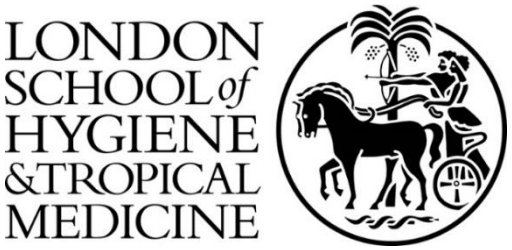

Estimating healthcare costs at scale in low- and middle-income countries

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The case of community-based HIV self-testing scale-up in Southern and Western Africa

MARC d'ELBÉE

Thesis submitted in accordance with the requirements for the degree of Doctor of Philosophy of the University of London

September 2021

Funded by UNITAID

Department of Global Health and Development

Faculty of Public Health and Policy

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

Declaration by candidate

I have read and understood the LSHTM's definition of plagiarism and cheating. I declare that this thesis is my own work, and that I have acknowledged all results and quotations from the published or unpublished work of other people.

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Date: September 18th , 2021

Abstract

This thesis aims to gain understanding of current methods used to forecast the costs at scale for a new technology in low- and middle-income countries (LMIC) and to propose improved methods for cost predictions at scale, using community-based HIV self-testing (HIVST) kits distribution programmes in southern and western Africa as a case study.

Following the review of ~8,000 studies through seven databases on quantitative analyses of costs for informing the scale-up of an intervention in LMIC, I propose a framework to guide the decision process of fitting cost functions by study objective. I then conduct costing studies for implementing community-based HIVST distribution models in southern and western African regions. I also explore potential efficiency gains arising from the addition of HIVST to HIV testing services (HTS) and from continuous programme development in Lesotho, and the importance of distinguishing between full and incremental HIVST costs for country financial planning. I deepen our understanding of the variation of HIVST costs at scale up by fitting an empirical econometric costs function using data from Malawi, Zambia, Zimbabwe, South Africa, and I test it against the observed HIVST scale-up in Lesotho to inform on its external validity. In western Africa, I use an accounting cost function to quantify the expected returns on investment of adding HIVST to civil society organisation-led HTS programmes in Côte d'Ivoire, Senegal and Mali.

This research provides insights into the economic considerations for integrating and scaling up the community-based HIVST distribution programmes in southern and western Africa. These findings inform costing studies design for data collection and analysis, encourage the use of cost functions that are the most relevant to the policymaker research questions, ultimately to guide the scale-up of the most promising health interventions in LMIC.

Acknowledgments

I would like to express my gratitude to Prof Fern Terris-Prestholt, supervisor and line manager for the past six years, for offering me this unique work experience, for your support, patience, and vision. Thank you for keeping me on track, I learned a lot throughout the years, it was intense, and incredibly rewarding.

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Finally, thank you to my parents Jean and Monique, my sister Claire, and my brothers Jean-Marie, Raphael, and Christian; for creating and protecting our family cocoon, a space for love and calm, in a noisy world. You all inspire me, immensely. I am proud, and deeply grateful.

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List of Abbreviations

AF: Allocation Factor

ART: antiretroviral treatment

ATLAS: HIV Self-Testing: Free to know your status

CB: Community-based

CEA: Cost Effectiveness Analysis

CHOICE project: CHOosing Interventions that are Cost-Effective

CI: Confidence Interval

CSO: Civil Society Organisations

G-CEA: Generalized-Cost-Effectiveness Analysis

HIC: High Income Countries

HIVST: HIV Self-Testing

HTS: HIV Testing Services

ICER: Incremental Cost-Effectiveness Ratio

LMIC: Low- and Middle-Income Countries

LSHTM: London School of Hygiene and Tropical Medicine

M&E: Monitoring and Evaluation

MoH: Ministry of Health

NGO: Non-Governmental Organization

ORPHEA: Optimizing the Response in Prevention: HIV Efficiency in Africa

PANCEA: Prevent AIDS: Network for Cost-Effectiveness Analysis

PSI: Population Services International

RDT: Rapid Diagnostic Test

STAR: HIV Self-Testing AfRica

TB: Tuberculosis

UNAIDS: The Joint United Nations Programme on HIV/AIDS

VMMC: Voluntary Medical Male Circumcision

WHO: World Health Organization

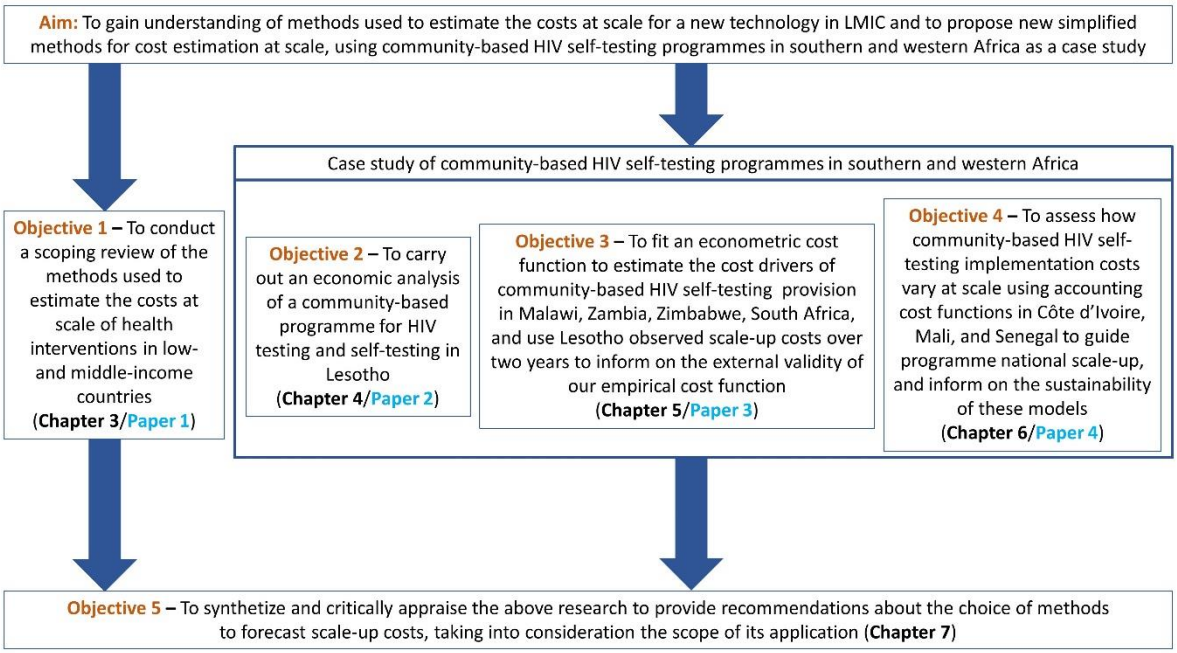
Chapter 1 – Introduction

This chapter aims to present the scope and an outline of the thesis, and also provides background information on HIV self-testing programmes scale-up in southern and western Africa which is my case study. I then present the thesis aim and objectives, as well as the study timelines and intellectual ownership.

Scope of the thesis

This thesis adopts a research paper style and is composed of seven chapters with appendices including four research papers. This thesis was conducted as a part-time PhD while I was working as a research fellow at the LSHTM on the STAR (HIV Self-Testing AfRica) and ATLAS (HIV Self-Testing: Free to know your status) projects. In a nutshell, this thesis is an evaluation of methods used to predict health care costs at scale in low- and middle-income countries (LMIC), with applications using community-based HIV self-testing (HIVST) programmes scale up in southern and western Africa as a case study. An overview is presented in the thesis framework (**Figure 1**).

Figure 1. Thesis framework



Outline of thesis

Chapter 1 is the introduction and presents the background to the thesis. It sets the context and presents our case study used for the application of methods used to estimate costs at scale: the implementation and scale up of HIV self-testing programmes in southern Africa (Malawi, Zambia, Zimbabwe, South Africa, and Lesotho) with the STAR Initiative, and in west Africa (Côte d'Ivoire, Senegal, and Mali) with the ATLAS project. I provide an overview of the HIV epidemic in these countries, and the role that HIVST can potentially play as a prevention strategy to control the epidemic. I also present the thesis aims and objectives, as well as the intellectual ownership.

Chapter 2 summarises the literature on HIV prevention programme costs and cost drivers. I then present the theory of production for the purpose of scaling-up health interventions in LMIC.

Chapter 3 builds upon the theory discussed in chapter 2 and presents a scoping review of cost functions used to predict costs at scale of health interventions in LMIC. I synthesise the various

methods applied and I propose different frameworks to guide the decision process of fitting the cost function by study objective (Paper 1). I also summarise the research gaps related to operational and economic considerations for scaling up HIVST in sub-Saharan Africa, introducing the research papers 2-4.

Chapter 4 provides a micro-costing analysis of HIVST integration into HTS services using longitudinal data from a real-world intervention over two-years of implementation in Lesotho (Paper 2). I find that adding HIVST to community-based HTS improves its overall affordability regarding HIV-positive case finding. I also highlight how the reporting of both full and incremental cost estimates can increase transparency for use in priority setting, budgeting and financial planning for scale-up. This analysis is published in the *AIDS* journal (August 2020).

Chapter 5 identifies the drivers of costs of community-based HIVST interventions in southern Africa (Paper 3). An empirical cost function is estimated using cost and programme data from Malawi, Zambia, Zimbabwe, and South Africa and then modelled for Lesotho to project costs over a two year scale up period. The cost function scale up predictions are then compared with observed scale up costs to assess the external validity of this cost function for out-of-sample countries. I published this work in *BMJ Global Health* (May 2021).

Chapter 6 presents a costing study of HIVST implementation through civil society organisations (CSO)-led models for key populations in Côte d'Ivoire, Mali and Senegal (Paper 4). I also model costs for programme transition and early scale-up using accounting cost functions to inform the budgeting of country national HTS plans. I explore the potential returns on investment of a progressive integration of the HIVST programme to CSO activities and contextual challenges (COVID-19 pandemic, country safety concerns). I also assess how, in transition to scale-up and integration of the HIVST programme into CSO activities, this model is likely to exhibit substantial economies of scale. This study is published in *Frontiers in Public Health* (May 2021).

Chapter 7 provides a general discussion of the key findings from the results chapters 5-8. I synthetise the contribution to new knowledge from this thesis. I then present the limitations and strengths of these findings. Finally, I discuss the implications of these findings for research and for policy making, followed by a general conclusion.

The importance of HIV self-testing programmes scale-up to control the HIV epidemic in southern and western Africa

Epidemiological contexts of HIV in southern and western Africa

In December 2013, the Joint United Nation Programme on HIV/AIDS (UNAIDS) developed a narrative to end AIDS as a public health threat with access to antiretroviral treatment (ART) central to its success. New operational targets were defined - the 90-90-90 targets [1, 2]. These targets refer to 90% of all people living with HIV (PLHIV) knowing their HIV status, 90% of all people with diagnosed HIV infection receiving sustained ART, 90% of all people receiving antiretroviral therapy being virally suppressed by 2020. These targets are now set for 95-95-95 by 2030. Despite these laudable targets, in 2019, there were globally 38 million people living with HIV, of which 25.4 million had access to ART and every year an estimated 1.7 million people become newly infected [3]. The two regions most affected by the epidemic are east and southern Africa (20.7 million PLHIV) and west and central Africa (4.9 million PLHIV) in 2019 [3].

The eastern and southern Africa region is estimated to be the most affected region with 730,000 new infections in 2019 (44% of new infections)[2]. At the end of 2019, 87% of PLHIV were aware of their status in this region (**Figure 2**). The gap to achieving the first 95 of the 95–95–95 targets in 2019 was a total of 530,000 PLHIV [3].

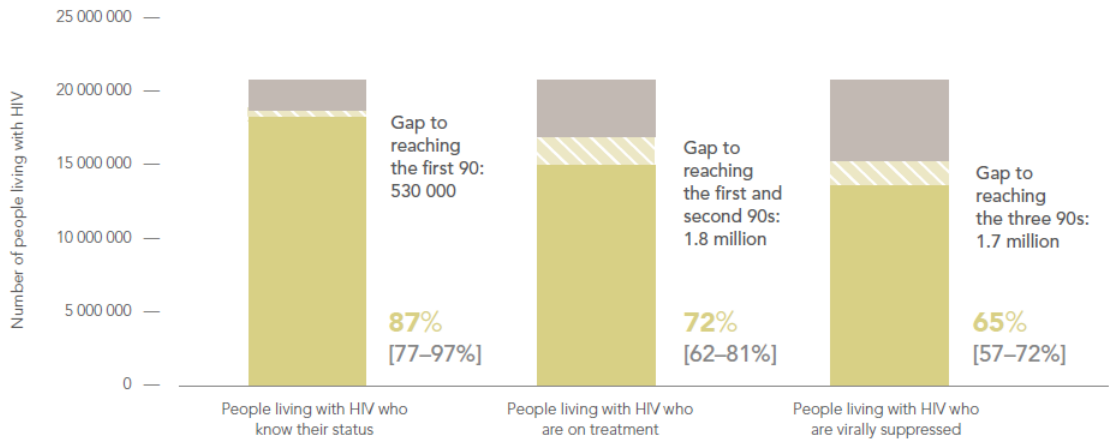


Figure 2. HIV testing and treatment cascade, eastern and southern Africa, 2019, Source: UNAIDS Data report, 2020 (p. 40)

There is wide variation in HIV prevalence between countries, with an estimated adult (aged 15-49 years) prevalence among the general population ranging between 9% in Malawi and 23% in Lesotho in 2019 (**Table 1**) [2].

Table 1. Overview of key HIV data by case study countries for the adult population aged 15-49 years in 2019

Country	% of HIV prevalence	Number of PLHIV	Number of new HIV infection yearly	% PLHIV who know their status (first target)
Malawi	8.9	790,000	29,000	90
Zambia	11.5	950,000	43,000	90
Zimbabwe	12.8	1,000,000	33,000	90
South Africa	19.0	5,900,000	170,000	92
Lesotho	22.8	250,000	9,500	93
Côte d'Ivoire	2.4	290,000	9,200	73
Senegal	0.4	27,000	1,100	71
Mali	1.2	110,000	Unknown	43

Source: UNAIDS, AidsInfo, 2021: https://aidsinfo.unaids.org/

In western and central Africa region, we are further away from reaching UNAIDS' first 95 with an estimated 68% of PLHIV knowing their status, with a remaining PLHIV who do have not yet been identified of 1.1 million (**Figure 3**). As in most countries of the region in 2019, the HIV epidemic is mixed in Côte d'Ivoire, Senegal, and Mali, with national prevalence ranging between 0.4% and 2.4% and much higher prevalence at 5% to 30% in key populations (KP) including female sex workers (FSW), men who have sex with men (MSM), and people who use drugs (PWUD) [3]. In 2019 in western and central Africa, HIV prevalence was 9% for FSW, 13% for MSM, and 3% for PWUD. In 2019, seven out of ten new HIV infection were among these key populations and their sexual partners (**Figure 4**).

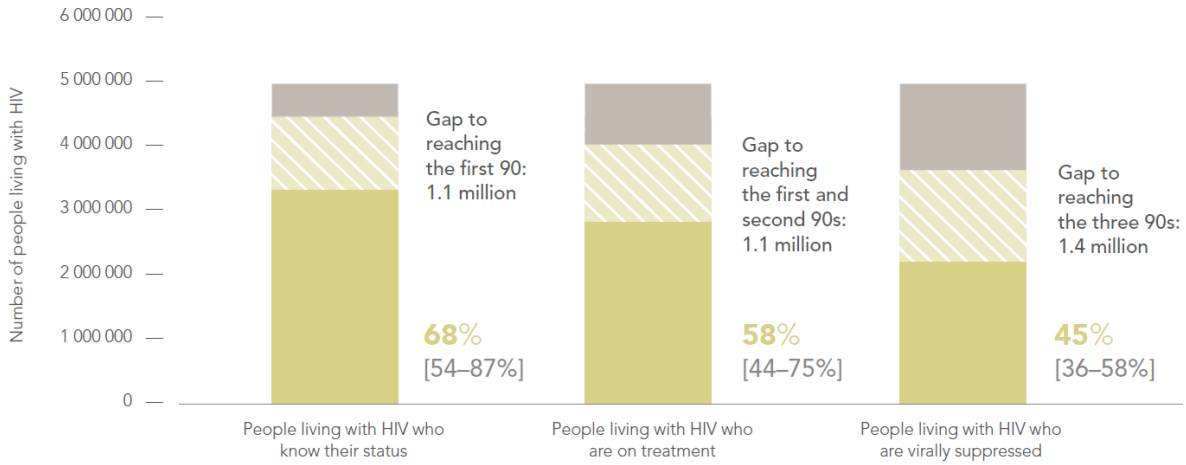


Figure 3. HIV testing and treatment cascade, western and central Africa, 2019, Source: UNAIDS Data report, 2020 (p. 100)

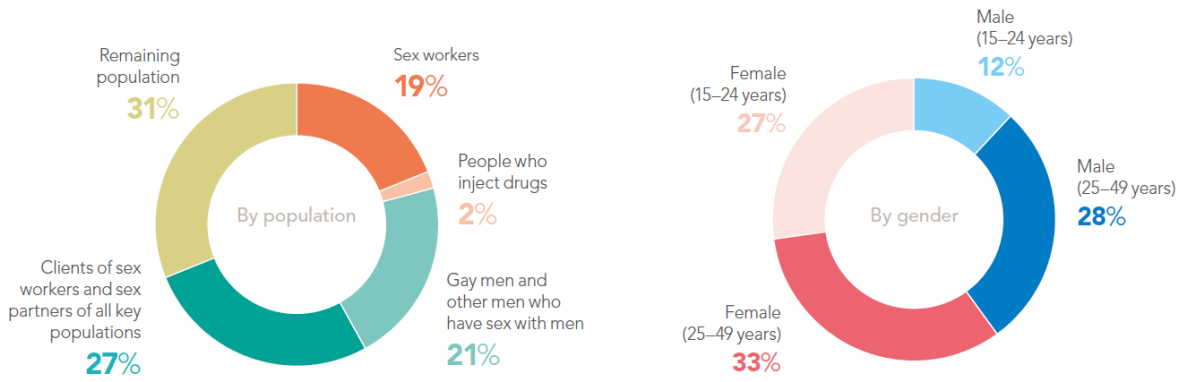


Figure 4. Distribution of new HIV infections by population (aged 15-59 years), western and central Africa, 2019, Source: UNAIDS Data report, 2020 (p. 95)

The potential of HIV self-testing using community-based approaches to reach the first UNAIDS 95 target in Sub-Saharan Africa

HIV self-testing (HIVST), where an individual collects their own oral fluid or blood sample, conducts the test and interprets results[4], is an additional testing modality introduced in Sub-Saharan Africa in 2015 [5]. According to the World Health Organization (WHO) guidelines, a reactive HIVST result should be followed by further confirmatory testing by a trained provider [5]. In 2016, WHO released a supplement to the "Consolidated guidelines on HIV testing services" on HIV self-testing and partner notification[4, 5]. They highlighted the potential of HIVST to increase HTS access, especially among men, key populations and young people and aimed to support the implementation and scale-up of effective, and evidence based approaches to HIVST [5].

STAR was the first and largest implementation project to introduce HIVST in sub-Saharan Africa, funded by the donor UNITAID [6]. The first phase (2015-2017) delivered almost 650,000 HIVST kits in three countries: Malawi, Zambia, Zimbabwe, the largest global assessment of HIVST. Strategies for distribution were mainly community-based with distribution of HIVST kits at home door-to-door [7]. STAR has generated important information about efficient and ethical ways to distribute HIVST kits,

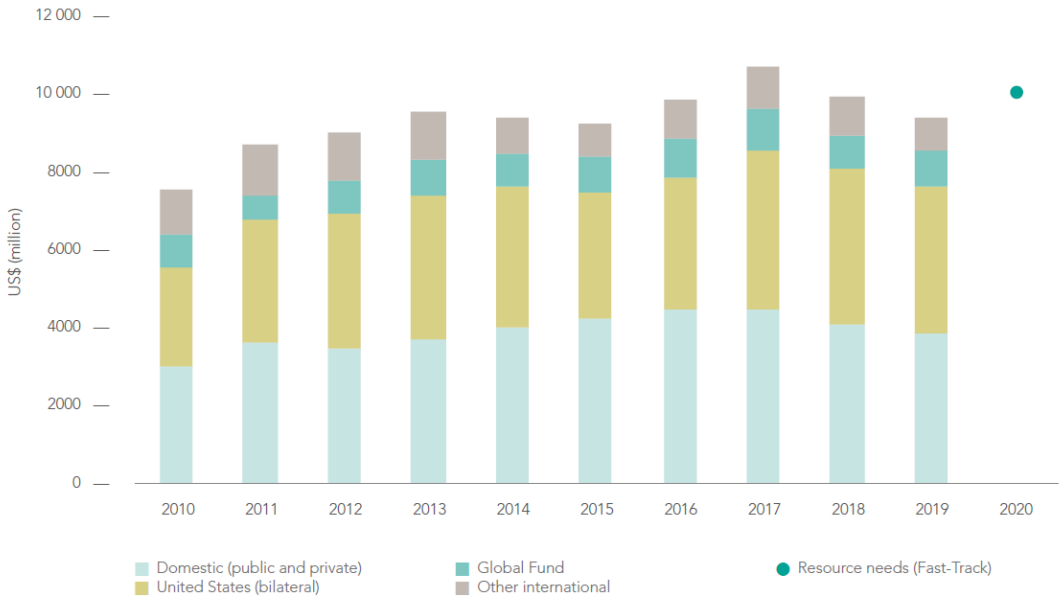
including post-test tips to respond to questions about the feasibility, acceptability and impact of interventions in Sub-Saharan Africa. These data were used for the development of new recommendations, and the development of national public policies on self-testing of HIV. The second phase of the STAR Initiative (2018-2020) extended this programme to three additional countries (South Africa, eSwatini and Lesotho) and distributed over 4.8 million HIVST kits in six countries. Following STAR, UNITAID supported the ATLAS project that aimed to introduce HIVST in western Africa, coordinated by the non-governmental international organisation Solthis. ATLAS supported HIV self-testing implementation in three west African countries (Côte d'Ivoire, Mali, Senegal) [8]. Up to December 2020, in close collaboration with the national AIDS programmes/councils, over 150,000 HIVST kits were distributed across the three countries through ten delivery channels combining fixed and advanced strategies of primary and secondary distribution [8, 9].

