evidence base around the effective use of HIVST through formative research and impact evaluation.

2.3.2 Overall project objectives

The primary objective is to increase the uptake of quality-assured HIVST among general and key populations in Malawi, Zambia and Zimbabwe.
The secondary objectives are:

1. *To increase access to quality-assured HIVST among target populations:* This includes directly addressing the availability, adaptability and affordability of HIVST and developing context-specific distribution models to more effectively reach target consumers.
2. *To increase informed demand for quality-assured HIVST:* The project will conduct formative market research to increase product responsiveness to client needs and preferences for HIVST, as well as improve package inserts and other IEC products so that clients are provided with the information they need to effectively use the tests and access relevant post-test services.
3. *To reduce policy barriers to market entry for quality-assured HIVST products:* This means using evidence around preferences and demand for HIVST to estimate the market size and to inform global and national policy and guidelines, thereby helping to create a supportive policy and regulatory environment in which quality products can be introduced.

2.3.3 Summary of UNITAID/PSI HIV STAR activities

In 2016 and 2017, PSI plans to provide a total of 171,054 HIVST kits to underserved general population adults and key populations in Malawi using multiple distribution channels.

Figure 2. HIV STAR objectives and activities

Objectives	Implementation Activities	Research Activities	Policy Activities
1. Increase access to quality-assured HIVST among target populations in intervention areas.	• Distribute HIVST kits through CBDAs, social marketing franchises, peer educators, and VMMC mobilisers to target populations.	• Conduct formative research and preparatory work for HIV distribution models. • Pilot and conduct interim evaluations of HIV distribution models.	• Partner with MoH on developing training curriculum and tools for CBDAs and defining acceptable CBDA cadres. • Work with MoH to include HIVST in national algorithms.
2. Increase informed consumer demand for quality-assured HIVST.	• Develop marketing and communication strategy using marketing planning processes. • Strategically design and test branded packaging and inserts.	• Conduct formative market research to better understand barriers and motivators to using HIVRDT for self-testing. • Perform economic and mathematical modelling of HIVST delivery.	• Share findings on user preferences with MoH collaborators.
3. Reduce policy barriers to market entry for quality-assured HIVST products.	• Establish expert HIVST Advisory Board to provide scientific oversight on project implementation and to inform global quality standards and guidelines.	• Provide technical support and assistance for global and national-level policy makers and regulators. • Disseminate findings at key intervals with local, national and international stakeholders.	• Develop normative guidance on HIVST.

Among the general population, HIV STAR will target rural and peri-urban populations, urban populations, and young men, with corresponding distribution models for each sub-group. The launch of multiple channels for HIVST distribution will help HIV STAR to reach all sub-groups as well as increase the evidence around effective models for HIVST delivery and linkage to HIV prevention and care.

The distribution of HIVST kits to the general population will take place through the following PSI-led mechanisms:

1. *CBDAs* – Community-based distribution agents (CBDA) will distribute HIVST kits, among other health products, to populations in rural and peri-urban areas, which generally have been underserved by HTC services.
2. *Tunza* – Tunza franchise providers, which are contracted by PSI and provide socially marketed products through the private sector, will deliver HIVST kits to urban populations. For this sub-group, lack of privacy and confidentiality often are the biggest barriers to HTC.

3. *VMMC mobilisers* – VMMC mobilisers will offer HIVST kits to men ages 15 to 49, who are the target of VMMC campaigns. A frequently cited barrier to VMMC uptake is the perceived requirement for HTC. Therefore, HIVST among this sub-group has the potential to increase the uptake of this critical HIV prevention service.

MLW-LSHTM will conduct a series of research studies, packaged as *HIV STAR Malawi*, to inform and evaluate PSI HIVST implementation. The HIV STAR Malawi study is then divided into three protocols based on the target population segment:

1. *HIV STAR Malawi General Population (HIV STAR Malawi GP)* – This protocol consists of a cluster randomised trial (CRT) to evaluate HIVST interventions among the general population. The study will also conduct formative research to inform the design of HIVST distribution models.
2. *HIV STAR Malawi Key Populations (HIV STAR Malawi KP)* – MLW-LSHTM will conduct formative research to inform peer-led delivery models among FSWs and MSM. The study will also carry out social harms research to monitor unintended consequences from accessing HIVST.
3. *HIV STAR Malawi Workplace (HIV STAR Malawi WP)* – MLW-LSHTM will evaluate urban distribution of HIVST kits through a workplace model, with supplementary qualitative research around implementation.

Figure 3. Breakdown of target populations

Target Populations	Target Number of Self-Tests*			Districts	Distribution models
	Year 1	Year 2	Total		
1. General population					
Rural and peri-urban populations	25,000	96,000	121,000	Blantyre, Mwanza, Machinga, Thyolo	CBDAs
Tunza social franchise clients	3,600	27,000	30,600	Mchinji, Lilongwe, Salima, Dedza, Nkhotakota, Kasungu	Tunza providers
Potential VMMC clients	1,500	4,800	6,300	Blantyre	VMMC mobilisers
2. Key populations					
MSM	540	2,592	3,132	Blantyre, Lilongwe, Mzuzu	MSM peer educators
SSWs	1,728	8,294	10,022	Blantyre, Lilongwe, Mzuzu	FSW peer educators
Total	**32,368**	**138,686**	**171,054**		

*Includes cases of repeat testing with the same individual.

3. Research question, aims, objectives

HIVST research findings have so far have been limited to a single delivery model in urban Blantyre. Findings such as acceptability and accuracy of HIVST may not be

generalizable to other target populations, including rural adults, and may also change along with cost and cost-effectiveness when different service delivery models are used.

Here we investigate the uptake, acceptability, safety, population-impact and costs of adding HIVST to the remit of two existing cadres of community volunteers working in Malawi:

1. Rural-based community-based distribution agents (CBDAs) who provide reproductive health and child survival commodities through social marketing in rural areas.
2. VMMC mobilisers who provide information on voluntary male circumcision services.

The main research questions to be addressed are

- Does HIVST provided through multifunctional community volunteers maintain high willingness to self-test, safety, accuracy, and acceptable uptake of post-test services?
- Does adding HIVST to reproductive health CBDA services increase coverage of recent HIV-testing at population-level?
- Does adding HIVST to reproductive health CBDA services increase demand for ART?
- Does the offer of home assessment and HIV care initiation improve linkage into post-test services?
- What are the social effects (benefits and harms) of introducing HIVST through community health
- What are the incremental costs and cost-effectiveness of adding community-based HTC?

3.1 Research objectives

3.1.1 Research objectives

The broad objectives are to investigate the incremental costs and health benefits of adding HIVST to the remit of existing cadres of community volunteers to adults in the general population in Malawi. Ultimately this may contribute to the ability to meet and sustain National 90-90-90 targets as well as informing regional policy and practice.

The specific objectives are to:

1. Evaluate the impact of introducing HIVST into the remit of reproductive health CBDAs, with and without the option of home-assessment and initiation of HIV care, on HIV testing coverage and ART initiation rates.
2. Evaluate the impact of adding HIVST into the remit of VMMC mobilisers on VMMC initiation rates.
3. Establish the expected costs and benefits of introducing HIVST to Malawi.
4. Evaluate preferences for HIVST delivery and linkage to care models.

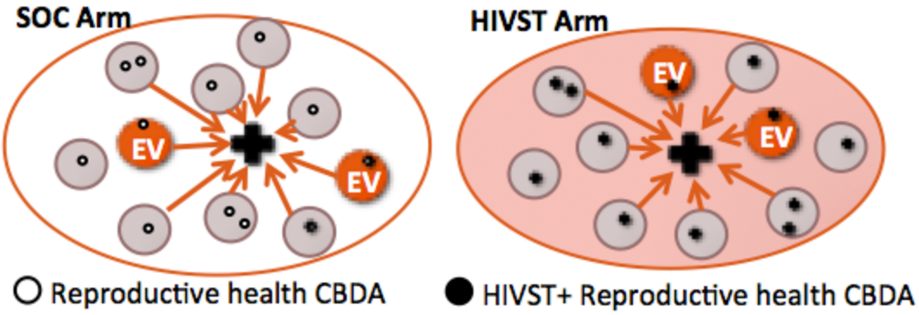
5. Identify policy and regulatory barriers and enablers to the scale-up of HIVST and actions needed to support the market introduction of quality-assured HIVST product

4. Study design

4.1 Main trial

The main study will be a cluster-randomised trial in up to 5 high HIV prevalence districts (provisionally Blantyre, Machinga, Mwanza, Neno and Thyolo) that already have community-based reproductive health services provided by PSI under funding provided by the German Technical Cooperation Agency (GTZ). This programme supports volunteers to socially-market reproductive and child health products in villages, with products stored and managed by collaborating primary care clinics.

Figure 4. Schematic illustration of Standard of Care and HIVST intervention clusters intervention provided by village-based CBDAs.



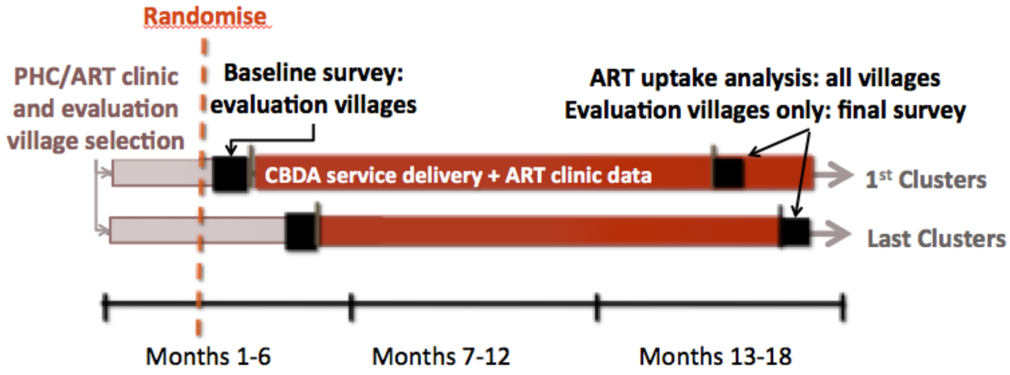
Unit of randomisation is the Primary Care + ART Clinic (black cross) and surrounding catchment area villages (large circles with feed-in arrows) to clinic. CBDAs in the HIVST Arm villages will be trained to provide HIVST services as well as reproductive health services (**small solid circles**). CBDAs in the SOC Arm villages will remain with reproductive health services only (**small open circles**). Two separate units of evaluation will be pre-defined before randomisation: one or two evaluation villages that will have baseline-final household surveys, and a wider catchment area including all villages with CBDA activities.

The unit of randomisation will be the **primary care clinic.** The **unit of evaluation** will be defined by **clinic records of adult ART initiations** from villages within the wider CBDA catchment area, and through household survey of **1 to 2 evaluation villages** contained within the catchment population (Figure 5).

