Reaching the First 90%: Cost-effectiveness of HIV self-testing services in Zambia

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ABSTRACT

Adult HIV prevalence in Zambia is approximately 12%, and an estimated 28% of people living with HIV remain undiagnosed. In 2016 Zambia adopted HIV self-testing (HIVST) as an additional approach to expand coverage and access to those in need of testing and who may not otherwise test. To inform HIV testing scale-up, this thesis aims to:

1. Assess state of the art in cost and cost-effectiveness analyses on HIV testing services in sub-Saharan Africa through a systematic review;
2. Estimate the costs of HIV self-testing in voluntary medical male circumcision (VMMC) and health facilities in Zambia; and
3. Evaluate the incremental cost-effectiveness ratio (ICER) of adding community-based (door-to-door) HIVST kit distribution to conventional facility-based HIV testing services (HTS) to reach people who otherwise will not access HTS while visiting health facilities in Zambia.

A systematic literature review summarized the literature on costs and cost-effectiveness analyses of HTS in sub-Saharan Africa over the past decade. The costs to test individuals through health facility, home-based, and mobile services are comparable; however, the costs are higher for campaign-style and stand-alone HTS. Moreover, the review shows that few studies have undertaken cost-effectiveness analyses of HTS. Different HIV testing models are potentially cost-effective but will increase HIV testing budgets. Thus, it is essential to do more cost-effectiveness and budget analyses of different combinations of HIV testing modalities to inform HIV testing policy and budgets.

A cost analysis of HIV testing (HTS and HIVST) across Malawi, Zambia, and Zimbabwe generated a detailed summary of observed resources used for HIV testing and how these vary across settings. The corresponding unit cost per community-based distribution by VMMC mobilizers are US$24.83 for Malawi and US$7.71 for Zimbabwe. The corresponding unit cost per HIVST kits distributed at the VMMC clinic are US$9.65, US$13.01, and US$7.71 for Malawi, Zambia, and Zimbabwe, respectively. For Zambia and Zimbabwe, the outpatient department (OPD) and integrated models distribution unit cost per kit distributed are US$15.81 and US$9.85.

Lastly, the age- and sex-specific Markov microsimulation model evaluated the costs and impact of a one-year HIVST program in Zambia. The model simulated 100,000 individuals over a 20-year time horizon. Using HIV Self-Testing Africa (STAR) consortium's endline survey data, the model inputs reflected observed uptake of HTS and assumed that only those

who had not tested within the last 12 months were eligible for home-based HIVST; these people could then accept or reject HIVST with its associated costs and consequences. ICERs were calculated for the intervention relative to the HTS status quo. Effects were presented building on the HIV prevention and treatment cascade framework, ultimately estimating disability-adjusted life years (DALY) averted. The age and sex-stratified Markov microsimulation model predicted that the implementation of community-based (door-to-door) HIVST distribution would avert more DALYs relative to the standard facility-based HTS. The ICERs for adolescent men and women ages 15-24 were $101.81 and $154.73 per DALY averted. The ICERs for men and women were $35.26 and $25.18 for ages 25-34 and $32.10 and $23.03 for ages 35-49.

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Most of all, thanks to my beloved Allah for all Your sense of humour throughout out my life, only to leave me with millions of Alhamdulillahs.

DEDICATION

This thesis is dedicated to the memory of my grandmother Zemzem Osman (Ummiyee), for showing me the path to higher education with conviction, tenacity, and resilience to serve others.

You are the light, and you live in me.

LIST OF ACRONYMS

ANC	Antenatal care
ART	Antiretroviral therapy
CBA	Cost-benefit analysis
CBDA	Community-based distribution agent
CDC	Centers for Disease Control and Prevention
CEA	Cost-effectiveness analysis
CHCT	Couple HIV counselling and testing
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
COMREC	Malawi College of Medicine Research Ethics Committee
CRT	Cluster-randomized trials
CUA	Cost-utility analysis
DALY	Disability-adjusted life year
GDP	Gross domestic product
GFATM	Global Fund to Fight AIDS, Tuberculosis, and Malaria
GHCC	Global Health Cost Consortium
HIA	HIV infection averted
HIVST	HIV self-testing
HTS	HIV testing services
ICERs	Incremental cost-effectiveness ratios
IHME	Institute of Health Metrics and Evaluation
ILO	International Labour Organization
Intl $	International dollars
LSHTM	London School of Hygiene and Tropical Medicine
LYG	Life years gained
M&E	Monitoring and evaluation
MRCZ	Medical Research Council of Zimbabwe
MWK	Malawian Kwacha
NSC	New Start Centre
OPD	Outpatient department
PHC	Primary health clinics
PEPFAR	President's Emergency Plan for AIDS Relief
PITC	Provider-initiated testing and counselling
PLHV	People living with HIV

PrEP	Pre-exposure prophylaxis
PMTCT	Prevention mother to child transmission
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PSI/Z	Population Services International Zimbabwe
QALY	Quality-adjusted-life-year
RCT	Randomized control trial
RDT	Rapid diagnostic test
SFH	Society for Family Health
STAR	HIV-Self-Testing Africa
STI	Sexually transmitted infection
UCL	University College London
USAID	United States Agency for International Development
UNAIDS	United Nations Programme on HIV/AIDS
UNICEF	United Nations International Children's Emergency Fund
UNODDC	United Nations Office on Drugs and Crime
UNZAREC	University of Zambia Biomedical Research Ethics Committee
US$	United States Dollar
US$ppositive	Cost per HIV-positive identified
US$pptested	Cost per person tested
VCT	Voluntary counselling and testing
VMMC	Voluntary medical male circumcision
VL	Viral load
WHO	World Health Organization
YLL	Years of life lost
YLD	Years lived with disability
ZMW	Zambian Kwacha

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THESIS OUTLINE

This is a paper style thesis with five chapters with appendices. This thesis presents three result papers, hereafter referred to as papers 1, 2, and 3 in chapters 2, 3, and 4 respectively. These three papers are linked by an overall introduction and description of the aims (chapter 1) and conclusion (chapter 5). The appendices include supplementary documents for paper 1 and paper 3 and the additional three supporting papers I co-authored as part of the HIV self-test in Africa (STAR) project.

Overall, this thesis aims to examine the cost-effectiveness of HIVST compared to the existing standard HIV testing services in Zambia. The outcomes from the systematic literature review on costs and cost-effectiveness of HTS in sub-Saharan Africa (Paper 1 – chapter 2), cost analysis (Paper 2 – chapter 3), and the Markov microsimulation model for cost-effectiveness analysis (Paper 3 – chapter 4) are investigated.

The introduction chapter (chapter 1) provides an overview of the HIV epidemic, national response to the epidemic, alternative HIV test services in Zambia, and discusses the research aim, objectives, and methodological approaches for the result papers. Chapter 2 reviews the theory and practice of economic evaluation in health care and systematic literature review findings on previous costing and cost-effectiveness studies of HTS in sub-Saharan Africa (Paper 1).

Chapter 3 presents the cost analyses of three models of HIVST distribution across Malawi, Zambia, and Zimbabwe (Paper 2). Chapter 4 examines a cost-effectiveness analysis of community-based (door-to-door) HIVST kits distribution (Paper 3). Chapter 5 brings together the key findings from the previous chapters and constructs emerging knowledge and empirical evidence from this thesis. It also highlights key policy recommendations and future research priorities.

CHAPTER 1 INTRODUCTION

1.1. Overview of HIV epidemics

Globally, approximately 37.9 million (32.7-44.0 million) people are living with HIV/AIDS in 2019. Eastern and Southern Africa account for 20.6 million adults and children living with HIV globally (1). In Eastern and Southern Africa, between 2000 and 2018, the number of new HIV infections decreased by 28%, the number of AIDS-related deaths by 44% and the incidence prevalence ratio by 3.9% (Figure 1.1) (1, p.22). In the previous decade, sub-Saharan Africa has scaled-up biomedical HIV prevention strategies (5, 6). These include HIV testing services (HTS), early HIV diagnosis, and early initiation of antiretroviral therapy (ART) (7, 8). Despite the findings from qualitative studies and population surveys demonstrating a high willingness for HIV testing, uptake of free facility-based HTS remains low (9-11). To increase linkage to ART and to maximize the public health impact of HTS, sub-Saharan Africa has yet to establish optimal testing and linkage strategies (12-16).

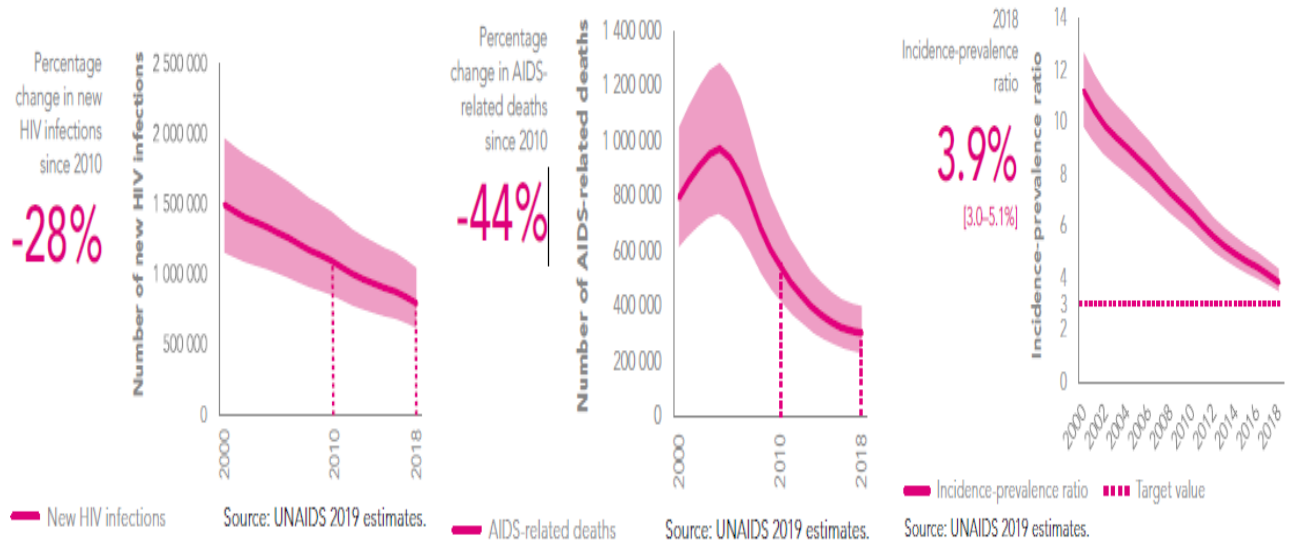

Figure 1.1 Number of new HIV infections, number of AIDS-related deaths, and incidence-prevalence ratio in Eastern and Southern Africa between 2000 and 2018 UNAIDS 2019 (1 p.22)

1.2. Zambian HIV epidemic and response

Zambia's total population is estimated at 17 million (17), and around 1.1 million people are living with HIV. There are 48,000 new HIV infections every year and a national HIV prevalence of 12% (14.6% among females and 9.3% among males) among adults ages 15-59 years (4). HIV prevalence rates among the female population ages 40-44 and 45-49 years are the highest: 29.6% and 23.0%, respectively (4). The HIV prevalence is four times higher among females ages 20-24 years (8.3%) compared to males (2.0%) (Figure 2) (4, p.48). Key drivers of the Zambian HIV epidemic include low rates of HIV testing, multiple concurrent sexual partners, low rates of male circumcision, mother to child transmission, commercial sex work, and migrant workers (4).

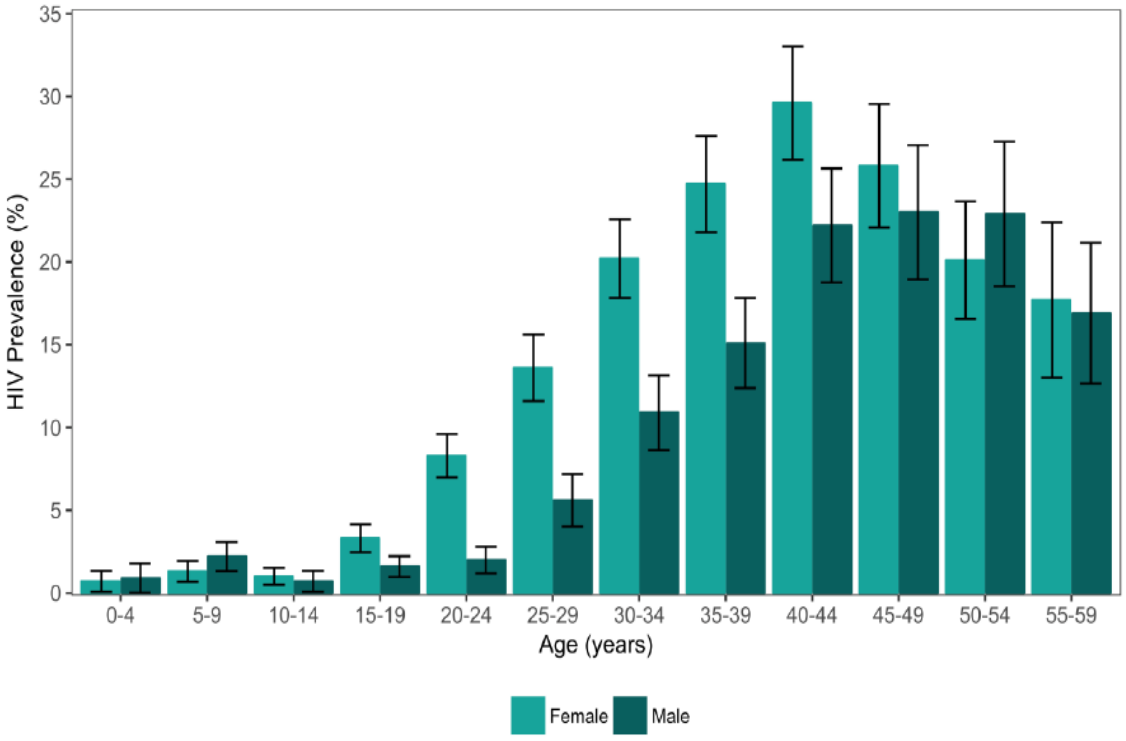

Figure 1.2 HIV prevalence among persons ages 0-59 by sex and age Ministry of Health Zambia 2019 (4, p.48)

Between 2000 and 2015 in Zambia, the number of new HIV infection and AIDS-related deaths decreased by 13% and 37%, respectively. However, the incidence prevalence ratio was 0.04, where the expected target was 0.03 (Figure 3) (1, p.71).

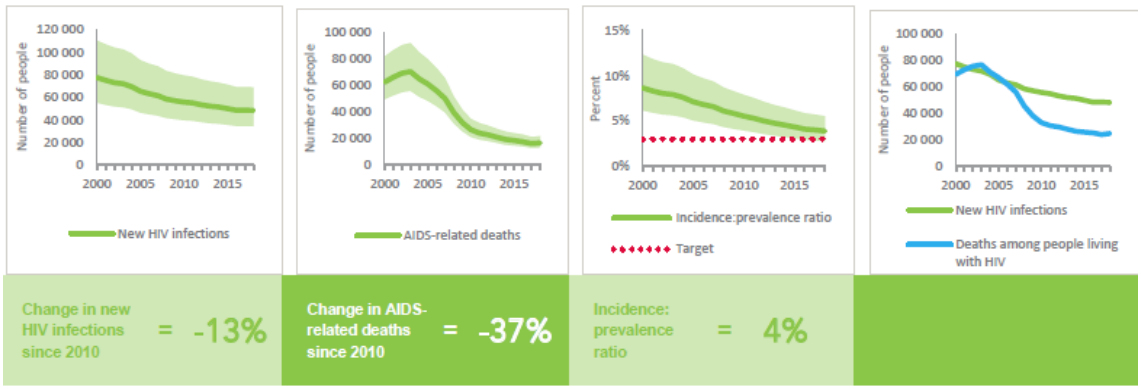

Figure 1.3 Zambian HIV epidemic estimates UNAIDS 2019 (1, p.71)

In 2014, United Nations Programme on HIV/AIDS (UNAIDS) launched the 90-90-90 targets for 2020: 90% of all HIV-positive persons know their status, 90% of those diagnosed are provided with ART, and 90% of those treated achieve viral load suppression. The latest report on the progress toward this aim among the population ages between 15-59 years showed that 71% of the population are aware of their HIV status, out of the 71%, 87% are on treatment, and out of the 87%, 89% are virally suppressed (Figure 4) (4, p.74). However, among young adults ages 15-24 years, only 41% (males) and 40% (females) are aware of their HIV positive status (4). For those ages between 15 and 49 years, only 59% (males) and 67% (females) self-reported knowing their HIV positive status (4). These findings showed that there are HIV testing gaps when the Zambian population is stratified by age and gender that fail to achieve reaching the UNAIDS 90-90-90 and the fast-track UNAIDS 95-95-95 targets to end the AIDS epidemic by 2030 (Figure 4) (18).

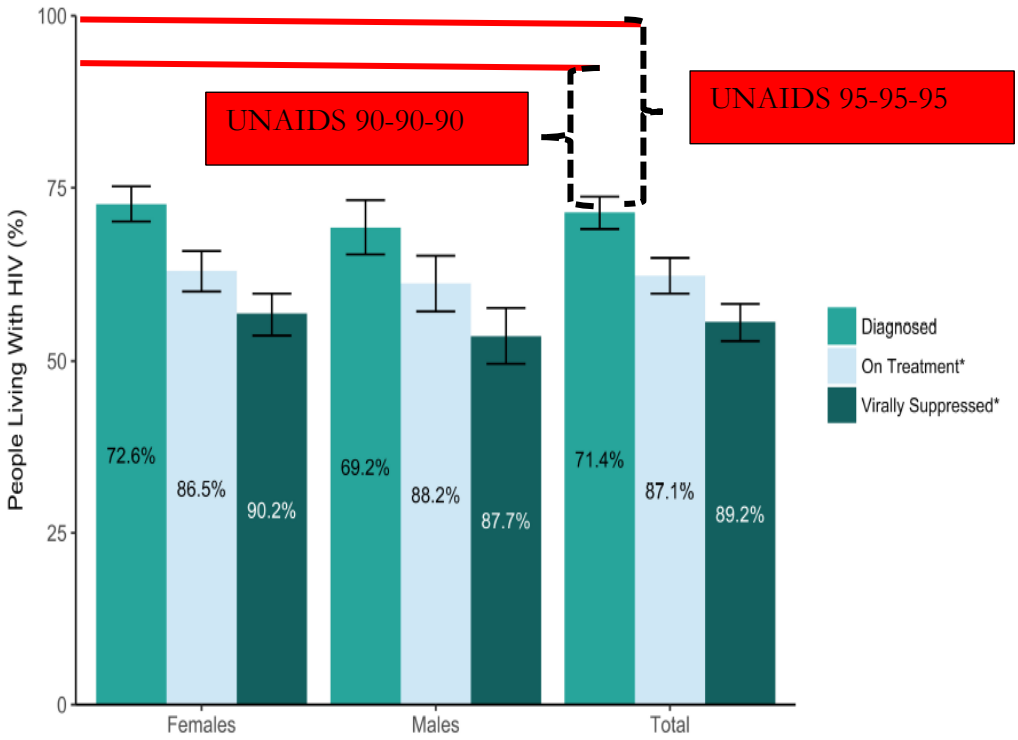

Figure 1.4 Zambia adult 90-90-90 and the gaps to reach 95-95-95 among adults ages 15-59 years (1, p.71), Ministry of Health Zambia 2019 (4, p74)

Many reasons have been mentioned for the gaps in HIV testing, including fear of abandonment by a sexual partner, fear of taking ART, and continued stigma around HIV in Zambia (19). The Zambian government continues its effort to increase HTS using alternative HIV testing modalities, including community-based testing, mobile outreach, and door-to-door testings (20). Yet, the most considerable gaps in meeting the 90-90-90 targets are among young people and men who do not know their HIV status. Therefore, the Zambian Ministry of Health (MoH) has recognized that HTS coverage remains below the UNAIDS targets, and it has supported research studies to investigate the addition of HIV self-testing (HIVST) to conventional HIV testing approaches to increase uptake of HIV testing among new and repeat testers (21).

Since 2015, the Zambian MoH has been working to introduce HIVST as an additional testing modality to meet its HIV testing targets. Evidence from other African countries has demonstrated the accuracy, acceptability, and performance of HIVST in general and key populations (22-28). However, more studies are needed to generate evidence on the costs and cost-effectiveness to have the HIV testing service distribute HIV self-test kits in Zambia. This is needed to inform programming decisions regarding a scale-up of HIVST in Zambia. Because the same budget will fund both HIVST provision and other MoH activities, it is essential to show comparative cost and effectiveness of HIVST to ensure optimal allocation of resources. These could potentially influence programming decisions about which HIV

testing service to include in the national HIVST scale-up plan (29). This thesis ultimately seeks to examine the impact of different HTS, the cost of distributing HIVST using different distributing modalities, and the cost-effectiveness of HIVST provision for one year compared to the existing standard HIV testing services in Zambia.

1.3. Different HIV testing services

The most recent published report, *Differentiated service delivery for HIV: A decision framework for HIV testing services,* categorizes HIV testing models into health facility, community-based, and self-testing (29). Health facility HIV testing services included the provision of HIV testing within the department of voluntary counseling and testing (VCT), antenatal clinic (ANC), and provider-initiated HIV counseling and testing (PITC) or outpatient department (OPD), and within voluntary medical male circumcision (VMMC) centres. Community-based HTS includes home-based, mobile, and campaign style HIV testing. Home-based HTS includes the provision of pre-test counseling, HIV rapid tests, and post-test counseling by a trained HTS provider in the client's home. Mobile HTS uses tents and mobile vans to provide HIV testing in different community locations, such as near markets, transport hubs, and open fields. The trained HTS provider selects the specific location on an ad hoc basis. Stand-alone HTS is immobile HTS located near transport hubs and markets where it serves community members. Self-testing is where a person performs and interprets his or her own HIV test, often in private. Self-testing can be done within health facilities or the community.

Delivering HIV testing services alongside other health interventions was more cost-effective than delivering either HIV testing or the other intervention alone (30, 31). Studies have found that the provision of either home-based HIV testing (32), mobile testing services (33), or HIV self-testing (34-37) in addition to routine facility-based HIV testing were potentially cost-effective at cost-effectiveness thresholds equivalent to one to three times the gross domestic product per disability-adjusted life year (DALY) averted, quality-adjusted-life-year (QALY) gained, or life year gained in the respective studies (38).

1.4. HIV self-testing

"HIV self-testing (HIVST) is a process whereby a person who wants to know his or hers HIV status collects a specimen, performs a test, and interprets the test result in private" (39, p.2). The specimen can be taken from a person in two different ways: the first one is a fingerstick test to extract a whole blood sample from a finger to detect evidence of antibody. The second technique is a mouth swab of oral mucosal transudate specimen; again, it is used to detect evidence of antibodies. HIVST is not considered a diagnostic HIV test, meaning it does not provide a definitive HIV positive diagnosis. A negative HIVST test result or non-reactive self-test results are considered negative; however, a positive or a reactive self-test results require a confirmatory HIV test according to the country's national HIV testing algorithms. WHO does not recommend HIVST for people with HIV who are on ART, as a false-negative HIVST result can occur. Retesting is highly encouraged for those at ongoing risk as a key population and those who reported HIV exposure in the preceding 12 weeks (40).

OraQuick® HIV Self-Test, which uses an oral mucosal transudate specimen, is manufactured by OraSure Technologies Inc. In 2012, the Food and Drug Administration (FDA) approved OraQuick as a rapid home-use HIV test kit (41). In 2016, the WHO issued new guidelines on HIV self-testing and partner notification, and in 2017 OraQuick was pre-qualified to increase HIV diagnosis and treatment (42, 43).

In line with 2016 WHO recommendation of HIVST, many countries developed their own HIVST guidelines to optimise HIVST implementation, including consideration of different service delivery models followed by effective linkage to care services. Key findings from HIVST systematic review showed that compared with standard facility-based HIV testing, the provision of HIVST increased the uptake of HIV testing, and the proportion of people diagnosed and referred to linkage to care services with HIVST are comparable to those with facility-based testing (40). The same WHO systematic review reported on the acceptability and feasibility of HIVST in a range of population and settings, the effectiveness of a range of HIVST service delivery models and the rarity of misuse and social harms associated with HIVST (40). The different HIVST service delivery models include: community-based, health facility-based, ordering online an receive via mail, secondary distribution (to partner or peers), retail outlets, pharmacies and vending machines, faith-based settings and workplace (40). Multiple studies also demonstrated the acceptability and accuracy of self-testing (22-24, 27, 44, 45). Lay users can perform confidential HIVST and interpret results effectively comparable to that of a trained healthcare provider. At present, the only HIV self-test kit

available in Zambia is the OraQuick ADVANCE rapid HIV I/II Antibody test (OraSure Technologies), which uses an oral mucosal transudate specimen. HIV self-testing has the potential to increase the proportion of the population who know their HIV status and ultimately lead to linkage to care for ART initiation.

1.5. HIV self-testing in Africa and the (STAR) project background

The Population Service International (PSI), in collaboration with the WHO, LSHTM, Liverpool School of Tropical Medicine, and University College London are implementing the self-testing in Africa (STAR) project with support from UNITAID. The STAR project has strategised its implementation work in two phases. Phase one was a two-year project from 2015-2017 in Zambia, Malawi, and Zimbabwe, and in-country institutes led the research activities: Zambart in Zambia, Malawi-Liverpool Wellcome Trust Clinical Research Programme in Malawi, and Centre for Sexual Health and HIV/AIDS Research in Zimbabwe.

In phase one, four different models for distributing HIVST were evaluated in Zambia, Malawi, and Zimbabwe. These four models were community-based door-to-door distributing agents (CBDA), voluntary medical male circumcision (VMMC), health facility (HF), workplace distribution models. In phase one, Zambia and Malawi conducted cluster-randomised trials and all three countries conducted robust economic evaluations, including 54 health facility costings.

In phase one, the overall evaluation of the STAR project showed that over one million HIVST kits were distributed: 628,705 in Malawi, 190,787 in Zambia and 265,091 in Zimbabwe. The community-based door-to-door distribution model distributed 519,658 HIVST kits compared with VMMC (23,561), health facility (21,183), and workplace (9,850). These different HIVST kits distribution models reached a higher proportion of men, young people, and first time testers in Zambia, Malawi, and Zimbabwe. Men constituted a higher proportion of first-time testers than women, (25.4% vs 17.7%) in Zambia, (27.9% vs 25.9%) in Malawi, and (16.2% vs 11.4%) in Zimbabwe. The young (16 to 24 years) and older men (>50 years) were the highest proportion of first-time testers (46).

The effectiveness of the community-based door-to-door distribution model was assessed using cluster-randomised trials in Zambia and Malawi. In Zambia, six matched-pairs catchment areas of clusters from four districts were selected. The clusters were randomised to receive HIVST in the intervention arm and the national standard HIV testing service in the control arm. The primary outcome was self-reported HIV testing within the previous 12

months and after 12 months of the intervention (HIVST). A total of 65,585 HIVST kits were distributed and HIV testing data were collected using a cross-sectional survey among individuals aged ≥16 years, living in households in randomly selected blocks in each cluster.

Despite the higher number of HIVST kits distributed, the results from the cluster-randomised trial on a community-based distribution of HIVST kits at population level among those who HIV tested in the last 12 months did not identify a significant impact on recent (last 12 months) or lifetime testing (RR 1.08, Adj 95% CI 0.94-1.24; p=0.15) (47). This study also showed that a higher proportion of surveyed adults in the intervention arm (HIVST) vs the standard of care arm (88.9% vs 31.5%) had heard of HIVST and ever self-tested (42.5% vs 8.3%). Before embarking on a cost-effectiveness analysis of HIVST compared with standard HIV testing, further investigation went into why the intervention (HIVST) did not significantly increase HIV testing at the community-level, considering novel HIV testing strategies had shown promise to expand access to HIV testing services (46). The investigation identified that the lack significant impact was attributable to poor targeting of the intervention population, with high rates of migration between the time that the baseline and end line survey were conducted. The fact that ineffective result was attributed to incorrect target coverage not to the intervention (HIVST) itself validated the importance of conducting cost-effectiveness analysis HIVST. In this thesis, chapter 4 explored the cost-effectiveness of HIVST in Zambia

was because of incorrect targeted coverage where the population migrated between the time when baseline and endline surveys were conducted. The fact that an ineffective result was attributed to incorrect target coverage and not to the intervention (HIVST) itself validated the importance of conducting cost-effectiveness analysis HIVST. In this thesis, chapter 4 explored the cost-effectiveness of HIVST in Zambia.

In Malawi, in contrast, the cluster-randomised trials in Malawi stratified 11 health facilities in the intervention arm and 11 health facilities in the control arm. The study found that the community-based door-to-door HIVST kits distribution model among those who self-reported HIV testing in the last 12 months significantly increases recent or lifetime testing (RR 1.33, Adj 95% CI 1.12-1.59; p=0.003) among populations in a rural setting, including men and adolescents (48). This study, however, did not identify a measurable impact on population-level ART initiation (RR 1.14, Adj 95% CI 0.75-1.75; p=0.52).

STAR's economic team conducted an economic cost analysis of community-based door-to-door HIV self-test kits distribution in Malawi, Zambia, and Zimbabwe and reported the unit cost per HIVST kit distributed. HIVST kits were distributed across 71 sites: 152,671 in Malawi, 103,589 in Zambia, and 93,459 in Zimbabwe, and reported an average cost per HIVST kits distributed of US$8.15, US$16.42, and US$13.84 in Malawi, Zambia, and Zimbabwe, respectively (49). In this thesis, the cost analysis (Paper 2) presents the cost of delivering HIVST kits within 13 VMMC services and 21 health facilities in Malawi, Zambia, and Zimbabwe. The cost-effectiveness analyses of HIVST in these three countries are underway.

Phase two of the STAR project (2017-2019) has adapted lessons from phase 1 to scaleup successful distribution models and evaluate the health impact of HIVST in South Africa, Swaziland, and Lesotho. The overall evaluation of the project is underway, including the multidisciplinary studies' findings. The evaluation is expected to inform policymakers, implementers, external donors, and new manufacturers about how to introduce HIV self-testing as part of a comprehensive HIV testing service in sub-Saharan Africa.

This thesis is embedded in the STAR phase one project in Zambia. The STAR project in Zambia has been assessing CBDA, VMMC, and HF models for HIVST distribution. This thesis will focus on the cost-effectiveness of CBDA (door-to-door) distribution of HIVST kits in Zambia.

1.6. Aim, research questions, and methodology

In this section, I present the: (I) aim and research questions, (II) conceptual framework and relevance to my hypotheses and methodology, (III) intellectual ownership, (IV) ethical considerations, and (V) conclusion.

Aim and research questions

The overarching aim of this thesis was to estimate the incremental cost and cost-effectiveness of community-based HIV self-test kit distribution compared to the standard of care HIV testing services in Zambia. The main research questions were as follows:

1. What is the cost of providing HIV testing in sub-Saharan Africa through different HIV testing models, and how does the scale of the service impact the costs (Paper 1)?
2. How much does self-test kit distribution cost within health facilities and within the community in Zambia (Paper 2)?
3. What is the incremental cost-effectiveness of community-based (mainly door-to-door) self-test kit distribution compared with the standard of care HTS in Zambia (Paper 3)?

Figure 5 presents how the three papers together provide key policy insight into evidence-based HIV testing programmes in Zambia.

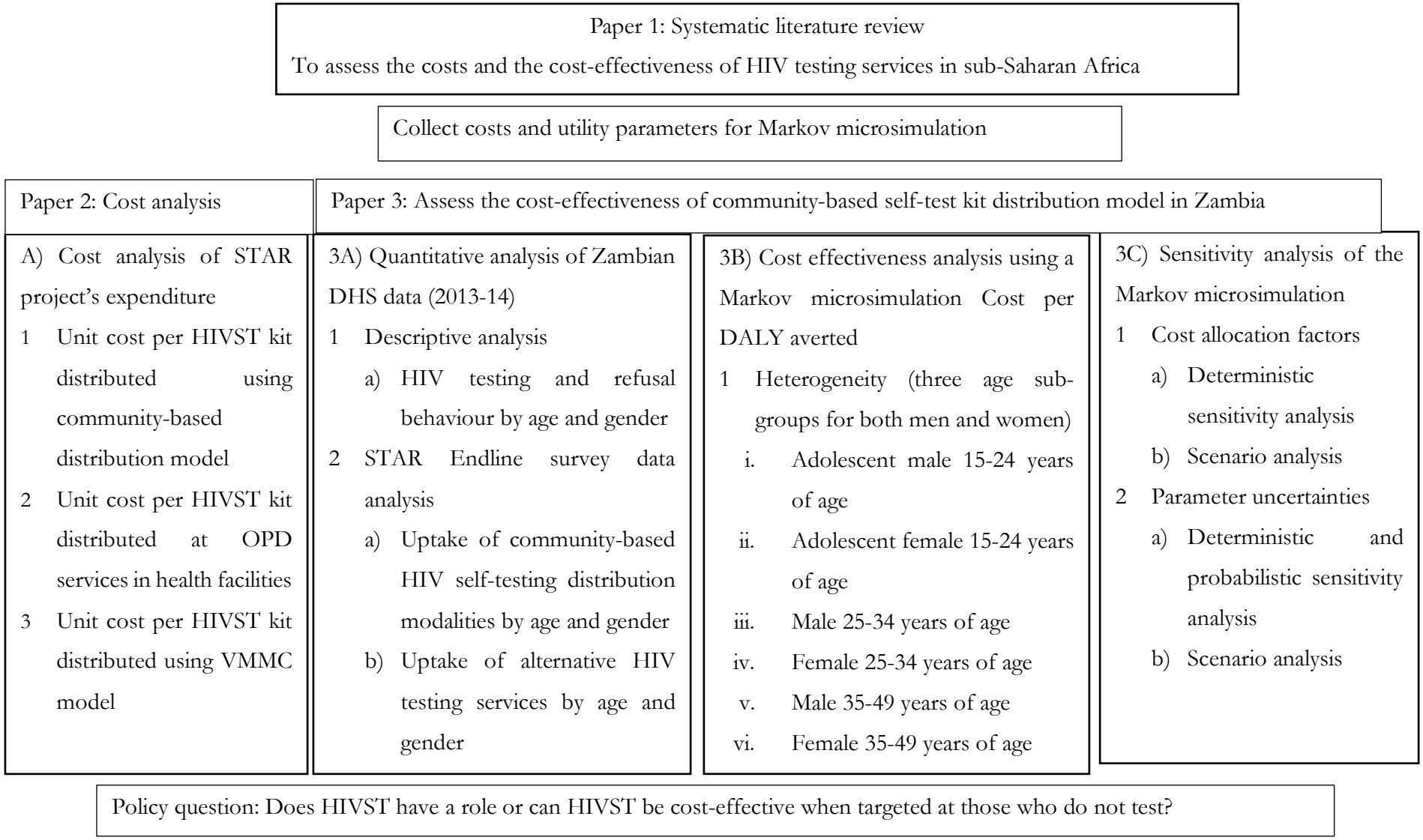

Figure 1.5 Framework of the study and linkage between chapters

1.7. Conceptual framework and relevance to hypothesis

The objectives of the three papers were developed based on the following hypothesis. First, the costs and cost-effectiveness studies are influenced by several factors, namely, study perspective, comparators, time horizon, discount rate, choice of health outcomes, measurement of effectiveness, choice of model, assumptions, and characterisation of uncertainty. These points are captured in Paper 1. The results from Objective Paper 1 are used to parametrise the Markov microsimulation model in Paper 3 and will identify the critical gaps in costs and cost-effectiveness studies of different HIV testing services in sub-Saharan Africa.

The STAR economic team led the cost analyses of three HIVST distribution models: (1) community-based distribution; (2) VMMC; and (3) outpatient department (OPD) services in health facilities. A colleague from Zimbabwe led the writing of a cost analysis of community-based HIVST distribution model for Malawi, Zambia, and Zimbabwe (50). In the cost analysis, I led the Zambian portion of data collection and analysis while also leading the cross country write up (Appendix II). The unit cost of community-based HIVST distribution helped to parametrise the Markov microsimulation model in Paper 3. I, as part of the STAR economic team, led the cost analyses of HIVST kit distribution through existing VMMC and outpatient department services for Malawi, Zambia, and Zimbabwe (Paper 2). Paper 2 also contributed methods identifying appropriate allocation factors for attributing shared HIVST programme costs to specific HIVST models and sites. These allocation factors are the methodological contribution to guide future cost analysis, particular in similar settings, using different cost inputs.

Second, concerning the "optimal investment in HIV prevention programmes," governments and donors place a strong emphasis on efficiency in HIV testing services, i.e., producing testing at the lowest possible cost. Thus, it is imperative to explore how the costs and cost-effectiveness of new health interventions, including HIVST, could be optimised with the lowest possible cost and/or highest impact in Zambia. Findings from Paper 3, which uses a Markov microsimulation model, are valuable for exploring the cost-effectiveness of HIVST because HIVST is an emerging technology in Zambia that may be added as an alternative HIV testing option to those who do not access facility-based HIV testing. Also, there is currently insufficient understanding of the use of different HIV testing approaches for HIVST distribution and of the costs and effectiveness of HIVST. It is possible that, despite

the tremendous progress being made toward achieving the UNAIDS 90-90-90 goals, the Zambian government and donors may consider HIVST too expensive and not cost-effective enough to incorporate into the national scale-up of testing. The Markov microsimulation model in Paper 3 follows individuals over time and accounts for heterogeneity by age and gender. It can, therefore, help address which specific age group and gender to target and how this can be achieved. The Zambian government may choose a stepwise approach to invest in expanding HIVST to a particular age-group or gender first (the most cost-effective option) then choose the next most cost-effective option and so on.

I conducted a descriptive quantitative analysis of Zambian Demographic Health Survey (DHS) data to capture the proportion of HIV testing and refusal behaviour and utilisation of alternative HIV testing services by three age groups of both men and women (51). I also analysed the STAR ndline survey data to provide the proportion of community-based HIVST distribution to the three male and female age groups. The cost analyses of the STAR project expenditure provided unit costs for community-based HIVST distribution models. All research questions and objectives (Table 1) were drawn together to develop the conceptual framework shown in Figure 5.

Table 1.1 Summarising research questions, research objectives, and corresponding methods

Research question (RQ)	Objective	Main method
RQ 1: What is the cost of providing HIV testing in sub-Saharan Africa through different HIV testing models, and how does the scale of the service impact on the costs?	Paper 1: To undertake a systematic literature review to assess the costs and the cost-effectiveness of HIV testing services in sub-Saharan Africa.	Systematic literature review.
RQ 2: How much does it cost to add HIV self-testing into male circumcision, outpatient, and HIV testing services in Malawi, Zambia, and Zimbabwe?	Paper 2: To estimate the costs of distributing HIVST through VMMC and OPD models in Zambia.	Cost analysis.
RQ3: Is community-based self-test kits distribution cost-effective compared to the standard of care HTS?	Paper 3: To assess the cost-effectiveness of community-based HIVST kit distribution model in Zambia.	Markov microsimulation model and optimization of ICERs.

1.8. Intellectual ownership

This research was undertaken as part of the STAR project supported by Unitaid which covered the cost of data collection. The cross-country cost analyses (Paper 2) were conceptualised by the STAR Economics team with my input. I led all stages of the Zambian portion of data collection and cost analysis in collaboration with Lawrence Mwenge.

I led all other elements of this DrPH research with the support of my supervisors, advisory committee members, and upgrading examiners. A summary of my role and contribution to the research activities in this thesis is provided in the Table 1.2.

Table 1.2 Summary of the role of the candidate in research activities

Component	Activity	Responsibility	Additional input
Preparatory work	Development of thesis objectives and work plan	NA, FTP	STAR
	Ethics submission and amendments	STAR	
	Local authority permissions	STAR	
Data collection	Cost data collection	NA, LM	FTP
	Cost analysis	NA, LM	FTP
	Selection of survey sites	STAR	
	STAR Endline survey enumeration	STAR	
	Survey Endline survey data analysis	NA	JO, FTP, STAR
Model development	Model design	NA	JO
	Model estimation	NA	JO, FTP, STAR
	Analysis of model results	NA	JO, FTP
	Interpretation of model results	NA	JO, FTP
Research Papers	Paper 1: A systematic literature review of costs and cost-effectiveness analyses of HIV testing services in sub-Saharan	NA	HH, FTP, JO, STAR
	Paper-2: Distributing HIV self-test kits through voluntary medical male circumcision services, outpatient departments, and integrated centres in Malawi, Zambia, and Zimbabwe: A cost analysis	NA	FTP, JO, HH, STAR

	Paper-3: Cost-effectiveness of community-based (door-to-door) HIV self-testing distribution models for HIV testing in Zambia: Markov microsimulation model	NA	JO, FTP, STAR
Supervision	Overall STAR project	FTP	STAR
	Overall DrPH thesis	FTP, JO, GM	

NA: Nurilign Ahmed, FTP: Fern Terris-Prestholt (Primary supervisor), GM: Graham Medley (Primary supervisor), JO: Jason Ong (Secondary supervisor), HH: Hendramoorthy Maheswaran (Advisory committee)**,** STAR Project (Helen Ayles, Lawrence Mwenge, Marc d'Elbée, Valentina Cambiano, Elizabeth Corbett, Karin Hatzold, Cheryl Johnson)

1.9. Ethical considerations

Ethics approval

This study was carried out according to the LSHTM standard on Good Research Practice (52). It was also approved by the University of Zambia biomedical research ethics committee and the National Health Research Authority (Zambia Ministry of Health) and is in line with applicable guidelines and regulations in Zambia. The Zambian DHS dataset was obtained upon consent from the DHS programme online database and was only used for this thesis.

Funding

The STAR research consortium funded by Unitaid partially supported this thesis. The National Institute of Health Fogarty Global Health Fellowship funded one year of doctoral work.

1.10. Conclusion

This thesis sought to synthesize and examine the gaps in cost and cost-effectiveness studies of HTS in sub-Saharan Africa. The cost analysis calculated the unit cost of HIVST distribution using VMMC and outpatient department models. The Markov microsimulation model estimated the cost-effectiveness of community-based (door-to-door) self-test kits distribution in Zambia. A wide range of data analyses techniques were used, including collaboration in primary costing data collection and analysis and secondary data analysis using Zambian DHS and STAR endline survey datasets. Results from all research questions were synthesized to provide policy recommendations.

CHAPTER 2 ECONOMIC EVALUATION OF NEW HEALTH INTERVENTIONS - PRINCIPLES AND USES

This chapter presents background information on economic evaluation methods and a systematic literature review on cost and cost-effectiveness studies of HTS in sub-Saharan Africa (Paper 1). This chapter seeks to understand the advantages and the disadvantages of different economic evaluation methods, and the systematic literature review aims to synthesize the extant literature and identify gaps in cost and cost-effectiveness studies of HTS in sub-Saharan Africa.

First, I present an overview of economic evaluation of new health interventions by summarizing key methodologies used to inform policymakers and funders. Second, I present a full systematic literature review paper along with the findings and rationale that inform the modeling work. Third, I summarize the key gaps and their implications for this thesis.

2.1. Economic evaluation of new health interventions

An economic evaluation of new health interventions systematically evaluates alternatives to optimize health gains within budget-constrained settings (53-55). This is achieved by evaluating the new intervention through the lens of cost and consequences (overall health benefits). Most policymakers and funders are willing to pay for an intervention whose specific cost and consequences are known. Consequently, economic evaluation is a tool that allows a comparison of the costs and consequences of alternative health interventions (53, 54, 56). This is done to inform policymakers using empirical evidence about which intervention delivers the maximum health benefit with minimum cost before adopting and expanding the new intervention. The integration of costs and consequences can commonly be evaluated through cost-effectiveness analysis, cost-benefit analysis, or cost-utility analysis.

2.2. Cost analysis

Cost analysis estimates the cost of a health intervention or service in a specific population, time, and location. The outcome of a measurement is expressed as a unit cost or an average cost of an intervention, service, or output (57). Unit costs are calculated as total cost divided by the unit of intervention for the service or output. The calculation of cost functions is applied when costs are determined by input cost, scale of production, or quality of the intervention being provided. Different types of costs are appropriate for different purposes: financial vs. economic cost, incremental vs. marginal unit cost. Financial costs capture the monetary values of the resources that are paid for while excluding the costs of donated goods and services. Thus, financial costs analysis focuses on money or health budgets that are planned to be spent or have been spent. Economic costs aim to capture the cost of paid resources, donated goods and services, and opportunity costs. In most functional markets, the price of resources reflects opportunity costs. Marginal cost is defined as the cost of producing an additional unit of output as service levels increase (57). Incremental cost captures the difference in cost between two or more interventions, services, or outputs (57).

2.3. Cost-benefit analysis

Cost-benefit analysis (CBA) compares the benefits and costs of interventions in monetary terms. Monetary values can be estimated through a group of individuals or society's willingness –to pay for years of life or improvement in health and well-being (53, 54). The

basic principle of CBA is that an intervention will improve a group of individuals or society as a whole if the benefit associated with the health intervention exceeds the costs. In CBA, both direct and indirect benefits and costs can be accounted for (53, 54). The advantage of CBA for decision making is that it allows for comparison across investments, e.g., education and health programmes.

2.4. Cost-effectiveness analysis

Given the difficulty of placing monetary values on life and health benefits, cost-effectiveness analysis (CEA) often provides more practical evidence to facilitate the decision-making process for policymakers (53, 54, 56). For instance, CEA can compare the cost of achieving a non-monetary value or natural unit of outcomes such as lives saved, infection averted, or viral load suppressed. CEA conceptually aims to produce more health benefits among alternative health interventions at the lowest possible cost. CEA has been applied to determine the most cost-effective means of different HTS to optimize HIV testing at the population level (30-37, 58-64). Moreover, CEA is a key step before undertaking a cost-benefit analysis, which compares the cost of intervention with its outcome valued in monetary terms. If there is a challenge in undertaking a CEA, it is improbable that cost-benefit analysis will be feasible (53, 54).

2.5. Cost-utility analysis: QALYs and DALYs

Cost-utility analysis (CUA) compares the cost of intervention with its outcome values in generic health outcomes (53, 54). Outcomes are presented either as cost per quality-adjusted life years (QALY) gained or cost per disability-adjusted life years (DALY) averted. The estimation of preferences for health states along with the cost is useful for decision-makers to maximize health gains and determine how best to allocate the existing budget across health areas.

QALY

Discounted QALYs are calculated as follows (65):

$$QALYs\ gained = \sum_{t=a}^{a+L^i} \frac{Q_t^i}{(1+r)^{t-a}} - \sum_{t=a}^{a+L} \frac{Q_t}{(1+r)^{t-a}} \qquad Equation\ (1)$$

Q is the health-related quality of life weight attached to the relevant period of life.

Q^t is a vector of health-related quality of life weights predicted (or observed) for each time period *t* following the intervention, while r is the discount rate expressed as a decimal

L is the duration of the disease in the absence of treatment, while L^t is the period over which the individual enjoys the benefits of treatment

a is the age of the individual

r is the discount rate

DALY

DALYs are calculated by adding the number of years lived with disability (YLDs), and the number of years of life lost due to premature mortality (YLLs) (66).

YLL = Number of deaths X life expectancy at the age of death

$$YLL\,[r,K,B] = \frac{KCe^{ra}}{(r+B)^2}\{e^{-\frac{r+B}{L+a}[-(r+B)(L+a)-1]-\ e^{-(r+B)a[-(r+B)a-1]}} + \frac{(1-K)}{r}(1-e^{-rL})$$

Equation 2

Where:

r = discount rate expressed as a decimal

K = age weighting modulation factor

C = constant

B= parameter from the age weighting function

a = age of death

L = standard expectation of life at age a (age of death)

A disability weight is a weight factor that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (death).

YLD = Number of cases X duration till remission or death

X disability weight for the condition

The formula for YLDs [*r, K, B*] differs from YLLs [*r, K, B*] by incorporating D (the disability weight) and different interpretation of **a** and **L** as described below:

$$YLDs[r,K,B] = \frac{D\{KCe^{ra}}{(r+B)^2}\left\{e^{-\frac{r+B}{L+a}[-(r+B)(L+a)-1]-\ e^{-(r+B)a[-(r+B)a-1]}} + \frac{(1-K)}{r}(1-e^{-rL})\right\}$$

Equation 3

Where:

r = discount rate expressed as a decimal

K = age weighting modulation factor

C = constant

B = parameter from the age weighting function

a = age of HIV diagnosed

L = duration of disability

DALY [r, K, B] = YLL [r, K, B] + YLD [r, K, B] *Equation (4)*

Therefore, the incremental cost-effectiveness ratio (ICER) of a health care intervention can be calculated by the difference in cost between two possible interventions divided by the difference in their effect (54).

$$ICER = \frac{C_1 - C_0}{E_1 - E_0} \qquad Equation\ 5$$

C_1 = Cost of the new intervention

C_0 = Cost of the status quo

E_1 = Effect of the new intervention

E_0 = Effect of the status quo

2.6. QALYs and DALYs - praise and criticism

The advantage of applying QALY as a measure of health outcome is that it combines the reduced morbidity (quality gained) and reduced mortality (quantity gained) into a single unit of measure (65, 67-70). The quality gain is the gain in health-related quality of life during the time the individual benefits from the intervention. The quantity gain is the amount of life extension gained by the intervention (69). The challenge with QALY is that it conflicts with the basis of equal health provision for all because it favours more treatable conditions and those with the potential for more excellent health (71).

On the other hand, DALY is a widely used measure of economic evaluations in low- and middle-income countries and is recommended by WHO for use in CEA (72). In principle, DALY assumes that every person is born to live in optimal health for a certain number of years (66, 73, 74). However, people can lose these healthy life years due to illness or by dying before average life expectancy (75). Thus, DALYs capture lost years due to morbidity, mortality, or both (66, 72-74, 76). Challenges with DALY include its implication with age-

weighting, discounting, and difficulties with distinguishing between measuring the burden of diseases and allocating resources (77, 78).

2.7. Modelling of health interventions – what is useful for policymakers?

In economic evaluation, decision-analytic models synthesize data from randomized control trials (RCT), clinical trials, or observational studies, or the literature to model an intervention beyond the research population, settings, or time to evaluate the intervention at the population or cohort level (53, 54). The systematic literature review on the CEA of different HTS in this chapter will present different modelling approaches that evaluated varying models of HTS within diverse settings and target populations. Despite the differences in research objectives and design, economic evaluation models aim to extrapolate the intervention's cost and health benefits over time while providing intermediate outcomes (for example number of positive cases identified, number of ART initiations, number retained in ART care, and number with viral load suppression) and a final utility measure (for example, cost per DALY averted). With the utmost transparency and sensitivity/uncertainty analysis, models often have to combine multiple data sources to parametrize the model.

Modelling studies using microsimulations, discrete event simulation or dynamic transmission models have been used for CEA of different HTS (31-37, 60, 62-64)(31-37, 60, 62-64). The two decision-analytic models of interest are decision tree models and Markov models. A decision tree model provides a logical structure for a decision and possible events over a fixed time horizon (53, 54). A decision tree is important because it provides a simple, logical decision structure with all HIV testing approaches available to the decision-maker. Markov models are based on a series of 'health states' that an individual can occupy and it simulates a hypothetical cohort's recurrent events through the set of health states over time (53, 54). One limiting assumption of the Markov model is that transitions to a state depend only on the current state and do not depend on the events that preceded, which makes the Markov model memoryless (53).

Policymakers in low and middle-income countries face difficult decisions about which healthcare intervention to invest in and which cost-effectiveness threshold (CET) to apply that truly reflect the likely health effects of changes in healthcare expenditures (79, 80). The traditional "WHO-CHOICE threshold (81)" of 1-3x GDP per capita has been criticized for

doing more harm than good (79). In the absence of a locally defined CET, countries may consider using half of gross domestic product (GDP) per capita (82, 83) instead of the previously suggested 1x-3 GDP per capita rule (72). The current GDP per capita for Zambia is US$1,430 (80). The cost-effectiveness threshold needs to reflect the opportunity cost of the health service forgone to provide for other interventions (79, 80). Because Zambia does not have a defined local threshold, this study considered Zambia's 1x GDP per capita per DALY averted as CET.

2.8. A systematic literature review of costs and cost-effectiveness analyses of HIV testing services in sub-Saharan Africa (Paper 1)

Overview of Paper 1

Cost and cost-effectiveness data on HTS can be used to parametrize models to estimate the incremental cost-effectiveness ratio of existing HTS or new testing technology in a given population, time, and place. However, it is vital to understand the gaps before applying the cost and cost-effectiveness estimates in an economic evaluation of HTS.

This research paper systematically reviews the cost and the cost-effectiveness of providing HIV testing in sub-Saharan Africa through various HIV testing modalities.

This chapter provides evidence as well as information about the gaps on the cost and cost-effectiveness estimates of various HIV testing modalities.

This paper is in preparation to be submitted to *AIDS* in July 2020. One supplementary document is included at the end of the thesis.

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Student ID Number	159519	**Title**	Miss
First Name(s)	Nurilign		
Surname/Family Name	Ahmed		
Thesis Title	Reaching the First 90%: Cost-effectiveness of HIV self-testing services in Zambia		
Primary Supervisor	Fern Terris Prestholt		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

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Where is the work intended to be published?	AIDS
Please list the paper's authors in the intended authorship order:	Nurilign Ahmed, Fern Terris-Prestholt, Jason J. Ong, Marc d'Elbée1, Stephanie Rotolo1, Cheryl Johnson, Valentina Cambiano, Hendramoorthy Maheswaran
Stage of publication	**Not yet submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I planned the conceptulization data search, extraction, data analyses and writing and reviewing of draft paper.

SECTION E

Student Signature	[redacted]
Date	23 Sep 2019

Supervisor Signature	[redacted]
Date	23-9-2019

Title: A systematic literature review of costs and cost-effectiveness analyses of HIV testing services in sub-Saharan Africa

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Keywords: Cost analysis, Cost-effectiveness analysis, HIV testing services, Sub-Saharan Africa.

Abstract

Objective: To review the costs and cost-effectiveness of HIV testing services (HTS) in sub-Saharan Africa.

Design: A systematic literature review of costing and cost-effectiveness studies reported from January 2006 to June 2019.

Methods: We searched ten electronic databases for studies that reported estimates for cost per person tested (US$pptested), cost per HIV-positive identified (US$ppositive), and cost-effectiveness (CE) analysis where health outcomes were quantified in quality-adjusted life years (QALYs), disability-adjusted life years (DALYs), HIV infections averted, or life-years gained (LYG). We explored variations in costs and CE estimates by different testing modalities. All costs are presented in 2019 US$.

Results: Fifty-four studies were identified: cost studies (n = 44), CE studies (n = 15), both cost and CE studies (n = 5), reporting estimates for six HIV testing modalities: health facility, home-based, mobile, self-testing, campaign-style, and stand-alone. The mean cost per test was lowest with self-testing services (US$11.94, range: US$8.89-US$14.23) and highest with campaign-style (US$40.64, range: US$13.78-US$57.93). The mean US$ppositive was lowest with self-testing services (US$79.583range: US$33.40-US$115.08) and highest with campaign-style (US$722.11). The 15 CE studies reported 31 estimates. For facility-based testing, the cost per HIV infection averted ranged from US$112.06 to US$44,203.96. Additionally, mobile-service compared to facility-based testing would cost US$1,952.23 per LYG. An additional provision of self-testing to the standard of care would result in ICER of US$280.23 and US$289.92 from a provider and societal perspective, respectively.

Conclusion: Home-based HIV testing and self-testing in the community and through existing health facilities were the least costly approaches. In general, the costs of the different testing modalities were comparable. Providing a combination of these modalities is more likely to achieve universal awareness of HIV status. The few cost-effectiveness studies identified highlighted the value of averting HIV transmission in targeting pregnant women and their sexual partners potentially through couples testing, home-based testing, or HIVST.

Key messages

- The costs to test individuals through health facility, home-based, and mobile services were comparable; however, the costs were higher for campaign-style and stand-alone HTS.

- Few studies have undertaken cost-effectiveness analyses of HTS models. Though expanding testing choice is likely to increase coverage, it comes at increased cost. More work is needed to identify the optimal combination of HTS models and funding strategies.

- Future cost and CE studies should follow standardized guidelines for estimating and reporting cost and cost-effectiveness estimates using the Global Health Cost Consortium (GHCC) reference case and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist, respectively, to better allow for evidence synthesis.

Research in context

Evidence before this study

Previous systematic reviews (84-86) have assessed either the cost or cost-effectiveness of HIV prevention. They reported costs for different HIV testing modalities across different setting, populations, and contexts.

Added value of this study

In our study, we systematically reviewed the findings of previous costing and cost-effectiveness studies of HIV testing services in sub-Saharan Africa. We explored how the costs of different testing modalities vary by the costs per person tested for HIV and costs per HIV-positive case identified. Our study systematically reviewed both the cost and cost-effectiveness of HIV testing services to adequately inform HIV testing planning with the most up to date economic evidence by including studies published after the year 2006. We used the Global Health Cost Consortium (GHCC) reference case and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statements to assess the quality of cost and cost-effectiveness studies, respectively.

Implications of all the available evidence

Our findings add to existing publications reviewing the cost-effectiveness of HIV testing services in sub-Saharan Africa. Together, they will help policymakers better understand optimal and affordable approaches to delivering universal access to HIV testing.

Introduction

HIV continues to be a major global health concern affecting 37.9 million people, with 1.7 million newly infected every year (1). Eastern and Southern Africa (ESA) continue to be disproportionately affected, accounting for 45% of incident HIV infections and 53% of people living with HIV (PLWH) globally (87). Out of the 53% PLWH in ESA, 19% (3.1 million PLHIV) remain undiagnosed (87). The UNAIDS 90-90-90 targets recommend that by 2020, 90% of all PLHIV should know their HIV status, 90% of individuals diagnosed with HIV infection should receive antiretroviral therapy (ART), and 90% of those on ART should be virally suppressed to end the HIV epidemic (88). At the end of 2017, only 81% of PLHIV knew their HIV status (87, 89). Disparities in HIV testing coverage, knowledge of HIV positive status among men and adolescents, and mortality from HIV in men remain major concerns (90-92). Universal access to HTS is also essential to ensure uninfected individuals at risk of HIV infection are referred to effective HIV prevention interventions, including voluntary male medical circumcision (VMMC) and pre-exposure prophylaxis (93-102).

HTS are abundant in many African countries with testing delivered in health facilities and various other testing modalities such as home-based, mobile-service, campaign-style, and stand-alone HTS, by a range of healthcare professionals and more recently with users able to self-test for HIV. These testing approaches have been found to have varying degrees of success, with evidence suggesting Africans prefer HIV testing to be delivered closer to their homes or provided through more convenient and confidential approaches like HIV self-testing (103-114). Policymakers striving to ensure universal access to HTS in Africa need to balance these objectives with the financial pressures they face to ensure cost-efficient spending. In order to achieve this, they urgently need to better understand the costs and cost-effectiveness of different HIV testing modalities.

In this study, we sought to systematically review the findings of previous costing and cost-effectiveness studies of HTS in sub-Saharan Africa. First, we explored how the costs of different testing modalities vary by outcomes, such as costs per person tested for HIV and costs per HIV-positive case identified. Second, we reviewed all cost-effectiveness studies and presented results such as DALY, QALY, $/LYG, $HIA, $/DALY or $/QALY. The implications of the findings for the variation in reported cost and cost-effectiveness estimates and identified cost drivers are discussed.

Methods

This systematic review aims to review the costs and the cost-effectiveness of different HIV testing modalities in sub-Saharan Africa. The review was limited to sub-Saharan Africa because it experienced a generalized epidemic. A description of the different HIV testing approaches in sub-Saharan Africa is provided in Table 2-1 (29) and is used to classify studies into models. Study results are also categorized as cost or cost-effectiveness depending on how the results are presented.

Table 2.1 Definition of model HTS included in the review (29)

HTS model	Description
Health facility	Health facility HIV testing includes the provision of pre-test counseling, HIV rapid tests, and post-test counseling offered to clients within the department of voluntary counseling and testing (VCT), antenatal clinic (ANC), and provider-initiated HIV counseling and testing (PICT) or outpatient department (OPD).
	HTS provided within voluntary medical male circumcision centres.
Community-based	Home-based HTS includes the provision of pre-test counseling, HIV rapid tests, and post-test counseling by trained HTS provider in the client's home.
	Mobile HTS uses tents and mobile van to provide HIV testing in different community locations such as near markets, transport hubs, and open fields. The trained HTS provider selects the specific location on an ad hoc basis.
	Campaign-style HIV testing uses more accessible community spaces that are organized by the MoH or specific organizations. It is more connected to the community, and it is designed to address specific community needs.
	Stand-alone is immobile HTS located near transport hubs and markets where it serves community members.
Self-testing	Self-testing is where a person performs and interprets his or her own HIV test, often in private. Self-testing can be done within health facilities or the community.

Search strategy and identification of studies

The literature searches were undertaken in December 2019 and updated on May 2020. We searched ten databases: Medline, PubMed, Embase, Popline, Scopus, Global Health, COCHRANE, Social Policy and Practice, Web of Science, and Tuft University cost-effectiveness analysis registry (115). The search terms were formulated around the following three concepts: (1) HIV, (2) HIV testing (including couples testing and self-testing), and (3) cost and cost-effectiveness analysis. Authors and experts in HIV economics were contacted by email for any further references, missing outcomes, and clarifications. References of included studies were reviewed for additional relevant articles. The full search strategy is described in Supplementary Table S2.

Inclusion and exclusion criteria

Studies were eligible for inclusion if they reported any costs or cost-effectiveness estimates for HTS in a sub-Saharan African country. This included unit cost -- cost per person tested (US$pptested) and cost per HIV-positive case identified (US$ppositive) -- and for cost-effectiveness studies cost per HIV infection averted (HIA), cost per life-year gained (LYG), cost per disability-adjusted life years (DALYs) averted or cost per quality-adjusted-life-years (QALYs) gained. Studies were included in the analysis more than once if they had reported the results of costs for more than one HIV testing model. We included studies that explored HIV testing in all population groups except those that focused on infant HIV testing. The language was limited to English, including original or translated sources. Supplementary Table S1 provides detailed PICOS (Population, Intervention, Comparators, Outcomes, and Study type), inclusion, and exclusion criteria.

Study selection and data extraction

Two independent reviewers (N.A. and S.R.) scrutinized titles and abstracts independently for eligibility according to the inclusion criteria. Discrepancies were resolved through discussion and consensus by reviewing the full study. N.A reviewed full studies and created the data extraction template using the Global Health Cost Consortium (GHCC) reference case (116) and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (117) checklist to characterize eligible studies. This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Supplementary Table S2-3) (118).