Decentralisation of HTS has proven effective for reaching UNAIDS targets, for instance with the universal HIV testing and treatment strategy of the PopART trials in South Africa and Zambia [10]. Decentralisation of HTS can also be supported by HIVST. Bringing HIVST to the community has the potential to reduce societal costs for accessing HIV testing, increase efficiency gain by only incurring costs for skilled providers to conduct confirmatory testing, and is has shown able to reach people who would otherwise not test, in particular men and young groups [11, 12]. Community-based HIVST distribution models use agents (community-based agents, peer distributors, peer educators, volunteers) to deliver HIVST either at people's homes or within the community with mobile outreach [13, 14]. Potential users consider this model convenient, reducing long waiting times at health facilities and helping them avoid transport fees [15-17]. Although community-based approaches incur additional costs for transport and outreach from a provider perspective, they decrease users' costs in accessing HIV testing, in particular among working men whose time might be more expensive [14, 18, 19].

Resource availability for HIV in southern and western African regions

To end AIDS as a public health threat by 2030, UNAIDS estimates that US$26.2 billion are required for the global HIV response in 2020 alone [20]. This means that the amount of resources available for HIV should have increased by US$1.5 billion each year between 2016 and 2020, a situation that did not happen [20]. A shared commitment to the HIV response among the region's governments and the international community has translated into levels of funding that are in line with the 2020 target in southern Africa whereas the resources available for HIV responses in western and central Africa in 2019 were only 46% of the 2020 target (**Figure 5**).

Resource availability for HIV by source, 2010–2019, and estimated Fast-Track resource needs in 2020, eastern and southern Africa



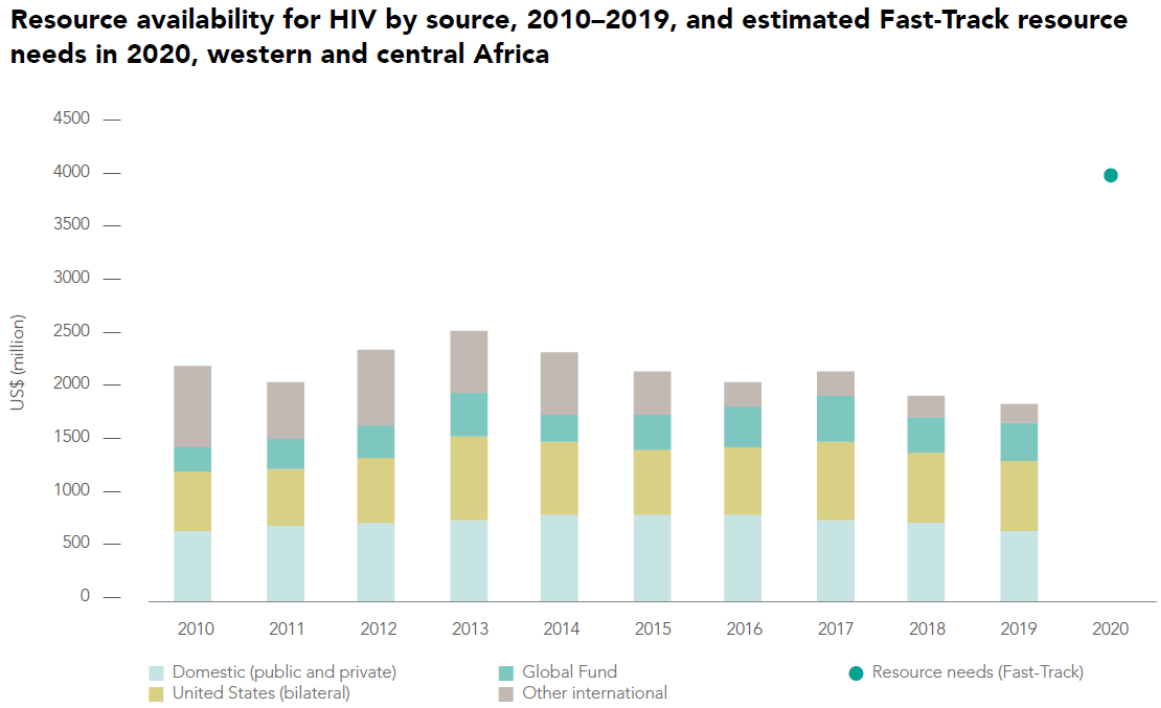


Figure 5. Resource availability for HIV by source, 2010–2019, and estimated Fast-Track resource needs in 2020, eastern and southern Africa (top), western and central Africa (bottom), Source: UNAIDS Data report, 2020 (p. 47 and 103)

In 2012, the African Union endorsed the 'Roadmap on Shared Responsibility and Global Solidarity for AIDS, TB and Malaria in Africa', and highlights the need for country ownership, efficiency and sustainable financing of the HIV response and reflects increasing political commitment [21]. In recent years, high-income countries have reduced funding for the HIV response in LMIC, with a 7% decrease reported between 2015 and 2016 [22]. The Fast-Track approach proposed by UNAIDS requires a rapid increase in funding for HIV over the next few years to have a decisive impact on the epidemic and ensure the long-term sustainability of the HIV response [23]. With increasingly scarce funds to fight the HIV epidemic in LMIC, priority setting for HIV testing programmes becomes critical. The decision to scale-up a promising programme such as community-based HIVST relies, among other factors, on the estimation of the intervention's its cost-effectiveness as well as its affordability when introduced at scale. There is a need to better understand how costs evolve with scale and how to best project costs at scale for both budgeting and assessing affordability.

Thesis aim

To gain understanding of current methods used to forecast the costs at scale for a new technology in LMIC and to propose improved methods for cost estimation at scale, using community-based HIVST distribution programmes scale-up in southern and western Africa as a case study.

Research objectives

Objective 1 – To conduct a scoping review of methods used to date to estimate the costs at scale of health interventions in LMIC and describe the relationship between the choice of the estimation method and the intended use of the costs projections – **Chapter 3**/***Paper 1***

Objective 2 – To carry out a cost analysis of the community-based programme for HTS and HIVST with the highest level of testing coverage in Lesotho over a two-year observation period - **Chapter 4**/***Paper 2***

Objective 3 – To estimate the costs drivers of community-based HIVST distribution in Malawi, Zambia, Zimbabwe and South Africa, using econometric methods and, based on the model outputs, project costs at scale using community-based HIVST national scale-up in Lesotho as a case study - **Chapter 5**/***Paper 3***

Objective 4 – To apply accounting approaches to estimate costs at scale using the case of community-based HIVST national scale-up in Côte d'Ivoire, Senegal, and Mali - **Chapter 6**/***Paper 4***

Objective 5 – To synthetize and critically appraise the above research to discuss recommendations about the choice of methods for predicting scale-up costs, taking into consideration the scope of its application, whether it is priority setting, budgeting, or financial planning - **Chapter 7**

We present below the specific objectives of each chapter 3 to 6 corresponding to the research papers 1-4.

Chapter 3: Objectives - Research paper 1: ***Estimating health care costs at scale: A review of cost function applications in low- and middle-income countries***

1. To synthetize the literature on methods used to estimate costs of health interventions at scale in LMIC,
2. To propose new algebraic formula for cost functions based on the synthesised literature,
3. To summarize key factors considered by researchers for the fitting of cost functions using qualitative methods,
4. To critically review the studies' quality and validity of cost projections,
5. Considering the above findings, to propose frameworks on the use of cost functions for the estimation of costs at scale for health interventions in LMIC based on the intended use of these cost estimates

Chapter 4: Objectives – Research paper 2: ***Using HIV self-testing to increase the affordability of community-based HIV testing services: A longitudinal analysis in Lesotho***

1. To estimate the costs of community-based HTS implementation in Lesotho before and after integration of HIVST,
2. To investigate potential efficiency gains from the addition of self-testing and from continuous programme development

Chapter 5: Objectives – Research paper 3: ***Modelling costs of community-based HIV self-testing programmes in Southern Africa at scale: An econometric cost function analysis across five countries***

1. To fit an econometric cost function to estimate the cost drivers of the community-based HIVST programmes in Southern Africa using data from Malawi, Zambia, Zimbabwe, and South Africa,
2. To inform the use of econometric cost functions to predict costs at scale by comparing econometric cost function models with different level of data requirements,

3. To assess the validity of our empirical econometric cost function by comparing projected costs with observed costs at scale in Lesotho

Chapter 6: Objectives – Research paper 4: ***Costs and scale-up costs of integrating HIV self-testing into civil society organisation-led programmes for key populations in Côte d'Ivoire, Senegal, and Mali***

1. To estimate the costs of implementing HIVST through civil society organisations-led programmes for key populations in Côte d'Ivoire, Senegal, and Mali,
2. To assess the costs of scaling up this model to guide project national scale-up, propose costed operational plans, and inform on the sustainability of this distribution model

Intellectual ownership

As staff member of LSHTM, I should justify that the proposed research arises from my own independent research alongside the research project I am professionally involved with. I highlight below and in the **Figure 6** my role and responsibilities for this research.

Scope of work related to the STAR project

Between 2016 and 2019 I have been working as a full-time research fellow on the STAR research project. Between 2016 and 2018, I supported the design of discrete choice experiments in Malawi, Zambia and Zimbabwe to understand potential user's preferences for various models of HIVST distribution and linkage to care following a positive self-test. To a lesser extent, I also contributed to the costing studies in these countries as a coordinator for cross-country weekly review of progress during the cost data collection, cleaning, and analysis. I am a co-author on the publication of this costing study (**Appendix I**), from which I use data for the econometric cost function analysis in Paper 3. In addition, I collected data with the local economist for one model of HIVST distribution in Malawi (Private health facility).

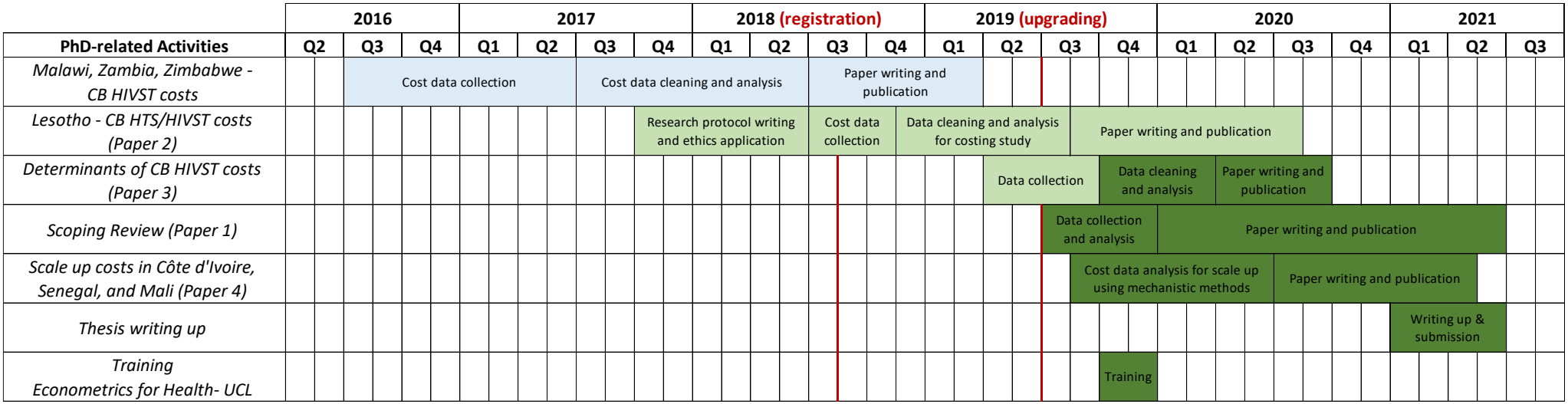
During STAR phase 2 (2018 and 2019), the STAR consortium grew to cover South Africa, Lesotho and eSwatini (six countries in total). I supported the coordination of costing studies in Malawi, Zambia, Zimbabwe, South Africa with a similar role as in phase 1. I led the costing studies in Lesotho where I am the only researcher involved. I wrote the costing research protocol, collected, cleaned and analysed data.

Scope of work related to the ATLAS project

Following the STAR initiative, a sister intervention – the ATLAS project – was funded by the same donor UNITAID to inform the design of HIVST programmes in West Africa. Since September 2019, I work full-time on the ATLAS project where I am the field coordinator for the economics work package. I wrote the costing protocol (**Appendix II**) and led the design of the cost data collection and analysis with the support of two research assistants (one based in Côte d'Ivoire, and the other in Senegal). I supervised the cost data collection and analysis conducted by the research assistants. I fully designed the scale-up cost modelling approach.

Scope of work related to my PhD

Because of the successful introduction of HIV self-testing in southern and western Africa in the first phase of the STAR initiative and the ATLAS projects, interest in evidence to inform the scale-up of this new technology has been growing. It has been mentioned in my research costing protocols that I would be looking at costs at scale, for which I received ethical approval. The PhD research aims to explore and compare various methods used to estimate costs at scale is my own original idea. Given the large scale of these research programmes, a significant amount of primary cost data has been collected, and the aim of this PhD is to take full advantage of these data. However, the scope of this PhD is distinct from the STAR and ATLAS project deliverables in that I am focusing on methods and the projects focus on the policy-relevant results of the evaluation. Nevertheless, my findings are relevant to explain the STAR/ATLAS recommendations and, therefore, of interest to the research teams.



Roles and responsibilities

STAR team and PhD candidate
PhD candidate for STAR+PhD research
PhD candidate for PhD research

Figure 6. Timelines and intellectual property

I presented in this chapter the background to the thesis. It sets the context and presents our case study used for the application of methods used to estimate costs at scale: the implementation and scale up of HIV self-testing programmes in southern Africa (Malawi, Zambia, Zimbabwe, South Africa, and Lesotho) with the STAR Initiative, and in west Africa (Côte d'Ivoire, Senegal, and Mali) with the ATLAS project. I provided an overview of the HIV epidemic in these countries, and the role that HIVST can potentially play as a prevention strategy to control the epidemic. In line with the scope of this thesis, I focus on community-based HIVST distribution models as opposed to facility-based distribution models. The following chapter provides background information of the economics of scaling up health care interventions in LMIC. I also present in this chapter the existing literature on HIV Testing Services (HTS) and HIVST costs of implementing these programmes in preparation for scale-up.

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Chapter 2 – Economics of scaling up health interventions in low- and middle-income countries: The case of HIV programmes in Sub-Saharan Africa

This chapter reviews the costs and cost drivers of HTS and HIVST programmes in sub-Saharan Africa. I then present the theory of production and the concept of returns to scale with its application for the scale up of health interventions in LMIC. Finally, I discuss the various applications of cost estimation at scale in LMIC and we highlight the research gaps in this area.

Costs of HIV testing and HIV self-testing programmes in sub-Saharan Africa

A systematic review conducted in 2021 by Ahmed and colleagues reports 169 costs per HIV test from 65 studies in sub-Saharan Africa published between 2006 and 2020 (**Appendix III**). The authors explored variations in incremental cost estimates by different testing modalities: health facility-based (n=57), home-based (n=29), mobile services (n=13), self-testing (n=19), campaign-style (n=4), and stand-alone (n=3). They also presented costs by primary or secondary/index HTS and by type of population tested (general population, people living with HIV, antenatal care male partner, antenatal care/postnatal women and key populations).

In this analysis, as the distributions of cost estimates across the studies was quite skewed, I report the median costs instead of mean costs. The main findings are, for facility-based testing the median cost per person tested was US$10 (interquartile range (IQR): $6-28) for negative test and $140 (IQR: $67-414) for positive test. For home-based testing, the median cost was US$13 (IQR: $8-23) and US$247 (IQR: $141-382) for HIV negative and positive test respectively. For self-testing the median cost was US$12 (IQR: $9-14) per person tested, and the cost for positive result was US$113 (IQR: $78-516).

Because costs per test were largely comparable ($10-$13), this review concludes that the choice of one testing modality over another should be driven by which HIV testing approach is most feasible to implement and most likely to reach their untested groups. It should also encourage policymakers to consider delivering a mixture of testing modalities. Self-testing services, attracting harder-to-reach groups such as men, young groups, and key populations, play a key role in the HIV response and are being added to national HTS programmes across sub-Saharan Africa. Nevertheless, with increasingly scarce resources to sustain HIV programmes, there is a need to accurately estimate the costs of scaling up HIVST programmes for the purpose of budgeting and financial planning.

Costs drivers of HIV preventions programmes globally

Understanding the drivers of costs is essential for implementers to run HIV testing models that are both effective and efficient [1, 2]. Costs functions can help monitoring programme efficiency and identify drivers of costs. They can help to identify areas where the allocation of resources is not optimal and take corrective actions [3, 4]. I conducted a narrative review of economic evaluations alongside multi-country HIV testing and treatment programmes and we present here the cost drivers of HIV prevention programmes identified in these large scale studies.

Given the significant amount of data required to conduct such analysis, only a few studies have been able to analyse the determinants of costs for HIV prevention programmes using econometrics methods [5, 6]. To my knowledge, no study has focused on HIV testing services only but rather on a package of HIV prevention services. Well-known applications of costs functions to HIV prevention programmes include the PANCEA, ORPHEA, Integra, and Avahan research projects [2, 7-9].

The PANCEA (Prevent AIDS: Network for Cost-Effectiveness Analysis) project assessed the efficiency of HIV prevention programmes by collecting 2003 and 2004 cost and output data from 206 HIV prevention programmes in five countries (Uganda, South Africa, India, Mexico, and Russia). They

assessed the direction, shape, and strength of association between scale and efficiency for each country by fitting bivariate regression lines to scatter plots of output levels and unit costs. Overall, the authors found efficiency gains with scale, with variation across countries and interventions [1].

The ORPHEA (Optimizing the Response in Prevention: HIV Efficiency in Africa) project, built on PANCEA and other past work, is one of the most comprehensive studies on the cost and technical efficiency of HIV prevention interventions and looked at over 300 delivery sites in Kenya, Rwanda, South Africa, and Zambia between 2012 and 2013 [8]. The research team assessed the cost, cost structure, cost variability, and the determinants of efficiency for major HIV interventions including: HIV testing and counselling, prevention of mother-to-child transmission, voluntary medical male circumcision, and HIV prevention for sex workers. Using the ORPHEA data, Gallaraga et al. applied multivariate regression methods to analyse predictors of log-transformed average costs and found that HIV prevention costs could be contained by using task shifting, outside of hospital sites, service integration and bringing services to the community [10].

The Integra Initiative evaluated the costs and benefits of integrating HIV and sexual and reproductive health services in Kenya, Swaziland and Malawi. To determine the existence of economies of scale and scope, Obure et al. used a quadratic cost function using data collected between 2008 and 2011 from 40 health facilities in Kenya and Swaziland [9]. They found that efficiency gains from the integration of HIV and other services are likely to be modest or in sites operating at a low scale with high levels of fixed costs.

Finally, an example of estimating cost functions has been done by Lepine et al. to examine a public health programme for HIV prevention using data from 138 non-governmental organisations over four years in India (Avahan – The India AIDS Initiative) [7]. Using a fixed-effect panel estimator and a random-intercept model, they find that the NGO scale, the community involvement, and the organisation of clinical services are the major determinants of average costs.

Production function, short and long run, returns to scale and scale economies

Healthcare's goal is to maximize health and the analysis of health production processes and supply presents two challenges: one is that the outputs – the goods produced – are health outcomes. The health outcomes aim to increase the patient utility – happiness or satisfaction gained from consuming a good – but its assessment can be highly subjective between individuals and cultural settings. The second one is that the *production function* (i.e. the relationship between inputs and outputs) needs to be defined in terms of intermediate outputs (e.g. vaccinations carried out, or HIV self-testing kits distributed) and not outcome ("good" health) [11].

The production process in healthcare has two distinct timeframes, differentiating the variability of inputs to production. In the *short run*, some fixed inputs (e.g. hospital building) will not vary with the level of output (e.g. number of patients seen) while other inputs (e.g. number of nurses) will vary. In the *long run*, all inputs to production will vary. When considering alternative methods to estimate costs at scale, the timeframe of costs projections (short or long run) will be critical. The relationship between inputs and outputs defines the *production function* and is characterised by the output elasticity (the percentage change of output divided by the percentage change of an input) used to estimate returns to scale [11]. In situations where a percentage increase in inputs leads to the *same* percentage increase in output, we observe *constant* returns to scale. When a given percentage increase in input leads to either a *larger* or a *smaller* percentage increase in output, we are in the case of *increasing* or *decreasing* returns to scale, respectively [12]. The concept of *increasing*/*decreasing* returns to scale is closely linked to that of *economies*/*diseconomies* of scale. Whereas returns to scale focuses on how output changes in proportion to the quantity of input used in production, economies of scale looks at how costs change in proportion to the output produced. Economies of scale happen when increasing the scale of production leads to a lower cost per unit of output, and vice-versa [12].
When considering costs of production, the variation in the level of production of output or *scale*, will be associated with varying marginal benefits (or intermediate outcome in healthcare) and marginal

costs in the short and the long run. This relationship between costs and output is explored to achieve scale efficiency (**Figure 1**). In the short run, as output increases, fixed costs are spread across more units of output and the average cost per output is decreasing, exhibiting economies of scale. After a certain point in scale, average costs start increasing, related to either the law of diminishing marginal return (short run), or theoretical diseconomies of scale such as management challenges at large scale (long run) [12-14]. The law of diminishing marginal return states that when one or more factors of production are held fixed (short run), there will come a point beyond which the extra output for additional units of the variable factor will diminish [12]. The evaluation of the impact of (dis)economies of scale on costs implies that the analyst adopt a perspective from the provider (health system, implementer).