The trial will compare **population-level uptake of ART** (as defined by ART clinic records of new initiators listing study villages as their home address) and **coverage of recent HIV testing** (as defined by household surveys) between two arms:

1. **Intervention arm**: Addition of HIVST kits, with brief training and IEC material, to the products carried by PSI-supported reproductive health CBDAs, or
2. **SOC arm**: CBDAs will continue to offer reproductive health services, but without the addition of HIVST kits

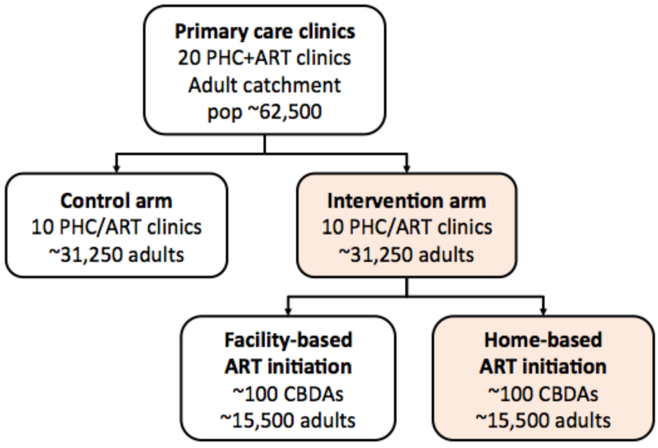
Figure 5. Trial timelines



In a **second-stage randomisation arm**, villages included in the HIVST intervention will be further randomised to

1. **Arm 1A: HIVST plus optional home assessment for HIV care.** CBDAs will offer all clients willing to confide their preliminary positive result the option of having their confirmatory testing and initial HIV care assessment (registration card and the first 2 weeks of cotrimoxazole and ART, if eligible) at home, or
2. **Arm 1B: HIVST only:** CBDAs will offer advice and encouragement to all clients to confide a preliminary positive result, in order to allow the OraQuick test to be repeated by the CBDA who will then provide a written referral slip to the nearest ART clinic.

Figure 6. Summary of HIVST CRT arms and second stage randomisation



Home-based assessment from HIV care following HIVST was shown to be effective in urban Blantyre (MacPherson, et al. 2012).

4.2 Sub-Studies

Accompanying substudies, including quantitative, qualitative and economic evaluations, are described in detail below.

4.3 Primary and secondary outcomes

4.3.1 Primary Outcome for main HIVST versus SOC CBDA intervention

The primary outcome is: Comparison between randomisation arms in coverage of recent (within the last 12 months) HIV testing among adult (16 years and above) village residents 12 months after the initiation of the intervention.

A related pre-specified analysis is to compare between randomisation arms the coverage of ever (lifetime) HIV testing among adult (16 years and above) village residents.

These analyses will be based on household surveys carried out in the pre-defined evaluation villages in each randomisation arm.

4.3.2 Secondary Outcome for main HIVST versus SOC CBDA intervention

The secondary outcome is: Comparison between randomisation arms of ART initiation rates for adult (16 yrs or older) cluster residents, during months 1 to 12 of intervention.

This analysis will be based on data extraction from routine ART clinic records. Residential address will be used to identify all new initiations among adults (16 years or older) living within the the wider CBDA catchment area relating to that clinic.

4.3.3 Second stage randomisation: home-based versus facility-based assessment for HIV care

Villages in the HIVST intervention area will be randomised to either **HIVST only,** or to **HIVST plus offer of home assessment and HIV care initiation** (first assessment and first 14 days of HIV care medications) with this additional intervention aimed at facilitating linkage into care.

The **primary outcome** for this second-stage randomisation will be comparison between randomisation arms of number of adult (16 yrs or older) village residents disclosing a positive results to the CBDA during months 1 to 12 of intervention, with a confidential post-test log book used to capture these data.

The **secondary outcome** for this second-stage randomisation will be comparison between randomisation arms of ART initiation rates for adult (16 yrs or older) village residents during months 1 to 12 of intervention, with ART clinic records used for this assessment.

4.4 Study population and timeline

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Phase 1 of the study is funded from 1st Sept 2015 to August 2017. A second two-year funding phase has been requested, and will if successful allow continuation of the implementation and research. The decision on Phase 2 funding will be made in April 2017.

The main study population will be adults living in selected evaluation villages located within the 5 Southern Districts that have an existing reproductive CDBA programme (Blantyre, Machinga, Mwanza, Neno and Thyolo).

20 Primary care clinics that are actively participating in PSI-CBDA scheme and have an active ART clinic will be selected, with preference given to sites with evidence of high HIV burden in surrounding villages (based on ANC clinic data).

Selection of 20 to 40 evaluation villages for the purposes of household surveys will be based on distance from the primary care clinic (aiming for sites that are at least 10km away), plus considerations affecting ease of access and follow-up. Ideal villages will have an active CDBA volunteer, an adult population of greater than 250, with no alternative HIV care facility nearby, and with no major access problems during the rainy season. If necessary, 2 villages will be selected from any given primary care clinic catchment area to meet the requirement for 250 adults evaluated.

Additional populations will be included for the purposes of the formative studies, the interviews with policymakers, and the VMMC mobilisers.

1. Formative studies will include initial cognitive interviews with a convenience sample of up to 144 participants attending routine HTC clinics, to establish ability to understand and follow the new instructions for use before moving into the village residents
2. HIVST ICE materials will be piloted for accuracy and acceptability in 2 non-intervention villages within the intervention Districts
3. Policymakers and opinion leaders on HIV testing will be included in key informant interviews aiming to support scale up of HIVST if these evaluation studies are promising
4. Mobile VMMC clinics operate in overlapping districts and sites to the main cluster randomised trial. The initial evaluation of adding HIVST to VMMC mobilisers will be carried out within the catchment area of the study primary care clinics. However, if results are promising then the intervention will be extended to all PSI VMMC clinic sites, which include other districts.

5. Methods

HIVST will use the OraQuick ADVANCE Rapid HIV-1/2 Antibody Test. The kits, which are manufactured by Orasure, contain the HIVOFT kit, stand, buffer solution, IFUs, materials on counselling and linkage to care, and primary and secondary packaging.

A toll-free telephone number will also be provided with the HIVST kit, which can be used to access verbal pre-test information, test instructions, and results-based post-test information. Participants will also be given information on the nearest clinic for confirmatory testing and ART initiation.

The kits will be distributed for free across all of the distribution models. All distributors will receive a training package in HIVST promotion and support that has been developed in consultation with MoH HIV Department.

The study has five main phases:

1. Formative studies
2. Piloting in non-intervention area 2 villages
3. Cluster enumeration in all 20 ART clinics and evaluation villages
4. Intervention and outcome evaluation
5. Economic and qualitative studies

5.1 Formative studies and piloting

Formative studies are intended to

- Establish ability to follow HIV implementation the instructions-for-use and confirm high accuracy of supervised HIVST in rural settings
- Inform our understanding of needs through key informant interviews with stakeholders working in HIV policy, product regulation and HIV implementation

5.1.1 Cognitive interviews

Convenience sampling will be used to recruit clients from VCT clinics for the cognitive interviews (PS101A). Eligibility criteria include clients who are 16 years or older, and willing to provide written informed consent for participation in the study. A witnessed thumbprint will be sufficient for those who are unable to read or write. Participants will be purposively selected to ensure a range in location and literacy level.

Four to 12 participants will be recruited for each iteration of the cognitive interviews, with a maximum of 12 iterations of adaptation and trial of the intended IFUs (n = 144). Cognitive interviewing and iterative adaptation will continue until saturation occurs and no further modifications to user materials are made.

5.1.2 Key informant interviews and participant observations

Approximately 45 participants will be selected purposively through snowball sampling for the KIIs (PS201). MLW-LSHTM, using their professional networks and PSI country

staff, will identify appropriate stakeholders. Interviews will be with written informed consent, will use semi-structured questionnaires and will be audiotaped.

Participant observations will be conducted during HIV testing Technical Working Group (TWG) meetings to investigate critical opportunities to advocate for national HIVST policy in Malawi. Researchers will be involved in the TWG meetings and take notes on key observations and actions during the meeting. If allowed, the researcher will also record the meeting with an audiotape. At the end of the meeting, the researcher will generate a meeting report with analysis on discussions and emerging issues. Prior permission will need to be obtained from the TWG in order to conduct the participant observations.

5.1.3 Village selection and community mapping

Primary care clinics and evaluation villagers will be selected in consultation with the program lead for PSI's CBDA programme, and in consultation with the relevant District Health Offices, Primary care clinics and the CBDAs themselves.

Once villages have been selected, preliminary mapping exercises will be initiated including demarcation of the village boundaries and location of dwellings with geographical position system (GPS) and a brief household-level questionnaire (name of household head, demographics of household members).

Sensitisation will include village-level meetings, as well as introduction of the project to village health committees, village governance bodies (e.g., traditional councils), community peer groups, and community-based organisations engaged in HIV and other social services. Membership size and gender and age structure of active community peer-groups (church groups, sports, micro-finance etc) will also be listed during sensitisation.

5.1.4 Pilot study of uptake and accuracy

Two villages not included in the main study will be selected from rural Blantyre or Machinga for pilot studies of accuracy and acceptability. From these villages, 200 to 250 participants in total will be recruited from either randomly selected households (n = 150-200) or community peer groups (n = 48) for the accuracy and acceptability studies.

Peer group members

Two peer groups identified during community mapping exercises will be purposively selected from each of the villages to participate in FGDs (PS301) on HIVST. The groups should broadly represent men, women and youth. Written consent will be required by members in order to participate in the FGDs. Should a peer group refuse, another group will be selected to take its place.

Each FGD will consist of 8 to 12 individuals (n = 48). FGDs will cover barriers and motivators to self-testing and linkage to care as well as group-based dynamics around information sharing and HIVST demonstration. The FGDs will also assess background

preferences for service delivery and linkage to care approaches and identify the most salient service attributes that drive decision-making.

Randomly selected households

In addition, 150 to 200 adults will be recruited from a random selection of 60 to 80 households (with an estimated 2-5 adults per household) using randomly selected GPS waypoints. All household members aged 16 years or older will be asked for written consent to answer a brief questionnaire (socio demographics, past HIV testing experience, chronic care including ART) and will be offered HIVST followed immediately by confirmatory HTC (PS303A). Parental consent will be taken for 16 and 17-year-olds and witnessed thumbprint for individuals unable to read or write.

Offer of HIVST and exit interviews

Participants who opt to self-test as well as undergo standard HTC will be given a HIVST kit and a test results forms to record their own reading of the results (PS303B). They will then be provided with a demonstration and instructions before carrying out the self-test procedure in a private room and completing the test results forms. Participants who themselves recognise that they have made a user error or find that their first result is uninterpretable will be given a second test kit to repeat the procedure if they wish to do so.

Following self-testing, trained HTC counsellors will record their own reading of the test kit before completing the standard HTC process (parallel Unigold and Determine finger prick blood) and entering the results of blood-based testing. All patients testing HIV+ve will be referred to HIV care services.

Specimens will not be stored. However, if discordant test results are obtained, the participant will be asked to consent to providing a dried blood spot sample for subsequent laboratory Enzyme-Linked Immunosorbent Assay (ELISA) and ART drug assay.