For each included study, we first classified the studies by whether they undertook a cost analysis, cost-effectiveness analysis, or both. Studies were deemed to have undertaken a cost analysis if they only estimated the costs of delivering the HTS and related this to either the number of HIV tests performed, or a number of HIV-positive individuals identified. Studies were deemed to have undertaken a cost-effectiveness analysis if they compared one HIV testing modality to either provision of no HTS or another HIV testing modality and reported results such as (but not limited) DALY, QALY, $/LYG, $HIA, $/DALY or $/QALY.

Cost studies

For cost studies, we extracted data on the country of the study, HIV testing modality, costing year, costing perspective, costing method, the total number of HIV tests provided, the total number of HIV-positive cases identified, cost per person tested (US$pptested) and cost per HIV-positive individual identified (US$ppositive). For US$pptested, the total costs of a given HIV testing modality were divided by all individuals that were tested (the sum of person tested HIV negative and person newly tested HIV positive : $\text{US\$pptested} = \frac{total\ cost\ a\ given\ HTS}{(\text{Person tested HIV}-)+(\text{Person tested HIV}+)}$. For US$ppositive, the total costs of a given HIV testing modality are divided by all individuals that newly tested HIV positive: $\text{US\$ppositive} = \frac{total\ cost\ a\ given\ HTS}{\text{Person tested HIV}+}$. For studies that reported costs for a package of interventions targeted at HIV testing services and other health provisions, such as family planning or TB, we subtracted cost for other health provisions and only reported costs that were part of the HIV testing services to improve the comparability of studies. For the costing year, we extracted the year the costing exercise was conducted, rather than the year the study was published. For studies that did not report the costing year, we assumed it to be the year before the publication date. The included studies reported costing perspectives using different terminologies. We categorized the costing perspective as provider, patient, or societal. A provider perspective captured the costs an organization spent to deliver the health intervention, a patient perspective only included the costs incurred by the users, and societal perspective included all the costs incurred by the organization delivering the intervention and by the users and possibly second or third parties affected (119).

We classified the costing methods used at three levels. First, we determined whether the researchers had estimated incremental or full costs. The incremental costs estimate the cost of adding a new health intervention onto an existing health programme by reporting the additional capital and recurrent costs incurred without accounting for the cost of the existing

infrastructure and overhead costs borne by the existing health programme. An incremental cost analysis may underestimate the cost of delivering a new health intervention or the investment needed to sustain current provision (54). By contrast, a full cost analysis includes the costs of all resources used to introduce the new health intervention, including the infrastructure and overhead costs. Second, we determined whether the costs represent financial or economic costs. Financial costs estimate the actual expenditure on goods and services purchased. Economic costing estimates the value of all resources used, including donated goods and services (120). Third, we determined whether the cost represented estimates from primary costing studies or modelled costs. Primary costing studies are ones that observed actual resource use in order to estimate costs, whilst modelled costs are ones that assumed likely resource use in order to estimate costs (120).

Cost-effectiveness studies

For studies that reported findings from a cost-effectiveness analysis, we extracted data on the country of the study, costing year, study perspective, HIV testing modalities compared, and the incremental cost-effectiveness estimate. We extracted the incremental cost-effectiveness estimate for each comparison of HIV testing modality undertaken. Measures of effectiveness included HIA, LYG, DALY, and QALY.

Study quality assessment

Two independent reviewers (N.A. and M.D.) assessed the quality of the costing methods using the GHCC reference case (116). The GHCC is comprised of 17 principles to guide the process of cost estimation; for each cost study, we assessed whether the study had met these guidelines (Table S4). The CHEERS checklist consists of 24 items to guide the minimum amount of information that should be included when reporting economic evaluations (117). We applied the CHEERS checklist to summarise the quality of cost-effectiveness studies (Table S5). These two scoring systems explore reporting of different issues and therefore may result in discrepancies. A detailed quality assessment for individual studies is included in Supplementary Tables S6 and S7.

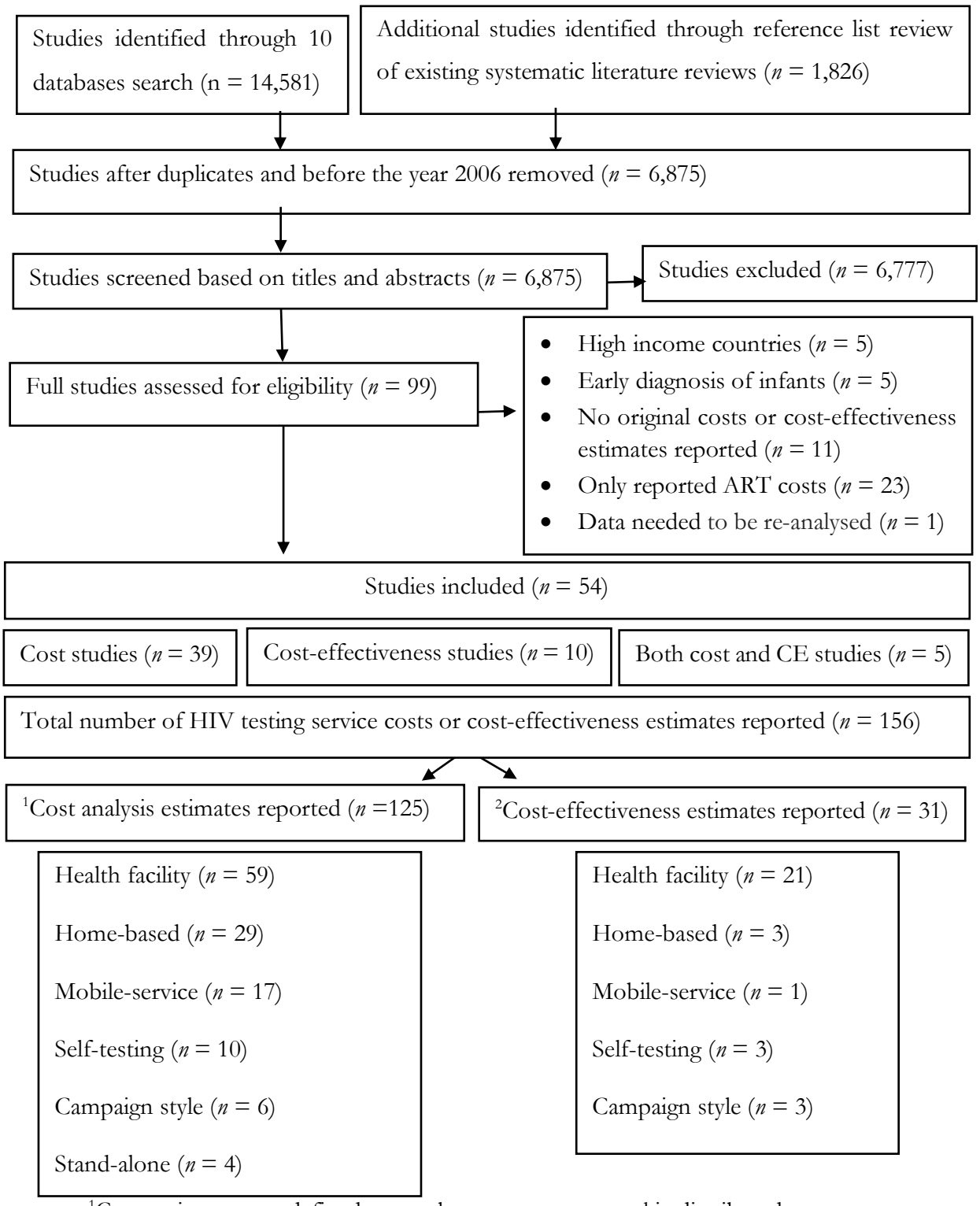
Data analysis

All cost and cost-effectiveness estimates were adjusted for inflation using local inflation rates and consumer price index and are expressed in 2019 US dollars based on the World Bank's consumer price index (121) and the official exchange rate (122). First, costs expressed in US$ were converted back to the local currency using the World Bank's exchange rate based on

the time the cost analysis was done. Second, the costs were inflated using the World Bank's consumer price index and converted back to US$ using the exchange rate of the base year (2019)(123). It is important to estimate costs using purchasing power parities and health care specific indices in different countries by applying purchasing power parities conversion factors to the non-tradable portion of the costs. This was impossible, because not all costs in the literature review were clearly presented into tradable and non-tradable cost inputs. This systematic literature review did not conduct a meta-analysis on cost and cost-effectiveness estimates due to variation in HTS approaches, population served, costing perspective and costing methods in different African countries. Moreover, to conduct a meta-analysis of economic evaluation, *Crespo et al.* suggest using net monitory benefit. Unfortunately, in SSA, we don't have a formal ICER threshold, which is required to determine NMB. Thus, it is not possible to conduct a meta-analysis (124).

Results

We identified 99 eligible studies out of 6,875 abstracts and the findings from 54 studies are included in our review (Figure 2-1). Table 2-2 summarizes the findings from studies that only undertook a cost analysis (n = 39), and Table 2-3 shows findings from studies that undertook cost-effectiveness analysis (n = 10). Five studies undertook both cost and cost-effectiveness analyses and are presented in both tables, presenting the unit cost results separately from cost-effectiveness results.



[1]Cost estimates are defined as total cost, cost per test kit distributed, per person tested, and per HIV + person identified

[2]Cost-effectiveness estimates are defined as having effect present in QALYs, DALYs, HIA or LYG

Figure 2.1 PRISMA flow diagram of the systematic literature review

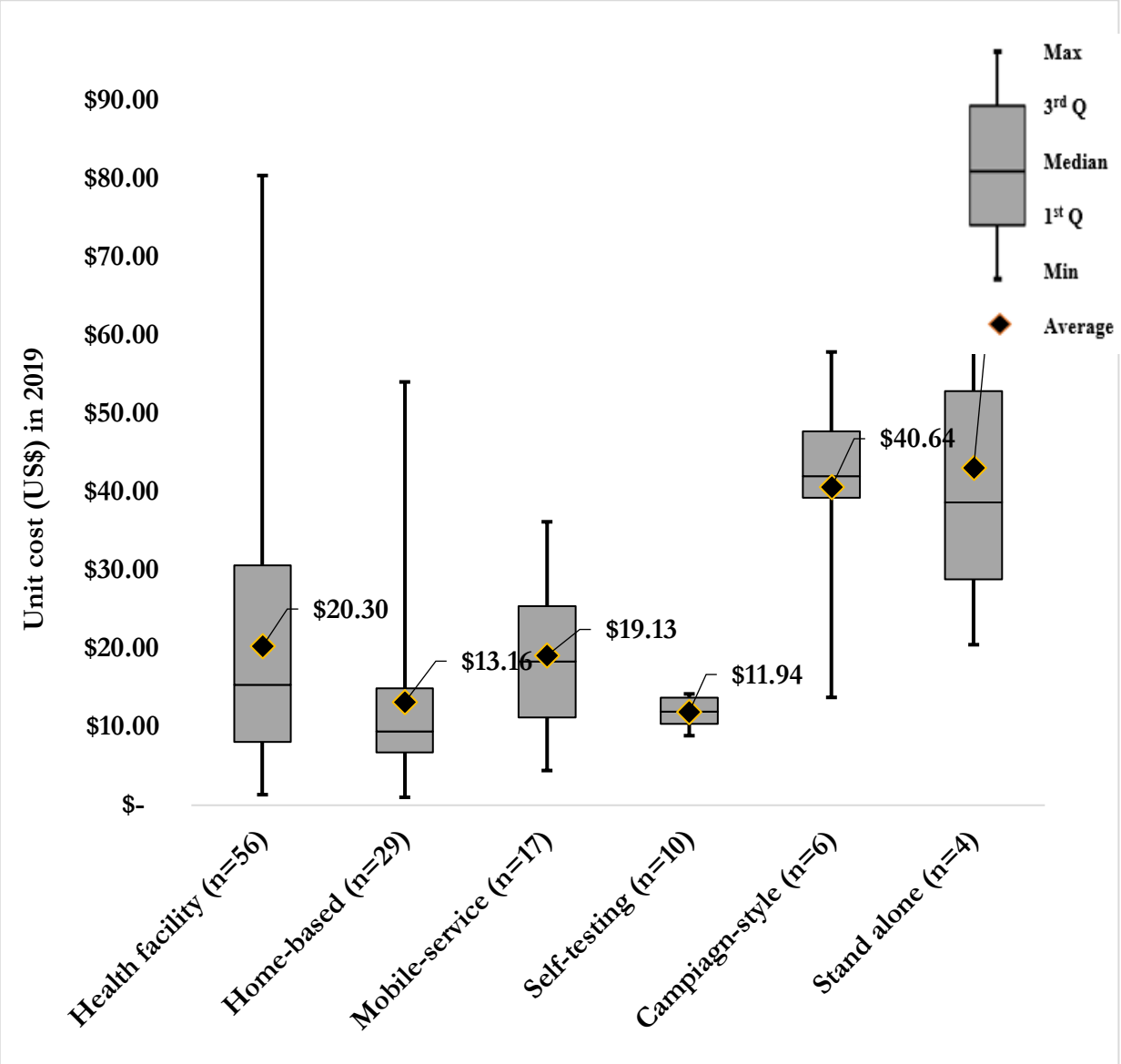
Cost analysis studies

The 44 studies (39+5) that undertook cost analysis represented findings from 13 countries in sub-Saharan Africa: 28 were from Southern Africa, 20 were from East Africa, three were from West Africa, and two were from sub-Saharan Africa. For costing perspectives, 43 studies presented costs from the providers' perspective, one study presented patients' perspectives, and one study presented both provider and societal perspectives. For costing methods, 29 studies undertook incremental costing, 12 studies undertook a full costing method, and three studies modelled costs from another study. Twenty-four studies reported the financial costs, 17 studies reported the economic costs, and three studies modelled costs from another study. Of the 44 studies, primary (empirical) costing was undertaken to estimate costs in 41 studies, whilst in three studies estimates were modelled based on likely resource use. Ten studies did not report the costing year (Table 2-2). The 54 studies present 123 cost estimates of different HIV testing modalities. Out of the 123 reported cost estimates, 59 reported costs for facility-based HTS, 29 home-based testing, 17 mobile services, 10 self-testing, 5 campaign-style, and 4 stand-alone HTS.

Figure 2-2 shows the estimates for US$pptested by HIV testing modalities from provider perspectives. For facility-based HTS, the mean US$pptested was US$20.30 (range: US$1.35-US$80.48) (30, 32, 59, 61, 97, 125-141) and for home-based testing, the mean US$pptested was US$13.16 (range: US$1.01-US$54.10) (130-132, 137, 140, 142-151). For mobile-service services, the mean US$pptested was US$19.13 (range: US$4.43-US$36.22) (33, 125, 137, 145, 146, 148, 149, 152-154). For self-testing, the mean US$pptested was US$11.94 (range: US$8.89-US$14.23) (50, 155, 156). For campaign-style, the mean US$pptested was US$40.64 (range: US$123.78-US$57.93) (154, 157, 158). For stand-alone HTS the mean US$pptested was US$43.12 (range: US$20.52-US$74.63) (130, 153). For the one study that reported costs from patients' perspective, the US$pptested ranged from US$1.35 to US$2.37 (138) (Figure 2-2). Most results were identified from facility-based testing (n = 55) with only ten estimates for HIV self-testing.

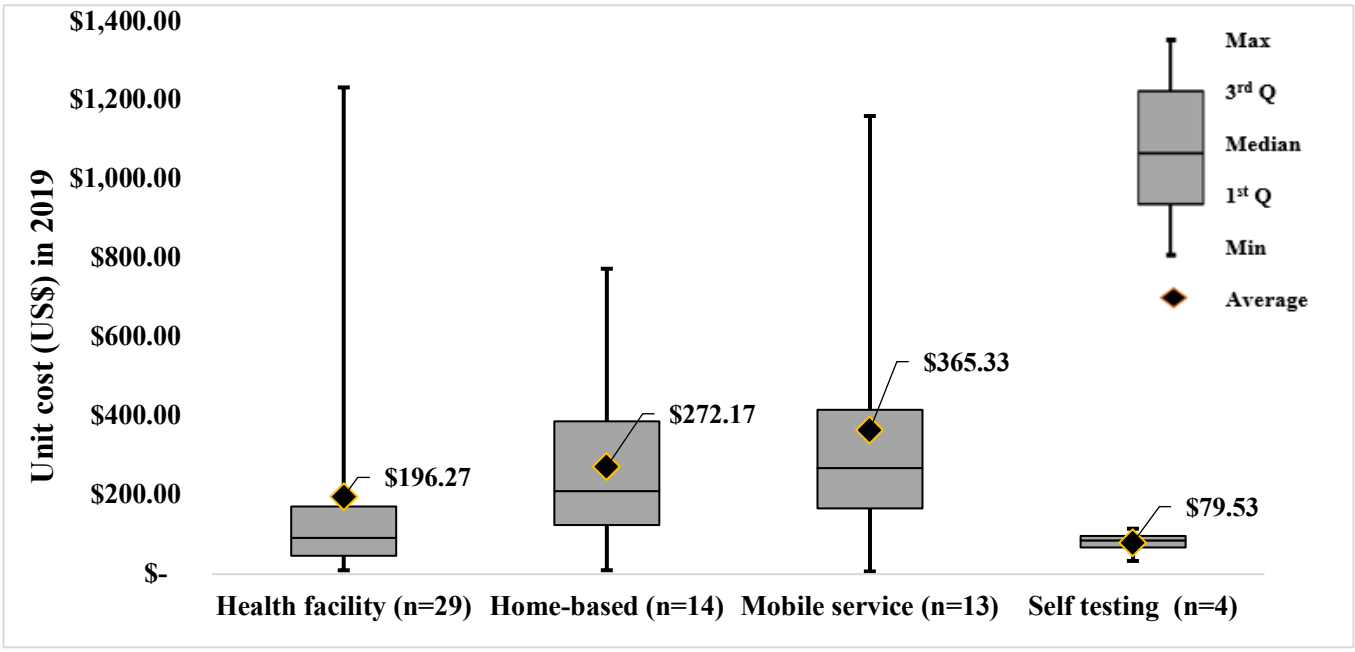
Figure 2-3 shows the estimates for US$ppositive by testing modality. For facility-based HTS, the mean US$ppositive was US$196.27 (range: US$9.69-US$1,823.04) (59, 127, 128, 130, 132, 133, 139, 141) and for home-based testing, the mean US$ppositive was US$272.17 (range: US$9.87-US$773.70) (130, 132, 143-151). For mobile-service services, the mean US$ppositive was US$365.33 (range: US$6.74-US$1,160.67) (127, 145, 146, 148, 149, 152-154). For self-testing, the mean US$ppositive was US$79.53 (range: US$33.40-US$115.08)

(156). For campaign-style, the mean US$ppositive was US$723.11 (154). For stand-alone, the mean US$ppositive was US$215.11 (range: US$107.15-US$323.08) (130) (Figure 2-3).



***One study reported the unit cost of US$200.63 per person tested for the second round of first-time testers for home-based testing (144).**

Figure 2.2 Unit cost per person tested by mode of HIV testing services in 2017 US$



*One study reported the unit cost of US$1823.04 per case identified for health facility PMTCT testing (128).

Figure 2.3 Unit cost per HV+ case identified by mode of HIV testing services in 2017 US$

Table 2.2 Summary of HTS cost studies included 2006-2019 in 2019 USD (n = 43)

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Adebajo, 2013 (125)	Nigeria	Health facility	Clients at a health facility	Provider	Inc/Fin/Emp	44.92	-	1,988	177	Not specified
		Mobile service	Mobile service-referred clients			9.49	-	14,726	480	
		Mobile service	Peer-led mobile service			6.51	-	14,895	1,853	
Ahmed, 2018 (155)	Zambia	Self-testing	Clients at a health facility	Provider	Inc/Fin/Emp	13.34	-	12,885	NA	• Training • Sensitization • Building and storage • Equipment
			Clients at the VMMC centre			11.50	-	11,330	NA	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			Community-based HIVST			14.23	-	103,589	NA	• Vehicles and bicycle • Recurrent training • HIV self-test kits • Personnel supplies • Vehicle operation and maintenance • Building operation and maintenance • Other recurrent
Aliyu, 2012 (159)	Nigeria		Clients at a health facility[1]	Provider	Inc/Fin/Emp	9.69	-	NS	NA	• Rapid test kits and other

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
		Health facility	Clients at a tertiary facility			24.23	-	NS	NA	

			Clients at secondary facilities			8.28	-	NS	NA	• Rapid test kits and other medical consumables for HTC • Health commodities (ARV, opportunistic infections drugs, laboratory reagents and other medical consumables for ART • Infrastructure (structure, furniture, and equipment) • Human resources

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
										• Training • Global HIV/AIDS initiative in Nigeria (GHAIN) technical support

Allen, 2014 (126)	Zambia	Health facility	CHCT at a health facility	Provider	Inc/Fin/Emp	41.02	-	68,000	NA	• Overheads • Training in counseling • Training in promotional and data recording and equipment • HIV test kits and supplies • Monitoring and evaluation • Salaries for counselors and promotion agents and trainers • Salaries for monitoring and

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
										evaluation staff • Vehicle fuel and maintenance • Administrative supplies • Back-up test kits
Armbruster, 2010 (142)	Malawi	Home-based	Home-based-contact tracing of the current husband in high awareness scenario	Provider	Inc/Fin/Emp	9.11	-	91	NA	• Tracing • Providing HTC

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			Home-based-contact tracing of a formal husband with high awareness scenario			5.06	-	82	NA	
			Home-based-contact tracing of a non-marital partner with high awareness scenario			4.05	-	184	NA	
			Home-based-contact tracing of a current husband with low awareness scenario			2.02	-	91	NA	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			Home-based-contact tracing of a former husband with low awareness scenario			1.52	-	82	NA	
			Home-based-contact tracing of a non-marital partner with low awareness scenario			1.01	-	184	NA	
Bassett, 2007 (127)			Clients at OPD	Provider	Inc/Fin/Emp	7.29	21.98	137	102	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
	South Africa	Health facility	Clients at VCT services			7.66	11.47	1,414	463	• HIV testing kits • Confirmatory HIV testing kits • Salaries • Space
Bassett, 2014 (33)	South Africa	Mobile service	General population	Provider	Inc/Fin/Emp	23.83	25.46	18,870	939	• Mobile van purchase and modification • Medical/counsellor salary • Administrative salary and maintenance
Bautista-Arredondo, 2016 (128)	Kenya	Health facility	Clients at VCT services	Provider	Inc/Fin/Emp	8.09	168.80	1,270	491	• • Capital training
			Clients at ANC			68.21	778.11	288	105	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
	Rwanda	Health facility	Clients at VCT services			4.51	1233.10	2,340	106	• Supervision • Personnel • Recurrent inputs and services
			Clients at ANC			16.24	1823.04	812	14	
	South Africa	Health facility	Clients at VCT services			28.03	156.45	808	1,019	
			Clients at ANC			80.48	512.75	426	172	
	Zambia	Health facility	Clients at VCT services			13.92	89.35	242	291	
			Clients at ANC			35.89	413.81	618	104	
Bogart, 2017 (160)	Uganda	Home-based	Clients tested at home	Provider	Inc/Eco/Emp	37.63	-	822	-	• Personnel • Per-diems • Transport • Test kits
		Campaign style	Outreach testing			39.62	-	344	-	
Change, 2016 (152)	Uganda (West)	Mobile service	Campaign attendees	Provider	Inc/Eco/Emp	11.22	166.17	4,417	287	• Personnel • Recurrent supplies and services
			Campaign-non-attenders			24.36	288.84	771	57	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
	Uganda (East)	Mobile service	Campaign attendees			12.27	329.38	4,260	153	• Capital and equipment • Facility space
			Campaign-non-attenders			27.75	1160.67	675	14	
	Kenya	Mobile service	Campaign attendees			15.46	86.47	2,969	519	
			Campaign-non-attenders			36.22	203.97	832	136	
Grabbe, 2010 (153)	Kenya	Mobile service	Community members	Provider	Ful/Eco/Emp	25.47	268.54	47,539	4,265	• Overheads • Building rentals • Personnel • Vehicles • Equipment • Supplies • Per diems
			Community members-new person tested			28.32	-	41,829	3,782	
		Stand-alone	Community members			45.69	323.08	14,634	2,063	
			Community members-new person tested			74.63	-	8,415	1,612	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Hauck, 2018 (143)	Zambia	Home-based	First-round clients tested	Provider	Inc/Fin/Emp	26.78	367.17	126,208	9,196	• Administration • Personnel • Transport • Equipment • Supplies
			Second-round clients tested			25.43	692.20	136,966	4,921	
Hausler, 2006 (30)	South Africa	Health facility	Clients at the community health centre	Provider	Ful/Eco/Emp	15.05	-	NS	NA	• Personnel • Training and support services • Health education
			Clients at the primary health facility			18.40	-	NS	NA	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			Clients at the STI clinics			11.71	-	NS	NA	• HIV testing and follow-up • Management of opportunistic infections • Supervision • Training • Mentorship • Personnel • Building, furniture, equipment, and vehicle maintenance
Helleringer, 2013 (144)	Malawi	Home-based	First-round clients tested	Provider	Inc/Fin/Emp	12.35	153.16	597	40	• Training • Stipends

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			First-round new person tested			16.91	-	434	NA	• Transport • Accommodation • Community meetings • Consumables
			Second round client tested			13.67	400.76	586	45	
			Second round new person tested			200.43	-	40	NA	
Ibekwe, 2017 (59)	Nigeria	Health facility	Clients at VCT services	NS	Inc/Fin/Emp	-	476.26	NA	15	• Not specified*
			Clients at ANC			-	349.54	NA	44	
Kahn, 2011 (157)	Kenya	Campaign style	Campaign attendees	Provider	Ful/Eco/Emp	57.93	-	NS	NA	• Personnel

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			Campaign attendees-scale-up			44.47	-	NS	NA	• Training and support services • Services (campaign planning, advertising, promotion, transportation, accommodation) • Supplies

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Kahwa, 2008 (161)	Tanzania	Health facility	Clients at health facility	Provider	Inc/Eco/Emp	16.14	-	53,926	NA	• Vehicle • Building • Furniture • Laboratory equipment • Recurrent laboratory supplies and consumables • Personnel
Labhardt, 2014 (145)	Lesotho	Home-based	Household members	Provider	Inc/Fin/Emp	14.14	393.33	1,083	39	• Personnel

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
		Mobile service	Campaign attendees			12.87	206.60	1,207	75	• Transportation • Test kits and supplies • Point-of-care CD4-counter • Staff accommodation, perdiems, horse rent
Lasry, 2019 (146)	Botswana	Home-based	Household members	Provider	Ful/Eco/Emp	54.10	773.70	12,415	870	• Labour

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
		Mobile service	Campaign attendees			34.70	583.85	12,820	766	• Equipment and supplies • Facilities and administration • Events and travel • HIV rapid test kits

Liambila, 2008 (129)	Kenya	Health facility	Clients at VCT	Provider	Inc/Fin/Emp	46.12	-	27	NA	• Stakeholder meetings • Development & production of job aids • Production of Information, Education, and Communication (IEC) materials • Curriculum development • Training • Personnel • HIV test kits and supplies • Additional supervisory
Maheswaran, 2016 (156)	Malawi	Health facility	Clients at health facility-1	Provider	Ful/Eco/Emp	8.89	79.47	6,759	756	• Personnel • Training

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
		Health facility	Clients at health facility-2			12.48	90.16	5,372	743	• Monitoring and evaluation • Consumables and equipment • Capital/over heads
		Health facility	Clients at health facility-3			10.50	33.40	9,488	2,984	
		Self-testing	Clients at health facility			10.36	115.08	15,190	1,367	
Meehan, 2017 (154)	South Africa	Campaign-style	Community members	Provider	Inc/Fin/Emp	48.85	723.11	1,909	128	• Overheads

		Mobile service	Community members			23.94	1006.61	3,057	74	• Service provision • Capacity building • Administration cost • Monitoring & evaluation • Data • Planning • Recurrent goods &services (rental, utilities, telephone, cleaning, & security costs)
Mangenah, 2019 (50)	Malawi	Self-test	Home-based	Provider	Ful/Eco/Emp	9.99	-	152,671	-	• Training • Sensitization

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
	Zambia	Self-test	Home-based			14.23	-	103,589	-	• Building and storage

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
	Zimbabwe	Self-test	Home-based			13.84	-	93,459	-	• Equipment • Personnel • HIV self-test kits • Supplies • Vehicle operation, maintenance • and transport • Building operation/maintenance • Recurrent training • Waste management • • Other recurrent

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Menzies, 2009 (130)	Uganda	Stand-alone	Clients accessing stand-alone HTS	Provider	Inc/Fin/Emp	20.52	107.15	8,391	1,616	• Building and utilities • Equipment • Personnel • HIV testing supplies • Vehicles • Training
		Health facility	Clients accessing health facility testing			12.44	45.91	21,755	5,872	
		Home-based	Household-member of an index client			14.75	246.75	1,861	80	
		Home-based	Household members			8.83	174.62	38,799	2,072	
		Stand-alone	New person tested			31.64	-	6,227	1,511	
		Health facility	New person tested			15.69	-	18,428	5,807	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
		Home-based	Household members of an index client-new person tested			15.49	-	1,916	101	
		Home-based	Household members new person tested			9.81	-	44,523	2,350	
Muhumuza, 2012 (131)	Uganda	Health facility	Clients at VCT services	Provider	Inc/Fin/Emp	4.49	-	34,119	3,753	• Not specified*
		Home-based	Household members			10.68	-	31,770	953	
Mulogo, 2013 (132)	Uganda	Health facility	Clients at VCT services	Provider	Inc/Fin/Emp	6.07	82.10	454	36	• Building • Furniture

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
		Home-based	Household members			4.75	51.92	444	45	• Training • Personnel • Supplies • Building operation and maintenance • Recurrent training • Transport
Mwenge, 2017 (133)	Malawi	Health facility	Clients accessing the health facility	Provider	Ful/Eco/Emp	6.62	107.01	3,404	304	• Building and storage • Equipment
	Zambia					4.24	73.66	2,789	251	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
	Zimbabwe					8.87	180.55	1,542	93	• Vehicles • Personnel • HIV test kits • Supplies • Operation and maintenance • Recurrent training • Waste management
Negin, 2009 (147)	Kenya	Home-based	Household members	Provider	Inc/Fin/Emp	8.18	116.80	2,780	209	• Training • Stipends • Transport • Consumables test kits

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Obure, 2012 (135)	Kenya	Health facility	Clients from provider-initiated testing and counseling	Provider	Ful/Eco/Emp	7.66	-	5,486	780	• Building • Furniture and equipment • Staff training • Personnel • Building maintenance • Communication • Stationary • Diagnostics • Supplies
			Clients at VCT services			11.09	-	9,005	1,527	
	Swaziland		Clients from provider-initiated testing and counseling			8.03	-	4,872	1,851	
			Clients at VCT services			9.73	-	6,061	2,698	
Obure, 2015 (134)	Kenya	Health facility	Clients at a health facility	Provider	Ful/Eco/Emp	7.66	-	NS	NS	• Overhead • Personnel

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
	Swaziland		Clients at a health facility			11.09	-	NS	NS	• Administrative costs • Building • Building maintenance • Diagnostics • Supplies
Orlando, 2010 (162)	Malawi	Health facility	Clients at ANC	Provider	Inc/Fin/Emp	67.82	-	5,457	-	• Personnel • Diagnostics • Lab examination • Building • Vehicle • Furniture
Parker, 2015 (148)	Swaziland	Home-based	Household members	Provider	Inc/Fin/Emp	8.43	262.74	170	75	• Transport

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
		Mobile service	Campaign attendees			18.38	415.94	228	60	• Human resources • Testing equipment • Infection control • Information education and counseling • Other (trailer, tents, furniture, accommodation, food, and airtime)
Perchal, 2006 (136)	Ethiopia	Health facility	Clients tested at a health facility during 1st-year	NS	Inc/Fin/Emp	33.17	-	NS	NA	• Personnel • Supplies (diagnostics)

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			Clients tested at health in subsequent years			8.92	-	NS	NA	• Indirect cost
Perez, 2016 (137)	South Africa	Mobile service	Campaign attendees	Provider	Inc/Fin/Emp	9.88	-	22,152	699	• Diagnostics • Personnel • Sensitization • Infrastructure • Transport • Communication • Equipment
		Health facility	Clients at a health facility			9.69	-	17,678	807	
		Home-based	Household members			6.78	-	48,330	896	
Pinto, 2013 (138)	Malawi	Health facility	Clients tested in a centralized health facility	Patient	Inc/Fin/Emp	2.37	-	120	NA	• Travel cost • Income loss • Additional costs (food & medication)
			Clients tested in a decentralized health facility			1.35	-	120	NA	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Rutstein, 2013 (61)	Malawi	Health facility	Partner testing via provider notification	Provider	Inc/Fin/Emp	16.33	-	2436	NA	• Personnel • Cost of tracing and transport • Cost of testing and treatment
			Partner testing via contract notification			7.74	-	2537	NA	
			Partner testing vis passive referral			3.44	-	1207	NA	
			New partner testing via provider notification			30.95	-	1267	NA	
			New partner testing via contract notification			15.47	-	1320	NA	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			New partner testing via passive referral			6.88	-	627	NA	
Shade, 2013 (139)	Kenya	Health facility	Clients tested at an integrated health facility	Provider	Inc/Fin/Emp	-	19.31	NA	4,135	• Initial training • Space • Refresher training • Mentoring • Supervision • Supplies • Other costs
			Clients tested at a non-integrated health facility			-	9.69	NA	3,429	
Sharma, 2014 (149)	South Africa	Mobile service	Campaign attendees	Provider	Inc/Eco/Emp	4.43	6.74	890	381	• Programme cost of mobile HTS
		Home-based	Household members			6.69	9.87	NS	NS	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Sharma, 2016 (32)	Kenya	Health facility	CHCT-concordant negative couples	Provider	Inc/Eco/Emp	33.99	-	NS	NA	• Personnel • Transportation • Equipment • Supplies • Building and overhead • Start-up • Data capturing and use
			CHCT-concordant positive couples			38.43	-	NS	NA	
			CHCT-discordant couples			40.23	-	NS	NA	
			CHCT-concordant negative couples (Task-shifting to community health workers)			15.25	-	NS	NA	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			CHCT-concordant positive couples (Task-shifting to community health workers)			15.65	-	NS	NA	
			CHCT-discordant couples (Task-shifting to community health workers)			17.17	-	NS	NA	

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Smith, 2015 (150)	South Africa	Home-based	Household members	Provider	Inc/Fin/Emp	7.08	19.01	NA	NA	• Personnel • Transportation • Equipment • Supplies • Buildings • Overhead • Start-up • Recurring meetings • Data capture and use
Tabana, 2015 (140)	South Africa	Health facility	Clients at the health facility	Provider	Inc/Eco/Emp	30.60	-	3,818	NA	• Startup • Office rentals • Personnel

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
		Home-based	Household members			23.35	-	8,177	NA	• On-going training • Testing equipment • Stationary • Field material • Dry blood spot (DBS) • Vehicles • Office equipment

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
Terris-Prestholt, 2006 (163)	Uganda	Campaign-style	Campaign attendees	Provider	Inc/Eco/Emp	39.18	-	1,526	NS	• Buildings • Equipment • Vehicles • Start-up • Personnel • Supplies • Vehicles operation and maintenance • Building operation and maintenance • Central support costs
Terris-Prestholt, 2008 (141)	Zambia	Health facility	Clients at VCT-Chawama health facility	Provider	Ful/Eco/Emp	31.01	95.76	1,381	455	• Buildings • Equipment

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			Clients at VCT-Matero health facility			32.83	46.51	239	166	• Indirect cost Vehicles • Training/workshops • Personnel • Opening ceremony • Supplies • Vehicles operation and maintenance • Building operation and maintenance • Outreach
Tumwesigye, 2010 (151)	Uganda	Home-based	Household members	Provider	Ful/Eco/Emp	7.51	148.40	264,953	10,012	• Personnel

Author, year, ref	Country	HTS approach	Population served	Costing perspective	Costing method[1]	Cost/person tested ($pptested)	Cost/case identified ($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs
			Household members- new person tested			12.48	-	238,290	NA	• HIV testing supplies • Transportation

[1]Ful=Full costing, Inc=Incremental cost, Fin=Financial cost, Eco= Economic cost, Emp= Empirical (primary) cost, Mod=Modelled cost

Cost-effectiveness analysis studies

We identified 15 (10+5) studies that undertook cost-effectiveness analysis (Table 3) across seven countries in sub-Saharan Africa: eight from Southern African, four from East Africa, one from West Africa, and two studies that stated the location as sub-Saharan Africa. For these 15 studies, 12 studies undertook the analysis from the provider's perspective, one from both provider and societal perspectives, and two did not specify their perspective. On the analytical approach, all the 15 studies applied different types of modeling approaches to measuring cost-effectiveness estimates and impacts (Table 2-3). The 15 studies presented 31 cost-effectiveness estimates for different HIV testing modalities. Out of the 31 reported cost-effectiveness estimates, 21 reported estimates for health facility testing, three for home-based testing, one for mobile service, three for self-testing, and three for campaign-style HTS.

Thielman *et el.* undertook cost-effectiveness analysis regarding removing user fees to access HIV testing at community-based HIV services in Tanzania. The estimated cost per HIV infection averted with standard fee VCT, with two-weeks free VCT campaign, and with sustained free VCT service were US$242.43, US$149.73 and US$131.20, respectively (62). The Kahn and colleagues study in Kenya found that integrating HIV testing, malaria, and diarrhea prevention interventions would be more effective and less costly than delivering them separately, suggesting economic of scope in community screening programmes (31).

Two studies modelled the cost-effectiveness of couples HIV testing and counseling (CHCT) at health facilities (58, 60). Allen *et al.* estimated that CHCT would cost US$359.71 per HIV infection averted compared to the standard individual VCT in sub-Saharan Africa (58). John *et al.* estimated cost per DALY averted for individual VCT (US$26.20) to be comparable to that estimated for CHCT (US$26.29) at ANC in Kenya (60). Ibekwe *et al.* estimated the cost-effectiveness of delivering HIV testing to pregnant women through ANC services and routine VCT in Nigeria (59). The authors estimated the cost per HIV infected averted for HIV testing through ANC services and routine VCT as US$2,040.58 and US$1,519.02 respectively (59).

Rutstein *et al.* undertook a cost-effectiveness analysis of different partner notification strategies amongst HIV-positive cases attending an STI clinic in Malawi (61). The authors estimated that contract notification (while maintaining index case anonymity) would cost US$3,060.35 per HIV infection averted compared to the passive notification, whilst provider notification would cost US$44,203.96 per infection averted compared to contract

notification (61). Sharma and colleagues undertook cost-effectiveness analysis of adding a home-based partner education and HIV testing (HOPE) intervention amongst pregnant women attending ANC clinics in Kenya (32). They estimated the cost-effectiveness of adding the HOPE intervention to be US$978.46 per DALY averted. However, if community health workers delivered the HIV testing (task-shifting) rather the intervention the additional cost per DALY averted would be US$679.18 (32).

Hausler *et al.* estimated the cost-effectiveness of delivering HIV testing in community health centres, primary health care clinics, and sexually transmitted infection (STI) clinics (30). The authors reported that HIV testing at community health centres, primary healthcare clinics, and STI clinics would cost US$155.55, US$187.33, and US$112.06 per HIV infection averted, respectively (30).

Two studies (Bassett and Walensky) used the Cost-Effectiveness of Preventing AIDS Complications-International (CEPAC-I) computer simulation model, which is a stochastic microsimulation model for undertaking cost-effectiveness analysis of mobile testing services (33) and periodic HIV screening (63) in South Africa. Bassett *et al.* estimated it would cost an additional US$1,952.23 per life-year saved to add a mobile HIV testing service to standard VCT (33). Walensky reported incremental cost-effectiveness ratios (ICER) of US$1,732.78 per QALY saved for HIV screening every 5 years compared to ICER of US$1,898.33 per QALY saved for annual screening (63). Waters *et al.* estimated the cost-effectiveness of different retesting intervals (3 months to 30 years) amongst those who tested HIV-negative (64). The authors reported the most cost-effective strategy in low-risk populations (i.e., HIV incidence of 0.8%) was re-testing every 7.5 years (US$773.68 per QALY gained), in medium-risk populations (i.e., HIV incidence of 1.3%) every 5 years (US$751.61 per QALY gained), and in high-risk populations (i.e., HIV incidence of 4.0 %) every 2 years (US$700.84 per QALY gained) (64).

Three studies estimated the cost-effectiveness of providing HIV self-testing in addition to routine facility-based HTS in Zimbabwe (34, 35) and Malawi (36). Cambiano *et al.* found that implementing self-testing would be cost-saving if it could be delivered at the full cost of US$3 per unit, and only cost-effective at ICER thresholds above US$10,000 per DALY averted if the cost of providing each episode was below US$9 (34) Maheswaran *et al.* estimated the additional provision of self-testing was associated with an ICER of US$280.23 and US$2389.92 per QALY gained from a provider and societal perspective, respectively

(36). Leigh and colleagues estimated the cost-effectiveness of self-testing in the context of antenatal partner testing and home-based testing (37). The authors reported the incremental cost of US$1,941.72 and US$1,111.85 per life-year gained for providing self-testing for the partner of pregnant women at antenatal care and home-based self-testing, respectively (37) (Table 2-3).

Table 2.3 Summary of HTS with CEA included 2006-2019 in 2019 USD (n = 15)

Author, year, ref	Country	HTS approach	Population served	Comparator	Costing perspective	Costing method[1]	Modeling approach	Cost-effectiveness estimate
Allen, 2010 (58)	Sub-Saharan Africa	Health facility	Couples accessing HIV testing at a health facility	Couples HIV testing counseling compared to facility testing	Provider	Modelled	Not specified	US$359.71 per HIA
Bassett, 2014 (33)	South Africa	Mobile-service	Campaign attendees	Additional mobile-service compared to standard of care	Provider	Emperical	Stochastic microsimulation model	US$1,952.23 per LYG
Cambiano, 2015 (34)	Zimbabwe	Self-testing	Clients at the health facility	HIV self-testing compared to provider-delivered HIV testing and counseling	Provider	Modelled	Individual-based stochastic model	7000 DALYs over 20 years
Cambiano, 2019 (35)	Sub-Saharan Africa	Self-testing	Clients self-tested in the community	Different scenarios	Provider	Empirical	Individual-based stochastic model	Targeting adult men with community-based HIV self-testing avert 1500 HIV infections and 520 deaths per year.

Author, year, ref	Country	HTS approach	Population served	Comparator	Costing perspective	Costing method[1]	Modeling approach	Cost-effectiveness estimate
Hausler, 2006 (30)	South Africa	Health facility	Clients at the community health centre	Community health centre compared to primary health care compared to STI clinic	Provider	Empirical	Not specified	US$155.55 per HIA
			Clients at the primary health facility					US$187.33 per HIA
			Clients at the STI clinics					US$112.06 per HIA
Ibekwe, 2017 (59)	Nigeria	Health facility	Pregnant women at antenatal care	Antenatal HIV testing compared to routine volunteer counseling and testing	Provider	Empirical	Not specified	US$2,040.58 per HIA
			Women in routine volunteer counseling and testing					US$1,519.02 per HIA
John, 2008 (60)	Kenya	Health facility	Couples accessing HIV testing at antenatal care	Couples testing at the antenatal care compared to individual voluntary counseling and testing	Not specified	Modelled	Stochastic microsimulation model	US$26.29 per DALY averted
			Clients accessing individual voluntary HIV testing and counseling					US$26.20 per DALY averted

Author, year, ref	Country	HTS approach	Population served	Comparator	Costing perspective	Costing method[1]	Modeling approach	Cost-effectiveness estimate
Leigh, 2018 (37)	South Africa	Campaign-style	Men who have sex with men (MSM) attending community-based testing	Comparing the population-level impact of MSM testing to a partner of pregnant women to home-base self-testing	Provider	Modelled	Stochastic microsimulation model	US$182.62 per LYG
		Self-testing	Partners of pregnant women tested at antenatal care					US$1,941.72 per LYG
		Self-testing	Clients self-tested at home					US$1,111.85 per LYG
Kahn, 2012 (31)	Kenya	Campaign-style	Campaign attendees accessing integrated HIV malaria and diarrheal testing	Comparing the integrated mass campaign to early case identification	Provider	Modelled	Stochastic microsimulation model	359 DALY averted
		Campaign-style	Campaign attendees and early HIV case identification					82 DALY averted
Maheswaran, 2017 (36)	Malawi	Self-testing	Clients self-tested in the community	Comparing solo facility-based	Provider			US$280.23 per QALY gained

Author, year, ref	Country	HTS approach	Population served	Comparator	Costing perspective	Costing method[1]	Modeling approach	Cost-effectiveness estimate
				testing to the additional provision of self-testing	Societal	Empirical	Stochastic microsimulation model	US$289.92 per QALY gained
Rutstein, 2013 (61)	Malawi	Health facility	Partner testing of HIV positive index cases	Contract notification compared with passive referral	Provider	Empirical	Decision-analytic model	US$ 3,060.35 per HIA
				Provider notification compared with contract notification				US$ 44,203.96 per HIA
Sharma, 2016 (32)	Kenya	Home-based	Partner of pregnant women	Home-based partner education and HIV testing (HOPE) for pregnant women compared to facility testing	Provider	Empirical	Dynamic transmission model	US$978.46 per DALY averted for partner education and HIV testing, and US$679.18 per DALY averted for Task-shifting to

Author, year, ref	Country	HTS approach	Population served	Comparator	Costing perspective	Costing method[1]	Modeling approach	Cost-effectiveness estimate
								community health workers
Thielman, 2006 (62)	Tanzania	Health facility	Clients accessing health facility testing	Free VCT compared to HIV testing integrated into community-based AIDS services.	Not Specified	Empirical	Deterministic compartmental population-based model	US$242.43 per HIV infection averted, and US$12.44 per DALY averted
			Clients accessing two-weeks free VCT campaign					US$149.73 per HIV infection averted, and US$7.70 per DALY averted
			Clients accessing sustained free VCT					US$131.20 per HIV infection averted, and US$6.73 per DALY averted
Walensky, 2011 (63)	South Africa	Health facility	Clients accessing HIV testing at the health facility	Comparing routine (annual) HIV screening to screening every 5-year	Provider	Modelled	Stochastic microsimulation model	5-years ICER: US$1,732.78 per QALY
								Annual ICER: US$1,898.33 per QALY

Author, year, ref	Country	HTS approach	Population served	Comparator	Costing perspective	Costing method[1]	Modeling approach	Cost-effectiveness estimate
Waters, 2011 (64)	Sub-Saharan Africa	Health facility	Clients accessing HIV testing at the health facility	Comparing HIV testing every 7.5 years to every 5-years to every 2-years	Provider	Modelled	Stochastic microsimulation model	US$773.68 per QALY gained for testing frequency every 7.5 years
								US$751.61 per QALY gained for testing frequency every 5-years
								US$700.84 per QALY gained for testing frequency every 2-years

[1] **Empirical (primary) cost and modelled cost**

Table 2.4 Quality assessment: Proportion of the cost and cost-effectiveness studies compliant with GHCC and CHEERS guidelines[a,b]

Quality assessment of cost studies (*n* = 44) following the GHCC principles (116) in %									
Reported cost estimated by testing modality	**Study purpose and population (P1)**	**Study perspective and types of costing approach used (P2-3)**	**Unit cost, time horizon, scope, the quantity of inputs, sampling, and data source strategy (P4-9)**	**Timing of data collection sources for price data (P10-11)**	**Annualisation or depreciation of capital cost and discounting (P12-13)**	**Shadow prices for goods and for the opportunity cost of time (P14)**	**Characterizing heterogeneity (P15)**	**Characterizing uncertainty (P16)**	**Communicated limitations, conflicts of interest (P17)**
Health facility (*n* = 59)	100	80	73	87	87	22	26	17	91
Home-based (*n* = 29)	100	85	77	88	77	8	8	31	100
Mobile-services (*n* = 17)	100	93	91	100	86	0	14	71	100
Self-testing (*n* = 10)	100	100	100	100	100	33	33	100	100
Campaign style (*n* = 6)	100	100	100	100	100	0	50	50	100
Stand-alone (*n* = 4)	100	100	83	50	100	0	0	0	100
Quality assessment of cost-effectiveness studies (*n* = 15) following the CHEERS guidelines (117) in %									
Reported CE estimated by testing modality	**Describe the intervention compared,**	**Target population and subgroups, setting, time**	**Choice of health outcomes and measurement**	**Resources and costs, currency, price date,**	**Choice of model, assumptions and analytical method**	**Study parameters, increment**	**Characterizing uncertainty (Q20)**	**Characterizing heterogeneity (Q21)**	**Communicated limitations, conflicts of interest**

	study perspective and objectives (Q1-3)	**horizon and discounting (Q4-9)**	**of effectiveness (Q10-11)**	**and conversion (Q12-14)**	**(Q15-17)**	**al outcomes (Q18-19)**			**(Q22-24)**
Health facility (*n* = 21)	88	83	100	83	63	81	63	80	79
Home-based (*n* = 3)	100	100	100	100	100	100	100	100	100
Mobile-service (*n* = 1)	100	100	100	83	83	100	100	50	100
Self-testing (*n* = 3)	100	100	100	100	100	100	100	100	100
Campaign style (*n* = 3)	100	50	50	33	33	50	0	0	33

[a] Data are presented as % unless otherwise indicated, [b] The full quality assessment results for each cost and CEA studies are in the Supplementary table S2-5 &S2

Discussion

This review adds to existing reviews on the effectiveness of HIV testing (84, 85, 104, 164) by exploring the costs and cost-effectiveness of HIV testing strategies in sub-Saharan Africa. We identified cost estimates for six different HIV testing modalities. We found the costs to test individuals through health facility, home-based, and mobile services were comparable: US$20.33, US$11.16, and US$19.13 respectively. The costs were higher for campaign-style and stand-alone HTS: US$40.64 and US$43.12 per person tested respectively. The costs were lowest for HIV self-testing: US$11.94 per person tested. The cost per HIV-positive individual identified varied across the six HIV testing modalities. The mean cost per HIV-positive identified at the health facility, home-based, and mobile services were US$196.27, US$272.17, and US$365.33, respectively. Although there were a small number of cost studies for campaign-style and stand-alone HIV testing modalities, the mean costs were US$723.11 and US$215.11 per HIV-positive identified, respectively. The mean cost per HIV-positive individual identified was lowest through HIV self-testing at US$79.53.

Interpreting these cost estimates should be done with caution. Some of the differences observed in cost estimates are likely to be explained by variation in HIV prevalence across settings. For example, low HIV prevalence in Rwanda led to low yields, and higher cost per HIV+ case identified (128). One study presented cost estimates for two rounds of home-based HIV testing and reported the cost per HIV-positive person tested nearly doubled between the two rounds (first round US$367.17 vs second round US$692.20) and this was partly explained by a reduction in the HIV positivity rate. The authors also stated costs are sensitive to community specific factors such as service delivery and population characteristics (143).

Additionally, we observed variation in costing methods used (incremental vs. full, economic vs. financial). Studies that used incremental costing methods will likely under-estimate costs as they do not include the existing infrastructure and overhead costs borne by the existing health programme. These costs would potentially be incurred by those wishing to implement the same testing service in another setting where existing infrastructure may not be available. Studies that estimated the financial costs might have costed a service that utilized donated goods or volunteer staff. The same service in another setting may have to purchase these goods or pay for staff.

We found that, in general, the costs of the different testing modalities were comparable. This should encourage policymakers wishing to provide different options of HTS modalities in their populations. The choice of one testing modality over another can be driven by which HIV testing approach is most feasible to implement and most likely to reach their untested and under-served populations. Additionally, the cost findings may encourage policymakers to consider delivering a mixture of testing modalities.

We identified a few cost-effectiveness studies of HIV testing services. These studies did identify a few important issues. Removing user fees to access HIV testing improved their cost-effectiveness (62). Delivering HIV testing services alongside other health interventions was more cost-effective than delivering either HIV testing or the other intervention alone (30, 31). Couples testing and ensuring pregnant women have access to HIV testing were potentially a cost-effective approach to preventing new infections (58, 59). In comparison, partner notification was associated with a higher cost per HIV infection averted (61) unless it targeted pregnant women and offered partners HIV testing in their homes (32). A recent study in Malawi provided further evidence to support this approach (106). Studies found the provision of either home-based HIV testing (32), mobile testing services (33), or HIV self-testing (34-37), in addition to routine facility-based HIV testing, potentially cost-effective at a cost-effectiveness thresholds equivalent to one to three times gross domestic product per gain in DALY, QALY, or life year (38). Implementing these testing models may be cost-effective but will increase total spending on HIV testing. Finally, amongst those who have tested, the cost-effective time to the next HIV test is 5-8 years depending on the population's risk (63).

We used the GHCC, and the CHEERS statements to assess the quality of cost and cost-effectiveness studies, respectively (116, 117) (Table S4 & Table S5). Though there has been a significant improvement in adherence to best practices for conducting and reporting findings from economic evaluations, the wide variability of unit costs is partly due to the non-standardized definition of unit cost and approaches to data collection, cost analysis, and reporting. The included cost components varied considerably. Not only cost components but sources for cost data collection also varied, including estimating cost from a single health facility and aggregating data from all regions in a country without accounting for variations in HIV prevalence and population demographics (Table S6 & Table S7).

The paucity of standardized cost and CEA estimates for different HIV testing modalities in sub-Saharan African countries imposes technical challenges in translating the resource needs and findings from one country to another. It is apparent that high-quality cost and CE studies are crucial for sub-Saharan Africa, where scarce resources must be allocated efficiently. Thus, we strongly recommend that cost and CE data collection, estimation, and reporting should follow the GHCC reference case, and reporting of published findings adhere to CHEERS guidelines (116, 117) to improve the validity and comparability of studies across the region. The scarcity of cost-effective estimates for home-based, mobile-service, self-testing, and campaign-style testing modalities highlights the need for more studies. Also, it is essential to do more CE analysis of the different combinations of testing modalities to inform HIV testing policies better.

Limitations

This review has several limitations. This review acknowledges the diversity and complexity of healthcare systems in sub-Saharan Africa. Thus, the review presented the costs and the CE results following the study perspective. Furthermore, there is no consensus on what should be reported as direct and indirect costs, and studies might have defined direct and indirect costs differently. In no one single country were all six HIV testing modalities assessed, which made the comparison of different testing modalities difficult. The methods used to undertake the economic analysis were not always comprehensive or comparable, limiting the generalizability of findings. Some studies proposed checklists of transferability of economic evaluations (165-168). Moreover, this review acknowledges the diverse published data sources, for example, peer-reviewed papers, posters, abstracts, and presentations, which limited the quality assessment and comparison between studies.

Conclusion

In summary, our review identified a large number of studies reporting the costs of different testing modalities but few studies that undertook full cost-effectiveness analysis. Although we found cost and cost-effectiveness estimates to vary widely, we did identify that in general, the costs of the different testing modalities were comparable. The few cost-effectiveness studies identified highlighted the value in ensuring users do not pay fees and in targeting pregnant women and their sexual partners potentially through couples testing, home-based testing, or HIVST. Finally, home-based and mobile are potentially cost-effective if providers

are willing to pay the additional money needed to deliver these services and thereby realize the potential health benefits from their use.

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Authors' contributions

NA and FTP planned the study. NA and SR searched. NA extracted, analyzed, interpreted the data, and produced a draft manuscript. NA and MD conducted study appraisals. FTP, JO and HM oversaw the progression of the review, provided guidance, and contributed to various versions of the manuscript. All contributing authors read and approved the final manuscript. NA is the overall patron of this work.

Competing interests

The authors have no conflicts of interest to declare.

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Quality assessment: Proportion of the cost and cost-effectiveness studies compliant with GHCC and CHEERS guidelines [a,b]

Supplementary Table S1 to Table S7

Supplementary document

A systematic literature review of costs and cost-effectiveness analysis of HIV testing services in sub-Saharan Africa

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Additional files
Supplementary Tables

Table S1 PICOS Inclusion and exclusion criteria

PICOS	Inclusion criteria	Exclusion criteria
Population	Adolescents, adult men, and adult women	Infants and children (<age 16)
Intervention	Different types of HIV testing services (differentiated HIV testing services)	Infant and children HIV testing approaches
Comparators	Any stated comparators	None
Outcomes	Cost estimates are cost per person tested, and per HIV + person identified Cost-effectiveness estimates are cost per infection averted, cost per DALY averted, cost per QALYs gained	Not stating costs measures or units of health outcomes in the study
Study types	Costing and cost-effectiveness analysis of HTS in sub-Saharan Africa	Costing: where no new primary costs data are presented. Cost-effectiveness: where outcomes are not presented in generic health outcomes, including QALYs, DALYs, HIA or LYG

Table S2 Systematic literature review search strategy and strings

Searched databases	Search terms	Result
Medline		
Concept 1(C1)	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immunedeficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR Sexually Transmitted Diseases	211,320
Concept 2(C2)	Counselling OR Counseling OR Counse*OR Testing OR Test*	386,102
Concept 3 (C3)	Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	1,800,445
C1 AND C2 AND C3		461
Concept 4	hiv self-testing OR self-test* OR "self test" OR hiv self-test OR hivst OR home test*	1,581
Pubmed*		
C1 AND C2 AND C3	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immunedeficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR Sexually Transmitted Diseases AND Counselling OR Counseling OR Counse* OR Testing OR Test* AND Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness	980

	analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	
Concept 4	hiv self-testing OR self-test* OR "self test" OR hiv self-test OR hivst OR home test*	639
EMBASE		
Concept 1	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect$ OR human immunodeficiency virus OR human immunedeficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immune$) AND (deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immune$) AND (deficiency syndrome)) OR Sexually Transmitted Diseases	256,689
Concept 2	Counselling OR Counseling OR Counse*OR Testing OR Test*	495,348
Concept 3	Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	2,320,362
C1 AND C2 AND C3		569
Concept 4	hiv self-testing OR hiv self-test OR hivst OR home test* OR rapid test*	1993
Popline		
C1 AND C2 AND C3	HIV Infections* OR HIV OR human immunodeficiency virus* OR acquired immunodeficiency syndrome* OR AIDS **And** Counselling OR Counseling OR Counse*OR Testing OR Test* **AND** Cost OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives*	175
Concept 4	hiv self-test* OR hiv self-testing	68

SCOPUS*		
C1 AND C2 AND C3	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect$ OR human immunodeficiency virus OR human immunedeficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immune$) AND (deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immune$) AND (deficiency syndrome)) OR Sexually Transmitted Diseases AND Counselling OR Counseling OR Counse*OR Testing OR Test* AND Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	2,452
Concept 4	HIV* OR hiv self-testing OR hiv self-test* OR hivst OR home test* OR rapid test*	1,536
Global Health		
Concept 1	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immunedeficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR Sexually Transmitted Diseases	110,964
Concept 2	Counselling OR Counseling OR Counse*OR Testing OR Test*	62,706
Concept 3	Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	338,534
C1 AND C2 AND C3		313

Concept 4	hiv self-testing OR self-test* OR "self test" OR hiv self-test OR hivst OR home test*	972
COCHRANE*		
C1 AND C2 AND C3	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immunedeficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR Sexually Transmitted Diseases AND Counselling OR Counseling OR Counse*OR Testing OR Test* AND Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	51
Concept 4	hiv self-testing OR self-test* OR "self test" OR hiv self-test OR hivst OR home test*	0
Social policy and practice		
Concept 1	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immunedeficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR Sexually Transmitted Diseases	5,138
Concept 2	Counselling OR Counseling OR Counse*OR Testing OR Test*	18,579
Concept 3	Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	83,039

C1 AND C2 AND C3		161
Concept 4	hiv self-testing OR self-test* OR "self test" OR hiv self-test OR hivst OR home test*	0
Web of Science		
C1 AND C2 AND C3	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immunedeficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR Sexually Transmitted Diseases AND Counselling OR Counseling OR Counse*OR Testing OR Test* AND Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	513
Concept 4	hiv self-testing OR self-test* OR "self test" OR hiv self-test OR hivst OR home test*	1,060
Tuft's cost effectiveness analysis registry	HIV	98

*Pubmed, SCOPUS, COCHRANE and Web of Science databases search were conducted using "AND" conjugation concept 1, 2, and 3.

Table S3 PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported in section
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title section
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Supplemental appendix
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Introduction
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Introduction
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Systematic literature review not registered
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Methods and supplemental table
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Methods and supplemental table
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplemental table

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Methods
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Methods
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Methods
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Methods
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Methods
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Methods and supplemental table
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Discussion
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Supplemental table

RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Results and supplemental table
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Results and supplemental table
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Results and supplemental table
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Meta analysis not done
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Discussion
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression- see Item 16).	Results
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Discussion
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Discussion
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Discussion
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Funding statement

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**

Table S4 Quality assessment using the GHCC's principles and methods reporting checklist for cost studies (57)

Principle	Item No	GHCC reference case checklist items included
Principle 1	P1	The purpose of the study, the population, and the intervention and/or service/output being costed should be clearly defined.
Principle 2	P2	The perspective (extent of the resource use captured) of the cost estimation should be stated and justified relevant to purpose.
Principle 3	P3	The type of cost being estimated should be clearly defined, regarding economic vs. financial, real-world vs. guideline, and incremental vs. full cost, and whether the cost is 'net of future cost,' should be justified relevant to purpose.
Principle 4	P4	The 'units' in the unit costs for strategies, services, and interventions should be defined, relevant for the costing purpose, and generalizable.
Principle 5	P5	The time horizon should be of sufficient length to capture all costs relevant to the purpose, and consideration should be given to disaggregating costs into separate periods where appropriate.
Principle 6	P6	The scope of the inputs to include in the cost estimation should be defined and justified relevant to purpose.
Principle 7	P7	The methods for estimating the number of inputs should be described, including data sources and criteria for allocating resources (Describe the measurement of each input as either top-down or bottom-up, a method to allocate human resources inputs, overhead and other resources and methods for excluding research costs).
Principle 8	P8	The sampling strategy used should be determined by the precision demanded by the costing purpose and designed to minimize.