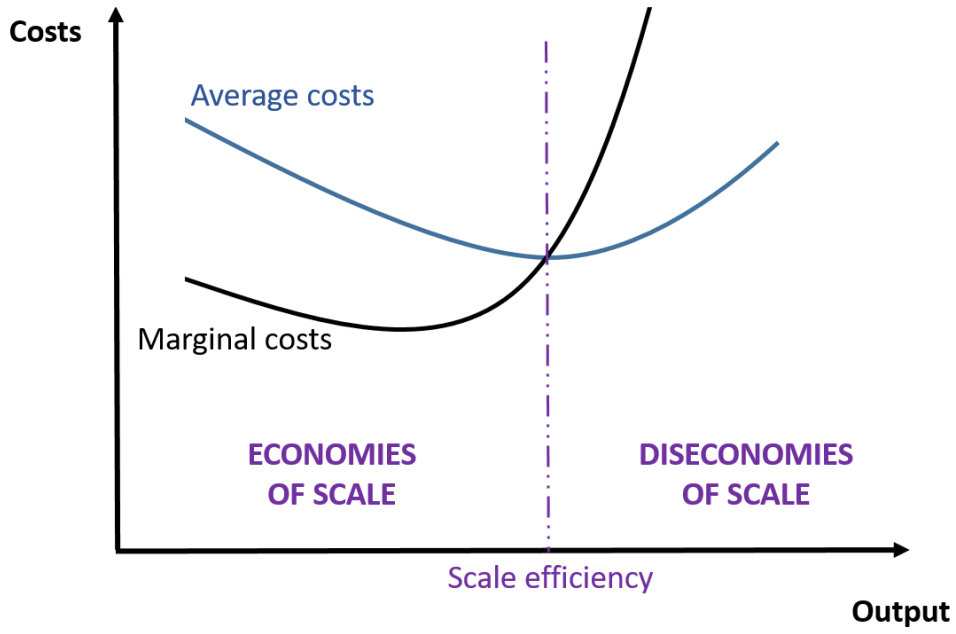

Figure 1. Average, marginal cost curves and (dis)economies of scale, Source: Guinness L, Wiseman V. Introduction to Health Economics. 2nd edition ed: Open University Press; 2011

Although the short and long run average costs curves are commonly presented as "U-shaped" [12, 15], with initial economies of scale followed by diseconomies of scale for higher levels of inputs, there are many reasons for (dis)economies of scale to happen: they can be context specific and its nonlinear effects are still subject of debate today among economists [16, 17]. The literature on cost functions usually agree on a L-shaped average cost curve versus scale, rather than the theoretical U-shaped curve as diseconomies of scale are rarely empirically observed [7, 18, 19].

Research on the scale-up of health interventions in LMIC

The concept of scaling up an intervention can be defined either as an intrinsic characteristic or as a process. The former refers to "*the ability of a health intervention shown to be efficacious on a small scale and/or under controlled conditions to be expanded under real world conditions to reach a greater proportion of the eligible population, while retaining effectiveness*" [20]; while the latter refers to the "*deliberate efforts to increase the impact of successfully tested health interventions so as to benefit more people and to foster policy and programme development on a lasting basis"* [21]. These deliberate efforts, in certain situations, can also include the successful integration of new interventions into existing programmes [22].

Research on scale-up of intervention has described frameworks for scaling health interventions as a process, the majority of which have an explicit focus on LMIC [23-40]. The constraints to scale-up can be different between high-income countries (HIC) and LMIC, in terms of human resources, infrastructures, or health system organisation[20, 21, 24, 27, 33, 36, 41-48]. Furthermore, the scarcity, quality and accessibility of data in LMIC explain the development of costing methods specific to LMIC [49].

Two reviews have looked at conceptual frameworks for scaling up health interventions in LMIC. Subramanian et al., in a systematic review published in 2011, identified six conceptual models [35]. Most models highlighted the importance of organisational, functional, and political capabilities through experimentation and adaptation of strategies in addition to increasing the coverage and

range of health services. They suggested that approaches such as a “learning by doing” would allow for engagement of key stakeholders, used data to address constraints, and incorporated results from pilot projects. A second review, a narrative review conducted in 2015 by Milat et al., identified eight scale-up frameworks [50], where the key factors for success included the importance of establishing monitoring and evaluation systems, strong infrastructure to support implementation, costing and economic modelling of interventions, engagement of implementers and the target community, the systematic use of evidence, and a well-defined strategy tailored to local context with strong leadership and political will. Although these two reviews compared different frameworks (except one framework which was present in both reviews [41]), both suggested an adaptive strategy for the successful scale-up of health interventions in LMIC, with a “learning by doing” approach i.e. the systematic use of evidence throughout the scale-up process. Both reviews also highlighted the evaluation of resource needs as a major constraint to scale-up [35, 50]. Milat et al. ranked the appropriate costing and economic modelling as the second most important success factor based on the literature review citations.

Estimating costs at scale for health interventions in LMIC: for what purpose?

Costs estimated at scale have various applications for budgeting, planning using projections from budgetary expenditures, priority setting using cost-effectiveness analysis, or the (global/regional/national) estimation of resource needs for the introduction of packages of priority health interventions [51]. Depending on the purpose of the estimation, there are different needs for precision and accuracy. Precision and accuracy will be more relevant for budgeting purposes in order to avoid the risk of under-funding a programme while a cost-effectiveness analysis can accommodate larger uncertainty that can then be taken into account. Therefore, the intended use (or purpose) of the cost estimate will influence the selection of the appropriate method to use in order to minimize data requirements while improving accuracy when critical.

Appropriate estimation of costs at scale is needed to inform policies aiming to expand or introduce new interventions. Various methods have been applied to estimate costs of health interventions at scale in LMIC. However, the relationship between the choice of the method and the intended use of the estimates produced is unclear. This chapter presented that the theory of returns to scale is often not, or partially, accounted for in cost projection methods. As it is increasingly relevant to account for decreasing returns to scale for the application of cost functions to epidemic such as HIV, malaria where it costs more to reach the last percentage of the target population (remote areas, groups harder to reach, etc.), I will explore how to account for decreasing return to scale with cost functions. The following chapter is a scoping review of methods used to estimate the costs at scale of health interventions in LMIC, their ability to include the theory of returns to scale, and the purpose for which those estimates have been produced. The focus of this review is to assess how the choice of methods used and the purpose of the cost estimate are related. More specifically, I present a review of existing frameworks to inform the intervention scale-up in these countries and the importance of estimating accurate resource needs. I then present the different methods usually applied to estimate costs of scaling up, namely accounting methods, and econometric (or statistical) methods. Finally, I present the main areas where estimated scale-up costs can be applied: for budgeting, for the estimation of global resource needs for financial planning, or for priority setting with economic evaluation of cost-effectiveness. This chapter is presented in a paper format as submitted to the Health Economics journal on August 2021.

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Chapter 3 – Paper 1: Estimating health care costs at scale: A review of cost function applications in low- and middle-income countries

Overview of Paper 1

As presented in chapter 2, the appropriate estimation of costs at scale is needed to inform policies aiming to expand or introduce new interventions. This paper reviews methods used in LMIC to estimate the costs at scale of health interventions. Furthermore, this paper assesses how the choice of methods used and the purpose of the cost estimate are related.

In total, forty research articles are included in this review and critically assessed. Accounting and econometric cost function frameworks are developed based on the intended use of these cost estimates. These proposed frameworks also include ways to account for variable returns to scale in cost estimation methods at scale.

Additional details on methods and findings are presented in the supplemental material. Appendix A1 presents in details the search strategy for each data base. Appendix A2 provides an overview of the data extracted from each paper. Appendix A3 presents the qualitative methods used for the themes identification for the classification of factors considered by authors when fitting a cost function. Appendix A4 presents methodological approach taken to conduct the qualitative data extraction and classification by study objective. Appendix A5 provides a summary of study characteristics by year, outlet of publication, world region, country, and intervention sector. Appendix A6 presents a synthesis of estimators used for econometric cost functions, based on healthcare cost data features (adapted from Mihaylova et al, 2011). Appendix texts present factors considered by authors when fitting a cost function, examples of application of cost functions to economic evaluations, and further details on the choice of statistical method for cost data analysis. Finally, Appendix Figure A1 shows the factors considered when fitting a cost function by type of cost function.

Data extraction and analysis is conducted following the guidelines from the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA) - Scoping Review Extension.

This review was submitted to the *Health Economics* journal in August 2021.

This paper fulfil research objective 1 by reviewing methods used to date to estimate the costs at scale of health interventions in LMIC and describing the relationship between the choice of the estimation method and the intended use of the costs projections.

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Student ID Number	1805320	**Title**	Mr
First Name(s)	Marc		
Surname/Family Name	d'Elbée		
Thesis Title	Estimating healthcare costs at scale in low- and middle-income countries – the case of community-based HIV self-testing scale-up in southern and western Africa		
Primary Supervisor	Prof 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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Stage of publication	**Submitted**

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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 designed the study, conducted data search, extraction, analysis. I wrote the first draft and incorporated co-authors comments.

SECTION E

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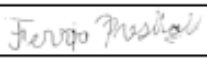
Supervisor Signature	
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Estimating health care costs at scale: A review of cost function applications in low- and middle-income countries

Authorship:

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Abstract (193/200 words limit)

Appropriate costing and economic modelling are major factors for the successful scale-up of health interventions. Various cost functions are currently being used to estimate costs of health interventions at scale in low- and middle-income countries (LMIC) potentially resulting in disparate cost projections. The aim of this scoping review is to gain understanding of current methods used and provide guidance to inform the use of cost functions that is fit for purpose.

We reviewed seven databases covering the economic and global health literature to identify studies reporting a quantitative analysis of costs informing the projected scale-up of a health intervention in at least one LMIC between 2003 and 2019 without language restrictions.

Of the 8,725 articles identified, 40 met the inclusion criteria. We classified studies according to the type of cost functions applied – accounting or econometric and described the intended use of cost projections. Our critical review finds reporting issues related to sampling approach, reporting of uncertainty measure, and selection of the right estimator based on sample size and cost data features. Building on the review results, we proposed a framework to guide the fitting of cost functions by study objective including mathematical notations.

Key words:

Health Economics, Microeconomics, Econometrics, Production costs, Cost functions, Low- and middle-income countries

Introduction

The research in implementation science for intervention scale-up in low- and middle-income countries (LMIC) is gaining interest in the field of health economics [1]. Whether it is related to changes of the donor landscape where LMIC are transitioning to more reliance on domestic funding (e.g. HIV epidemic), or an evolution to decentralised health services delivery systems aiming to increase access to care (or in response to the COVID-19 pandemic), stakeholders need robust estimates of programme costs at scale to better inform decisions. Two recent systematic reviews have looked at conceptual frameworks for the successful scale-up of health interventions in LMIC [2, 3], both highlighted the misevaluation of resource needs as a major challenge to scale-up. Milat and colleagues ranked the appropriate costing and economic modelling as the second most important success factor, after establishing monitoring and evaluation systems, based on the literature review citations [2].

The constraints to scale-up differ between high-income countries (HIC) and LMIC, in terms of human resources, infrastructures, and health system organisation. In LMIC, these constraints are often related to data scarcity (relying solely on routine cost accounting systems and patient-information systems), shortages of human resources, the health financing system in countries with high out-of-pocket expenditures, and weak governance [4-17].

According to the World Health Organisation, scaling up in the health sector means "doing something in a big way to improve some aspect of a population's health" [18]. This broad definition encompasses multiple dimensions including inputs/resources (mobilising more funds), outputs (providing more services), outcomes (reaching more people), and/or impact (reducing morbidity or mortality). We distinguish ''costs at scale'' – assessing resource needs at various quantities of outputs, from ''costs of scaling-up'' - estimating all costs incurred in the process of increasing the quantity of outputs of an intervention.

Originally, the production function, developed by Cobb and Douglas in 1927, describes the relationship between outputs and factors of productions (inputs) [19]. Cost functions are derived then from the

production function and estimate the total cost of production given a specific quantity of output produced. The simplest cost function multiplies a single unit cost by a quantity - the commonly used "simple cost multiplier" (SCM) [20]. Accounting cost functions (ACF) - also called accounting identity cost functions [21] - are broad in nature because they aim to follow step-by-step the intervention production process as close as possible to the reality [20, 21]. ACF identify fixed and variable costs, typically assumed to vary linearly with the scale of output produced such as that used in input-output analysis as originally developed by Leontief [22] (e.g. *total costs of scaling up HIV testing = cost of a HIV testing site* (fixed cost) + *HIV testing session cost*number of person to test* (variable cost*scale)) [23]. In contrast to accounting approaches, econometric cost functions (ECF) do not follow the production process and apply statistical inference to project costs. The challenge of ECF is to reflect the complexity of real-world production process with a relatively simple statistical model of dependent (costs) and independent variables.

The applications of cost functions have developed largely independently in the context of budgeting, medium- and long-term financial planning, technical efficiency analyses, and priority setting. These applications differ regarding their economic assumptions, complexity and data requirements ultimately resulting in disparate cost projections.

In 2005, as part of the WHO CHOICE project (CHOosing Interventions that are Cost-Effective), Johns and colleagues systematically reviewed factors affecting costs as coverage increased. The authors outlined various methods used and identified accounting methods, projections from budget expenditures, and econometric models from thirty-seven studies [24]. In 2008, Kumaranayake systematically reviewed methods used in thirty-four studies to estimate costs at scale for HIV/AIDS interventions and identified that the majority of methods were using either an ACF where costs were modelled with or without adjustment for scale, empirically estimated, or using econometric models [25]. Studies were used for cost-effectiveness analysis or resource needs estimates.

We conducted a scoping review of methods used to estimate the costs at scale of interventions in LMIC and the purpose for which those estimates have been produced. This review aims to update and expand previous works to identify potentially innovative approaches for projecting costs at scale, better accounting for variable returns to scale [24, 25]. Since the relationship between the choice of cost function and the intended use of the estimates produced is unclear, we also aim to assess how the choice of methods used and the purpose of the cost estimate are related to draw lessons on the suitability of different methods for each purpose. Specifically, the objectives of the review are: (1) to synthetize the literature on methods used to estimate costs of health interventions at scale in LMIC, (2) to propose new algebraic formula for cost functions based on the synthesised literature, (3) to summarize key factors considered by researchers for the fitting of cost functions using qualitative methods, (4) to critically review the studies' quality and validity of cost projections, (5) considering the above findings, to propose a mathematical framework on the use of cost functions for the estimation of costs at scale for health interventions in LMIC based on the intended use of these cost estimates.

Methods

2.1. Search strategy

Research questions in scoping reviews are broad in nature as the focus is on summarizing breadth of evidence [26]. We followed the Arksey and O'Malley methodological framework for scoping studies revised by Levac et al. and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews [26-28]. Seven databases covering the economic and global health literature were reviewed (Pubmed, Embase, Global Health, Econlit, The Cost-Effectiveness Analysis Registry, Global Health Cost Consortium unit cost database and the Latin American and Caribbean Health Science Literature database). We included studies reporting a quantitative cost analysis, using a provider perspective, and informing the scale-up of an intervention in at least one LMIC between 2003 (corresponding to the end of Johns' review [24]) and 2019 without language

restrictions. Eligible studies in other development economic sectors than health, such as agriculture and education, were also included in the search to capture the broader scale-up literature available across economic fields, allowing for cross fertilization across disciplinary foci.

The intended readers of this review are researchers or planners tasked with generating information for financial planning decisions, conducting economic evaluations at scale and technical efficiency analyses for estimating costs at scale. Therefore, program budgeting methods used by health managers for routine health services, funding application, price setting methods (e.g. in the insurance sector), patient cost analysis, and technical efficiency analyses not used for estimating costs at scale (performance analysis such as frontier models, data envelopment analysis or stochastic frontier approach) - are judged beyond the scope of the review.

We excluded the SCM method from the search because it is commonly found in the literature, and our focus was on innovative approaches. However, we include this method as a comparator with new approaches identified in the review. We looked at the first fifty hits (i.e. results in Google) of our search in additional key economics sources such as the World Bank (WB), and sources for health research in developing countries, including the World Health Organisation, The Joint United Nations Programme on HIV/AIDS, Clinton Health Access Initiative, Médecins Sans Frontières, with the aim of including approaches not captured with our database search. No additional studies were found with the grey literature search.

The concept of costing at scale is broad, therefore the search strategy covered a wide range of research areas, these can be found in Appendix Table A1. The search strategy was composed of three dimensions: (1) costs: including economic evaluations, econometric cost functions, programme financing, expenditure analysis, efficiency analysis, cost sharing analysis; (2) scale: related to implementation sciences, programme organization/evaluation, health service assessment/monitoring, health planning, management of health resources, delivery of care, operational and organizational research; and finally (3) setting: low- and middle-income countries as

per the 2020 WB classification [29]. We validated our search strategy using a list of fourteen pre-identified research articles applying diverse cost projection methods that we knew should be included in the review to ensure our search strategy was capturing studies of interest.

2.2. Data extraction and analysis

We conducted two types of data extraction (Appendix Table A2). One approach was more descriptive, related to the article information (e.g. name of first author, year of publication), the intervention setting and scale-up (e.g. countries, study objectives), and the cost projection method (e.g. accounting or econometric, fixed/variable costs, uncertainty measure).

The second data extraction phase was more analytical and synthetized the factors, explicitly presented by the authors, that were considered when fitting the cost functions. The approach taken extracted text and summarized data as bullet points then identified themes of analysis (Appendix Tables A3 and A4).

Results

3.1. Search results

The screening process is presented in Figure 1. The database searches identified 8,725 published studies for screening. A total of 40 articles were included for the complete methods review [21, 30-68].

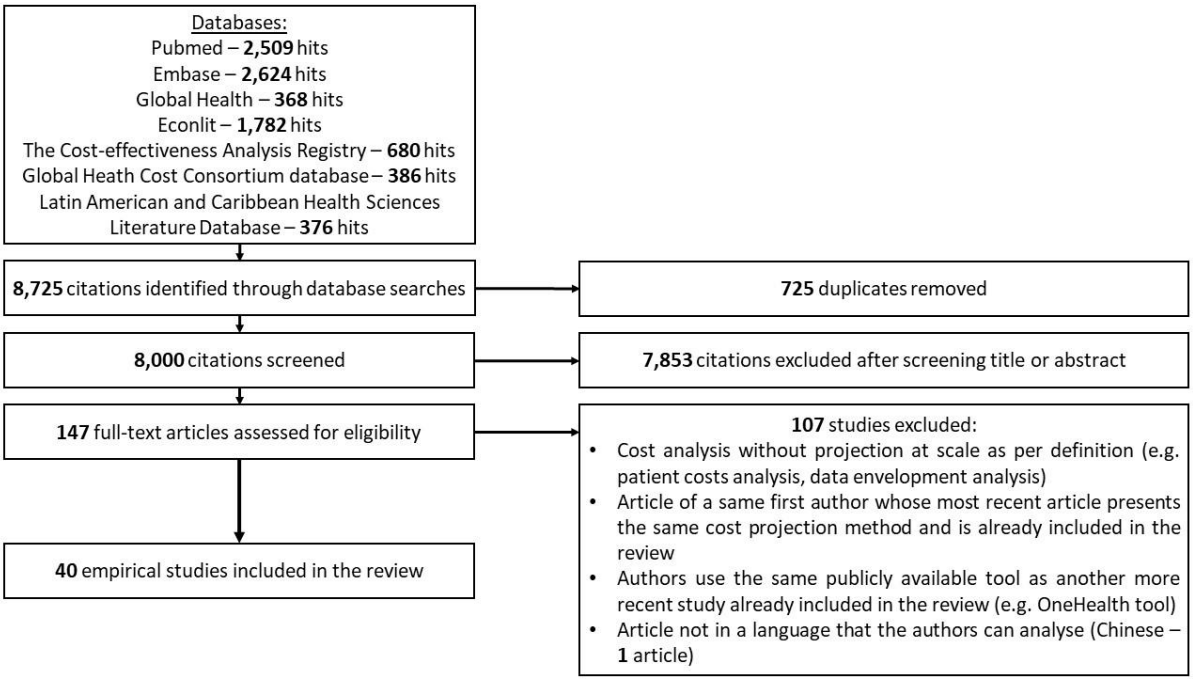


Figure 1. Database search and screening process

3.2. Study characteristics

Study characteristics are presented in Table 1. and Appendix Table A5. We observe an increasing number of relevant studies over time, and half of the studies (48%) are published in the five most recent years. Studies are published in a wide range of journals in the fields of health economics (n=7, 19%); health management, policy, and planning (n=5, 13%); health service delivery (n=27, 65%); and waste management research (n=1, 3%). The most common publication journals are PloS one (n=6, 12%), Cost Effectiveness and Resource Allocation (n=4, 11%), Health Policy and Planning (n=3, 7%) and

The Lancet journals (n=3, 7%). Most studies are conducted in Sub-Saharan Africa (n=19, 48%), followed by South Asia (n=10, 23%), multiple regions (n=6, 15%), East Asia & Pacific (n=4, 11%), and Latin America & Caribbean (n=1, 3%). Many studies are multi-country analyses ranging from 2 to 188 countries (n=9, 20%) and a high number of studies are conducted in India (n=9, 20%). Although we included other development economics sectors in our review, most studies are in the health sector (n=39, 97%) and one study is related to waste management research (n=1, 3%). Finally, a third of studies are related to HIV (n=16, 38%), followed by health-related expenditure analysis (n=5, 12%), packages of primary health care services (n=6, 14%), and maternal and childcare (n=3, 7%).