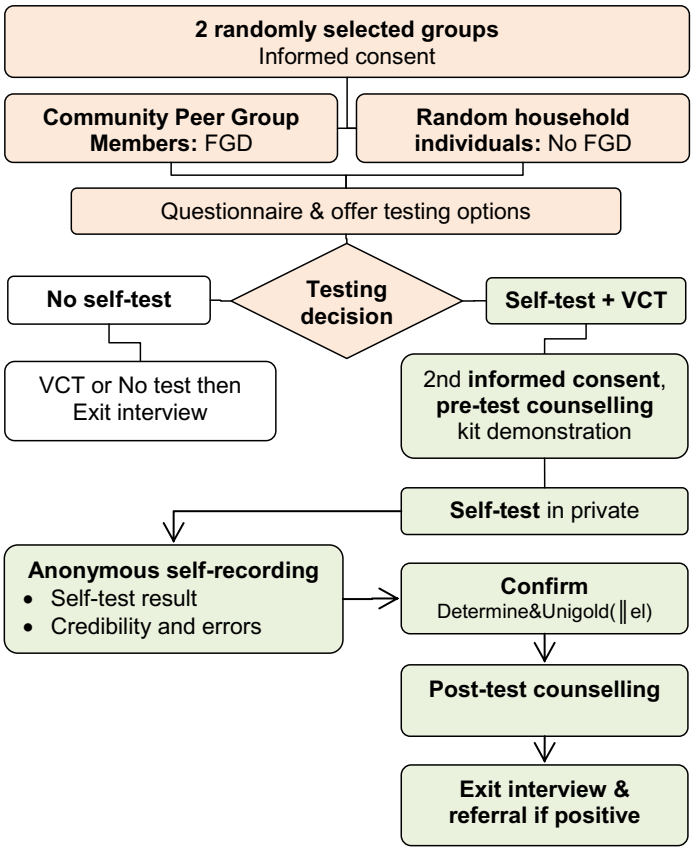
Finally, all participants will undergo a brief semi-structured exit interview (PS303C/PS303D) exploring the reasons why a particular HTC option was chosen, asking about their self-testing experience. Feedback will be sought to improve piloted information materials and instructions.

Use of pilot accuracy results

Under the most likely range of scenarios (point estimate of accuracy 95% to 98%), then 200 participants accepting HIVST will be sufficient to exclude (at $p = 0.05$) an accuracy of below 90%. If the observed accuracy is as high as 98%, then these numbers would be sufficient to exclude an accuracy of below 95% at $p = 0.05$.

If accuracy is below 90% then the accuracy component of this study will be repeated after IEC supportive materials have been refined.

Figure 7. HIV testing flow chart



5.1.5 In-depth interviews

Following the accuracy study, 40 eligible participants will be identified for in-depth interviews (IDIs) according to the categories listed in the purposive sampling framework. An information sheet on the study will be provided to obtain informed, written consent. Researchers will then move on to the next listed household until a sufficient number of participants have been recruited.

Figure 8. Stratified IDI framework

		Village 1		Village 2		Total
		Previous testing	No previous testing	Previous testing	No previous testing	
HIV negative	Aged 16 to 39	2	2	2	2	8
	Aged 40+	2	2	2	2	8
	Aged 16 to 39	2	2	2	2	8
	Aged 40+	2	2	2	2	8
HIV positive		2	2	2	2	8
Total		10	10	10	10	40

The IDI (PS302A/302B) will collect data on perceived barriers and motivators to HTC and linkage to care, as well as HTC preferences. The data will be used to analyse readiness and acceptability of self-testing, user preferences for different self-testing options, and factors influencing HIVST uptake and linkage to onward services in different contexts.

Input will also be obtained for two intended study tools: a component of the baseline household questionnaire that will use pictorial representations of salient attributes for different HTC scenarios, and an illustrated self-completed questionnaire that HIVST participants will be asked to complete during the intervention study.

IDI participants will be presented with the proposed images and self-completed questionnaires and asked what they think they represent. If the pictures are not immediately clear, the concepts will be explained and the images shown again at the end of the IDI to check for recognition. Over the sequence of the IDIs, the tool will be iteratively adapted until it is suitable for inclusion as a Selection of villages

20 primary care facilities offering ART services across the 5 districts will be included in the intervention. Clinic eligibility will be constrained on a specific set of criteria, including:

- CBDA activity in at least one village within its catchment area.
- Location in a district with relatively high HIV prevalence estimates.
- Well-functioning ART services and operations, as assessed by the Department of HIV and AIDS.

5.2 Cluster enumeration

5.2.1 Definition of the study population

20 primary care clinics offering ART services will be included in the intervention. The broader catchment population required for ART uptake evaluation (10 to 20 villages) will be defined in consultation with the clinic staff and PSI CBDA Project Manager. A catchment area that does not cross District boundaries and does not have major alternative ART providers will be selected if possible.

Following this, one or 2 evaluation villages within the ART clinic catchment area will be selected. Eligibility requirement for the evaluation villages include:

- Location within the catchment area of an eligible ART clinic, with the clinic acting as the most dominant source of ARTs for the village.
- Presence of at least one active PSI CBDA.
- Population of 250 to 500 adults.
- Road access for most/all of the year.
- Sufficient distance and separation from administrative boundaries and other intended evaluation villages to minimise 1) 'contamination' between HIVST and control villages, and 2) missed linkage to events from seeking HIV care at a remote clinic not included in the evaluation.

5.2.2 Baseline and endline household surveys

All households in the evaluation villages will be visited for enumeration and invited to participate in the baseline household survey (PS401A). Village boundaries will be defined by obtained GPS coordinates.

An appointment will be made to visit the head of household or authorised individual to explain the study. All adults and older adolescents will be asked for verbal consent to participate, with verbal consent from guardians required in the case of adolescents.

As part of the baseline household survey, a household-level questionnaire of household size, age and gender composition, and socioeconomic indicators will be administered. Each adult household member will then be asked for verbal consent to participate in a brief individual questionnaire on demographic characteristics and experience with HIV testing and care.

A random selection of participants will then also be asked for written consent to complete an extended individual questionnaire on sexual behaviour, stigma, and health service utilisation, including costs. A discrete choice module will investigate user preferences for HIV delivery and linkage to care.

One in 4 household survey participants will be randomly allocated to a longer questionnaire (PS401B/PS402A), includes an approach to establishing user preferences by asking participants to make a series of trade-off choices (discrete choice experiment: DCE).

Written or witnessed informed consent (or assent with guardian consent in the case of adolescents) will be obtained beforehand. Selection will be determined based on a random number generated by the electronic survey device at the time of the household survey (Choko, et al. 2015).

A post-intervention survey will be conducted with the same evaluation villages 12 months after the start of HIVST services. The post-intervention survey will consist of the household and brief individual questionnaires as well as an additional section on self-testing.

5.2.3 Midline household surveys

A midline round of surveys and analysis will be conducted 4-6 months after distribution begins to assess the implementation of the intervention. Midline data collection will occur within intervention communities only, and will include a subset of questions asked at baseline about sociodemographic background and recent HIV testing and self-testing.

We propose a sample size of 550 individuals across 11 clusters (50/cluster) to detect a prevalence of 55% recent testing (as reported in the baseline survey) with 15% precision and ρ=0.03 (calculated using baseline data).

5.3 Randomisation and investigator blinding

Following baseline enumeration, ART clinic-evaluation village pairs will be randomly allocated to the intervention or control arm at a public ceremony using constrained randomisation.

Balls or discs numbered 1-N (where N represents the number of possible randomisation combinations) will be selected from an opaque bag by a stakeholder representative. The selected number will correspond to a pre-specified combination of clinics in Arms A and B.

A second opaque bag containing 2 balls – one for HIVST and one for SOC – will then be used to allocate the arm to the selected combination in a second drawing process. It will not be possible to blind participants, community workers, or their supervisors to the cluster intervention allocation, but all specimens and forms and data analysis conducted by laboratory, data, and health facility staff will be managed without reference to the intervention arm.

Outcome data will not be analysed by intervention arm until the final data analysis after completion of the trial, with the exception of data analysis by an independent statistician for presentation to the Data Safety Monitoring Board.

5.4 Intervention procedures and process evaluation

5.4.1 Intervention procedures

CBDAs linked to PHC clinics allocated to the intervention arm will be provided with training in HIVST and IEC materials including flipboards, used kits to show clients how to interpret positive, negative and inconclusive results, a cotton bud and vial of water to demonstrate the mouth swabbing and development process, leaflets and a buffer stock of OraQuick ADVANCE HIV I/II test kits, to be stored in a locked container in their own home.

Adult (16 years or older) participants wishing to know their status will be provided with brief pre-test counselling together with the kit, and an envelope containing a self-completed questionnaire for return of the used test, a telephone hotline number, a self-referral slip for the nearest PHC offering ART services in case of a positive result, and information on how to access VMMC for HIV-negative men. The kit contains instructions for use and results interpretation in Chichewa.

Clients will be encouraged to return their used kits confidentially to the CBDA, either in person or by posting in the sealed envelope into an opaque locked “ballot box” container kept in the counsellor’s house. Clients will also be encouraged to seek post-test advice from the CBDA, which can be “generic” (i.e. not results based) or results-based.

Kits will be replaced by the PHC clinic supervisors on presentation of used kits, and following inspection of an HIV test logbook to confirm recording of names and

addresses, but not results, of clients. Numbers of used kits, and results on late re-read, will be recorded by the CBDA/PHC supervisor. HIVST logbooks will be kept at the CBDAs home in a locked container.

There are no sharps or hazardous materials.
Couple's testing will be encouraged. In the case of couples wanting to self-test together, both partners will be asked to attend the IEC session, but clients will also be allowed to take up to 2 kits home if the partner cannot attend.

Testing of children (aged 15 years or less) will not be permitted as part of this trial, but can be arranged through special arrangement with the PSI Supervisors.
For CBDAs participating in the **Home-initiation Arm** of the second stage randomisation, additional training will be provided on how to advise the client about the availability of this option, and the need to share a provisionally positive HIVST result in order to access this option.

Once a client requests home assessment, the CBDA will be responsible for arranging a clinical (ART trained nurse) visit to the participant's home or designated meeting point within 3 days to carry out confirmatory HIV testing, WHO staging, CD4 cell count (Alere PIMA CD4), and TB screening. They will also provide 2 weeks of Co-trimoxazole and ART if the participant meets eligibility requirements. Participants will then be provided with a completed ART registration card and follow-up appointment at the ART clinic.

5.4.2 Participant selection, inclusion and exclusion criteria

The inclusion criteria for clients are:

- Age 16 years or above
- Usual residence within a study PHC catchment area
- Able and willing to provide oral consent to HTC

The exclusion criteria for participation in the ACF intervention will be:

- Age 15 years or below
- Usual residence outside of the intervention cluster

5.4.3 VMMC mobilisers and Tunza Network

Using adaptations of the methods developed for the main CDBA trial, training packages, IEC materials, use of returned kits plus SQC for quality control, and social harms reporting will be used to evaluate the potential role for HIVST delivered through VMMC mobilisers and the Tunza Network.