Principle 9	P9	The selection of the data source(s) and methods for estimating service use should be described, and potential biases reported in the study limitations.
Principle 10	P10	Consideration should be given to the timing of data collection to minimize recall bias and, where relevant, the impact of seasonality and other differences over time.
Principle 11	P11	The sources for price data should be listed by input, and clear delineation should be made between local and international price data sources, and tradeable, non-tradeable goods (Report the sources of price data by input and where local and international prices were uses).
Principle 12	P12	Capital costs should be appropriately annuitized or depreciated to reflect the expected life of capital inputs (Describe the depreciation approach, discount rate used from capital goods, and expected life years of capital goods and data source).
Principle 13	P13	Where relevant an appropriate discount rate, inflation and exchange rates should be used, and clearly stated (discount rate used for future costs, currency year, conversion made and inflation type, and rate used).
Principle 14	P14	The use and source of shadow prices for goods and for the opportunity cost of time should be reported (Report methods for valuing volunteer time and adjustments for input prices for donated or subsidized goods).
Principle 15	P15	Variation in the cost of the intervention by site size/organization, sub-populations, or by other drivers of heterogeneity should be explored and reported.
Principle 16	P16	The uncertainty associated with cost estimates should be appropriately characterized (describe sensitivity analyses conducted and list of possible sources of bias).
Principle 17	P17	Cost estimates should be communicated clearly and transparently to enable decision-maker(s) to interpret and use the results (limitations, conflicts of interest and open access).

Table S5 Quality assessment using Consolidated Health Economics Evaluation Reporting Standard (CHEERS) statement for published costs and CEA studies [105]

Section	Item No	CHEERS checklist—Items to include when reporting economic evaluations of health interventions	Included/not applicable*
Title and abstract			
Title	Q1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis," and describe the interventions compared	Included
Abstract	Q2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Included
Introduction			
Background and objectives	Q3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance to health policy or practice decisions.	Included
Methods			
Target population and subgroups	Q4	Describe the characteristics of the base case population and subgroups analyzed, including why they were chosen.	Included
Setting and location	Q5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Included
Study perspective	Q6	Describe the perspective of the study and relate this to the costs being evaluated.	Included
Comparators	Q7	Describe the interventions or strategies being compared and state why they were chosen.	Included
Time horizon	Q8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Included
Discount rate	Q9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Included
Choice of health outcomes	Q10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Included

Measurement of effectiveness	Q11a	Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Included Did the study describe fully the design and measurement of effectiveness? Q11
	Q11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	
Measurement and valuation of preference-based outcomes	Q12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable
Estimating resources and costs	Q13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with alternative interventions. Describe primary or secondary research methods for valuing each resource item regarding its unit cost. Describe any adjustments made to approximate to opportunity costs.	Included Did the study describe approaches to estimate resources and costs? Q13
	Q13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item regarding its unit cost. Describe any adjustments made to approximate to opportunity costs.	
Currency, price date, and conversion	Q14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate	Included
Choice of model	Q15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show the model structure is strongly recommended.	Included
Assumptions	Q16	Describe all structural or other assumptions underpinning the decision-analytical model.	Included

Analytical method	Q17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half-cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty	Included
Results			
Study parameters	Q18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Included
Incremental costs and outcomes	Q19	For each intervention, the report means values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Included
Characterizing uncertainty	Q20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Included Did the study characterize uncertainty? Q21
	Q20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Included Did the study characterize uncertainty? Q21
Characterizing heterogeneity	Q21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Included

Discussion			
Study findings, limitations, generalizability, and current knowledge	Q22	Summarize key study findings and describe how they support the conclusions reached. Discuss limitations and the generalizability of the findings and how the findings fit with current knowledge	Included
Source of funding	Q23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support	Included
Conflicts of interest	Q24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of journal policy, we recommend authors comply with the International Committee of Medical Journal Editors recommendations	Included Did the study describe any potential conflict of interest?

*Not applicable refers the CHEER assessment question, which is not applicable for that given study; for example, Q11 is assessing if the study reported effectiveness (QALYs, DALYs, infection averted) and if the study is a costing study Q11 is not applicable.

Table S6 Findings from a quality assessment using the GHCC's principles and methods reporting checklist for cost studies included in review [47] (n=44)

Author, year	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13[1]	P14	P15	P16	P17	Type of data source	Score[1]
Adebajo, 2013 (125)	Y	N	N	N	N	N	N	N	N	N	N	N/A	N/A	N	N	N	N	Slides	3/17
Ahmed, 2018 (155)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	Poster	15/17
Aliyu, 2012 (159)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	Y	N	Y	PRP	15/17
Allen, 2014 (126)	Y	Y	N	N	Y	N	N	N	N	N	Y	N	N/A	N	N	N	N	Abstract	5/17
Armbruster, 2010 (142)	Y	Y	N	Y	N	N	N	N	Y	Y	N	N	N	N	N	N	Y	PRP	6/17
Bassett, 2007 (127)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N/A	N	N	N	N	Y	PRP	12/17
Bassett, 2014 (33)	Y	Y	N	Y	Y	Y	Y	Y	N	Y	Y	N/A	Y	N	N	Y	Y	PRP	13/17
Bautista-Arredondo, 2016 (128)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	N	Y	PRP	16/17
Bogart, 2017 (160)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	N	Y	PRP	16/17
Chang, 2016 (152)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	14/17
Grabbe, 2010 (153)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	PRP	14/17
Hauck, 2018 (143)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	Slides	15/17
Hausler, 2006 (30)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	PRP	14/17
Helleringer, 2013 (144)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	14/17
Ibekwe, 2017 (59)	Y	N	N	Y	N	N	N	N	N	N	N	N/A	N/A	N	N	N	N	Abstract	4/17
Kahn, 2011(157)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	PRP	14/17
Kahwa, 2008 (161)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N	N	N	Y	PRP	14/17

Author, year	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13[1]	P14	P15	P16	P17	Type of data source	Score[1]
Labhardt, 2014 (145)	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	12/17
Lasry, 2019 (146)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	PRP	15/17
Liambila, 2008 (129)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	Y	N	Y	Report	15/17
Maheswaran, 2016 (156)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	PRP	17/17
Meehan, 2009 (154)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	PRP	13/17
Mangenah, 2019 (50)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	PRP	15/17
Menzies, 2009 (130)	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	N/A	N/A	N	N	N	Y	PRP	12/17
Muhumuza, 2012 (131)	Y	N	N	Y	Y	N	N	N	N	Y	N	N	N	N	N	N	Y	Abstract	5/17
Mulogo, 2013 (132)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	14/17
Mwenge, 2017 (133)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	PRP	15/17
Negin, 2009 (147)	Y	N	Y	Y	Y	Y	N	Y	N	Y	Y	N/A	N/A	N	N	N	Y	PRP	11/17
Obure, 2015 (134)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N	N	Y	PRP	16/17
Obure, 2012 (135)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N	N	Y	PRP	15/17
Orlando, 2010(162)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N	N	Y	Y	PRP	15/17
Parker, 2015 (148)	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	N	N	N	N	N	Y	PRP	10/17
Perchal, 2006 (136)	Y	N	Y	Y	Y	N	Y	N	Y	Y	Y	N/A	N/A	N	N	N	Y	Slides	11/17
Perez, 2016 (137)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	Poster	14/17
Pinto, 2013 (138)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	N	Y	PRP	16/17
Rutstein, 2013 (61)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	14/17
Shade, 2013 (139)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	Y	N	Y	PRP	15/17

Author, year	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13[1]	P14	P15	P16	P17	Type of data source	Score[1]
Sharma, 2016 (32)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	PRP	16/17
Sharma, 2014 (149)	Y	Y	N	Y	N	Y	N	Y	Y	Y	N	N	N	N	N	N	Y	Abstract	8/17
Smith, 2015 (150)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	PRP	15/17
Tabana, 2015 (140)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	PRP	15/17
Terris-Prestholt, 2006 (163)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	PRP	16/17
Terris-Prestholt, 2008 (141)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	14/17
Tumwesigye, 2010 (151)	Y	Y	Y	Y	Y	N	N	Y	N	Y	N	Y	Y	Y	N	N	Y	PRP	11/17

[1]Non applicable = N/A was assigned to discount if the analysis was limited to one year. Additional points were awarded to the "Score" column if the cost principle(s) was/were N/A for the study.

PRP: Peer-reviewed papers

Table S7 Findings from a quality assessment using Consolidated Health Economics Evaluation Reporting Standard (CHEERS) statement for published CEA studies included in the review [105] (n=15)

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9[1]	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Q17	Q18	Q19	Q20	Q21	Q22	Q23	Q24	Type of data source	Score
Allen, 2010 (58)	N	Y	Y	Y	Y	Y	Y	N	N	Y	Y	N/A	Y	N	N	N	N	N	Y	Y	N	Y	N	N	Abstract	13/24
Bassett, 2014 (33)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	PRP	22/24
Cambiano, 2015 (34)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	24/24
Cambiano, 2019 (35)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	24/24
Hausler, 2006 (30)	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y	PRP	20/24
Ibekwe, 2017 (59)	Y	Y	N	N	Y	Y	Y	N	N	Y	Y	N/A	N	N	N	N	N	N	Y	N	N	N	N	N	Abstract	9/24
John, 2008 (60)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	PRP	23/24
Leigh, 2018 (37)	Y	Y	Y	N	N	Y	Y	Y	N	Y	N	N/A	N	N	Y	N	N	N	Y	N	N	Y	N	N	Abstract	11/24
Kahn, 2012 (31)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	N	Y	Y	Y	N/A	Y	Y	Y	PRP	23/24
Maheswaran, 2017(36)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	24/24
Rutstein 2013 (61)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	24/24
Sharma, 2016 (32)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	24/24
Thielman, 2006 (62)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N	N	N	N	Y	Y	Y	N	Y	Y	Y	PRP	19/24
Walensky, 2011 (63)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	24/24
Waters, 2011 (64)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	23/24

[1]No discount if the analysis was limited to one year. Non applicable =N/A was assigned to discount if the analysis was limited to one year. Additional points were awarded to the "Score" column if the cost principle(s) was/were N/A for the study.

2.9. Implication for thesis

The systematic leterature review demostaated that few studies estimated the cost-effectiveness of providing HIV self-testing in addition to routine facility-based HTS in Zimbabwe (34, 35) and Malawi (36). Cambiano *et al.* applied Individual-based stochastic model from provider perspective to demonstrate implementing self-testing at the health facility would be cost-saving if it could be delivered at the full cost of US$3 per unit, and only cost-effective at ICER thresholds above US$10,000 per DALY averted if the cost of providing each episode was below US$9 (34). Maheswaran *et al.* applied stochastic microsimulation model to estimate the additional provision of self-testing was associated with an ICER of US$280.23 and US$2389.92 per QALY gained from a provider and societal perspective, respectively (36). In South Africa, Leigh and colleagues again applied stochastic microsimulation model to estimate the cost-effectiveness of self-testing in the context of antenatal partner testing and home-based testing (37). The authors reported the incremental cost of US$1,941.72 and US$1,111.85 per life-year gained for providing self-testing to the partner of a pregnant women at antenatal care and home-based self-testing, respectively (37).

This thesis will use a Markov microsimulation model (Paper 3) that accounts for the steps in HIV prevention and HIV care cascade to estimate the cost-effectiveness of HIVST compared with standard HIV testing services in Zambia. The HIV prevention cascade is an emerging approach and is similar to the HIV treatment cascade (169, 170). This prevention cascade can facilitate how those at risk of acquiring HIV can avoid infection through HIV interventions (such as HIV testing) and how to reach the optimal gain in impact on the demand side, supply-side (supporting linkage) or combination of both (169, 171)(168, 170).

This model is selected because it can help model different scenarios for each of the respective testing options being compared. Therefore, the Markov microsimulation model can assist policymakers in formulating informed scale-up plans of HIVST to reach adult populations who are unaware of their HIV status. Because HIVST is an emerging technology in Zambia, there is insufficient understanding of the use of alternative HIV testing approaches for HIVST distribution, and of the costs and effectiveness of HIVST. Thus, applications of Markov microsimulation model to inform programmatic decisions based on cost-effective approaches are essential to maximizing the uptake and impact of HIVST scale-up.

CHAPTER 3 HOW MUCH DOES IT COST TO ADD HIV SELF-TESTING INTO MALE CIRCUMCISION, OUTPATIENT, AND HIV TESTING SERVICES IN MALAWI, ZAMBIA, AND ZIMBABWE? AN ECONOMIC EVALUATION (PAPER 2)

Overview of Paper 2

The systematic literature review Paper 1 in chapter 2 demonstrated the cost of different HIV testing services in sub-Saharan Africa; however, only three studies estimated the cost of HIVST. This chapter presents the cost analysis of distributing HIVST within voluntary medical male circumcision services and health facilities in Malawi, Zambia, and Zimbabwe.

In this cost analyses, I refine the allocation factors that were applied in Mwenge et al. 2017 and Mangenah et.al 2019 papers that I co-authored (Appendix I & II). The formulation of different allocation factors of different cost inputs was guided by a bottom-up costing approach in each country.

This paper is in preparation to be submitted to *The Journal of the International AIDS Society* in July 2020. Two supplementary tables are included at the end of the thesis.

This paper fulfils research question two: calculating the cost of HIVST distribution within health facilities and within communities in Zambia.

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

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Surname/Family Name	Ahmed		
Thesis Title	Reaching the First 90%: Cost-effectiveness of HIV self-testing services in Zambia		
Primary Supervisor	Fern Terris Prestholt		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	The Journal of the International AIDS Society
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	Johnson, Elizabeth L Corbett, Frances M Cowan, Helen Ayles, Hendramoorthy Maheswaran, Fern Terris-Prestholt
Stage of publication	**Not yet submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I planned the conceptualization, data curation, cost analysis and writing of the first draft.

SECTION E

Student Signature	[redacted]
Date	23 Sep 2019.

Supervisor Signature	[redacted]
Date	23-9-2019

Title: How much does it cost to add HIV self-testing into male circumcision, outpatient, and HIV testing services in Malawi, Zambia, and Zimbabwe? An economic evaluation

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Abstract

Background: HIV self-testing (HIVST) is a novel approach to HIV testing where people can perform and interpret their own HIV test. This study presents the cost of delivering HIVST within 13 voluntary medical male circumcision (VMMC) services and 21 health facilities in Malawi, Zambia, and Zimbabwe.

Methods: The annual incremental economic costs of distributing HIVST kits were estimated from a providers' perspective. We performed a prospective cost analysis between 2016 and 2018, using expenditures analysis and field observations. A sensitivity analysis was conducted to test key assumptions, and scenario analyses explored potential programmatic and setting specific variations on unit costs.

Results: Across the 34 sites implementing these models, the intensity of distribution varied widely, achieving distribution from as low as 733 HIVST kits through VMMC mobilizers in Malawi to 14,886 kits distribution within integrated testing service in Zimbabwe. The costs of distributing these kits ranged from $7.71 in the Zimbabwean VMMC model to $24.83 in the less intensive mobilizer distribution model in Zambia. The smallest sites experienced the highest costs, and the largest sites observe lower costs.

Conclusions: The cost analysis has shown that for both models the costs are slightly higher than the standard facility-based finger prick testing. It also demonstrated the importance of cost reduction on the HIVST kit price to ensure access to HIVST and the scalability of the intervention. Continued efforts are needed to reach new testers, particularly men and adolescents to achieve national and global goals – including the 90-90-90 targets and soon to be 95-95-95 goals.

Trial registration numbers: Malawi (NCT02793804), Zambia (NCT02718274); and Zimbabwe (PACTR201607001701788)

Keywords: HIV self-testing; costs; cost analysis; HIV testing services; Malawi; Zambia; Zimbabwe.

Introduction

Despite substantial progress towards combating the HIV epidemic globally, the greatest burden continues to be in Eastern and Southern Africa (ESA). In 2017, it was estimated that 45% of all new HIV infections occurred in ESA, where 53% of people living with HIV (PLHIV) live (87). Despite substantial scaled-up of HIV testing in Malawi, Zambia, and Zimbabwe, 90%, 72% and 85% of PLHIV, respectively are aware of their status (87). Particularly, disparities in HIV testing and knowledge of HIV positive status among young people (ages 15-24) and men remain critical (90, 92, 172). Men have not benefited as much from this scale-up in conventional HIV testing services (HTS) because most are integrated into sexual and reproductive health and antenatal services focused on women. While HIV related mortality has decreased among women it has flat-lined for men in ESA (87), largely due to delayed diagnosis, with men often diagnosed during the late disease stage.

To reach undiagnosed groups and achieve the United Nation's 90-90-90 targets by 2020, which starts with diagnosing 90% of all PLHIV (88), innovative HIV testing approaches are needed. HIV self-testing (HIVST) is one such approach recommended by WHO (42) and has been shown to be acceptable, safe, accurate, and effective in reaching those who may not test otherwise (27, 49, 106, 108, 156, 173-183). Recent studies of community-based HIVST suggest that wide-scale distribution successfully reached first-time testers, particularly men and young people in ESA (46) at a providers' cost of slightly more than conventional HTS (49, 184-187), and is likely to significantly reduce user costs, particularly among men (188). This study complements the existing costings of HIVST by presenting the costs of HIVST distribution within the following health services: voluntary medical male circumcision (VMMC) and provider-initiated testing services within the outpatient department (OPD) and integrated into other clinical services.

It was hypothesized that HIVST distribution could increase uptake of VMMC services by providing men the opportunity to test for HIV themselves, either prior to presenting for VMMC or in private at the VMMC clinic. Additionally, using facility-based counsellors and health care workers to promote HIVST, the health facility model was designed to reach undiagnosed HIV positive people while at their routine OPD in Zambia and HTS visits in Zimbabwe, successfully increasing uptake by men in Zambia and Zimbabwe, with 45.8% and 29.0% of HIVST kits taken by men, respectively (46). Moreover, facility-based distribution of HIVST in outpatient waiting rooms in Malawi increased HIV testing uptake and identified more HIV positive cases than provider-initiated testing (189). While these approaches may achieve impact, it is increasingly challenging to maximize HIV testing

coverage because of limited and declining domestic and donor resources for additional testing. As more countries work to implement HIVST effectively and efficiently, efforts to understand the cost of HIVST implementation are critical. In this study, we examine the full programme costs (including a share of central PSI costs) of distributing HIVST within VMMC services in Malawi, Zambia, and Zimbabwe, to the OPD model in Zambia, and integrated model with existing HTS (New Start Centres) in Zimbabwe.

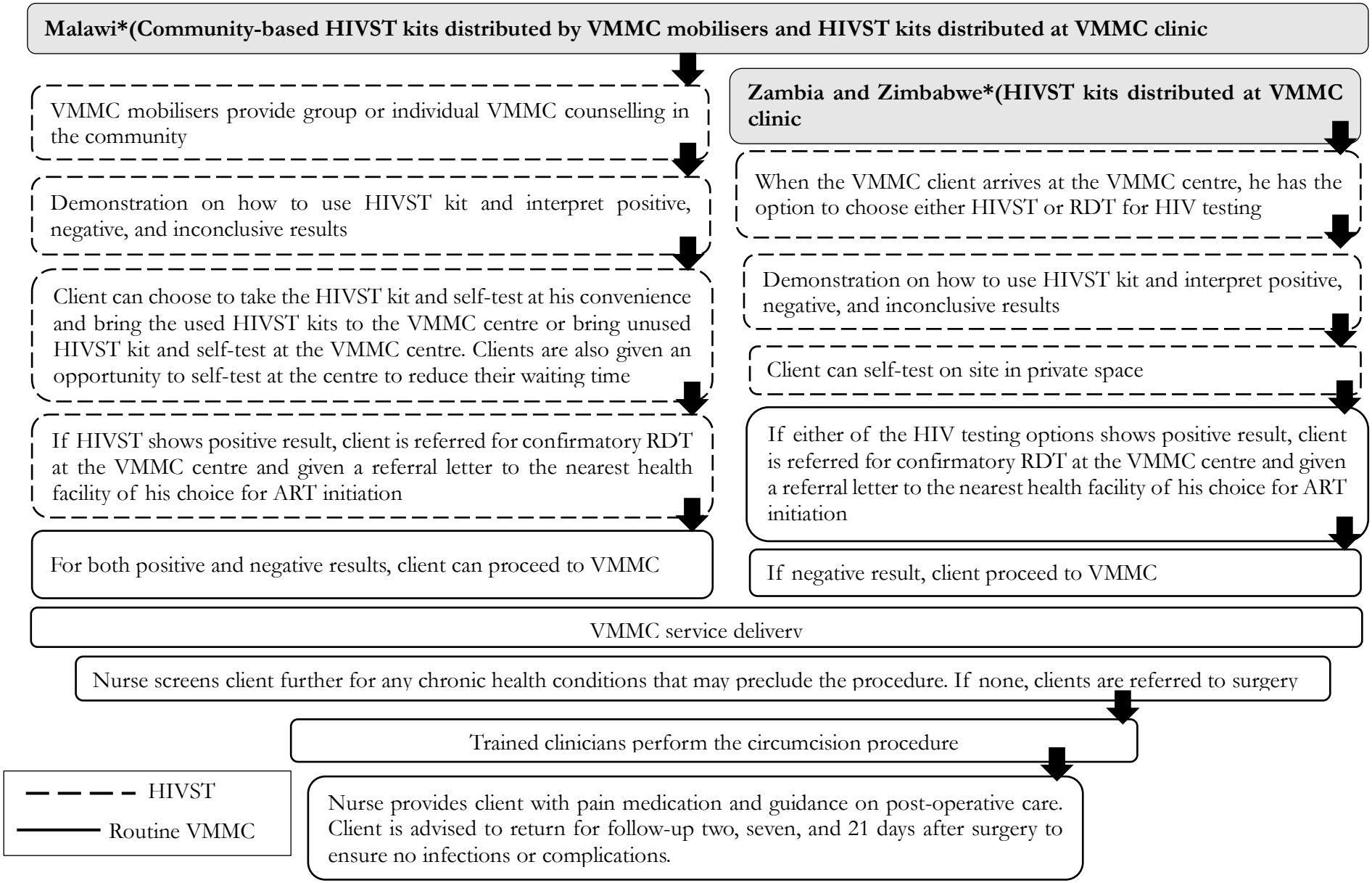
Methods

The intervention and setting

The aim of community-based distribution using VMMC mobilizers and distribution at the VMMC clinic focused on VMMC demand creation to reduce barriers for men (age 16 years and older) who fear to get tested for HIV before VMMC at the VMMC clinic and to improve time and efficiency efforts by offering HIVST to adult males who are mobilized for VMMC to self-test at home or at the clinic before accessing the VMMC services. The VMMC model for HIVST kits distribution varied across countries. In Malawi, the VMMC model applied distribution at the VMMC clinic as well as community-based distribution using VMMC mobilizers. In Zambia and Zimbabwe, the VMMC model implemented HIVST kits distribution at the VMMC clinics. In Zimbabwe, 40.2% of men have received HIVST kits from VMMC mobilizers before going for male circumcision (46).

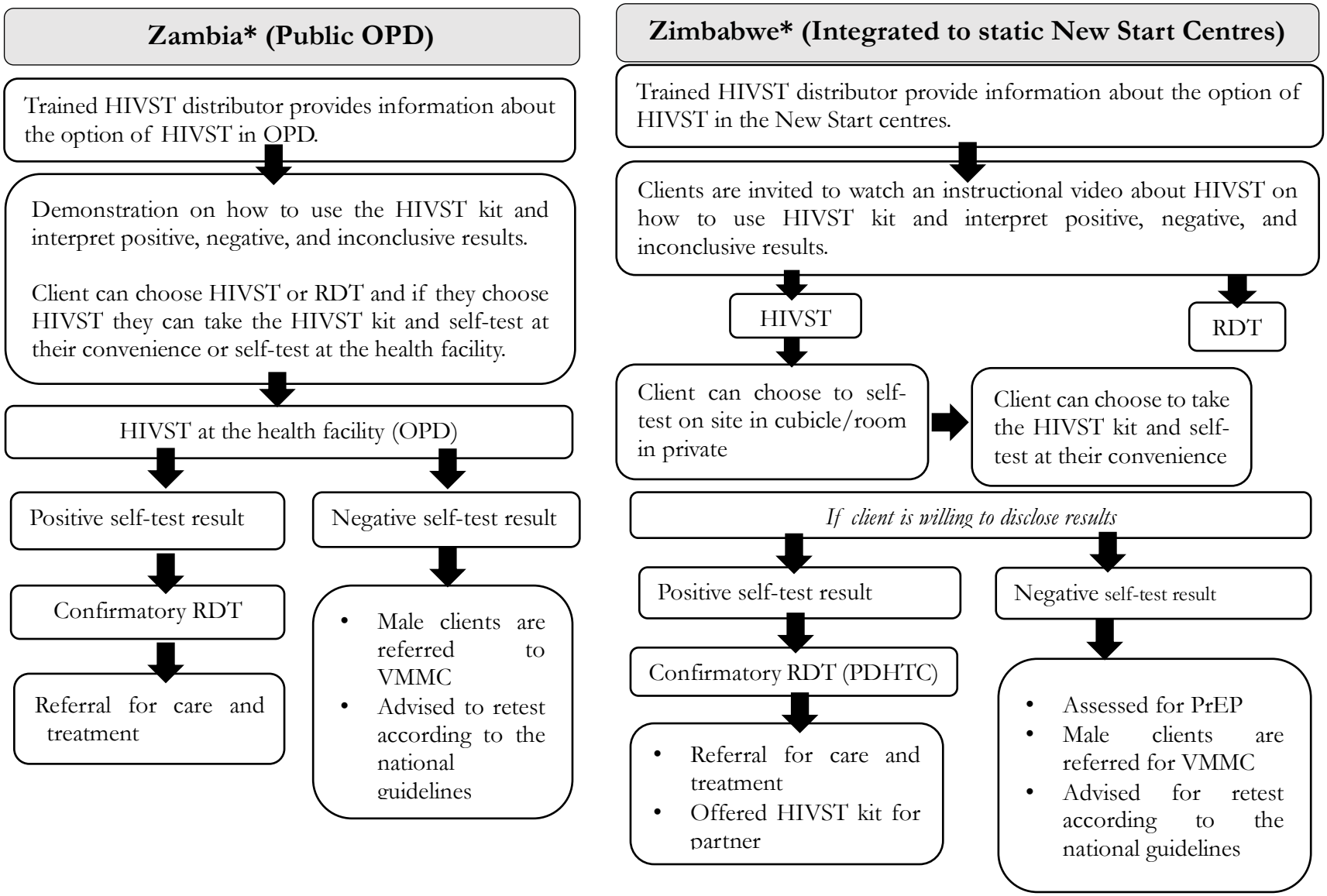
The aim of the OPD model (Zambia) and integrated model (Zimbabwe) was a case finding among clients (age 16 years and older) who were accessing health facilities to maximize HIV diagnosis, ART initiation, and increase prevention service uptake. In Zambia, the OPD model assigned a trained HIVST distributor to provide information about the option of HIVST in OPD and to demonstrate on how to use the HIVST kits and interpret positive, negative, and inconclusive results. In Zimbabwe, the integrated model provided an instructional video on how to use HIVST and interpret results. Figures 3.1 and 3.2 provide an overview of the VMMC, OPD, and integrated models, respectively. Additional implementation details have been published elsewhere (46, 190).

This study costed a total of 13 VMMC clinics (two in Malawi, eight in Zambia and three in Zimbabwe), and a total of 21 health facilities (16 in Zambia and five in Zimbabwe). The characteristics of the VMMC clinics and the health facilities included both urban and semi-urban settings (Table 3.1).



**Both in Zambia and Zimbabwe, all clients were advised to places used kits together with the result form in a drop box located at health facility*

Figure 3.1 Flow diagram for VMMC demand creation after HIVST and client flow – VMMC model



**Both in Zambia and Zimbabwe, all clients were advised to places used kits together with the result form in a drop box located at health facility*

Figure 3.2 Flow diagram for HIVST kits distribution using OPD and integrated models

Table 3.1 Characteristics of setting and overview of HIVST kits distribution models (in 2017 US$)

Characteristics	VMMC model			Facility model		Source
	Malawi	Zambia	Zimbabwe	Zambia	Zimbabwe	
				OPD model	Integrated model	
National HIV prevalence among adults 15 to 49 years (%)	10%	12%	14.1%	12%	14.1%	(90, 92, 172)
Number of districts	1	3	2	4	5	
Number of sites	2	8	3	16	5	
Catchment population*	181,549	311,566	79,369	182,655	89,480	(133, 191-193)
Location (Urban/Semi-urban/Rural)	Urban	Semi-urban	Urban	Semi-urban	Urban	
Average number of VMMC mobilizers	39	13	5	16	38	
Number of community-based HIVST kits distributed by VMMC mobilizers	733	NA	NA	NA	NA	
Number of HIVST kits distributed	2,742	11,330	2,870	12,885	14,886	
Services offered to HIV self-test clients	Demonstration of how to use the HIVST kits and how to interpret positive, negative and inconclusive results					
VMMC mobilisers compensation	Allowances for VMMC demand creation. No additional payment for HIVST distribution.	Allowances for VMMC demand creation. No additional payment for HIVST distribution.	Allowances for VMMC demand creation. No additional payment for HIVST distribution	Allowances	Salaried	

* Catchment population around the health facility

Costing methods

Using a provider's perspective, we estimated the annual incremental economic costs of each intervention model by country. The incremental costs for the VMMC model only included costs for community-based VMMC demand creation and distribution at the VMMC clinic and did not include the costs for VMMC services. For the OPD and integrated models, all resources used were accounted for including donated resources by calculating the opportunity cost for the unpaid voluntary time (54). Annual financial expenditures (in USD) were collected from Population Services International (PSI) country offices and their sub-grantees over one year: ranging from February 2017 to January 2018 for Malawi and July 2016 to June 2017 for Zambia and Zimbabwe. Field observations were conducted during this period to further document implementation; capture donated goods and services, and derived allocation factors for apportioning shared costs.

The activity-based allocation factors applied are presented in Table 3.2 and are consistent with those used in the cost analysis of HIVST kits distribution using community-based distributing agents (49). Table 3.2 was developed over two years using activity-based allocation in which we assigned cost of each activity to all products and services to specific cost inputs. This cost inputs are used to present the cost analysis results in Table 3.3 and 3.4. The activity-based allocation factor could offer a practical approach to estimating unit costs from project expenditures (i.e., using a top-down method). Drummond detailed the four methods for allocating shared costs: direct allocation, step-down allocation, step-down allocation with interactions, and simultaneous allocation (54). The direct allocation methods "ignores the interaction of overhead department." Moreover, step-down allocation and step-down allocation with interactions and simultaneous allocation methods apply allocations to account for all unallocated costs (54). The activity-based allocation aim to guide the process of calculating the unit cost for new intervention implementation at the site level in detail. Although this study used both bottom-up and top-down approaches to construct cost inputs using the activity-based allocation, it is vital to recognize the prominent role of the unit cost calculation in scaling up of the intervention. For example, costs for supplies such as t-shirt and bags might be important during the pilot stage of HIVST distribution; however, these costs can be exempted when the programme matures and moves to the scale-up stage.

The expenditure analysis started by categorizing each expenditure line item by cost input type and resource use level (central, warehouse and site level). Capital costs included project start-up costs, such as initial training and sensitization, and equipment and building space. The start-up period was defined as including all costs which were incurred before the first day of

HIVST kit distribution. Capital goods were annualized over their useful years of life using a 3% discount rate. Recurrent costs included costs of training, personnel, HIVST kits, and other supplies, building utilities, vehicle operation, and maintenance, and other recurrent costs such as project administration and coordination. Using standardized allocation factors adapted from Mangenah [26] (see Table 3.2) each cost input line item was allocated across each HIVST distribution model. Lastly, we applied costs from the HIVST distribution model to site level (individual VMMC clinic, OPD, and integrated New Start centres). Overheads, including centrally shared costs were shared across models and sites by their respective share of direct site level expenditures.

The cost per HIVST kit distributed was estimated by dividing the total cost by the total number of HIVST kits distributed. We have used nominal exchange rates rather than purchasing power parities as this are the most important for projecting costs and informing global fund applications. Costs are presented in 2017 US$.

Table 3.2 Cost allocation factors across the interventions by cost input type

Cost input type	Allocation factors to site level		
	Malawi	**Zambia**	**Zimbabwe**
Training	% of direct expenditure	% of distributors	% of distributors
Sensitization	% of direct expenditure	% of direct expenditure	% of direct expenditure
Other Start-up	N/A	% of HIVST kits distributed	% of HIVST kits distributed
Building and storage			
- Central	% of HIVST kits distributed	% of direct expenditure	% of direct expenditure
- Warehouse	N/A	% of HIVST kits distributed	% of HIVST kits distributed
- Site-level	Equally between sites	% of direct site level expenditure	% of direct site level expenditure
Equipment			
- Central equipment	% of HIVST kits distributed	% of direct expenditure	% of direct expenditure
- Site-level	Equally between sites	% of direct site level expenditure	% of direct site level expenditure
Vehicles and bicycles	% of mileage/distance (in km)	N/A	N/A
Other capital	N/A	% of HIVST kits distributed	% of HIVST kits distributed
Personnel	% Staff time allocations	% of distributors	% of distributors
HIVST Kits	observed HIVST kits distributed by site	observed HIVST kits distributed by site	observed HIVST kits distributed by site
Supplies			
- T-shirts, bags, flipcharts	% of HIVST kits distributed	% of distributors	% of distributors
- Other supplies	% of HIVST kits distributed	% of HIVST kits distributed	% of HIVST kits distributed
Vehicle maintenance and transportation	% of mileage/distance (in km)	% of mileage/distance (in km)	% of mileage/distance (in km)

Building operations and maintenance	% of direct expenditure	% of direct expenditure	% of direct expenditure
- Central	N/A	% of HIVST kits distributed	% of HIVST kits distributed
- Warehouse	Equally between sites	% of direct site level expenditure	% of direct site level expenditure
- Site-level			
Waste management	N/A	N/A	% of HIVST kits returned
Other recurrent	% of HIVST kits distributed	% of HIVST kits distributed	% of HIVST kits distributed

Sensitivity and scenario analyses

Sensitivity and scenario analyses were conducted to explore the robustness of the cost analysis by examining the extent to which the unit costs are affected by changes in key assumptions (unmeasured cost inputs) and how these would vary under different scenarios. Univariate sensitivity analyses focused on: discount rate (base case 3%, range 0% to 15%); allocation of central cost (base case % of direct expenditures range % of HIVST kits distributed to % of distributors); economic life years of other capital (base case 5 years, range 2.5 years to 7.5 years); economic life years of start-up training and sensitization (base case two years, range one to three years); HIVST kit price (base case US$2.78 range US$1 to US$5.56). A multivariate sensitivity analysis applied the values of the most optimistic (best-case scenario) and pessimistic (worst-case scenario) parameters. The scenario analysis was used to explore the impact of higher and lower resource costs or service outputs. This included varying personnel salary costs (+/-10%), the quantity of HIVST kits distributed (+/-10%), and vehicle operation costs (+/-10%).

Results

VMMC model

Table 3.3 presents the total number of HIVST kits distributed, the incremental total and unit costs of HIVST distribution through community-based distribution using VMMC mobilizers and distribution at the VMMC clinic across the three countries over the 12-month study period. Table 3 presents the outputs, total, and unit costs for the 13 VMMC clinics. The community-based distribution by VMMC mobilizers distributed 733 HIV kits in Malawi across two VMMC clinics at a total cost of US$18,198 and an average cost of US$24.83. The initial training of distributors was relatively intensive with 39 distributors trained at an annualized cost of $8075. The recurrent cost of the VMMC mobilizer model is just $12.83 per kit distributed. The distribution at the VMMC clinic distributed 2,742 HIVST kits in same two sites in Malawi, and 11,330 HIVST kits in eight VMMC clinics in Zambia, and 2,870 HIVST kits in three VMMC clinics in Zimbabwe. The country average costs per HIVST kit distributed at the VMMC clinics were US$9.65, US$13.01 and US$7.71 for Malawi, Zambia and Zimbabwe, respectively (Table 3.3).

Table 3.3 HIV self-test kit distribution cost breakdown and key cost contributors VMMC model (in 2017 US$)

Cost input type	Malawi			Zambia		Zimbabwe	
	HIVST kits distributed at VMMC clinic	Community-based HIVST kits distributed by VMMC mobilizers	Facility-based HIV finger prick test	HIVST kits distributed at VMMC clinic	Facility-based HIV finger prick test	HIVST kits distributed at VMMC clinic	Facility-based HIV finger prick test
	Kits distributed: 2,742	Kits distributed: 733	Number of people tested 5,620	Kits distributed: 11,330	Number of people tested: 3,161	Kits distributed: 2,870	Number of people tested: 1,542
	Total Cost	Total Cost	Total Cost	Total Cost	Total Cost	Total Cost	Total Cost
Start-up							
Training	$5,383	$8,075	$0	$3,067	$0	$0.11	$0
Sensitization	$722	$722	$0	$2.79	$0	$1.82	$0
Other start-up	$0	$0	$0	$7,356	$0	$1,234	$0
Total start-up	$6,105	$8,797	$0	$10,426	$0	$1,236	$0
Capital costs							
Building & storage	$195	$0	$1722	$0	$133	$59	$190
Equipment	$0	$0	$0	$0	$0	$267	$0
Central equipment	$1,244	$0	$0	$1,186	$0	$554	$0
Site level	$0	$0	$598	$0	$160	$0	$180
Vehicles and bicycles	$249	$0	$0	$0	$91	$0.64	$22
Other capital	$0	$0	$0	$0	$43	$882	$0
Total capital costs	$1,688	$0	$2,320	$1,186	$427	$1,763	$392
Total start-up and capital costs	$7,793	$8,796	$2,320	$11,612	$427	$2,999	$392
Recurrent Costs							

Recurrent training	$0	$0	$0	$1,416	$0	$879.58	$0
Test kits	$7,617	$2,036	$4,078	$20,561	$3,421	$6,745	$1,826
Other supplies	$362	$97	$3,802	$6,940	$450	$0	$441
Other supplies	$0	$0	$0	$0	$0	$1,490	$203
Sensitization	$0	$0	$0	$4,468	$0	$0	$0
Building & storage							
Central	$0	$0	$0	$4,528	$0	$0	$0
Site level	$103	$0	$0	$0	$0	$0	$0
Personnel	$3,623	$5,435	$1,568	$74,900	$6,678	$10,045	$7,670
Vehicle operation & maintenance	$4,665	$1,247	$710	$14,461	$0	$237	$0
Building operation/maintenance							
Central	$103	$0	$0	$1,690	$0	$0	$56
Warehouse	$0	$0	$0	$0	$0	$250	$0
Site level	$0	$0	$84	$0	$751	$0	$0
Other recurrent	$2,196	$587	$2,720	$6,781	$309	$352	$2
Waste Management	$0	$0	$1,187	$0	$0	$0	$0
Total recurrent costs	$18,698	$9,402	$14,149	$135,745	$11, 609	$19,999	$10,198
Total costs	$26,491	$18,198	$16,469	$147,357	$12,036	$22,998	$10,590
Total costs without start up	$20,386	$9,402	$16,468	$136,931	$12,036	$21,762	$10,590
Cost per HIVST kits distributed	$9.65	$24.83		$13.01		$7.71	
Cost per person tested using facility-based HIV finger prick test			$2.93		$4.24		$8.79

Figure 3.3 shows the number of HIVST kits distributed and cost per kit distributed at site level across the three countries via VMMC model. A wide variation in cost across sites was identified. The site-level costs per HIVST kit distributed by VMMC mobilizers were US$19.24 and $32.04, while lower costs were seen where kits were distributed within the VMMC service, at US$9.47 and US$9.72, respectively. In VMMC clinics in Zambia, the cost per kit distributed across the sites ranged from US$8.08 to US$29.13, and in Zimbabwe, it ranged from US$6.09 to US$11.93 (Figure 3.3). For more detailed information, see Table 3.6 at the end of this paper.

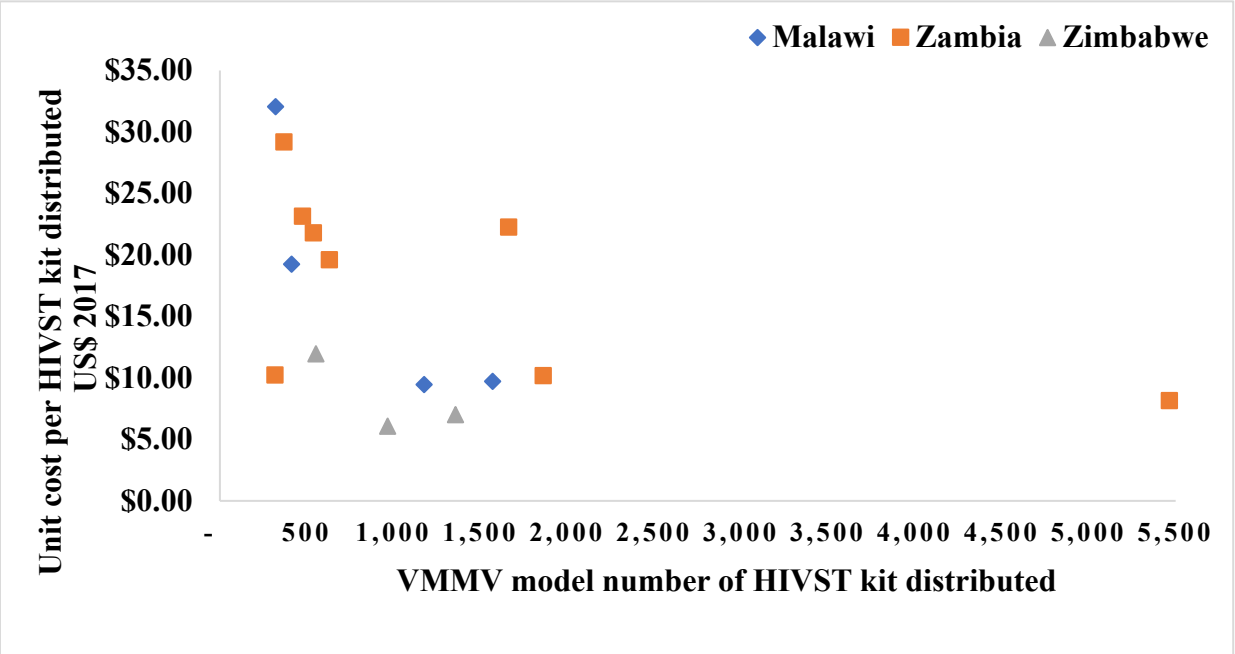


Figure 3.3 VMMC model site-level unit costs by the quantity of HIVST kits distributed (in 2017 US$)

OPD and integrated models

Table 3.4 presents the economic costs of incorporating HIVST distribution into OPD services in Zambia and into the integrated model in Zimbabwe. In Zambia, the OPD model distributed 12,885 HIVST kits across 16 sites. The total cost was US$203,659, and the average cost per kit distributed was US$15.81. In Zimbabwe, the integrated HTS model distributed 14,886 HIVST kits across five sites. The total cost was US$146,577, averaging US$9.85 per kit distributed (Table 3.4).

Table 3.4 HIV self-test kit distribution cost breakdown and key cost contributors facility-based models (in 2017 US$)

Cost input type	Zambia		Zimbabwe	
	Facility-based OPD model	Facility-based HIV finger prick test	Faculty based Integrated model	Facility-based HIV finger prick test
	Kits distributed: 12,885	Number of people tested: 3,161	Kits distributed: 14,886	Number of people tested: 1,542
	Total Cost	Total Cost	Total Cost	Total Cost
Start-up				
Training	$3,670	$0	$0.73	$0
Sensitization	$3.86	$0	$12.05	$0
Other start-up	$10,144	$0	$8,278	$0
Total start-up	$13,818	$0	$8,291	$0
Capital costs				
Building & storage				
Central	$0	$0	$392	$0
Site level	$0	$133	$0	$190
Equipment				
Central equipment	$1,632	$0	$1,772	$0
Site level	$0	$160	$2,898	$108
Vehicles and bicycles	$0	$91	$0	$22
Other capital	$0	$43	$4.22	$0
Total capital costs	$1,632	$427	$5,067	$320
Total start-up and capital costs	$15,450	$427	$13,357	$320
Recurrent Costs				
Recurrent training	$2,377	$0	$5,618	$0
HIV Self-Test Kits	$28,417	$3,421	$34,982	$1,826
Sensitization	$6,729	$0	$0	$0
Building & storage				
Central	$6,413	$0	$0	$0

Personnel	$105,544	$6,678	$82,047	$0
Supplies	$0	$450	$0	$441
T-shirts, bags, flipcharts	$9,467	$0	$0	$0
Other supplies	$0	$0	$6,353	$203
Vehicle operation & maintenance	$17,953	$0	$1,028	$0
Building operation/maintenance				
- Central	$2,304	$0	$0	$56
- Warehouse	$0	$0	$1,081	$0
Other recurrent	$9,005	$309	$2,111	$0
Total recurrent costs	$188,209	$11, 609	$133,220	$2.01
Total costs	$203,659	$12,036	$146,577	$10,198
Total costs without start up	$189,841	$12,036	$138,286	$10,518
Cost per HIVST kits distributed	$15.81		$9.85	
Cost per person tested using facility-based HIV finger prick test		$4.24		$8.79

Figure 3.4 suggests that unit costs drop as the quantity of kits distributed on-site increases using the OPD model. Variation in site costs again show a 10- and 3-fold variation in cost per kit distributed, ranging from US$5.20 to US$58.92 and US$6.49 to US$22.78 in Zambia and Zimbabwe, respectively. More detail is provided at the end of the chapter in Table 3.7). Table 3.5 provides the unit cost for each distribution modality without start-up cost and the unit cost for facility-based finger prick testing to reflect the incremental unit cost of HIVST.

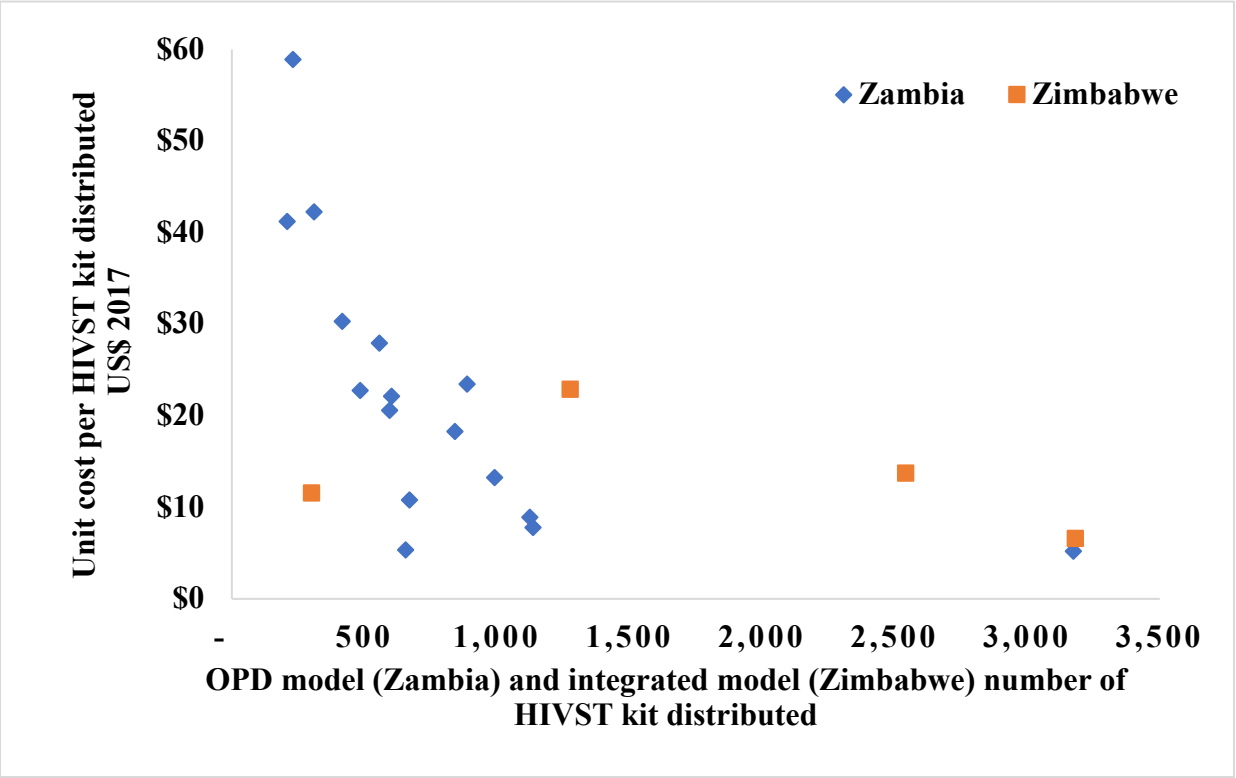


Figure 3.4 OPD and integrated model site-level unit cost by the quantity of HIVST kits distributed (in 2017 US$)

Table 3.5 Summary of costs and annual HIV testing outputs

HIV testing outputs	Malawi				Zambia				Zimbabwe			
	Community-based HIVST kits distributed by VMMC mobilizers	**HIVST kits distributed at VMMC clinic**	**Community-based (door-to-door) HIVST kits distribution (49)**	**Facility-based finger prick testing (133)**	**HIVST kits distributed at VMMC clinic**	**HIVST distribution at OPD**	**Community-based (door-to-door) HIVST kits distribution (49)**	**Facility-based finger prick testing (133)**	**HIVST kits distributed at VMMC clinic**	**Integrated model**	**Community-based (door-to-door) HIVST kits distribution (49)**	**Facility-based finger prick testing (133)**
Number of HIVST kits distributed	733	2,742	152,671	NA	11,330	12,885	103,589	NA	2,870	14,886	93,459	NA
Average annual number of people tested	NA	NA	NA	5,620	NA	NA	NA	3,161	NA	NA	NA	1,542
Total cost without start-up cost	$9,401	$20,356	$1,065,734	$16,468.28	$136,931	$189,841	$1,526,677	$12,036	$20,879	$138,286	$1,211,348	$10,518
Unit cost	$24.83	$9.65	$8.15	NA	$13.01	$15.81	$16.42	NA	$7.71	$9.85	$13.84	NA
Unit costs without start-up	$12.82	$7.43	$6.98	$ 2.93	$12.08	$14.73	$14.73	$4.24	$7.58	$9.29	$12.96	$8.79

Sensitivity and scenario analysis

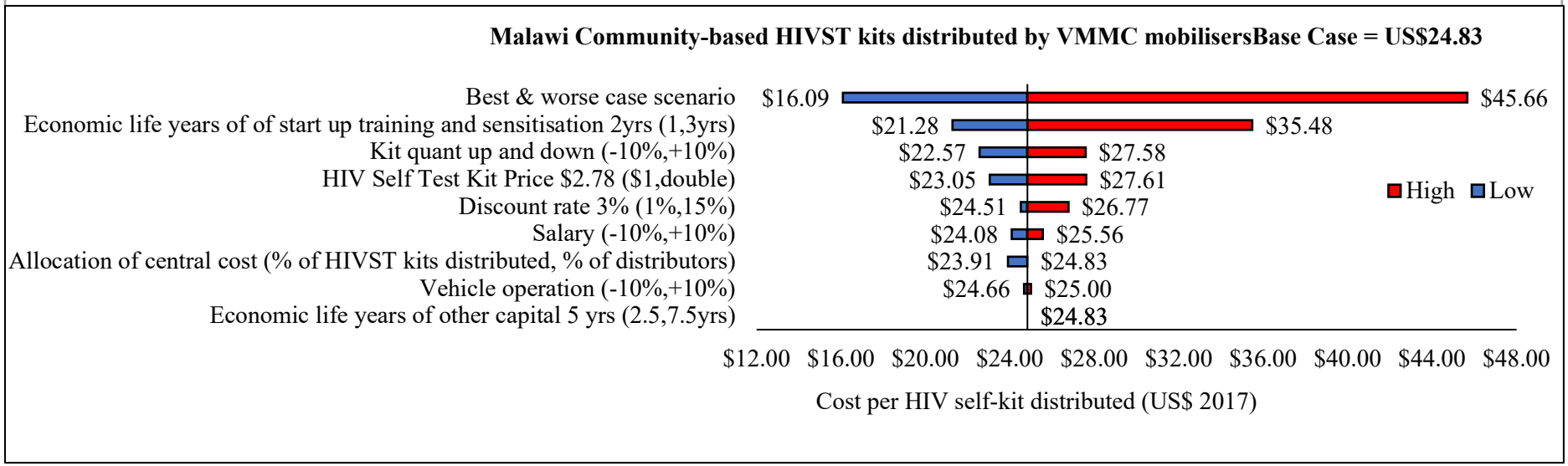
VMMC model

Figure 3.5 shows the findings from the sensitivity and scenario analyses undertaken for VMMC models in each of the three countries. In Malawi, for the community VMMC mobilizers distribution, the greatest impact scenarios/assumptions on the cost per kit distributed were the life years of capital items (range: US$21.28-US$35.48) and allocation of central costs (range: US$23.91-US$24.83). For VMMC clinic distribution sensitivity analysis, the allocation of central costs (range: US$8.85-US$9.61) and HIV self-test kit price (US$7.84-US$12.40) had a large influence. Applying all most advantageous and least advantageous assumption generates an estimate of the best and worst-case unit costs. In Malawi, the best-worst case scenario ranged from US$16.09-US$45.66 and US$5.54-US$16.23 for community-based and VMMC clinic HIVST kits distribution, respectively. For Zambia, the VMMC clinic model ranged from US$11.12 to US$16.05, primarily driven by allocation of central costs. For Zimbabwe, the two scenarios/assumptions that had the greatest impact on the cost per kit distributed were how central costs were allocated (range: US$6.80-US$10.28) and the HIVST kit price (range US$6.52-US$8.87) (see supplemental Table 3.10 for more detail).

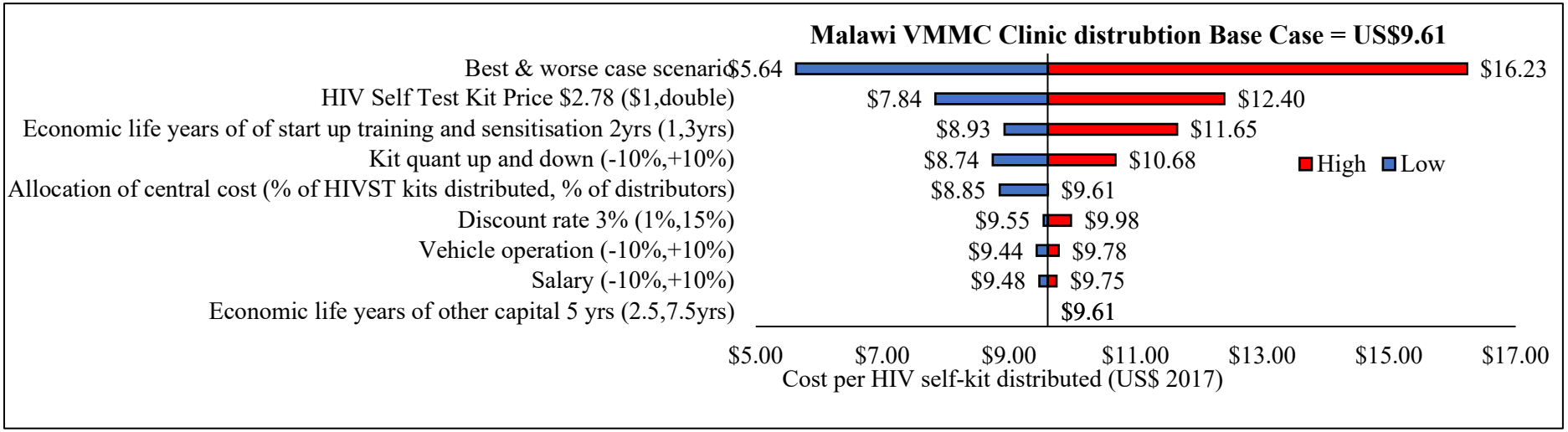
OPD and integrated HST models

For Zambia, in the OPD model, the two scenarios/assumptions that had the greatest impact on the cost per kit distributed were the HIVST kit price (range: US$14.59-US$16.95 per kit distributed) and the number of kits distributed (range: US$14.79-US$17.10 per kit distributed). Similar patterns were observed in the sensitivity and scenario analyses for the integrated models (Figure 3.6). In Zambia and Zimbabwe, the best-case scenarios were US$13.47 and US$6.45 per kit distributed, and the worst-case scenarios resulted in US$19.36 and US**$**16.91 per kit distributed in Zambia, and Zimbabwe, respectively (see supplemental Table 3.11 for more detail).

A. Sensitivity analysis for cost per HIVST distributed via community-based HIVST kits distributed by VMMC mobilisers-Malawi



B. Sensitivity analysis for cost per HIVST distributed via VMMC clinic distribution- Malawi



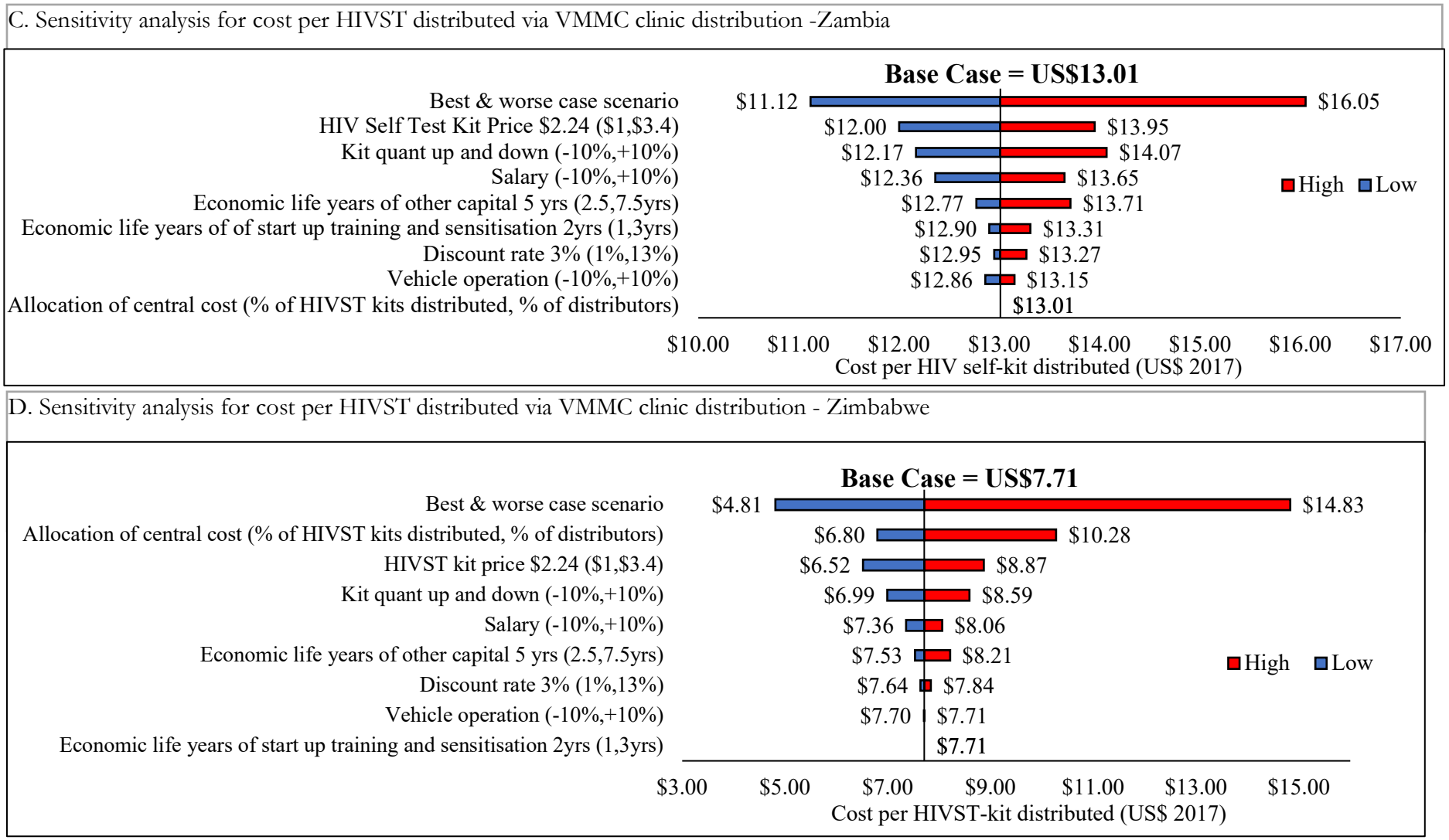


Figure 3.5 Country-level sensitivity analysis of unit cost per HIVST kit distributed via VMMC model (in 2017 US$)

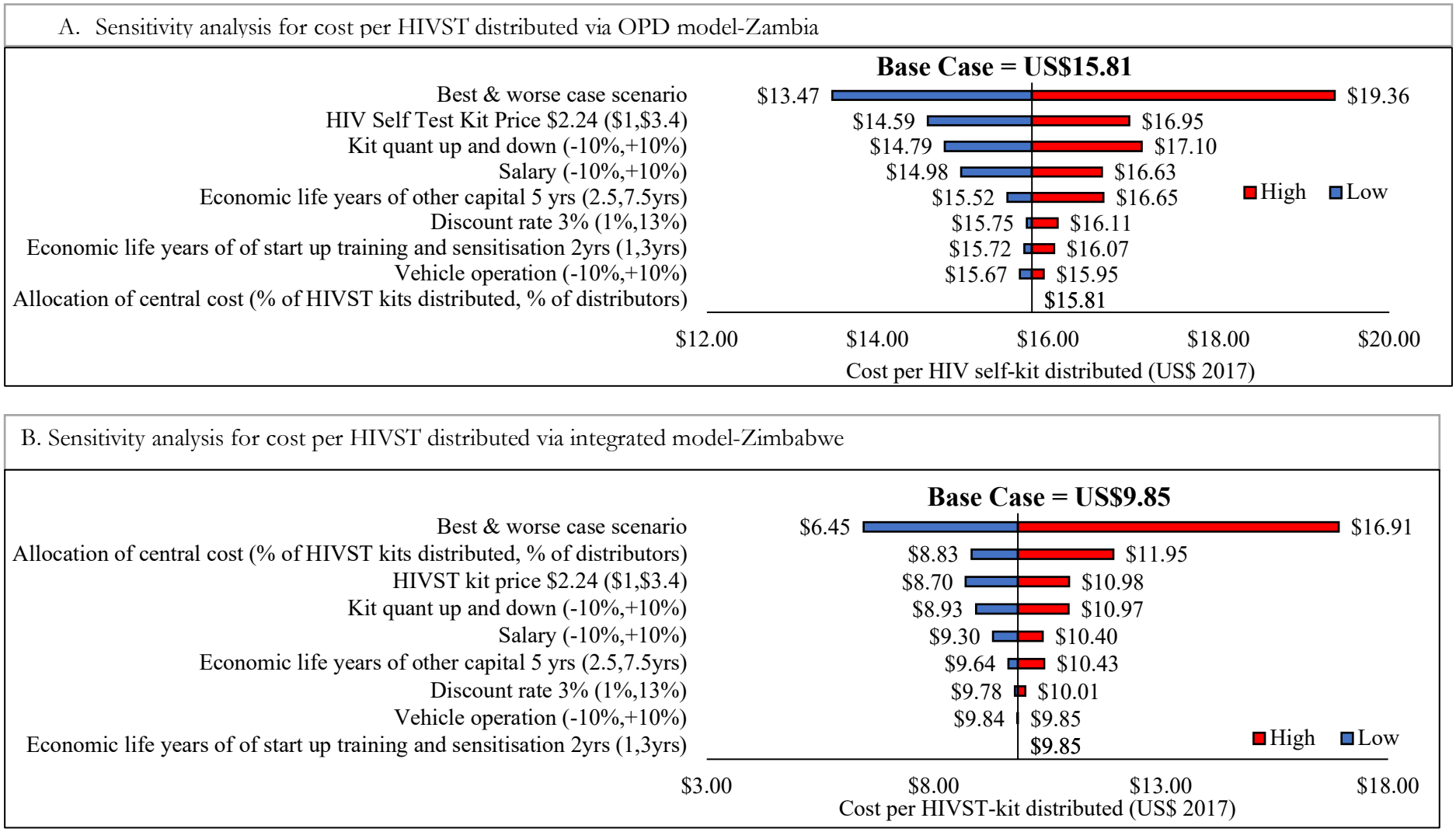


Figure 3.6 Country-level sensitivity analysis of unit cost per HIVST distributed via OPD and integrated model (in 2017 US$)

Discussion

In this study, we presented the costs of distributing HIVST kits integrated into VMMC services and in facility-based services in the OPD and HST services. Costs of adding HIVST to service's testing offer could be as low as $7.71, such as in Zimbabwe's VMMC model, and comparable to conventional HTS, but could be relatively high if only few kits are distributed, such as through the VMMC mobilizers model in Malawi. These full costs include the initial start-up costs and central support. These fixed costs are expected to substantially decrease as they are more fully incorporated into routine activities and as operations scale up. In the facility integrated models, costs ranged from US$5.20 to US$58.92 per kit distributed.