Table 1. Overview of individual study characteristics (N=40)

First author, year	Study objective	Cost function	Intervention field	World region	Country
Kerr, 2015	Econ. Eval.†	Accounting	HIV	Multiple regions	Not reported
Turner, 2016	Econ. Eval.	Accounting	Parasitology - Helminthiasis	Sub-Saharan Africa	Uganda
Winskill, 2017	Econ. Eval.	Accounting	Malaria	Sub-Saharan Africa	Unknown
Marseille, 2012	Econ. Eval.	Econometric	HIV	Sub-Saharan Africa	Zambia
Abdullah, 2012	Fin. Plan.‡	Accounting	Basic Package of Health Services	East Asia & Pacific	Indonesia
Barasa, 2012	Fin. Plan.	Accounting	Maternal and Child Care	Sub-Saharan Africa	Kenya

Cantelmo, 2018	Fin. Plan.	Accounting	Basic Package of Health Services	East Asia & Pacific	Cambodia
Castaneda-Orjuela, 2013	Fin. Plan.	Accounting	Vaccination	Latin America & Caribbean	Colombia
Deghaye, 2006	Fin. Plan.	Accounting	HIV	Sub-Saharan Africa	South Africa
Deo, 2019	Fin. Plan.	Accounting	Tuberculosis	South Asia	India
Ensor, 2012	Fin. Plan.	Accounting	Basic Package of Health Services	East Asia & Pacific	Indonesia
Marschall, 2008	Fin. Plan.	Accounting	Basic Package of Health Services	Sub-Saharan Africa	Burkina Faso
Prinja, 2018	Fin. Plan.	Accounting	Maternal and Child Care	South Asia	India
Rodrigues, 2014	Fin. Plan.	Accounting	HIV	South Asia	India
Terris-Prestholt, 2006	Fin. Plan.	Accounting	Adolescent Health	Sub-Saharan Africa	Tanzania
Verguet, 2015	Fin. Plan.	Accounting	Surgery	Multiple regions	88 countries
Castro, 2016	Fin. Plan.	Econometric	Health Care Expenditures	Multiple regions	156 countries
GBD Health Financing Collaborator Network, 2018	Fin. Plan.	Econometric	Health Care Expenditures	Multiple regions	188 countries
Berman, 2018	Fin. Plan.	Mixed	Basic Package of Health Services	Sub-Saharan Africa	Ethiopia
Adam, 2003	Fin. Plan.	Econometric	Hospital Expenditures	Multiple regions	6 countries

Ameli, 2008	Tech. Eff. An.§	Econometric	Basic Package of Health Services	South Asia	Afghanistan
Bautista-Arredondo, 2018a	Tech. Eff. An.	Econometric	HIV	Sub-Saharan Africa	Nigeria
Bautista-Arredondo, 2018b	Tech. Eff. An.	Econometric	HIV	Sub-Saharan Africa	4 countries
Bollinger, 2014	Tech. Eff. An.	Econometric	HIV	Sub-Saharan Africa	6 countries
Chandrashekar, 2010	Tech. Eff. An.	Econometric	HIV	South Asia	India
Dandona, 2005	Tech. Eff. An.	Econometric	HIV	South Asia	India
Galarraga, 2017	Tech. Eff. An.	Econometric	HIV	Sub-Saharan Africa	Kenya
Guinness, 2007	Tech. Eff. An.	Econometric	HIV	South Asia	India
Johns, 2013	Tech. Eff. An.	Econometric	Maternal and Child Care	Sub-Saharan Africa	Malawi
Lepine, 2015	Tech. Eff. An.	Econometric	HIV	South Asia	India
Lepine, 2016	Tech. Eff. An.	Econometric	HIV	South Asia	India
Menzies, 2012	Tech. Eff. An.	Econometric	HIV	Multiple regions	6 countries
Meyer-Rath, 2012	Tech. Eff. An.	Econometric	HIV	Sub-Saharan Africa	South Africa
Mujasi, 2015	Tech. Eff. An.	Econometric	Pharmaceutical Expenditures	Sub-Saharan Africa	Uganda
Obure, 2016	Tech. Eff. An.	Econometric	HIV	Sub-Saharan Africa	2 countries

Parthan, 2012	Tech. Eff. An.	Econometric	Solid Waste Management	South Asia	India
Pitt, 2017	Tech. Eff. An.	Econometric	Malaria	Sub-Saharan Africa	Senegal
Schneider, 2007	Tech. Eff. An.	Econometric	Health Insurance	Sub-Saharan Africa	Rwanda
Weaver, 2004	Tech. Eff. An.	Econometric	Hospital Expenditures	East Asia & Pacific	Vietnam
Ahanhanzoa, 2015	Tech. Eff. An.	Econometric	Vaccination	Sub-Saharan Africa	2 countries

† Economic Evaluation, ‡ Financial Planning, § Technical Efficiency Analysis

3.3. Cost functions – Algebra and description of terms

We classify studies by type of cost functions – accounting and econometric and we propose a formula for each cost function that encompass all reported methods. We further account for variable returns to scale in our notations beyond what is done in most studies. We also report the simple cost multiplier approach to allow for comparison between methods. The algebra is presented in Table 2 and applied examples are provided in Appendix Table A6.

Table 2. Cost functions – Derived mathematical notations

Simple cost multiplier (comparator)	Accounting cost function	Econometric cost function
$$C = s \cdot UC$$ with $UC = \sum_i P_i \cdot Q_i$	$$C = \sum_j c_j + \sum_k \left[\frac{s_k}{D_k}\right] \cdot c_k + \sum_l s_l \cdot c_l + \sum_m s_m \cdot \left(\left(\frac{s_m}{S_m^{full}}\right)^x \cdot (C_m^{full} - c_m) + c_m\right)$$ with $c_j = f(P_j, Q_j)$ in the short run, with $c_k = f(P_k, Q_k)$; $c_l = f(P_l, Q_l)$; $c_m = f(P_m, Q_m)$, with $\left[\frac{s_k}{D_k}\right]$, where [ ] is the rounded-up value to the nearest higher integer and is > 0	$$C = \sum_v C_v \quad \text{with} \quad C_v = \beta_0 + \sum_w \beta_{vw} \cdot X_{vw}$$ OR $$C = \sum_v UC_v \cdot s_v \quad \text{with} \quad UC_v = \beta_0 + \sum_w \beta_{vw} \cdot X_{vw}$$
Where: C: Total cost	Where:	Where: β_0: Model intercept

s: Scale variable to reach desired number of outputs UC: Unit cost per output i: input (building, personnel, supplies, etc.) differentiated by intervention level (health facility, district office, central, etc.) P_i: Price of an input i Q_i: Quantity of input i required for one output	c: Cost by type of input (building, personnel, supplies, etc.) differentiated by intervention level (health facility, district office, central, etc.) s: Scale is defined as a number of outputs c and s vary by type of input. We differentiate the type of inputs into j, k, l, m defined by their behaviour at scale (j = fixed, no variation to scale; k = semi-variable, increasing return to scale; l = variable, constant return to scale; m = variable, decreasing return to scale) P: Price of an input Q: Quantity of input required for one output D_k: Maximum capacity per input k C_m^{full}: Input cost m when outputs are produced at full scale-up S_m^{full}: Number of outputs at full scale-up for an input m x: Scale factor - varies typically from 2 to 5	v: Unit of analysis: district, facility, catchment area of health facility w: Number of regressors introduced in the model β_{vw}: Model coefficients computed using empirical dataset X_{vw}: Regressors introduced in the model - quality variables, organisational characteristics of the unit v, characteristics of the population reached by v, environmental characteristics, and observed scale variable

3.3.1. Simple cost multiplier

The SCM approach estimates total costs at scale (C) using a unit cost per output (UC) multiplied by the scale variable (s) to reach desired number of output (e.g. number of HIV test to conduct). The unit cost per output is the sum of the multiplied input prices (P_i) by the input quantities (Q_i) for one output, for each cost input i, identified at different intervention levels - national, regional, district, health facility, community, etc.

3.3.2. Accounting cost functions

The costs (C) are total programme costs at scale for one or more interventions, regardless of whether scale-up happens at sub-national, national, or international level.

The cost inputs j, k, l, and m are defined by their behaviour as scale changes, where: j = fixed cost, no variation with scale; k = semi-variable cost, exhibiting increasing return to scale; l = variable cost, exhibiting constant return to scale; m = variable cost, exhibiting decreasing return to scale; as illustrated in Figure 2. Inputs k are categorised as 'semi-variable' because they are fixed costs for a set level of production, that become variable after a certain production level is reached.

The inputs are identified at various intervention level and differentiated between: (1) *service delivery:* health facility – primary health centre [30, 39, 40, 54, 62, 64] or secondary hospital health centre [34, 39], the entire site or part of it related to the intervention (e.g. operating room) [66]; outreach (community, village) [30, 39, 61]; and (2) *above service delivery:* government/central or health system level [39, 40, 62], state [61], district [46, 61, 64], block [61], ward [64], department [40], municipality [40], community council, etc. - depending on the country's administrative structure.

Fixed cost inputs j are identified at different intervention levels. Fixed costs include a broad range of costs related to intervention start-up phase [34, 62], sensitization [45], production of information, education, and communication material [45, 62, 65], training [34, 65], meetings, workshops [34], capital goods

(building, vehicle, equipment) [46], administrative central cost, central/national/sub-national /overheads [45, 46, 62], personnel (management/programme, supervision, monitoring, data management) at sub-national level, health facility level [34, 44-46, 54, 62, 65]. Fixed costs can be a total cost (e.g. initial set up of a hotline at national level) or an average cost (average capital costs at primary care health facility level for a specific intervention).

Almost all variable costs from these studies are assumed to exhibit constant return to scale (input l) and include a broad range of inputs. These costs can be varied depending on the intervention and magnitude of scale-up. Most commonly, these costs include medical personnel costs [40, 54, 64, 68], and medical supplies such as drugs or biological tests [30, 39, 40, 44, 46, 54, 64, 65]. Only two studies account for variable returns to scale, for instance related to delivery costs, increasing with scale to account for diminishing marginal returns associated with a higher unit cost at high levels of coverage [65, 68].

Scale variables (s) can be classified in the following areas:

Inputs (or resources): hospital bed, per field officer, lab reagent, diagnostic test [45]

Outputs:

per service (e.g. dose of vaccine delivered or administered, hospital visit with/without admission, home visit, medical consultation, screening or diagnostic test for HIV or tuberculosis, treatment administered, surgical operation, long-lasting insecticide-treated net delivered) [34, 40, 46, 54, 65, 66, 68]

per health intervention as a package or not (e.g. primary health care: health promotion, sanitation and environment health, maternal and child health and family planning, nutrition, immunization and communicable diseases control, and treatment of common illness) [39, 54]

Outcomes: per beneficiary/target individual (e.g. general population, patient, pregnant woman, child under five years old, fully vaccinated child, school child) [30, 40, 44, 61, 62, 64, 68]

Impact: per disease to prevent/treat, health expenditure (e.g. HIV infection averted) [30, 45]

Setting: per administrative structure (e.g. village, district, block, ward, health centre) [30, 61, 64, 66]

These variables are used as a combination of variables in half of the studies to follow closely a production process (e.g. input/setting/outcome or setting/output) [34, 61].

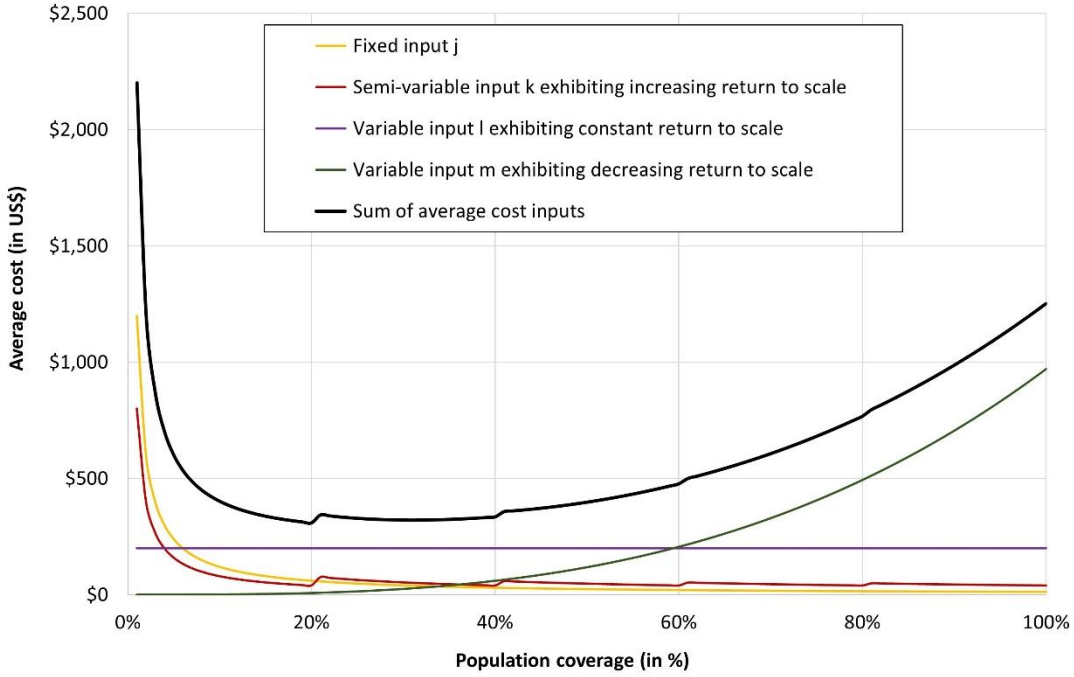


Figure 2. Average cost of inputs j, k, l, m, and sum of inputs by % population coverage

The following three parameters need to be defined by the analyst (observed or arbitrarily): D_k (maximum capacity per input k), C_m^{full} (input cost m when outputs are produced at full scale-up), and S_m^{full} (number of outputs at full scale-up for an input m).

Finally, the scale factor x applied for cost inputs m defines how steep the curve slope is, i.e. the lower the power, the stronger is the assumed effect of decreasing return to scale (e.g. transport costs are

rapidly increasing at scale-up if roads are in a bad state and require 4*4 with high petrol consumption) (Appendix Figure A1).

3.3.3. Econometric cost functions

The costs are represented by total programme costs (C) or total cost at the unit of analysis v (C_v) [32, 33, 41, 43, 48-50, 58, 67] or unit costs per unit of analysis (UC_v) [21, 31, 35-38, 42, 47, 52, 53, 55, 56, 59, 60, 63], single or a set of cost dependent variables [36, 41, 47, 48, 52, 55, 57, 63], and log transformed or not [21, 33, 42, 43, 48, 50, 55, 57-59].

The selection of w regressors (X_w) includes environmental characteristics and organisational characteristics specific to the intervention production function, aiming to include measures such as quality. The functional form is normal, quadratic (assuming U-shaped following the economic theory), log transformed (L-shaped), or cubic, and several forms are sometimes included in the equation [32, 36, 41, 47, 52, 53]. The scale variable is a combination of variables defining scale-up of simultaneous interventions or a single variable in the equation [21, 31-33, 35, 41-43, 47, 48, 52, 53, 55, 57, 59]. The functional form of the scale variable(s) is either normal, squared, cubic, or log transformed, and sometimes, several forms are included in the same equation [36-38, 49, 50, 56, 58, 60, 67]. The classification of scale variables follows the one proposed for ACF. The most common categories of scale variables are related to *outcomes* (e.g. number of clients tested) [35-38, 42, 43, 47, 49, 50, 52, 53, 55-57, 60] or *outputs* (beneficiaries or coverage of eligible population) [31, 32, 38, 43, 57, 58, 60, 63, 67]. Other scale variables related to *inputs*, *impact*, and *setting* are less commonly used. Only one category of scale variable is used in each cost function, with one exception [57].

The unit of analysis v is broad, the most commonly observed units are health facility [21, 32, 33, 35, 36, 38, 47, 50, 55, 56, 58, 60, 63, 67], NGO [43, 49, 52, 53], country [41, 42, 48]. The unit of analysis is sometimes time-dependent, affecting the choice of estimator for time series and/or panel data models [41, 48, 52, 53, 58].

3.4. Understanding factors considered when fitting a cost function

Several themes are identified through qualitative data analysis and are presented by projection approach in Appendix Figure A2. The intended use of cost projections is the major factor considered and is discussed here. Other motivators are scope of analysis, complexity of cost function, data-related considerations, method being easy to use, transparent, replicable, or whether the analysis tool is available online (Appendix Text A1). ACF have a broader range of motivators suggesting its wider range of applications, the main motivators are the intended use of the cost projection, scope of analysis, and the complexity of the cost function.

Intended use of cost projections

The reported uses of costs are the estimation of resource needs to inform budget preparation or funding application, to assess affordability of an intervention (feasibility study before investing resources) or to conduct scenario analyses of various strategies to inform planning. The focus can also be on the methodological approach for further institutionalisation to ensure regular update of resources projections for multi-year operational planning or mid-year review of strategic plan (integration to routine financial activities).

Studies also explore technical efficiency to optimize an existing programme, quantify potential economies of scale and scope, identify, and estimate determinants of cost variation between intervention sites, and identify variables that predict health care needs between sites and use them to develop weights for allocating resources between geographical areas.

Other studies aim to promote a new intervention by generating information on its scale-up and present the costs of scaling-up to higher coverage levels as a secondary analysis of a costing analysis. Finally, some studies conducted a cost-effectiveness analysis at scale.

A synthesis of study objectives by cost projection approach is presented in Figure 3 and follow the classification proposed by the Global Health Costing Consortium reference case [20]. Data extraction

methods are presented in Appendix Table A4. In summary, most studies informing short- and medium-term financial planning use ACF with one exception [31]. Long-term financial planning present nuanced approaches with either accounting, econometric or mixed approaches [37, 41, 48, 66].

For technical efficiency analyses, a few studies specifically explore how to measure the efficient scale of operation [21, 38, 49, 53, 67], while other studies analyse drivers of technical efficiency between sites more broadly, and all use ECF.

Only a few studies conduct an economic evaluation at scale using cost functions as per our inclusion criteria (excluding SCM) [51, 55, 65, 68]. We report a descriptive analysis of these applications in Appendix Text A2.

3.5. Critical review of studies included

Our critical review assesses the reporting of a list of key information related to the method used to project costs. This list of items can potentially provide guidance on how to assess the study quality and validity of projection results (Tables 3.a. and 3.b.). The list of reported information is not exhaustive and only capture the most critical criteria that should be reported.

For ACF, we find that most studies report in detail the composition of fixed costs (n=12, 80%) and variable costs (n=14, 93%), intervention levels (n=11, 73%) and scale variable (n=10, 67%). However, the sampling approach is not often representative (n=6, 40%) and uncertainty measures on cost projections are not always reported (n=7, 47%).

For ECF, several studies do not appropriately justify the choice of the estimator based on sample size and cost data features (n=5, 20%). When applicable (n=9), only a few studies assess the effect of the allocation method of costs incurred above the unit of analysis to sites (n=3, 33%). In most studies, the choice of the relevant scale variable is discussed (n=23, 92%). However, only a minority are reporting results of standard statistical tests of heteroscedasticity (n=7, 28%), endogeneity (n=5, 20%) and multicollinearity (n=7, 28%).