PSI-VMMC mobilisers will be trained to offer HIVST kits to men ages 15 to 49, who are the target of VMMC campaigns. Research evaluation will be limited to safety reporting aspects and analysis of the effect of introducing this method through comparison of before-after time trends in demand for VMMC at any given VMMC site, using a difference-in-differences analysis approach.

The Tunza Network are a social franchise of private practitioners who use with PSI reproductive health products. Tunza practitioners will be trained to offer HIVST kits to their patients. Research evaluation will be limited to safety reporting and analysis of the effect of introducing this method through comparison of before-after time trends in demand for ART referrals at any given Tunza site, using a difference-in-differences analysis approach.

5.5 Health economics

5.5.1 Costing studies

Costing will estimate the societal-level costs of providing HIVST interventions, both from the perspective of the health provider and the user. The MLW-LSHTM team will also collect costs on current MoH HIV prevention, testing and counselling, and treatment services.

The costing study will feed into estimates of cost-effectiveness, which are to be projected on different time scales and population levels. The first cost-effectiveness study will be a short-term, trial-based evaluation using costs and impacts directly measured within the scope of PSI HIVST distribution. The second study will be model-based and explore the long-term population costs and effects at scale using mathematical modelling.

Costing data will be collected initially within the CBDA evaluation villages, but will be expanded to all locations where PSI will be distributing HIVST kits through CBDA, peer, Tunza, and VMMC mobiliser models.

5.5.2 Study period

The costing study will run in parallel with the distribution of HIVST kits by PSI. During this period, MLW-LSHTM will collect programmatic expenditure data from PSI on a monthly basis. Data on user costs of accessing HIVST and HTC services will be gathered through the extended baseline questionnaire administered to adults living in Evaluation Villages.

Data from relevant HIV prevention, testing, and care facilities will be extracted throughout the project period, with data from ART clinics obtained from interview of staff and analysis of primary care clinic and District expenditure records, with permission of MOH and DHOs.

5.5.3 Study population and study size

Full financial and economic costs from the providers' perspective will be collected through PSI and MoH facilities. User costs of accessing existing and new forms of HIV testing and linkage to care will be gathered using the extended baseline questionnaire, which will be assigned to a random sample of ~1000 enumeration participants.

5.5.4 Data Collection

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Costing tools will be used in conjunction with service-related financial and activity reports in order to determine the unit costs of providing HTC and subsequent HIV care. Obtaining costs from MoH will require permission from MoH and District Health Officers (DHO). MLW-LSHTM will also carry out detailed micro-costing, including time and motion studies, to clinics assigned to the intervention and control arms of the impact evaluation. This is important in order to identify instances of reduced crowding in ART clinics due to HIVST decentralisation.

Full PSI costs for HIVST distribution will be derived from programme expenditure reports, while user costs will be collected through questions asked on service utilisation costs in the extended baseline questionnaire.

5.5.5 Data analysis

Gathered costing data will be used to conduct an economic evaluation, using decision-analytic modelling, to compare the costs of the different HIVST models to current MoH HTC models. Key outcomes include the incremental cost per Disability Adjusted Life-Year (DALY) averted, which will allow the cost-effectiveness of HIVST and linkage to care models to be determined.

Additionally, a model of scale-up costs will be developed that takes into consideration budgetary constraints. This will include costs from the providers' perspective, but also changes in total societal costs once user costs have been taken into account.

5.6 Outcome evaluation

5.6.1 Data Capture

Four data collection channels will be employed for the impact evaluation:

1. Pre- and post-intervention household surveys
2. CBDA registers and forms
3. ART clinic registers and forms, and
4. Harms monitoring records.

Data will be collected using tablet computers and paper-based forms.

CBDA logbooks and forms

Process data on HIVST distribution by CBDAs will be captured using HIVST logbooks (date, name, village and number of test-kits taken), returned kits, self-completed questionnaires (SCQ), and self-referral cards for ART clinics.

The SCQ will include questions about the self-read HIVST result, satisfaction, coercion, and HIV testing and ART history. The returned kits will be collected and read against the SCQ by field supervisors before disposal. This will allow the study team to conduct confirmatory readings of HIVST results and provide an ongoing measure of accuracy. CBDAs will also use registers to track the age, sex and HIV and ART history of participants and the nature of support received for HIVST.

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ART registers and forms

To monitor the number of referrals, HIV diagnoses and ART initiations, the study will extract routine facility records and, if applicable, self-referral cards from ART clinics serving the evaluation villages.

Harms monitoring records
Identified community leaders will provide weekly reports of deaths and any known episodes of domestic violence. CBDAs will then investigate any possible links to HIVST.

Data capture forms and questionnaires are shown in the Appendices

5.6.2 Data security

Hard copies of data and study documentation will be kept in locked offices, and long term storage will be in locked cupboards in a locked repository.

Electronic copies of data will be saved in password-protected files. All data will be backed up daily by the MLW Data Office, with offsite back up once weekly. Backup data will be stored in a locked filing cabinet away from the office by the PI.

5.6.3 Quality assurance

Data will be checked for internal inconsistencies during verification and following data entry. Quality assurance protocols will be developed for each stage of the study, detailed as SOPs.

PSI supervisors will carry out periodic spot-checks on CBDAs, with visit at home of recent HIVST participants.

ART clinic data will be extracted by PSI supervisors. MLW data team will check data and raise any queries, and will also visit each ART clinic quarterly.

5.6.4 Outcome evaluation

For the comparison of **coverage of recent / ever HIV testing**, outcomes will be evaluated through household surveys as detailed above.

For evaluation of **ART initiations within study area villages**, maps showing study area boundaries and names of participating villages will be produced and displayed in HCT and ART clinics. ART register completion will be adjusted in collaboration with MoH to allow previous HIVST / home-initiation episodes to be documented in the "Comments" column.

Clinic staff will be asked to ensure that all clients are asked directly if they are attending following HIVST results and that the village of residence is clearly recorded in the ART register. The self-referral cards, which are presented by the participants to the clinic, will contain spaces for ART clinic staff to log confirmatory results, the

national ART number for clients entering HIV care, and any other relevant referrals (e.g., VMMC).

PSI CBDA supervisors will extract these data on a monthly basis from each of the 20 ART clinics included in the study. Retrospective data extraction will also be used to provide an indication of pre-intervention ART initiations from the 20 study clinics. In **Home-Initiation villages**, where participants have the option of requesting home initiation of care, PSI CBDA supervisors will fill out HIV care registration cards and maintain a logbook allowing cross-reference by ART number with the local ART clinic. Total numbers of clients confiding positive HIVST results will be recorded by all CBDAs in post-test logbook recording disclosure and other referral events without name.

5.7 Qualitative studies

Qualitative studies will be embedded into the main study to explore individual and community experiences within large-scale HIVST distribution. This includes understanding community members' experiences throughout the HIVST pathway, specifically barriers and facilitators to HIVST and linkage to HIV treatment and prevention services, perceptions around community-based distribution models, particularly around the role of counselling, and social harms and benefits from HIVST. Following the intervention period, we will also conduct FGDs to explore how the community-based distribution model could be modified for scale-up by MoH outside of research.

FGDs and IDIs for the process evaluation will start in October 2017 and will be conducted in 4 intervention clusters (one per district). FGDs for scale-up preparation will start in January 2018 and will be conducted in districts, such as Mangochi, identified by MoH for scale-up.

5.7.1 Process evaluation

IDI participants (n=48) will be purposively selected to ensure sufficient representation by sex, age group, those who did or did not self-test, and those who did or did not link to care after self-testing positive. Participants will be identified through CBDAs and are eligible if they are at least 16 years old, lived in the evaluation villages at the time of HIVST distribution, and can give informed assent or consent.

Figure 9. Stratified IDI framework

		Male			Female			Total
		Age 16-19	Age 20-25	Age 26+	Age 16-19	Age 20-25	Age 26+	
No HIVST		2	2	2	2	2	2	12
HIVST	Neg	2	2	2	2	2	2	12
	Pos + linked	2	2	2	2	2	2	12

	Pos + not linked	2	2	2	2	2	2	12
Total		8	8	8	8	8	8	48

Forty IDIs will also be conducted with CBDAs (n=20) and public sector health care workers (n=20). CBDAs in catchment areas of intervention clinics will be purposively selected to ensure representation from all districts and inclusion of both 'low' and 'high' performing CBDAs based on client uptake of HIVST. Health care workers who provide HTC or ART services in the 4 intervention clinics will be purposively sampled to ensure representation of all cadres who provide HIV services. Both CBDAs and HCWs will be identified through the assistance of PSI implementers.

Follow-up interviews will be conducted with HIVST clients reporting severe or life-threatening incidents through established social harms reporting systems and the Community Liaison Officer. Clients will be confidentially followed up and asked if they would like to participant in Critical Incident Narratives (CIN) to understand the nature of the reported event. FGDs will also be conducted with members of the social harms reporting system to understand the functionality and quality of the system.

5.7.2 Planning for MoH scale-up

Following the intervention period, we plan to conduct additional FGDs to explore how the community-based distribution model evaluated in the trial could be pragmatically adapted for scale-up by MoH. This includes exploring alternative models for delivery at community level, potential implementation roles for existing community networks, and willingness of communities to deliver HIVST kits themselves. FGDs will be conducted in high-burden priority districts, such as Mangochi, that have been identified by MoH.

We plan to conduct a total of 16 FGDs across four villages identified by MoH. In each village, FGDs will be conducted with Group Village Heads and Village Health Committees. Additional FGDs will be conducted with community groups, each representing women, men and youth, selected by the Group Village Heads.

5.8 Data management

5.8.1 Quantitative data management

Quantitative data will be captured using electronic devices (Tablets) or onto Optical Character Recognition forms, and entered into a dedicated database (Microsoft Access). Incoming electronic data will be checked on a daily basis for errors, with supplemental training provided to field staff if required. In the case of external manual data, MLW-LSHTM will provide training on data collection and assess quality and accuracy through quarterly (initially monthly) supervisory visits.

All data will be cleaned and analysed using Stata software (Stata Corporation, College Station, Texas, USA). All participants will be assigned a study ID number. Participant names will not be linked except through paper-based recruitment logs, which will be stored in locked cupboards and not entered into electronic form.

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5.8.2 Qualitative data management

Qualitative data will be recorded in two forms – observational notes and digital audio recordings – and cross-referenced for accuracy. A backup copy of the audio file will be saved on RedCAP, the MLW data management programme, while another copy will be sent to the transcription and translation team. The audio file will be transcribed verbatim into written chiChewa. Transcriptions and notes will then be translated into English. All data will then be transferred to a qualitative data analysis software package, NVIVO 10 (QSR, Melbourne, Australia) and filed according to document type. Coded data will be transferred to a Microsoft Excel spreadsheet for broader thematic analysis.