The estimated unit costs of HIVST distribution through these models are within the wide range of standard facility-based counselor-led HIV testing services (US$2.60-22.42) (133), and to HIVST delivery through community-based distribution agents (US$8.15-16.42) (49), that we previously estimated using the exact same methods across the same sites in these three countries (49, 133). While the unit cost of these three distribution models may be higher, the implementation trials across these countries suggests HIVST has value in reaching first-time testers (men and adolescent boys) (46, 194) and groups that are underserved including key populations as well as underserved truck drivers (106, 175, 195-197).

Estimated unit costs for these four HIVST distribution models may not be comparable with the cost of standard HTS or HIVST distribution through community-based distribution agents (49, 133) (Table 3.5). The distribution numbers were relatively small for these four models compared to community-based distribution, which accounted for 82.7% of HIVST kit distribution (46). The current estimated unit costs for VMMC, OPD, and integrated models should be interpreted with caution. For example, the aim of HIVST distribution through community-based distribution by VMMC mobilizers and distribution at the VMMC clinic focused on VMMC demand creation among men to increases uptake of VMMC services as it reduces the barrier of men to test for HIV. The OPD model aims to expand HIV testing capacity within OPD to increase coverage of targeted provider-initiated testing, maximize HIV diagnosis, ART initiation, and uptake of prevention service. For example, across the two countries personnel cost accounted for close to 50% of the recurrent costs. It is likely that real-world integration of HIVST into OPD could be achieved with fewer human resources and routine training reduces additional costs of future integrated HIVST distribution. Additionally, start-up and capital costs are likely to be dependent on PSI's different implementation strategies across the three countries. Thus, the scaling-up processes need more detailed planning and budgeting to reduce cost.

Currently, in all three countries, the HIVST kit was available through the funded STAR project for US$2.00 – which is only available for 50 low- and middle-income countries for four years. In our study, the sensitivity analysis demonstrated important cost reductions when the HIVST kit price is lowered to near the standard HIV kit price of around US$1.00. To ensure access to HIVST and the ability to scale-up implementation, continued efforts are needed to make affordable HIVST kits available, including partnerships with donors. Emerging evidence suggests opportunities in the private sector, public-private partnerships, and through workplace programmes may be promising for broader and affordable HIVST scale-up.

The sensitivity analysis showed the impact of different rates of uptake of HIVST (+/-10%) on the unit cost and the total cost. The impact of lower than optimal uptake on unit costs, resulted in an eight-fold increase in the OPD model (i.e., ranging from US$5.20 to US$42.24 per kit distributed). However, among non-testers who refuse to access health facility testing, the OPD model case-finding approach is unlikely to achieve large scale, and additional innovative approaches need to be identified for HIVST to be integrated within health facilities. For instance, offering of HIVST kits to HIV positive index to take to a sexual partner or partners and giving HIVST kits to all pregnant women regardless of HIV status to take to male partners (secondary distribution) are being explored (46).

Limitations

This study has a number of limitations. First, we reported unit costs per kit distributed, but do not have observed data linking our costs to numbers of new people linked to care, etc. Since HIVST is intended to be used in private, we were unable to estimate the unit cost per person tested or per HIV positive individuals linked to care and treatment after self-testing or negative person linked to prevention – notably in this case VMMC. Second, STAR is the first implementation project that introduced HIVST in the Southern Africa region. Thus the distribution numbers were relatively small for these three models compared to community-based distribution, which accounted for 82.7% of HIVST kit distribution (46). If respective MOHs scale-up HIVST using these two distribution modalities, it is likely that unit costs would be significantly lower due to the higher number of test kits distributed and spreading of fixed costs.

Conclusions

The cost analysis has shown that the costs, though slightly higher, fit within the range of estimated costs of HIV testing. If shown to increase coverage of new testers, particularly

men and adolescents, or reducing barriers to VMMC, it is likely that adding HIVST into routine service delivery will support the achievement of the 90-90-90 and soon to be 95-95-95 goals. Continued efforts are needed to optimize HIVST particularly around alternative models that motivate trained distributors to deliver more kits to the right people.

List of abbreviations

ART	-	Antiretroviral therapy
COMREC	-	Malawi College of Medicine Research Ethics Committee
FSWs	-	Female sex workers
ESA	-	Eastern and southern Africa
HIVST	-	HIV self-testing
LSHTM	-	London School of Hygiene and Tropical Medicine
HTS	-	HIV testing services
MRCZ	-	Medical Research Council of Zimbabwe
NSC	-	New Start Centre
OPD	-	Outpatient department
PrEP	-	Pre-exposure prophylaxis
PITC	-	Provider-initiated testing and counseling
PSI	-	Population Services International
PSI/Z	-	Population Services International Zimbabwe
RDT	-	Rapid diagnostic test
SFH	-	Society for Family Health
STAR	-	HIV-Self-Testing AfRica
UNZAREC	-	University of Zambia Biomedical Research Ethics Committee
US$	-	United States Dollar
VMMC-		Voluntary medical male circumcision
WHO	-	World Health Organization

Ethics approval and consent to participate

The study was approved by the London School of Hygiene and Tropical Medicine (LSHTM) Ethics Committee, Malawi National Health Sciences Research Committee, University of Zambia Biomedical Research Ethics Committee, Medical Research Council of Zimbabwe (MRCZ) and University College London Ethics Committee. The STAR trials are registered under the Clinical Trials Network (ClinicalTrials.gov) under registration numbers NCT02793804 (Malawi); NCT02718274 (Zambia); Pan African clinical trials registry (Zimbabwe) PACTR201607001701788. No incentives were given to any individual who tested for HIV using the HIVST kits.

Consent for publication

Authors gave consent for publication.

Additional file

Table 1- 1 Total & site level unit costs of HIVST kits distribution VMMC model (in 2017 US$)

Table 1- 2 Total & site level unit costs of HIVST kits distribution OPD and integrated models (in 2017 US$)

Table 8 Sensitivity analysis data input and output for HIVST kits distribution VMMC model (in 2017 US$)

Table 9 Sensitivity analysis data input and output for HIVST kits distribution OPD and integrated models (in 2017 US$)

Competing interests

The authors have no conflicts of interest to declare.

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Authors' contributions

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Data curation: NA, LM, CM, LS, SR, SK

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Writing-original draft: NA, LM, HM, FTP

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Supplementary document

Table 3.6 Total & site level unit costs of HIVST kits distribution VMMC model (in 2017 US$)

Country & Site number	Total HIVST kits distributed	Total intervention cost (Full)	Site-level unit cost per kit distributed	Total number of people tested using facility-based HIV finger prick (133)	Total HTC cost without start-up cost	Facility-based HIV finger prick unit cost per person tested(133)
Malawi (Community-based HIVST kits distributed by VMMC mobilizers model)						
1	413	$7,947	$19.24	1,899	$9,250	$4.81
2	320	$10,251	$32.04	2,727	$9,520	$3.45
Malawi (HIVST kits distributed at VMMC clinic)						
1	1174	$11,121	$9.47			
2	1568	$15,238	$9.72			
Zambia (HIVST kits distributed at VMMC clinic model)						
1	540	$11,740	$21.74			
2	1862	$18,830	$10.11			
3	631	$12,343	$19.56	1,976	$11,705	$6.14
4	478	$11,034	$23.08	3,196	$12,195	$3.87
5	5467	$44,151	$8.08			
6	1663	$36,954	$22.22			
7	318	$3,246	$10.21			
8	371	$10,806	$29.13	4,673	$8,684	$3.64
Zimbabwe (HIVST kits distributed at VMMC clinic model)						
1	963	$5,862	$6.09	24,126	$77,611	$3.22
2	553	$6,598	$11.93	5,051	$82,728	$16.38
3	1354	$9,524	$7.03	4,679	$89,888	$19.21

Table 3.7 Total & site level unit costs of HIVST kits distribution OPD and integrated models (in 2017 US$)

Country & Site number	Total HIVST kits distributed	Total intervention cost (Full)	Site-level unit cost per kit distributed	Total number of people tested using facility-based HIV finger prick (133)	Total HTC cost without start-up cost	Facility-based HIV finger prick test $/per person tested (133)
Zambia (OPD model)						
1	596	$12,266	$20.58			
2	992	$13,148	$13.25			
3	484	$11,021	$22.77	1,976	$11,705	$6.15
4	208	$8,568	$41.19	3,196	$12,195	$3.87
5	3175	$16,495	$5.20			
6	1136	$8,834	$7.78			
7	1124	$9,988	$8.89			
8	670	$7,232	$10.79			
9	556	$15,529	$27.93			
10	231	$13,611	$58.92	4,192	$10,860	$2.64
11	887	$20,768	$23.41			
12	311	$13,136	$42.24			
13	656	$13,331	$5.30			
14	416	$12,599	$30.29	2,691	$6,344	$2.49
15	841	$15,376	$18.28			
16	602	$13,306	$22.10	4,673	$8,684	$3.64
Zimbabwe (Integrated model)						
1	7,576	$56,592	$7.47	85,725	$346,805	$4.05
2	1,278	$29,109	$22.78	13,204	$98,241	$7.44
3	3,184	$20,668	$6.49	24,126	$199,222	$8.26
4	303	$3,473	$11.46	2,855	$69,607	$24.38
5	2,545	$34,782	$13.67	8,411	$148,616	$17.67

Table 3.8 Sensitivity analysis data input and output for HIVST kits distribution VMMC model (in 2017 US$)

Malawi Cost per Community-based HIVST kits distributed by VMMC mobilisers Base Case = US$24.83						
	Input			**Output**		
Sensitivity analysis inputs	**Low**	**Base case**	**High**	**Low**	**Base case**	**High**
Discount rate 3% (1%, 13%)	1%	3%	13%	$24.51	$24.83	$26.77
Allocation of central cost (% of HIVST kits distributed, % of distributors)				$23.91	$24.83	$24.83
Economic life years of start-up training and sensitization 2yrs (1,3yrs)	1yr	2yrs	3yrs	$21.28	$24.83	$35.48
Economic life years of other capital 5 yrs. (2.5,7.5yrs)	2.5yrs	5yrs	7yrs	$24.83	$24.83	$24.83
Best & worst-case scenario				$16.09	$24.83	$45.66
HIV Self-Test Kit price $2.24 ($1, $3.4)	$1.00	$2.24	$3.40	$23.05	$24.83	$27.61
Salary (-10%, +10%)	90%	100%	110%	$24.08	$24.83	$25.56
Kit quant up and down (-10%, +10%)	90%	100%	110%	$22.57	$24.83	$27.58
Vehicle operation (-10%, +10%)	90%	100%	110%	$24.66	$24.83	$25.00

Malawi cost per HIVST distributed via VMMC clinic distribution Base Case = US$9.61						
	Input			**Output**		
Sensitivity analysis inputs	**Low**	**Base case**	**High**	**Low**	**Base case**	**High**
Discount rate 3% (1%, 13%)	1%	3%	13%	$9.55	$9.61	$9.98
Allocation of central cost (% of HIVST kits distributed, % of distributors)				$8.85	$9.61	$9.61
Economic life years of start-up training and sensitization 2yrs (1,3yrs)	1yr	2yrs	3yrs	$8.93	$9.61	$11.65
Economic life years of other capital 5 yrs. (2.5,7.5yrs)	2.5yrs	5yrs	7yrs	$9.61	$9.61	$ 9.61
Best & worst-case scenario				$5.64	$9.61	$16.23
HIV Self-Test Kit price $2.24 ($1, $3.4)	$1.00	$2.24	$3.40	$7.84	$9.61	$12.40
Salary (-10%, +10%)	90%	100%	110%	$9.48	$9.61	$ 9.75
Kit quant up and down (-10%, +10%)	90%	100%	110%	$8.74	$9.61	$10.68
Vehicle operation (-10%, +10%)	90%	100%	110%	$9.44	$9.61	$ 9.78

Zambia cost per HIVST distributed via VMMC clinic distribution Base Case US$13.01						
		Input			Output	
Sensitivity analysis inputs	**Low**	**Base case**	**High**	**Low**	**Base case**	**High**
Discount rate 3% (1%, 13%)	1%	3%	13%	$12.95	$13.01	$13.27
Allocation of central cost (% of HIVST kits distributed, % of distributors)				$13.01	$13.01	$13.01
Economic life years of start-up training and sensitization 2yrs (1,3yrs)	1yr	2yrs	3yrs	$12.90	$13.01	$13.31
Economic life years of other capital 5 yrs. (2.5,7.5yrs)	2.5yrs	5yrs	7yrs	$12.77	$13.01	$13.71
Best & worst-case scenario				$11.12	$13.01	$16.05
HIV Self-Test Kit price $2.24 ($1, $3.4)	$1.00	$2.24	$3.40	$12.00	$13.01	$13.95
Salary (-10%, +10%)	90%	100%	110%	$12.36	$13.01	$13.65
Kit quant up and down (-10%, +10%)	90%	100%	110%	$12.17	$13.01	$14.07
Vehicle operation (-10%, +10%)	90%	100%	110%	$12.86	$13.01	$13.15

Zimbabwe cost per HIVST distributed via VMMC clinic distribution Base Case US$7.71						
		Input			Output	
Sensitivity analysis inputs	**Low**	**Base case**	**High**	**Low**	**Base case**	**High**
Discount rate 3% (1%, 13%)	1%	3%	13%	$7.64	$7.71	$7.84
Allocation of central cost (% of HIVST kits distributed, % of distributors)				$6.80	$7.71	$10.28
Economic life years of start-up training and sensitization 2yrs (1,3yrs)	1yr	2yrs	3yrs	$7.71	$7.71	$7.71
Economic life years of other capital 5 yrs. (2.5,7.5yrs)	2.5yrs	5yrs	7yrs	$7.53	$7.71	$8.21
Best- & worst-case scenario				$4.81	$7.71	$14.83
HIV Self-Test Kit price $2.24 ($1, $3.4)	$1.00	$2.24	$3.40	$6.52	$7.71	$8.87
Salary (-10%, +10%)	90%	100%	110%	$7.36	$7.71	$8.06
Kit quant up and down (-10%, +10%)	90%	100%	110%	$6.99	$7.71	$8.59
Vehicle operation (-10%, +10%)	90%	100%	110%	$7.70	$7.71	$7.71

Table 3.9 Sensitivity analysis data input and output for HIVST kits distribution OPD and integrated models (in 2017 US$)

Zambia cost per HIVST distributed via OPD Base Case US$15.81						
	Input			**Output**		
Sensitivity analysis inputs	**Low**	**Base case**	**High**	**Low**	**Base case**	**High**
Discount rate 3% (1%, 13%)	1%	3%	13%	$15.75	$15.81	$16.11
Allocation of central cost (% of HIVST kits distributed, % of distributors)				$5.81	$15.81	$15.81
Economic life years of start-up training and sensitization 2yrs (1,3yrs)	1yr	2yrs	3yrs	$15.72	$15.81	$16.07
Economic life years of other capital 5 yrs. (2.5,7.5yrs)	2.5yrs	5yrs	7yrs	$15.52	$15.81	$16.65
Best & worst-case scenario				$13.47	$15.81	$19.36
HIV Self-Test Kit price $2.24 ($1, $3.4)	$1.00	$2.24	$3.40	$14.59	$15.81	$16.95
Salary (-10%, +10%)	90%	100%	110%	$14.98	$15.81	$16.63
Kit quant up and down (-10%, +10%)	90%	100%	110%	$14.79	$15.81	$17.10
Vehicle operation (-10%, +10%)	90%	100%	110%	$15.67	$15.81	$15.95

Zimbabwe cost per HIVST distributed via OPD Base Case US$9.85						
	Input			**Output**		
Sensitivity analysis inputs	**Low**	**Base case**	**High**	**Low**	**Base case**	**High**
Discount rate 3% (1%, 13%)	1%	3%	13%	$9.78	$9.85	$10.01
Allocation of central cost (% of HIVST kits distributed, % of distributors)				$8.83	$9.85	$11.95
Economic life years of start-up training and sensitization 2yrs (1,3yrs)	1yr	2yrs	3yrs	$9.85	$ 9.85	$9.85
Economic life years of other capital 5 yrs. (2.5,7.5yrs)	2.5yrs	5yrs	7yrs	$9.64	$9.85	$10.43
Best & worst-case scenario				$6.45	$9.85	$16.91
HIV Self-Test Kit price $2.24 ($1,$3.4)	$1.00	$2.24	$3.40	$8.70	$9.85	$10.98
Salary (-10%, +10%)	90%	100%	110%	$9.30	$9.85	$10.40
Kit quant up and down (-10%, +10%)	90%	100%	110%	$8.93	$9.85	$10.97
Vehicle operation (-10%, +10%)	90%	100%	110%	$9.84	$9.85	$ 9.85

3.1. Implication for thesis

The results presented in this paper offer important insights regarding how to optimize HIVST distribution to reach different population groups. For instance, the VMMC model is designed to reach men and the health facility model to identify HIV positive cases.

The most practical implication of these unit costs of different HIVST distribution models will fully inform policy.

CHAPTER 4 COST-EFFECTIVENESS OF COMMUNITY-BASED (DOOR-TO-DOOR) HIV SELF-TESTING DISTRIBUTION MODELS FOR HIV TESTING IN ZAMBIA: MARKOV MICROSIMULATION (PAPER-3)

Overview of Paper 3

The cost-effectiveness model on HTS can be used to estimate cost and effectiveness measurements to understand its impact in a given population, time, and place. No modelling work assessed the cost-effectiveness of door-to-door HIVST distribution in Zambia.

This research paper applies a microsimulation model to estimate the incremental cost-effectiveness of adding home-based HIVST distribution to conventional facility-based HIV testing services (HTS) to reach people who otherwise would not access HTS while visiting health facilities.

This paper is in preparation to be submitted to *AIDS* in July 2020. One supplementary document is included at the end of the thesis.

This chapter provides the ICERs per DALY averted as well as the gaps on cost-effectiveness estimates of the microsimulation model.

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Student ID Number	159519	**Title**	Miss
First Name(s)	Nurilign		
Surname/Family Name	Ahmed		
Thesis Title	Reaching the First 90%: Cost-effectiveness of HIV self-testing services in Zambia		
Primary Supervisor	Fern Terris Prestholt		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

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Stage of publication	**Not yet submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I planned the conceptualization, data curation, methodology and writing and reviewing of the draft.

SECTION E

Student Signature	[redacted]
Date	23 Sep 2019.

Supervisor Signature	[redacted]
Date	23-9-2019

Cost-effectiveness of community-based (door-to-door) HIV self-testing distribution models for HIV testing in Zambia: Markov microsimulation model

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Abstract

Background: Adult HIV prevalence in Zambia is approximately 12%, and it is estimated that 28% of people living with HIV remain undiagnosed. In 2016 Zambia adopted HIV self-testing (HIVST) as an additional approach to expand coverage and access to those in need of testing and who might not otherwise test. While early introduction focused on small-scale HIVST distribution in specific districts and regions, the programme seeks to expand nationwide. This study evaluates the incremental cost-effectiveness of adding home-based HIVST distribution to conventional facility-based HIV testing services (HTS) to reach people who otherwise would not access HTS while visiting health facilities.

Methods: This study developed a sex- and age-specific Markov microsimulation model for Zambia. Costs and health outcomes were evaluated for a one-year door-to-door HIVST programme over a 20-year time horizon using a discount rate of 3%. The model applied Self-test in Africa (STAR) endline survey data to reflect uptake of facility HTS and assumed that only those untested in the past year were eligible for home-based HIVST and could accept or reject HIVST with its accompanying costs and consequences. Costs are presented from the health providers' perspective and effects in terms of disability-adjusted life year (DALY) averted. All costs are reported in 2017 US$.

Results: The model applied 100,000 simulations to estimate the incremental cost-effectiveness ratio (ICER) per DALY averted of a one-year HIV testing service of door-to-door HIVST compared with facility-based HTS for men and women across three age groups. The ICERs (cost per DALY averted) for men and women ages 15-24, 25-34, and 35-49 were $101.81 & $154.73, $35.26 & $25.18 and $32.10 & $23.03, respectively. The sensitivity analyses showed increasing the uptake of HIVST, linkage to ART initiation, ART retention and viral load suppression could lower the ICER.

Conclusion: Overall, to reach the 28% who remain undiagnosed at facility testing, door-to-door HIVST provides a cost-effective complement to current testing approaches and can play an essential role in reaching national testing targets.

Keywords: Modelling; microsimulation; Markov model; HIV testing; HIV self-testing; cost-effectiveness analysis; Sub-Saharan Africa

Background

Zambia has one of the highest HIV prevalence rates in the world. Adult HIV prevalence in Zambia is approximately 12% (4), yet it is estimated that 28% of people with HIV remain undiagnosed. In 2014, the joint United Nations Programme on HIV/AIDS (UNAIDS) put forward the 90-90-90 targets recommending that by 2020, 90% of all people living with HIV should know their HIV status, 90% of all individuals with diagnosed HIV infection should be enrolled and receive antiretroviral therapy (ART), and 90% of those receiving ART should achieve viral suppression (88). Moreover, Zambia adopted the 2015 World Health Organization (WHO) test and treat guidelines for immediate ART initiation for all HIV positive adults and adolescents (198). These ambitious targets have brought changes in Zambia and are likely to require increasing innovative and alternative HIV testing services (HTS).

The government of Zambia continues its effort to increase HIV testing using alternative HTS, including community-based testing, mobile services, home-based testing, voluntary medical male circumcision (VMMC), prevention of mother to child transmission (PMTCT), and integrating HTS to centres offering sexually transmitted infection (STI) services (20). The most considerable gaps in meeting the 90-90-90 targets are adolescents and men who do not know their HIV status. Therefore, the Zambian Ministry of Health (MOH) has recognized that HTS coverage remains below the UNAIDS targets and it has supported research to investigate HIV self-testing (HIVST) to complement conventional HTS in order to increase uptake of HIV testing (21).

Since 2015, the HIV-Self Testing Africa (STAR) project has been leading the implementation of HIVST (using oral-fluid) in Zambia. The STAR project also aimed to understand the costs of distributing HIVST kits using different distribution modalities to ensure the efficient use of financial and human resources. Careful costing and cost analysis of various HIVST distributing modalities were conducted, including door-to-door (50) and static site HIV self-test kit distribution (199) to ensure the provision of HIVST to achieve high testing coverage. Evidence from other African countries has demonstrated the accuracy, acceptability, and performance of HIVST in general and key populations (22, 23, 25, 26, 28, 195, 200). In Zambia, results from a cluster-randomized trial on a community-based distribution of HIVST kits at population level among those whom HIV tested in the last 12 months did not identify a significant impact on recent or lifetime testing (RR 1.08, Adj 95% CI 0.94-1.24; p = 0.15) (47). However, more studies are needed to generate evidence on efficient approaches to reaching ambitious targets and the cost-effectiveness of each HTS to consider distributing

as HIVST kits in Zambia. These data are critical to inform the programmatic decision of HIVST scale-up in Zambia.

To inform this evidence gap, this study used a Markov microsimulation model to determine the cost-effectiveness of a package of standard facility based HTS with an addition of a door-to-door HIVST kit distribution model compared with standard facility-based HTS from the health providers' perspective in Zambia.

Methods and Materials

Cost analysis

This study analysed the annual cost incurred between June 2016 and July 2017 for HIVST kit distribution in Zambia using a door-to-door community-based distribution model. This includes the cost of reaching communities, demonstration of how HIVST works, and distribution of HIVST kits (50). The cost data collection employed both ingredients-based (bottom-up) costing for allocation factors and direct resource use and top-down costing for overhead and administrative costs allocation. The detailed financial expenditure for the project period was readily available through the Society for Family Health (SFH) Lusaka office. In this study, the financial costs represented actual STAR project expenditures, and the economic costs represented the estimated market value of all resources that were used in expanding the HIVST intervention, including donated goods and services. Cost data were disaggregated by specific input types. For instance, capital costs included the costs of project start-up, including initial training, sensitization, and equipment. Recurrent costs included costs of recurrent training, personnel, HIVST kit price, building and vehicle operation and maintenance, utilities, and other recurrent costs such as project administration and coordination. We adjusted for cost and converted all costs into 2017 US$ (201). Capital costs, including start-up and training costs were annualized over their economic life year using a 3% discount rate in the base case costs.

The cost per HIVST kit distributed was estimated by dividing the total cost by the total number of HIVST kits distributed using a door-to-door community-based distribution model for those individuals who accepted the HIV self-test kit to be used at home. The cost that is used in this model is the unit cost per HIV self-self-kit distributed. This is discussed as a limitation to highlight that this analysis did not consider unit cost for individuals who refused to test. The intervention cost for HIV testing using HIVST and status quo were only incurred once (one-year intervention cost, see Table 4.1 along with Supplementary Table S2). The annual ART cost (US185.86) included the cost of provider, health facility visit and the

drug (36), and the costs were incurred for a 20-year time horizon (sensitivity analysis: 5, 10, 15 20 years, and lifetime) in the model. This cost does not include the cost of hospitalization or receiving end of life care.

Cost-effectiveness analysis

To examine the potential impact of the introduction of a one-year HIVST campaign and its impact over 20 years, we developed a Markov microsimulation model using TreeAge Pro 2017, R2.0 *TreeAge Software, Williamstown, MA, USA (202)*. This model used the primary observed cost data from the STAR project to parameterize the intervention cost and extrapolated missing parameters from a systematic literature review (203).

The model simulated a heterosexual population representing Zambian adults ages 15 to 49 from the point of offer of HIV testing to viral load suppression and death (if it occurred within the 20-year time horizon). Thus, the model incorporated the HIV care cascade, which included individuals going through confirmatory rapid diagnostic HIV testing (RDT), accepting HIV positive status, initiating ART, being retained in ART care, and obtaining viral load suppression. This is described in the Markov health states (Figure 4.1). The age- and sex-specific HIV prevalence and mortality data were obtained from the Zambia Population-Based HIV Impact Assessment (ZAMPHIA) (91) and the Zambia Demographic Health Survey (DHS) respectively (51). When an individual is confirmed to be HIV positive, they would be initiated on ART without the consideration of CD4 cell count in accordance with the Zambian national ART guidelines (204). In the HIV care cascade, individuals could be lost to follow-up at any stage. Those who refused to initiate ART after the HIV-positive confirmatory test or those lost to follow-up after initiating ART could subsequently re-enter the care cascade (Table 4.1, Supplementary Tables S3-S14).

This study calculated the incremental cost-effectiveness ratio (ICER) for adding a door-to-door HIVST kit distribution model to the facility-based standard HTS (status quo). The ICER was calculated as incremental costs divided by the incremental health benefit (DALYs averted). The observed costs and health effects (DALYs averted) related to door-to-door HIVST kit distribution model was compared to inform which one was likely to represent the most cost-effective modality for HIVST kit distribution for three age groups for both men and women. This includes adolescent male/female 15-24 years of age, male/female 25-34 years of age and male/female 35-49 years of age. Indirect health effects, such as secondary infection averted, were not estimated.

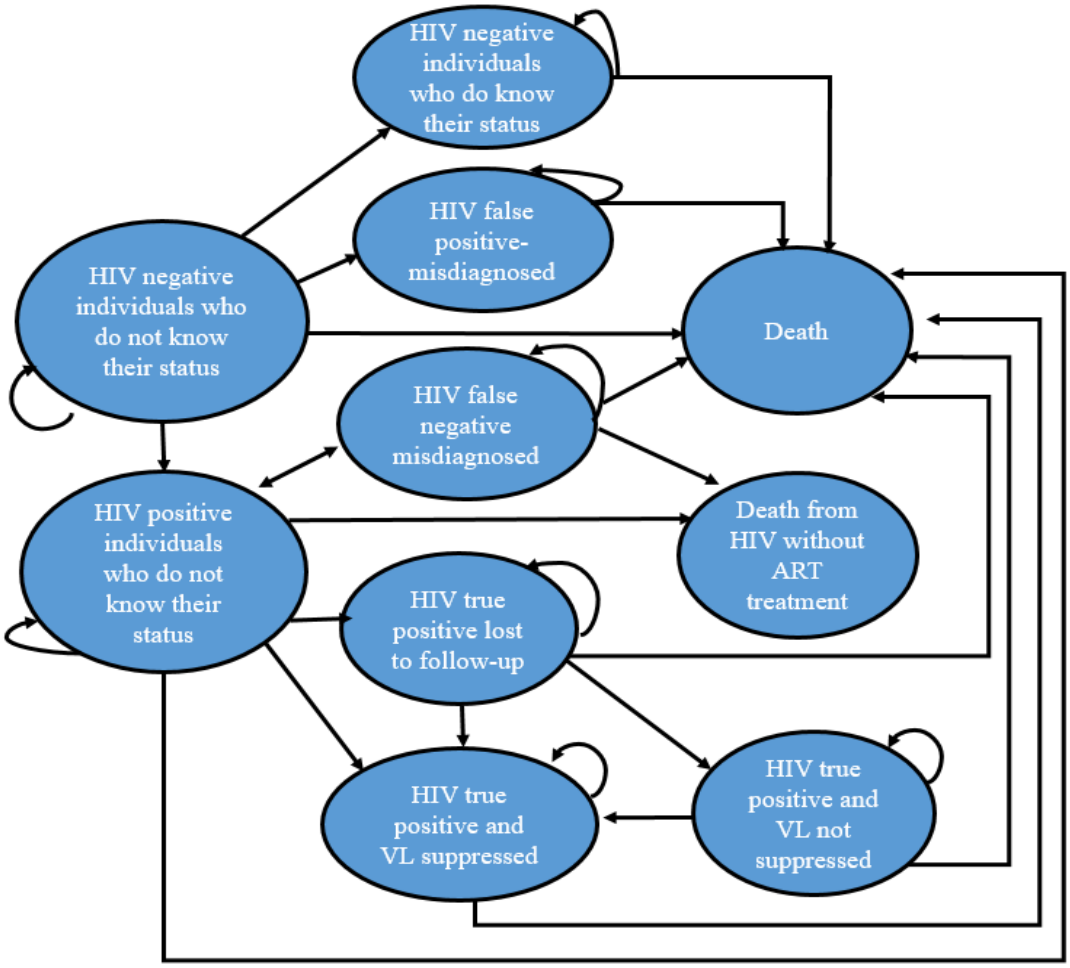


Figure 4.1 The structure of the Markov microsimulation model for the provision of HIV self-testing for those not tested in the last 12 months.

Table 4.1 HIV testing strategies evaluated

Strategy	Description	Frequency of HIV testing per person
Status quo or standard facility-based HTS: PITC, ANC, VCT (Comparator)	PITC - health facility provider-initiated testing and counselling ANC - health facility antenatal care HIV testing VCT - health facility voluntary counselling and testing	Once/year
Intervention: Adding community-based door-to-door HIV self-testing to the status quo (offered only to those who did not accept HTA)	Community-based (door-to-door) self-test kit distribution via community-based distributing agents	Once/year

Model structure

Individuals entered in one of two health states: 1) HIV negative individuals who do not know their HIV status, and 2) HIV positive individuals who do not know their HIV status (Figure 4.1). The transitions between health states experienced by individuals were assigned health utility and cost pertinent to each of these health states. The transition probabilities were extracted from ZAMPHIA (91) and the Zambia DHS respectively (51). The model has ten mutually exclusive health states: 1) HIV negative individuals who know their HIV status, 2) HIV negative individuals who do not know their HIV status, 3) HIV positive individuals who do not know their HIV status, 4) HIV false positive (misdiagnosed), 5) HIV false negative (misdiagnosed), 6) HIV true positive viral load suppressed, 7) HIV true positive viral load not suppressed, 8) HIV true positive lost to follow-up, 9) death from HIV without treatment, and 10) death from other natural causes (Figure 4.1).

Model calibration

The model was calibrated to match the most recently available HIV prevalence estimates, mortality rate, ART, and viral load suppression data from ZAMPHIA and Zambian DHS (51, 91). The population was divided by age, gender, and risk of HIV infection (91). Both HIV specific and other causes of mortality were incorporated into the model (51, 91).

Model validation

The model was developed after reviewing the literature, descriptive analysis of Zambian HIV epidemiology (local survey), demographics, and mortality from natural cause stratified by age and gender (Zambian DHS). The model validation was done to ensure the model's fidelity to satisfy the analysis objectives and by visiting HIV testing facilities in Zambia. The internal validity of the model was tested using extreme numbers in the parameters.

Status quo HTS

The current status quo (comparator) HTS available at the government health facilities are provider-initiated testing and counselling (PITC), voluntary counselling and testing (VCT) and antenatal care (ANC) HIV testing using RDT (Table 4.1). In the status quo scenario, individuals (HIV negative individuals who do not know their HIV status, and HIV positive individuals who do not know their HIV status) accessed a health facility for HIV screening through either PITC, VCT, or ANC. We calculated the proportion of men and women who tested at the status quo across the three age stratifications using the STAR endline survey. Uni-Gold is the confirmatory rapid diagnostic test (RDT) used in Zambia (205). The sensitivity and specificity for Uni-Gold were 99.8% and 99.9% (206). Per Zambian HIV

treatment guidelines, individuals identified as HIV positive were initiated with ART regardless of CD4+ cell count (204). Following HIV diagnosis and initiation with ART, it was estimated that 83% of the patients would be retained in ART care for the subsequent two years (207). The 83% ART retention was extended to the 20-year time horizon. We applied ZAMPHIA's published average coverage of ART for males and for females across the three age categories (91).

Intervention strategies

We compared the impact of adding door-to-door HIVST kits distribution onto existing standard HTS, and these were compared with the standard facility-based HTS at the government health facility (Table 4.1). In the intervention arm, individuals (HIV negative individuals who do not know their HIV status, and HIV positive individuals who do not know their HIV status) who did not test at a health facility through PITC, VCT, or ANC in the last 12 months were offered HIVST kits. This is different from the STAR trial and avoids substitution. The sensitivity and specificity of OraQuick among intended users were 94.2% and 99.7%, respectively (208). Specifically, we compared the 20-year impact of adding a one-year targeted intervention of HIVST onto the existing HTS on healthcare cost, DALYs averted, and the ICER.

HIV prevention and treatment cascades

The HIV prevention cascade helps identify the people who are unaware of their HIV negative status and people unaware of their HIV infection (169, 171, 209). The HIV treatment cascade helps monitor people after they enrol in HIV care services. This includes: 1) initiating ART, 2) alive and remaining in care for 90 or more days, and 3) alive and viral load suppressed (210-213). We modelled the steps between becoming HIV positive to achieving viral load suppression as provided within government-approved HIV programmes. All input parameters for the model are listed in Table 4.2.

Discounting and time horizon

As standard practice, future costs and effects were discounted and expressed in present values in order to better inform current decision making (54). The 3% per year discount rate for costs (in 2017 US$) and health benefits were applied as a central estimate (214). The impact of varying the discount rate was explored in a sensitivity analysis. A 20-year time horizon was used in the model to adequately capture both the benefits and cost associated with HIVST.

Uncertainty and sensitivity analysis

Deterministic (univariate and multivariate (best/worst-case scenarios)), and probabilistic sensitivity analyses (PSA) were performed to ensure the robustness of the input parameters and assumptions in the decision model (53, 54). Using sensitivity analyses, we also explored the impact of using a 5-, 10-, and 15-year time horizon. A deterministic sensitivity analysis was applied to identify parameters that affected the ICER the most. The following parameters were varied in the deterministic sensitivity analyses: discount rate of cost (base case 3%, range 1% to 13%), discount rate of effects (base case 3%, range 1% to 13%), ART initiation (base case 78%, range 37% to 90%), ART retention (base case 78%, range 60% to 90%), viral load suppression (base case 78%, range 60% to 90%), and sensitivity of OraQuick among intended users (base case 94%, range 90% to 99%). In any age category, if the base case ART initiation, retention, or viral load suppression had already reached 90%, the one-way sensitivity analysis applied high targets of ART initiation (95%), ART retention (95%), and viral load suppression (95%).

Scenario analyses were used to explore the impact of higher and lower resource cost or service outputs. This included varying the cost of HIVST (base case US$16.42, range US$7.91 to US$50.01) as observed in STAR; lifetime ART cost after (base case US$185.86, range from US$139.39 to US$232.32), and uptake of HIVST (+/- 25%).

PSA using Monte Carlo simulations for 10,000 trials (individual patient simulation) was conducted to assess combined uncertainty related to any number of parameters. We used gamma distributions for costs and beta distributions for health utility (215). By randomly sampling from each parameter distribution, 10,000 simulations of incremental costs and incremental effects were obtained. The results of the PSA are presented as the cost-effectiveness acceptability curve (CEAC). The CEACs summarize the impact of uncertainty in relation to different possible values of the cost-effectiveness threshold (CET) (54). In the absence of a locally defined CET, countries may consider using half of gross domestic product (GDP) per capita (82, 83) instead of the previously suggested 1-3x GDP per capita rule (72). The current GDP per capita for Zambia is US$1,430 (216). Until Zambia defines its local threshold, this study considered 1x GDP per capita (US$1,430) as CET and also to present CEAC.

Table 4.2 HIV testing, treatment, and cost input parameters

Variable	Base-case assumption	Sensitivity analysis range	Source
Population and testing			
Proportion of HIV-negative individuals who do not their status	Male ages 15-24: 0.96 Male ages 25-34: 0.90 Male ages 35-49: 0.86 Female ages 15-24: 0.96 Female ages 25-34: 0.87 Female ages 35-49: 0.85		(51)
Proportion of HIV-positive individuals who do not know their status	Male ages 15-24: 0.04 Male ages 25-34: 0.10 Male ages 35-49: 0.14 Female ages 15-24: 0.04 Female ages 25-34: 0.13 Female ages 35-49: 0.15		(51)
Annual self-reported HIV testing (status quo-proportion)	**PITC** Male ages 15-24: 0.46 Male ages 25-34: 0.56 Male ages 35-49: 0.65 Female ages 15-24: 0.53 Female ages 25-34: 0.55 Female ages 35-49: 0.65 **ANC** Male ages 15-24: 0.02 Male ages 25-34: 0.06 Male ages 35-49: 0.06 Female ages 15-24: 0.11 Female ages 25-34: 0.16 Female ages 35-49: 0.10 **VCT** Male ages 15-24: 0.12 Male ages 25-34: 0.12 Male ages 35-49: 0.09 Female ages 15-24: 0.09 Female ages 25-34: 0.08 Female ages 35-49: 0.07		STAR endline survey
Annual uptake of door-to door HIV self-testing (proportion)	Male ages 15-24: 0.57 Male ages 25-34: 0.57 Male ages 35-49: 0.53 Female ages 15-24: 0.41 Female ages 25-34: 0.60 Female ages 35-49: 0.60		STAR endline survey

Variable	Base-case assumption	Sensitivity analysis range	Source
Mortality rates of HIV uninfected person (proportion per year)	Male ages 15-24: 0.03 Male ages 25-34: 0.08 Male ages 35-49: 0.14 Female ages 15-24: 0.02 Female ages 25-34: 0.07 Female ages 35-49: 0.11		(217)
Testing frequency	Once per year	-	Assumption
Discount rate for cost and utility outcomes	3% per year	(0%-13%) for cost (1%,- 13%) for utility	(214)
HIV care and treatment			
Initiation of ART care for intervention-door-to-door HIVST (%) (~ annual)	Male ages 15-24: 0.78 Male ages 25-34: 0.72 Male ages 35-49: 0.86 Female ages 15-24: 0.78 Female ages 25-34: 0.78 Female ages 35-49: 0.88	(37%[a], -90%)	(218)
Initiation of ART care for status quo (%) (90 days)	Male: 79.7% Female: 82.3%		(213)
On treatment among those diagnosed (annual) for both intervention and status quo (%)	Male ages 15-24: 0.78 Male ages 25-34: 0.72 Male ages 35-49: 0.86 Female ages 15-24: 0.78 Female ages 25-34: 0.78 Female ages 35-49: 0.88		(4)
VL suppression among those on treatment (annual) for intervention and status quo (%)	Male ages 15-24: 0.78 Male ages 25-34: 0.91 Male ages 35-49: 0.88 Female ages 15-24: 0.78 Female ages 25-34: 0.88 Female ages 35-49: 0.91		(4)
Annual lost to follow-up from HIV care (%)	17%	(10-31)	(207)
Annual lost to follow-up from HIV care and died (%)	2.9%	(1.5- 6)	(207)
Annual mortality rates while on HIV care (%)	8.8%	(6.40-12.10)	(207)
Cost of intervention and status quo HTS in 2017 US$[*]			
Intervention (Community-based door-to-door self-test kit distribution)- average cost/person tested	16.42	(4.00-20.00)	(50)

Variable	Base-case assumption	Sensitivity analysis range	Source
Status quo – PITC-average cost/person tested	10.76		(135)
Status quo – ANC-average cost/person tested	57.59		(128)
Status quo – VCT- average cost/person tested	4.41		(133)
Average cost of false-positive confirmatory test	1.60		(133)
Cost of HIV care and treatment in 2017 US$*			
Intervention (door-to-door self-test following linkage into care) and Status quo			
Annual cost of ART per client	185.86	(139.39-232.32)	(36)
Health-related quality of life-utility description (disability weight)			
HIV negative individuals	0	-	(76)
HIV/AIDS receiving antiretroviral treatment	0.053	(0.034-0.079)	(76)
HIV asymptomatic (also don't know their HIV positive status)	0.221	(0.146-0.310)	(76)
AIDS not receiving antiretroviral treatment (viral load not suppressed)	0.547	(0.382-0.715)	(76)

***** The costs for the prevention cascade include the costs for HIV testing at the health facility in three departments: provider-initiated testing and counselling (PITC), antenatal care (ANC) and voluntary counselling and testing (VCT). The costs for the treatment cascade include the costs to identify a HIV positive individual and link to the treatment cascade. See supplemental tables for further explanation on the variables

[a]37% is calculated by dividing 181 adults who self-tested and initiated ART at home by 490 adults who reported positive HIV self-testing in the home group (218).

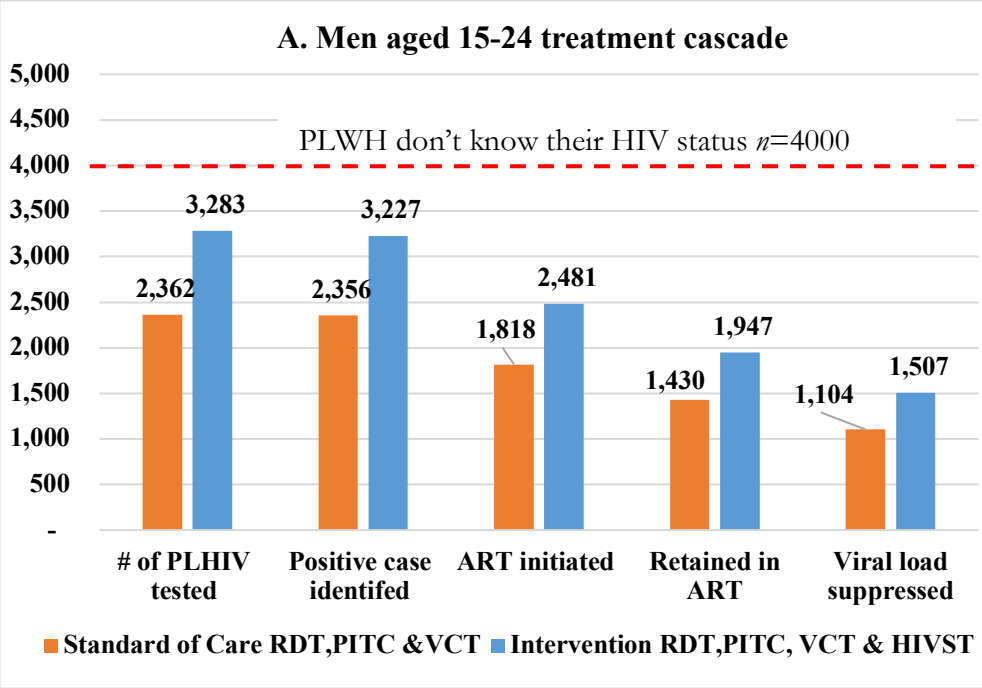
Results

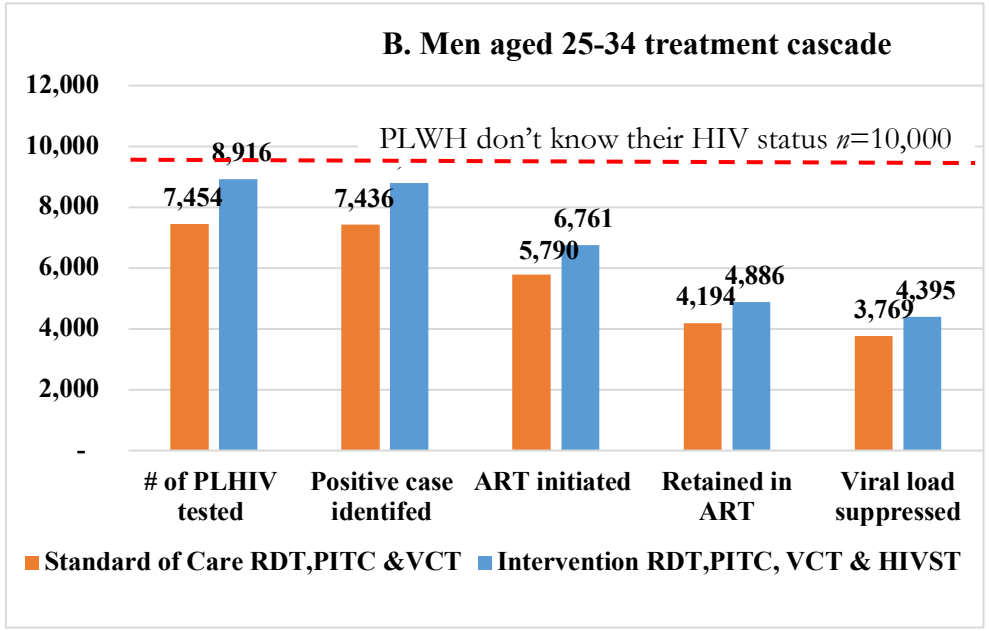
Table 4.3 shows the total costs for intervention (HIVST) and standard of care for the three age groups stratified by men and women in Zambia. The intervention arm, which includes the provision of HIVST, incurred an additional total cost for reaching additional people. One-year community-based HIV self-testing reached an additional 22,722 new men (ages 15-24), 14,925 (ages 25-34) and 10,695 (ages 35-49) and 11,192 new women (ages 15-24), 12,594 (ages 25-34) and 10,879 (ages 35-49) who had not tested for HIV in the previous 12 months. The one-year provision of HIV self-testing for those who did not test for HIV in the previous year resulted in identifying an additional 921 (ages 15-24), 1,462 (ages 25-34), and 1,494 (ages 35-49) HIV positive cases for men and 449 (ages 15-24) 1,612 (ages 25-34), and 1,605 (ages 35-49) for women. The cost per case identified using HIV self-testing for the adolescent age group was US$409.29 for men (age 15-24) and US$ 405.29 for women (ages 15-24), which differed substantially from $167.63 for men (ages 25-34), $117.54 for men (ages 35-49), $128.28 for women (ages 25-34), and $111.30 for women (ages 35-49) (Table 4.3), Figure 4.2 and 4.3.

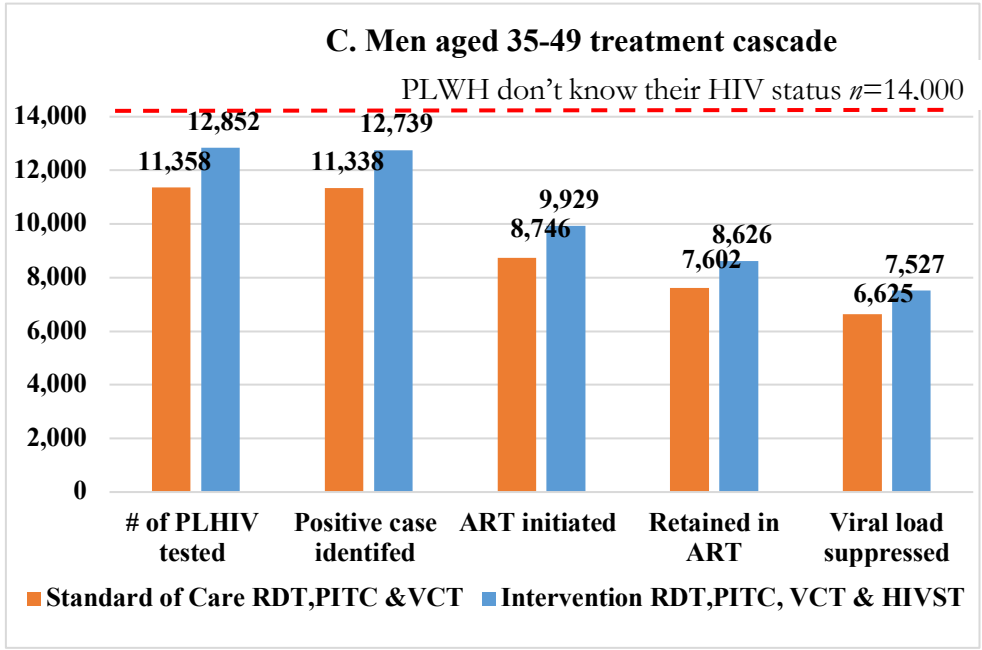
Table 4.3 Incremental costs and uptake of HIVST

	Intervention (HIVST)				
Age (years)	**Total number of people tested**	**Cost/person tested**	**Total cost**	**Number of HIV positive people tested**	**Cost/case identified**
Men					
15-24	22,722	$16.42	$373,095	921	$405.10
25-34	14,925	$16.42	$245,069	1,462	$167.63
35-49	10,695	$16.42	$175,612	1,494	$117.54
Women					
15-24	11,192	$16.42	$183,773	449	$409.29
25-34	12,594	$16.42	$206,793	1,612	$128.28
35-49	10,879	$16.42	$78,633	1,605	$111.30

In Table 4.4, we present the ICERs (cost-per DALY averted) of door-to-door HIVST compared with the status quo, for 100,000 simulations over 20 years for both men and women by the three age categories. The ICERs for adolescent men and women ages 15-24 were $101.81 and $154.73 per DALY averted. The ICERs for men and women were $35.26 and $25.18 for ages 25-34, and $32.10 and $23.03 for ages 35-49, respectively.



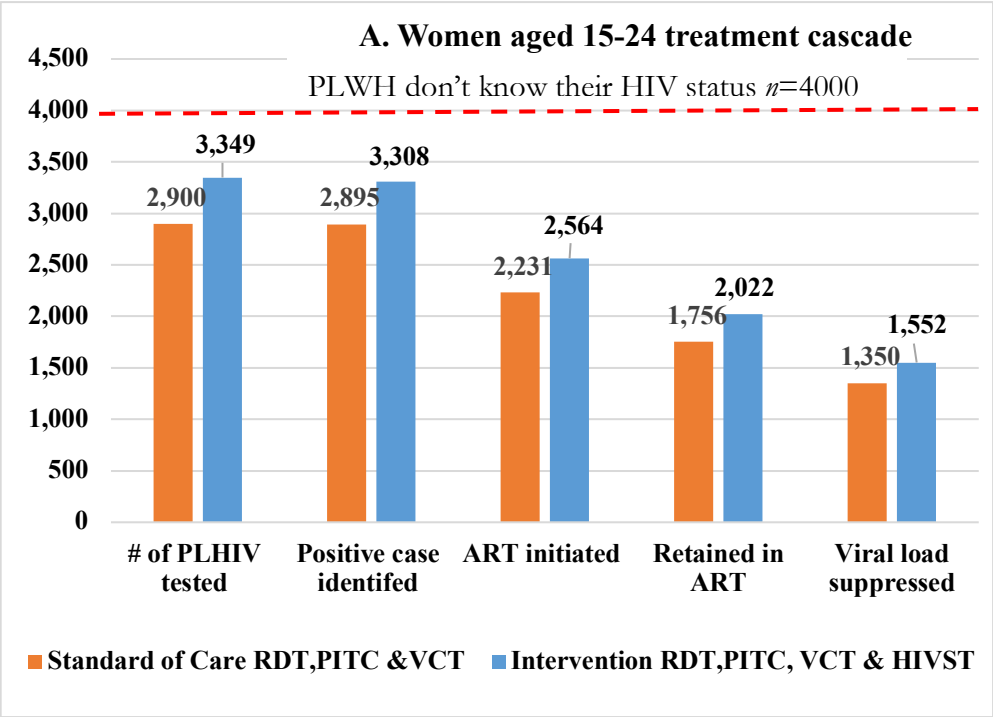


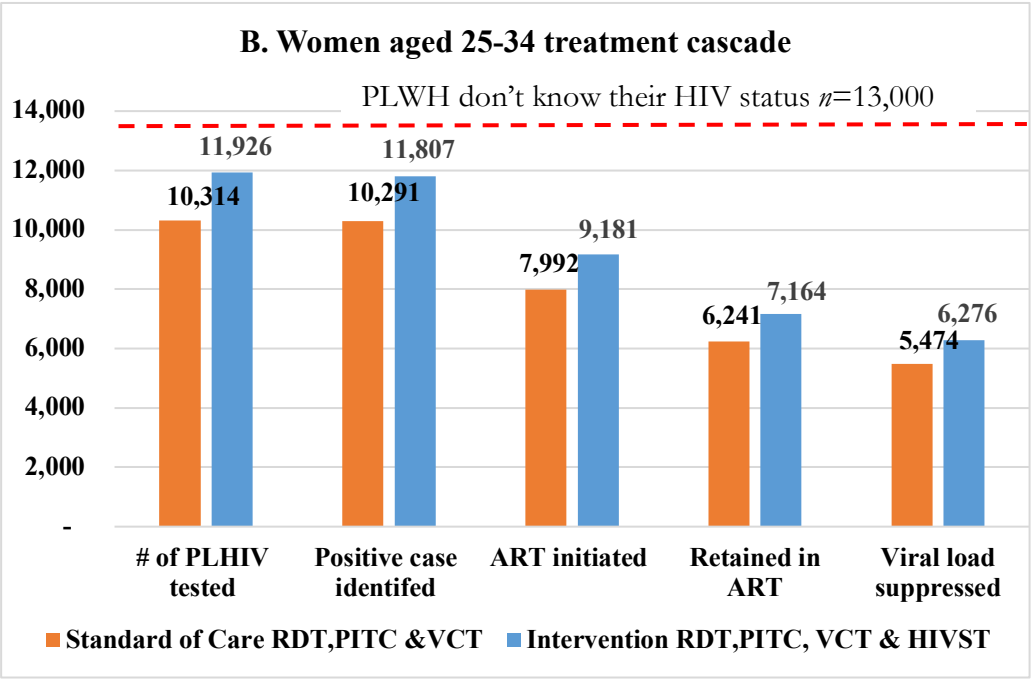


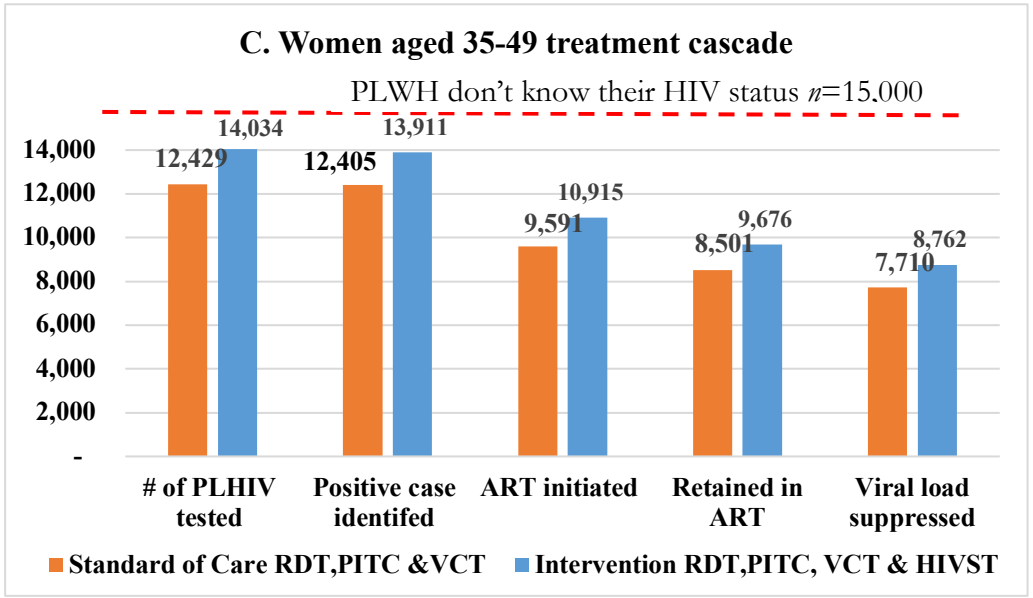
# of PLHIV tested= Number of HIV positive individuals who tested for the HIV for the first-time using HIV self-test kit.

Positive case identified= Number of confirmed HIV positive cases using rapid diagnostic tests.

Figure 4.2 (A-C) Men HIV treatment cascade







# of PLHIV tested= Number of HIV positive individuals who tested for the HIV for the first-time using HIV self-test kit.

Positive case identified= Number of confirmed HIV positive cases using rapid diagnostic tests.

Figure 4.3 (A-C) Women HIV treatment cascade

Table 4.4 ICER values of comparative HTS (HIVST vs. status quo) by age and gender, Zambia (2017 USD)

Age (years)	Comparative HTS (Status quo vs. HIVST)	Total cost (US$)	Incremental cost	YLD	YLL	DALYs	Incremental DALYs averted	ICER per DALY averted	Prioritization by ICER
Men									
15-24	Status quo	$1,004,359.78	$534,842.81	26,243	83,104	109,348	5,253.30[1]	$101.81	5
	Intervention	$1,539,202.59		28,356	75,738	104,094			
25-34	Status quo	$2,100,248.17	$451,887.20	34,341	132,253	166,594	12,816.97[1]	$35.26	4
	Intervention	$2,552,135.37		35,140	118,637	153,777			
35-49	Status quo	$2,100,248.17	$413,887.20	21,196	95,484	116,680	12,881.73[1]	$32.10	3
	Intervention	$3,155,537.04		21,682	82,116	103,798			
Women									
15-24	Status quo	$1,666,298.07	$262,736.87	29,850	100,353	130,203	1,698.07[1]	$154.73	6
	Intervention	$1,929,034.95		32,204	96,301	128,505			
25-34	Status quo	$3,061,346.61	$449,887.89	44,613	173,602	218,216	17,870.25[1]	$25.18	2
	Intervention	$3,511,234.50		44,445	155,900	200,346			
35-49	Status quo	$3,122,012.18	$442,989.40	34,156	131,626	165,783	19,237.38[1]	$23.03	1
	Intervention	$3,565,001.58		26,234	120,311	146,545			

[1]DALYs are unfavourable utilities and the negative incremental DALYs averted are the inverse of incremental DALYs.