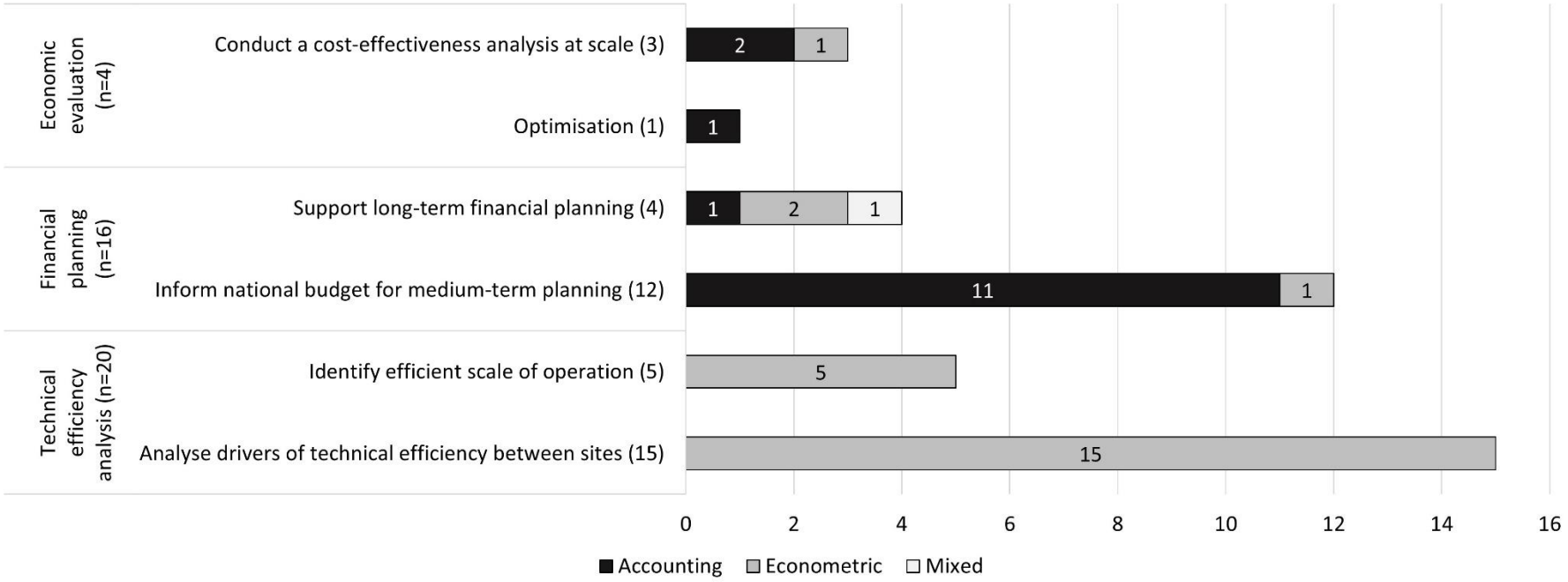


Figure 3. Synthesis study objectives by type of cost function (N=40)

Table 3.a. Accounting cost functions - Critical review of studies using key criteria for the assessment of transparency identified throughout the review process (N=15)

Criteria area	Accounting cost function method	Abdullah, 2012	Barasa, 2012	Cantelmo, 2018	Castaneda-Orjuela, 2013	Deghaye, 2006	Deo, 2019	Ensor, 2012	Kerr, 2015
Cost data	Composition of fixed costs is clearly reported and consistent with objectives of analysis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Cost data	Composition of variable costs are consistent with the scale variable applied	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Intervention levels	Intervention levels for scale-up projection estimates are clearly presented	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Scale	Scale variables are selected to follow as closely as possible the production function	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sampling approach	Sampling strategy is likely to be representative	Yes	No	Yes	Yes	No	No	Yes	NA†
Uncertainty	Measure of uncertainty on cost projections is reported (including sensitivity analysis)	No	No	No	No	Yes	No	Yes	No
Criteria area (continued)	Accounting cost function method (continued)	Marschall, 2008	Prinja, 2018	Rodrigues, 2014	Terris-Prestholt, 2006	Turner, 2016	Verguet, 2015	Winskill, 2017	

Cost data	Composition of fixed costs is clearly reported and consistent with objectives of analysis	Yes	Yes	Yes	Yes	No	No	No	
Cost data	Composition of variable costs are consistent with the scale variable applied	Yes	Yes	Yes	Yes	Yes	No	Yes	
Intervention levels	Intervention levels for scale-up projection estimates are clearly presented	Yes	Yes	Yes	Yes	No	No	No	
Scale	Scale variables are selected to follow as closely as possible the production function	No	Yes	No	Yes	No	No	No	
Sampling approach	Sampling strategy is likely to be representative	No	No	No	Yes	Yes	No	No	
Uncertainty	Measure of uncertainty on cost projections is reported (including sensitivity analysis)	No	Yes	Yes	No	Yes	Yes	Yes	

† Not Applicable

Table 3.b. Econometric cost functions - Critical review of studies using key criteria for the assessment of transparency identified throughout the review process (N=25)

Criteria area	Econometric cost function method	Adam, 2003	Ahanhanzoa, 2015	Ameli, 2008	Bautista-Arredondo, 2018a	Bautista-Arredondo, 2018b	Berman, 2018	Bollinger, 2014
Estimator	Choice of the estimator is appropriately justified given sample size and cost data features	Yes	No	No	Yes	Yes	Yes	Yes
Cost data	Effect of allocation method of costs incurred above the unit of analysis is assessed	No	NA†	No	NA	NA	NA	NA
Scale	Choice of the most relevant scale variables is discussed	Yes	Yes	Yes	Yes	Yes	No	Yes
Statistical tests	Test of heteroscedasticity is reported	No	Yes	No	No	Yes	No	Yes
Statistical tests	Test of endogeneity is reported	No	No	No	No	No	No	No
Statistical tests	Test of multicollinearity is reported	Yes	No	No	No	Yes	No	No
Criteria area (continued)	Econometric cost function method (continued)	Castro, 2016	Chandrashekar, 2010	Dandona, 2005	Galarraga, 2017	GBD Health Financing Collaborator	Guinness, 2007	Johns, 2013

						Network, 2018		
Estimator	Choice of the estimator is appropriately justified given sample size and cost data features	Yes	No	No	Yes	Yes	Yes	Yes
Cost data	Effect of allocation method of costs incurred above the unit of analysis is assessed	NA	No	NA	NA	NA	No	NA
Scale	Choice of the most relevant scale variables is discussed	Yes	Yes	No	Yes	Yes	Yes	Yes
Statistical tests	Test of heteroscedasticity is reported	NA	No	No	No	No	Yes	No
Statistical tests	Test of endogeneity is reported	Yes	No	No	No	Yes	No	No
Statistical tests	Test of multicollinearity is reported	No	No	No	No	No	Yes	No
Criteria area (continued)	Econometric cost function method (continued)	Lepine, 2015	Lepine, 2016	Marseille, 2012	Menzies, 2012	Meyer-Rath, 2012	Mujasi, 2015	Obure, 2016
Estimator	Choice of the estimator is appropriately justified given sample size and cost data features	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Cost data	Effect of allocation method of costs incurred above the unit of analysis is assessed	Yes	Yes	Yes	NA	NA	NA	No
Scale	Choice of the most relevant scale variables is discussed	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Statistical tests	Test of heteroscedasticity is reported	No	No	No	No	No	No	No
Statistical tests	Test of endogeneity is reported	Yes	No	No	No	No	No	No
Statistical tests	Test of multicollinearity is reported	No	Yes	No	No	No	No	No
Criteria area (continued)	Econometric cost function method (continued)	Parthan, 2012	Pitt, 2017	Schneider, 2007	Weaver, 2004			
Estimator	Choice of the estimator is appropriately justified given sample size and cost data features	Not available	Yes	Yes	Yes			
Cost data	Effect of allocation method of costs incurred above the unit of analysis is assessed	NA	No	NA	NA			
Scale	Choice of the most relevant scale variables is discussed	Yes	Yes	Yes	Yes			
Statistical tests	Test of heteroscedasticity is reported	No	Yes	Yes	Yes			
Statistical tests	Test of endogeneity is reported	No	Yes	No	Yes			
Statistical tests	Test of multicollinearity is reported	Yes	Yes	No	Yes			

† Not Applicable

Discussion

In their review, Johns et al. provide general guidance on factors to consider when adjusting costs to account for scale including : calculating separate unit costs for urban/rural setting; identifying (dis)economies of scale, separating the fixed and variable components of the costs; assessing the availability and capacity of health human resources; and including above service level costs [24]. We identified similar factors through the classification of fixed/variable costs at various intervention levels for ACF or, the classification of regressors for ECF. We further explore how to consistently apply these factors by proposing frameworks for each cost function based on the intended use of the cost estimates. We propose an approach to estimate variable returns to scale in cost projection methods, which is currently ignored in most studies. The development of these frameworks is based on the synthesis of cost function algebra from our study sample, the qualitative analysis of authors' motivators guiding the fitting of a cost function, and complemented by the methodological literature on healthcare cost data analysis. The following sections propose a framework to guide the decision process of fitting the ACF and ECF by study objective (Figures 4.a. and 4.b.).

As the review is broad in nature, and the aim is to synthesize information on the most innovative approaches, we excluded the commonly found SCM method from the search. However, we recognize the usefulness of this simplified approach for two reasons: (1) its simplicity and transparency, desirable for certain types of analysis, and (2) although intuitively less accurate as it assumes constant return to scale, there is no method obviously superior to another, i.e. no defined gold standard for each study objective.

1. Application of cost functions in the short and long run, implications for returns to scale

The analysis of costs at scale should account for the notion of time and application of economic concepts related to short and long run situations. In the short run, at least one input is fixed, whereas,

in the long run, all inputs can vary [69]. Based on the algebra, SCM is therefore applied only in the long run, ACF in both the short run (if some inputs are fixed) and the long run, and ECF ignores the notion of time because it does not use inputs in the regression model to project costs at scale.

SCM, following our definition, always uses linear relationship between variable inputs and output quantities, a given percentage increase in inputs leads to the same percentage increase in output. Therefore, SCM only accounts for constant returns to scale, and (dis)economies of scale are not measured.

In the short run, ACF identifies fixed input costs. As output increases, fixed costs are spread across more units of output and the average cost per output is decreasing, exhibiting increasing returns to scale. After a certain point in scale, average cost increases related to either the law of diminishing marginal return (short run), or theoretical diseconomies of scale such as management challenges at large scale (long run) [69-71]. However, the literature on cost functions usually agrees on a L-shaped average cost curve versus scale, rather than the theoretical U-shaped curve as diseconomies of scale are rarely empirically measured [49, 52, 72].

As it is increasingly relevant to account for decreasing returns to scale for the application of cost function formula to epidemics such as HIV, malaria where it costs more to reach the last percentage of the target population (remote areas, groups harder to reach, etc.), we identified how to account for decreasing return to scale with ACF. Winskill and colleagues applied a fixed delivery cost of malaria prevention technologies per person reached at a baseline amount, then after a given threshold, derived a logarithmic relationship between coverage and the delivery costs to account for higher costs of reaching the last percentage of the population [68]. Therefore, because of the flexibility in fitting non-linear relationship between output and input costs, ACF can account for variable (increasing then decreasing) return to scale contrary to SCM.

For ECF, the relationship between inputs and outputs is specific to each unit of analysis. Observed constant or variable returns to scale are identified by looking at the entire sample of sites. The values

of scale can be transformed to improve the goodness of fit in the regression model – in theory, log-transformation provides the best fit as it accounts for some increasing return to scale (economies of scale), and is often observed in the literature [35, 37, 38, 52]. A combination of transformed scale variables is sometimes found (e.g. logarithmic and quadratic), potentially accounting for increasing then decreasing returns to scale. The sign and value of the scale variable coefficient allow to measure (dis)economies of scale, other things being equal. Other cost determinants in the model (e.g. percentage of hard-to-reach group tested) can be varied as scale is increasing to account for variable returns to scale.

2. Accounting cost functions – Application for medium- and long-term financial planning, economic evaluation at scale

2.1. Fixed and variable costs

As a rule of thumb, most capital costs can be considered as fixed costs whereas recurrent costs usually compose the variable costs (Figure 4.a.). However, the treatment of costs as fixed or variable will depend on the type of intervention (costs that are considered fixed in a study can be considered variable in another study), the magnitude of intervention scale-up (high coverage of the population), the intervention level (more variable costs at service delivery level than above service delivery level), the intervention phase (development, start-up, and implementation), and whether the analysis is conducted in the short- or long-run [20].

Fixed costs can be both related to health programme costs and cross-cutting health system costs following the OneHealth costing tool classification [39]. Consideration of fixed costs depends on the intervention, some interventions have a small proportion of fixed costs compared to overall intervention costs [62], or considered insignificant [30, 39, 61, 66]. A major assumption with ACF using average fixed/variable costs is that for each intervention levels, we assume similar costs between units

(e.g. health facility, district) ignoring efficiency considerations (economies of scale and scope). Another issue relates to the consideration of joint costs and methods to allocate them to average costs, this is further explained in the Global Health Cost Consortium reference case [20]. This formula also assumes that average costs are constant over time, which might be acceptable in the medium-term but a limitation in long-term planning. Meyer-Rath and Over showed with the modelling of antiretroviral treatment costs at scale in South Africa that delivery costs can significantly change depending on how services are delivered and the rate of scale-up [21]. A measure of variability such as range or standard deviations should be reported, which is currently not done in most studies.

2.2. Intervention levels

Intervention levels are context-specific and consideration of costs and resources at each level depends on data availability, and the level of planning (e.g. national or district level). There is a need to acknowledge the considerable data challenges in LMIC because of the lack of routine cost data collection through accountancy systems or a simple way to extract this data. Consideration of different intervention levels also reflect the degree of integration of an intervention within the existing healthcare system. One should note that the composition of fixed and variable costs will depend on the intervention level.

2.3. Scale variables

Following the World Health Organisation classification, we classify scale variables into areas related to *inputs*, *outputs*, *outcomes*, and *impact* [18]. We also identify in this review, a new area related to *setting*. Scale variables correspond mostly to input, output and outcome variables at the service delivery level but might be less intuitive for above service levels where *setting* is more commonly used. The diversity of variables used implies a necessary choice from the authors on the selection of variable that replicate as realistically as possible a scale unit that follows the production process.

However, one should note that multiple output variables can act as proxies for scale. The choice of output variables also defines the composition of the relevant average variable cost and might lead to wide variation in the estimation of total costs. It also ignores the concept of quality of health care services which influences both scale and costs [21, 73].

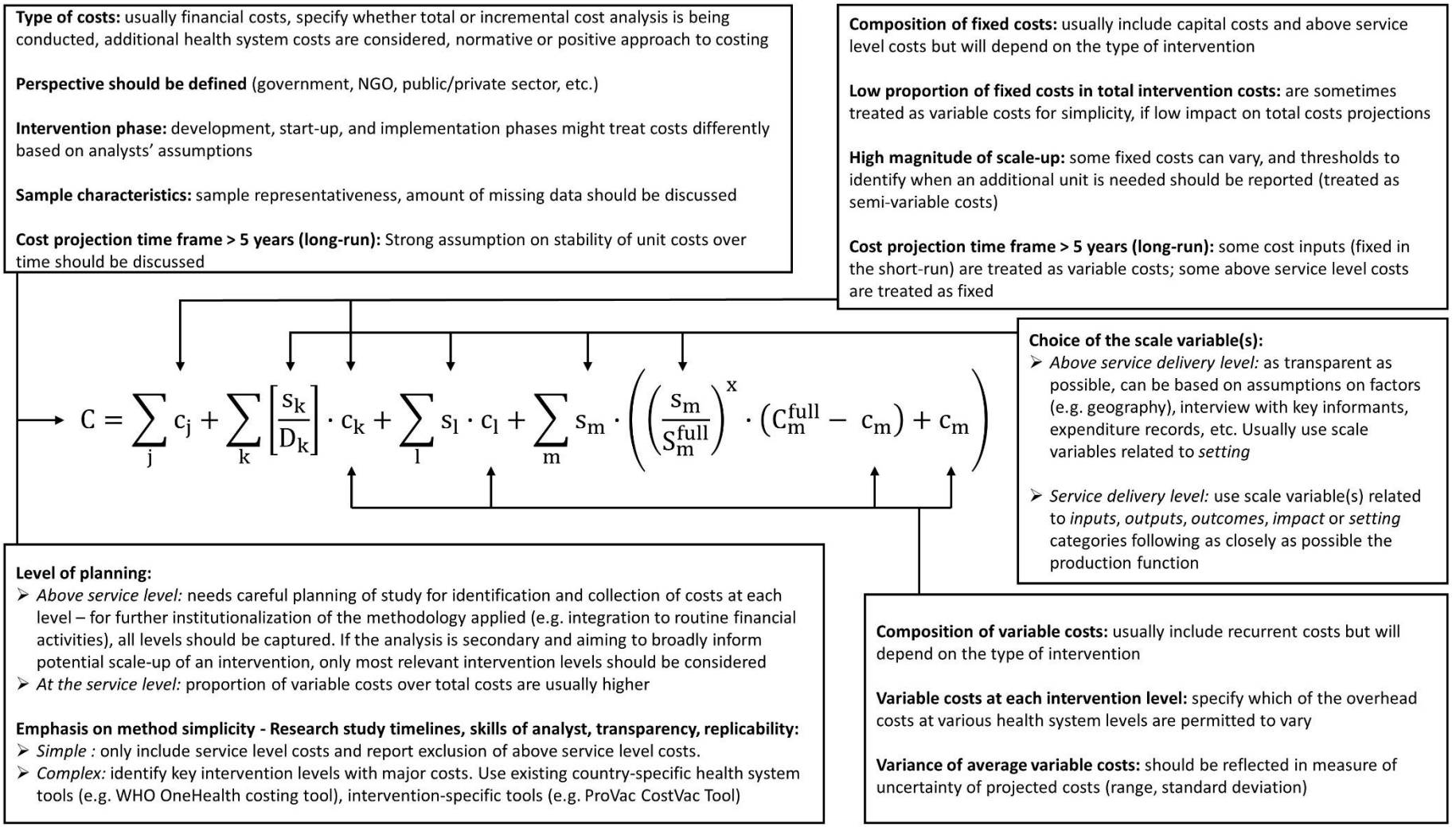


Figure 4.a. Framework – Fitting of accounting cost functions

3. Econometric cost functions – Application for technical efficiency analysis for estimating costs at scale, economic evaluation at scale

3.1. Choice of statistical method for cost data analysis

Challenges in finding the right specifications for regression models are well documented in the literature and choosing the best estimator for health care cost analysis is not simple [74-84] (Figure 4.b.). Several literature reviews and comparative studies exist to guide the choice and specification of a regression model [85-91], we find the review by Mihaylova and colleagues particularly useful [92]. We summarise in Appendix Text A3 the features of cost data to consider for model selection and in Appendix Table A7 the different estimators that can be used based on Mihaylova's review and empirical applications from our study sample [92]. However, in LMIC, most of studies are conducted on relatively few sites where data access is sometimes limited, posing a major challenge for the validity of statistical methods applied in this context. Apart from a few exceptions [21, 31, 36, 37, 41, 48, 52, 53, 59, 67], most econometric analyses in our review are conducted with a sample below one hundred. The feature of cost data is guiding the choice and specification of the regression models. Cases where there is a need to back transform to produce inferences on the original cost variable, rather than on the transformed cost variable are complex, and are out of the scope of this review.

3.2. Treatment of the dependent cost variable (total/average costs, inclusion/exclusion of above service level costs)

In studies included this review, researchers are either using total costs or dividing it by total output in a specified time period to obtain average costs. The choice of using average or total cost need to account for several factors. The choice to use average costs might be made to avoid the higher error terms due to heteroscedasticity in the estimated regression. Sometimes, standardised unit costs can be used across studies, such as cost per bed-day [31, 93, 94]. In other cases, an average cost function on

cost per sexual health consultation at a clinic could use cost per HIV test conducted or cost per sexually transmitted disease treated as the dependent variable. However, average cost functions depend on which of many outputs used in the denominator is arbitrarily chosen and might lead to ambiguous results. For instance, an average cost function can ignore the effect of economies of scope associated with the chosen output variable. The Breusch-Pagan test of heteroscedasticity can potentially help to assess whether to use total or average costs as a dependent variable [36] or a heteroscedastic robust estimator can be applied.

The inclusion of programme cost should also be considered carefully. As many above service level costs are intuitively fixed such as management, information system set up, and invariant with the scale of production, their inclusion or exclusion might have a big impact in the estimation of economies of scale, as discussed by Lepine and colleagues in the Avahan HIV prevention programme in India [52]. Their results highlight the importance of ensuring that above service level costs are considered when examining optimal operational size. In cases where the proportion of above service level costs is substantial, the allocation method to the unit of analysis should also be clearly reported. In these cases, two cost functions can be estimated, with and without inclusion of above service level costs [52].

3.3. Selection of variables including scale

A challenge in developing cost prediction models is the presence of many covariates. Therefore, variable selection methods should be applied to achieve a balance of prediction accuracy and avoid over fitting the model [84, 86, 92]. However, in economics, independent variable selection should be based on theory and not on fit, making model fitting challenging. In LMIC, the availability of good proxy variables is sometimes limited due to data scarcity and may require a less than optimal choice of covariates, for instance, when assessing quality proxied by a share of supervisory team or how well a site reached target groups of an intervention (e.g. sex workers for HIV care services).

Broadly, several groups of independent variables are identified in this review, including scale, quality, and organizational variables, following the classification proposed by Lepine and colleagues [52]: (1) quality: share of management staff in total staff, proportion of drugs out of stock during observation period ; (2) unit organizational characteristics: type of hospital, cost inputs (labor, drug costs), experience of medical staff/NGO; (3) environmental time-variant factors: GDP, target population size within unit of analysis; (4) environmental time-invariant factors: country, urban/rural setting, geographical characteristics (e.g. distance to nearest health facility); (5) characteristics of population targeted: socio-economic status, clinical characteristics (e.g. proportion of high-risk population reached). The purpose of this exercise can also guide the choice of explanatory variables. For instance, when the aim is to estimate average costs for countries where the data are not available, the chosen explanatory variables must be available in the out-of-sample countries [31]. Efficiency, or ''economies of scope'' parameters can be included as an independent variable to assess their impact on site-level costs. Ideally, incentives for increasing service efficiency should also be captured in the cost function.

When there is no commonly agreed measure as a proxy of scale (e.g. dose of vaccine delivered), the choice of variable(s) defining scale can sometimes be arbitrary (as for accounting methods) and can use wide range of variables related to *outputs* or *outcomes*. The economic theory can guide the choice of how to transform the scale variable. A number of studies have shown that, when using average cost as dependent variable, the cost function may be more consistent with an L-shaped curve in practice [49, 52], rather than the theoretical U-shape [72]. In addition, the scale can be tested whether a logarithmic form versus a quadratic, cubic functional form, or normal form explains a larger share of the variance. The issue of endogeneity for the estimation of unbiased economies of scale also needs to be addressed. It can arise from key independent variable omission, simultaneous relationship between scale and costs, and random measurement error, and has been described empirically by Lepine and colleagues [53].