5.9 Data analysis

Standard approaches to analysis CRT data will be used. Sample size calculations are detailed in the Statistical Considerations section.

5.9.1 Description of the HIVST and SOC arms in the baseline survey

The characteristics of participants recruited into the baseline survey will be described by arm (HIVST and SOC). Cluster-level factors will be summarised at baseline using the mean, median and range, by intervention arm, based on data from the facility assessment, conducted at baseline.

5.9.2 Description of the HIVST and SOC arms in the follow-up survey

The characteristics of participants recruited into the follow-up survey, by arm (HIVST and SOC) will be described. All characteristics will be compared by arm of the trial to assess for comparability. Any variables for which there is a substantial imbalance will be noted so that final analysis can take this into account. This assessment will not be based on the results of hypothesis tests, and p-values will not be shown.

5.9.3 Missing data

Missing data will be examined for each variable and for each cluster or individual participant. A systematic assessment of missingness will be conducted to ascertain the reason and possible mechanism for missing data by identifying the quantity of missing data and patterns within the data. Missingness will be particularly examined by cluster and between randomised arms to assess for systematic biases. Sensitivity analysis for the primary outcome of recent test for HIV will be carried out – comparing complete case analysis results with those where missing outcome status are re-classified as yes and no.

5.9.4 Outcomes

Overall numbers of ART initiations per 1,000 total adult population will be calculated for each clinic during months 1 to 12, and will be compared between intervention and control arms after adjusted for any major imbalance between the trial arms in factors such as pre-intervention ART initiation rates.

The proportion of residents accepting HIV testing will be estimated both overall and within sex, age and village strata, using population denominators from the post-intervention household prevalence survey. Participant characteristics during different time periods of the study will also be compared.

Estimates of linkage into newly accessed care will be assessed using the referral completion rate. This will compare the number of participants who disclosed positive results to CBDAs during a specific period of time to the number of participants accessing confirmatory testing following HIVST over the same time period.

The number of new HIV-positive cases will be ascertained through re-reading of returned kits and participants sharing results with CBDAs.

5.9.5 Methods

All statistical analyses will be based on methods used for CRTs with a small number of clusters (Campbell, et al. 2012). The analysis for the first randomisation is based on a total of 20 clusters.

Summary measures
For binary outcomes the overall risk, combining data across clusters, and means of cluster-level risk will be reported by intervention arm. For quantitative outcomes, the overall mean and cluster-level means will be reported by intervention arm.

Unadjusted analysis
The analysis will give each cluster equal weight. The overall risk/mean for each cluster will be calculated.

A log transformation (where necessary) will be applied to the risk/rate/mean for each cluster. For binary outcomes where there are clusters with no events, one event will be added to all clusters so that the log transformation can be conducted. The mean and standard deviation of these log risks/rates/means will be used to obtain the geometric mean (GM) and associated 95% CI for each arm of the study.

The risk/mean ratio, 95% confidence interval and p-value is estimated using a t test and the log risks/rates/means by arm, based on 18 degrees of freedom.

Adjusted analysis
Factors for adjustment will be determined as stated above.

Depending on the outcome to be analysed, logistic/linear regression will be used to adjust for confounders at the individual level and cluster level, adopting a two-stage approach.

The regression model will include terms for the individual level adjustment factors, but not study arm. For each cluster the fitted model will be used to obtain the ratio of observed to expected (O/E) events, and a log transformation will be applied to this ratio,

where appropriate. A t test of the log (O/E) by arm will be used to estimate the risk ratio, 95% CI and p-value. If adjustment for cluster level factors is considered necessary, this will be conducted at the second stage using linear regression of the log (O/E) on arm and cluster level factors, with appropriate adjustment for the degrees of freedom.

Stratified (subgroup) analyses

Stratified analyses (sub-group) for the primary outcome will be pre-specified before the end of data collection,

Stratified analyses based on effect modification by cluster- or individual-level covariates will be analysed as follows: the effect of the intervention will be estimated for each strata. For individual-level covariates this will be accompanied with p-values for effect modification using the approach by Cheung et al (Cheung, et al. 2018).

6. Adverse Event Reporting and Management

6.1. HIVST

HIV testing and counselling including HIVST is well established, and known to have a high level of safety and favourable risk: benefit ratio. However, harmful reactions can occur. For the purposes of this trial, we will focus on capture of the following **Serious Adverse Events.**

- Death or hospitalisation due to self-inflicted injuries within 30 days of a positive HIVST results
- Death or hospitalisation resulting from violent assault by others (intimate partner violence, assault by family members, assault by community members) within 30 days of a positive HIVST result

Deaths and hospitalisations will be captured through the Social Harms System established in each cluster. The PSI Supervisor will interview the client and relatives to establish relatedness where possible.

6.2. Institutional responsibilities

SAEs will be reported immediately to the PI or MLW Coordinator. All other adverse events will be logged and reported through regular follow-up reports.

As this is a public-health scale-up evaluation, following an intervention trial that showed low risk of harm from HIVST (no suicides from 27,000 HIVST episodes), expected SAEs will be reported through 6-monthly progress reports that will report on safety as well as other important process indicators and will be sent to the Technical Advisory Group members and local and international collaborators.

12 monthly reports with full listings of SAEs will be submitted to Ethics Review Boards at the time of annual reporting.

6.3. Reporting procedures

SAE forms will be completed by the MLW Trial Coordinator and responsible CBDA Supervisor and reported to the PI. The PI will check the form, make changes as necessary.

SAEs will be evaluated for seriousness, and likely relatedness by the PI.

7. Statistical considerations and sample size

7.1. Precision for the pilot accuracy study

Figure 9. Sample size calculation – tested for HIV in last 12 months

The table below summarises precision obtained from the pilot accuracy study for a range of scenarios around participation in HIVST

# people conducting self-tests	**Proportion results concordant with confirmatory tests**	
	95%	**98%**
114[1]	94.7% (89.0%, 98.0%)	98.2% (93.8%, 99.8%)
127[2]	95.3% (90.0%, 98.2%)	
200	95.0% (91.0%, 97.6%)	98.0% (95.0%, 99.5%)
250	94.8% (91.3%, 97.2%)	98.0% (95.4%, 99.3%)
278[3]	95.0% (91.7%, 97.2%)	97.8% (95.4%, 99.2%)

[1] Assumes 228 eligible individuals identified, with 50% participation in self-testing
[2] Minimum sample size that allows an accuracy of 95% to have a 95% CI that is above 90%
[3] Assumes 308 eligible individuals identified, with 80% participation in self-testing
Shaded area indicates the range of scenarios considered most likely

7.2. CRT sample size calculations

This trial has one primary and one secondary outcome, with a number of other analyses to be specified in the Statistical Analysis Plan. The sample size considerations here relate to the main Primary Outcome (comparison between arms of recent HIV testing).

A survey sample of 250 to 500 adults per cluster will provide sufficient power for a two sample comparison of unmatched proportions for HTC coverage was performed across the intervention and control arms to determine the number of clusters per arm.

The cluster size is based on the typical size of a rural village (250-500 people) from previous experience in Malawi. Using 2010 DHS data, baseline rates for individuals tested in the last 12 months is estimated at 25% to 40%, with a 45% to 60% predicted effect size in the intervention arm compared to the control arm. Baseline coverage for individuals who have ever tested is estimated at 42% to 60% with predicted effect size 30%-45%.

Figures 10 and 11 contain a table of scenarios for each of the outlined assumptions. To detect a 50% increase in rate of people testing in the past 12 months and a 45% increase in the percentage of people who have ever tested in the intervention villages, there should be approximately 8 clusters per arm and approximately 4,000 participants total. This study will aim to reach 10 clusters per arm and 5,000 participants to provide contingency for a lower than anticipated effect size.

Figure 10. Sample size calculation – tested for HIV in last 12 months

1-type I	Power	Baseline testing	Effect size	Intervention testing	Cluster size	k	Number of clusters	Total participants
0.95	0.8	0.35	0.6	0.56	250	0.25	6.19	3094.21
0.95	0.8	0.3	0.6	0.48	250	0.25	6.30	3148.20
0.95	0.8	0.25	0.6	0.4	250	0.25	6.45	3223.78
0.95	0.8	0.35	0.55	0.5425	250	0.25	6.92	3460.38
0.95	0.8	0.3	0.55	0.465	250	0.25	7.05	3523.39
0.95	0.8	0.25	0.55	0.3875	250	0.25	7.22	3611.61
0.95	0.8	0.35	0.5	0.525	250	0.25	7.87	3933.04
0.95	0.8	0.3	0.5	0.45	250	0.25	8.02	4007.80
0.95	0.8	0.25	0.5	0.375	250	0.25	8.22	4112.45
0.95	0.8	0.35	0.45	0.5075	250	0.25	9.12	4560.03
0.95	0.8	0.3	0.45	0.435	250	0.25	9.30	4650.47
0.95	0.8	0.25	0.45	0.3625	250	0.25	9.55	4777.08

Figure 11. Sample size calculation – ever tested for HIV

1-type I	Power	Baseline testing	Effect size	Intervention testing	Cluster size	k	Number of clusters	Total participants
0.95	0.8	0.6	0.45	0.87	250	0.25	8.67	4333.93
0.95	0.8	0.5	0.45	0.725	250	0.25	8.79	4397.24
0.95	0.8	0.42	0.45	0.609	250	0.25	8.94	4469.59
0.95	0.8	0.6	0.4	0.84	250	0.25	10.28	5139.67
0.95	0.8	0.5	0.4	0.7	250	0.25	10.44	5218.16
0.95	0.8	0.42	0.4	0.588	250	0.25	10.62	5307.86
0.95	0.8	0.6	0.35	0.81	250	0.25	12.58	6291.61
0.95	0.8	0.5	0.35	0.675	250	0.25	12.78	6391.99
0.95	0.8	0.42	0.35	0.567	250	0.25	13.01	6506.71
0.95	0.8	0.6	0.3	0.78	250	0.25	16.06	8030.49
0.95	0.8	0.5	0.3	0.65	250	0.25	16.33	8164.21
0.95	0.8	0.42	0.3	0.546	250	0.25	16.63	8317.04

Extended individual questionnaire and post-intervention household survey

The sample size for the extended individual questionnaire is based on the minimum sample size needed for the DCE to measure choice probabilities with a high level of accuracy. Though sample size calculations for DCEs have not been formalised in the same manner as trials, conventional sample sizes tend to be around 200 participants per population strata, though new efficient experimental designs do allow for smaller samples.

The study will use five strata in total, generating a sample size of 1,000 participants. Strata of interest include low and high HIV risk, young (16 to 30 years) and old (31 years or more), male and female, self-identified HIV positive and negative, and Socio-Economic Status (SES) quintiles.

8. Results presentation and dissemination

Descriptive and inferential findings will be presented through tables and histograms, line graphs and other figures, where relevant.