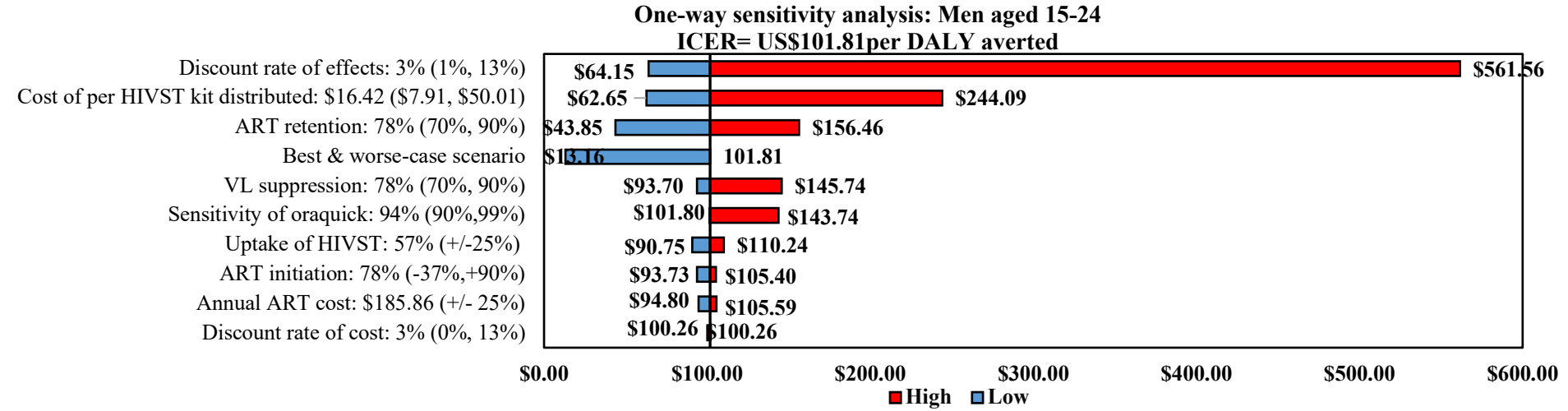
YLD = Years lost to disability; YLL = Years of life lost

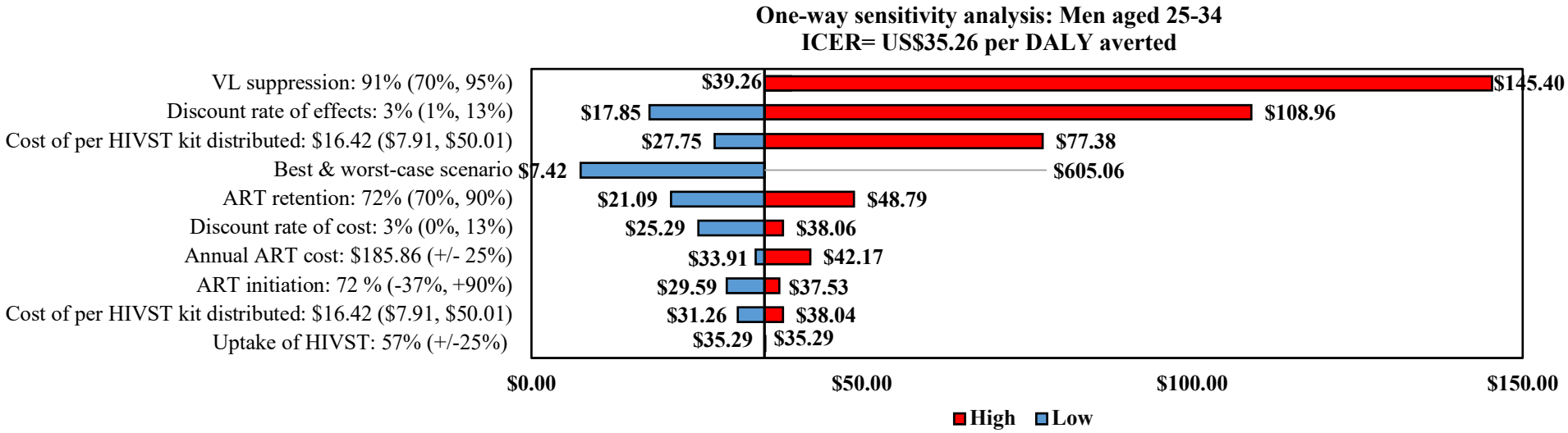
Sensitivity analyses

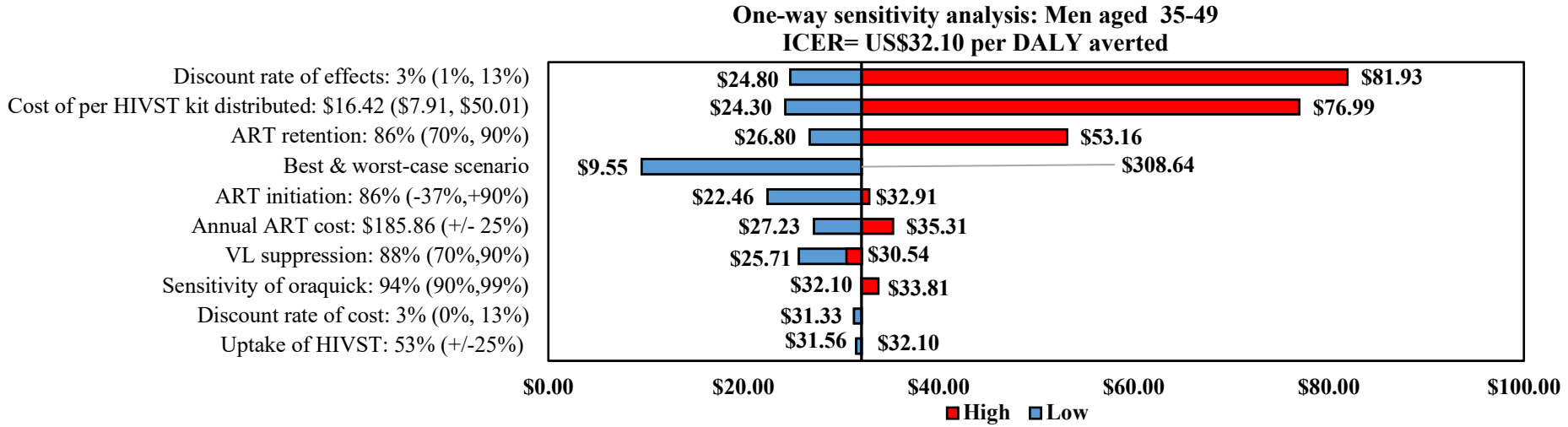
Figure 4.5 shows one-way sensitivity analyses for men and women by age group. The base-case values are shown, and the red-right and the blue-left bars demonstrate the ICER estimates at the upper and lower assumptions, respectively. In all age groups for both men and women, varying the discount rate of effects from 13% to 1% lowered the ICERs. Per our previously published study of onsite level cost per HIVST kit distributed (50) (Supplementary Table S-3), we varied cost per HIVST kit distributed between $7.91 and $50.01, and in all age groups, this significantly affected the ICERs on both lower and higher values. For adolescent men aged 15-24, the upper values for ART initiation (90%) resulted in higher ICER ($105.40 per DALY averted). ART retention (90%) and viral load suppression (90%) could bring down the base-case ICER (US$ 101.81 per DALY averted) to US$43.85 and US$93.70, respectively. If the ART initiation was 37%, ICER lowered from US$105.40 to US$93.73. For adolescent women, increasing ART initiation, retention, and viral load suppression to 90% resulted in higher ICERs of US$239.66, US$230.27, and US$240.14, respectively. In almost all age groups for both men and women, increasing the sensitivity of OraQuick among intended users from 94% to 99% resulted in lower ICER per DALY averted. Moreover, lowering the lifetime ART cost results lowered ICERs. Varying the uptake of HIVST by +25% lowers the ICER for both adolescent men and women.

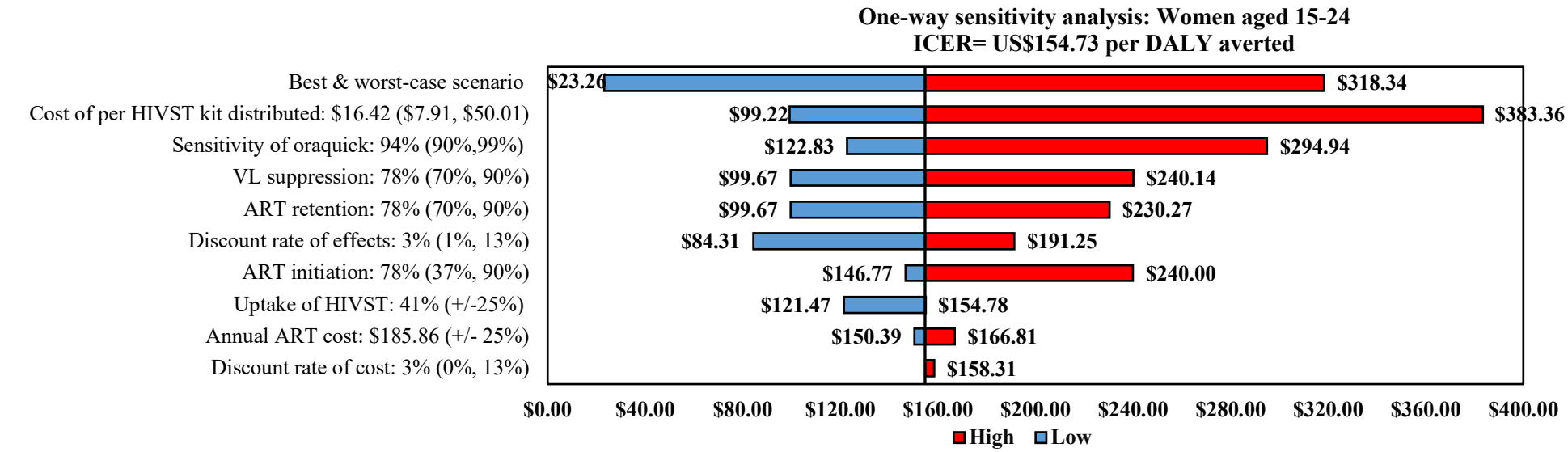
The multivariate (best/worst-case scenarios) analysis applied the values of the most optimistic (best-case scenario) and pessimistic (worst-case scenario) parameters, and this resulted in lower and higher ICER per DALY averted, respectively. For adolescent men, the best-case scenario lowered the base-case ICER from $101.81 to $13.16 per DALY averted. The worst-case scenario resulted in negative ICER of $1028.32 with fewer DALYs averted. For adolescent women, the best-case scenario lowered the base-case ICER from $154.73 to $23.26 per DALY averted. The worst-case scenario resulted in a higher ICER of $318.34 per DALY averted. The sensitivity analysis also explored the impact of 5, 10, and 15-year time horizons, and the five-year time horizon resulted in lower ICER per DALY averted in all age groups (Supplementary Figure S5-4).

Figure 4.5 presents cost-effectiveness acceptability curves for each age group for both men and women. The simulation plots on the cost-effectiveness plane are included in Supplementary Figure S5 and S6. For all age groups, HIVST is less likely to be cost-effective relative to the status quo. The PSA also shows that for all age groups for both men and women, HIVST is less cost-effective and each group was approximately 50% probability unlikely to be cost-effective at the 1x GDP, respectively (Figure 4.6).


One-way sensitivity analysis: Men aged 15-24
ICER= US$101.81per DALY averted
Discount rate of effects: 3% (1%, 13%)
Cost of per HIVST kit distributed: $16.42 ($7.91, $50.01)
ART retention: 78% (70%, 90%)
Best & worse-case scenario
VL suppression: 78% (70%, 90%)
Sensitivity of oraquick: 94% (90%,99%)
Uptake of HIVST: 57% (+/-25%)
ART initiation: 78% (-37%,+90%)
Annual ART cost: $185.86 (+/- 25%)
Discount rate of cost: 3% (0%, 13%)
$64.15
$561.56
$62.65
$244.09
$43.85
$156.46
$13.16
101.81
$93.70
$145.74
$101.80
$143.74
$90.75
$110.24
$93.73
$105.40
$94.80
$105.59
$100.26
$100.26
$0.00
$100.00
$200.00
$300.00
$400.00
$500.00
$600.00
High
Low


One-way sensitivity analysis: Men aged 25-34
ICER= US$35.26 per DALY averted
VL suppression: 91% (70%, 95%)
Discount rate of effects: 3% (1%, 13%)
Cost of per HIVST kit distributed: $16.42 ($7.91, $50.01)
Best & worst-case scenario
ART retention: 72% (70%, 90%)
Discount rate of cost: 3% (0%, 13%)
Annual ART cost: $185.86 (+/- 25%)
ART initiation: 72 % (-37%, +90%)
Cost of per HIVST kit distributed: $16.42 ($7.91, $50.01)
Uptake of HIVST: 57% (+/-25%)
$39.26
$145.40
$17.85
$108.96
$27.75
$77.38
$7.42
$605.06
$21.09
$48.79
$25.29
$38.06
$33.91
$42.17
$29.59
$37.53
$31.26
$38.04
$35.29
$35.29
$0.00
$50.00
$100.00
$150.00
High
Low


One-way sensitivity analysis: Men aged 35-49
ICER= US$32.10 per DALY averted
Discount rate of effects: 3% (1%, 13%)
Cost of per HIVST kit distributed: $16.42 ($7.91, $50.01)
ART retention: 86% (70%, 90%)
Best & worst-case scenario
ART initiation: 86% (-37%,+90%)
Annual ART cost: $185.86 (+/- 25%)
VL suppression: 88% (70%,90%)
Sensitivity of oraquick: 94% (90%,99%)
Discount rate of cost: 3% (0%, 13%)
Uptake of HIVST: 53% (+/-25%)
$24.80
$81.93
$24.30
$76.99
$26.80
$53.16
$9.55
$308.64
$22.46
$32.91
$27.23
$35.31
$25.71
$30.54
$32.10
$33.81
$31.33
$31.56
$32.10
$0.00
$20.00
$40.00
$60.00
$80.00
$100.00
High
Low


One-way sensitivity analysis: Women aged 15-24
ICER= US$154.73 per DALY averted
Best & worst-case scenario
Cost of per HIVST kit distributed: $16.42 ($7.91, $50.01)
Sensitivity of oraquick: 94% (90%,99%)
VL suppression: 78% (70%, 90%)
ART retention: 78% (70%, 90%)
Discount rate of effects: 3% (1%, 13%)
ART initiation: 78% (37%, 90%)
Uptake of HIVST: 41% (+/-25%)
Annual ART cost: $185.86 (+/- 25%)
Discount rate of cost: 3% (0%, 13%)
$23.26
$318.34
$99.22
$383.36
$122.83
$294.94
$99.67
$240.14
$99.67
$230.27
$84.31
$191.25
$146.77
$240.00
$121.47
$154.78
$150.39
$166.81
$158.31
$0.00
$40.00
$80.00
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$200.00
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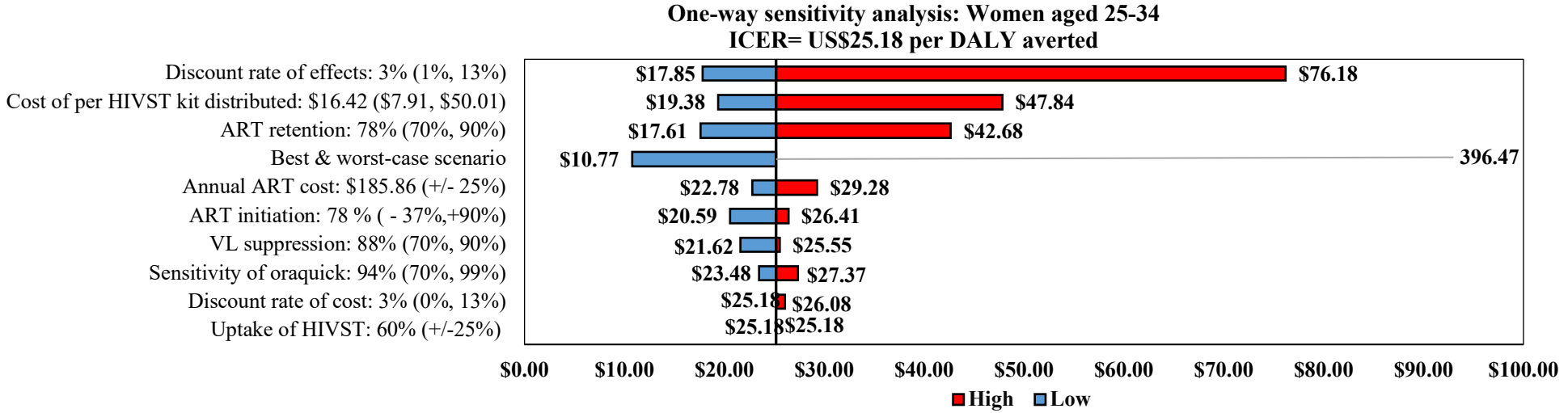
$360.00
$400.00
High
Low


One-way sensitivity analysis: Women aged 25-34
ICER= US$25.18 per DALY averted
Discount rate of effects: 3% (1%, 13%)
Cost of per HIVST kit distributed: $16.42 ($7.91, $50.01)
ART retention: 78% (70%, 90%)
Best & worst-case scenario
Annual ART cost: $185.86 (+/- 25%)
ART initiation: 78 % (- 37%,+90%)
VL suppression: 88% (70%, 90%)
Sensitivity of oraquick: 94% (70%, 99%)
Discount rate of cost: 3% (0%, 13%)
Uptake of HIVST: 60% (+/-25%)
$17.85
$76.18
$19.38
$47.84
$17.61
$42.68
$10.77
396.47
$22.78
$29.28
$20.59
$26.41
$21.62
$25.55
$23.48
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$100.00
High
Low

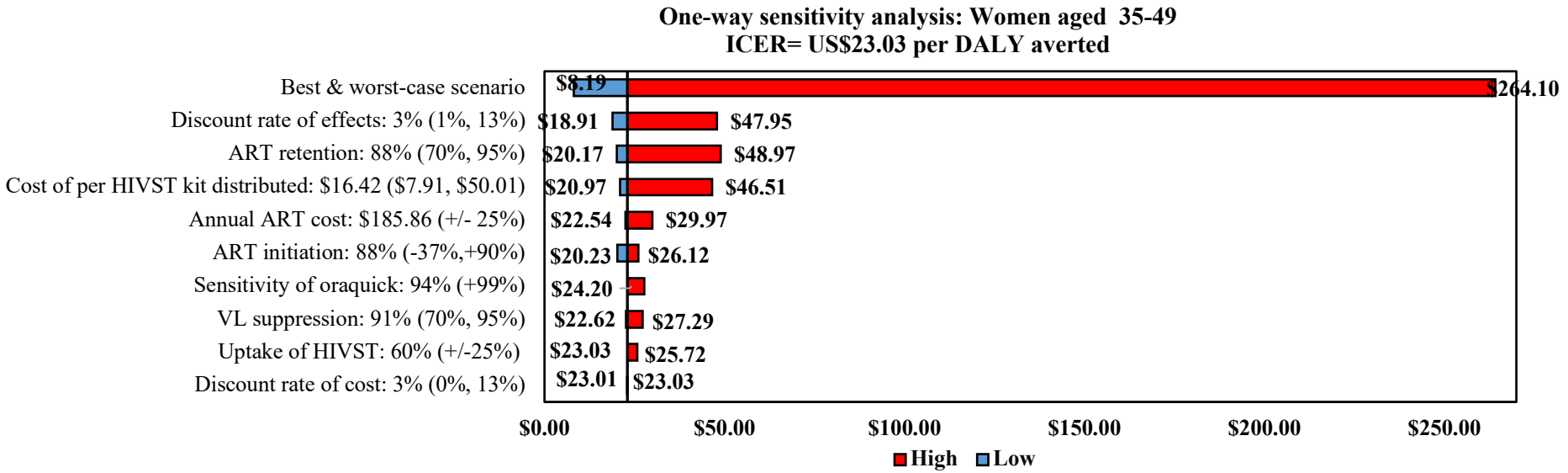
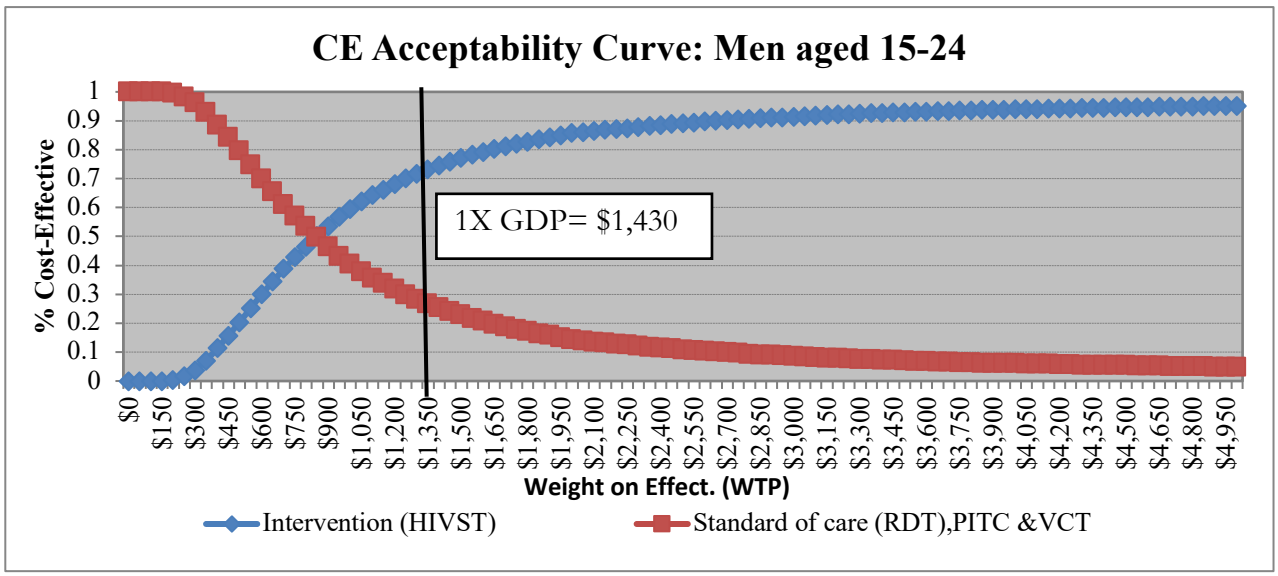
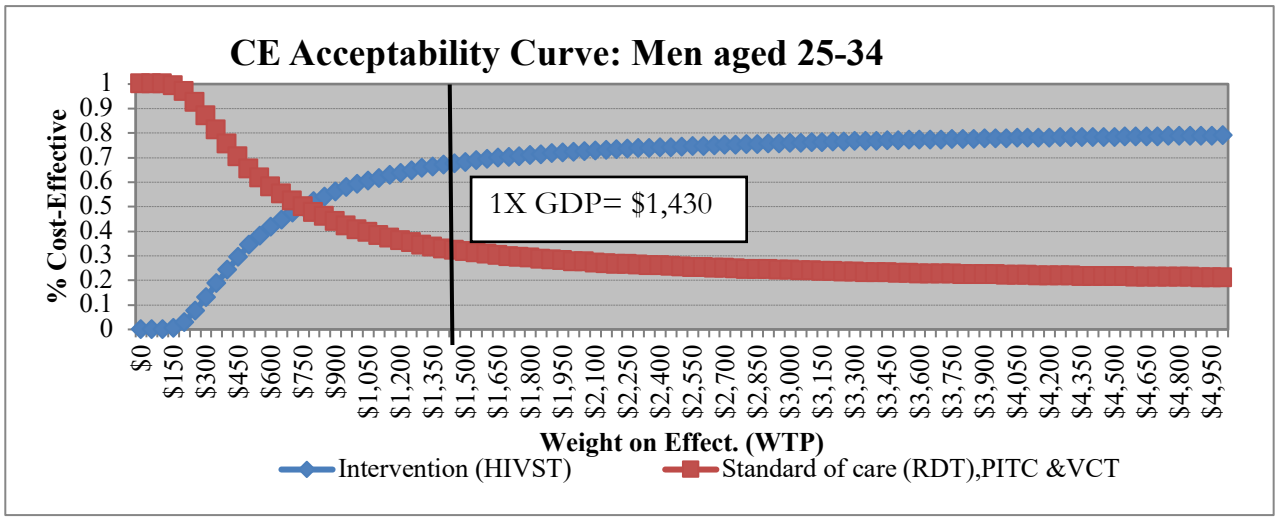
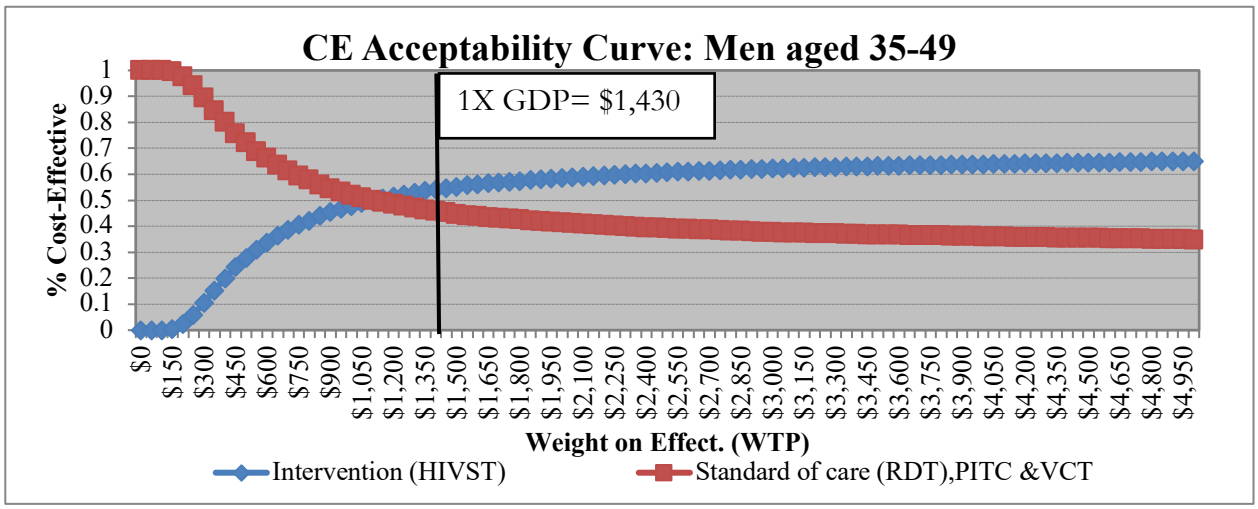
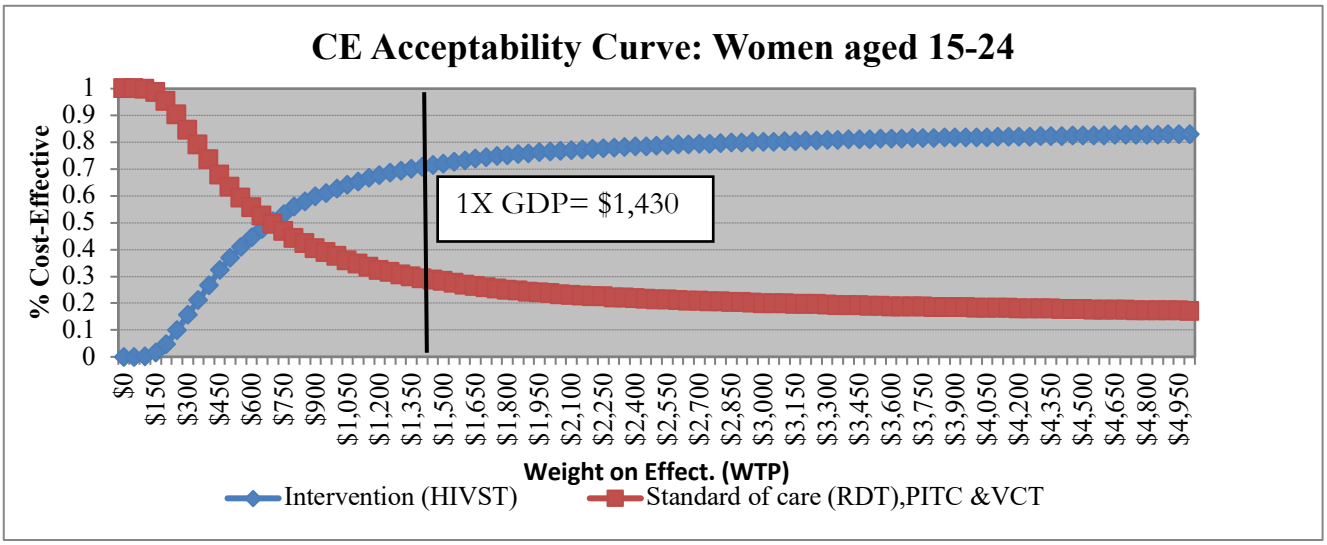


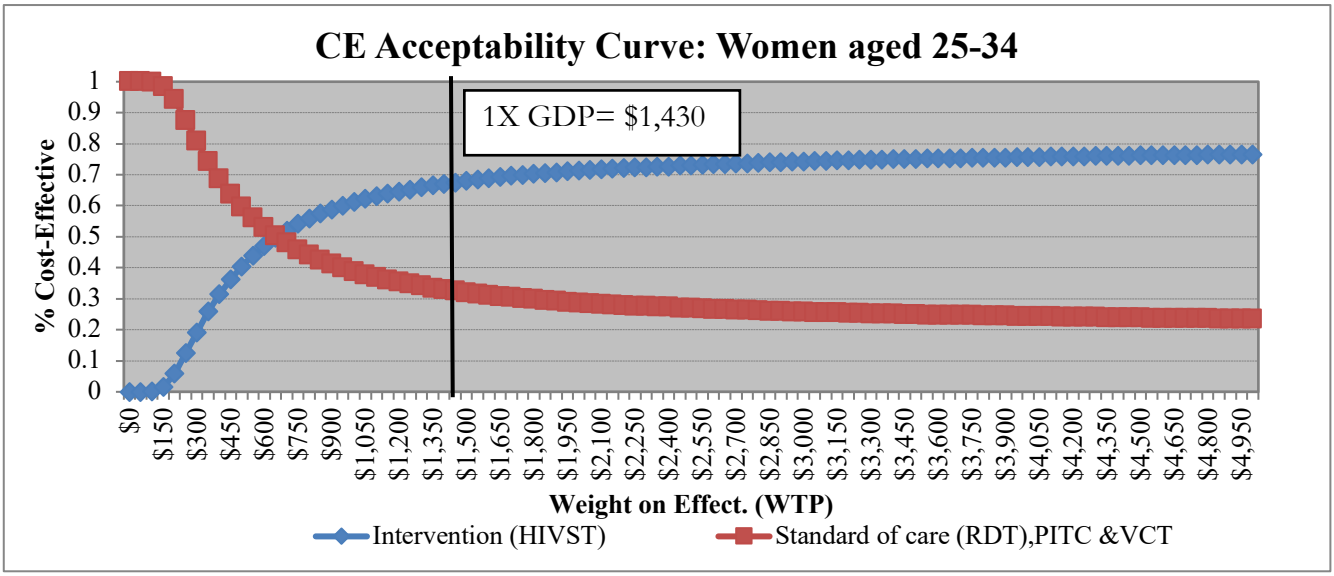
Figure 4.4 One-way sensitivity analyses


CE Acceptability Curve: Men aged 15-24
% Cost-Effective
1X GDP= $1,430
Weight on Effect. (WTP)
Intervention (HIVST)
Standard of care (RDT),PITC &VCT


CE Acceptability Curve: Men aged 25-34
% Cost-Effective
1X GDP= $1,430
Weight on Effect. (WTP)
Intervention (HIVST)
Standard of care (RDT),PITC &VCT


CE Acceptability Curve: Men aged 35-49
% Cost-Effective
1X GDP= $1,430
Weight on Effect. (WTP)
Intervention (HIVST)
Standard of care (RDT),PITC &VCT





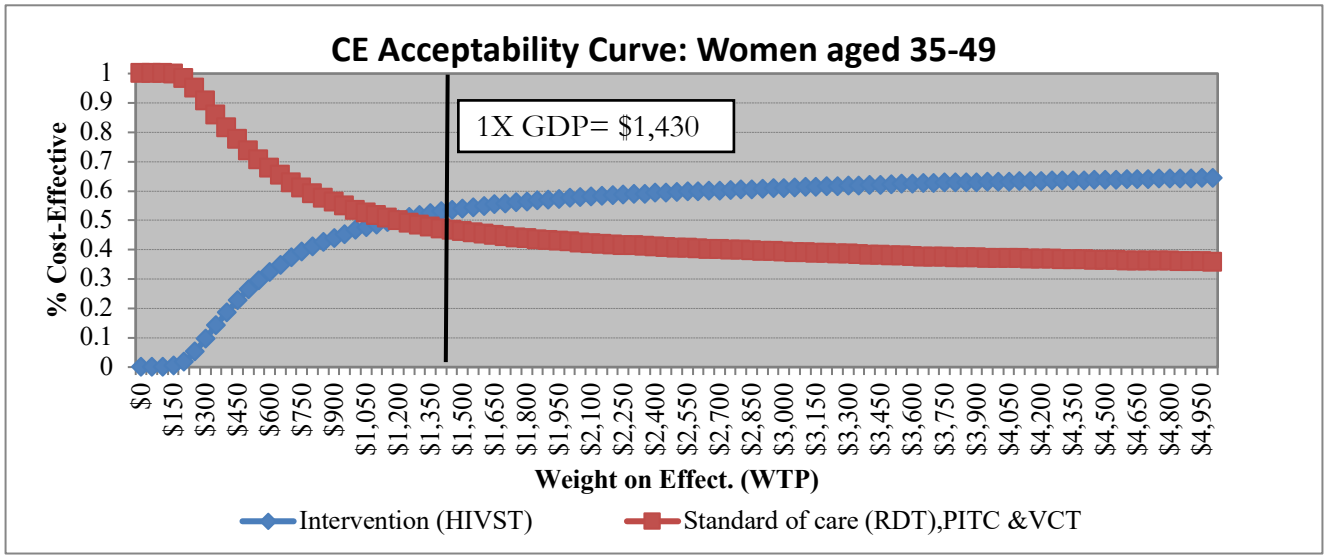


Figure 4.5 Cost effectiveness acceptability curves

Discussion

This study is the first to estimate the cost-effectiveness of HIVST in Zambia. At the population level, HIVST may not be very cost-effective; however, HIVST is a promising intervention to reach those who do not come to a health facility to test for HIV that is targeted at those not reached at the health facility. These estimates of cost and cost-effectiveness are comparable to published studies (35, 50, 156, 219-221). Our results are modelled from empirical data from a trial, costing exercises, and nationally representative population-based studies. This model simulates the provision of HIVST for those who did not test for HIV in the past 12 months using facility-based HTS and calculates six ICERs per DALY averted. For adolescent men and women, we reported higher ICER per DALY averted. These population groups have been reported to not access facility-based HIV testing. Thus, reaching them to distribute HIVST kits would incur more cost as would reaching them through other testing approaches.

Based on the uptake evidence, HIVST reached a higher proportion of men (all age groups) and adolescents (both men and women) than conventional testing, including some of who may not test otherwise as shown in Malawi, Zambia, and Zimbabwe (222). Our results also suggest which age group to prioritize to identify the newest HIV positive cases. Although the implementation of HIVST for adolescent men and women resulted in higher ICER per DALY averted relative to those ages 25-34 and 35-49 in the 20-year analysis, the ICERs were cost-effective at the 1x GDP per DALY averted threshold. However, despite being cost-effective, our HIV care cascade projection suggests that HIVST is unlikely to result in a dramatic increase in the absolute numbers of those who initiated ART, were retained in care or had viral load suppression. These results suggest that to lower the cost and maximize the health effect of HIVST, a higher number of individuals need to initiate ART, be retained, and have their viral load suppressed in the care cascade. These care cascade outcomes are highly dependent on the Zambian government effort to achieve UNAIDS' 90-90-90 targets (88). One study suggested the importance of immediate ART initiation after HIVST at homes or in community-based HIVST strategies (221). However, there should also be additional efforts to achieve high ART retention rates at the government health facilities in Zambia.

This study has an important programmatic contribution to previous studies. In Zambia, a nested cluster-randomized trial for door-to-door HIVST kits distribution demonstrated that 68% of the HIVST group had knowledge of their HIV status compared with 65% in the non-HIVST group (110). The effect was higher among men in the HIVST group (*OR* =

1.31) (110). The results from STAR's cluster-randomized trial found no evidence that HIVST significantly increased HIV testing at the population level in Zambia (47). The authors speculated that sampling challenges at the time of endline survey might be the reason for ineffective results. Thus, this allowed the cost effectiveness study to assess the impact of HVST. From the health providers' perspective, the prioritization of HIVST is likely to increase programme cost-effectiveness for two reasons. First, the self-testing nature of the product, in which one can perform the HIV test and interpret the result in a private setting, makes it more attractive especially to populations with low access to a health facility. Second, averting years lost to disability and years of life lost due to undiagnosed HIV could increase the benefit of DALYs averted, but cost-effective criteria tell us that more DALYs could be averted for a given budget by targeted testing.

This study has several limitations. First, we used a static Markov microsimulation model instead of a dynamic transmission model because the STAR research design did not collect impact data such as data on the number of people who initiated ART after positive HIVST result, the impact of reducing secondary HIV transmissions over time, or the prevention benefit of identifying and treating new HIV positive cases. With these data limitations, a Markov model was the appropriate model choice to answer the cost-effectiveness research question. Our model thus provides conservative values of the ICER of HIVST, underestimating its full impact. Although dynamic transmission models are designed for infectious diseases (such as HIV) to capture the long-term health benefits of an intervention and secondary infections averted, the numerous assumptions involved can make the estimated result uncertain. Second, we estimated the total cost for HIVST additively, which may underestimate the true cost by not accounting for the total fixed cost that is needed to sustain the programme and variations in health care practices and relative prices of resource inputs. This means that our estimate for the total cost of HIVST may be too low and make HIVST seem more cost-effective than the status quo. Although the estimated ICER per DALY averted for the adolescent groups are substantially higher in this study, they are significantly lower than other cost-effectiveness studies of HIVST in Southern Africa (16, 35, 37, 156). Third, the ICERs were sensitive to the probability of ART initiation. This model applied uniform ART initiation rate across by age and gender in the intervention and status quo. This was done because no previous studies reported the ART initiation proportion after following HIVST by age and gender. This was tested in the one-way sensitivity analyses: lowering the ART initiation to 37% results in lower ICER per DALY averted, and increasing the ART initiation to 90% results in higher ICER per DALY averted. The latter demonstrated that reaching the first 90% of the UNAIDS targets might cost more because

of additional costs related to ongoing ART costs. Fourth, this study acknowledges as a limitation on the generalizability of the cost and cost-effectiveness results to other settings because of variations in health care practices including patient flows and behaviour, different approaches to reaching people with HIV testing, and cross-country salary differences.

This study has important programmatic implications. The six ICERs show that in all age groups the additional cost of HIVST provision can result in a lower cost per DALY averted relative to the threshold of 1x GDP per DALY averted. Thus, targeted HIVST provision (by age and gender) among those who do not regularly test at the standard of care could be prioritized. The Zambian Ministry of Health and implementing partners could start scaling-up HIVST first among women ages 35-49 years, second among women ages 25-34 years, third among men ages 35-49 years, fourth among men ages 25-34 years, fifth among men ages 15-24 years, and sixth among women ages 15-24 years. The scaling-up of HIVST might be expensive, but it might be necessary to reach 90-90-90 and fast-track 95-95-95. Insights from this cost-effectiveness analysis can inform policymakers in Zambia and other comparable African countries with similar HIV testing targets.

Conclusion

This study estimates the cost-effectiveness of HIVST in Zambia. Our estimates of ICERs per DALY averted for all age groups are substantially below half of Zambian 1xGDP of US$1,430 threshold. However, when modelling costs from pilots for national scale-up, it is important to consider how costs change, as screening programmes are successful in identifying those easily reached. To identify the remaining undiagnosed HIV cases, testing budgets will need to expand.

List of abbreviations

ART	-	Antiretroviral therapy
ANC	-	Antenatal care
CEA	-	Cost-effectiveness analysis
DALYs	-	Disablity-adjusted life years
HIVST	-	HIV self-testing
HTS	-	HIV testing services
ICER	-	Incremental cost-effectiveness ratio
LSHTM	-	London School of Hygiene & Tropical Medicine
OPD	-	Outpatient department
PITC	-	Provider-initiated testing and counselling
RDT	-	Rapid diagnostic test
US$	-	United States dollar
VCT	-	Voluntary counselling and testing
WHO	-	World Health Organization
STAR	-	HIV-Self Testing AfRica
VL	-	Viral load
ZAMPHIA	-	Zambia population-based HIV impact assessment
ZDHS	-	Zambian demographic health survey

Ethics approval and consent to participate

The London School of Hygiene and Tropical Medicine (LSHTM) Ethics Committee and University of Zambia Biomedical Research Ethics Committee approved the study. The STAR trials are registered under the Clinical Trials Network (ClinicalTrials.gov) under registration numbers NCT02718274. No incentives were given to any individual who tested for HIV using the HIVST kits.

Consent for publication

The authors gave consent for publication.

Additional file

Text. Supplementary Tables

Competing interests

The authors have no conflicts of interest to declare.

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Authors' contributions

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Cost analysis: NA, LM, FTP

Methodology: NA, JJO, FTP

Writing –original draft: NA

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Supplementary document

Cost-effectiveness of community-based (door-to-door) HIV self-testing distribution models for HIV testing in Zambia: Markov microsimulation model

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Online supporting information

Modelling definition

Overview

We developed a Markov microsimulation model of a heterosexual population representing Zambians ages 15 years and over. This analysis aimed to evaluate the health impact and cost-effectiveness of one year of community-based (door-to-door) HIV self-test screening to reach those who did not test at the health facility in the last 12 months compared to a 'status quo' scenario of standard health facility testing. The model incorporated both HIV prevention and antiretroviral therapy (ART) cascades, which included individuals going through confirmatory rapid diagnostic HIV testing (RDT), receiving HIV positive results, initiating on ART, being retained in ART care, and attaining viral load suppression. The costs and health impacts of one year of screening were calculated over a time horizon of 20 years from a health provider perspective. The model was developed using TreeAge Pro 2017, R2.0 *TreeAge Software, Williamstown, MA, USA* (Table S1).

Table S1 Overview of the cost-effectiveness analysis

Key element	Reference case
Introduction	
Background of the problem	Introduction of HIV self-testing in Zambia.
Study Design and Scope	
Objectives	To assess the cost-effectiveness of a one-year community-based (door-to-door) HIVST kit distribution model compared to the standard of care HTS from a health provider's perspective in Zambia
Audience	Zambia Ministry of Health (MoH), implementing partners, funders
Type of analysis	Cost-effectiveness analysis
Target populations	Men and women aged 15 and above in the Zambian population
Intervention	One-year community-based HIV self-testing screening
Comparator	Standard HIV testing services: provider-initiated testing and counselling (PITC), antenatal care (ANC) and voluntary counselling and testing (VCT)
Time horizon	Twenty years. (Sensitivity analysis: 5, 10,15, 20 years and lifetime)
Analytic perspective	*Health provider*
Whether this analysis meets the requirements of the reference case	It meets the Consolidated health economic evaluation reporting standards (CHEERS) statement
A measure of health effects	Disability-adjusted life years (DALYs)
Primary analysis plan	Cost per DALY averted
Methods and data	
Description of the model	Markov microsimulation model
Software used	*TreeAge Software, Williamstown, MA, USA*

Methods for obtaining estimates of costs	Society for Family Health annual Self-testing in Africa project expense data Both ingredients based (bottom-up) and top-down costing data of HIV testing services in Zambia
Preference disability weights	HIV symptomatic, pre-AIDS- 0.221[0.146-0.310](76) HIV/AIDS: receiving antiretroviral treatment-0.053[0.034-0.079](76) AIDS: not receiving antiretroviral treatment-0.547[0.382-0.715](76)
Statement of discount rates	All costs (in 2017 US$) and health benefits discounted by 3% per year
Results of sensitivity analysis	Deterministic (one-way univariate), multivariate, probabilistic sensitivity analyses (PSA) and scenario analyses

Model Structure

The Markov microsimulation model started the simulation using two groups of individuals: 1) HIV negative individuals who do not know their HIV status, and 2) HIV positive individuals who do not know their HIV status (Figure S1). The health states experienced by individuals were assigned disability weights and costs pertinent to each of these health states. The model has ten mutually exclusive health states: 1) HIV negative individuals who know their HIV status, 2) HIV negative individuals who do not know their HIV status, 3) HIV positive individuals who do not know their HIV status, 4) HIV false positive (misdiagnosed), 5) HIV false negative (misdiagnosed), 6) HIV true positive viral load suppressed, 7) HIV true positive viral load not suppressed, 8) HIV true positive lost to follow-up, 9) death from HIV without treatment and 10) death from other natural causes (Figure S1).

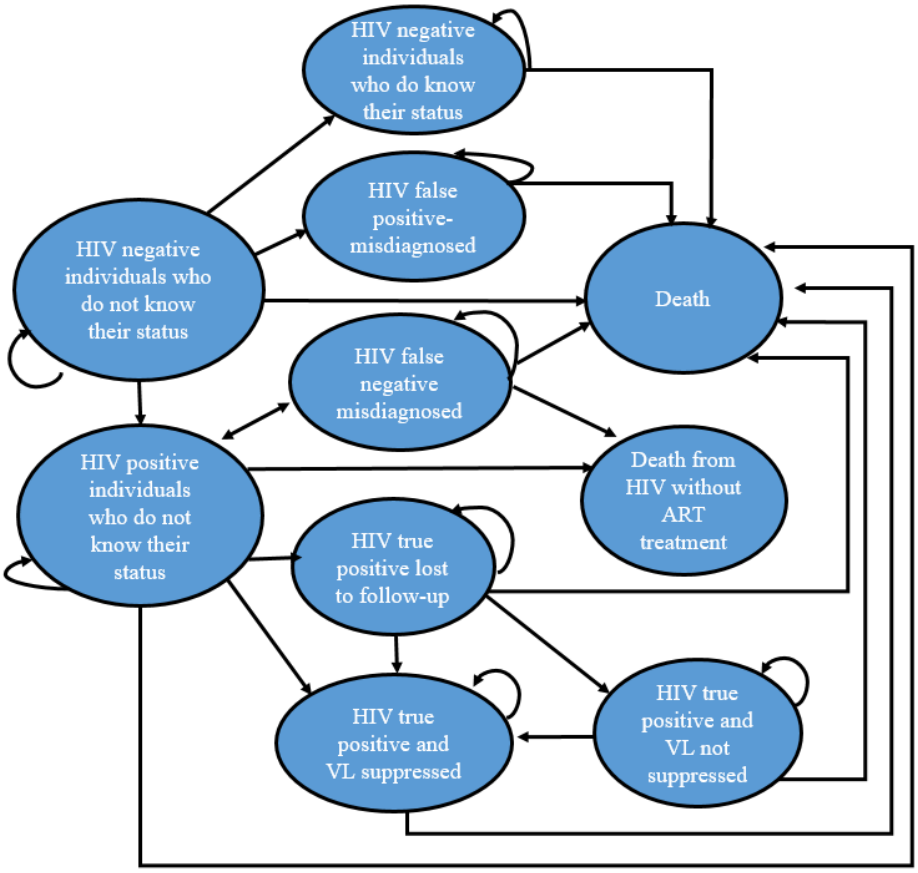


Figure S 1 The structure of the Markov microsimulation model for the provision of HIV self-testing for those not tested in the last 12 months

Cost inputs

The Markov microsimulation model incorporates both HIV prevention and treatment cascades. The costs for the prevention cascade include the costs for HIV testing at the health facility in three departments: provider-initiated testing, counselling (PITC), antenatal care (ANC), voluntary counselling, and testing (VCT). The costs for the treatment cascade include the costs to identify HIV positive individual and link to the treatment cascade (Table S2).

Table S2 Cost inputs

Cost inputs (2017 USD)	**Average cost**	**Standard error (SE)**	**95% confidence interval**		**Markov model estimation**				
		SE* = (d-b)/3.92	**Low (b)**	**High (d)**	**Beta (SE^2)/average cost**	**Lambada (1/beta)**	**Alpha (mean/SE) ^2**	**Distribution**	**Reference**
Cost of intervention and Status quo HTS in 2017 US$									
Intervention Community-based (door-to-door) self-test kit distribution									
Average cost per negative person tested	16.42	10.74	7.90	50.00	7.02	0.14	2.33	Gamma	(50)
Status quo - Provider initiated testing and counselling									
Average cost per negative person tested	10.76	1.65	7.53	13.99	0.25	3.97	42.68	Gamma	(135)
Status quo - Antenatal care HIV testing									
Average cost per negative person tested	57.59	8.81	40.31	74.87	1.35	0.74	42.68	Gamma	(128)
Status quo - Voluntary counselling and testing									

Average cost per negative person tested	4.41	1.01	2.59	6.55	0.23	4.33	19.69	Gamma	(133)
Average cost of false positive confirmatory test	1.6	0.24	1.12	2.08	0.037	26.68	42.68	Gamma	(133)
Cost of HIV care and treatment in 2017 US$									
Intervention (door-to-door self-test following linkage into care)									
Annual cost of ART per client	185.86	4.75	176.55	195.16	0.12	8.25	1532.67	Gamma	(36)
Status quo- Linkage to care									
Average cost of ART	190.36	2.28	185.89	194.84	0.027	36.51	6951.73	Gamma	(36)

SE = (d-b)/3.92 is applied when there is no SE data available

Site-level unit cost for community-based HIVST distribution

Table S3 shows the site level cost per HIVST kit distributed in 16 health facilities in Zambia. The average cost $16.42 is applied in the model per Table S2. The table below is included to show the unit cost variation by health facility (site-level) where it ranged from $7.90 to $50.01 per HIVST kits distributed. These two minimum and maximum values are applied in the one-way sensitivity analysis and for best & worst-case scenario (Table S3).

Table S3 Total and site-level unit cost for community-based door-to-door HIVST kit distribution model

Zambia site number	Total number HIVST kits distributed	Total cost for HIVST distribution (Full)	Site-level unit cost per HIVST kit distributed
1	5587	$ 105,822.48	$ 18.94
2	7370	$ 101,485.07	$ 13.77
3	3113	$ 81,341.94	$ 26.13
4	3090	$ 61,563.63	$ 19.92
5	20450	$ 161,774.90	$ 7.91
6	8029	$ 76,522.03	$ 9.53
7	8759	$ 93,243.83	$ 10.65
8	8768	$ 70,206.19	$ 8.01
9	7752	$ 158,721.75	$ 20.47
10	1758	$ 87,921.17	$ 50.01
11	5030	$ 130,696.73	$ 25.98
12	7270	$ 157,551.93	$ 21.67
13	4902	$ 116,784.17	$ 23.82
14	2452	$ 81,773.42	$ 33.35
15	5895	$ 121,294.01	$ 20.58
16	3364	$ 90,732.00	$ 26.97
Min	1758	$ 61,563.63	$ 7.91
Max	20450	$ 161,774.90	$ 50.01

Population-level HIV testing uptake

Intervention - Adding community-based HIV self-test distribution to the status quo

The community-based HIV self-test distribution enumerated all individuals in a community of four provinces of Zambia. Self-testing kits were distributed only to those ages 15 and over. The Self-test in Africa (STAR) endline survey data were analysed to calculate the proportion of community-based HIV self-test distribution by males/females age 15-24 years, 25-34 years, and 35-49 years who did not test in the last 12 months (Table S4).

Table S4 Observed proportion of community-based HIV self-test distribution uptake by male and female in (n = 314) (STAR endline Survey)

Age	Community-based (door-to-door) self-test distribution	
	Men	Women
15-24	0.57	0.41
25-34	0.57	0.60
35-49	0.53	0.60

Comparator 'status quo' health facility testing

The 'status quo' health facility testing provided testing to individuals age 15 and above who did not test in the past 12 months. The STAR endline survey data were analysed to calculate the proportion of men/women age 15-24 years, 25-34 years, and 35-49 years of age who tested at the standard of care in the last 12 months (Table S5).

Table S5 Proportion of men and women HIV testing through the standard of care HIV testing services in the last 12 months (n = 2,334) (STAR endline survey)

Age (years)	Provider initiate test and counselling (PITC)		Antenatal care (ANC) testing		Volunteer counselling and testing (VCT)	
	Men	Women	Men	Women	Men	Women
15-24	0.46	0.53	0.02	0.11	0.12	0.09
25-34	0.56	0.55	0.06	0.16	0.12	0.08
35-49	0.65	0.65	0.06	0.10	0.09	0.07

Epidemiology of HIV

The model starts the simulation by allocating individuals into two health states: HIV negative people who do not know their HIV negative status and HIV positive people who do not know their HIV positive status, stratified by age and gender. These proportions were calculated using the Zambia DHS 2013-14 dataset. The proportion for HIV negative and HIV positive who do not know (stratified by age and gender) (Table S7) were calculated by cross tabulating of those who responded 'No' to ever been tested for HIV (stratified by age and gender) (Table S6 and S7).

Table S6 Proportion of men and women ever been tested for HIV (51)

Age	Men ever been tested for HIV (*n* = 13,574)		Women ever been tested for HIV (*n* = 15,388)	
	No	Yes	No	Yes
15-24	0.54	0.46	0.33	0.67
25-34	0.22	0.78	0.07	0.93
35-49	0.23	0.77	0.14	0.86

Table S7 Proportion of HIV status for men and women who never been tested for HIV in the last 12 months and their HIV status (51)

Age	Men never been tested for HIV in the last 12 months		Women never been tested for HIV in the last 12 months	
	HIV negative	HIV positive	HIV negative	HIV positive
15-24	0.96	0.04	0.96	0.04
25-34	0.90	0.10	0.87	0.13
35-49	0.86	0.14	0.85	0.15

Population-level HIV treatment

In the model, after confirmed HIV testing, individuals who were tested HIV positive were linked to care for both intervention and standard of care arm. Since there is a data gap on linkage after confirmed HIV positive test per PITC, ANC, and VCT testing services, self-reported ART status from Zambia population-based HIV impact assessment (ZAMPHIA) were used to parametrize the model (Table S8). The model assumed the same proportion of linkage (Table S8) regardless of testing modality.

Table S8 Proportion of Men and women self-reported antiretroviral therapy (ART) status [9]

Age	Men	Women
15-24	0.78	0.78
25-34	0.72	0.78
35-49	0.86	0.88

For the intervention arm where individuals tested for HIV using door-to-door HIVST, the proportion of 37% ART initiation was applied (218) (Table S9).

Table S9 Proportion of men and women in HIV care (223)

HIV Care	Men	Women
Initiation of ART care for intervention-door-to-door HIVST	0.37	0.37
Annual lost to follow-up from HIV care (%)	0.17	0.17
Annual lost to follow-up from HIV care and died (%)	0.029	0.029
Annual mortality rates while on HIV care	0.088	0.088

Viral Load Suppression among those on treatment

Among those who reported being on ART, Table S10 shows the proportion of viral load suppression stratified by age and gender.

Table S10 Proportion of men and women viral load suppression (VLS) among those on treatment [9]

Age (years)	Men VLS (< 1,000 copies/ml)	Women VLS (< 1,000 copies/ml)
15-24	0.78	0.78
25-34	0.91	0.88
35-49	0.88	0.91

The model incorporated the performance of both OraQuick HIV self-test and rapid diagnostic tests (Table S11).

Table S11 List of HIV diagnostic test kits quality assurance

Type of HIV test	Sensitivity (CI)	Specificity (CI)	Reference
Performance of OraQuick*	94.2% (90.4-96.8)	99.7% (99.3-99.9)	(208)
Uni Gold*	99.8%	99.9%	(224)
Bioline*	100%	99.1%	(224)

*****WHO Prequalified, CI = confidence interval

Clinical course of HIV infection

In the model, for individuals who are HIV positive and remain unaware of their HIV positive status (refused to test) and for individuals with no viral load suppression, the disability weights were applied according to the clinical course of HIV infection (Figure S2). In the 20-year time horizon, the following disability weights were applied:

- Year 1-7: disability weight of 0.221
- Year 8-12: disability weight of 0.547
- Year 13-20: disability weight of 1 (individuals without treatment are expected to die from AIDS after 12 years)

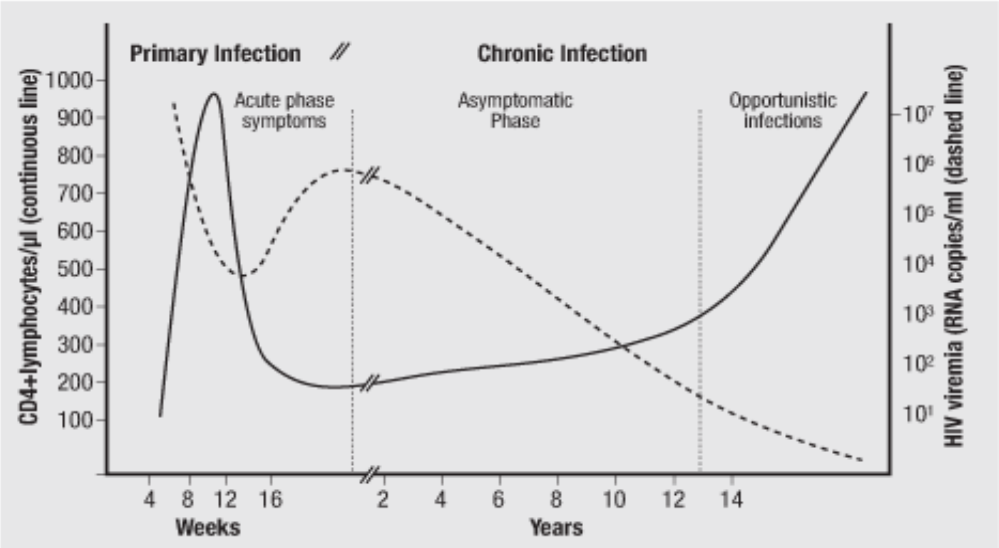


Figure S 2 Clinical course of HIV infection (3)

Annual mortality proportions

Annual all-cause mortality proportions were applied to individuals who would assume to die other than HIV/AIDS (Table S12).

Table S12 Men and women annual all causes of mortality (Zambia DHS, 2015)

Age (years)	Men	Women
15-19	0.02	0.02
20-24	0.03	0.03
25-29	0.03	0.04
30-34	0.08	0.07
35-39	0.09	0.09
40-44	0.14	0.10
45-49	0.14	0.11

DALY calculation

Classification of disability weight for HIV health states

The mean HIV disability weights were applied at the Markov health states using a beta distribution. The utility descriptions for the different health states are discussed in Table S13. The application of these classified disability weights aided to calculate the mean years of life lived with disability (YLD). It also helped identify age-specific YLD for individuals who died from HIV within the 20-year time horizon (either not knowing HIV positive status or failed viral load suppression) (Equation 1).

Table S13 Health-related quality of life

Utility description	Standard Error		95% Confidence interval		Markov model estimation		Reference
	Mean	SE	Lower CI	Upper CI	alpha	beta	
HIV-negative individuals	0.005	0.002	0.002	0.011	4.71	938.08	(76)
HIV-positive receiving antiretroviral treatment	0.053	0.011	0.034	0.079	20.13	359.73	(76)
HIV-positive, asymptomatic (who don't know their HIV positive status)	0.221	0.042	0.146	0.310	21.51	75.84	(76)
AIDS not receiving antiretroviral treatment	0.547	0.085	0.382	0.715	18.23	15.10	(76)

CI = confidence interval, SE = standard error

Formulas for calculating DALYs

DALYs are calculated by adding the adjusted number of years lived with disability (YLDs) and the number of years of life lost due to premature mortality (YLLs) (66).

DALY [r, *K, B*] = YLL [r, *K, B*] + YLD [r, *K, B*] equation (1)

YLL [r, *K, B*] = Number of deaths X life expectancy at the age of death equation (2)

YLD [r, *K, B*] = Number of cases X duration till remission or death
X disability weight equation (3)

The formulas here are taken from Fox-Rushby (74)

$$YLLs[r,K,B] = \frac{KCe^{ra}}{(r+B)^2}\{e^{-\frac{r+B}{L+a}[-(r+B)(L+a)-1]-\ e^{-(r+B)a[-(r+B)a-1]}} + \frac{(1-K)}{r}(1-e^{-rL})$$

Where:

r = discount rate expressed as a decimal

K = age weighting modulation factor

C = constant

B = parameter from the age weighting function

a = age of death

L = standard expectation of life at age a (age of death)

The formula for YLDs [r, K, B] differs from YLLs [r, K, B] by incorporating D (the disability weight) and different interpretation of **a** and **L** and it is described below:

$$YLDs[r,K,B] = \frac{D\{KCe^{ra}}{(r+B)^2}\{e^{-\frac{r+B}{L+a}[-(r+B)(L+a)-1]-\ e^{-(r+B)a[-(r+B)a-1]}} + \frac{(1-K)}{r}(1-e^{-rL})\}$$

Where:

r = discount rate expressed as a decimal

K = age weighting modulation factor

C = constant

B= parameter from the age weighting function

a = age of HIV diagnosed

L = duration of disability

Life expectancy by age and gender - Zambia

The life expectancies at the age of death for Zambia in Table S14 were provided by the Institute of Health Metrics and Evaluation (IHME) (225).

Table S14 Life expectancy at the age of death by age and gender - Zambia

Age (years)	Men	Women
15-19	50.59	55.66
20-24	46.11	51.03
25-29	41.74	46.48
30-34	37.47	42.10
35-39	33.37	37.87
40-44	29.40	33.76
45-49	25.59	29.77
50-54	21.96	25.87
55-59	18.59	22.14
60-64	15.34	18.41
65-69	12.45	14.97
70-74	9.88	11.85
75-79	7.70	9.12

Calculating the years of life lost (YLL)

In order to count the number of individuals who died from HIV, two absorbing states of individuals who died from HIV were created: one for the intervention arm and the second for the standard of care arm. The only function of these two absorbing states was to transition individuals who died from HIV into these absorbing states. To understand the steps in the model better, let us follow a 15-year-old male who was not tested in the last 12 months. For example, within the first year, this 15-year-old individual gets tested using HIV self-test and learns his HIV positive status. After a confirmatory diagnostic HIV test, he gets linked to ART. Within the 20-year time horizon (20 cycles, 1 cycle = 1 year), he might fail to adhere to ART, which could lead to no viral load suppression and death from HIV. At the time of his death, the model transitions this individual into the absorbing state of individuals who died from HIV at the intervention arm. This absorbing state counts the number of cycles this individual stayed in this absorbing state. Since the model runs using a 20-year time horizon, the number of cycles in this absorbing health state counting cannot be greater than 20 cycles. Then the age when this 15-year-old male who tested HIV positive died can be calculated as follows:

Age of HIV positive test = 15
Number for cycles in absorbing state = 17
Model's time horizon = 20 years (or 20 cycles)
Age of 15-year-old died from AIDS = 15+ (20-17) = 18 years
Standard life expectancy at age of death in years = 50.59 (the life expectancy at age 18, using the data provided for Zambia by Institute of Health Metrics and Evaluation 2017)

In this example, the calculation of the YLLs requires two steps:
First, to calculate the life lost from age 18 onwards and secondly to discount this value to age 15.
$r = 0.03$
$K = 1$
$C = 0.1658$
$B = 0.04$
$a = 18$
$L = 50.59$

$$YLL\,[r,K,B] = \frac{KCe^{ra}}{(r+B)^2}\{e^{-\frac{r+B}{L+a}[-(r+B)(L+a)-1]-\ e^{-(r+B)a[-(r+B)a-1]}} + \frac{(1-K)}{r}(1-e^{-rL})$$

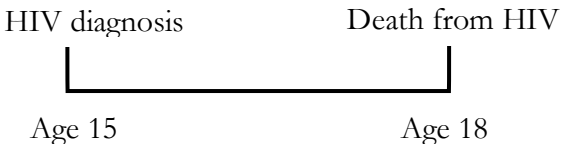
Equation 2

(Undiscounted) YLL[r,*K,b*] in this example is

=(1*0.1658*EXP(0.03*18)/(0.03+0.04)^2)*(EXP(-1*(0.03+0.04)*(50.59+18))*(-(0.03+0.04)*(50.59+18)-1)-EXP(-1*(0.03+0.04)*18)*(-(0.03+0.04)*18-1))+((1-1)/0.03)*(1-EXP(-1*0.03*50.59))

(Undiscounted) YLL [r, *K, b*] = 34.45

Discounting this value back to age 15 uses this formula



Discounted YLL[r,*K,b*] = undiscounted YLL X EXP(-r*s)

Where:

r = 0.03

s = number of years to be discounted

Discounted YLL[r,*K,b*] = 34.45*EXP(-0.03*(18 -15))

=31.49

Calculating the years of life lost with disability (YLD)

The model is parameterized with HIV disability weights per Salomon et al. (Table S13). The application of these classified disability weight aided to calculate age-specific YLD for individuals who died from HIV within the 20-year time horizon (Figure S4). Again, the calculation for YLD differs from YLL by incorporating D (the disability weight) and different interpretation of **a (**age of HIV diagnosed) and **L (**duration of disability).