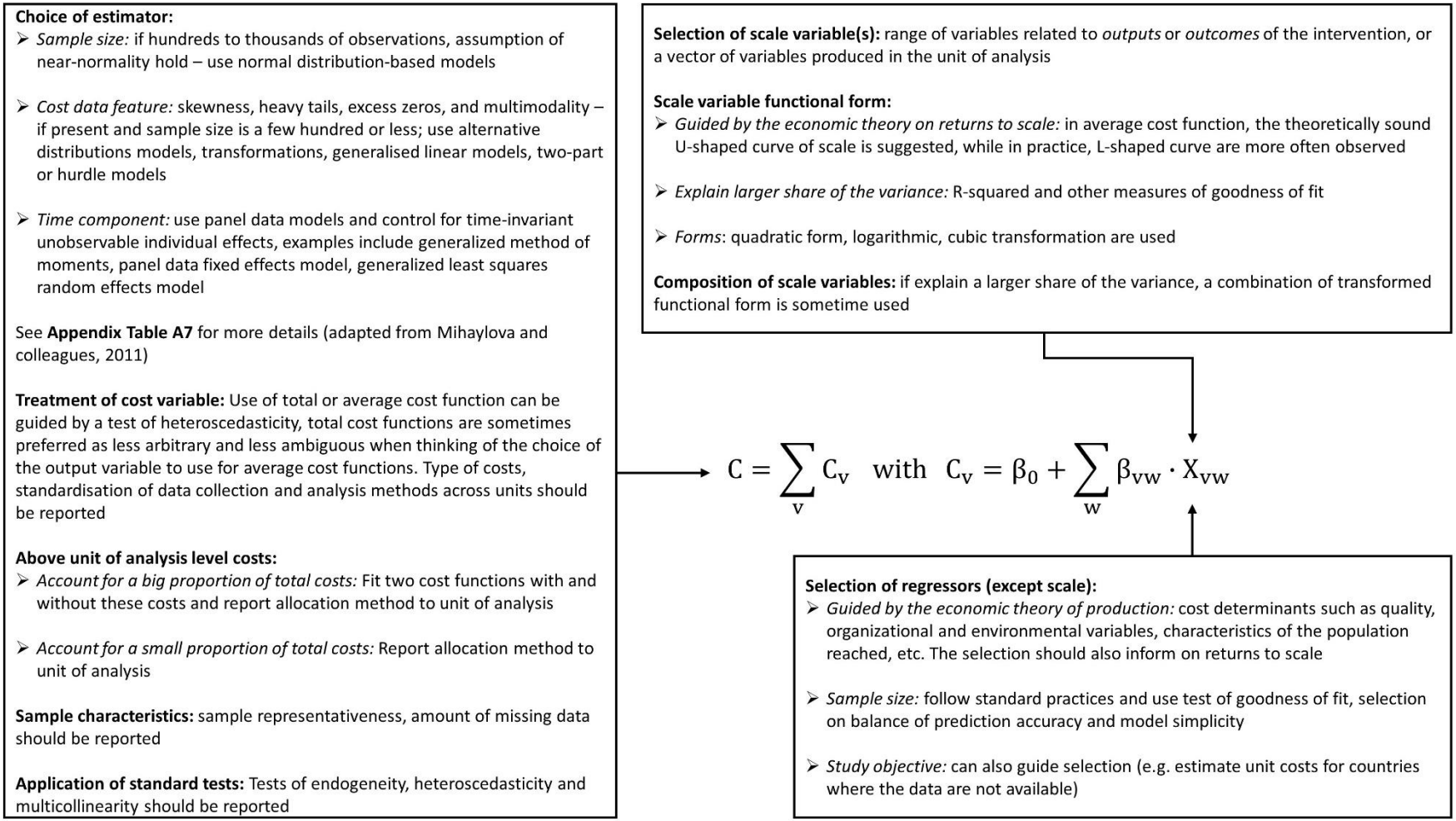


Figure 4.b. Framework – Fitting of econometric cost functions

4. Conclusion

The proposed notations and frameworks can offer a more consistent use of cost functions in LMIC by guiding the choice of the relevant approach based on the intended use of the cost estimate. We hope to facilitate the analysts' decision process of balancing simplicity versus accuracy when critical and increase the overall transparency in the reporting of methods.

Our study has a few limitations. First, the review is in majority based on the published peer-reviewed literature potentially missing other innovative methods. However, the aim was to select studies which already passed a peer-review process. Second, for ECF, the interpretation of coefficient of cost determinants, including scale, can be challenging (related to issues of back transformation), and is not discussed in this review because it is specific to each study. Third, because we almost never have information on observed costs at scale to compare with projected costs, the validation of cost projection approach in each study cannot be done, therefore only method reporting transparency, and expected validity of cost projections were assessed in our critical review.

Areas of future research include comparative analysis of these various cost function based on empirical data to further characterise similarities and differences between approaches, further integration of cost functions into economic evaluations, the development of a validated reporting checklist for study transparency and validity, and the development of econometric approaches that can address the issues specific to LMIC including working on a small sample of sites and restricted access to routine information and financial data.

Appendices – Chapter 3

Appendix Table A1. Search strategy – Research data bases

Data base	Search (06/02/2020)
Pubmed	Search ((((((((("Costs and Cost Analysis"[MeSH]) OR "Economic Development/organization and administration"[Mesh] OR "Economic Development/statistics and numerical data"[Mesh] OR "Economics, Hospital"[MeSH] OR "Economics, Medical"[MeSH] OR "Economics, Pharmaceutical"[MeSH] OR "Financial Management"[MeSH] OR "Financial Support"[MeSH] OR "Financing, Organized"[MeSH] OR "Health Care Sector"[MeSH] OR "Public Expenditures"[MeSH] OR "Models, Econometric"[MeSH] OR "cost function"[tiab] OR "cost functions"[tiab] OR "cost analysis"[tiab] OR "cost analyses"[tiab] OR "cost analyzis"[tiab] OR "cost analyzes"[tiab] OR "cost-effectiveness"[tiab] NOT "Cost Sharing"[MeSH] NOT "Drug Costs"[MeSH] AND ("2003/01/01"[PDat] : "2019/12/31"[PDat])))))))) AND ((((((((((((((("Implementation Science"[Mesh] OR "Program Evaluation/economics"[Mesh] OR "Program Evaluation/methods"[Mesh] OR "Program Evaluation/organization and administration"[Mesh] OR "Program Evaluation/statistics and numerical data"[Mesh] OR "Health Plan Implementation"[Mesh] OR "Health Priorities"[Mesh] OR "Health Resources"[Mesh] OR "Health Services Needs and Demand"[Mesh] OR "Needs Assessment"[Mesh] OR "Single-Payer System"[Mesh] OR "State Medicine"[Mesh] OR "Regional Health Planning"[Mesh] OR "Delivery of Health Care, Integrated"[Mesh] OR "Population Health Management"[Mesh] OR "Program Development"[Mesh] OR "Operations Research"[Mesh] OR "Efficiency, Organizational "[Mesh] OR "Linear Models"[Mesh] OR "Logistic Models"[Mesh] OR "Models, Economic"[Mesh] OR "Nonlinear Dynamics"[MeSH] OR "cost function"[tiab] OR "cost functions"[tiab] OR "mathematical modelling"[tiab] OR "mathematical modeling"[tiab] OR "mathematical model"[tiab] OR "mathematical models"[tiab] AND ("2003/01/01"[PDat] : "2019/12/31"[PDat])))))))))))))))) AND ((((Afghanistan[tiab] OR Benin[tiab] OR "Burkina Faso"[tiab] OR Burundi[tiab] OR "Central African Republic"[tiab] OR Chad[tiab] OR Congo[tiab] OR Eritrea[tiab] OR Ethiopia[tiab] OR Gambia[tiab] OR Guinea[tiab] OR Guinea-Bissau[tiab] OR Haiti[tiab] OR "North Korea"[tiab] OR Liberia[tiab] OR Madagascar[tiab] OR Malawi[tiab] OR Mali[tiab] OR Mozambique[tiab] OR Nepal[tiab] OR Niger[tiab] OR Rwanda[tiab] OR Sierra Leone[tiab] OR Somalia[tiab] OR "South Sudan"[tiab] OR Syria[tiab] OR Tajikistan[tiab] OR Tanzania[tiab] OR Togo[tiab] OR Uganda[tiab] OR Yemen[tiab] OR Afghanistan[ot] OR Benin[ot] OR "Burkina Faso"[ot] OR Burundi[ot] OR "Central African Republic"[ot] OR Chad[ot] OR Congo[ot] OR Eritrea[ot] OR Ethiopia[ot] OR Gambia[ot] OR Guinea[ot] OR Guinea-Bissau[ot] OR Haiti[ot] OR "North Korea"[ot] OR Liberia[ot] OR Madagascar[ot] OR

	Malawi[ot] OR Mali[ot] OR Mozambique[ot] OR Nepal[ot] OR Niger[ot] OR Rwanda[ot] OR Sierra Leone[ot] OR Somalia[ot] OR South Sudan[ot] OR Syria[ot] OR Tajikistan[ot] OR Tanzania[ot] OR Togo[ot] OR Uganda[ot] OR Yemen[ot] OR "Afghanistan"[Mesh] OR "Benin"[Mesh] OR "Burkina Faso"[Mesh] OR "Burundi"[Mesh] OR "Central African Republic"[Mesh] OR "Chad"[Mesh] OR "Democratic Republic of the Congo"[Mesh] OR "Eritrea"[Mesh] OR "Ethiopia"[Mesh] OR "Gambia"[Mesh] OR "Guinea"[Mesh] OR "Guinea-Bissau"[Mesh] OR "Haiti"[Mesh] OR "Democratic People's Republic of Korea"[Mesh] OR "Liberia"[Mesh] OR "Madagascar"[Mesh] OR "Malawi"[Mesh] OR "Mali"[Mesh] OR "Mozambique"[Mesh] OR "Nepal"[Mesh] OR "Niger"[Mesh] OR "Rwanda"[Mesh] OR "Sierra Leone"[Mesh] OR "Somalia"[Mesh] OR "South Sudan"[Mesh] OR "Syria"[Mesh] OR "Tajikistan"[Mesh] OR "Tanzania"[Mesh] OR "Togo"[Mesh] OR "Uganda"[Mesh] OR "Yemen"[Mesh] OR "South Africa"[Mesh] OR Angola[tiab] OR Bangladesh[tiab] OR Bhutan[tiab] OR Bolivia[tiab] OR "Cabo Verde"[tiab] OR Cambodia[tiab] OR Cameroon[tiab] OR Comoros[tiab] OR Congo[tiab] OR "Cote d'Ivoire"[tiab] OR Djibouti[tiab] OR Egypt[tiab] OR "El Salvador"[tiab] OR Ghana[tiab] OR Honduras[tiab] OR India[tiab] OR Indonesia[tiab] OR Kenya[tiab] OR Kiribati[tiab] OR Kyrgyz*[tiab] OR "Lao PDR"[tiab] OR Lesotho[tiab] OR Mauritania[tiab] OR Micronesia[tiab] OR Moldova[tiab] OR Mongolia[tiab] OR Morocco[tiab] OR Myanmar[tiab] OR Nicaragua[tiab] OR Nigeria[tiab] OR Pakistan[tiab] OR "Papua New Guinea"[tiab] OR Philippines[tiab] OR "Sao Tome and Principe"[tiab] OR Senegal[tiab] OR "Solomon Islands"[tiab] OR Sudan[tiab] OR Eswatini[tiab] OR Timor-Leste[tiab] OR Tunisia[tiab] OR Ukraine[tiab] OR Uzbekistan[tiab] OR Vanuatu[tiab] OR Vietnam[tiab] OR Zambia[tiab] OR Zimbabwe[tiab] OR "South Africa"[tiab] OR Angola[ot] OR Bangladesh[ot] OR Bhutan[ot] OR Bolivia[ot] OR "Cabo Verde"[ot] OR Cambodia[ot] OR Cameroon[ot] OR Comoros[ot] OR Congo[ot] OR "Cote d'Ivoire"[ot] OR Djibouti[ot] OR Egypt[ot] OR "El Salvador"[ot] OR Ghana[ot] OR Honduras[ot] OR India[ot] OR Indonesia[ot] OR Kenya[ot] OR Kiribati[ot] OR Kyrgyz*[ot] OR "Lao PDR"[ot] OR Lesotho[ot] OR Mauritania[ot] OR Micronesia[ot] OR Moldova[ot] OR Mongolia[ot] OR Morocco[ot] OR Myanmar[ot] OR Nicaragua[ot] OR Nigeria[ot] OR Pakistan[ot] OR "Papua New Guinea"[ot] OR Philippines[ot] OR "Sao Tome and Principe"[ot] OR Senegal[ot] OR "Solomon Islands"[ot] OR Sudan[ot] OR Eswatini[ot] OR Timor-Leste[ot] OR Tunisia[ot] OR Ukraine[ot] OR Uzbekistan[ot] OR Vanuatu[ot] OR Vietnam[ot] OR Zambia[ot] OR Zimbabwe[ot] OR "South Africa"[ot] OR "Angola"[Mesh] OR "Bangladesh"[Mesh] OR "Bhutan"[Mesh] OR "Bolivia"[Mesh] OR "Cabo Verde"[Mesh] OR "Cambodia"[Mesh] OR "Cameroon"[Mesh] OR "Comoros"[Mesh] OR "Congo"[Mesh] OR "Cote d'Ivoire"[Mesh] OR "Djibouti"[Mesh] OR "Egypt"[Mesh] OR "El Salvador"[Mesh] OR "Ghana"[Mesh] OR "Honduras"[Mesh] OR "India"[Mesh] OR "Indonesia"[Mesh] OR "Kenya"[Mesh] OR "Micronesia"[Mesh] OR "Kyrgyzstan"[Mesh] OR "Laos"[Mesh] OR "Lesotho"[Mesh] OR "Mauritania"[Mesh] OR "Moldova"[Mesh] OR "Mongolia"[Mesh] OR "Morocco"[Mesh] OR "Myanmar"[Mesh] OR "Nicaragua"[Mesh] OR "Nigeria"[Mesh] OR "Pakistan"[Mesh] OR "Papua New Guinea"[Mesh] OR "Philippines"[Mesh] OR "Sao Tome and Principe"[Mesh] OR "Senegal"[Mesh] OR "Melanesia"[Mesh] OR "Sudan"[Mesh] OR "Timor-Leste"[Mesh] OR

	"Tunisia"[Mesh] OR "Ukraine"[Mesh] OR "Uzbekistan"[Mesh] OR "Vanuatu"[Mesh] OR "Vietnam"[Mesh] OR "Zambia"[Mesh] OR "Zimbabwe"[Mesh] OR "developing countries"[tiab] OR "developing country"[tiab] OR "Low- and middle-income countries"[tiab] OR "Low- and middle-income country"[tiab] OR "developing countries"[ot] OR "developing country"[ot] OR "Low- and middle-income countries"[ot] OR "Low- and middle-income country"[ot] OR "Sub-Saharan Africa"[tiab] OR "South Asia"[tiab] OR "Middle East & North Africa"[tiab] OR "Latin America & Caribbean"[tiab] OR "Europe & Central Asia"[tiab] OR "East Asia & Pacific"[tiab] AND ("2003/01/01"[PDat] : "2019/12/31"[PDat]))))))
Embase, Global Health	1. "program cost effectiveness"/ or "cost"/ or "nursing cost"/ or "hospital cost"/ or "health care cost"/ or "hospital running cost"/ or "hospitalization cost"/ or "cost of reproduction"/ 2. economic model/ or economic status/ or economics/ or finance/ 3. economic development/ or financial management/ or health economics/ or informal sector/ or private sector/ or public sector/ or sustainable development/ or economic evaluation/ 4. statistical model/ or econometric*.ti,ab. 5. cost function*.ti,ab. 6. 1 or 2 or 3 or 4 or 5 AND 1. (low- and middle-income countries).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 2. (Africa or Asia or Caribbean or West Indies or South America or Latin America or Central America).hw,ti,ab,cp. 3. (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or Burkina Faso or Burkina Fasso or Upper Volta or Burundi or Urundi or Cambodia or Khmer Republic or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or Cape Verde or Central African Republic or Chad or Chile or China or Colombia or Comoros or Comoro Islands or Comores or Mayotte or Congo or Zaire or Costa Rica or

	Cote d'Ivoire or Ivory Coast or Croatia or Cuba or Cyprus or Czechoslovakia or Czech Republic or Slovakia or Slovak Republic or Djibouti or French Somaliland or Dominica or Dominican Republic or East Timor or East Timur or Timor Leste or Ecuador or Egypt or United Arab Republic or El Salvador or Eritrea or Estonia or Ethiopia or Fiji or Gabon or Gabonese Republic or Gambia or Gaza or Georgia Republic or Georgian Republic or Ghana or Gold Coast or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or Kyrgyzstan or Kirghizia or Kyrgyz Republic or Kirghiz or Kirgizstan or Lao PDR or Laos or Latvia or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania or Macedonia or Madagascar or Malagasy Republic or Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or Marshall Islands or Mauritania or Mauritius or Agalega Islands or Mexico or Micronesia or Middle East or Moldova or Moldovia or Moldovian or Mongolia or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or Netherlands Antilles or New Caledonia or Nicaragua or Niger or Nigeria or Northern Mariana Islands or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or Puerto Rico or Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or Saint Kitts or St Kitts or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Samoa or Samoan Islands or Navigator Island or Navigator Islands or Sao Tome or Saudi Arabia or Senegal or Serbia or Montenegro or Seychelles or Sierra Leone or Slovenia or Sri Lanka or Ceylon or Solomon Islands or Somalia or South Africa or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadzhik or Tanzania or Thailand or Togo or Togolese Republic or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR or Uzbekistan or Uzbek or Vanuatu or New Hebrides or Venezuela or Vietnam or Viet Nam or West Bank or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia).ti,ab. 4. ((developing or less* developed or under developed or underdeveloped or middle income or low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or population? or world)).ti,ab. 5. ((developing or less* developed or under developed or underdeveloped or middle income or low* income) adj (economy or economies)).ti,ab. 6. (low* adj (gdp or gnp or gross domestic or gross national)).ti,ab. 7. (low adj3 middle adj3 countr*).ti,ab.

	8. (lmic or lmics or third world or lami countr*).ti,ab. 9. transitional countr*.ti,ab. 10. Developing Country.sh. 11. south africa.mp. or South Africa/ 12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 AND 1. resource allocation/ or organizational efficiency/ or organizational structure/ or planning/ 2. implementation science/ 3. planning/ 4. health care management/ 5. health care management/ 6. program development/ 7. system analysis/ 8. program evaluation/ 9. process control/ or process design/ or process development/ or process model/ or process monitoring/ or process optimization/ 10. health care distribution/ 11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 AND Date: 01/01/2003 to 31/12/2019

Econlit	1 (low- and middle-income countries).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 00:01 _____ 2 (Africa or Asia or Caribbean or West Indies or South America or Latin America or Central America).hw,ti,ab,cp. 00:01 _____ 3 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or Burkina Faso or Burkina Fasso or Upper Volta or Burundi or Urundi or Cambodia or Khmer Republic or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or Cape Verde or Central African Republic or Chad or Chile or China or Colombia or Comoros or Comoro Islands or Comores or Mayotte or Congo or Zaire or Costa Rica or Cote d'Ivoire or Ivory Coast or Croatia or Cuba or Cyprus or Czechoslovakia or Czech Republic or Slovakia or Slovak Republic or Djibouti or French Somaliland or Dominica or Dominican Republic or East Timor or East Timur or Timor Leste or Ecuador or Egypt or United Arab Republic or El Salvador or Eritrea or Estonia or Ethiopia or Fiji or Gabon or Gabonese Republic or Gambia or Gaza or Georgia Republic or Georgian Republic or Ghana or Gold Coast or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or Kyrgyzstan or Kirghizia or Kyrgyz Republic or Kirghiz or Kirgizstan or Lao PDR or Laos or Latvia or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania or Macedonia or Madagascar or Malagasy Republic or Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or Marshall Islands or Mauritania or Mauritius or Agalega Islands or Mexico or Micronesia or Middle East or Moldova or Moldovia or Moldovian or Mongolia or Montenegro or Morocco

	or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or Netherlands Antilles or New Caledonia or Nicaragua or Niger or Nigeria or Northern Mariana Islands or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or Puerto Rico or Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or Saint Kitts or St Kitts or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Samoa or Samoan Islands or Navigator Island or Navigator Islands or Sao Tome or Saudi Arabia or Senegal or Serbia or Montenegro or Seychelles or Sierra Leone or Slovenia or Sri Lanka or Ceylon or Solomon Islands or Somalia or South Africa or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadzhik or Tanzania or Thailand or Togo or Togolese Republic or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR or Uzbekistan or Uzbek or Vanuatu or New Hebrides or Venezuela or Vietnam or Viet Nam or West Bank or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia).ti,ab. _____ 4 ((developing or less* developed or under developed or underdeveloped or middle income or low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or population? or world)).ti,ab. _____ 5 ((developing or less* developed or under developed or underdeveloped or middle income or low* income) adj (economy or economies)).ti,ab. _____ 6 (low* adj (gdp or gnp or gross domestic or gross national)).ti,ab. _____ 7

	(low adj3 middle adj3 countr*).ti,ab. _____ 8 (lmic or lmics or third world or lami countr*).ti,ab. _____ 9 transitional countr*.ti,ab. _____ 10 Developing Country.sh. _____ 11 south africa.mp. or South Africa/ _____ 12 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 AND 1 econometric*.ti,ab. _____

	2 (cost* adj3 analy*).ti,ab. _____ 3 (cost* adj3 estimat*).ti,ab. _____ 4 (cost* adj3 evaluat*).ti,ab. _____ 5 cost* function*.ti,ab. _____ 6 economic* model*.ti,ab. _____ 7 economic* development*.ti,ab. _____ 8 economic* evaluation*.ti,ab.