The results of this research will be used to guide the introduction of self-testing into community-based HTC models and the formation of national and international policies around HIVST. Results will be disseminated to the MoH HIV Unit, COMREC and UNITAID. A report on the study will be produced and disseminated to COMREC, the College of Medicine (COM) Library, the Health Sciences Research Committee and the University Research and Publication Committee. Findings will also be distributed internationally to global health policy makers, nationally to the Malawian government, and regionally to District and Council Health Offices. Presentations will be given at the COMREC research dissemination day and at MLW research-in-progress meetings. Copies of peer-reviewed publications from the research will be submitted to COM, MLW, and LSHTM.

In terms of public engagement, the MLW-LSHTM team will work with the MLW Science Communication team to disseminate the project results and raise the profile of HIVST in Malawi. MLW actively engages with both urban and rural communities, and has already hosted a range of programmes including science cafes, radio projects, and mobile exhibitions about HIVST. These mediums will be employed to educate the general public about the UNITAID project and the results.

9. Ethical considerations

9.1 Confidentiality

Participants will not have their names used during any stage of data collection except in recruitment logbooks and will be given a unique identifier. Hard copies of questionnaires and transcripts will be kept in locked cupboards in a secure location in MLW and electronic transcripts will be password protected on a computer accessible only to authorised staff members.

9.2. Informed consent

Informed consent will be taken for participation in certain parts of the study. If the sub-study requires that participants give written consent, the investigator will first provide the potential subject with an explanation of the study as well as an information sheet with study details. The investigator will answer any questions raised by the potential participant and allow them sufficient time to come to a decision. Participants will then be required to give consent. In cases where written consent is required and the participant is illiterate, they will be asked to give verbal consent plus a thumb print. Parental consent will be required if participants are 16 or 17 years old.

Figure 12. Consent requirements for each research activity

Method	Consent Requirements
Cognitive interviews	Written
Key Informant inerviews	Written
FGD	Written
IDI	Written
HIVST + HTC for pilot accuracy studies	Written
Baseline household survey	Verbal
Extended individual questionnaire	Written
Post intervention household survey	Written
PSI-led HIVST distribution	Request waiver of informed consent; leaflets provided in lieu of participant information sheets
Process evaluation	N/A
DCE	Written
Costing study	N/A

9.3. HTC and HIVST

All individuals selecting to self-test will be offered pre- and post-test information and referral to the most convenient clinic offering ART services. Participants will also be given the opportunity to discuss any fears about the process or results prior to testing and to disclose their status and receive advice and support for post-test services.

Participants are not required to disclose the results of HIVST to the distribution agent, but such will be encouraged so that they can receive results-based, post-test information. The only exception is during the pilot accuracy study, where self-testing will need to be disclosed in order to verify the accuracy of HIVST results against confirmatory results.

All disclosed HIV status results will remain confidential.

9.4. Compensation for participation

Study participants will be compensated for their time away from income-earning activities, but this will be packaged as compensation rather than payment. This will include refreshments, refund of any transport costs incurred. For those exposed to the HIVST intervention, the decision to self-test or not will not influence the amount of compensation.

Compensation will be as follows:

- MWK 1000 per household for participation in the Household Surveys
- MWK 1000 for individuals participating in cognitive interviews, pilot studies, and the process evaluation
- MWK 7000 for individuals participating in qualitative studies on scale-up planning.

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10. Constraints and limitations

10.1. Risk mitigation

Social harms monitoring will be conducted by MLW-LSHTM and PSI throughout the HIVST distribution period to respond to incidences of coercion, GBV, and other potential unintended consequences from self-testing. Systems for tracking social harms include a community-based reporting network using community stakeholders and leaders and hotline for HIVST participants to call and report adverse events. Tracking of social harms will then enable MLW-LSHTM to assess and mitigate adverse events arising from HIVST.

10.2. Data quality

MLW-LSHTM has considerable expertise in supporting all aspects of quality data management in Malawi. Standard Operating Procedures (SOP) will be used on study design, data collection instruments and data analysis procedures, with routine data quality audits conducted for quality assurance purposes. PSI and MLW-LSHTM have also invested in electronic data collection, using open source software and computer tablets. This approach improves data collection efficiency and reduces traditional weaknesses associated with data collection such as completeness, consistency, and timeliness. Additionally, MLW has substantial experience with bridging any gaps in MoH records and project data requirements, using extraction of registers onto Optic Character Recognition forms.

The Research Governance unit in MLW will conduct periodic (usually annual) internal audits to ensure that all documentation and data capture is within acceptable international standards. Should PSI Malawi data be found to be not compliant with SOPs or fail a data quality audit, they will be required to revise their practices with close supervision from external technical staff, i.e., Regional Researchers and Health Area Research Advisors.

10.3. Governance

HIV STAR will form a Technical Advisory Group (TAG) to review data and provide expert opinion on whether a product should be pre-qualified, and to support post-market surveillance reports and supervision when products enter the market place.

HIV STAR has the support of key officials in the Government of Malawi. The MoH has collaborated in a number of HIVST projects to date and supported publications and presentations from projects hosted by MLW. The Director of the Department of HIV and AIDS of the MoH, is a collaborator with the MLW HIVST project and has provided a letter of support for the UNITAID project.

11. Capacity building and training

This research will contribute to qualitative and quantitative data capacity at the College of Medicine both in terms of establishing a resource base of qualified and trained researchers to conduct qualitative and quantitative fieldwork and a system for accurate and timely transcription and translation services and data management.

Data and field staff employed on the project will be trained in both qualitative and quantitative techniques, in Good Clinical Practice, and on the protocol, and will be uniquely placed to understand the complementarity of triangulation between quantitative and qualitative methods.

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12. HIV STAR Malawi Budget

DESCRIPTION	Inflation	Type of unit	Unit cost	2015 (Sep. - Dec.) # of Units	2015 (Sep. - Dec.) Total Cost	2016 (Jan. - Dec.) # of Units	2016 (Jan. - Dec.) Total Cost	2017 (Jan. - Nov.) # of Units	2017 (Jan. - Nov.) Total Cost	TOTAL # of Units	TOTAL Total Cost	Crosswalk
III. HOST COUNTRY NATIONAL STAFF												
A. PROJECT SALARIES - PROGRAM	-											
MLW Data Manager (8% LOE) 1 month per year	L	month	2,870	0.60	1,722	1.00	2,956	0.40	1,228	2	5,906	staff costs
Country Research Coordinator (100% LOE)	L	month	2,130	7.00	14,910	12.00	26,327	5.00	11,299	24	52,535	staff costs
Project Data Manager (50% LOE for Months 2-22 inclusive)	L	month	1,391	1.50	2,087	6.00	8,596	2.50	3,689	10	14,372	staff costs
Research Assistant (quanititative) (100% LOE months 4-24)	L	month	1,136	4.00	4,544	12.00	14,041	5.00	6,026	21	24,611	staff costs
Data Collector (100% LOE months 4-24)	L	month	352	4.00	1,408	12.00	4,351	5.00	1,867	21	7,626	staff costs
Post-doc Social Scientist (100% LOE months 4-21)	L	month	3,004	4.00	12,016	12.00	37,129	2.00	6,374	18	55,519	staff costs
Social Science Research Assistant (100% LOE months 4-21)	L	month	1,136	4.00	4,544	12.00	14,041	2.00	2,410	18	20,995	staff costs
Translator Transcriber Assistant (100% LOE months 4-21)	L	month	852	4.00	3,408	12.00	10,531	2.00	1,808	18	15,746	staff costs
Data Clerk (100% LOE months 4-24)	L	month	496	4.00	1,984	12.00	6,131	5.00	2,631	21	10,746	staff costs
Economics Fellow (100% LOE months 4-21)	L	month	1,391	4.00	5,564	12.00	17,193	2.00	2,951	18	25,708	staff costs
C. PROJECT SALARIES SUPPORT	-											
Admin Officer/Bookkeeper (37.5% LOE)	L	month	1,391	2.6	3,631	4.5	6,447	1.9	2,789	9	12,867	staff costs
Administrator (50% LOE)	L	month	1,391	3.5	4,841	6.0	8,596	2.5	3,719	12	17,156	staff costs
SUBTOTAL HCN STAFF	-	-	-	-	**$60,658**	-	**$156,339**	-	**$46,791**	-	**$263,788**	-
V. FRINGES												
B. LOCAL FRINGES												
Fringe - Local	%	salary	29.0%		17,591		45,338		13,569		76,498	staff costs
SUBTOTAL FRINGES	-	-	-	-	**$17,591**	-	**$45,338**	-	**$13,569**	-	**$76,498**	-
VII. TRAVEL												-
Regional Airfare Star Project Kickoff (Harare)	US	RT	750	2	1,500	0	0	0	0	2	1,500	operating costs
Regional Per Diem Star Project Kickoff (Harare)	US	day	334	12	4,008	0	0	0	0	12	4,008	operating costs

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DESCRIPTION	Inflation	Type of unit	Unit cost	2015 (Sep. - Dec.) # of Units	2015 (Sep. - Dec.) Total Cost	2016 (Jan. - Dec.) # of Units	2016 (Jan. - Dec.) Total Cost	2017 (Jan. - Nov.) # of Units	2017 (Jan. - Nov.) Total Cost	TOTAL # of Units	TOTAL Total Cost	Crosswalk
International Airfare Star Project Planning Mtg (JBG)	US	RT	750	0	0	1	773	0	0	1	773	operating costs
International Per Diem Star Project Planning Mtg (JBG)	US	day	306	0	0	6	1,891	0	0	6	1,891	operating costs
Regional Airfare Star Project Planning Mtg (JBG)	US	RT	750	0	0	1	773	0	0	1	773	operating costs
Regional Per Diem Star Project Planning Mtg (JBG)	US	day	306	0	0	6	1,891	0	0	6	1,891	operating costs
Regional Airfare Star Project Planning Mtg (Lusaka)	US	RT	750	0	0	0	0	1	796	1	796	operating costs
Regional Per Diem Star Project Planning Mtg (Lusaka)	US	day	285	0	0	0	0	6	1,814	6	1,814	operating costs
International Airfare Symposium (Geneva)	US	RT	1,250	0	0	1	1,288	0	0	1	1,288	operating costs
International Per Diem Symposium (Geneva)	US	day	469	0	0	6	2,898	0	0	6	2,898	operating costs
International Airfare Post-Doc HIV Conf (US/UK)	US	RT	2,500	1	2,500	1	2,575	0	0	2	5,075	operating costs
International Per Diem Post-DocHIV Conf (US/UK)	US	day	300	7	2,100	7	2,163	0	0	14	4,263	operating costs
Local Vehicle Costs and Field staff per diem (mileage/fuel)	L	month	2,000	5	10,440	9	18,540	3.8	8,020	18	37,000	operating costs
SUBTOTAL TRAVEL					**$20,548**		**$32,791**		**$10,630**		**$63,969**	
VII. FURNITURE/EQUIPMENT												
Smart Phone for data capture	US	unit	403	15	6,045	0	0	0	0	15	6,045	operating costs
SUBTOTAL FURNITURE/EQUIPMENT					**$6,045**		**$0**		**$0**		**$6,045**	
XV. RESEARCH, MONITORING AND EVAL.												
Research - accuracy (300 participants)	L	study	36,000	1.00	36,000	0.00	0	0	0	1	36,000	operating costs
Research - DCE (150+300 participants) and costing	L	study	60,800	**1.00**	60,800	**0.50**	31,312	0	0	2	92,112	operating costs
SUBTOTAL RESEARCH, MONITORING AND EVAL.					**$96,800**		**$31,312**		**$0**		**$128,112**	
XVI. PROGRAM RELATED TRAINING/CONF./MTGS.												
Program Related Training	L	year	8,200	1	8,200	1	8,446	0	0	2	16,646	operating costs
Program-Related Conferences	L	year	1,000	1	1,000	1	1,030	0	0	2	2,030	operating costs
Program-Related Meetings	L	year	1,500	1	1,500	1	1,545	0	0	2	3,045	operating costs