Following the above example, YLD [r, *K, b*] is calculated as follows:

Where:

r = 0.03

K = 1

C = 0.1658

B= 0.04

a = 15

$L = 3$

D = 1.788 (from the individual model output)

$$YLDs[r,K,B] = \frac{D\{KCe^{ra}}{(r+B)^2}\left\{e^{-\frac{r+B}{L+a}[-(r+B)(L+a)-1]-\ e^{-(r+B)a[-(r+B)a-1]\}}} + \frac{(1-K)}{r}(1-e^{-rL})\right\}$$

Equation 3

YLD [r, *K, B*] =

=1.788*(1*0.1658*EXP (0.03*15)/ (0.03+0.04) ^2)*(EXP (-1*(0.03+0.04)*(3+15))*(-(0.03+0.04)*(3+15)-1)-EXP(-1*(0.03+0.04)*15)*(-(0.03+0.04)*15-1))+((1-1)/0.03)*(1-EXP(-1*0.03*3))

YLD [r, *K, B*] = 7.21

Therefore, from the time of HIV diagnosis at age 15, the total numbers of discounted YLLs lose due to premature death equals 31.49. Adding this to the year of life lost with disability YLDs = 7.21, gives the total number of DALYs loss of 38.70.

DALY [r, *K, B*] = YLLs + YLDs

= 31.49 + 7.21

=38.70

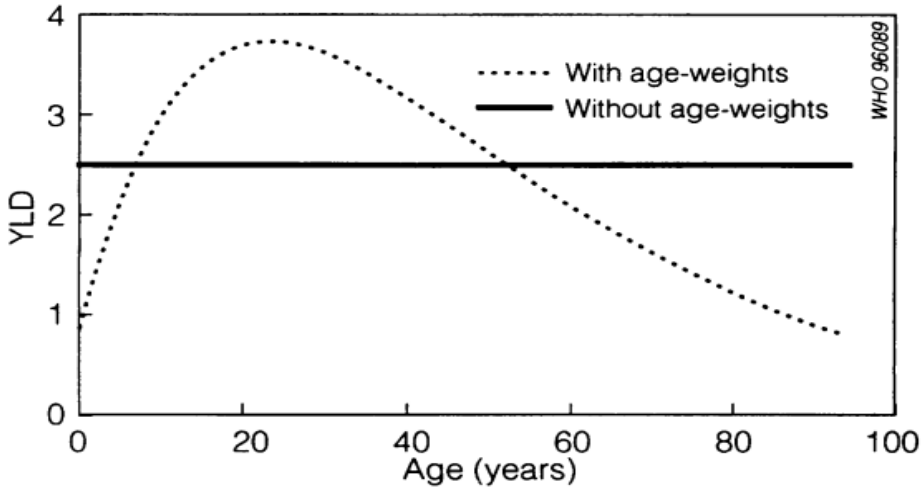
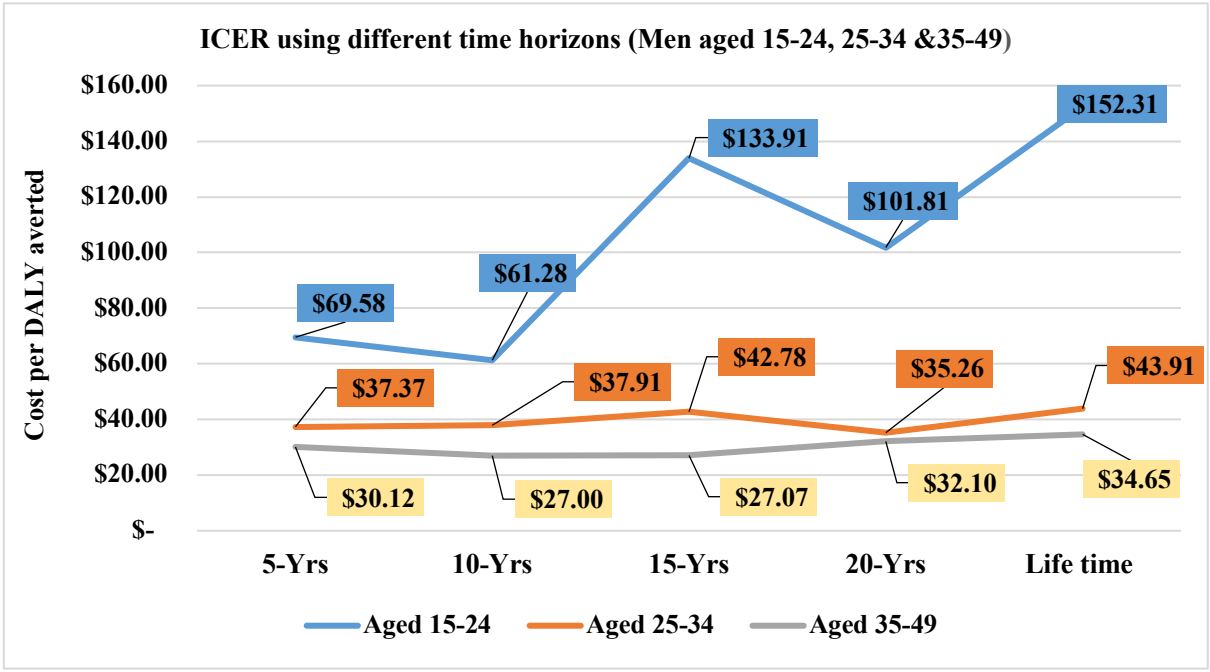


Figure S 4 YLD with and without age weighting (2)

Sensitivity analyses

We explored different time horizons over which the intervention could be modelled by applying 5, 10, 15, 20-year, and lifetime horizons (Figure S5). For all age groups, the incremental cost for the different time horizons varied, while the number of DALYs averted each year increases over time.



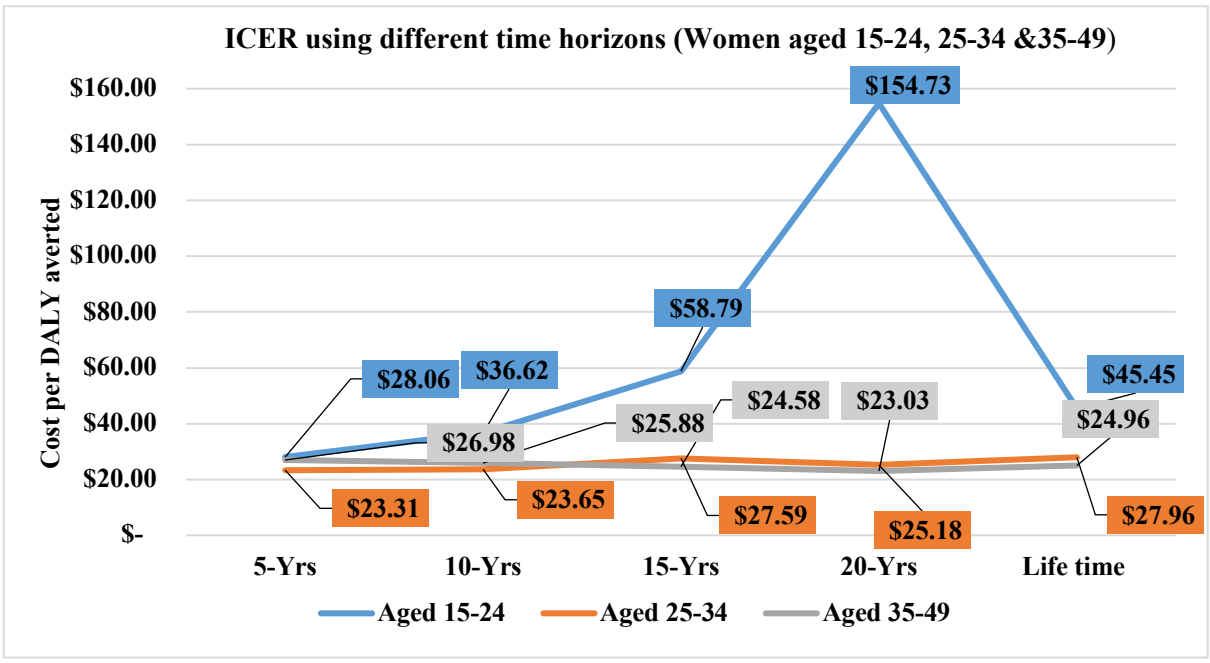


Figure S 5 ICERs using different time horizons

Probabilistic sensitivity analyses

Figure S6 and S7 reflect the simulation plots on the cost-effectiveness plane for men and women by the three age groups with 1x GDP per capita (US$1,4300 per DALY averted.

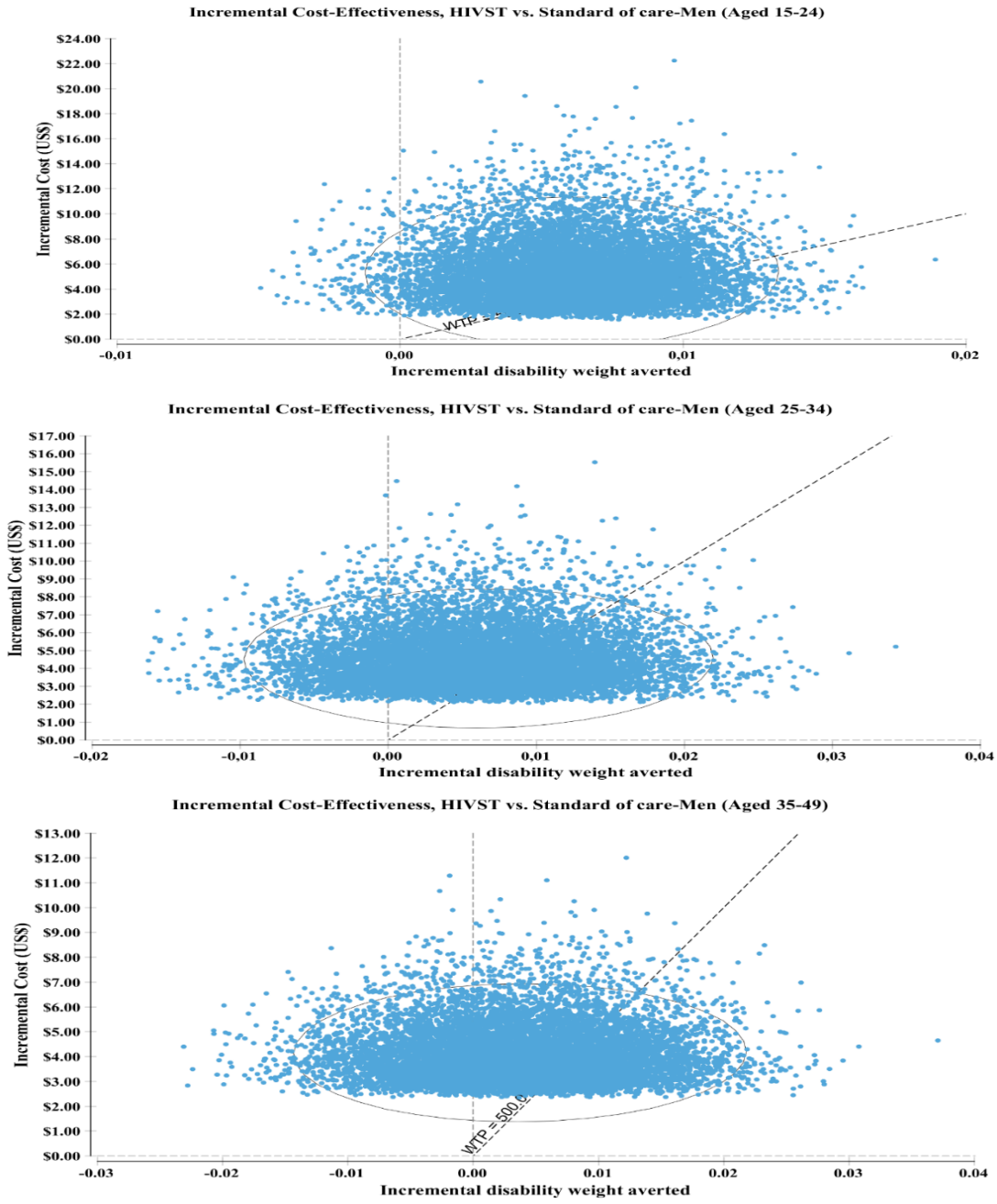


Figure S 6 Incremental cost-effectiveness scatterplots (Men)

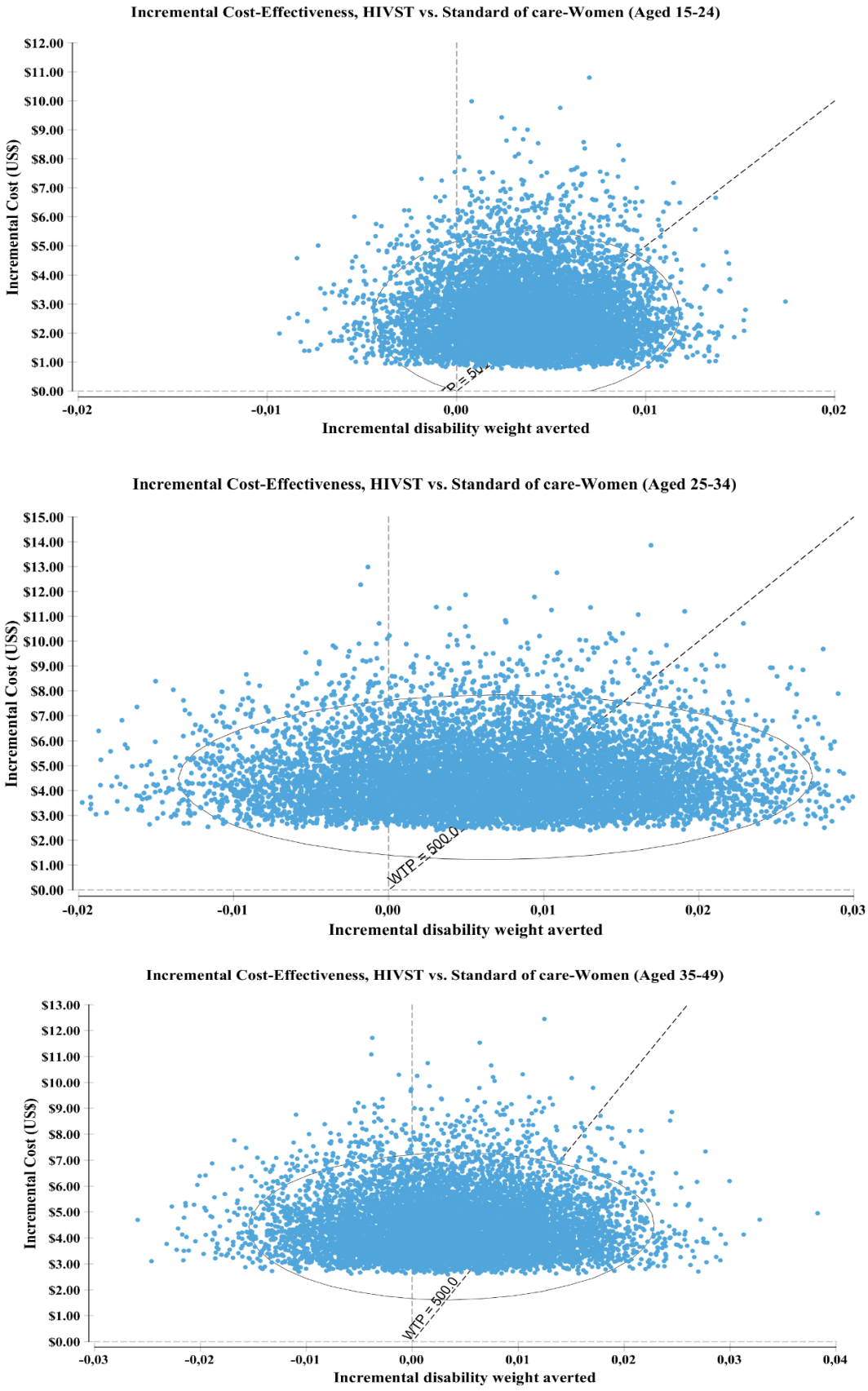


Figure S 7 Incremental cost-effectiveness scatterplots (Women)

CHAPTER 5 DISCUSSION AND CONCLUSIONS

This thesis set out to investigate the costs and cost-effectiveness of different HIV testing services in sub-Saharan Africa, the costs of HIVST kit distribution, and the cost-effectiveness of HIV self-testing added on to the standard of care in Zambia. This chapter provides a critical assessment of the key findings of the thesis, discusses their strengths and limitations, and highlights future research and policy implications. This chapter aims to answer the one overall policy question stated in the conceptual framework (Chapter 1 Figure 1.5): does HIVST have a role or can HIVST be cost-effective when targeted at those who do not test?

5.1. Key findings

This section summarizes the key results arising from the thesis research question outlined in Chapter 1.

Research Q1: What is the cost of providing HIV testing in sub-Saharan Africa through different HIV testing models, and how does the scale of the service impact the costs?

The first research question sought to examine the gaps in cost and cost-effectiveness studies of HIV testing services in sub-Saharan Africa using a systematic literature review (Paper 1). The review found that a large number of studies reported the cost of different HIV testing modalities, but few studies undertook a cost-effectiveness analysis. Although cost and cost-effectiveness estimates varied widely, this review identified that in general, the costs of the different testing modalities were comparable to each other.

The few cost-effectiveness studies identified and highlighted the importance of ensuring users do not pay fees, and of targeting pregnant women and their sexual partners potentially through couples testing, home-based testing, or HIVST. In addition, home-based, mobile, and HIVST are potentially cost-effective if providers are willing to pay the additional money needed to deliver these services and thereby realize the potential health benefits from their use. Policymakers and implementing partners would find the result of the systematic literature review helpful and could do more cost-effectiveness and budget analyses of the different combination of HIV testing modalities to inform HIV testing policy and budgets.

Research Q2: How much does it cost to add HIV self-testing into male circumcision, outpatient, and HIV testing services in Zambia (Paper 2)?

The second research question was addressed in Paper 2, where costs of different HIVST distribution modalities were calculated. The VMMC model distributed 2,742 HIVST kits in Malawi, 11,330 HIVST kits in Zambia, and 2,870 HIVST kits in Zimbabwe. The average cost per HIVST kit distributed was US$9.65, US$13.01, and US$7.71 for Malawi, Zambia, and Zimbabwe, respectively. In Zambia, the OPD model distributed 12,885 HIVST kits that resulted in an average cost of US$15.81 per kit distributed. In Zimbabwe, the integrated HTS model distributed 14,886 HIVST kits and reported the average cost as US$9.85 per kit distributed.

HIVST distribution costs varied substantially by model and location, and a model with higher numbers of HIVST kits distributed generally showed lower unit costs (i.e., economies of scale). HIVST kits distributed via the VMMC model were designed to create demand and increase uptake of VMMC services among HIV negative men for HIV prevention benefits. The OPD model was designed to increase more targeted provider-initiated testing to reach undiagnosed HIV positive people. The impact of this approach is significant when removing the start-up cost, and this substantially lowered the average cost of each HIVST distribution modality. This paper strengthens the evidence for integrating HIVST into existing HTS.

Research Q3: What is the incremental cost-effectiveness of community-based (door-to-door) self-test kit distribution compared with the standard of care HTS in Zambia (Paper 3)?

The third research question was addressed in Paper 3, in which a microsimulation model showed the cost-effectiveness of HIVST distribution among men/women ages 15-24 years, 25-34 years, and 35-49 years who did not test in the last 12 months.

The ICERs for adolescent men and women ages 15-24 were $101.81 and $154.73 per DALY averted, respectively. The ICERs for men and women were $35.26 and $25.18 for ages 25-34 and $32.10 and $23.03 for ages 35-49. Men and women in the 25-34 and 35-49 age groups could benefit greatly from HIV self-testing. Although the ICERs for adolescent men and women were highest, the ICERs per DALY averted were below the US$1,430 per DALY averted threshold. Thus, policymakers could use these age-stratified ICERs to prioritize for targeted HIVST provision.

The microsimulation modeling paper outlined in greater detail how to simulate individuals using both HIV prevention and treatment cascades. The HIV prevention cascade specifically helped to present the provision of HIVST among HIV negative and HIV positive individuals who do not regularly test at a facility-based HTS. The treatment cascade helped visualize treatment flows of individuals after they tested HIV positive and enrolled in HIV care services. Bringing these two cascades together facilitated the building and parametrization of the model. Most importantly, it helped to identify the weakest decision point in the cascade that might affect the impact of the intervention. In a series of one-way sensitivity analyses, I tested the sensitivity of the model parameters and found that the calculated ICER results were sensitive to the variation in cost per HIVST kit distributed, lifetime ART cost, discount rate of effects, ART initiation, ART retention and viral load suppression, and the sensitivity of OraQuick among intended users.

5.2. Contribution to knowledge

The contribution of this thesis can be summarized in terms of both empirical findings and methods.

Contribution to empirical findings

The first contribution of this thesis is the systematic literature review. This review will extend the scope of the existing literature by contributing the costs and cost-effectiveness of HIV testing services in sub-Saharan Africa. The key findings of the systematic literature review (Paper 1) showed that the costs of different HIV testing modalities are comparable and that more cost-effectiveness analyses are needed. More cost-effectiveness analyses are critical before substantial financial and human resources are spent in scaling-up the HTS. Large-scale spending on HTS that may not be cost-effective and demonstrate impact (e.g., identify new HIV positive cases) and may result in misallocation of scarce resources. Notably, in recent years bilateral and multilateral donors significantly reduced funding for HIV response in low and middle-income countries (LMIC) (226). This has started to increase pressure on LMIC to finance their own HIV responses, which makes opportunity cost decisions and sustainability of HIV responses even more crucial (227). Thus, LMIC needs to find more efficient and cost-effective HTS approaches for individuals who need HIV testing.

A second contribution involves the cost analyses, in which this thesis calculated the incremental unit cost for HIVST kits distribution within 13 VMMC services and at 21 health facilities from the providers' perspective in Malawi, Zambia, and Zimbabwe (Paper 2). For these models, the unit cost per HIVST kit distributed are slightly higher than the standard

facility-based finger-prick testing services (US$2.60-22.42) (133), and HIVST delivery through community-based distribution agents (door-to-door distribution) (US$8.15-16.42) (49), that we had previously estimated using the same methods in the same sites. Despite the higher unit costs that were observed within the VMMC and OPD HIVST distribution models, it is important to evaluate these unit costs in relation to the target population of interest for HIV testing. The VMMC model not only targets men but also aims to increase the uptake of VMMC services by encouraging men to HIV test themselves prior to VMMC services. Additionally, the OPD model targets undiagnosed HIV positive individuals during their routine OPD visits and provides the opportunity to test themselves to maximize HIV diagnosis, ART initiation, and uptake of other HIV prevention services. Therefore, in both models, the higher unit costs achieved more than covering the cost of HIV testing and went beyond enhancing HIV prevention and ART initiations targets.

The third important contribution of this thesis is the Markov microsimulation model that evaluated the incremental cost-effectiveness of an additional one-year home-based HIV self-testing campaign (Paper 3). This was the first cost-effectiveness model to incorporate age and gender heterogeneity and present results by gender across three age groups in Zambia. Men and women 25-34 and 35-49 age groups could benefit greatly from HIV self-testing. In the model, the different proportions for HIV testing uptakes for HIVST had an impact on both HIV prevention and the HIV care cascade.

In addition, the findings from Papers 1 and 2 strengthen the parameterization of the model and highlight which parameters to test for uncertainty using sensitivity analyses. For instance, the unit cost per HIVST kits distributed ($16.42) through a door-to-door distribution modality was applied in the model to estimate the incremental cost of HIVST provision. Our previously published work (50) showed the variation of unit cost at the site level based on the scale of HIVST kits distributed. The sensitivity analyses in Papers 2 and 3 showed the impact of lower than optimal uptake to HIVST on the unit cost and ICERs, respectively.

Taken together, Papers 1 and 3 highlight the importance of using high-quality parameters to closely estimate the impact and the cost-effectiveness of an intervention. Most importantly, the high-quality parameters extend to the sensitivity analysis as well. Ideally, programmes for the introduction of new interventions should support both cost and cost-effectiveness analysis to generate reliable cost and effectiveness estimates, respectively.

Contribution to methods

This thesis has also made several important contributions to methods. The systematic literature review on the cost and cost-effectiveness of HIV testing services in Chapter 2 employed two recently published frameworks: the Global Health Cost Consortium (GHCC) reference case (116) and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (117) to assess the quality of the cost and cost-effectiveness studies respectively. The 17 GHCC principles that were applied to assess the costing studies stressed the gaps in designing costing studies and reporting the results in a standardized manner. Also, it highlighted the importance of following the 17 principles for future costing studies. This will facilitate budget allocation for HIV testing services and estimating future scale-up costs using programme costs. The 24-item CHEERS checklist could also be used as standard checklist practice to follow in reporting cost-effectiveness estimates. This could also identify technical challenges in predicting the resources needed to adopt the same interventions from one country to another. It is apparent that high-quality cost and CE studies are especially crucial for sub-Saharan Africa, where scarce resources must be allocated efficiently. Thus, these two frameworks for standard reporting of cost and cost-effectiveness results could improve the validity and comparability of studies across sub-Saharan Africa.

The cost analyses in Chapter 3 employed cost allocation factors by cost input types. These allocation factors aim to guide the process of allocating aggregated financial costs to specific cost inputs to calculate total and unit cost of new interventions in greater detail and transparency. Thus, this study provides methodological guidance about which allocation factors to apply for a given cost input for expenditure-based cost analysis. I also hope these allocation factors will invite future cost studies to expand these allocation factors based on study setting and type of health intervention.

The Markov microsimulation model in Chapter 4 is the first cost-effectiveness study simulating a heterosexual population representing Zambian adults aged 15 to 49, incorporating each decision an individual makes in the process, beginning with uptake of HIV testing, confirmatory testing, linkage to ART, retention in care, and eventually leading to viral load suppression, which encompasses both HIV prevention and HIV care cascades. The HIV prevention cascade helps present the flow of people who are unaware of HIV negative status and people unaware of HIV infection (not in care) (169, 171, 209,168, 170, 208). The HIV treatment cascade helps present how to move people along with treatment services after they enroll in HIV care services. This includes: 1) initiating ART, 2) alive and remaining in care for 90 or more days, and 3) alive and viral load suppressed (210-213, 209-

212). The model is parameterized in a way that can easily be updated with the most recently published data to generate the most up-to-date cost-effective estimates. This can be done not only in the context of Zambia but also in other comparable countries such as Malawi and Zimbabwe, which are STAR countries where HIV self-testing was introduced using different HIV testing modalities and is currently in the process of being scaled-up to reach high-risk groups.

5.3. Limitations of thesis approach

The strengths and limitations of specific methodological and analytical approaches are discussed in greater detail at the end of this chapter. This section focuses on overarching limitations.

Comparability and transferability of cost and cost-effectiveness estimates

Chapter 2 (Paper 1) presents the cost and cost-effectiveness of different HTS in sub-Saharan Africa. Although the review shows the variation in reported costs and cost-effectiveness estimates, the review acknowledges the diversity and complexity of healthcare systems in sub-Saharan Africa. Thus, the review presented the costs and the CE results following the study perspective. The six HIV testing modalities could not all be assessed in one country, which made it difficult to compare different testing modalities. The methods used to undertake the economic analysis were not always comprehensive or comparable, limiting transferability of findings.

Unit of measurement cost per HIVST kit distributed

The first limitation of the cost analysis (Paper 2) is reporting unit costs per kit distributed for the different distribution modalities but without observed data linking the unit costs to numbers of new HIV case identified and those linked to care. In Zambia, the STAR endline survey design did not incorporate the monitoring of the number of people tested, new HIV positive cases, or linkage to ART. As a result, I was unable to estimate the unit cost per person tested or per HIV positive individual tested or linked to care after self-testing or a negative person linked to prevention – notably to VMMC services. Second, STAR is the first implementation project that introduced HIVST in the Southern Africa region. Thus, the distribution numbers were relatively small for VMMC, OPD, and integrated models compared to community-based distribution, which accounted for 82.7% of HIVST kit distribution (46). If respective MOHs scale-up HIVST using the community-based

distribution modalities, it is posible that unit costs may reduce due to the higher number of test kits distributed.

Simplification of static Markov microsimulation model

First, this study recognized that HIV is an infectious disease and models with individual interactions were necessary to capture the disease transmission rate. The static Markov microsimulation model did not allow individual interaction. For example, individuals in the model who were screened might be infected at a later time, and individuals who were enrolled in ART might have a lower possibility of infecting others (228), which in turn might decrease the cost-effectiveness of each alternative HTS. However, this study tried to minimize this limitation by incorporating stratification of HIV prevalence and testing behavior by gender and age, and transitioning individuals through the 10 different health states.

Second, the model in this thesis was designed in order to explore the cost of one-year of HIVST provision and explore its impact over a 20-year time horizon for different age groups. Due to a lack of observed data, the model applied assumptions around important parameters such as the proportion of ART initiation after HIV-self test. The model applied the same proportion for ART initiation in the intervention and standard of care arm. One study published the effect of home initiation of HIV cases following HIVST (221), though no other study published the follow-up of home ART initiation to linkage in HIV care at the health facilities. Sensitivity analyses were conducted to mitigate the impact of the assumed parameters.

Moreover, I acknowledge that costs were additive, and the proportions of ART initiation, ART retention, and viral load suppression were applied in a linear manner, where in reality these three cascades in HIV care represent complex behaviors. This study also identified data gaps for ART initiation, ART retention, and viral load suppression post-HIVST. Having these parameters would have improved the accuracy of the model prediction.

5.4. Strength of thesis approach

Combination of cost and cost-effectiveness analysis

The key strength of this thesis is in generating empirical evidence of unit cost using cost analysis and cost-effectiveness estimates using the microsimulation model. The microsimulation model allowed this study to objectively track people in 10 health states due to the complexity of the model parameters. Particularly, variation in HIV testing uptake,

ART initiation, ART retention, and viral load suppression by sex and the three age groups offered a great understanding of complex nuance in order to estimate the impact of HIVST intervention. Paper 3 used our previously published cost data plus new data, and it was the first microsimulation model for HIVST for the Zambian population.

Zambia as a research context

Zambia was chosen as a study site for the STAR project and this study is embedded in STAR's research. Zambia has a very high HIV prevalence, and there is political will from the Zambian MOH to include HIVST in its HIV testing strategic framework and to scale-up HIVST provision. With available funding and social acceptability of HIVST as an additional HTS, the results of this thesis have the potential to reach those who do not test regularly at the health facility. The available ICERs per DALY averted estimates in Paper 3 could inform funders to allocate HIV test resources accordingly.

Generalizability to other settings

The parameterization of the model applied weightings to quantitatively make the results generalizable to the Zambian population. However, the generalizability of these results outside of Zambia may not be possible. As noted in the modelling paper, the parameterization of the model was only done using data from studies done in Zambia. Moreover, the conceptualization of the model structure is grounded in the Zambian healthcare system following the HIV prevention and care cascade. Thus, the structure of the model can be adapted to other countries following the country's HIV testing and treatment guidelines.

A number of studies highlighted that the transfer of economic evaluation estimates to other settings should only be done following the proposed checklists (165-168, 164-167).

5.5. Implications for research

This section lays out the broad research implication of this thesis, along with its generalizability to other settings.

More routine cost-effectiveness analysis

Results from this thesis suggest that future HIV programmes need to incorporate both HIV prevention and HIV care cascades in their programme design and conduct cost-effectiveness analyses. As UNAIDS 90-90-90 targets are approaching, HIV prevention programmes need to target individuals who do not test regularly. Adolescent men and women and men in other

age groups could benefit significantly from the provision of targeted HTS. Additionally, programmes that support HIV care cascade need to do more research to generate accurate data on ART initiation, ART adherence, and viral load suppression. Thus, cost-effectiveness analyses can combine these two cascades and generate complete empirical evidence to optimize HIV response.

5.6. Implications for policy

Prioritizing adolescent men and women

In high HIV burdened countries such as Zambia, the health systems are likely to have limited resources. Thus, it is critical to identify which population could benefit the most from prioritized HVST provision. Although this thesis demonstrated that HIVST is cost-effective for all age groups (i.e. below the $1,430 per DALY averted threshold) for scaling up of HIVST, it could prioritize men and women ages 25-34 and 35-49 years and adolescents second.

This work will also inform national HIV testing services guidelines and policies in multiple ways. First, the findings from this study can inform the government of Zambia about strategies for the next National Strategic Framework on HIV testing services and integrate HIVST as one of the HIV testing options. Moreover, it provided evidence about cost-effective modalities for scaling-up HIVST.

The need for investment for ART initiation and adherence after HIVST

A large number of studies evaluated adherence-enhanced interventions to improve adherence to ART (229). HIVST has the potential to reach undiagnosed HIV positive people. Given the adherence assumptions in Paper 3 of this thesis, I would recommend investment in ART initiation and ART adherence after the provision of HIVST to have a high probability of being cost-effective. Promoting HIVST alone will not generate a long-term impact because it requires enhancing and maintaining complex ART initiation and adherence programmes. Policymakers and funders should work together to facilitate the HIV care system to make it more attractive and as integrated as possible to improve ART initiation and adherence after HIVST.

5.7. Conclusion

HIVST is a promising intervention to reach people who do not test regularly at facility-based HTS. This thesis explored the cost and cost-effectiveness of HIVST. It found that the

provision of HIVST may be cost-effective among all age groups who did not test in the last 12 months. Cost analysis also calculated the unit cost of delivering HIVST using the VMMC and OPD models to increase VMMC uptake and identify new HIV positive people, respectively. This thesis has shown the value of combining systematic literature review, cost analysis, and cost-effectiveness modeling to explore the full potential of HIVST. Further research is needed to assess the rate of ART initiation and adherence after HIVST.

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APPENDIX I: CO-AUTHORED PAPER 1: COSTS OF FACILITY-BASED HIV TESTING IN MALAWI, ZAMBIA, AND ZIMBABWE

This first paper, *Costs of facility-based HIV testing in Malawi, Zambia, and Zimbabwe,* is a cross-country collaboration paper published in *PLOS ONE,* which provided evidence on unit cost per person tested and positive case identified at the standard health facility (standard of care) in these three countries. The Zambian unit cost per person tested was used to parametrizes the model in Chapter 5. This paper is added in Appendix 1 as published, and PLOS ONE permitted this.

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Primary Supervisor	Fern Terris Prestholt		

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RESEARCH ARTICLE

Costs of facility-based HIV testing in Malawi, Zambia and Zimbabwe

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Abstract

Background

Providing HIV testing at health facilities remains the most common approach to ensuring access to HIV treatment and prevention services for the millions of undiagnosed HIV-infected individuals in sub-Saharan Africa. We sought to explore the costs of providing these services across three southern African countries with high HIV burden.

Methods

Primary costing studies were undertaken in 54 health facilities providing HIV testing services (HTS) in Malawi, Zambia and Zimbabwe. Routinely collected monitoring and evaluation data for the health facilities were extracted to estimate the costs per individual tested and costs per HIV-positive individual identified. Costs are presented in 2016 US dollars. Sensitivity analysis explored key drivers of costs.

Results

Health facilities were testing on average 2290 individuals annually, albeit with wide variations. The mean cost per individual tested was US$5.03.9 in Malawi, US$4.24 in Zambia and US $8.79 in Zimbabwe. The mean cost per HIV-positive individual identified was US$79.58, US $73.63 and US$178.92 in Malawi, Zambia and Zimbabwe respectively. Both cost estimates were sensitive to scale of testing, facility staffing levels and the costs of HIV test kits.

Conclusions

Health facility based HIV testing remains an essential service to meet HIV universal access goals. The low costs and potential for economies of scale suggests an opportunity for further

Competing interests: The authors have declared that no competing interests exist.

scale-up. However low uptake in many settings suggests that demand creation or alternative testing models may be needed to achieve economies of scale and reach populations less willing to attend facility based services.

Introduction

Over 35 million people are living with HIV, the majority in sub-Saharan Africa [1]. In particular, HIV prevalence stands at 10.6%, 12.3% and 14.6% among individuals aged 15–64 in Malawi, 15–59 in Zambia and 15–64 in Zimbabwe, respectively [2–5]. Timely initiation of antiretroviral treatment (ART) has the potential to ensure those infected can lead healthy lives, potentially living as long as uninfected individuals in the region [6], and reduces the probability for further sexual and vertical transmission through suppressed viral load [3, 7]. Despite efforts to increase access to ART in the region, millions continue to die [1], while those who do start treatment do so late [8]. Achieving universal and timely access to ART relies on ensuring those who are infected with the virus are aware of their status [9].

In the last decade Southern Africa has seen significant scale up of HIV testing services (HTS). In Zambia, this has led to the proportion of 15-49-year-olds who have tested and received their HIV test result in the previous 12 months increasing from 19% of women and 12% of men in 2007 to 70% of women and 63% of men in 2015 [3]. According to the Malawi Population-Based HIV Impact Assessment (MPHIA), 76% of women and 67% of men aged 15–64 who are living with HIV know their HIV status [10]. In Zimbabwe, 71% of women and 70% of men aged between 15 and 64 who are living with HIV know their HIV status [4]. Conversely, though national statistics group all HTS indicators together, it is known that the scope of HTS has expanded beyond facility based activities [11]. For example community based HTS has been said to increase number of individuals with known HIV status and improve HIV knowledge in general [12–15]. This has mainly been achieved by increasing the availability of health facility-based HTS [16, 17].

Moreover countries have adopted the 2015 World Health Organisation (WHO) guidelines, which recommend immediate ART for all HIV-positive adults and children [18], and are aiming to achieve the UNAIDS 90-90-90 target (i.e. by 2020 90% of all people living with HIV should know their HIV status, 90% of all individuals with diagnosed HIV infection will receive sustained ART, and 90% of all individuals receiving ART will have viral suppression [19]. Clearly meeting these goals requires further scale-up and better targeting of HTS. Understanding the costs of delivering HTS is critical to ensure efficient use of resources and improve planning and budgeting. However, information on HTS costs remains sparse in the region, and where available, estimates show wide variation in costs per person tested ranging from US$5 to US$50 [20, 21].

This paper presents the costs of health provider delivered facility-based HTS in Malawi, Zambia and Zimbabwe and explores cost drivers and economies of scale. In addition, cost estimates presented in this paper will inform the cost-effectiveness analysis of HIVST implementation in the HIV-Self Testing AfRica (STAR) project.

Methods

Setting

In 2016 UNITAID commissioned STAR project to assess the feasibility, acceptability and the potential health impact of distributing HIV self-test kits in Malawi, Zambia and Zimbabwe.

We undertook a cost analysis of facility-based HTS services provided at 54 health facilities serving the STAR study populations in Malawi (15), Zambia (10) and Zimbabwe (29). Health facilities included both primary and secondary care facilities.

In the STAR project community-based distribution of HIVST is being evaluated in Malawi, Zambia and Zimbabwe. In these countries, communities were selected for the purposes of the main implementation evaluation being undertaken. Briefly, communities were selected in collaboration with the countries' Ministry of Health. The selected communities had to be served by a local government health facility providing HIV care, with no alternative HIV care facility nearby. Preference was given to communities with high HIV prevalence. For this costing study, in Malawi and Zimbabwe all health facilities included in the impact evaluation were included while in Zambia 12 facilities were randomly selected. Data collection occurred prior to HIVST implementation.

In Malawi, all 15 facilities were rural primary health clinics located in Blantyre, Machinga, Mwanza and Neno districts. In Zambia, there were two peri-urban and eight rural primary health clinics located in four districts, Ndola, Kapiri Mposhi, Choma and Lusaka. In Zimbabwe, all 29 health facilities evaluated were in rural areas including one mission hospital, one mine hospital, two district government hospitals, and 25 rural primary health clinics. There were between one and six HIV testing staff full-time equivalents (FTEs) working at each health facility in the three countries. For Zambia, unlike Malawi and Zimbabwe, HIV testing staff included a mix of paid and volunteer counselors. Table 1 presents a detailed description of study sites.

At all health facilities individuals may voluntarily attend the health facility to request HIV testing or may be referred to the HTS service because they are unwell, pregnant or have an illness that warrants HIV testing (e.g. Tuberculosis). In all three countries, HIV testing is performed using finger-prick rapid diagnostic test (RDT) kits and follows standard serial testing algorithms where those who test positive on the first RDT undergo confirmatory testing using a different RDT kit [22]. In each of the countries, a different RDT kit is used for the confirmatory testing. For those found to have discordant test results on serial testing are an immediate

Table 1. Sample overview and facility description.

Characteristic	Description	Malawi	Zambia	Zimbabwe
Number of districts	Number of districts	4	3	6
Number of sites	Sample size	15	10	29
Type of facility	Primary health clinic (Hospital)	15 (0)	10 (0)	27 (3)
Population	Mean catchment population at sampled facilities (median; range[$])	27,439 (19,172; 5,500–82,581)	18,266 (15,223; 7673–50,094)	3,196 (3,088; 549–6,699)
Location	Rural (urban/peri-urban)	15 (0)	8 (2)	29 (0)
Personnel	Mean HTS* FTEs[&] per facility (median; range[$])	2 (2; 1–4)	6 (6; 2–10)	5 (4; 2–11)
	Mean HTS FTEs per 10,000 population (median, Range)	16 (13; 5–35)	31 (31; 13–53)	68 (52; 24–184)
	Mean Paid counsellors per facility (median; range[$])	2 (2; 1–4)	1 (1; 0–5)	5 (4; 2–11)
	Mean Volunteers per facility (median; range[$])	-	4 (4; 2–7)	-
National HIV prevalence (%) [2–5]	Adults 15 to 49 years	9.1	12.3	14.6

FTE = Full time Equivalent.

[&]HTS = HIV testing services.

[$]Range is presented in terms of minimum—maximum.

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parallel repeat test is done on both testing is done on both tests. For those found to have discordant test results on serial testing an immediate parallel repeat test is done. If both test 1 and test 2 are reactive results are reported positive; if both are non-reactive, results are reported negative. If the results from parallel testing are discordant, clients are advised to repeat HIV test after 4 weeks in Malawi and 14 days in Zambia and Zimbabwe. All those who test HIV-negative are advised to re-test in three months. A detailed description of the national HIV testing algorithms in the three countries is provided in the Supplemental figures S1–S3 Figs. HTS department is a unit in the facility with a physical space where all HTS data within the facility are aggregated. HIV testing is done by trained counselors, either employed or volunteers, at the facility. Counselors may also be placed in different locations within the facility (e.g. Antenatal clinic) to perform HIV testing.

Cost data collection

The study was undertaken from the health providers' perspective to estimate the costs of routine provider delivered facility-based HTS and understand key determinants of these costs. Full annual financial and economic costs were estimated. Financial costs represent all expenditures for resources used in the intervention, while economic costs capture the full value of all resources used, including valuation of donated goods or services, here the opportunity cost of volunteer counsellors' time [23]. Volunteer time was valued as a product of the number of hours that volunteers spent on doing HTS activities and the average stipend rate which non-government organizations (NGOs) pay volunteers for providing similar activities in Zambia. Annual resource use data were sequentially and retrospectively collected with end dates rolling between June 2016 and April 2017, depending on the date of the data collection visit. Costs were adjusted to 2016 United States dollars (US$) using the average exchange rates, ZMK722.99 for Malawi, ZMW10.03 for Zambia and US$1 for Zimbabwe, over the period of the costing [24] and deflators [25].

Standardised costing methods were developed collaboratively by economists across the three countries to ensure consistency of data collection and analysis. We employed both ingredients based (bottom up) costing and top-down costing where we apportioned costs stepwise to their respective cost centers [10, 26]. Types, quantities and unit costs of cost items were collected through interviews, expenditure and outcome review at facility and district levels. Where unit costs were not present in the expenditure records, market prices were used. See S1 Table for details of the allocation of each cost item. Capital costs included: buildings, equipment and vehicles whilst recurrent costs captured personnel, HIV testing commodities, general supplies, facility level operations including transportation and waste management. Capital costs were annualised and discounted at a 3% rate in accordance with WHO guidelines [27]. Overhead costs were considered at two levels; facility overhead which included all the costs that are needed to ensure the overall running of the facility, and HTS centre-specific costs, which are the costs of running the HTS department where HIV-related activities are conducted. Due to difference in financial reporting system across the three countries overhead costs were allocated differently in each country, particularly costs related to health systems management (Above-facility administration, supervision & mentorship) and facility administration. Supply chain costs were apportioned using allocation factors from literature [28]. See supplemental table S1 Table for details.

Outputs and allocation factor data collection

Alongside cost data collection we collected data on the catchment population, number of outpatient department (OPD) visits, number of staff, number of HTS visits and number of HIV-

positive results, through reviewing facility registers. Data sources were facility registers and heath information aggregation forms. These data were also used in the allocation of overhead and shared costs.

Data analysis

Total annual costs of running HTS at each facility and the respective unit costs were estimated by dividing the total facility costs by the annual number of people tested and the number of HIV-positive individuals identified. Descriptive statistical analysis was performed to calculate mean and median (with the minimum and maximum ranges) for unit costs per HIV test and HIV-positive identified for each country. To explore potential drivers of costs descriptively, Pearson correlations were calculated. A univariate sensitivity analysis was undertaken to understand the impact of HIV test kit price and staff time on the unit costs. The impact of price on unit costs was explored by applying the lowest and highest observed test kit prices across the three countries. The impact of staffing was explored by considering variation in staffing in a +/-20% range to; (a) cope with increased testing demand; (b) explore impact of introduction of community-based HIV testing or HIV self-testing requiring fewer facility based counsellors. We also assessed the impact of the size of facility on the unit costs in Zimbabwe, where the costing sample included both clinics and hospitals. All facilities from Malawi and Zambia were clinics; we only had a clinic-hospital mix in Zimbabwe (3 rural hospitals out of 29 facilities). In our analysis facility size is defined by the catchment population and HTS department by the number of annual HTS visits.

Ethics

Ethical approvals for the project were secured from the appropriate research review boards. This included the London School of Hygiene and Tropical Medicine (LSHTM) Ethics Committee, Malawi National Health Sciences Research Committee, University of Zambia Biomedical Research Ethics Committee, Medical Research Council of Zimbabwe (MRCZ) and University College London Ethics Committee. The STAR trials are registered under the Clinical Trials Network (ClinicalTrials.gov) under registration numbers NCT02793804; NCT02718274; Pan African clinical trials registry (Zimbabwe) PACTR201607001701788.

Results

HTS output summary

The mean number of HIV tests conducted per clinic during the 12-month costing period was 2,359 with 3,404, 3,161 and 1,542 in Malawi, Zambia and Zimbabwe, respectively (Table 2). The mean HIV prevalence amongst those who accessed HIV testing at the health facilities was 7% (9% for Malawi, 9% for Zambia, and 6% for Zimbabwe). While the annual number of HTS visits was significantly associated with the size of the health facility catchment population when pooling across the three countries ($R^2 = 0.53$, N = 53, P<0.000), when estimated at the country level the correlation only remained significant in Malawi (($R^2 = 0.55$, N = 15, P<0.002) and Zambia ($R^2 = 0.76$, N = 10, P = 0.001) but no longer in Zimbabwe ($R^2 = 0.030$, N = 28, P<0.379).

Fig 1 shows the number of HTS visits each month for all the health facilities sampled in the three countries. In Malawi, the majority of the health facilities appears to have experienced gradual increases in number of HTS visits over the study period. In Zambia, the number of HTS visits every month appears relatively constant over the year, with two clinics experiencing

Table 2. Test kit prices and average (mean; median) annual facility HTS outputs.

	Malawi	Zambia	Zimbabwe
Test kit price[&] First	Determine $1.00 Unigold $1.00	Determine $1.00-$1.20 Unigold $1.60	Determine $1.07 First response $0.71
HIV tests	3404 (3461; 835–7953)	2789 (2338; 852–6957)	1542 (1132; 368–5735)
HIV+ identified (median; range*)	304 (230;25–950)	251; (120; 48–907)	93; (63; 12–409)
Facility HIV+ reactivity rate	9% (8%; 3%-16%)	9% (7%; 2%-16%)	6% (6%; (1%-14%)

*Range is presented in terms of minimum—maximum

[&]Test kit prices were derived from national laboratory and medical supplies procurement catalogues from each country complimented by discussion with key stakeholder

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a peak in visits in July and August. In Zimbabwe, many of the health facilities experienced significant fluctuation in monthly HTS visits.

The mean annual number of HIV testing episodes per HTS staff FTE was 1132 (519–2075) in Malawi, 597 (238–1257) in Zambia and 895 (237–2285) in Zimbabwe. Country-level analysis did show the number of HTS staff was strongly correlated with the size of the facility catchment population in Zambia, though not in Malawi and Zimbabwe. Cross-country analysis shows that there was no significant relationship between the number of HIV counsellors employed at each health facility and the facility catchment population ($R^2 = 0.01$, N = 53, P = 0.4039). At country-level, the results showed that the correlation was significant in Zambia, but not in Malawi and Zimbabwe. Overall, there was no correlation between the number of HIV counsellors employed and the number of HIV testing episodes ($R^2 = 0.01$, N = 54, P = 0.53).

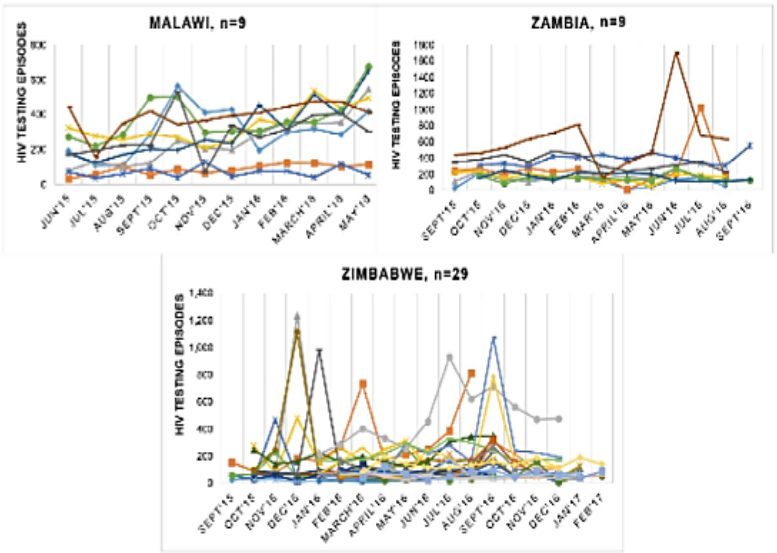

Fig 1. Monthly HTS visits by facility*. *monthly service statistics were not available for all clinics.

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Table 3. Total and mean economic costs (minimum-maximum).

Cost item	Malawi (US$)			Zambia (US$)			Zimbabwe (US$)		
	Total annual costs	Cost per test performed	Cost per HIV+	Total annual costs	Cost per test performed	Cost per HIV+	Total annual costs	Cost per test performed	Cost per HIV+
Capital costs									
Buildings and storage	347 (54–777)	0.13 (0.01–0.28)	1.9 (0.34–7.52)	133 (59–254)	0.07 (0.02–0.21)	0.97 (0.17–1.87)	190 (32–514)	0.22 (0.01–1.40)	4.62 (0.44–24.47)
Equipment	169 (57–300)	0.08 (0.01–0.28)	1.43 (0.12–8.70)	160 (41–391)	0.1 (0.01–0.46)	1.44 (0.06–3.35)	108 (38–304)	0.11 (0.01–0.45)	2.36 (0.15–11.16)
Vehicles	-	-	-	91 (21–249)	0.06 (0.01–0.26)	0.69 (0.04–1.86)	22 (0–633)	0.01 (0.00–18)	0.06 (0.00–1.77)
Other	-	-	-	43 (29–61)	0.02 (0.01–0.05)	0.39 (0.04–1.24)	-	-	-
Total capital cost	*517 (162–938)*	*0.2 (0.04–0.51)*	*3.33 (0.61–16.22)*	*428 (211–844)*	*0.24 (0.05–1.00)*	*3.49 (0.32–697)*	*320 (72–1,095)*	*0.33 (0.03–1.85)*	*7.04 (0.66–32.36)*
Recurrent costs		-	-						
Personnel	8,375 (2,893–13,828)	2.97 (1.35–6.00)	46.57 (13.05–115.72)	6,678 (1,373–32,665)	2.05 (0.51–4.70)	36.83 (5.82–115.76)	7,670 (3,141–34,398)	6.69 (1.85–118.88)	131 (26.36–313)
Supplies—test kits	3,713 (912–9,064)	1.19 (1.13–1.26)	19.16 (8.51–41.58)	3421 (1,128–8,692)	1.22 (1.14–1.35)	21.34 (8.21–46.39)	1826 (439–6,747)	1.2 (1.12–1.29)	28.71 (9.39–84.61)
Supplies	1,231 (783–1,632)	0.46 (0.79–1.09)	7.83 (1.22–31.32)	450 (163–596)	0.21 (0.08–0.58)	3.32 (0.62–5.95)	441 (130–2,032)	0.38 (0.09–2.9)	7.82 (1.61–31.27)
Supply chain	111 (70–147)	0.04 (0.01–0.10)	0.7 (0.11–2.82)	307 (101–779)	0.11 (0.10–00.12)	1.91 (0.76–4.16)	203 (63–676)	0.14 (0.03–0.34)	3.22 (0.41–9.26)
Operation & maintenance	393 (67–1325)	0.36 (0.06–1.22)	3.64 (0.62–12.27)	751 (210–1,427)	0.42 (0.05–1.14)	6.85 (0.32–13.71	56 (0.00–682)	0.1 (0.00–01.15)	0.7 (0.00–8.42)
Recurrent training	-	-	-	-	-	-	-	-	-
Waste management	31 (2–136)	0.01 (0.00–0.05)	0.24 (0.01–1.46)	2 (1–4)	-	0.02 (0.00–0.07)	2.01 (0.38–7.32)	-	0.06 (0.00–0.43)
Total recurrent costs	*14304 (4,4981–24228)*	*4.85 (2.96–890)*	*76.24 (25.50–199.22)*	*11,609 (4,440–43,071)*	*4 (2.34–6.19)*	*70 (16.30–184.39)*	*10198 (4198–4162)*	*8.46 (3.33–20.68)*	*171.88 (41-97-426.05)*
Total cost / unit cost	**14,822 (5,386–25,124)**	**4.92 (2.95–8.33)**	**79.58 (26.45–215.44)**	**11,652 (4,486–43,106)**	**4.24 (2.49–6.24)**	**73.63 (16.62–191.35)**	**10,517 (4,476–38,514)**	**8.79 (3.38–21.51)**	**178.92 (43.81–442.43)**

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Total HTS costs

S2 Table presents resource utilization for key recurrent supplies. The total annual economic costs for the health facilities sampled in the three countries are shown in Table 3, financial costs are presented in Supplemental Table S3 Table. The median total annual costs were US $14,822 (range: US$5,386-US$25,124) for Malawi, US$8,797 (range: US$4,486-US$43,106) for Zambia and US$8,774 (range: US$4,476-US$38,514) for Zimbabwe. In the three countries,

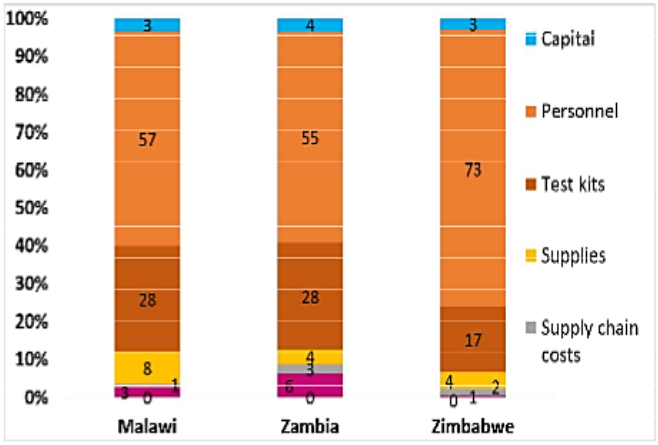

Fig 2. Input shares by country (%).

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salaries for personnel accounted for 57%, 55% and 73% of the total annual cost in Malawi, Zambia and Zimbabwe, respectively (Fig 2). The variation in costs across the countries was significantly correlated with variation in staffing levels ($P = 0.04$ for Malawi, $P = 0.04$ for Zambia, and $P<0.01$ for Zimbabwe); some facilities relied heavily on volunteer/ lay providers (mainly in Zambia) whereas others tended to employ highly trained and paid staff. The cost of the HIV RDT kit and supplies accounted for 28% in Malawi, 28% in Zambia and 17% in Zimbabwe of the total annual cost. Capital costs accounted for approximately 4% of the total annual cost for Zambia, and 3% for Malawi and Zimbabwe.

Unit costs

The median costs per individual tested for HIV in Malawi, Zambia and Zimbabwe were US $4.56, US$3.96, US$6.25, respectively. The median cost per HIV-positive individual identified were US$58.044 for Malawi, US$54.33 for Zambia and US$141.67 for Zimbabwe. Average unit costs are reported in Table 3.

To identify the presence of economies of scale, Fig 3 shows the cost per individual tested and cost per HIV-positive individual identified by the annual number of HIV testing episodes performed at the health facility and the annual number of HIV-positive individuals identified at each of the health facilities, respectively. The cost per individual tested for HIV was lower at health facilities that were testing more individuals. Likewise, the cost per HIV-positive individual identified was lower at health facilities that were identifying more HIV-positive individuals.

Sensitivity analysis

When varied the prices of HIV test kits from the observed prices for each country (base prices) to the observed minimum price (US$1.00 for Determine in Malawi and US$0.71 in Zimbabwe, both the mean cost per individual tested for HIV and mean cost per HIV-positive individual identified changed by 13% for Malawi, 11% for Zambia and 18% for Zimbabwe. When test kit prices were set at the observed maximum prices (US$1.10 for Determine and US$1.60 for Uni-Gold in Zambia), the mean cost per individual tested for HIV changed by 11% for Malawi, 9%

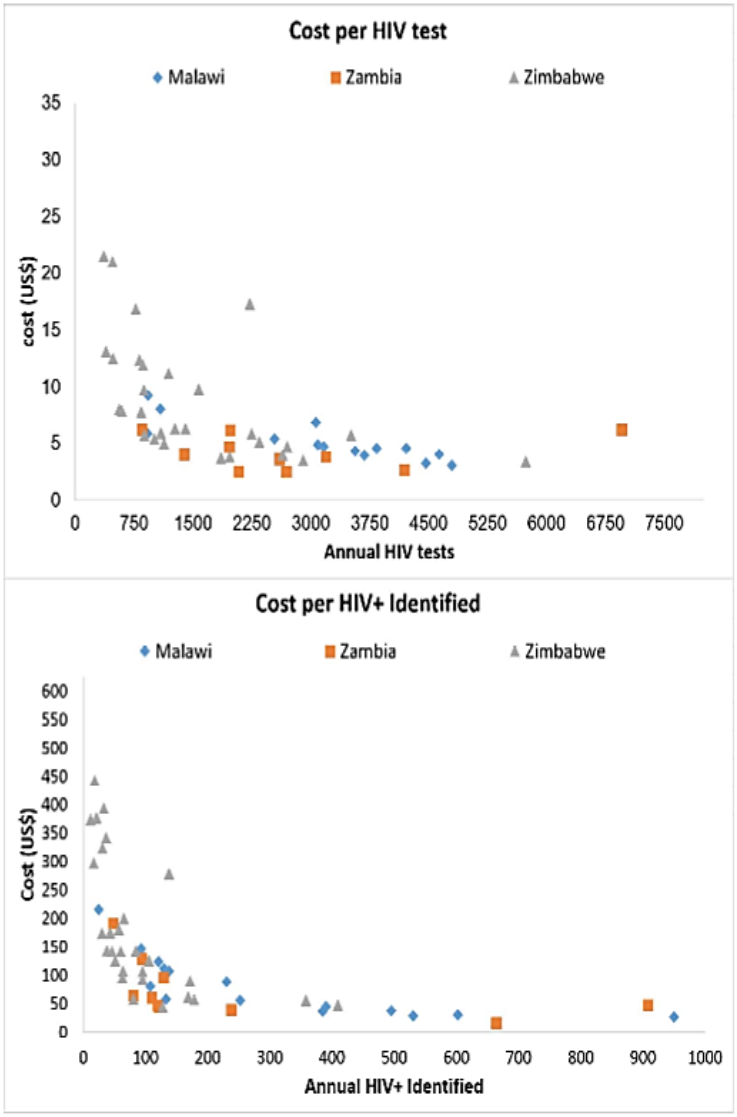

Fig 3. Economies of scale.

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for Zambia and 13% for Zimbabwe. The mean cost per HIV-positive individual identified changed increased by the same magnitude for each country.

When we set personnel costs were set at 20% lower than actually observed, both the mean cost per individual tested for HIV and mean cost per HIV-positive individual identified reduced by 13% for Malawi, 11% for Zambia and 18% for Zimbabwe. When personnel costs were 20% higher than that observed, the mean cost per individual tested for HIV increased by

Table 4. Sensitivity analysis results.

Parameter	Malawi (US$)		Zambia (US$)		Zimbabwe (US$)	
	Per HIV test	Per HIV+	Per HIV test	Per HIV+	Per HIV test	Per HIV+
Base case	5.05	79.58	4.24	73.63	8.79	178.92
HIV Test kit Prices						
Observed low prices (Determine = US$0.87; UniGold = US$0.71)	5.02	75.93	3.88	67.44	8.70	176.91
Observed Higher prices (Determine = US$1.10; UniGold = US$1.60)	5.22	82.05	4.24	73.63	8.93	181.88
Personnel costs						
20% reduction	4.45	70.27	3.83	66.26	7.45	152.68
20% increase	5.64	88.90	4.65	80.99	10.13	205.25

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11% for Malawi, 9% for Zambia and 13% for Zimbabwe. The mean cost per HIV-positive individual identified increased by 10% for Malawi, 9% for Zambia and 13% for Zimbabwe. Only Zimbabwe included hospitals in the costing. When these were excluded, mean cost per individual tested for HIV ranged from US$8.79 to US$7.65, and mean cost per HIV-positive individual identified dropped from US$178.92 to US$150.40. Table 4 shows details of outcomes from sensitivity analysis.