	_____ 9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 _____ AND 1 scale-up.ti,ab. _____ 2 scaling-up.ti,ab. _____ 3 (financial* adj3 planning*).ti,ab. _____ 4 (organi#ational* adj3 efficienc*).ti,ab. _____ 5 (program* adj3 evaluat*).ti,ab. _____

	6 (process* adj3 optimi#ation*).ti,ab. _____ 7 (process* adj3 control*).ti,ab. _____ 8 (process* adj3 develop*).ti,ab. _____ 9 (process* adj3 model*).ti,ab. _____ 10 (process* adj3 monitor*).ti,ab. _____ 11 (program* adj3 implement*).ti,ab. _____ 12 (process* adj3 implement*).ti,ab.

	_____ 13 (intervention* adj3 implement*).ti,ab. _____ 14 (system* adj3 implement*).ti,ab. _____ 15 (process* adj3 analy$*).ti,ab. _____ 16 (program* adj3 analy$*).ti,ab. _____ 17 (intervention* adj3 analy$*).ti,ab. _____ 18 (project* adj3 implement*).ti,ab. _____ 19

	(project* adj3 analy$*).ti,ab. _____ 20 (resource* adj3 allocat*).ti,ab. _____ 21 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 AND Date: 01/01/2003 to 31/12/2019
The Cost-effectiveness Analysis Registry, Global Health Cost Consortium unit costs database	All data extracted
Latin American and Caribbean Health Sciences Literature database	Subject descriptors: “Costs and Cost Analysis” OR “Economies of Scale” - ~ 370 results (after removed duplicates and filtered after 2003) – no restriction to LMIC because limited with filters and no proper mesh term for this. Given the reasonable # of ouputs, we did not restrict to the “scale” dimension

Search strategy – Grey literature

We reviewed the first 50 documents that result from the algorithm used in Google for different websites starting with tables of content and summary.

Web page	Organization	Search algorithm in google + filter by date (after 2003)	Documents reviewed	Notes
worldbank.org	World Bank	site:worldbank.org (cost AND (scale OR scale-up OR scaling-up) AND health) filetype:pdf	Many reports – mostly nutrition (health filter), cost multipliers, sometimes consider fixed costs and scale economies, one author comes back ''Shekar'' – no added value of these reports to our current selection of papers	+++ 0 included
who.int	World Health Organisation	site:who.int (cost AND (scale OR scale-up OR scaling-up)) filetype:pdf	Simple cost multiplier approach or published in academic literature	50 hits 0 included
clintonhealthaccess.org	Clinton Health Access Initiative	site:clintonhealthaccess.org (cost AND (scale OR scale-up OR scaling-up)) filetype:pdf	They have plenty of tool to guide budgeting and financial planning, but use simple cost multiplier	47 hits 0 included
unaids.org	The Joint United Nations Programme on HIV/AIDS	site:unaids.org (cost AND (scale OR scale-up OR scaling-up)) filetype:pdf	By Johns: incremental cost multiplier – accounting for some fixed costs and economies of scale – in academic literature Costing guidelines – cost multiplier based on population size Catch up plan - unit cost approach (Stover et al.)	42 hits 0 included
msf.org	Medecins Sans Frontieres	site:msf.org (cost AND (scale OR scale-up OR scaling-up)) filetype:pdf	Reasons for exclusion were: papers from journals already covered in academic database, or out of scope of review (cost analysis only)	1190 hits, 0 included

Appendix Table A2. List of data extracted for review

Field	Type of extraction	Extracted variable
Article information	Descriptive	Name of first author(s)
		Year of publication
		Name of the journal featuring the study
		Title
Intervention setting and scale-up process	Descriptive	Intervention sector and sub-classification (health, others)
		World region(s)
		Country(ies)
		Whether the study is conducted on LMIC only (yes/no)
		Primary study objective
		Secondary study objective(s)
		Health system level(s)
		Definition of the ''scale'' variable(s)
Cost projection method	Descriptive	Category of cost projection method (accounting, econometric, mixed, others)
		Definition of costs (total/average costs and financial/economic)
		Year(s) of cost data collection
		Year(s) of cost data analysis
		Time frame of analysis
		Cost variable in sample – highest value - (in USD – year of analysis)
		Cost variable in sample – standard deviation of highest value - (in USD – year of analysis)
		Cost variable in sample – lowest value - (in USD – year of analysis)
		Cost variable in sample – standard deviation of lowest value - (in USD – year of analysis)
		Cost variable projected – highest value - (in USD – year of analysis)
		Cost variable projected – standard deviation of highest value - (in USD – year of analysis)
		Cost variable projected – lowest value - (in USD – year of analysis)
		Cost variable projected – standard deviation of lowest value - (in USD – year of analysis)
		Uncertainty measure (standard deviations retrieved)
		Whether a sensitivity analysis on scale-up costs is conducted (yes/no)

		Estimator(s) (econometric approach only)
		Algebraic formula
		Independent variables except for scale (econometric approach only)
		Sample size(s) of cost variable (min-max) (mostly econometric approach)
	Analytical	Determinant(s) of the choice of the cost projection method
		Advantage(s) of the cost projection method
		Limitation(s) of the cost projection method

Appendix Table A3. Factors considered when fitting a cost function – Data extraction and theme identification

First author, year	Full text extractions	Bullet points	Theme 1	Theme 2	Theme 3	Theme 4	Theme 5
Abdullah, 2012	A key strength of the model is the capacity to accommodate these differences in costs and also in the way in which services are delivered (e.g., proportion of outreach and facility provided) in different localities. The relatively simple Excel-based model also enables managers to adjust the model to suit differences in costs and in program characteristics for different areas and thus makes more explicit and transparent the differences in costs to reach populations in different contexts. In addition, the key strength of the model is the transparency of the linkage between inputs, activities and key outputs, in terms of population targets. This enables health service managers to better see and understand these linkages and the implications for funding requirements and budget preparation. It also provides potentially a powerful advocacy tool to explain to district governments the linkage between budget allocations and expected outputs.	Differentiate costs between facility- and community-based delivery of intervention. Simple tool (excel) allow managers to adjust the model to suit differences in costs and in program characteristics for different areas and thus makes more explicit and transparent the differences in costs to reach populations in different contexts. Transparent links between inputs/outputs - enables health service managers to better see and understand these linkages and the implications for funding requirements and budget preparation. Useful for funding	Scope of analysis – differentiate between intervention levels	Ease of use – simple tool	Transparent – for health managers	Intended use – inform budget allocation	

		application/budget preparation. Advocacy tool to district government for linkage between budget allocation and expected outputs.					
Adam, 2003	Econometric models explain how total costs change in response to differences in service mix, inputs, input prices, and scale of operations. They allow cost and production functions to be specified with sufficient flexibility that a non-linear relationship can be demonstrated between costs and quantity of inputs: total costs can rise at a lower rate than prices. As the relationship between unit costs and the explanatory variables are expected to be non-linear, the Cobb-Douglas transformation was used to approximate the normal distribution of the model variables. Natural logs were used. The choice of explanatory variables is partly related to economic theory and partly determined by the purpose of the exercise, which is to estimate unit costs for countries where the data are not available. There are other possible uses of this model such as estimating the possible costs of scaling-up health interventions for the poor, which is receiving increasing attention with the activities of such bodies as the Global Fund to Fight AIDS, Tuberculosis and Malaria. This can be done in many ways, according to the objectives of the analysis. It may be used, for instance, to estimate: - unit costs at different capacity levels for purposes of efficiency analysis or economic evaluation of health interventions; - the "hotel" component of average cost per bed-day;	Allow cost and production functions to be specified with sufficient flexibility that a non-linear relationship can be demonstrated between costs and quantity of inputs. Choice of explanatory variables is partly related to economic theory and partly determined by the purpose of the exercise. Application to estimating costs of scaling up health intervention in many ways according to the objectives of the analysis. Application for use in cost-effectiveness analysis, cost estimates can be generated, including the costing of various coverage levels as well as the scaling-up of costs to the level of	Complexity - non linearity costs/inputs, economic theory	Intended use - cost of scaling up / CEA			

	- unit costs, excluding specific items such as drugs or food costs. Application for use in CEA (Baltussen, 2004): generate these cost estimates, including the costing of various coverage levels as well as the scaling-up of costs to the level of the epidemiological subregions.	the epidemiological subregions.					
Ahanhanzoa, 2015	Results from this type of analysis can support development of more targeted interventions to improve immunization program efficiency. These data should allow countries in the region to make some assessment of the impact of various strategies on overall costs. In terms of future research, these results also highlight the importance of full costing approaches in economic evaluations due to the significant contribution of human resource costs to total cost. The use of all resources (full costing) has been underestimated or not considered in other studies.	Can support the development of more targeted interventions to improve program efficiency. The model can assess the impact of various strategies on overall costs.	Intended use - improve program efficiency / scenario analysis				
Ameli, 2008	We were interested in seeing if there were any predictors of the relative cost, utilization and quality of services at the supported facilities, which provided nearly universal access in these provinces, as preparations began for renewing contracts with NGOs in 2008. This research reflects a priority policy issue for the Afghan health system. The optimal cost of implementing the BPHS is unknown and has been disputed since the programme began in 2003. In addition, little information is available about how expenditure on the BPHS is affected by environmental factors and various aspects of healthcare provision (e.g. inputs, outputs and quality).	Estimate determinants of costs, utilization and quality of services at health facilities. Identify optimal costs of implementing basic package of health services taking into account environmental factors and various aspects of healthcare provision (e.g. inputs, outputs and quality).	Intended use - determinants of costs/optimal implementation strategy				
Barasa, 2012	We estimated the cost ofscaling up this intervention with a number of assumptions: (1) Development costs do not vary with scale-up; given that they are only incurred once, they are not a function of the scale of the intervention; (2) That	Can differentiate between fixed costs, and other costs such as training, supervision,	Complexity - fixed/variable costs	Scope of analysis			

	training, supervision, and follow-up costs (implementation) vary as a function ofthe number of hospitals; (3) That treatment costs vary as a function of the number of pediatric admissions; (4)That the intervention would reach all 121 hospitals when at scale.	and follow-up costs (implementation) varying as a function ofthe number of hospitals; treatment costs varying as a function of the number of pediatric admissions Can define the scale of the intervention (121 hospitals here)					
Bautista-Arredondo, 2018a	Our study is the first to rely on a relatively large and representative sample of facilities in Nigeria. through this type ofanalysis we can learn what makes small facilities with lower costs different from other comparably small facilities providing services more efficiently (at lower costs), and implement interventions or programs that ensure or at least facilitate this result. A second implication is that programs should be aware ofthe higher costs per patient that inevitably will be observed in smaller facilities and budget appropriately for that. Results from this study support this service delivery model and show that task shifting is associated with lower unit costs. In terms ofmethods, studies can vary in the elements ofthe service provision included in the measurement of cost (staff, drugs, laboratory tests, capital, utilities, training, supervision, etc.). Some studies collected data on health care utilization at the facility level to estimate costs (patient charts, electronic data sets, pharmacy and other records), whereas others use a normative approach based on guidelines, or a combination ofboth. Our study aims to provide a reference point by reporting extensively on the methods used, including the largest sample	Can measure efficiency between facilities because can learn what makes small facilities with lower costs different from other comparably small facilities providing services more efficiently (at lower costs). Can measure eco/diseco of scale and budget appropriately for that. Can show task shifting effect on unit costs. Flexibility regarding the elements of service provision included in the measurement of costs (staff, drugs, laboratory tests, capital, utilities,	Intended use - measure efficiencies, eco. scale, task shifting	Scope of analysis - flexible regarding inputs included in measurement of costs			

	size thus far in a costing study in Nigeria, and relying on microcosting methods as much as possible.	training, supervision, etc.).					
Bautista-Arredondo, 2018b	This method allowed for more flexibility in the assumption of the error variance distribution. We assumed an identity link function and a Gaussian probability distribution, following the results of the modified Park test . We explored the role ofscale by estimating three specifications of the model; we began without adjusting for scale and then sequentially added the linear and quadratic terms of the log of VMMC clients. In all specifications, we tested for heteroskedasticity applying the Breusch-Pagan test and applied robust standard errors when appropriate. We also examined the Variance Inflation Factor (VIF) to assess the presence of multicollinearity.	Flexibility in the assumption of the error of variance distribution.	Scope of analysis				
Berman, 2018	Though we found no ideal way to project future costs of government primary care in Ethiopia, we feel that the two cost approaches (HSTP or cost function approach) likely represent high or low estimates of future resources needed to deliver primary care services. The HSTP cost estimates are potentially overestimates of the resource need because they are based on normative costs and standards to provide primary care. The cost function approach is an underestimate of the resources needed due to limited inclusion of capital investments, future changes in services offered among primary care facilities to meet changes in health needs, and future improvements that may be made in quality of services provided. We believe that the best estimate value probably lies between these two projections. These two approaches are likely to give different results. The cost function approach is based on actual spending on services adjusted for increases in coverage, scope, and time-varying factors. This estimate incorporates any underspending from existing gaps in utilization, quality differences, and scale and	Combination of cost projection methods to estimate high and low estimates. Cost multiplier based on standards to provide primary care and normative unit costs of services multiplied by planned utilization overestimate costs The cost function approach is based on actual spending on services adjusted for increases in coverage, scope, and time-varying factors. The cost function approach is an	Intended use - Estimate future scenarios of health care spending	Combination of cost projection methods	Complexity - method can include local sources of funding as well as development assistance for health		

	scope efficiencies in delivery. In addition, the woreda-based costs probably suffer from data quality problems. Data quality concerns consist of possible reporting errors in the HMIS (e.g., due to multistep aggregation from paper-based records before data are entered electronically) and incomplete woreda data on spending because of off-budget spending or in-kind provisions either from community contributions or external support. The HSTP estimates are based on normative unit costs of services multiplied by planned utilization.	underestimate of the resources needed due to limited inclusion of capital investments, future changes in services offered among primary care facilities to meet changes in health needs, and future improvements that may be made in quality of services provided.					
Bollinger, 2014	Econometric analyses can contribute to identifying potential cost savings associated with delivering HIV services. Various methodologies have been utilized to estimate potential efficiency gains for HIV prevention, including estimating efficiency frontiers and using a generalized linear mixed model to estimate the effect of cost determinants on annual per-patient HIV treatment costs.	Can estimate efficiencies (economies of scope/scale) and determinants of costs of the intervention.	Intended use - measure efficiencies, determinants of costs				
Cantelmo, 2018	To estimate resource requirements for the strategic plan, the Cambodian health ministry selected the OneHealth tool, a tool developed to inform national strategic health planning. To estimate costs of expanding public sector service provision, the health ministry chose the OneHealth tool, which incorporates many other disease or programme-specific tools used previously in Cambodia. The tool is a freely available software platform, whose development is overseen by the World Health Organization (WHO) and other agencies. The health ministry, development partners and other stakeholders attended tool training and data validation workshops and a high-level consultation meeting to discuss	The toold OneHealth incorporates many other disease or programme-specific tools used previously in Cambodia, is specifically designed to estimate resource requirements for a strategic plan and inform national health planning. Freely available software platform, whose development is overseen	Scope of analysis - not disease-specific, flexible regarding inputs included in measurement of costs	Availability - Free	Ease of use	Complexity - vary parameters such as quality/utilization of public sector services, public/private sector health	

	investment strategies, targets, cost scenarios and funding gaps. The health ministry formed the OneHealth tool costing team, who used the tool to estimate approximately 74% of total projected costs of the strategic plan; they calculated the remaining costs using Excel spreadsheets. The health ministry designed two scenarios for discussion due to uncertainty in the percentage of people who will access services in the public versus private sector. The first scenario assumed that the proportion of total health services delivered in the public sector remains constant. The secondassumed that the quality of public sector service delivery would improve under the strategic plan, resulting in a 25% increase in public versus private sector health service utilization. The health ministry selected the second scenario for inclusion in the new strategic plan due to planned quality improvements. The OneHealth tool was particularly useful for understanding health system requirements, which we found to be either lacking from costing exercises for vertical disease programmes or could have been double-counted when estimated separately by programme and then summed across programmes. Institutionalization requires further investment in health ministry capacity to ensure that regular updates of resource projections are made during multi-year operational planning or during the mid-term review of the strategic plan.	by WHO Can be institutionalized - The health ministry formed the OneHealth tool costing team, who used the tool to estimate approximately 74% of total projected costs of the strategic plan; they calculated the remaining costs using Excel spreadsheets. The team can ensure regular update of resources projections during multi-year operational planning or mid-year review of strategic plan Can vary parameters such as quality/utilization of public sector services, public/private sector health service utilization. OneHealth tool useful for understanding health system requirements (either lacking from costing exercises for vertical disease programmes or double-counted when estimated separately by				service utilization	

		programmes and then summed across programmes).					
Castaneda-Orjuela, 2013	provide comprehensive cost estimates for the entire EPI. The newly developed ProVac CostVac Tool is a valuable tool for collecting and estimating economic costs at different administrative levels of the EPI. It provides users with a detailed list of cost items that should be evaluated to generate precise total cost estimates of the EPI and includes a handbook that provides guidance to users on how to define the number of health facilities that should be sampled to conduct the exercise at local or lower administrative levels. There is an important link between the sampling strategy used and the extrapolation method and the relationship between the two should be kept in mind in order to develop unbiased estimates at the national level. Given the importance of developing a robust sampling design, this issue will continue to be explored in future pilots of the ProVac costing tool. The choice of applying the average cost-per-dose method in the Colombian setting, based on the empirical evidence from the data, allowed us to extrapolate the costs for the items captured in the lower level survey and generate reliable national-level estimates (Table 4) despite the heterogeneity in the unit cost per health facility. A costing tool with a valid and transparent methodology will be a useful instrument to generate EPI costs. Cost analysis of the routine EPI is an important input for cost-effectiveness analysis.	Tool (ProVac Costvac) is valuable for collecting and estimating economic costs at different administrative system levels of the expanded program on immunization Includes handbook to guide users on how to define the number of health facilities that should be sampled to conduct the exercise at local or lower administrative levels. Possibility to discuss impact of the sampling strategy used for estimating unit costs and the extrapolation method to national level - risk of bias - robust sample design will continue to be explored for this tool. Valid and transparent methodology to generate expanded program on	Scope of analysis - different health system levels	Ease of use	Data-related - Can deal with missing data	Transparency	Intended use - use in CEA

		immunization costs and can input into cost-effectiveness analysis.					
Castro, 2016	Given the presence of individual effects, vi (country specific effects), the model can be estimated assuming those effects as fixed or random. However, the lagged value of the dependent variable would be correlated with the error term even if the latter is not serially correlated. This implies that OLS estimates (random or fixed effects) will be biased and inconsistent (Baltagi, 2013). The estimators that take into account that bias can be grouped into: (i) bias-corrected estimators; and (ii) instrumental variables estimators. Bias-corrected estimators, like the one proposed by Bruno (2005a, 2005b) – the bias-corrected least squares dummy variable estimator (LSDVC) for dynamic panel data models – are suitable when the number of individuals (N) is small (and T is not very large). Although T is not large in this study, the number of individuals cannot be considered small (N= 156). Hence, this estimator is not a suitable tool to solve the bias problem caused by the inclusion of the lag of the dependent variable in the list of regressors. According to the large sample properties of the generalized method of moments (GMM), the dynamic estimator proposed by Arellano and Bond (1991) is adequate when there is a clear dominance of cross sections (N) over time periods (T) in the sample. This is what happens in our panel, which means that this estimator is a more appropriate procedure to solve the bias problem.	Can analyse determinants of cost using econometric methods. Generalized method of moments is adequate when there is a clear dominance of cross sections (N) over time periods (T) in the sample and can solve the bias problem, allowing to estimate future scenarios of health care spending.	Intended use - costs determinants	Data-related			
Chandrashekar, 2010	Multivariate linear regression analysis was used to give an initial insight into the causes of the variation in average cost between local implementing NGOs.	Multivariate linear regression analysis can provide initial insight into the causes of variation in average cost	Intended use - heterogeneity in costs				

		between local implementing non-governmental organizations.	between sites				
Dandona, 2005	The outputs, cost and efficiency estimates, relationship of efficiency with scale, and the unit incremental costs for each of the major activities of the sex worker programmes, presented in this paper could be useful for planning sex worker programmes and estimating the resources needed by them in Andhra Pradesh and other states in India.	The regression method can explore the relationship of efficiency with scale.	Intended use - can explore efficiency with scale				
Deghaye, 2006	Excel based model. This model is unique as it allows researchers to determine the changing resource requirements of a programme as patient numbers increase. The proportion of total staff time and facility time allocated to the programme is calculated for different patient numbers. This model estimates how per patient cost of HAART changes with patient numbers and estimates at what point new investment in facilities is needed. This is an advantage over other models that assume a static cost per patient and do not allow for economies of scale. Human resource costs of programmes are often neglected. This model focuses on human resource costs.	Determine the changing resource requirements of a programme as patient numbers increase nonlinearly. This model estimates how per patient cost of HAART changes with patient numbers and estimates at what point new investment in facilities is needed - advantage over other models that assume a static cost per patient and do not allow for economies of scale.	Intended use - assess resource requirements	Complexity - non-linear relationship between scale-up and cost, estimate at what point new investment in facilities is required			
Deo, 2019	We used quantitative and qualitative programmatic data ofthe three pilots from their respective launches (July to September 2014) until May 2016 to conduct a retrospective activity-based costing analysis. Realistic estimate of the budget required for a successful	Use real-world and country-specific data to realistic estimate the budget required for a successful national scale up using scale factors for	Complexity - use real-world and country-	Intended use - estimate the budget required			