DESCRIPTION	Inflation	Type of unit	Unit cost	2015 (Sep. - Dec.) # of Units	2015 (Sep. - Dec.) Total Cost	2016 (Jan. - Dec.) # of Units	2016 (Jan. - Dec.) Total Cost	2017 (Jan. - Nov.) # of Units	2017 (Jan. - Nov.) Total Cost	TOTAL # of Units	TOTAL Total Cost	Crosswalk
SUBTOTAL PROGRAM RELATED TRAINING/CONF./MTGS.					**$10,700**		**$11,021**		**$0**		**$21,721**	
XVII. OTHER DIRECT COSTS												
Office Supplies	L	month	300	7	2,088	12	3,708	5	1,604	24	7,400	operating costs
Communications	L	month	200	7	1,392	12	2,472	5	1,069	24	4,933	operating costs
Postage & Delivery	L	service	25	3	87	6	155	3	67	12	308	operating costs
SUBTOTAL OTHER DIRECT COSTS					**$3,567**		**$6,335**		**$2,740**		**$12,642**	
SUBTOTAL ALL DIRECT COSTS					**$215,908**		**$283,136**		**$73,731**		**$572,775**	
SUBTOTAL ALL COMMON COSTS (8% COMREC)					**$14,442**		**$24,900**		**$10,458**		**$49,800**	common costs
GRAND TOTAL WITH Common Costs					**$230,350**		**$308,036**		**$84,189**		**$622,575**	

13. Budget justification

Budget assumptions: Local costs are adjusted annually due to inflation by 3%. All costs are budgeted in U.S. dollars.

Scope of work: A total of US $622,575 is requested for the scope of work covered by Malawi Liverpool Wellcome Trust Clinical Research Programme. MLW is responsible for the overall coordination and delivery of research outputs in Malawi, one of the 3 tier countries participating in the HIVST project under UNITAID/PSI. Core functions to be coordinated by MLW will include hiring and training of core team for implementation of activities, development and adaptation of tools to be used, procurement, coordinating local meetings, data management and dealing with local ethical aspects.

I. Commodities
N/A

II. Operating Costs

A. Travel

International and Regional Airfare

- A total of 8 international flights have been budgeted:
- Attending biannual project meetings to discuss project progress (4 trips)
- One AIDS conference flight per year for the post-doc social scientist (2 trips)
- Attending harmonisation workshop at CeSSHAR for key populations protocol finalisation in Harare (1 trip, Year 1)
- Attending international symposium (LSTM hosting) in Year 2 (1 trip)

Estimated Flight costs and 50 days for per diems are summarized below. Per diems use the US State Department rates.

Airfare/Retreats/Conferences

Destination	Travellers	Purpose of travel	Number of airfares	RT airfare /person	Per diem/day
YEAR 1 Harare	TBD	Project Kick-off Meeting	1	$750	$334/day for 6 days
YEAR 1 TBD	Post Doc researcher	International HIV conference	1	$2500	$300/day for 7 days
YEAR 1 Harare	TBD	Harmonization w/key pops workshop	1	$750	$334/day for 6 days

YEAR 2 Johannesburg	TBD	Project planning Meeting	1	$750	$306/day for 6 days
YEAR 2 Johannesburg	TBD	Project planning Meeting #2	1	$750	$306/day for 6 days
YEAR 2 Geneva	TBD	HIV testing symposium	1	$1250	$469/day for 6 days
YEAR 2 Durban SA	Post Doc researcher	To attend World AIDS Conference Durban	1	$2500	$248/day for 7 days
YEAR 3 Lusaka	TBD	Project planning meeting	1	$750	$285/day for 6 days

Per Diem and Lodging-Local in-country

18 months years of local vehicle lease costs, mileage and lodging-local in-country are budgeted at US $2,000 (2,000 km per month) for the LOP. This includes a total of 128 nights accommodation and per diem for MLW project staff supervising key populations studies in Lilongwe and Mzuzu, and for field staff to attend monthly District meetings and to supervise the extraction of HIV testing and ART initiation data from routine facilities serving the 10 intervention and 10 control villages that will make up the impact evaluation cohort. Local per diem and accommodation is costed at US $79.25 per night. Mileage during the LOP is estimated at 26,500 km. MLW charges 1 USD per km for use of institutional vehicles, including service, fuel and a driver.

B. Furniture/Equipment
   - Smart phones (15) for LOP will be purchased for STAR project data capture with total budget at US $6,045.

C. Research, Monitoring and Evaluation
   - Field, temporary staff and participant related costs during accuracy study in Year 1 budgeted at US $36, 000.
   - Participant and costs related to Rapid DCE (accuracy: 150 participants, year 1) and full DCE (300 participants linked to initial household survey). Economics sub-studies budgeted at US $92,112

D. Program Related Training/Conf./Mtgs.
   - National protocol meetings and GCP training are budgeted at US $16,646 in Years 1-2.
   - Local Conference fees (MLW annual scientific meeting or National AIDS Council Annual Conference: one per year for the Postdoc Social Scientist or other academic presenter) is budgeted at US $2,030
   - Meeting costs (DHO staff and local investigators) are budgeted at US $3,045. These meetings will be held monthly in the districts hosting the 10 HIVST evaluation villages, in order to allow data extraction from routine facility records.

Collaborating MoH staff will be paid for transport and per diem in order to present and allow supervision of all data relating to ART initiation.

E. Other Direct Costs

- Office supplies essential for the project function (study files, hard file records for storage, leaflet production) are budgeted at US $300 per month.
- Communications including cell phone airtime and internet are budgeted at US $200 per month.
- Postage at US $308 (US $25/service), including use of couriers as is occasionally necessary.

III. Staff Costs: Host Country National Staff (Malawi)

A. Salaries

Staff responsible for providing programmatic, financial and logistical support to the project will be locally recruited through MLW in order to run project activities. Actual charges to the project will be based on actual assignments and time spent supporting this project.

Apart from the country research coordinator (available immediately), a three-month delay in recruitment is assumed for all research staff allowing for advertising, interview and receipt of funds.

Program and project support costs are budgeted at a total of US $263,788 for two years including:

- 2 years of a senior data manager with LOE of 1/12 (8%) for each year of the level of effort (LOP) at salary grade TC4. Total cost US $5,906
- 2 years of a country research coordinator with LOE 100% over the life of the project (LOP, Phase 1) (salary grade TC5). Total cost US $52,535
- 20 months of a data manager at 50% LOE for the LOP (salary grade TC3). Total cost US $14,372
- 21 months years of a quantitative research assistant at 100% LOE for months 4-7 in Year 1 and throughout Year 2 and 3, respectively, over the LOP (salary grade TC2). Total cost US $24,611
- 21 months of a data collectors at 100% LOE for months 4-7 in Year 1 and 100% LOE for Year 2 (salary grade G2). Total cost US $7,626
- 18 months of a post-doctoral social scientist at 100% LOE for months 4-7 in Year 1 and 100% LOE in Year 2 and months 1-2 in Year 3 over the LOP (salary grade Postdoc). Total cost US $55,519
- 18 months of a social science assistant at 100% LOE for months 4-7 in Year 1, 100% LOE in Year 2, and 100% LOE for months 1-2 of Year 3 over the LOP (salary grade TC3). Total cost US $20,995

- 18 months of a translator/transcriber at 100% LOE for months 4-7 in Year 1, 100% LOE in Year 2, and 100% LOE for months 1-2 of Year 3 (salary grade TC1). Total cost US $15,746
- 21 months of a data clerk at 100% LOE from month 4-24 over the LOP (salary grade G3). Total cost US $10,746
- 18 months of an economics fellow at 100% LOE for months 4-21 inclusive (salary grade TC3). Total cost US $25,708
- 9 months LOP of an admin officer / bookkeeper (38% LOE) across Phase 1. Total cost US $12,867
- 12 months LOP of an administrator at 50% LOE (salary grade TC3). Total cost US $17,156

B. Fringes

- Local fringes include medical insurance, pension contribution, severance pay, housing and leave allowances, and are budgeted at US $75,735 (29%) over the LOP.

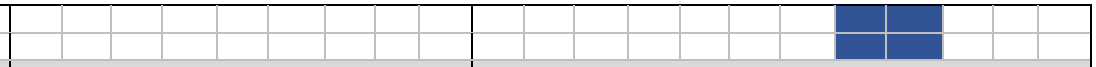
IV. Common Costs

Common costs totalling US $49,800 over Phase 1 include:

- COMREC submission fee at 8% of all direct costs is $45,822.
- Equipment: One (1) laptop computers will be purchased during the project period at a cost of US $1619 in year 1 including specialist software.
- Contribution to two years of professional institutional audit services budgeted at US $2,359 for the LOP are included in common costs.