Discussion

Health facility-based HIV testing remains the most common approach for individuals to learn their HIV status. Ensuring that 90% of all people living with HIV in sub-Saharan Africa know their HIV status by 2020 may require further scale-up of facility-based HTS. We found that the costs of delivering these HTS services in three southern African countries could be as low as US$3 per individual tested, especially in health facilities that were seeing a larger number of individuals.

The mean provider costs of facility-based HTS were similar in Malawi and Zambia and higher in Zimbabwe, ranging from US$4.24 to US$8.79 per person tested. Our findings are

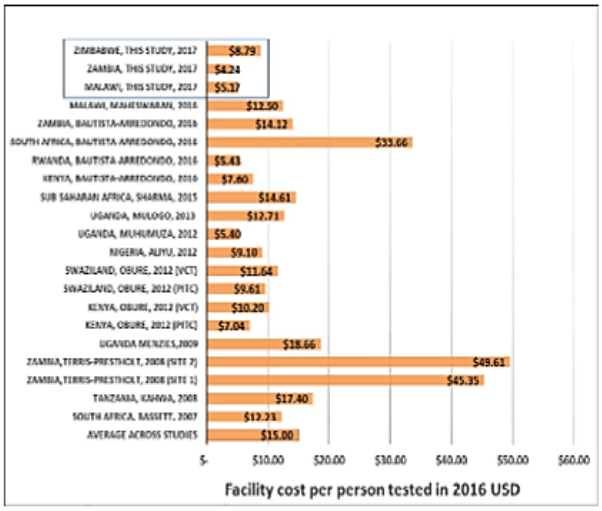

Fig 4. Comparison of cost per person tested for HIV in health facility in sub-Saharan Africa.

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fairly consistent with previous studies that estimated costs to test for and identify individuals with HIV at health facilities in the region (Fig 4) [29–39]. A facility-based costing study conducted in Malawi in 2014, with capital, overhead, staff salaries, consumables and equipment costs reported in 2014 prices, showed a higher cost of US$12.50 per person tested when adjusted to 2016 prices [40]. Notably, this estimate included costs of staff training, and service monitoring and evaluation, which was not observed in our study.

Previous studies in Zambia and South Africa, conducted between 2011 and 2012 with costs reported in 2013, estimated costs of US$14.12 and US$33.66 per person tested (in 2016 prices), respectively. Staff salaries were the main cost driver in South Africa [31]. The average economic costs were also estimated in 2009 for Kenya and Swaziland, with costs per person tested ranging from US$10.20 to US$11.64 for voluntary counselling and testing (VCT), and US$7.04 to US$9.61 (in 2016 prices) for provider initiated testing and counselling (PITC) [37]. These recent studies show large decreases as compared to cost estimates from the early years of HTS introduction (2001), costs reported in 2007, of which US$49.61 and US$45.35 (in 2016 prices) are reported costs per person tested [39]. It is important to note that, during early years of HTS introduction, HTS were delivered at high costs. HTS delivery was also surrounded by a lot of challenges (e.g. stigma, lack of confidentiality, fewer testing facilities) which required a lot of effort to create user demand [41–43]. Common across facility costing studies of HTS are the large contribution of human resources, training, test kits and consumables as drivers of costs.

We found considerable variation in cost estimates within and between countries and over time as the approach to and intensity of HTS evolved. Unit costs were especially low in larger health facilities that were seeing more individuals. These facilities often also provided a broader range of services. This suggests potential economies of scale, where inputs are more efficiently used due to fixed costs being spread across more outputs, and/or economies of scope, where fixed costs are spread across more services, both leading to lower unit costs. We did not find a strong relationship with the number of HIV counsellors working at the health facility and the number of individuals undergoing HIV testing. It is possible health facilities with greater numbers of HIV counselors are seeing fewer individuals for HIV testing during the time period of this study because past HIV testing was high and therefore fewer individuals in the community are unaware of their current HIV status. Conversely it is also possible that the demand for HIV testing amongst those served by these better staffed facilities, or the size of the facilities' catchment population are low. However, the findings suggests that existing HTS in health facilities could be seeing more individuals for HIV testing without needing additional resources except the consumables needed to perform the HIV test. We found that the monthly number of HTS episodes at health facilities in Malawi gradually increased over the study period. This may reflect the recent introduction of test and treat, where HIV treatment is initiated immediately upon an HIV-positive test result [18]. Conversely, we found major fluctuation in the monthly number of HTS episodes at health facilities in Zimbabwe. This could be due to supply issues, e.g. HIV test kit stock outs. Alternatively, demand side variation, for example anecdotal evidence suggests peaks in rural HTS around the Christmas period and subject to weather conditions, that may universally affect people presenting for HTS.

Observed cost variation across countries and facilities presents a room for HTS innovations as well as an opportunity to assess the additional resources and approaches needed to achieve the UNAIDS 90-90-90 targets. For example, engaging communities through outreach programmes may complement facility-based HIV testing in settings with low demand [44]. Personnel costs accounted for a significant component of the total provider costs of facility-based HTS. There have been suggestions that the counselling process could be optimised [45], enabling counsellors to see more individuals or facilities to be staffed by fewer personnel. Alternatively, providing HIVST kits to health facility attendees, allowing them to perform and

interpret their own test result, potentially in the privacy of their own homes or within private areas within facilities and discuss their results with healthcare providers. This approach could also reduce personnel needs at facilities or allow busy health facilities to meet HTS demand. HIVST has the additional benefit of high acceptability especially amongst men [46]. However, recognition of other potential bottle necks should be considered weighing the benefits of introducing new technological innovations because low output may also be caused by supply challenges such as stock-outs, which new test technology may or may not alleviate.

The cost per HIV-positive individual identified in our study ranged from as low as US$17 to as high as US$442. HIV testing and anti-retroviral treatment (ART) has been available in these three countries for over a decade, with recent estimates suggesting more than half of people living with HIV (PLHV) in the region are receiving treatment [1]. As there are fewer and fewer numbers of PLHV unaware of the infection, the cost per HIV-positive individual identified by HTS will continue to increase over time. In order to achieve the UNAIDS 90-90-90 targets this cost estimate should not inform decisions to fund or not fund HTS services, but may still provide useful insight into which HTS services are effective. It is important to note that we found approximately one in ten attendees of facility-based HTS in these three southern African countries to be HIV-positive. This confirms the fact that the three countries have made tremendous progress towards the 1st 90 of the USIAD 90-90-90 target [3, 4, 10], leading to having most of the people with known HIV status, and the remaining population comprising of 'hard-to-reach people who may not want to test. Our study shows similar HIV reactivity rate (6–8%) across the three countries despite having quite different national HIV prevalence. This could be attributed to the fact that most of our facilities were rural with low population density and more importantly HIV prevention and treatment activities are widely provided in these communities with notable impact [3, 4, 10]. Health facilities continue to provide an important route for individuals to learn their HIV status.

A major limitation of our findings is the different financial reporting systems used in the three countries that made it challenging to standardise the allocation of central overhead costs. Another challenge in our data collection was that, as in other similar studies, we faced poor record keeping in the facilities; missing information and inconsistency in financial reporting across facilities. Additionally, by not including costs borne by patients and their carers for accessing testing, this does not give a true reflection of the economic burden of HIV testing. Measurement of patients' costs can be essential for social planning as it gives insight into costs borne by individuals, households and society as a whole and can identify barriers to accessing HIV testing. However, an analysis of patient costs of accessing HTS in the same setting is underway. Thus, future research should consider direct and indirect costs of treatment from, at least, the provider and patient perspective as well as the long-term disability due to illness. This perspective can complement the provider's perspective taken in this study.

Facility-based HIV testing services remains an effective approach to identifying undiagnosed HIV-positive individuals and can be an affordable approach to reaching the first 90. There are potential opportunities to improve their efficiency, which would need to be complemented by approaches to address demand side constraints to have a beneficial impact.

Supporting information

S1 Fig. Malawian HIV testing algorithm.
(TIF)

S2 Fig. Zambian HIV testing algorithm.
(TIF)

S3 Fig. Zimbabwe HIV testing algorithm for children above 18 months, adolescents and adults.
(TIF)

S1 Table. Cost allocation factors.
(DOCX)

S2 Table. Resource utilization of key HTS key supplies.
(DOCX)

S3 Table. Financial cost: Mean (min-max).
(DOCX)

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APPENDIX II: CO-AUTHORED PAPER 2 – ECONOMIC COST ANALYSIS OF DOOR-TO-DOOR COMMUNITY-BASED DISTRIBUTION OF HIV SELF-TEST KITS IN MALAWI, ZAMBIA, AND ZIMBABWE

This second paper, *Economic cost analysis of door-to-door community-based distribution of HIV self-test kits in Malawi, Zambia, and Zimbabwe*, is also a cross-country collaboration paper published in *Journal of the International AIDS Society*, which provided evidence on unit cost per HIVST kits distributed using door-to-door distribution modality. The Zambian unit cost for HIVST kit distribution was used to parametrize the model in Chapter 5. This paper is added in Appendix 2 as published and *JIAS* permitted this.

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Primary Supervisor	Fern Terris Prestholt		

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RESEARCH ARTICLE

Economic cost analysis of door-to-door community-based distribution of HIV self-test kits in Malawi, Zambia and Zimbabwe

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Abstract

Introduction: HIV self-testing (HIVST) is recommended by the World Health Organization in addition to other testing modalities to increase uptake of HIV testing, particularly among harder-to-reach populations. This study provides the first empirical evidence of the costs of door-to-door community-based HIVST distribution in Malawi, Zambia and Zimbabwe.

Methods: HIVST kits were distributed door-to-door in 71 sites across Malawi, Zambia and Zimbabwe from June 2016 to May 2017. Programme expenditures, supplemented by on-site observation and monitoring and evaluation data were used to estimate total economic and unit costs of HIVST distribution, by input and site. Inputs were categorized into start-up, capital and recurrent costs. Sensitivity and scenario analyses were performed to assess the impact of key parameters on unit costs.

Results: In total, 152,671, 103,589 and 93,459 HIVST kits were distributed in Malawi, Zambia and Zimbabwe over 12, 11 and 10 months respectively. Across these countries, 43% to 51% of HIVST kits were distributed to men. The average cost per HIVST kit distributed was US$8.15, US$16.42 and US$13.84 in Malawi, Zambia and Zimbabwe, respectively, with pronounced intersite variation within countries driven largely by site-level fixed costs. Site-level recurrent costs were 70% to 92% of full costs and 20% to 62% higher than routine HIV testing services (HTS) costs. Personnel costs contributed from 26% to 52% of total costs across countries reflecting differences in remuneration approaches and country GDP.

Conclusions: These early door-to-door community HIVST distribution programmes show large potential, both for reaching untested populations and for substantial economies of scale as HIVST programmes scale-up and mature. From a societal perspective, the costs of HIVST appear similar to conventional HTS, with the higher providers' costs substantially offsetting user costs. Future approaches to minimizing cost and/or maximize testing coverage could include unpaid door-to-door community-led distribution to reach end-users and integrating HIVST into routine clinical services via direct or secondary distribution strategies with lower fixed costs.

Keywords: HIV self-testing; costs and cost analysis; community; Malawi; Zambia; Zimbabwe

Additional Supporting Information may be found online in the Supporting information tab for this article.

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1 | INTRODUCTION

In East and Southern Africa, freely available HIV services have led to a 42% reduction in AIDS-related deaths between 2010 and 2016. Despite such gains, 24% of people living with HIV (PLWH) remain undiagnosed [1]. UNAIDS has set global targets for 90% of PLWH to know their status, 90% of known HIV-positive individuals, to be on ART and 90% of those on antiretroviral therapy (ART) to have their viral load suppressed by 2020 [2]. To surpass and sustain high levels of awareness of HIV status, greater efforts are needed to ensure that HIV testing reaches those individuals who have not yet been tested for HIV. This, however, is likely to require more significant financial investments, innovative approaches and new technologies, including HIV self-testing (HIVST).

HIVST is defined as a process where a person collects his/her own specimen (oral fluid or blood) and then performs an HIV test and interprets the result, often in a private setting,

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Table 1. Key setting characteristics

	Malawi	Zambia	Zimbabwe	Source
National HIV prevalence among adults 15 to 59 years (%)	10.0	12.0	14.6	[8–10]
Number of districts	4	4	8	[11]
Number of sites	11	16	44	[11]
Catchment population of sites: mean (range)	27,439 (5500 to 82,581)	18,266 (7673 to 50,094)	3196 (549 to 6699)	[11]
Location: rural (urban or peri-urban)	11 (0)	16 (8)	44 (0)	[11]
Scale of current HTS – based on facility HTS in same communities and period	16,921	27,888	44,727	[16]
Men attendance at HTS – based on facility HTS – % men	34	37	26	[8–10]
Health facility HTS cost per person tested in US$: mean (range)	$5.03 ($2.96 to $9.24)	$4.24 ($2.49 to $6.24)	$8.79 ($3.38 to $21.51)	[16]

HTS, HIV testing services.

either alone or with someone they trust. The World Health Organization recommends HIVST to reach the "at risk" and "untested" populations including men as a complement to current conventional testing approaches, including facility-based and targeted community outreach-based testing [1,3-5]. The cost of HIVST kits has declined in some settings, with the OraQuick® HIV self-test now costing US$2 per kit in 50 low- and middle-income countries [6]. However, at US$2, it is around twice the price of standard HIV rapid diagnostic tests currently used for HIV testing in Africa [7]. Although HIVST kit price may be higher, impact analyses show that it can have an important public health benefit and offer value for money if implemented as a complement to current testing approaches [4,5].

The HIV Self-Testing AfRica (STAR) project has delivered over one million HIVST kits in Malawi, Zambia and Zimbabwe between 2016 and 2017 through a combination of distribution approaches, including facility-based distribution at outpatient departments, within voluntary medical male circumcision (VMMC) services and in the community. This study presents the costs of the model that uses community-based distribution agents (CBDAs) to deliver HIVST either at people's homes or within the community setting, hereafter "the CBDA model," to generate evidence to inform the scale-up of cost-effective HIV testing services (HTS).

2 | METHODS

2.1 | Setting, intervention and evaluation

Table 1 presents key setting characteristics across countries. In short, the adult HIV prevalence rates in Malawi, Zambia and Zimbabwe were approximately 10.0%, 12.0% and 14.6% respectively [8-10]. While Malawi and Zimbabwe CBDA model sites were exclusively rural, a third of Zambia sites were peri-urban or urban. Malawian and Zambian distribution sites were fewer and each served large populations, while Zimbabwe delivered kits to a larger number of smaller communities. This difference in site size is also reflected in the unit costs of conventional facility-based testing, with higher costs in the smaller facilities in Zimbabwe. It is also notable that men contribute only 26% to 37% of HTS clients in these facilities.

In the CBDA model, all individuals aged ≥16 years who were present in the homestead at the time of CBDAs' home visit were eligible for self-testing. Testing was done by the self-tester themselves after kit use demonstration and information on test result interpretation and linkage to follow-on care by the CBDAs. CBDAs provided a self-referral card to all testers to facilitate linkage to the local health facility for confirmatory testing and care for individuals with reactive HIVST results. In some cases, CBDAs were present during the self-test to provide reassurance and support if testers requested their presence or assistance. Table 2 presents the characteristics of the CBDA model implemented across countries. Narrative descriptions of the models can be found in Data S1. The impact of the CBDA model on uptake of HIV testing and ART is being evaluated in three cluster-randomized trials (CRTs). Detailed methodology of these CRTs is published elsewhere [11].

2.2 | Costing methods

We estimated the full economic cost of delivering HIVST within the CBDA model from the providers perspective, following international costing guidelines [12]. This included start-up and training costs, prior to the first HIVST kit distributed. Annual costs were estimated, with implementation costs collected between June 2016 and May 2017, depending on country implementation timelines. Start-up, training and all other capital costs were annualized using a 3% discount rate. All costs were converted to 2017 US dollars using average annual exchange rates and the dollar inflation rate [13-15].

This top-down costing collated all financial expenditures and categorized each line item by input type and distribution model. Inputs were allocated to distribution sites following predefined allocation factors, based on project monitoring and evaluation (M&E) data, including the percentage of kits distributed, percentage of distributors based in each site, distance from central office and percentage of direct expenditures, which is a weighted average of the preceding

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Table 2. Overview of door-to-door community-based HIVST delivery models

	Malawi	Zambia	Zimbabwe
Type of cadre used for distribution of HIVST kits	• Trained CBDAs • Some with prior experience distributing other reproductive health products for PSI	• Trained facility and CBDAs • Recruited from communities with prior links to respective health facilities	• Trained CBDAs • Information on HIVST and linkage to post-test services
Mode of distribution	• Door-to-door community-based distribution • PSI field teams-maintained stocks	• Door-to-door distribution by CBDA's within communities and households • Facility-based distributors-maintained stocks for CBDAs	• Campaign-style door-to-door community distribution to households for four to six weeks • PSI field teams-maintained stocks
Services offered to HIV self-test clients	• Introduction and demonstration of HIVST kit use (including interpretation of results) • CBDAs typically revisited clients a few days after dropping off the kit to: o enquire whether it had been used, o pick up the used kit o disclosed non-reactive HIVST: referral to VMMC o disclosed reactive HIVST: referral to linkage to HIV care	• Introduction and demonstration of HIVST kit use (including interpretation of results) • CBDAs typically revisited clients a few days after dropping off the kit to: o enquire whether it had been used o pick up the used kit o disclosed non-reactive HIVST: referral to VMMC o disclosed reactive HIVST: referral to linkage to HIV care	• Introduction and demonstration of HIVST kit use (including interpretation of results) • Follow-on services by PSI-Zimbabwe mobile outreach teams at one to two weeks post HIVST kit distribution o confirmatory HTS plus o family planning o blood pressure checks and CD4 count when available o clients alerted to linkages to government health facilities
Used HIVST kit returns	• Specially designed and locked drop-boxes to return used self-test kits located: o at all intervention sites	• Specially designed and locked drop-boxes were used to return used self-test kits, located: o at each facility and o local community public areas	• Specially designed and locked drop-boxes, located: o at CBDA's homestead o each health facility o local community public areas
CBDA reimbursement	• Per HIVST kit distributed US$0.15 (MWK 100)	• Monthly US$78 (ZMW 750) independent of performance.Later changed to: • Per HIVST distributed US$0.52 (ZMW 5) and per used HIVST kit returned US$0.21 (ZMW 2)	• Per ward campaign (four to six weeks) US$50 with a maximum of 100 kits per distributor • Per HIVST client linking to any PSI outreach service: $0.20 in half of the evaluation clusters

HIVST, HIV self-testing; CBDA, community-based distribution agent; PSI, Population Services International; MWK, Malawi Kwacha; ZMW, Zambian Kwacha.

allocation factors. Table S1 presents how each allocation factor was applied to input type. Further detail of the definitions of project phase and inputs can be found in Data S2.

To estimate economic costs, the expenditure analysis was complemented by a valuation of all other resources used in the CBDA model. Observations of distribution in each site strengthened the economists' understanding of the intervention and allowed for collection of data on donated goods and services. As a vertical model, these were relatively limited, and include a value for district or health facility storage contributed by the public health system. During the life of the project, the price of HIVST kits dropped from nearly $4 per kit to $2 per kit. The latter was imputed in place of the higher observed prices as it was considered the relevant kit price for any decision-making building upon this analysis. Total costs, total kits distributed and average cost per kit distributed were estimated at the country level, and for each country, at the site level. The latter provides a range of average costs by site and allows for identification of economies of scale.

2.3 | Sensitivity analysis

We undertook a series of one-way sensitivity analyses to assess the impact of key cost assumptions on the unit cost

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per HIVST kit distributed. We varied the discount rate used to annualize costs from the base case of 3% to 0% and 15% to capture the impact of not discounting or using a higher local central bank discount rate. Prevailing discount rates during the study period were 15% in Malawi, 12.5% in Zambia and 7% in Zimbabwe [13-15]. We further evaluated the impact of applying alternative allocation factors that is swapping % of kits distributed and % of CBDAs per site. We varied annualization (economic life years) time frames: training & sensitization was varied between one and three years (base case is two years) and project start-up life between 2.5 and 7.5 years (base case is five years) to assess impact if the project goes on for shorter or longer than assumed.

2.4 | Scenario analysis

In anticipation of planned programme scale-up by respective country ministries of health, we conducted scenario analysis varying salaries ±10% to assess the impact of integration into public health services, and variation in kit distribution by ±10%. We also modelled the impact of HIVST kit price between the observed average kit price (US$3.40), a recent Bill and Melinda Gates Foundation subsidized price (US$2) and a hypothetical price approximately equal to current rapid finger prick test price (US $1) [16]. Finally, we estimated a best- and worst-case scenario, the point where all the parameters yield the lowest/highest unit cost per kit distributed. To generate estimates that are comparable with the costs of ongoing facility HTS in the same communities in Malawi, Zambia and Zimbabwe [16], we also present costs without above site-level costs and start-up.

2.5 | Ethics

The study did not involve patient-level data collection; we did, however, obtain permission from ministries of health in the three countries to collate data from administrative, M&E records at facility level for cost allocation. Ethical approvals for the parent study were obtained from the Medical Research Council of Zimbabwe, Malawi College of Medicine Research Ethics Committee, University of Zambia Biomedical Research Ethics Committee, London School of Hygiene and Tropical Medicine Ethics Committee and University College London Ethics Committee. The trials are registered under the Clinical Trials Network (ClinicalTrials.gov) under registration numbers NCT02793804; NCT02718274; Pan African clinical trials registry PACTR201607001701788 for Malawi, Zambia and Zimbabwe.

3 | RESULTS

3.1 | Community-based distribution model programme outcomes

During the costing period, 152,671, 103,589 and 93,459 HIVST kits were distributed in Malawi, Zambia and Zimbabwe against the approximate targets of 62,500, 416,294 and 224,116 through a total of 138, 139 and 1009 CBDAs respectively. The average number of HIVST kits distributed was 12,538 (range: 4556 to 42,134) across 11 sites in Malawi, 7206 (range: 1758 to 20,450) across 16 sites in Zambia and 2124 (range: 319 to 4201) across 44 sites in Zimbabwe, where distribution was intentionally restricted by campaign duration (Table S2). Nearly half (49%, 51% and 43%, respectively) of the HIVST kits were distributed to men.

3.2 | Total HIVST costs and cost composition

Table 3 summarizes the findings of the cost analysis. The total distribution costs were calculated as US$1,243,940.66, US $1,700,730.45 and US$1,293,135.00 in Malawi, Zambia and Zimbabwe respectively. Capital costs accounted for 3%, 4% and 2% of the total costs with start-up costs accounting for 15%, 10% and 6% in Malawi, Zambia and Zimbabwe respectively. Within recurrent costs, personnel costs accounted for a significant portion of total costs, at 26%, 52% and 42% of costs in Malawi, Zambia and Zimbabwe respectively. Although the price of kits was centrally negotiated and thus the same across countries, kits contributed to the largest portion of total costs in Malawi (34%) and the second largest proportion in both Zambia and Zimbabwe (14% and 17% respectively).

3.3 | Unit costs

The country-level costs per HIVST kit distributed were US$8.15 for Malawi, US$16.42 for Zambia and US$13.84 in Zimbabwe. The cost per HIVST kit distributed across the sites ranged from US$7.20 to US$17.04 in Malawi, US$7.90 to U$50.00 in Zambia and from US$10.19 to US$54.44 in Zimbabwe. Figure 1 shows the unit cost per HIVST kit distributed plotted against the scale of HIVST kits across the three countries. Unit costs were generally lower at sites that were distributing a larger number of self-test kits, suggesting a spreading of fixed costs across variable numbers of kits. When above site-level and start-up costs are removed our estimates were comparable to the facility HTS unit costs estimated in the same communities [16]: US$6.67, US $10.42 and US$10.18 for the CBDA model, compared with facility HTS unit costs of $5.03 ($2.96 to $9.24), $4.24 ($2.49 to $6.24) and $8.79 ($3.38 to $21.51) in Malawi, Zambia and Zimbabwe respectively.

3.4 | Sensitivity and scenario analysis

Figures 2a,b,c show results from the univariate sensitivity and scenario analyses by country. Our unit costs per HIVST kit distributed remained robust when key cost parameters were varied. Varying life of start-up training and sensitization between one and three years resulted in costs of US$7.85 and US $16.42 versus US$9.07 and US$15.05 in Malawi and Zambia respectively. For Zimbabwe, however, there was no change to the base case cost of US$13.84 as training and sensitization costs were classified as recurrent due to the sequential and short-term nature of distribution across the eight districts, requiring training of CBDA who distribute for just four to six weeks. Varying life of start-up life or development phase between 2.5 and 7.5 years resulted in costs of US$8.23, US $15.40 and US$14.42 compared to US$8.13. US$14.28 and US $13.63 in Malawi, Zambia and Zimbabwe respectively.

Varying HIVST kit price between US$1 and US$3.40 yielded costs of US$6.44, US$15.15 and US$12.25 versus US $8.87, US$17.60 and US$14.99 in Malawi, Zambia and Zimbabwe respectively. Varying salaries by ±10% yielded costs of US$7.94, US$15.57 and US$13.24 versus US$8.37, US$17.27 and US$14.43 respectively. Varying kit quantity by ±10%

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Table 3. HIV self-test kit distribution cost breakdown and key cost contributors (in 2017 US$)

	Malawi Kits distributed: 152,671 12 months: June 2016 to May 2017		Zambia Kits distributed: 103,589 11 months: July 2016 to May 2017		Zimbabwe kits distributed: 93,459 10 months: August 2016 to May 2017	
Input type	**Intervention cost**	**%**	**Intervention cost**	**%**	**Intervention cost**	**%**
Start-up						
Training	$11,313.34	1%	$31,000.73	2%	$3,149.10	0%
Sensitization	$58,485.72	5%	$58,306.80	3%	$2,694.30	0%
Start-up other	$108,409.87	9%	$84,745.15	5%	$75,942.83	6%
Capital costs						
Building and storage						
Central	$16,755.33	1%	$54,077.43	3%	$3,266.62	0%
Warehouse	$–	–	$–	–	$–	–
Site level	$–	–	$–	–	$–	–
Equipment						
Central equipment	$28,026.91	2%	$13,597.20	1%	$14,759.28	1%
Site level	$–	–	$–	–	$7,621.29	1%
Vehicles and bicycles	$3,162.38	0%	$–	–	$–	–
Other capital	$–	–	$–	–	$35.14	0%
Total costs (capital and start-up)	$226,153	18%	$241,727	14%	$107,468	8%
Recurrent costs						
Personnel	$318,129.23	26%	$880,688.56	52%	$555,187.86	42%
HIV self-test kits	$418,584.61	34%	$237,303.53	14%	$219,627.52	17%
Supplies						
T-shirts, bags, flipcharts	$35,611.73	3%	$78,569.63	5%	$67,757.98	5%
Other supplies	$–	–	$–	–	$142,543.96	11%
Vehicle operation, maintenance and transport	$109,240.41	9%	$148,117.37	9%	$57,396.14	4%
Building operation/maintenance						
Central	$2,204.87	0%	$19,416.76	1%	$18,602.17	1%
Warehouse	$–	–	$–	–	$13,141.39	1%
Site level	$–	–	$–	–	$–	–
Recurrent training	$13,409.18	1%	$19,235.49	1%	$90,440.92	7%
Waste management	$–	–	$–	–	$554.89	0%
Other recurrent	$120,607.08	10%	$75,671.83	4%	$20,414.02	2%
Total costs (recurrent)	$1,017,787	82%	$1,459,003	86%	$1,185,667	92%
Total CBDA HIVST costs	$1,243,940	100%	$1,700,730	100%	$1,293,135	100%
Cost per kit distributed	$8.15		$16.42		$13.84	

Note that totals have been rounded to the nearest US$.
HIVST, HIV self-testing; CBDA, community-based distribution agent.

yielded costs of US$7.41, US$15.63 and US$12.83 versus US $9.06, US$17.60 and US$15.07 respectively. The best-case scenario was US$6.14, US$13.99 and US$12.32 per kit distributed, whereas the worst-case scenario was US$10.27, US $20.12 and US$21.85 per kit distributed.

4 | DISCUSSION

This is the first published study to present costs of door-to-door CBDA delivery of HIVST kits in Malawi, Zambia and Zimbabwe. Costs ranged from as low as US$7.20 at a very large distribution site where CBDA distribution of HIVST kits was integrated with the delivery of other health products, to US$54.55 with campaign-style delivery in a very small community in Zimbabwe that would otherwise not have access to testing. Staff costs contributed a substantial portion of the costs highlighting potential opportunities for lower cost models from reconfiguring distribution to rely on unpaid volunteers within door-to-door community-led distribution models. Additionally, economies of scale can clearly be optimized. In this analysis, we showed how unit costs fall as the number of

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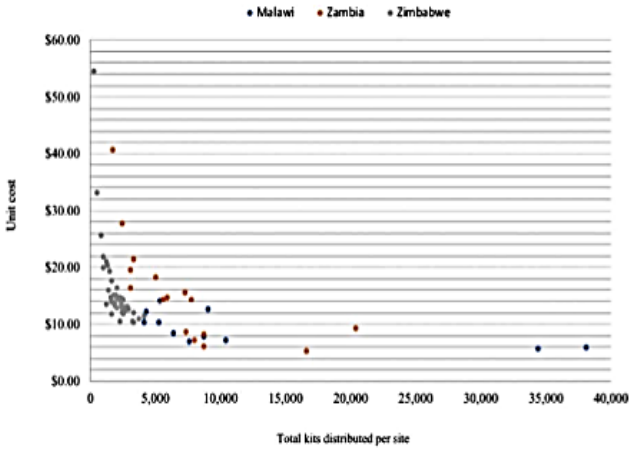

Figure 1. HIV self-testing (HIVST) costs per HIVST kit distributed by site and quantity in 2017 US$.

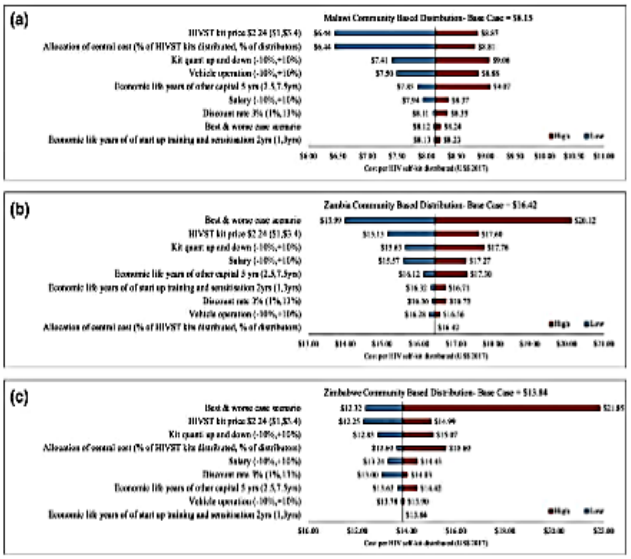

Figure 2. (a, b, c) Tornado diagrams of findings from deterministic sensitivity analysis (univariate and scenario analyses) in Malawi, Zambia and Zimbabwe.

kits distributed increases. As all modes of testing are scaled up and testing coverage increases, it will be critical to target populations efficiently, with special focus on communities underserved by facility-based HTS.

Although costs are presented from a provider's perspective, door-to-door community HIVST distribution relieves users from substantial direct and indirect costs of attending health facilities. A study in these same communities in Malawi showed the mean costs of accessing HIV testing among women and men as US$1.83 and US$3.81, respectively, with men reporting significantly higher opportunity costs (i.e. lost income) [17]. Community HIVST distribution reduces these costs to nearly zero, as kits are delivered in the home with no waiting times. We can, therefore, estimate the societal costs of facility-based HIV testing in Malawi as US$6.86 for women and US$8.84 for men (the user costs reported above and the provider costs as reported by Mwenge et al. [16]). This is comparable with our observed HIVST societal costs (excluding start-up and above service level costs: US$6.67) in Malawi. Thus, HIVST may provide for unmet testing needs among

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remotely or never-tested individuals, or others with high user costs of accessing facility-based testing.

HIVST costs reflected across all three countries are not dissimilar to those reported previously in Malawi ($8.78 in 2016 US$) [18]. We also found the cost of door-to-door community HIVST distribution to be comparable to standard community-based HIV testing in sub-Saharan Africa (range: US$7.37 to US $36.93) [19,20]. While we did find that CBDA delivered HIVST under this early demonstration and research programmes were more costly than facility-based HIV testing [16,18], we also found HIVST reached many more individuals. During the period of this costing study, health facilities serving the study communities provided HIV testing to approximately 17,000, 28,000 and 45,000 people, while the HIVST service distributed approximately 152,671, 104,000 and 94,000 kits in Malawi, Zambia and Zimbabwe respectively. Importantly, half of the HIVST kits were distributed to men, while only 26% to 37% of facility HIV testing clients were men [8-10], the population group primarily contributing to the HIV testing gap.

We anticipate potential for substantial economies of scale as HIVST programmes scale-up and mature. The door-to-door community HIVST distribution model costed for this current study was implemented by a non-governmental organization, under a research protocol, using paid and incentivized CBDAs and delivered to predominantly rural communities with no previous knowledge of, or experience with, HIVST. Interventions delivered in a research context tend to be associated with higher costs, as the primary objective is achieving effectiveness. Large-scale implementation through door-to-door community-led HIVST distribution with ordinarily paid government providers or community residents is likely to be significantly less costly. There are additional potential costs savings. First, we found costs were lower in high kit distribution sites suggesting economies of scale and ability to deliver at lower costs in more densely populated communities. Second, 10% to 20% of the costs were start-up and initial capital costs, which would decrease as services mature. Third, as general populations and providers gain a better understanding of HIVST as a screening technology, we would expect less intense need for CBDAs (and therefore, less intense need for training workshops) and community sensitization activities.

Additionally, CBDAs could incorporate HIVST delivery into other health service activities thereby delivering cost savings to providers through economies of scope in services delivered by the CBDAs. Finally, as the HIVST market grows, technology advances and newer manufacturers enter, the price of HIVST kits will likely fall to prices comparable to blood-based kits currently used in health facilities and in-person support requirements could, in theory, could become cheaper than provider-supervised testing. In this case, HIVST could save costs and allow providers to focus on confirmatory testing and strengthening linkage to ART [21,22]. To identify this, it will be important to take a full system costing approach. Such data have been collated and will be analysed jointly to inform cost-effectiveness modelling.

From a research perspective, the wide cost variations highlight the importance of evaluating costs across a variety of settings in order to generate means and confidence intervals. Future analyses of these data may generate useful insights into efficiency and provide key inputs into modelled cost-effectiveness analyses. It would also be important to expand conventional sensitivity analyses to assess unit costs when these observed ranges are included or when unit costs are incorporated as a function of scale. Furthermore, considering that our analysis only shows the costs of implementing CBDA model for a non-governmental perspective and that these costs can vary if the kits were distributed differently, an important next research question will be to explore the costs of possible HIVST distribution modalities such as secondary distribution and social marketing models among others.

4.1 | Limitations

The findings of our cost analyses are limited to unit costs per kit distributed as the private nature of the HIVST did not allow us to estimate the costs of identifying new HIV-positive individuals or those HIV-positive individuals linked to treatment through HIVST. In addition, our results are borne out of a research trial setting and may not truly reflect a real-world situation: for example, site fixed transport costs are likely higher due to the distances between the trial communities, while in routine scale-up, all communities would receive HIVST kits and transport would be shared across far higher scale.

Additionally, as HIVST was a new product, distribution was conservative, restricting the numbers of kits that each CBDA could distribute in Zimbabwe, and so constraining opportunities to operate at larger scale. Consequently, costs were likely higher than future routine implementation. The benefits of HIVST distribution may also be restricted by test performance characteristics such as sensitivity, specificity and ability of the user to read the test as well as rates of linkage to care. An important consideration would be the optimal, setting-specific incentive structure for door-to-door community-based distribution of the kits. It is important to highlight that for purposes of this analyses authors had not collated and analysed data on self-test kit utilization. However, previous work has not only shown high uptake of HIVST but also high levels of kit utilization by recipients [4]. Key strengths of this cost analysis are the estimation of costs across seventy-one sites in three Southern African countries. The costing teams used standardized costing guidelines and collaboratively analysed data ensuring consistency of methods across countries and application of a range of sensitivity and scenario analyses exploring the impact of our assumptions.

4.2 | Implications

Countries keen to achieve impact and meet the global testing and treatment targets will likely need to invest in a mixture of HIV testing approaches, including door-to-door community delivered HIVST targeted at populations with financial or other barriers to obtaining HIV testing in health services, that is people living in settings with high undiagnosed HIV or remote communities, and groups such as men and adolescents. Reducing costs during short-term scale-up and implementation of this model should focus on economies of scope and scale and ensure efficiencies in personnel and transportation costs. Alternative cost-minimization approaches also need to be explored for acceptability, impact and affordability, aiming to provide affordable access to HIVST nationally, for example integrating HIVST within the existing facility and community health services, secondary distribution from facilities including partner delivered and peer-network approaches.

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5 | CONCLUSIONS

Staff costs were a substantial cost contributor highlighting the potential for lower cost models if distribution relied on unpaid volunteers within door-to-door community-led distribution models.

Economies of scale can also be optimized with our costs showing reductions when kits are distributed in higher numbers. Across all three countries, our HIVST cost estimates were not dissimilar to previous door-to-door community-based HIVST and standard community-based HIV testing models costed in sub-Saharan Africa. Although the costs of CBDA delivered HIVST were higher than facility-based HIV testing the evidence shows HIVST reaches many more individuals. A significant portion (almost half) of HIVST kits were distributed to men (key contributors to the HIV testing gap) compared to only 26% to 37% for facility HIV testing.

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COMPETING INTERESTS

The authors have no conflicts of interest to declare.

AUTHORS' CONTRIBUTIONS

CM, LM, LS, NA, MD, HM and FTP conceptualized and designed the study. CM, LM, LS, NA, PC, TC and SK collected and facilitated the collection of data. CM, LM, LS, NA, PC, TC, SK, MD, JJO, HM and FTP analysed and interpreted the data. CM, LM, LS, NA, MD, PC, TC, SK, JJO, MM, MN, RC, PI, ELS, MNE, GN, OM, KH, CJ, HA, ELC, FC, HM and FTP drafted the manuscript and revised it critically. MM, MN, RC, PI, ELS, MNE, GN, OM, KH, CJ, HA, ELC, FC, HM and FTP supervised the study and facilitated the acquisition of the cost data. All co-authors approved the final version to be published.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1: Cost allocation factors across the interventions by cost input type.

Table S2: Site-level total and unit costs of HIVST and facility-based testing.

Data S1: Narrative description of the CBDA models across countries.

Data S2: Definitions of cost category and cost inputs and allocation factors.

APPENDIX III: CO-AUTHORED PAPER 3: COSTS OF ACCESSING HIV TESTING SERVICES AMONG RURAL MALAWI COMMUNITIES

This third paper, *Costs of accessing HIV testing services among rural Malawi communities,* is a co-authored paper published in *AIDS Care* journal, which helped to expand the understanding of cost beyond unit cost of HTS and explored the costs among HIV testing clients. This paper is added in Appendix 1 as published, and *AIDS Care* permitted this.

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Costs of accessing HIV testing services among rural Malawi communities

Linda Sande, Hendramoorthy Maheswaran, Collin Mangenah, Lawrence Mwenge, Pitchaya Indravudh, Phillip Mkandawire, Nurilign Ahmed, Marc d'Elbee, Cheryl Johnson, Karin Hatzold, Elizabeth L. Corbett, Melissa Neuman & Fern Terris-Prestholt

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Costs of accessing HIV testing services among rural Malawi communities

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ABSTRACT

HIV testing is free in Malawi, but users may still incur costs that can deter or delay them accessing these services. We sought to identify and quantify these costs among HIV testing service clients in Malawi. We asked residents of communities participating in a cluster randomised trial investigating the impact of HIV self-testing about their past HIV testing experiences and the direct non-medical and indirect costs incurred to access HIV testing. We recruited 749 participants whose most recent HIV test was within the past 12 months. The mean total cost to access testing was US$2.45 (95%CI: US$2.11–US$2.70). Men incurred higher costs (US$3.81; 95%CI: US$2.91–US$4.50) than women (US $1.83; 95%CI: US$1.61–US$2.00). Results from a two-part multivariable regression analysis suggest that age, testing location, time taken to test, visiting a facility specifically for an HIV test and district of residence significantly affected the odds of incurring costs to testing. In addition, gender, wealth, age, education and district of residence were associated with significant user costs.

Abbreviations: AIDS: Acquired Immune Deficiency Syndrome; ANC: Antenatal Care; ART: AntiRetroviral Therapy; CBDA: Community-Based Distribution Agent; CBHTS: Community-Based HIV Testing Services; CRT: Cluster Randomized trial; GLM: Generalised Linear Model; HIV: Human Immunodeficiency Virus; HIVST: HIV Self-Testing; HTC: HIV Testing and Counselling; IHS: Integrated Household Survey; OLS: Ordinary Least Squares; PCA: Principal Component Analysis; PITC: Provider Initiated Testing and Counselling; PLHIV: People Living with HIV; STAR: Self-Testing AfRica; TB: Tuberculosis; TPM: Two-Part Model; UNAIDS: The Joint United Nations Programme on HIV/AIDS; VCT: Voluntary Counselling and Testing

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Introduction

Eastern and Southern Africa account for the highest numbers of people living with HIV (PLHIV), newly infected with HIV, and dying from HIV (UNAIDS, 2017). HIV testing is an essential gateway to HIV prevention, treatment, care and support services since receipt of an HIV diagnosis empowers individuals to make informed decisions about follow on services in the cascade (World Health Organization, 2015; World Health Organization & UNAIDS, 2017). The global entities involved in AIDS eradication have adopted ambitious treatment targets: by 2020, 90% of all PLHIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy (ART) and 90% of all people receiving ART will have viral suppression (UNAIDS, 2014a). Ensuring that 90% of PLHIV are aware of their status will support enrolment in HIV care and achievement of these global treatment goals (UNAIDS, 2014a).

However, despite impressive efforts in scaling-up availability of HIV testing and treatment services in the region, including freely available HIV testing at nearly all healthcare settings, testing uptake remains inadequate to reach the global goals (Church et al., 2017). Malawi has been leading the way in scaling-up HIV services (Lowrance et al., 2008; UNAIDS, 2014b) but an estimated 35% of men and 18% of women have never tested for HIV and 60% of young people aged 15–19 years have never tested (CDC & GoM, 2017). Uptake of HIV testing also remains low amongst poorer individuals and those

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with less formal education (Kim, Skordis-Worrall, Haghparast-Bidgoli, & Pulkki-Brännström, 2016).

Previous studies in sub-Saharan Africa have cited location, distance, waiting time, costs, confidentiality concerns, low perceived risk and infrequent contact with the health-care system as barriers to accessing HIV testing (Angotti et al., 2009; Morin et al., 2006; Musheke et al., 2013; Sharma, Ying, Tarr, & Barnabas, 2015). Individuals often incur substantial access costs when utilising public sector HIV testing and treatment services even when they are provided free at point of use (Chimbindi et al., 2015; Lubega et al., 2013; Maheswaran et al., 2016; Pinto, Lettow, Rachlis, Chan, & Sodhi, 2013).

In urban settings, HIV testers incur costs close to twice their daily earning incomes (Maheswaran et al., 2016). These costs are likely to be higher in more rural settings, however little is known about these costs and whether these vary by different population groups or testing modalities, which limits efforts to minimise or offset testing costs to increase uptake. Awareness of costs incurred by rural HIV testers is particularly important since 84% of the Malawi population is rural with 57% of the rural population classified as poor compared to 17% of the urban population (International Monetary Fund, 2017; World Bank, 2014). The poor in developing countries like Malawi are even less likely than the better off to receive effective health care with existing costs barriers proposed as one of the deterrents of this low use (O'Donnell, 2007; Russel, 2004).

The World Health Organisation (WHO) guidelines have highlighted the need for strategic approaches to deliver HIV testing services (HTS) (World Health Organisation, 2016). HIV self-testing (HIVST) and community-based HIV testing are proposed as having the potential of increasing testing uptake especially for men, key populations and young people who would not normally access HIV testing services (Malawi Ministry of Health, 2016; World Health Organisation, 2016). Young people for instance, have previously demonstrated an aversion to price due to their limited access to resources (Indravudh et al., 2017; Sibanda, Maringwa, et al., 2017). Research on these costs is essential to appropriately targeting these sub-populations lagging behind in access to testing.

In this study, we sought to examine (1) the costs borne by users of HIV testing services in rural Malawi; (2) whether certain population subgroups incur higher costs; and (3) whether costs differ based on the mode of testing. To the best of our knowledge, this is the first study to identify and quantify specific costs of HIV testing in a rural setting. Other studies in the region have explored determinants of testing (Camlin et al., 2016; Helleringer, Kohler, Frimpong, & Mkandawire, 2009; Lépine, Terris-Prestholt, & Vickerman, 2014), costs of providing HIV services (Maheswaran et al., 2016; Mangenah, Mwenge, et al., 2017; Mwenge et al., 2017; Sharma et al., 2015), and costs of accessing tuberculosis (TB) treatment (Kemp, Mann, Simwaka, Salaniponi, & Squire, 2007) and ART (Bergmann, Wanyenze, & Stockman, 2017; Chimbindi et al., 2015; Pinto et al., 2013; Rosen, Ketlhapile, Sanne, & DeSilva, 2007). The few that have explored costs associated with HIV testing have either focused on urban settings (Maheswaran et al., 2016) or examined costs without considering lost income (Bergmann et al., 2017). The results of this study will inform the design of future HIV testing services and interventions aimed at overcoming financial barriers to testing.

Methods

Study setting and design

HIV testing in Malawi is freely provided. Individuals may voluntarily access HIV testing at a health facility; may be advised to test by a health professional [provider-initiated testing and counseling (PITC)]; may be offered testing as part of routine antenatal care (ANC) (accessed by both the pregnant women and their accompanying male partners) or TB care (also a form of PITC); or may have access to community-based HIV testing services (CBHTS) including through testing campaigns and outreach, home-based or door-to-door testing, workplace testing, mobile testing, and testing through educational institutions.

We undertook a baseline household survey as part of a cluster-randomised trial (CRT) investigating the impact of community-based distribution of HIVST in rural Malawi (ClinicalTrials.gov Identifier: NCT02718274). The CRT was conducted in rural villages of Blantyre, Machinga, Mwanza and Neno in Southern Malawi. The CRT comprised a population of approximately 62,500 residents with 22 clusters defined by the service catchment area of public primary health facilities with active ART clinics. The HIV prevalence in the four districts was approximately 11% (National Statistics Office & ICF Macro, 2017).

Within each cluster, villages were selected for inclusion in the baseline survey based on location, population size, road accessibility and presence of pre-existing reproductive health community-based distribution agents. Households in these evaluation villages were randomly sampled for a baseline household survey which was conducted between May and August 2016. The sampling of the survey ensured inclusion of at least 250 adults per cluster, with the

sample size calculated based on the primary outcome of the trial. All household members aged 16 years or older were eligible to participate in the survey. Details on the sample size calculation for the main trial can be found in the trial protocol available at http://hivstar.lshtm.ac.uk/.

Research assistants visited selected households and administered an electronic, face-to-face, questionnaire to all household members aged above 16 years who agreed to participate. The main questionnaire included questions about sociodemographics and HIV testing history. Due to time and resource constraints, an extended questionnaire was administered to a random 20% subset of participants responding to the main questionnaire. The extended questionnaire included questions on the costs of HIV testing as well as other questions on health care utilisation and stigma.

Assessing costs and location of HIV testing

Participants who reported testing within the previous 12 months were asked the location of testing, including whether facility- or community-based; if their most recent test was accessed separately from other health services or as part of antenatal care ANC or PITC; total time taken to access HIV testing; and the direct non-medical and indirect costs they incurred. The 12 months recall period is in line with other studies on health care use and/or out-of-pocket expenditure (van Doorslaer & Masseria, 2004; Heijink, Xu, Saksana, & Evans, 2011) and a similar recall period is used to collect household non-food expenditures in the Malawi integrated household survey which is a major socio-economic survey conducted by the Malawi National Statistical Office. It is worth noting that there is no general answer to the question of optimal recall period with the choice dependent on the primary objective of the data collection (Clarke, Fiebig, & Gerdtham, 2008).

We derived a list of potential costs based on the literature and previous work undertaken in Malawi to inform development of the study questionnaire (Kemp et al., 2007; Maheswaran et al., 2016; Pinto et al., 2013). We asked participants how much they had paid for the round trip to the testing facility (transport cost), and if they had paid any consultation or service fees (consultation cost) related to testing (sometimes incurred at private facilities), excluding any fees for other services they accessed at the same time. Participants were also asked if they spent money on any food and drink items (food costs) while accessing testing and, if so, how much they spent. Additionally, we asked participants about any costs they might have incurred by paying a caretaker to watch their children for the time they sought testing (child care costs), and about any other costs they might have incurred as they sought testing (other costs). We further asked participants to approximate the amount of money they would have earned during the entire time they took to access testing (lost income).

Other covariates

Participants were also asked questions on socio-demographics (age, gender and education), the number of children they have and ownership of eight household assets.[1] We estimated household wealth using the principal component analysis (PCA) method, with household assets as a proxy for wealth (Filmer & Pritchett, 2001), and we further classified wealth into quintiles. Table 1 further summarises all the covariates.

Ethical approvals were obtained from the College of Medicine Research Ethics Committee in Malawi and the Research Ethics Committee of the London School of Hygiene and Tropical Medicine. We obtained written informed consent from all participants in the extended questionnaire before their interview.

Statistical methods

All analysis was undertaken in STATA version 14.0 (Stata Corporation, Texas, USA). Costs were estimated in 2016 Malawi Kwacha (MWK) and converted to 2016 US dollars at an exchange rate of MWK 729.89/US$ (Reserve Bank of Malawi, 2017).

Cost data were categorised into direct non-medical costs and indirect costs. Direct non-medical costs included those directly incurred by participants and indirect costs refer to productivity and income losses due to accessing testing services. We include data for the entire sample who had complete cost data and present it using means with 95% confidence intervals. To assess the burden imposed on participants, we compared their total direct non-medical and indirect costs with the national poverty line of US$1.20/day. The poverty line was adopted from the Third Malawi Integrated Household Survey (IHS) of 2011, converted to US$ at the average 2011 exchange rate of MWK162.84/US$ (National Statistics Office, 2012; World Bank, 2018) and adjusted for inflation using the national gross domestic product (GDP) deflator for 2011 of 14% (World Bank, 2018).

To determine the significant predictors of costs, we estimated a multivariable two-part model (TPM). Individual-level user cost data pose estimation challenges since individual-level medical expenditures or costs of treatment typically feature a spike at zero and are strongly skewed with a heavy right-hand tail (Jones, 2010). There is no unique way to deal with these

Table 1. Descriptive statistics.

Variable	Regression Inclusion	Expected Direction
Gender	Indicator: Men (reference group) Women	Men are expected to incur higher costs than women to reflect their higher earning potential relative to women
Age (Years)	Indicator: 16–19 Years; 20–24 Years; 25–39 Years; 40–64 Years; 65+ Years	Financial productivity is expected to increase with age starting from age 20 hence raising the opportunity cost to testing up to age 65
Education	Indicator: No Formal education (reference group) Incomplete Primary education Some Secondary Education Complete Secondary Education or higher	Education as a proxy for earning potential, implying that the higher the level of education the higher the cost for testing
Number of Children	Continuous: The participant's number of children	Number of children is positively associated with any child care costs a participant might have incurred while accessing testing hence increasing the total costs incurred
Test Location	Indicator: Facility-Based Testing (reference group) Community HTC Other Place	Community-based HTC reduces logistic barriers hence lowers the opportunity cost of testing. Other place testing depends on where the person tested for example, if at home testing e.g., self-testing then lower costs than facility-based testing
Amount of Time Taken to Receive Testing	Continuous: Time taken (including travel) in hours to access HIV testing	The more time taken away from work to seek testing, the higher the cost of testing through lost income
Reason for visiting Testing Centre	Indicator: Had other reasons for visiting a testing centre aside from HIV testing (reference group) Visited a testing centre specifically for an HIV test	Visiting a testing centre for other reasons aside from HIV testing has potential of economies of scope hence reduced total costs
Wealth Index	Indicator: Households are ranked into wealth quintiles with the poorest as the reference group	Wealth is a proxy for ability to pay; the higher the wealth quintile, the higher the participant's expenditure to access testing
District of Residence	Indicator: Blantyre District (Reference Group) Machinga District Mwanza District Neno District	There should not be difference in costs of testing by district

estimation challenges associated with cost data with literature recommending that the choice of appropriate estimation approach should be determined by the research questions and the characteristics of the data (Buntin & Zaslavsky, 2004; Diehr, Yanez, Ash, Hornbrook, & Lin, 1999; Gregori et al., 2011; Griswold, Parmigiani, Potosky, & Lipscomb, 2004). The common proposed estimation approaches are the log-transformed OLS, Tobit model, TPM and generalised linear models (GLM) with a log-link function (Buntin & Zaslavsky, 2004; Gregori et al., 2011; Griswold et al., 2004; Jones, 2010; Nichols, 2010).

A Tobit regression model and a TPM were better fit for our data as they are both able to handle excess zeroes and positive distribution associated with cost data (Jones, 2010). GLM and log-transformed ordinary least squares (OLS) on the other hand, do not take into account the excess zeroes in the data and therefore generates biased estimates. We therefore, estimated a log-transformed Tobit and a TPM with a logit model for the first part and log-transformed OLS regression for the second part. Given our main objective, a TPM is the appropriate estimation approach as it can distinguish the probability of incurring costs for testing and assess significant cost drivers for those who incurred costs.

To account for the clustering of the data by district, a fixed effect approach was used. We then applied a likelihood ratio test to identify the most parsimonious model between the restricted and unrestricted TPM models. We further identified the most appropriate functional form for age (testing for non-linearity) using the likelihood-ratio test and did not find significant justification for this quadratic relationship.

We explored socio-demographic and socio-economic variables and accessibility of testing centres as

determinants of total costs:

$$\ln(\text{Total Costs}_i + 1) = f\left[\begin{array}{l} \textit{District},\ \text{Gender},\ \text{Wealth}_{hh},\ \textit{Age}\ \text{categories},\ \text{Education},\ \text{Number of Children}, \\ \text{Time Taken (Hours)},\ \text{Reason for visiting testing centre} \end{array}\right]$$

To reduce the skewness in the cost data, we modelled the costs using a log transformation. We log transformed user costs as ln (Total Costs$_i$ + 1) as suggested by the literature (McCune, Grace, & Urban, 2002). Table 1 summarises the a priori direction of association of the determinants.

Results

Participants' characteristics

A total of 5551 participants were recruited into the baseline survey and 1388 responded to the extended questionnaire. Seven hundred and forty-nine (14%) participants reported having had at least one HIV test in the previous 12 months, making them eligible for this sub-study. Baseline characteristics of these 749 participants are presented in Table 2. In brief, 32% of the participants were men, 33% of the participants were aged 16–24 years and 18% had no formal education. Most of the participants (83%) reported facility-based testing as their most recent testing approach. Among those who tested in a facility, more participants (76%) accessed testing through PITC. In addition, men reported spending an average of 2.9 h and women reported spending an average of 3.5 h to access testing services.

Direct non-medical and indirect costs

Direct non-medical and indirect costs stratified by gender and cost-category are summarised in Table 3. Twenty percent of the participants incurred zero costs for testing. The median cost for participants who incurred costs was US$2.06. The mean total cost per participant was US$2.45 (95%CI: US$2.11–US$2.70) with lost income accounting for 83% of the total costs. Men incurred higher mean total costs than women: US$3.81 (95%CI: US$2.91–US$4.50) versus US$1.83 (95%CI: US$1.61–US$2.00).

Cost determinants

The logit component of the TPM demonstrated that age, testing location, time taken to acquire a test, visiting a facility specifically for an HIV test and district of residence significantly affected the odds of incurring costs for testing. The odds of incurring testing costs are 18% higher for participants aged between 25–39 years than participants aged between 16–19 years. In addition, participants who tested within their communities (mobile testing) had 61% lower odds of incurring costs than participants who tested at facilities. Each additional hour spent seeking testing increased the odds of incurring costs by 48%. Participants who visited a testing site specifically for an HIV test had 48% higher odds of incurring costs for testing than those who accessed testing in addition to other health care services. And finally, residence in Mwanza district was associated with 95% higher odds of incurring costs when compared to residence in Blantyre district (Tables 4 and 5).

Table 2. Participant characteristics (n = 749)[a].

		Men (n = 237, 32%)		Women (n = 512, 68%)	
		N	Percentage	*N*	Percentage
Age (Years)	16–19	23	9.8%	52	10.2%
	20–24	35	14.8%	135	26.4%
	25–39	96	40.7%	205	40%
	40–64	63	26.7%	102	19.9%
	65+	19	8.1%	18	3.5%
Education	No formal Edu.	19	8.0%	112	21.9%
	Primary Edu.	160	67.5%	331	64.7%
	Some Secondary Edu.	38	16.0%	57	11.1%
	Complete Secondary or Higher Edu.	20	8.4%	12	2.3%
Wealth Index[b,c]	Lowest Quintile	64	27.0%	227	44.3%
	2nd Lowest Quintile	40	16.9%	57	11.1%
	Middle Quintile	28	11.8%	69	13.5%
	2nd Highest Quintile	45	19.0%	70	13.7%
	Highest Quintile	60	25.3%	89	17.4%
Test Location	Hospital/Clinic/ Health Centre	148	62.5%	295	57.6%
	ANC Clinic	17	7.2%	106	20.7%
	VCT Centre	24	10.1%	31	6.1%
	Community/ Mobile HTC	47	19.8%	74	14.5%
	Other Testing Place	1	0.42%	6	1.1%
Number of Children	Mean (min-max)	3	(0–12)	3	(0–13)
Reason for facility visit	HIV Test	168	70.9%	283	55.3%
	HIV Test + Other Services	69	29.1%	229	44.7%
Time Taken	≤1 h	73	30.8%	104	20.3%
	1–3 h	83	35.0%	181	35.4%
	3–6 h	66	27.9%	182	35.6%
	>6 h	15	6.3%	45	8.8%
District	Blantyre	62	26.2%	147	28.7%
	Machinga	70	29.5%	172	33.6%
	Mwanza	30	12.7%	51	10%
	Neno	75	31.7%	142	27.7%

[a]3 Participants had incomplete data.
[b]Wealth index estimated through undertaking principal component analysis of responses to asset ownership and housing environment.
[c]Assets selected in the baseline data did not do well in differentiating the poorest from one another.

Table 3. Direct non-medical and indirect costs by gender and cost category.

Cost Category		Men (US$) Mean (95% CI)	% of Men	Women (US$) Mean (95% CI)	Total Sample (US$) % of Women	Mean 95% CI	% of Total Sample
Direct non-medical costs	Transport	0.25 (0.15–0.36)	6.6%	0.16 (0.11–0.22)	8.7%	0.19 (0.14–0.24)	7.8%
	Consultation	0.03 (0.00–0.05)	0.8%	0.03 (0.01–0.04)	1.6%	0.03 (0.01–0.04)	1.2%
	Food	0.18 (0.14–0.22)	4.7%	0.13 (0.10–0.15)	7.1%	0.14 (0.12–0.17)	5.7%
	Other	0.05 (0.02–0.09)	1.3%	0.02 (0.01–0.04)	1.1%	0.03 (0.02–0.05)	1.2%
Indirect Costs	Child Care	0.06 (0.02–0.11)	1.6%	0.01 (0.00–0.03)	0.6%	0.03 (0.01–0.05)	1.2%
	Lost Income[a]	3.24 (2.45–4.03)	85.0%	1.48 (1.31–1.65)	80.9%	2.03 (1.75–2.31)	82.9%
Total direct non-medical and indirect cost		3.81 (2.91–4.50)	100%	1.83 (1.61–2.00)	100%	2.45 (2.11–2.70)	100%

[a]Lost Income had a median cost of US$1.37; US$2.06 for men and US$0.96 for women.

On the other hand, the log-transformed OLS component of the TPM demonstrated that gender, age, wealth, education and district of residence was associated with significant user costs. Holding everything else constant, men on average incurred 52% higher costs for testing than women.

Older age groups incurred significantly higher costs than the 16–19 age group. Participants aged between 20–24 years; 25–39 years incurred 61% and 96% higher costs respectively, than participants aged between 16–19 years. Participants aged between 40–64 years and 65+ years on average incurred more than double and 74% higher costs respectively, than participants aged between 16–19 years. There was no difference in average testing costs among participants with lower than complete secondary education and those without any formal education. However, participants with complete secondary education or higher on average incurred 63% higher costs than those with no formal education. Finally, participants in Mwanza district incurred on average 43% higher costs than participants resident in Blantyre district.

Table 4. Multivariable analysis of log-transformed Tobit regression model (Dependent Variable: total direct non-medical and indirect costs).

	Determinants (Reference Category)	Coefficient	95% CI	*P*-value
Gender	(Male)			
	Female	−0.323***	(−)0.457–(−)0.189	0.000
Wealth	(Lowest Quintile)			
	2nd Lowest Quintile	−0.049	(−)0.239–0.141	0.613
	Middle Quintile	0.169*	(−)0.024–0.362	0.086
	2nd Highest Quintile	0.003	(−)0.176–0.182	0.975
	Highest Quintile	0.175**	0.007–0.343	0.041
Age (Years)	(16–19)			
	20–24	0.411***	0.178–0.643	0.001
	25–39	0.640***	0.406–0.873	0.000
	40–64	0.685***	0.395–0.974	0.000
	65+	0.195	(−)0.169–0.56	0.293
Education	No Formal Edu.			
	Primary Edu.	0.013	(−)0.151–0.177	0.877
	Incomplete Secondary Edu.	0.253**	0.017–0.489	0.036
	Complete Secondary or Higher	0.530***	0.198–0.863	0.002
Children	No. of Children	0.000	(−)0.033–0.034	0.982
Testing Location	Facility			
	Community	−0.396***	(−)0.571–(−)0.220	0.000
	Other	−0.175	(−)0.858–0.508	0.614
Time Taken	Time (Hours)	0.049***	0.023–0.077	0.000
Reason for visiting	HIV Test + Other			
	HIV Test	0.079	(−)0.045–0.204	0.211
District	Blantyre			
	Machinga	0.059	(−)0.097–0.214	0.460
	Mwanza	0.350***	0.139–0.560	0.001
	Neno	−0.007	−0.164–0.149	0.927
	Constant	0.208	(−)0.113–0.529	0.164
	Observations			746[a]

Note: ***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.
[a]3 observations had incomplete data.