14. HIV STAR-M Work Plan

Activities	Lead	Group	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug
												Y2											
A. CRT																							
Partner with MoH to select evaluation clinics and villages	PI/LC/PM	MLW/PSI																					
Meet with community leaders and clinics to explain study	PM	PSI/MLW																					
Develop database for quantitative data	DM/PI	MLW																					
Identify and obtain GPS coordinates for village and household boundaries	PM/PI	PSI/MLW																					
Train field/data team on tools and SOPs	PI/DM/PM	MLW/PSI																					
Train ART clinic staff on tools and SOPs																							
Train CBDAs on tools and SOPs	PI/PM	MLW/PSI																					
Randomly assign intervention to evaluation villages	PI/LC	MLW																					
Collect and analyse data for baseline household survey																							
Pilot baseline survey and revise based on feedback	PI/PM	MLW/PSI																					
Enumerate households and randomly recruit participants for extended survey	PM/PI	PSI/MLW																					
Pilot extended baseline questionnaire and revise based on feedback	PI/PM	PSI/MLW																					
Conduct extended baseline questionnaire	PM/PI	PSI/MLW																					
Conduct quality and accuracy checks on incoming electronic data	PI/DM	MLW																					
Clean quantitative data	DM/PI	MLW																					
Conduct preliminary analysis of quantitative data	PI/LC/MN	MLW/LSHTM																					
Generate preliminary report on baseline findings	PI/LC	MLW																					
Conduct in-depth analysis of quantitative data	PI/LC/MN	MLW/LSHTM																					
Generate in-depth report on baseline findings	PI/LC	MLW																					
Collect and analyse data for interim household survey																							
Pilot extended interim household survey and revise based on feedback	PI/PM	PSI/MLW																					
Conduct interim household survey	PM/PI	PSI/MLW																					
Conduct quality and accuracy checks on incoming electronic data	PI/DM	MLW																					
Clean quantitative data	DM/PI	MLW																					
Conduct preliminary analysis of quantitative data	PI/LC/MN	MLW/LSHTM																					
Generate preliminary report on interim findings	PI/LC	MLW																					

Conduct in-depth analysis of quantitative data	PI/LC/MN	MLW/LSHTM	
Generate in-depth report on interim findings	PI/LC	MLW	
Collect and analyse data from CBDAs and ART clinics			
Pilot CBDA tools in intervention villages and revise based on feedback	PI/PM	MLW/PSI	
Collect SCQs and HIVST registers and kits from CBDAs in intervention villages	PI/PM/CC	MLW/PSI	
Collect harms monitoring records from community leaders in intervention villages	PI/PM/CC	MLW/PSI	
Collect patient registers and referral forms from ART clinics	PI/PM/CC	MLW/PSI	
Enter paper-based data into electronic files	DM	MLW	
Conduct quality and accuracy checks on incoming electronic data	PI/DM	MLW	
Clean quantitative data	DM/PI	MLW	
Conduct preliminary analysis of quantitative data	PI/LC/MN	MLW/LSHTM	
Generate preliminary report on impact evaluation findings	PI/LC	MLW	
Conduct in-depth analysis of quantitative data	PI/LC/MN	MLW/LSHTM	
Generate in-depth report on impact evaluation findings	PI/LC	MLW	
B. COGNITIVE INTERVIEWS			
Partner with MoH to select health facilities	PI/LC	MLW	
Meet with clinic staff and community leaders to ensure project buy-in	PI/LC	MLW	
Train SS-RA on tools and SOPs	PI/ND	MLW-SS	
Pilot tools and revise based on feedback	PI/SS-RA	MLW-SS	
Identify and recruit study participants	SS-RA/PI	MLW-SS	
Conduct cognitive interviews	SS-RA/PI	MLW-SS	
Conduct quality checks on collected data	PI/TT	MLW-SS	
Enter paper-based data into electronic files	DM/TT	MLW-SS	
Conduct ongoing analysis of qualitative data and iteratively revise IFUs	PI/ND/LC	MLW-SS	
Generate report on findings with recommendations on prototype IFUs/IEC materials	PI/ND/LC	MLW-SS	
C. KEY INFORMANT INTERVIEWS			
Conduct document review on HIV policy and regulation	SRA	LSTM	
Identify and recruit HIV policy and regulation stakeholders	SRA/ND	LSTM/MLW-SS	
Conduct KII with HIV policy and regulation stakeholders	SRA	LSTM	
Transcribe interviews into electronic files	TT	LSTM	
Clean and code qualitative data	SRA	LSTM	
Conduct analysis of qualitative data	SRA/ND	LSTM/MLW	

Generate report on findings with recommendations on policy/regulatory actions	SRA/ND	LSTM/MLW-SS	
D. PILOT STUDY			
Partner with MoH to select pilot villages	PI/LC	MLW	
Meet with community leaders to ensure project buy-in	PI/LC	MLW	
Train field and data team on tools and SOPs	PI	MLW	
Develop database for quantitative data	DM/PI	MLW	
Identify and obtain GPS coordinates for village and household boundaries	FM/PI	MLW	
Collect and analyse data for mapping exercises			
Conduct transect walks and mapping exercises in pilot villages	SS-RA/PI	MLW-SS	
Enter paper-based data into electronic files	TT	MLW-SS	
Conduct analysis of qualitative data	PI/ND/LC	MLW-SS	
Develop pilot social harms reporting system	PI/ND/LC	MLW-SS	
Collect and analyse data for feasibility, acceptability and accuracy study			
Identify and recruit households for accuracy study	FM/PI	MLW	
Identify and recruit peer organisations for accuracy study and FGDs	FM/PI/SS-RA	MLW-SS	
Identify and recruit household members for IDIs	FM/PI/SS-RA	MLW-SS	
Pilot tools and revise based on feedback	PI/FM/SS-RA	MLW-SS	
Conduct HTC/HIVST for accuracy study	FM/PI	MLW	
Conduct FGDs with peer groups	SS-RA/PI	MLW-SS	
Conduct IDIs with adults from randomly selected households	SS-RA/PI	MLW-SS	
Conduct quality and accuracy checks on collected data	PI/DM	MLW	
Enter paper-based data into electronic files	DM	MLW	
Clean quantitative data	DM/PI	MLW	
Transcribe and translate qualitative data	TT	MLW-SS	
Clean and code qualitative data	SSA	MLW-SS	
Conduct preliminary analysis of quantitative data	PI/LC/MN	MLW/LSHTM	
Conduct ongoing analysis of qualitative data	PI/ND/LC	MLW-SS	
Generate preliminary report on pilot findings	PI/LC/ND	MLW	
Conduct in-depth analysis of quantitative data	PI/LC/MN	MLW/LSHTM	
Conduct in-depth analysis of qualitative data	SSA/ND	MLW-SS	
Generate in-depth report on pilot indings	PI/LC/ND	MLW	
E. PROCESS EVALUATION			
Agree on key indicators and M&E data to be collected by PSI	PI/DM/MEO	MLW/PSI	

Assist PSI in developing M&E data collection tools and database	PI/DM/MEO	MLW/PSI	
Extract M&E data from PSI	DM/MEO	MLW/PSI	
Conduct preliminary analysis of M&E data	PI/LC	MLW	
Generate preliminary report on findings	PI/LC	MLW	
Conduct in-depth analysis of M&E data	PI/LC	MLW	
Generate in-depth report on findings	PI/LC	MLW	
F. DCE			
Collect and analyse data for DCE formative research (embedded in pilot study)			
Conduct DCE FGDs	RA-SS/PI	MLW-SS	
Develop scenarios and illustrations based on FGDs	FTP/PI	LSHTM/MLW	
Conduct DCE IDIs	RA-SS/PI	MLW-SS	
Conduct preliminary analysis of qualitative data	SRA/ERA	LSHTM/MLW	
Generate preliminary report on DCE findings	SRA/ERA	LSHTM/MLW	
Collect and analyse data for DCE (embedded in baseline household survey)			
Develop DCE survey based on qualitative research	ERA/SRA	MLW/LSHTM	
Pilot DCE survey and revise based on feedback	PM/PI	PSI/MLW	
Conduct DCE survey	PM/PI	PSI/MLW	
Conduct preliminary analysis of DCE data	SRA/ERA	LSHTM/MLW	
Generate preliminary report on DCE findings	SRA/ERA	LSHTM/MLW	
Conduct in-depth analysis of DCE data	SRA/ERA	LSHTM/MLW	
Generate in-depth report on DCE findings	SRA/ERA	LSHTM/MLW	
G. COSTING STUDY			
Meet with MoH to gain permission to access financial data	ERA	MLW	
Develop database for quantitative data	DM/ERA	MLW	
Train data team on tools and SOPs	PI/ERA/DM	MLW	
Collect user HTC cost data (as part of baseline household survey)	ERA/PI	MLW	
Collect provider cost data (as part of ART data collection)	ERA/PI	MLW	
Collect user HIVST cost data (as part of interim household survey)	ERA/PI	MLW	
Collect PSI HIVST financial data	ERA/PI	MLW	
Collect MoH HTC financial data	ERA/PI	MLW	
Enter paper-based data into electronic files	DM	MLW	
Conduct quality and accuracy checks on electronic data	PI/DM/ERA	MLW	
Clean quantitative data	DM/PI/ERA	MLW	
Conduct preliminary analysis of cost data	SRA/ERA	LSHTM/MLW	

Generate preliminary report on findings	SRA/ERA	LSHTM/MLW																					
Conduct in-depth analysis of cost data	SRA/ERA	LSHTM/MLW																					
Generate in-depth report on findings	SRA/ERA	LSHTM/MLW																					

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Addendum to COMREC submission

Study requirements

Requirements	Category	Item
1. Personnel	Core	Country research manager, admin offer/bookkeeper, administrator, driver*
	Field management	Field manager*
	Data management	Data manager, data collector, data clerk
	Quantitative/economics research	Quantitative research assistant, economics research fellow
	Qualitative research	Social scientist, assistant social scientist, translator/transcriber assistant
2. Training	Good Clinical Practice training (by COM prior to research implementation)	Country research manager, field manager*, data manager, data collector, data clerk, quantitative research assistant, economics research fellow
	Data management (by research coordinator and data manager prior to data collection)	Field manager*, data manager, data collector, data clerk, quantitative research assistant, economics research fellow, social scientist, assistant social scientist, translator/ transcriber assistant
	Protocol (by research coordinator prior to sub-study implementation)	Field manager*, data manager, data collector, data clerk, quantitative research assistant, economics research fellow, social scientist, assistant social scientist, translator/ transcriber assistant PSI: PSI lead, research and field staff, CBDAs MoH: ART facility staff
3. Data collection	Formative research and CRT	Paper-based forms, electronic tablets, audio recorded HIVST kits
4. Transport	Transport to and from research sites	

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Forms and Tools Guide

Form No.	Type	Form Name
PS01A	Information Sheet	Participant Information Sheet, Cognitive Interviews
PS01B	Consent Form	Consent Form, Cognitive Interviews
PS101	Qualitative	Cognitive Interview Guide
PS102	Tool	Prototype User Instructions
PS02A	Information Sheet	Participant Information Sheet, Policy and Regulation KII
PS02B	Consent Form	Policy and Regulation KII Consent Form
PS201	Qualitative	Policy and Regulation KII Guide
PS03A	Information Sheet	Participant Information Sheet, Acceptability/Feasibility and Accuracy
PS03B	Consent Form	Consent Form, FGD
PS03C	Consent Form	Consent Form, IDI + Formative DCE
PS03D	Consent Form	Consent Form, HIV Testing
PS301	Qualitative	Community Peer Group FGD Guide
PS302A	Qualitative	Random Household Adult IDI Guide - Individual
PS302B	Qualitative	Random Household Adult IDI Guide - Couple
PS303A	Quantitative	Demographic Questionnaire
PS303B	Quantitative	Self-Completed Test Results Form
PS303C	Quantitative	Exit Questionnaire - Individual
PS303D	Quantitative	Exit Questionnaire - Couple
PS04A	Information Sheet	Participant Information Sheet, Extended Baseline Questionnaire
PS04B	Consent Form	Consent Form, Extended Baseline Questionnaire
PS401A	Quantitative	Baseline HH Survey
PS401B	Quantitative	Baseline HH Survey – Brief Individual Questionnaire
PS402A	Quantitative	Extended Individual Questionnaire
PS501	Quantitative	CBDA Pre-Test Register
PS502	Quantitative	CBDA Post-Test Register
PS503	Quantitative	Self-Completed Questionnaire
PS504	Quantitative	Self-Referral Card

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