Table 5. Multivariable analysis of Two-Part Model on total direct non-medical and indirect costs with first part (logit) and second part (Log-transformed OLS).

		Two-Part Model	
Determinants (Reference Category)		logit	Log-transformed OLS
Gender	(Male)		
	Female	−0.221	−0.517***
Wealth	(Lowest Quintile)		
	2nd Lowest Quintile	−0.196	−0.0113
	Middle Quintile	−0.108	0.398***
	2nd Highest Quintile	−0.168	0.0644
	Highest Quintile	0.342	0.161
Age (Years)	(16–19)		
	20–24	0.468	0.610***
	25–39	0.777**	0.964***
	40–64	0.674	1.031***
	65+	−0.323	0.736***
Education	(No Formal Edu.)		
	Primary Edu.	0.177	−0.0569
	Incomplete Secondary Edu.	0.430	0.248
	Complete Secondary Edu.	0.951	0.628***
Number of Children	No. of Children	0.0604	−0.0164
Testing Location	(Facility)		
	Community testing	−0.946***	−0.204
	Other	−0.820	0.0617
Time Taken	Time (Hours)	0.203***	0.0161
		(0.0530)	(0.0197)
Reason for visiting	(HIV Test + Other)		
	HIV Test	0.393*	0.0374
District	(Blantyre)		
	Machinga	0.253	0.0857
	Mwanza	0.666*	0.434***
	Neno	−0.190	0.0594
	Constant	−0.0902	−0.118
	Observations	746[a]	746[a]
Pseudo R^2		0.116	
Adjusted R^2			0.1579
Log Likelihood		−335.04519	−847.03399

Note: ***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.
[a]3 observations had incomplete data.

Discussion

This study examined the costs borne by users when accessing HIV testing services in rural villages of Southern Malawi. Our findings indicate that the average cost of accessing HIV testing in rural Malawi is less than that reported in urban areas of the country (US$3.09 per test) (Maheswaran et al., 2016), yet rural testers incur costs that are equivalent to twice the daily minimum income required for their basic needs (national poverty line at US$1.20 a day) (National Statistics Office, 2012). In a country where at least 51% of the population live below the national poverty line and 71% live below the international poverty line of US$1.90 a day (National Statistics Office, 2012; World Bank, 2014), these costs are likely to be prohibitive for a large proportion of the population.

Our study also demonstrated that there are significant average cost differences between men (US$3.81) and women (US$1.83). Historically, there has been low uptake of HIV testing and poor linkage into care amongst men relative to women, particularly in sub-Saharan Africa (Camlin et al., 2016). It is likely that these high costs have contributed to the lower uptake. Seeking testing imposes both a direct non-medical cost but also the lost opportunity cost of hours away from productive activities (Angotti et al., 2009; Ganesh, 2015; Musheke et al., 2013; Wolff et al., 2005). Our findings show that these opportunity costs comprise a significant proportion (83%) of the total testing costs in this population. For most, the prospect of learning their HIV status may not be a sufficient incentive to bear these costs (Angotti et al., 2009), unless they are already sick. This is further evidenced by the large proportion of men in our sample who accessed testing through PITC (70%) and very few who voluntarily attended facilities for the sole purpose of learning their HIV status (10%), suggesting that most men in rural Malawi access testing as an add-on to other health care services, rather than seeking out testing independently.

The large proportion of total costs associated with lost income was driven by long travel times and long waiting times at testing facilities. On average, participants spent three hours to access HIV testing services, with men spending less time (2.9 h) than women (3.5 h). Similar long wait times (3.4 h) were observed among adults utilising public sector HIV and TB services in South Africa (Chimbindi et al., 2015). Taking measures to improve efficiency at HIV testing facilities, such as increasing staffing for this service, could reduce waiting times and therefore reduce the time taken from employment and other activities.

Delivering HIV testing closer to people's homes or at times convenient to users may also mitigate financial barriers to testing. We found that community-based testing is associated with a lower probability of incurring costs than facility-based testing, therefore decentralising testing services beyond static facilities may be necessary to increase uptake. The popularity, especially among men, of community-based HIV testing and HIVST models has been previously demonstrated (Angotti et al., 2009; Choko et al., 2015; Morin et al., 2006; Mwenge et al., 2017; Sebapathy, Van den Bergh, Fidler, Hayes, & Ford, 2012; Sharma et al., 2015; World Health Organization, 2015). HIVST and other home-based testing can be advantageous in that they substantially reduce or completely eliminate costs borne by users when testing (Maheswaran et al., 2016; Sharma et al., 2015).

Financial and non-financial incentives also offer an alternative to reducing or offsetting testing costs and

promoting uptake. Small non-monetary incentives are associated with significantly increased community testing and HIV case diagnosis (Sibanda, Tumushime, et al., 2017). It is worth noting that although small financial incentives have been effective in increasing health care uptake (Choko et al., 2017; Mangenah, Sibanda, et al., 2017; Pettifor, MacPhail, Nguyen, & Rosenberg, 2012), different amounts of incentives have different levels of effectiveness. Incentives that cover transport and opportunity costs are generally associated with better testing and linkage to care than incentives equivalent to transport reimbursement only (Choko et al., 2017).

Study limitations and strengths

Our study used retrospective interviews to collect expenditure data for participants' most recent HIV test. This approach introduces potential for recall bias. We limited this recall bias by recruiting participants with an HIV test within a period of 12 months preceding the interview. In addition, there is potential for downward bias of the testing costs because individuals with prohibitively high expected costs will not have tested. Our follow-up research will explore more advanced statistical models to reduce this downward bias.

Despite these limitations, our study adds valuable information to the literature on access to HIV testing. Unlike previous studies, we included lost income as a cost to testing which enabled us to determine the full economic burden of testing on users in a rural setting.

Conclusion

Though HIV testing services are "free" in Malawi, users incur costs to access these services in rural parts of the country that are double the national poverty line. In these contexts, men incur higher costs to access HIV testing services than women, with lost income as the largest cost component. Increasing uptake of testing services, especially for men, will likely require bringing testing services closer to the communities, improving efficiency of facility-based testing and potentially introducing financial or non-financial incentives as a way to motivate uptake and offset the total costs associated with this portion of the HIV cascade.

Note

1. Asset index: Electricity, radio, working television set, mobile phone, landline telephone, refrigerator and bed with mattress.

Acknowledgements

We acknowledge the participants who generously agreed to respond to the questionnaires, the entire Population Services International-Malawi research and implementation teams, researchers and data teams from the London School of Hygiene and Tropical Medicine and the Malawi-Liverpool Wellcome Trust Clinical Research Programme. The Data will be deposited to London School of Hygiene & Tropical Medicine's digital repository (http://datacompass.lshtm.ac.uk/).

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

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APPENDIX IV: ETHICS APPROVED FORMS

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Observational / Interventions Research Ethics Committee

Dr Helen Ayles
Reader
Department of Clinical Research (CRD)
Infectious and Tropical Diseases (ITD)
LSHTM

16 May 2016

Dear Helen

Study Title: Self-testing for HIV (HIVST) amongst urban, peri-urban and rural communities in Zambia, including a cluster-randomised trial of community-based HIVST distribution

LSHTM Ethics Ref: 10660

Thank you for responding to the Interventions Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Investigator CV	NH CV 201511	01/01/2015	1
Investigator CV	HA CV 201507	01/07/2015	1
Investigator CV	VB Biosketch 20150901	01/09/2015	1
Investigator CV	DT CV 201511	01/11/2015	1
Investigator CV	KNK CV 201511	01/11/2015	1
Investigator CV	MC CV 201503	01/11/2015	1
Investigator CV	MN CV 201511	01/11/2015	1
Investigator CV	AM CV 20151102	02/11/2015	1
Sponsor Letter	QA789_Sponsor letter_290116	16/01/2016	1
Investigator CV	JM CV 20160127	27/01/2016	1
Investigator CV	KM CV	02/02/2016	1
Investigator CV	MS CV	02/02/2016	1
Investigator CV	LM CV	02/02/2016	1
Information Sheet	STAR ZM info and consent 11 May	11/05/2016	1
Local Approval	STAR APPROVAL LETTER 20160215	11/05/2016	1
Covering Letter	ZM CRT Response to comments 11 May	11/05/2016	1
Protocol / Proposal	List of contents for baseline survey MN 4 May	11/05/2016	1
Protocol / Proposal	STAR Protocol Zambia (Trial) MN 12 May CLEAN	12/05/2016	1

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

[redacted]

Professor John DH Porter
Chair

ethics@lshtm.ac.uk
http://www.lshtm.ac.uk/ethics/

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BIOMEDICAL RESEARCH ETHICS COMMITTEE

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Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

Assurance No. FWA00000338
IRB00001131 of IORG0000774

15th February, 2016.

Our Ref: 013-11-15.

Dr. Helen Ayles,
ZAMBART,
University of Zambia,
School of Medicine,
Ridgeway Campus,
P.O Box 50697,
Lusaka

Dear Dr. Ayles,

RE: RESUBMITTED RESEARCH PROPOSAL: **"SELF-TESTING FOR HIV AMONGST PERI-URBAN AND RURAL COMMUNITIES IN ZAMBIA, INCLUDING A CLUSTER RANDOMIZED TRIAL OF COMMUNITY-BASED HIVST DISTRIBUTION" (REF. No. 013-11-15)**

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee on 12th February, 2016. The proposal is approved.

CONDITIONS:

- This approval is based strictly on your submitted proposal. Should there be need for you to modify or change the study design or methodology, you will need to seek clearance from the Research Ethics Committee.
- If you have need for further clarification please consult this office. Please note that it is mandatory that you submit a detailed progress report of your study to this Committee every six months and a final copy of your report at the end of the study.
- Any serious adverse events must be reported at once to this Committee.
- Please note that when your approval expires you may need to request for renewal. The request should be accompanied by a Progress Report (Progress Report Forms can be obtained from the Secretariat).
- **Ensure that a final copy of the results is submitted to this Committee.**

Yours sincerely,

[redacted]

M.C Maimbolwa PhD
CHAIRPERSON

Date of approval: 15th February, 2016. **Date of expiry:** 14th February, 2017.

APPENDIX V: STAR ENDLINE SURVEY

Version - 18 Sept. 2017

Overview of tabs

Tab	Question count	Notes
hh - response	11	
indiv - eligibility criteria	12	
indiv. - hh enumeration	18	
indiv - sociodem	20	
indiv ext. - sociodem	2	
indiv ext. - decision	1	
indiv - testing	16	
indiv ext. - testing	38	Includes costs
indiv - cbda	15	
indiv male only - circ	5	
indiv - sex beh	7	
indiv ext. - HIV care	9	
indiv ext - stigma	13	
indiv ext F - IPV	8	
indiv - end	3	This is the end of the individual survey - will need an option to add an additional respondent within the household (see below)

For YN, include don't know and declined to answer, with following coding: 1 Yes 2 No 8 Don't know 9 Declined to answer
Endline survey will be structured to loop individual responses within households to prevent problems merging households and individuals later
Households that refuse the survey or vacant units can be collected on the first few screens, with no need to associate individual responses.

Version - 18 Sept. 2017

Household questionnaire - response

To be completed by interviewer/head of household. ENDLINE NOTE: Have discussed collecting this on paper instead of tablet - to be discussed by teams

Question No.	Construct	Variable	Question	Data type	Skips	Ranges for continuous variables	Hint	Notes
HH01	Clinic ID	clinicid		Choose from list of clinics				
HH02	Village ID	villageid		Choose from list of villages				
HH03	Household ID/Barcode	hhbarcode		Unique ID or barcode?				
HH04	Interviewer ID	interviewerid		Choose from list of interviewers, or auto set by signing into tablet				
HH05	Device ID							
HH06	Date of interview	intdate		Current date		Should be set to date in device, with option to change if incorrect		
HH07	Start time	starttime		Time		Should be set to time in device		
HH08	Visit 1 outcome	visitlog1		Choose from list: household interview started; household interview refused; housing unit vacant				
HH09	Visit 2 outcome	visitlog2		Choose from list: household interview started; household interview refused; housing unit vacant				
HH10	Visit 3 outcome	visitlog3		Choose from list: household interview started; household interview refused; housing unit vacant				
HH11	Lat-Long	latlong		Automatic				GPS in phone/tablet

Version - 18 Sept. 2017

Individual questionnaire - eligibility to complete survey

To be completed by all people 16 years or older within the household
Note that length of residence will NOT be a criteria for exclusion/inclusion in Malawi/Zambia

Question No.	Construct	Variable	Question	Data type	Skips	Ranges for continuous variables	Hint	Notes
IE01	Clinic ID	clinicid		Choose from list of clinics				
IE02	Village ID	villageid		Choose from list of villages				
IE03	Interviewer ID	interviewerid		Choose from list of interviewers, or auto set by signing into tablet				
IE04	Device ID							
IE05	Date of interview	intdate		Current date		Should be set to date in device, with option to change if incorrect		
IE06	Start time	starttime		Time		Should be set to time in device		

Question No.	Construct	Measurement	Variable	Data type	Skips	Ranges for continuous variables	Hint	Notes
IE07	Age - older than 16y	Are you 18 years of age or older?	eligage	YN	If no, skip to elig16parent			

Version - 18 Sept. 2017

Question No.	Construct	Measurement	Variable	Data type	Skips	Ranges for continuous variables	Hint	Notes
IE08	Individual consent	Have you consented (or do you consent) to participate?	eligcons	YN	If no, skip to end			
IE09	Parental consent for ages 16-17	(If participant is 16-17 years old) Has parent/guardian consented to participation?	elig16parent	YN	If no, skip to end			
IE10	Individual ID	Individual ID	individ	Unique ID or barcode				
IE11	Selected for extended questionnaire	select		Randomly select 1/5 (or so) individuals for extended household/individual questionnaire.				

Version - 18 Sept. 2017

Individual questionnaire - household enumeration

To be completed by head of household or representative - all households

Question No.	Construct	Variable	Question	Data type	Skips	Ranges	Hint	Notes
HE01	Respondent for household SES questions	hhrespond	[Interviewer to select appropriate action]	1 Respondent is head of household 2 Respondent is reporting on behalf of head of household, who is not available to answer the questionnaire 3 Respondent is not head of household or reporting on behalf	If 3, skip to indiv - sociodem		[HINT TO INTERVIEWER: CHECK THAT ONLY ONE PERSON IDENTIFIES AS THE HEAD OF HOUSEHOLD OR IS REPORTING ON BEHALF OF THE HEAD OF HOUSEHOLD]	
HE02	First name	firstnamehoh	What is the first name of the head of household?	Short text				
HE03	Surname	surnamehoh	What is the surname of the head of household?	Short text				
HE04	Sex	hohsex	What is the sex of the head of household?	1 Male 2 Female	Skip if hhrespond=1			
HE05	Date of birth	hohdob	What is the date of birth of the head of household?	Select for Day Month Year	Skip if hhrespond=1 If year is known, skip to hohedu	TODAY'S DATE - 16]-[TOMORROW'S DATE-99]		
HE06	Age in years	hohageyrs	How old is the head of household?	Number	Skip if hhrespond=1	16-99		

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Question No.	Construct	Variable	Question	Data type	Skips	Ranges	Hint	Notes
HE07	Educational attainment	hohedu	What was the highest level of education that the head of household completed?	1 No formal schooling; 2 Primary incomplete or complete 3 Secondary incomplete 4 Secondary complete 5 Tertiary or higher 9 Decline to answer	Skip if hhrespond=1			

I would like to ask you information about this household.

HE08	Count of people in the household	hhct	How many people live in the household? Include all people who normally live and share meals in the household	Number		>0 & <30 hhct=sum(hhwmnct-hhchildct)	Include people who normally live in the household and share food together, including yourself [HINT TO INTERVIEWER: WRITE DOWN THE SEX AND AGES OF EVERYONE IN THE HOUSEHOLD WITH THE RESPONDENT]	
HE09	Count of people 18 years and older	hhadultct	How many adults 18 years or older live in the household?	Number		hhadultct=sum(hhwmnct-hhmnct)	Include people who were born before [TODAY'S DATE - 18 YEARS] [HINT TO INTERVIEWER: VERIFY WITH LIST]	
HE10	Count of women over age 18 years	hhwmnct	Of the adults in this household (18 years or older), how many are women?	Number		hhadultct=sum(hhwmnct-hhmnct) hhct=sum(hhwmnct-hhchildct)	Include women who were born before [TODAY'S DATE - 18 YEARS] [HINT TO INTERVIEWER: VERIFY WITH LIST]	

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Question No.	Construct	Variable	Question	Data type	Skips	Ranges	Hint	Notes
HE11	Count of men over age 18 years	hhmnct	Of the adults in this household (18 years or older), how many are men?	Number		hhadultct=sum(hhwmnct-hhmnct) hhct=sum(hhwmnct-hhchildct)	Include men who were born before [TODAY'S DATE - 18 YEARS] [HINT TO INTERVIEWER: VERIFY WITH LIST]	
HE12	Count of girls age 16-17 years	hhadgrlct	Of the people in this household aged 16-17 years, how many are girls?	Number		hhct=sum(hhwmnct-hhchildct)	Include girls who were born between [TODAY'S DATE - 16 YEARS] to [TOMORROW's DATE - 18 YEARS] [HINT TO INTERVIEWER: VERIFY WITH LIST]	
HE13	Count of boys age 16-17 years	hhadboyct	Of the people in this household aged 16-17 years, how many are boys?	Number		hhct=sum(hhwmnct-hhchildct)	Include boys who were born between [TODAY'S DATE - 16 YEARS] to [TOMORROW's DATE - 18 YEARS] [HINT TO INTERVIEWER: VERIFY WITH LIST]	
HE14	Count of children age 0-15 years	hhchildct	How many children 0-15 years are in this household?	Number		hhct=sum(hhwmnct-hhchildct)	Include children who were born after [TOMORROW'S DATE - 16 YEARS] [HINT TO INTERVIEWER: VERIFY WITH LIST]	
HE15	Identifying vulnerable subpopulations - orphans	orphan	In this household, is there any child whose mother and/or father has died or whose mother and/or father is not resident in the household and is very sick?	Y-N-DTA				Adapted from Malawi DHS

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Question No.	Construct	Variable	Question	Data type	Skips	Ranges	Hint	Notes
HE16	Identifying vulnerable subpopulations - persons with disabilities	disability	In this household, is there any person with a disability? Disability refers to a person who is limited in the kind or amount of activities that he or she can do because of on-going difficulties due to long term physical, mental or health problems	Y-N-DTA				Disability definition from Zambia 2000 census, but may be able to find something more recent?
HE17	Identifying vulnerable subpopulations - any domestic workers	domestics	In this household, is there anyone paid or otherwise supported in order to help with cleaning or other tasks in the home?	Y-N-DTA	If no or DTA, skip to next section			
HE18	Identifying vulnerable subpopulations - domestic workers living in	domlivein	Does this person live in this household?	Y-N-DTA				

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Household survey - questions asked to head of household

To be completed by head of household or representative - sampled households. ENDLINE NOTE - includes only household-level SES questions
(Note - assume this is all households surveyed [i.e., short and longer forms])

Question No.	Construct	Variable	Question	Data type	Skips	Ranges	Hint	Notes
HS01	Household assets - household level	hhasset_*	Does your household have or own:	A Electricity - Y-N-DTA B Radio - Y-N-DTA C Working television - Y-N-DTA E Non-mobile telephone (landline) - Y-N-DTA F Refrigerator - Y-N-DTA G Bed with mattress - Y-N-DTA H Table and chair Y-N-DTA Malawi only: MA Koloboyi - Y-N-DTA MB A paraffin lamp other than a koloboyi - Y-N-DTA		If decline to answer for one choice, must have decline to answer for all choices		assets from DHS surveys. ENDLINE NOTE: added assets that will help differentiate rural households
HS02	Household assets - any individual within household	hhassetind_*	Does any member of this household own:	A Mobile phone - Y-N-DTA B Working automobile (car or truck) - Y-N-DTA C Bicycle - Y-N-DTA D Working motorcycle or motor scooter - Y-N-DTA E An animal-drawn cart - Y-N-DTA				

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Question No.	Construct	Variable	Question	Data type	Skips	Ranges	Hint	Notes
HS03	Household agricultural land	hhland	Approximately how many acres of land have been cultivated by the household during the last production season?	Two digit number, 998 = d/k, 999=DTA				Adapted from Malawi HIS 2010-2011
HS04	Household cattle - y/n	hhcattle	Have you or anyone in your household raised or owned cattle during the past 12 months?	Y-N-DTA	If no/DTA, skip to hfiunceryn			
HS05	Household cattle - count	hhcattlect	How many cattle does your household own at present?	Two digit number, 998 = d/k, 999=DTA				
HS06	HFIAS - uncertainty	hfiunceryn	In the past four weeks, did you worry that your household would not have enough food?	Y-N-DTA	If no or DTA, skip to hfiqualiyn			
HS07	HFIAS - uncertainty frequency	hfiuncerfreq	How often did this happen?	1 Rarely (once or twice in the past four weeks) 2 Sometimes (3-10 times in past four weeks)				
HS08	HFIAS - quality	hfiqualiyn	In the past four weeks, were you or any household member not able to eat the kinds of foods you preferred because of a lack of resources?	Y-N-DTA	If no or DTA, skip to hfiquantyn			
HS09	HFIAS - quality frequency	hfiqualifreq	How often did this happen?	1 Rarely (once or twice in the past four weeks) 2 Sometimes (3-10 times in past four weeks) 3 Often (more than 10 times in past four weeks) 9 Decline to answer				

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Question No.	Construct	Variable	Question	Data type	Skips	Ranges	Hint	Notes
HS10	HFIAS - quantity	hfiquantyn	In the past four weeks, did you or any household member go to sleep hungry beause there was not enough food?	Y-N-DTA	If no or DTA, skip to end of section			
HS11	HFIAS - quantity frequency	hfiquantfreq	How often did this happen?	1 Rarely (once or twice in the past four weeks) 2 Sometimes (3-10 times in past four weeks) 3 Often (more than 10 times in past four weeks) 9 Decline to answer				

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Individual - sociodemographics

To be completed by all individuals consenting to participate within the household

I would now like to ask you information about yourself.

Question No.	Construct	Variable	Wording of question	Data entry	Skips	Ranges for continuous variables	Hint	Notes
A01	Relationship to head of household	hohrel	What is your relationship to the head of household?	1 I am the head of household 2 I am the wife or husband of the head of household 3 I am a son or daughter of the head of household 4 I am a son-in-law or daughter-in-law of the head of household 5 I am a grandchild of the head of household 6 I am a parent of the head of household 7 I am a parent-in-law of the head of household 8 I am a brother or sister of the head of household 9 I am a niece or nephew of the head of household 10 I am co-wife of the head of household 11 I am an adopted/foster/stepchild of the head of household 12 I am an other relative of the head of household 13 I am a domestic servant				From DHS 2010 with lodger and domestic servant added (asked in a separate question in DHS).

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Question No.	Construct	Variable	Wording of question	Data entry	Skips	Ranges for continuous variables	Hint	Notes
A09	Allowance income	allow	In a month, how much do you usually receive in allowances or gratuities, including in-kind payments such as uniform, housing, food and transport that were not included in the salary you just reported?	Number		0-??, 9999999	Estimate cash value of any in-kind payments received Enter 9999999 for decline to answer Enter 0 if no payments were received	from Linda
A10	Business income	businessinc	In a month, how much average profit do you earn on business enterprises that give you constant earnings?	Number		0-??, 9999999	Sum up the average profits for all enterprises owned Enter 9999999 for decline to answer Enter 0 if no payments were received	from Linda
A11	Informal income wage	informalwage	In a month, how much do you earn from informal income sources aside from those listed above?	Number		0-??, 9999999	Enter 9999999 for decline to answer Enter 0 if no payments	from Linda
A12	Self-reported health	srhealth	How do you rate your general health?	1 Very good 2 Good 3 Fair 4 Poor 9 Decline to answer				Prompt respondents to help reinforce that this is *all* health, not just HIV
A13	Usual household member	resid2mos	Have you resided in this community for the past two months?	Y-N-DTA	Not ZW?			

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Question No.	Construct	Variable	Wording of question	Data entry	Skips	Ranges for continuous variables	Hint	Notes
A14	Duration of residence	residlastyr	Did you live here 12 months ago? That is, did you live here in [MO] 2016?	Y-N-DTA	If yes, skip to marital			
A15	Move-in date if less than 1 year resident	movedate	In what month did you move to this dwelling?	Select for Month Year		If resid2mos is yes, [THIS MONTH - 12 MONTHS]-[THIS MONTH-2 MONTHS] If resid2mos is no, [THIS MONTHS - 2 MONTHS]-[THIS		
A16	Marital status	marital	What is your current marital status?	1 Married or living as married 2 Never married 3 Widowed/separated/ divorced 9 Decline to answer	If 1 or DTA, skip to widowed If 2 or 3, skip to children			
A17	Partnership	partnerlength	How long have you been together with your spouse or partner [or first spouse/partner for persons with multiple spouses]?	1 <1 year 2 1-5 years 3 More than 5 years 9 Decline to answer	If DTA, skip to widowed			
A18	Living with spouse/partner	livepartner	Are you currently living with your spouse/partner?	Y-N-DTA				
A19	Ever widowed	widowed	Have you ever lost a spouse due to death?	Y-N-DTA				

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Question No.	Construct	Variable	Wording of question	Data entry	Skips	Ranges for continuous variables	Hint	Notes
A20	Children	children	How many biological children do you have?	Number	0-20, 99		Enter 99 for decline to answer	

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Individual extended - sociodemographics

To be completed by SELECTED individuals ONLY

Question	Variable	Construct	Wording of question	Data entry	Skips	Ranges for continuous variables	Hint	Notes
AE01	phq1	PHQ-2 1	Over the past 2 weeks how often have you been having little interest or pleasure in doing things?	1 Not at all 2 Several days 3 More than half the days 4 Nearly every day 5 Decline to answer				PHQ-2
AE02	phq2	PHQ-2 2	Over the past 2 weeks how often have you been feeling down, depressed or hopeless?	1 Not at all 2 Several days 3 More than half the days 4 Nearly every day 9 Decline to answer				PHQ-2

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Individual - past testing (all individuals)

ENDLINE NOTE: removed "most important reason" question, added questions from midline and on CBDA

Core questions asked of all respondents
Core testing questions asked of all testers about lifetime testing
Non-tester questions

To be completed by all individuals consenting to participate within the household

Prompt: Now I would like to ask you some questions about your experiences testing with HIV.

Question #	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
B01	evertest	Ever tested for HIV	Have you ever been tested for HIV?	Y-N-DTA	If yes, skip to yrtestcount			
B02	thoughttest	Thought about testing	Have you ever thought about testing for HIV?	Y-N-DTA				
B03	whynottest_X	Why not tested?	What best describes why you haven' t tested for HIV?	A I am not at risk of being HIV positive or contracting HIV infection - Y-N-DTA B. I don't want to know my HIV status - Y-N-DTA C. I am afraid of testing positive or dying after HIV positive results - Y-N-DTA D. I am afraid of stigma and discrimination related to HIV testing - Y-N-DTA [COMMENT: ?? I AM AFRAID OTHER PEOPLE WILL JUDGE ME OR TREAT ME POORLY IF I TEST FOR HIV??] E. I don't feel sick enough to test for HIV - Y-N-DTA F. HIV testing is not a dignified or important thing to do at my age - Y-N-DTA G. I am too young to test or not yet sexually active - Y-N-DTA [COMMENT: DON'T KNOW ABOUT THIS - WOULDN'T THEY JUST PUT ANSWER A] H. My partner won't let me test or may blame me for bringing HIV into this relationship - Y-N-DTA [COMMENT: THE SECOND PART IS QUITE SPECIFIC. MAYBE INSTEAD: MY PARTNER WON'T LET ME TEST OR I AM AFRAID OF THE CONSEQUENCES OF TESTING ON MY RELATIONSHIP I. My family member(s) won't let me test - Y-N-DTA [COMMENT: COULD WORD SIMILAR TO THE SUGGESTED ANSWER FOR THE PARTNER QUESTION] J. It is too expensive for me to visit the facility, or the facility is too far away - Y-N-DTA K. I cannot take time off work to go test - Y-N-DTA [COMMENT: COMBINE WITH ANSWER BELOW: IT IS DIFFICULT FOR ME TO TAKE TIME OUT OF THE DAY TO GO TEST]		If decline to answer for one choice, must have decline to answer for all choices		Read out - revised categories for endline
B04	knowfac	Know of facility	Do you know any facilities offering HIV testing and counselling to people who live around here?	Y-N-DTA	If no or DTA, skip to thoughttest			Note that following non-user questions are from WHO generic tools
B05	faceasy	How easy to reach facility	If you wanted to go, how easy or difficult would it be for you to go the health facility from your home?	1 Very easy 2 Somewhat easy 3 Somewhat difficult 4 Very difficult 9 Decline to answer				
B06	offeredtest	Had test offered	Have you ever had an HIV test offered to you when you were at a health facility or in your home?	Y-N-DTA	Go to heardselftest			End of non-user section

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Question N	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
B07	yrtestcount	Testing in last twelve months	In the last 12 months, that is before [TODAY'S DATE-12 MONTHS], how many times have you tested for HIV?	Number	If 88 or 99, skip to testdate_1	0-15, 88, 99	If you had a test to confirm earlier results, this should be counted separately Enter 88 for don't know or	
B08	lifetestcount	Lifetime test count	In total, how many HIV tests have you had in your lifetime?	Number		1-50 (value must be greater than yrtestcount), 88, 99	If you had a test to confirm earlier results, this should be counted separately Enter 88 for don't know or 99 for decline to answer	
B09	testdate_1	Dates of last three tests	What was the date of your most recent HIV test?	MY	(MN additional note: all respondents to complete through end of section, then go to loop - skip next two questions if respondent has only tested one time)	[TODAY'S DATE]-[TODAY'S DATE-12 MONTHS] based on yrtestcount, otherwise [TOMORROW'S DATE-12 MONTHS]-[DATE OF BIRTH]	For dates prior to 2015, indicate only the year.	
B10	testdate_2	Dates of last three tests	What was the date of your second-most recent HIV test?	MY	If lifetestcount=1, 1 count If lifetestcount=2, 2 count If lifetestcount>=3, 3 count If lifetestcount=88 or 99 & yrtestcount=1, 1 field If lifetestcount=88 or 99 & yrtestcount=2, 2 count If lifetestcount=88 or 99 & yrtestcount>=3, 3 count If yrtestcount=88 or 99, 1 field	[TODAY'S DATE]-[TODAY'S DATE-12 MONTHS] based on yrtestcount, otherwise [TOMORROW'S DATE-12 MONTHS]-[DATE OF BIRTH]	For dates prior to 2015, indicate only the year.	
B11	testdate_3	Dates of last three tests	What was the date of your third-most recent HIV test?	MY	If lifetestcount=1, 1 count If lifetestcount=2, 2 count If lifetestcount>=3, 3 count If lifetestcount=88 or 99 & yrtestcount=1, 1 field If lifetestcount=88 or 99 & yrtestcount=2, 2 count If lifetestcount=88 or 99 & yrtestcount>=3, 3 count If yrtestcount=88 or 99, 1 field	[TODAY'S DATE]-[TODAY'S DATE-12 MONTHS] based on yrtestcount, otherwise [TOMORROW'S DATE-12 MONTHS]-[DATE OF BIRTH]	For dates prior to 2015, indicate only the year.	

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Question #	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
B12	heardselftest	Heard of self-testing	Have you heard about HIV self-testing as a method for testing for HIV? [Definition if needed from WHO technical report: HIV self-testing is a process whereby a person who wants to know his or her HIV status collects a specimen, performs a test, and interprets the test result in private.]	YN	If no and evertest=yes, skip to knowresults. If no and evertest=no or DTA, skip to knowfollowup			
B13	howheard_*	How heard of HIV self-testing	Where did you hear about HIV self testing?	Check all that apply: A. community-based distributor B. friend or family member C. other community member D. healthcare provider E. VMMC mobilizer F. Tunza/New Start counselor G. Workplace peer educator H. Targeted outreach communication I. Community drama J. National events (VCT day, national health week & World AIDS Day) K. Print media: leaflet/brochure L. Other media: whatsapp/Facebook M. Other person or event N. Decline to answer	If evertest=no or DTA, go to knowfollowup	If decline to answer for one choice, must have decline to answer for all choices		PHS to review with colleagues
B14	selftestever	Self test ever	Have you ever used a self-test to test for HIV?	Y-N-DTA	If no or DTA, skip to knowfollowup			
B15	selftest12mos	Self test within past 12 months	Within the past 12 months, have you used a self-test to test for HIV?	Y-N-DTA				
B16	knowfollowup	Awareness of follow-up - HIV care	If you were to test positive , do you know how to access appropriate follow-up services?	YN			Follow-up services include care and treatment services, including ART and confirmative testing for those testing positive.	Note that there is a similar question on VMMC in the VMMC section

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Individual - past testing

To be completed by SELECTED individuals ONLY
For each of last three tests
(Note that past year time is reflected in IPV questions)
Costs questions are in blue rows and should be asked only of the first test if this test occurred within the past 12 months

Prompt [OUTSIDE LOOP]: Now I would like to ask you more about your last [3] HIV tests. If you have had a test to confirm earlier results, I want you to tell me about each test separately.

Prompt [INSIDE LOOP]: For these sets of questions, I would like to ask you about your [last/second-to-last/third-to-last] test on [testdate_1]

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
C01	testloc_X	Location of test	Where did you have your [last/second-to-last/third-to-last] HIV test?	1 Health facility (not ANC) 2 ANC centre 3 VCT centre 4 HTC in the community (ie. Mobile VCT) 5 Self-test at the health facility 6 Self-test at home or in the community				In the community = not at a facility/not at home. Note that respondents will have already answered this for the first test in the indiv-testing questions and could be skipped or preanswered?
C02	testinit_X	Initiation of test	Who initiated the test?	1 Own initiative: I approached the provider or or distributor about testing 2 Partner initiative: My partner approached me about testing. 3 Offered by health worker or community volunteer (CBDA): A provider or health worker approached me and suggested testing 4 VMMC: A VMMC mobilizer approached me to test 5 Other person: Another person (not a health worker, VMMC mobilizer, or partner) approached me and suggested testing 6 Decline to answer	If testdate_X<12 months & selftest12mos=no, skip to C07 If selftestever=no, skip to C07			Split first item into own then partner (done)
C03	selftest_X	Self-test	Was this test a self-test?	Y-N-DTA	If no or DTA, skip to discusspart_X			Two sets of questions on partner tests based on self-test/not self test - this is potentially confusing for data analysis
C04	selftestsource_X	Self-test - where from	Who did you obtain the self-test from?	1 CBDA 2 VMMC mobilizer 3 Health care worker 4 Partner 5 Parent 6 Sibling 7 Other family member 8 Friend 9 Chief 10 Employer 11 Teacher 12 Religious leader 13 Other 99 Decline to answer				

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Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
C05	selftestalone_X	Self-test - anyone present?	Was anyone else with you when you self-tested?	Y-N-DTA	If no, skip to testdur or knowres_X			
C06	selftestpresent_X	Self-test - who present?	Who was with you when you performed the self-test?	(Check all that apply) A CBDA - Y-N-DTA B Health care worker - Y-N-DTA C Partner - Y-N-DTA D Parent - Y-N-DTA E Other family member - Y-N-DTA F Friend - Y-N-DTA G Chief - Y-N-DTA H Employer - Y-N-DTA I Teacher - Y-N-DTA J Religious leader - Y-N-DTA K Other - Y-N-DTA		If decline to answer for one choice, must have decline to answer for all choices		Added HCW to options
C07	discusspart_X	Discussion with partner	Did you discuss testing with your partner before you tested?	Y-N-N/A-DTA	If no or N/A or DTA, skip to testdur If no or N/A or DTAand not selected for extended survey or not the most recent test that occurred within past 12 months, skip to knowres_X	If testinit_X=2 or selftestsource=4 or seltestpresent_X_C=yes, then discusspart_X should probably be yes		
C08	testpart_X	Testing with partner	Did you test at the same time as when your partner also tested?	Y-N-N/A-DTA	If not selected for extended survey and not the most recent test that occurred within past 12 months, skip to knowres_X			Note rewording to differentiate between testing with partner present and testing while partner tested
C09	testpart_X	Testing with partner	Did you test with your partner in your [LAST/SECOND/THIRD TO-LAST] HIV test?	YN	Valid for non-self-tests only			Note - there is a question about partner testing in the short testing section adminstered to everyone. Reordered questions so testing with partner and self-testing with partner both before costs
C10	testdur	Costs - duration	**[Prompt for costs questions:] Now, I would like to ask you about the incurred costs from your last HIV test ?** How long did it take to have your test? Including travelling to the facility waiting to be tested and waiting for your results?	Select Minutes Hours	Only ask if selected for extended survey and the most recent test that occurred within past 12 months	Minutes: 0-59 Hours: 1-90	Enter 99 for decline to answer	
C11	testvisitreas	Costs - reason for travel	Was this visit to the [LOCATION OF TEST] primarily to be tested for HIV?	Y-N-DTA	Only ask if selected for extended survey and the most recent test that occurred within past 12 months			Note that [LOCATION OF TEST] will be gathered earlier in the questionnaire

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Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
C12	testtrans	Costs - transit mode	How did you get to the [LOCATION OF TEST] ?	1 Walked 2 Took bicycle 3 Took public transport 4 Used own car or motorcycle 5 Took taxi 6 Other	If 1 or 2, skip to C13 If C01=5, skip to C13 Only ask if selected for extended survey and the most recent test that occurred within past 12 months			
C13	costtrans	Costs - transit costs	How much did you pay to get to [LOCATION OF TEST] and back home?	Number	Only ask if selected for extended survey and the most recent test that occurred within past 12 months	1-??	Enter 888888 for don't know and 999999 for decline to answer	
C14	consultfee	Costs - consultation	Did you have to pay any fees to take the HIV test? This includes consultation, registration, the test kit, and health passport.	Y-N-DTA	Skip if selftest_X=yes If no or DTA, skip to C15 Only ask if selected for extended survey and the most recent test that occurred within past 12 months			
C15	costconsult	Costs - consultation costs	How much in fees did you pay to take the HIV test?	Number	Skip if selftest_X=yes Only ask if selected for extended survey and the most recent test that occurred within past 12 months	1-??	Enter 888888 for don't know and 999999 for decline to answer	
C16	childcare	Costs - child care	Did you have to pay for anyone to cover your regular duties while getting the HIV test? This includes to take care of your children, supervise your shop, or perform your agricultural activities.	Y-N-DTA	If no or DTA, skip to C17 Only ask if selected for extended survey and the most recent test that occurred within past 12 months			
C17	costchildcare	Costs - child care costs	How much did you pay for someone to cover your regular duties?	Number	Only ask if selected for extended survey and the most recent test that occurred within past 12 months	1-??	Enter 888888 for don't know and 999999 for decline to answer	

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Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
C18	food	Costs - food	Did you have to purchase food outside the home because of your HIV test?	Y-N-DTA	If no or DTA, skip to C19 Only ask if selected for extended survey and the most recent test that occurred within past 12 months			
C19	costfood	Costs - food costs	How much did you pay for food?	Number	Only ask if selected for extended survey and the most recent test that occurred within past 12 months	1-??	Enter 888888 for don't know and 999999 for decline to answer	
C20	other	Costs - other	Did you have any other incurred costs related to your last HIV test?	Y-N-DTA	If no or DTA, skip to C21 Only ask if selected for extended survey and the most recent test that occurred within past 12 months			
C21	costother	Costs - other costs	If yes, how much did you pay?	Number	Only ask if selected for extended survey and the most recent test that occurred within past 12 months	1-??	Enter 888888 for don't know and 999999 for decline to answer	
C22	costworklost	Costs - how much earned	How much would you have earned during the time you took off to get tested for HIV?	Number	Only ask if selected for extended survey and the most recent test that occurred within past 12 months	0-??	Enter 888888 for don't know and 999999 for decline to answer	Note: if in kind, need prompt to obtain value
C23	costsource	Costs - source	Who primarily provided the money to support the costs of accessing the test?	1 Myself 2 My partner 3 Myself and my partner jointly 4 Family 5 Friend 6 Employer 7 Other 9 Decline to answer	Only ask if selected for extended survey and the most recent test that occurred within past 12 months			
C24	knowres_X	Results of last HIV test	You don't have to tell me if you don't want to, but what were the results of this test? [COMMENT: DO WE WANT TO ASK AFTER IF THIS IS THE FIRST TIME THEY RECEIVED A POSITIVE TEST RESULT]	1 Positive 2 Negative 3 Indeterminate 9 Decline to answer	If knowres_X=1 go to firstpos_X; otherwise to regretimm_X			
C25	firstpos_X	First positive result?	Was this the first time you had received a positive result?	Y-N-DTA				

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
C26	regretimm_X	Regret testing immediately after testing	Aside from the results, did you have any regrets about this HIV test immediately after you completed the test?	Y-N-DTA				
C27	regretnow_X	Regret testing now	Looking back on this test now, do you regret taking this test now?	Y-N-DTA				
C28	relprob_X	Problems caused by test	Were there any problems in your relationship caused by this HIV test?	Y-N-N/A-DTA				
C29	testforce_X	Forced to test	If you were forced to test, who forced you?	(Check all that apply) A Not forced to test - Y-N-DTA B CBDA - Y-N-DTA C Health care worker - Y-N-DTA D Partner - Y-N-DTA E Parent - Y-N-DTA F Other family member - Y-N-DTA G Friend - Y-N-DTA H Chief - Y-N-DTA I Employer - Y-N-DTA J Teacher - Y-N-DTA K Religious leader - Y-N-DTA L Other - Y-N-DTA		A cannot be combined with other responses If decline to answer for one choice, must have decline to answer for all choices		
C30	disclose_X	Disclosed results	Did you disclose the result of this test to anyone? [COMMENT: WE ARE NOT ASKING ABOUT FORCED DISCLOSURE NOW?]	(Check all that apply) A Did not disclose this result Y-N-DTA B CBDA - Y-N-DTA C Health care worker - Y-N-DTA D Partner - Y-N-DTA E Parent - Y-N-DTA F Other family member - Y-N-DTA G Friend - Y-N-DTA H Chief - Y-N-DTA I Employer - Y-N-DTA J Teacher - Y-N-DTA K Religious leader - Y-N-DTA L Other - Y-N-DTA		A cannot be combined with other responses If decline to answer for one choice, must have decline to answer for all choices		
C31	forcedisc_X	Forced to disclose	If you were forced to disclose your results, or someone disclosed your status to another person without your permission, who forced this disclosure?	(Check all that apply) A Not forced to disclose result - Y-N-DTA B CBDA - Y-N-DTA C Health care worker - Y-N-DTA D Partner - Y-N-DTA E Parent - Y-N-DTA F Other family member - Y-N-DTA G Friend - Y-N-DTA H Chief - Y-N-DTA I Employer - Y-N-DTA J Teacher - Y-N-DTA K Religious leader - Y-N-DTA L Other - Y-N-DTA		A cannot be combined with other responses If decline to answer for one choice, must have decline to answer for all choices		

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Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
C32	aftercare_X	Confirmatory testing	After this HIV test, did you receive a test confirming your HIV diagnosis or additional care related to your HIV status?	Y-N-DTA	If no or DTA, go to C35			For log frame reporting, include positives only?
C33	afterdet_X	What care received	What care did you receive?	1 Confirmatory test only [COMMENT: CHANGE TO: FOLLOW-UP TEST TO CONFIRM THE RESULTS OF THIS TEST] 2 ART initiation [COMMENT: CHANGE TO: STARTED ON ART FOR THE FIRST TIME] 3 Restarted on ART 4 Other care (not including either confirmatory test or ART) 9 Decline to answer	If aftercare_X=yes and respondent is female, skip to next testing loop or partnerstatknwn			
C34	nocare	Reasons for not receiving care	Why have you not (yet) received a confirmatory test or obtained treatment?	Why have you not (yet) received a confirmatory test or obtained treatment? (Check all that apply) A. Afraid of stigma and discrimination from going to a clinic B. I don't want to be seen at the clinic C. I do not feel sick D. My partner won't let me go to the clinic E. Family member(s) won't let me go to the clinic F. It is too expensive for me to visit the facility, or the facility is too far away G. I cannot take time off work to go to receive an additional test or care H. It will take too much time to receive an additional test or care I. Health facilities offer poor quality HIV services J. I am afraid there will be drug shortages K. I do not believe that my status will be kept confidential L. I do not trust the results from HIV testing M. I don't know where to go to access services N. Other reason O. Decline to answer		If decline to answer for one choice, must have decline to answer for all choices		
C35	vmmc_X	VMMC after testing	[Asked of men only:] Did you go for VMMC (voluntary medical male circumcision) after this test?	1 Yes 2 No 3 I am already circumcised 9 Decline to answer	Valid only for men who do not report HIV+ status (knowres_X>1).			END of testing loop
C36	partnerstatknwn	Partner status known	Do you know the result of your current partner's [most recent] HIV test?	Y-N-N/A-DTA	If N/A, skip to C39			
C37	ownstatknwn	Partner knows respondent's status	Does your current partner know your HIV status?	Y-N-N/A-DTA				

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
C38	prefmode	Prefered mode of testing	If you were to test for HIV again, where would you prefer to have this next test?	1 Hospital, clinic or health center 2 - VCT centre 3 - Mobile HTC 4 At-home HTC 5 Self-testing with the distributor present 6 Self-testing without the distributor present 7 Decline to answer				

Version - 18 Sept. 2017

Individual - past testing (all individuals)
ENDLINE NOTE: removed "most important reason" question, added questions from midline and on CBDA

To be completed by all consenting individuals in the INTERVENTION clinics

Prompt: Now I would like to ask you some questions about your experiences with the community based distribution agents delivering HIVST kits

Questio	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
CA01	comdis	Awareness of community distribution	Before your discussion with study staff today, were you aware that community based distribution agents were distributing self-test kits near here?	Y-N-DTA	If no or DTA, skip to next section Skip if selftestsource_ X=1	Probe if no but selftestever=yes: You have stated that you have previously self-tested. Did you receive the kit outside of recent community distribution of self-test kits? [??OR SOMETHING LIKE THAT MIGHT BE NEEDED??] If yes, check if consistent with heardselftest (should be yes)		
CA02	cbdahouse	CBDA house visit	Did community based distribution agents come to your house to offer self-test kits? [COMMENT: IT COULD BE THEY RECEIVED THE KIT OUTSIDE THEIR HOUSE? CHANGE TO: DID COMMUNITY BASED DISTRIBUTION AGENTS OFFER A SELF-TEST KIT TO YOU OR MEMBERS OF YOUR HOUSEHOLD?]	Y-N-DTA-DK	If no or DTA or DK, skip to next section Skip if selftestsource_ X=1	Probe if no but selftestever=yes: You have stated that you have previously self-tested. Were you offered the kit from someone other than a community based distribution agent [??OR SOMETHING LIKE THAT MIGHT BE NEEDED??]		
CA03	stleft	ST kits left in house	Did community based distribution agents leave self-test kits at your house? [COMMENT: CBDAS DON'T REALLY LEAVE KITS AT HOMES. CHANGE TO: DID YOU OR MEMBERS OF YOUR HOUSEHOLD TAKE A SELF-TEST KIT?]	Y-N-DTA-DK	If no or DTA or DK, skip to next section Skip if selftestsource_ X=1	Probe if no but selftestever=yes: You have stated that you have previously self-tested. Did you take the kit from someone other than a community based distribution agent [??OR SOMETHING LIKE THAT MIGHT BE NEEDED??]		
CA04	stleftcount	Number ST left	How many kits were left at your house by the community health worker? [COMMENT: CHANGE TO: EXCLUDING YOURSELF, HOW MANY MEMBERS OF YOUR HOUSEHOLD TOOK A SELF-TEST KIT?	Number	If 88 or 99, skip to selfuse	1 One test 2 Two tests 3 Three tests 4 4 or more tests 5 Don't know how many tests were left 6 Decline to answer		Enter 88 for don't know or 99 for decline to answer
CA05	hhuse	Number of household members used ST	Excluding yourself, how many members of your household used the kits to test themselves for HIV?	Number		1 One other household member 2 Two other household members 3 Three other household members 4 Don't know how many household members have tested 5 Declined to answer		Enter 88 for don't know or 99 for decline to answer

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Questio	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
CA06	selfuse	ST selfuse	Did you get an HIV self-test kit for your use? [COMMENT: TO BE MORE CLEAR CHANGE TO: DID YOU TAKE AN HIV SELF-TEST KIT FROM THE COMMUNITY BASED DISTRIBUTION AGENT]	Y-N-DTA	If no or DTA, go to under16st Skip if selftestsource_X=1	Probe if no but selftestever=yes: You have stated that you have previously self-tested. Did you take the kit from someone other than a community based distribution agent [??OR SOMETHING LIKE THAT MIGHT BE NEEDED??]		
CA07	refuse	Possibilty of refusal	Did you feel you were able to refuse to accept the self-test kit from the community based distribution agent?	Y-N-DTA	If yes or DTA, go to testself			skip?
CA08	whynotrefuse	Reason for refusal	Why were you unable to refuse?	A The community based distribution agent pressured me to take it B My partner pressured me to take it C My parent pressured me to take it D Another family member pressured me to take it E My friend pressured me to take it F The chief pressured me to take it G My employer pressured me to take it H My teacher pressured me to take it I My religious leader pressured me to take it J Another person pressured me to take it		If decline to answer for one choice, must have decline to answer for all choices		tick all that apply
CA09	testself	Self use of testkit	Did you test yourself for HIV using the kit received by community based distribution agents?	Y-N-DTA	If no or DTA, go to stgiveaway. If yes and refuse=yes, goto firstst Skip if selftestsource_X=1	Probe if no but selftestever=yes: You have stated that you have previously self-tested. Did you self-test using a kit provided by someone other than a community based distribution agent [??OR SOMETHING LIKE THAT MIGHT BE NEEDED??]		
CA10	refuseregret	Regret testing after refusal	Now that you have self-tested for HIV and you did not feel able to refuse, do you regret having tested?	Y-N-DTA	Skip if selftestsource_X=1 & regretnow=yes Skip if selftestsource_X=1 & regretnow=no			

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Questio	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
CA11	firstst	first ST ever	Was the self-test received from the CBDA the first HIV test you have ever done? [COMMENT: SHOULD THIS BE ASKED IN THE LOOP INSTEAD? IF WE KEEP IT HERE, IT NEEDS TO PERTAIN TO A SELF-TEST DIRECTLY RECEIVED FROM A CBDA INSTEAD OF SELF-TESTING MORE GENERALLY REGARDLESS OF HOW THE TEST WAS RECEIVED]	1 Yes 2 No, I had been tested by a health worker (or health workers) before 3 No, I had previously done another self-test 9 Decline to answer	Skip if lifetestcount<= 3 and selftest_X=yes for latest date			
CA12	returnst	Test returned?	After testing, what did you do with the used test kit?	1 Return kit to the community based distribution agent 2 Return kit to drop box in the community 3 Return kit to the drop box at health facility [COMMENT: N/A IN MW - TAKE OUT] 4 Kept used kit in home 5 Disposed of used kit elsewhere 9 Decline to answer				
CA13	stgiveaway	Giving kit to someone else	Did you give your kit to someone else? [FOLLOW UP QUESTION: WHO DID YOU GIVE YOUR KIT TO?]	Y-N-DTA				
CA14	under16st	Testing child under 16	Were any of the test kits left in your household used to test a child who is younger than 16 years old?	Y-N-DTA	Asked of all respondents in households with tests, not just those who used the test			
CA15	unusedst	Unused test?	Were there any test kits left by the community health worker in your household that have not been used to test for HIV? [COMMENT: COULDN'T WE DERIVE THIS FROM CA04 AND CA05? COULD LEAD TO INCONSISTENCIES]	Y-N-DTA	Asked of all respondents in households with tests, not just those who used the test			

Version - 18 Sept. 2017

Individual - VMMC

To be completed by all MEN consenting to participate within the household
Note that question in pink row is for UNITAID reporting

Prompt: Now I will ask you questions regarding circumcision. Some men are circumcised; that is, the foreskin is completely removed from the penis

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges	Hint	Notes
E1	circstatus	Circumcision status - images	Please can you look at these pictures which show a penis that has had a foreskin completely removed. Does your penis look like this?	Y-N-DTA	If yes, skip to circdate. If no or DTA and in MW, skip to circaccess. If ZM, skip to E2			Images needed
E2	circ	Circumcision status - text only	Are you circumcised?	Y-N-DTA	If Y, skip to next section. ZM only			
E3	circdate	Circumcision date	When were you circumcised?	MY		After DOB		
E4	circaccess	Know where to access circumcision services	Do you know any facilities offering VMMC (voluntary medical male circumcision) to people who live around here?	Y-N-DTA				NEED TO BE CLEAR THIS IS MEDICAL NOT TRADITIONAL CIRCUMCISION IN TRANSLATION]
E5	circintent	Circumcision intention	How likely would you be to go for circumcision if it were offered within your neighborhood?	1 Very likely 2 Somewhat likely 3 Somewhat unlikely 4 Very unlikely 9 Decline to answer				

Version - 18 Sept. 2017

Individual - HIV care

To be completed by SELECTED individuals ONLY

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges for continuous variables	Hint	Notes
F01	posttest	Positive test result	Have you ever had a positive HIV test result?	Y-N-DTA	If no or DTA, skip to next section			If no, skip to end.
F02	modetest	Confirmation of positive ST result	Did you obtain this result from a self-test?	Y-N-DTA	If no or DTA, skip to artlifeuse Skip if selftestever=no and goto artlifeuse			
F03	confirmresult	Confirmation of positive ST result	Did you go to a health facilty to confirm the positive self-test result?	Y-N-DTA	Skip if selftestever=no			
F04	artlifeuse	ART lifetime use	Have you ever taken ART drugs?	Y-N-DTA	If no or DTA, skip to preartuse. If yes and respondent is male, skip to artcurruse			
F05	pmtctuse	PMTCT use	(If woman) Have you ever been given ART drugs at the the time of having a baby in order to prevent transmission of HIV?	Y-N-DTA				Women only

Version - 18 Sept. 2017

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Ranges for continuous variables	Hint	Notes
F06	artcurruse	ART current use	Are you currently using ART drugs?	YN	If yes, skip to artclinic			
F07	artwhydiscontir	ART - why discontinued	What best describes why you have stopped taking ART?	A Experienced side effects from the drugs B Afraid of stigma and discrimination from going to a clinic for ART C Partner won't let me go to the clinic to get ART D Other family won't let me go to the clinic to get ART E Do not have money to pay for transport to go to the clinic or to get ART F Cannot take time off work to go to the clinic G Not a dignified thing to do at my age H Health facilities offer poor quality HIV care services I Do not trust service providers J Did not feel sick enough K Other	If one item listed, set corresponding item in artdismain as main reason for discontinuing and continue to preartuse	If decline to answer for one choice, must have decline to answer for all choices		Read out responses
F08	preartuse	Pre-ART use	Are you currently using any medications besides ART to control your HIV and keep you healthy?	Y-N-DTA	If no or DTA, skip to next section			Reworded this using operational tools question but may need more help
F09	artclinic	ART/pre-ART provider	Which clinic is providing your ART or pre-ART care?	[Country-specific list of options]				

Version - 20 Nov. 2017

Individual - sexual behaviour
MN, 7 December 2015

To be completed by all individuals consenting to participate within the household

Prompt: Now I would like to ask you questions about your sexual activity in order to gain a better understanding of some important life issues. Let me asure you that your answers are completely confidential and will not be told to anyone. If we should come to any question that you don't want to answer, just let me know and we will go to the next question.

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Range	Hint	Notes
G01	steadyyn	In partnership YN	Do you have a steady partner?	Y-N-DTA	If no or DTA, skip to otheryn		[DO WE NEED DEFINITION OF STEADY PARTNER HERE?]	
G02	steadyct	Steady partner - count	If yes, how many steady partners have you had sex with in the last 3 months?	Number		1-25, 88, 99	Enter 88 for don't know or 99 for decline to answer	
G03	partnocond_X	Condomless sex indicator for each steady partner	In the past 3 months, how often have you not used condoms with your [COUNT] steady partner?	1 Condoms every time 2 Condoms some of the time 3 Condoms never used 9 Decline to answer		Asked for each partner from B2, with a maximum of 6 partners		**[NEED FOR A PARTNER MATRIX]**. Key construct is whether they had condomless sex with the steady partner in the last 3 months, so can be reworded to yes/no if this will be easier for respondents to understand?
G04	otheryn	Non-steady partner YN	[Apart from your steady partner(s)], have you had sex with anyone else in the last 3 months?	Y-N-DTA	If no, skip to next section		Modify wording as needed based on response to steadyyn	
G05	othernocond	Count of non-steady partners with condomless sex	If yes, with how many people apart from your steady partner have you had sex **without using a condom**, even if was only on one occasion?	Number		1-25, 88, 99	Enter 88 for don't know or 99 for decline to answer	Construct is number of casual partners they have condomless sex with in the last 3 months (don't need number of sexual partners in total)
G06	nocondposttest	Condomless sex after last HIV test	Thinking to the last time you tested for HIV, have you had sex without a condom since your more recent test?	Y-N-DTA	If no or DTA, skip to next section			

Version - 20 Nov. 2017

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Range	Hint	Notes
G07	count	How many partners	With how many different partners have you had sex without a condom with since your most recent test (even if it was only the one occasion)?	Number		1-25, 88, 99 If testdate_1<=3 months, count<=otherno cond If testdate_1>3 months, count>=otherno cond	Enter 88 for don't know or 99 for decline to answer	

Version - 18 Sept. 2017

Individual - stigma

To be completed by all SELECTED individuals only

For each of the following statements, please indicate whether you strongly agree, agree, are unsure, disagree or strongly disagree.

Question N	Variable name	Construct	Wording of question	Data type	Skips	Range	Hint	Notes
H01	txeffect4	Understanding of treatment effectiveness	I believe that HIV treatment makes people with HIV less infectious.	1 Strongly agree 2 Agree 3 Unsure 4 Disagree 5 Strongly disagree 9 Decline to answer				From WHO generic tools
H02	stigma1	Stigma 1	People are hesitant to take an HIV test due to fear of other people's reaction if the test result is positive for HIV	1 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H03	stigma2	Stigma 2	People sometimes talk badly about people living with or thought to be living with HIV	2 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H04	stigma3	Stigma 3	Health workers sometimes talk badly about people living with or thought to be living with HIV	3 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H05	stigma4	Stigma 4	People living with or thought to be living with HIV lose respect or standing	4 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H06	stigma5	Stigma 5	People living with or thought to be living with HIV are verbally insulted, harassed, and/or threatened	5 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study

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H07	stigma6	Stigma 6	People living with or thought to be living with HIV are sometimes phyiscally assaulted	6 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H08	stigma7	Stigma 7	I would be ashamed if someone in my family had HIV	7 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H09	stigma8	Stigma 8	I would not like to sit close to someone living with HIV,for example on public transport, at church, or in a waiting room	8 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H10	stigma9	Stigma 9	I fear that I could contract HIV if I come into contact with the saliva of a person with HIV	9 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H11	stigma10	Stigma 10	People sometimes disclose that other people are HIV positive without their permission	10 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H12	stigma11	Stigma 11	Health workers sometimes disclose that other people are HIV positive without their permission	11 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study
H13	stigma12	Stigma 12	People living with HIV who are taking ART are treated better by others than people living with HIV who are not taking ART	12 Strongly Agree 2 Agree 3 Disagree 4 Strongly disagree 9 Decline to answer				All from PopART stigma study

Version - 18 Sept. 2017

Individual extended - IPV

To be completed by SELECTED WOMEN ONLY

Prompt: The next questions are about things that happen to many women and men and that your current partner or any other partner may have done to you.

Question No.	Variable name	Construct	Wording of question	Data type	Skips	Range	Hint	Notes
J1	ipvpsychyn	Psychological IPV - YN	In the past 12 months did your partner do the following to you? Insulted you; made you feel bad; belittled, humiliated, scared you (yelled or smashed things), or threatened to hurt you?	Y-N-DTA	If no or DTA, skip to ipvphysicyn			Based on WHO VAW measure
J2	ipvpsychct	Psychological IPV - number of times	In the past month, would you say this has happened once or more than once?	1 Did not happen in past month 2 Once in past month 3 More than once in past month 9 Decline to answer				Based on WHO VAW measure
J3	ipvphysicyn	Physical IPV - YN	In the past 12 months did your partner do the following to you? Slapped, pushed, shoved, hit you with a fist, kicked, dragged, beaten you, choked, burned you, or threatened to use a gun, knife, or other weapon against you?	Y-N-DTA	If no or DTA, skip to ipvsexyn			Based on WHO VAW measure
J4	ipvphysicct	Physical IPV - number of times	In the past month, would you say this has happened once or more than once?	1 Did not happen in past month 2 Once in past month 3 More than once in past month 9 Decline to answer				Based on WHO VAW measure

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Question No.	Variable name	Construct	Wording of question	Data type	Skips	Range	Hint	Notes
J5	ipvsexyn	Sexual IPV - YN	In the past 12 months did your partner do the following to you? Forced you to have sexual intercourse by holding you down or making you afraid of him or forced you to do something sexual tht you found humiliating?	Y-N-DTA	If no or DTA, skip to ipveconyn			Based on WHO VAW measure
J6	ipvsexct	Sexual IPV - number of times	In the past month, would you say this has happened once or more than once?	1 Did not happen in past month 2 Once in past month 3 More than once in past month 9 Decline to answer				Based on WHO VAW measure
J7	ipveconyn	Economic violence - YN 1	In the past 12 months did your partner keep you from having the money you needed to buy food or other necessities even when he had money for other things?	Y-N-DTA	If no, skip to next section			Wording from SEA measure (Postmus et al.)
J8	ipveconct	Economic violence - YN 2	In the 12 months prior, were you forced away from your home?	Y-N-DTA				

Version - 18 Sept. 2017

Final items
MN, 4 December 2015

To be completed by interviewer

Question No.	Variable	Construct	Question	Data type	Skips	Ranges	Hint	Notes
X01	endtime	end time	Time interview ended	Should enter automatically based on device time				
X02	endstatus	Status of interview	Was this interview completed?	1 Complete 2 Incomplete - provide additional comments below				
X03	comments	Interviewer comments	Interviewer comments on specific questions, respondent, interview.	Long text				