	national scale up ofsuch models (use of various scale factors - in appendix).	different intervention levels.	specific data	for scale-up			
Ensor, 2012	The main approach to resource allocation has been to identify variables that explain need within a community and use them to develop weights for allocating resources between areas. In contrast, a low level of resources and intention to direct them to priority needs mean that many Low and Middle Income Countries (LMICs) aim to focus public funding for health care on a limited range of interventions that are of proven cost-effectiveness. A basic benefit package approach, focusing on a narrow range of mostly communicable disease and maternal and child health, has become a common feature of country sector strategies in many LMICs. The approach has been central to international initiatives advocating more but better targeted spending on health care [12,13]. A bottom up, approach to need for resource allocation may be practical for the limited range of services financed by the state in such countries and be more specific to needs than a general formula. Methods used to establish the normative costs of the package and the production of context specific scenarios. A user friendly interface to enter data and undertake simulations was constructed based on user forms in Visual Basic. Fixed overhead costs are permitted to vary across districts as they are directly related to the number of acilities that are required to serve a given population. Facility numbers are influenced by geography and topology so that a sparsely populated mountainous district will require, ceteris paribus, a larger number of facilities to serve population need. Similarly, while it is assumed that the proportion of patients with disease j requiring referral is similar across districts, the cost of referral (r) is influenced by proximity to referral facilities	The main approach to resource allocation has been to identify variables that explain need within a community (bottom up approach) and use them to develop weights for allocating resources between areas - practical for the limited range of services financed by the state in such countries and be more specific to needs than a general formula. A basic benefit package approach, focusing on a narrow range of mostly communicable disease and maternal and child health, has become a common feature of country sector strategies in many LMICs and is central to international initiatives advocating more but better targeted spending on health care Methods used to establish the normative	Scope of analysis - basic benefit package approach	Complexity - normative costs, fixed/variables costs	Intended use - resource allocation based on specific needs between sites, Indonesia (geographical specificity)		

	and so will vary across districts. The costing incorporates three types of fixed overhead (facility, SPM, district) Clearer costing that accounts for geographic differences in need provides a basis both for establishing the overall cost of SPMs over the entire country and indicate the level of (considerable) variation in different provinces and districts. The approach does not appear to be any more expensive or time consuming than an approach using proxy variables (based on application in Kenya and Timor Leste). In each country, the approach took approximately two months to develop and implement using available secondary data. Diverse scale factors are applied depending on the type of cost input.	costs of the package and the production of context specific scenarios. Costs are treated as fixed/variable - Fixed overhead costs are permitted to vary across districts as they are directly related to the number of facilities that are required to serve a given population - three types of fixed overhead (facility, minimum package of health services, district). The cost of referral is influenced by proximity to referral facilities and so will vary across districts Method that accounts for specific geographic characteristics of this country (Indonesia) and its impact on costs.					
Galarraga, 2017	Given the continued need for expanded services, while resources are diminishing, the main objectives of this paper are to document the costs of HIV prevention interventions, explore the predictors of economic efficiency, and quantify the potential economies of scale in the production of HIV prevention services.	Explore the predictors of economic efficiency, and quantify the potential economies of scale in the production of HIV prevention services.	Intended use - costs determinants, quantify economie				

	The dependent variable (average costs) was log transformed to more closely approximate a normal distribution, be able to apply linear regression methods, and to be able to interpret the scale coefficients as an elasticity. In addition, we included the following measures relevant to evaluating costs and efficiency determinants. Examining predictors of HIV prevention costs at the national level in sub-Saharan Africa Possibility to assess strength of relationships with R2. Cost function can explore task shifting.	Can explore task-shifting scenarios in cost projections.	s of scale, explore task shifting scenarios in cost projection s				
Global Burden of Disease Health Financing Collaborator Network, 2018	In brief, these methodological advances include the estimation of alternative (better and worse) future scenarios in addition to reference scenarios for each country; development of a structural framework to identify key covariates upon which to build our econometric models; and incorporation of several improvements to identify, rank, and pool the models that ultimately compose our final ensemble model and estimates of uncertainty.18 We then used these financing projections to estimate UHC index performance for each country-year through to 2040 using stochastic frontier analysis (SFA). We estimated the annual growth rate of GDP from 2018 to 2040 using an ensemble modelling approach. Out-of-pocket and prepaid private health spending, as well as total government spending were modelled as a share of GDP, whereas government health spending was modelled as a share of total government spending. We used a three-step process to estimate the future development assistance for health (DAH) disbursed to low-income and middle-income countries. For sources of DAH that are countries or national treasuries, we modelled DAH as a share of the source's government spending to make estimates of total DAH provided from 2018 to 2040. For sources without an	Method can estimate future scenarios of expected future health spending and pooled health spending for 188 countries over 2016-2040 period, with multiple financing sources (out-of-pocket, private insurance, development assistance, government spending), including transition from LMIC to HIC. Estimate alternative (better and worse) future scenarios in addition to reference scenarios for each country, develop a structural framework to identify key covariates upon which to build the	Scope of analysis - multi-country, multi-years, multiple financing sources	Intended use - estimate alternative future scenarios of health spending based on key covariates			

	associated GDP time series, such as corporate donations and private foundations, we estimated future DAH using autoregressive integrated moving average (ARIMA) models with no covariates. Second, we modelled DAH received for each recipient country, measured as a share of the total amount of DAH provided through 2040. Finally, we estimated the transition of countries from middle-income to highincome status on the basis of GDP per capita. This transition occurs when GDP per capita surpasses $13 741 per capita, the point of high-income transition defined by the World Bank. In addition to generating a reference scenario for each country from 2016 to 2040, we estimated two sets of alternative health spending scenarios for total, government, prepaid private, and out-of-pocket spending and DAH. Our projections highlight the large differences in expected future health spending and pooled health spending per capita across the globe, with high-income countries projected to spend 45·9 times (95% UI 37·1–54·6) more on total health expenditure per capita than low-income countries in 2040.	econometric models ; and incorporation of several improvements to identify, rank, and pool the models that ultimately compose the final ensemble model. As advances are made to quantify projections of a wider range of factors related to UHC, we aim to incorporate them into our models and increasingly narrow our estimates of uncertainty.					
Guinness, 2007	In the case of scale, economic theory suggests that as output increases average costs will first fall and then rise, resulting in a 'u' – shaped average cost curve. To test such a hypothesis for HIV prevention services estimates of the marginal cost (the change in total cost with each unit increase in scale) using a cost function approach are required. Expenditure data, for the financial year 2001/02, from 78 HIV state-funded prevention projects in Andhra Pradesh were analysed (the financial dataset) to explore the impact on costs of scale, target group, institutional history and price. This large sample allowed for statistically robust results. The model has a flexible functional form with linear, squared and cubed variables in output. The Cook-Weisberg (Breusch-Pagan) test was used to test for	Cost function method accounts for economies of scale and is flexible regarding choice of functional form of output variables.	Intended use - quantify economies of scale				

	heteroscedasticity. Multicollinearity is also assessed. In addition, differences between target groups are an important influence on cost. Total cost of vulnerable group projects are on average 11% higher than for the non-vulnerable group. This change in the intercept in the relationship between cost and coverage implies higher fixed costs in the vulnerable group projects. This is likely to reflect greater difficulty in reaching the more marginalized groups represented in vulnerable group projects (e.g. CSWs, men who have sex with men) and requiring greater investment in initiating the project, in particular in establishing a relationship with the community. When agency is included in the model, the case study data also confirms a difference in the production costs between funding agencies.						
Johns, 2013	This analysis will help policymakers understand the cost structure of child health services and will provide a baseline for determining how costs change over time and as the new programme expands.	Baseline for determining how costs change over time and as the new programme expands.	Intended use - estimate determinants of costs				
Kerr, 2015	To help national governments and other stakeholders understand their HIV epidemics and allocate limited resources most efficiently, we developed Optima (formerly known as Prevtool). A software toolbox that models (1) HIV transmission within and between population groups, (2) disease progression, (3) the effects of HIV prevention and treatment programs, and (4) the economic effects of policy choices. We designed it to be flexible and comprehensive enough to accommodate the regional, national, and epidemiological diversity of HIV epidemics. This article outlines the methodology underlying Optima and compares Optima to other commonly used HIV models, namely the Goals (Spectrum) Model, Epidemic Model	Help national governments and other stakeholders understand their HIV epidemics and allocate limited resources most efficiently. Designed to be flexible and comprehensive enough to accommodate the regional, national, and epidemiological diversity of HIV	Intended use - help governments/stakeholders to allocate resources more efficiently	Scope of analysis - various levels of intervention, link coverage/ costs/impacts			

	(AEM), Package (EPP), the AIDS the Estimation and Projection and the Modes of Transmission (MOT) model. For each HIV program, we derive one set of logistic curves that relate funding to program coverage levels and another set of curves (generally linear relationships) between coverage levels and clinical or behavioral outcomes (ie, the impacts that HIV strategies aim to achieve).	epidemics. For each HIV program, the authors derive one set of logistic curves that relate funding to program coverage levels and another set of curves (generally linear relationships) between coverage levels and clinical or behavioral outcomes (ie, the impacts that HIV strategies aim to achieve).					
Lepine, 2015	Regarding the GMM model presented in equation (3),it is important to point out that the lagged dependent variable was not statistically significant, justifying the use of the GMM in a nondynamic panel. The choice of the system GMM estimator is motivated by the fact that it has been found to be more efficient than the first-differenced GMM. The longitudinal nature of our data allows the use of a panel estimator with NGO fixed effects, which accounts for unobserved NGO time-invariant characteristics that are likely to be correlated both with the NGO size and its average cost. Finally, we use an IV method estimated by the two-stage least squares (2SLS) estimator, as presented in equations (4a) and (4b),in order to test the robustness of the results obtained from the system GMM - not the estimator of interest here.	Investigate the causal effect of scale on average cost and to estimate unbiased economies of scale: bias arising from endogeneity described in the paper: omission of pertinent variables in the analysis, simultaneous relationship between NGO size and average cost, and random measurement error, as well as another source of bias: method of allocation of above-level costs.	Intended use - quantify unbiased economies of scale				

Lepine, 2016	Panel data. Statistical tests to determine functional form, fixed or random panel estimator, etc. panel estimator with NGO fixed effects.	Method investigates into the drivers of cost of the Avahan programme during scale-up in order to inform programme managers to design economically efficient HIV prevention services using panel data.	Intended use - drivers of costs, efficiency analysis				
Marschall, 2008	The health planners of this district asked us to support them in assessing the impact on budgetary needs for primary care facilities if the needs of the population were covered as they see it to be necessary. Simplicity of methods have guided the choice of cost multiplier. Can show the important difference between average costs and marginal costs in order to convince policy-makers to base their decisions on marginal costs instead of average costs. fixed, step-fixed, variable costs.	Simplicity of methods guided the choice of deterministic approach using fixed, step-fixed, and variable costs, to guide health planners' decision in assessing the impact on budgetary needs.	Intended use - budgeting by health planners	Ease of use - simplicity of approach			
Marseille, 2012	These estimates can be used by policy makers to gauge the likely impact of scale-up on total ART expenditure depending on whether they primarily expand treatment in the types of facilities that have higher or lower estimated costs	Examine the correlates of variation in unit-costs and cost-effectiveness across the 45 health centers. Inform policy makers.	Intended use - cost determinants and impact on CE				
Menzies, 2012	Understanding the costs of HIV treatment serves two important functions. The first is to plan for future expenditure requirements: as HIV treatment requires lifelong care, initiation of patients on treatment implies a resource commitment both in the present and future. Gaining greater certainty about resource requirements puts funders in a better position to make long-term commitments about program targets. The second function is to suggest	Analysis of determinants of cost can help to plan for future expenditure requirements: as HIV treatment requires lifelong care, initiation of patients on treatment implies a resource	Intended use - costs determinants	Data-related - source of data: sufficient sample size for regression			

	strategies for improving the efficiency of HIV treatment programs. Big sample of facilities with consistent methodologies across countries - multi-country project.	commitment both in the present and future. Analysis of determinants suggest strategies for improving the efficiency of HIV treatment programs. Big sample of facilities with consistent methodologies across countries - allows to use regression analysis methods		analysis and standardized methods across countries/ sites			
Meyer-Rath, 2012	Most existing cost projections assume a single constant unit cost per patient-year, or per patient-year on a certain regimen, across large populations and often extended projection periods. A somewhat more complex approach is to assume a single unit cost for each of a set of services received by an HIV-positive patient, such as a unit cost for each type of laboratory test or outpatient visit or inpatient day, and then multiply these unit costs by an estimate of the number of each of these services per patient-year and by the number of patient-years delivered in a year. We call such an equation an accounting identity and designate a total annual cost so defined as an accounting identity cost function: TC = fixed +X*variable flexible cost function where TC is function of p and Z - vectors representing, respectively, the set of relevant input prices and all other policy and environmental determinants of cost.	Proposition of a more nuanced approach to estimate costs at scale, using flexible cost functions to better account for potential (dis)economies of scale (variation of assumption on scale elasticity - how those services will be delivered and how changes over time in the determinants of cost and quality will affect that delivery and estimated costs of scaling-up).	Intended use - quantify economies of scale	Complexity - flexible cost function	Data-related - source of data - sufficient sample size for regression analysis		
Mujasi, 2015	Andersen's behaviour model of health services utilization as a conceptual framework. This comprehensive model of the demand for health services was used in this study to identify independent variables likely	Andersen's behaviour model of the demand for health services was used in this study to identify	Intended use - analysis of cost				

	to influence essential medicines and health supplies utilisation at the health facilities in the districts and hence expenditure. The assumption is that since they determine utilisation of health services by the population, the identified independent variables influence the generated pharmaceutical expenditure as a result of utilization of the health services. Specifically, Andersen's model assumes that individuals' use of services is a function of their predisposition to use services (predisposing factors), factors that support or impede use (enabling factors), as well as their need for health care (illness level). According to Andersen, patients' illness level (representing the need factor) is considered as the major determinant of health care utilization. We run both linear-linear and loglinear models for each definition of pharmaceutical expenditure in order to select the model with the best fit. Table 2 shows the variables used in the multiple linear regression analysis to determine variations in pharmaceutical expenditure among the study districts.	independent variables likely to influence essential medicines and health supplies utilisation at the health facilities in the districts and hence expenditure. The assumption is that since they determine utilisation of health services by the population, the identified independent variables influence the generated pharmaceutical expenditure as a result of utilization of the health services. Specifically, Andersen's model assumes that individuals' use of services is a function of their predisposition to use services (predisposing factors), factors that support or impede use (enabling factors), as well as their need for health care (illness level).	variation between sites				
Obure, 2016	We estimate two specifications of the cost functions using the measures of integration. The first specification includes the individual measures of integration as covariates, while the	Use of cost function to evaluate the existence of economies of scale and	Intended use - determina				

	second includes the functional index of integration - can explore eco. scale/scope. The quadratic functional form is chosen because unlike the trans-logarithm functional form, it accommodates zero values for outputs therefore allowing for straightforward identification of economies of scope.	scope for integrated HIV and sexual and reproductive health service delivery in a sample of health facilities in Kenya and Swaziland.	nts of costs and measures of scale/scope efficiencies				
Parthan, 2012	The variable coefficients are best estimated using regression analysis, a statistical technique. Porter (2002) in his engaging book on the economics of waste shows how cost functions can be used by society to make decisions that are economically efficient. Stepwise regression was used to evaluate correlation. This method involves finding the best predictive variable, then controlling for its effect, and finding the next best predictor, and so on. This has the advantage of reducing the impact of co-linearity between predictive variables. A pre-set condition in stepwise regression procedure was that those variables below a significance level of 0.05 (p value associated with the t-test) would not be considered as statistically significant and would be automatically excluded from the model (Field, 2009). Inferences from costs correlated with population and costs correlated with waste quantity could be different - so 2 cost functions. Stepwise regression was used to evaluate correlation.	Analysis of determinants of costs for solid waste management - variable coefficients are best estimated using regression analysis and can be used by society to make decisions that are economically efficient. Stepwise regression was used to evaluate correlation. This method involves finding the best predictive variable, then controlling for its effect, and finding the next best predictor, and so on. This has the advantage of reducing the impact of co-linearity between predictive variables.	Intended use - determinants of costs and efficiency analysis				
Pitt, 2017	As our observations (health posts) were nested within a small number of clusters (districts), we fit a linear model with fixed effects at the district level (Mo¨ hring 2012) to account for this clustering.	Comprehensive analysis of cost drivers, the distribution of costs across the 3 months of	Intended use - determinants of	Data-related - source of data:			

	Scatter plots of all pairwise variable combinations were used to assess the linearity of relationships; logarithmic transformations were performed on skewed data and a quadratic term was added for any independent variables exhibiting a curvilinear relationship with costs.	administration and across health system levels, variation in costs between health posts, and economies of scale. As the observations (health posts) are nested within a small number of clusters (districts), the authors fit a linear model with fixed effects at the district level to account for this clustering.	costs, variation of costs between sites, economies of scale	observations nested within small number of clusters (choice of estimator)			
Prinja, 2018	Detail account expenditures to allow for progressive cost multiplier approach Only two blocks as unit - econometric approach would not be feasible. Approach is relevant from a fiscal planning point of view. Annualized unit cost for relevant cost inputs * number of units for scaling-up.	Only two blocks (level of subnational administrative division) as unit - econometric approach would not be feasible. This cost multiplier approach is relevant from a fiscal planning point of view.	Intended use - estimate costs of scale-up from fiscal planning point of view	Data-related - sample size too small for econometric approach			
Rodrigues, 2014	Costs for the mHealth intervention were studied from the perspective of the Indian NACP. Costs were collected based on the concept of avoidable costs specific to the mHealth intervention. The concept of avoidable costs refers only to the inclusion of costs that are contingent on the mHealth intervention, and all other costs were considered as sunk costs; that is, costs incurred even if the intervention was not undertaken. Sunk costs (e.g. costs of buildings) were not included in the study. The costs that were assessed were onetime costs as well as recurrent costs (the latter included	Estimate cost of national deployment of mHealth interventions from the perspective of the National AIDS Control Programme of India. Design of the costing study - Costs were collected based on the concept of avoidable	Intended use - costs of scale-up from the perspective of the National AIDS Control	Scope of analysis - incremental costing			

	fixed and variable costs). These costs were calculated as a function of fixed and variable costs using the formula: total cost for deployment of the IVR call plus SMS-programme-level costnumber of centrescentre-level costnpatient-level cost; where n- the number of patients.	costs specific to the mHealth intervention. The concept of avoidable costs refers only to the inclusion of costs that are contingent on the mHealth intervention, and all other costs were considered as sunk costs; that is, costs incurred even if the intervention was not undertaken (incremental costing approach). Sunk costs (e.g. costs of buildings) were not included in the study.	Program of India				
Schneider, 2007	Objective is to compare the effect on provider cost of two payment mechanisms: (1) user fees for drugs and services paid by the uninsured, and (2) capitation payment paid by MHI for the insured. To identify scale effects on payer-specific costs, the health centre cost structure is examined across different patient output levels.	The study objective is to compare the effect on provider cost of two payment mechanisms: (1) user fees for drugs and services paid by the uninsured, and (2) capitation payment paid by micro health insurance for the insured. The authors also examined the health centre cost structure across different patient output levels to identify	Intended use - determinants of costs and scale effects on costs				

		scale effects on payer-specific costs.					
Terris-Prestholt, 2006	Scale-up is geographical to other districts/wards - cost multiplier is transparent and can provide sufficient level of details. Unit cost per level (district, ward, facility, unit).	Estimation of the additional budget required to fund the 4-district scale-up of Mema kwa Vijana within an integrated public sector model. Scale-up is geographical to other districts/wards - cost multiplier approach can provide sufficient level of details by using unit cost per level (district, ward, facility, unit) - transparent and applicable for budgeting.	Intended use - estimation of budget required	Complexity - cost multiplier approach can provide sufficient level of details	Transparent		
Turner, 2016	In view of this need to rapidly scale up MDA,1–4 understanding how the cost and cost-eff ectiveness of MDA programmes might be affected by these reported economies of scale, and assessment of the potential eff ect of ignoring them on policy recommendations, is important. This finding is particularly relevant to NTDs because of the nature of the costs of MDA—many of which are fi xed, because the drugs themselves are often donated or inexpensive—but is also relevant to other large-scale control programmes. Formula is fixed costs + variable costs*number persons to treat.	Need to rapidly scale up mass drug administration programme targeting Ascaris lumbricoides, understanding how the cost and cost-effectiveness of mass drug administration programmes might be affected by reported economies of scale, and assessment of the potential effect of ignoring them on policy	Intended use - CEA at scale	Scope of analysis - nature of costs (important share of fixed costs)	Combination of cost projection methods - comparative analysis	Complexity - account for potential economies of scale	

		recommendations, is important. Compare use of a cost function (cost multiplier: fixed costs + variable costs*number persons to treat) to take into account economies of scale to the standard method of assuming a constant cost per treatment (simple cost multiplier) when investigating the cost and cost effectiveness of scaling up a soil-transmitted helminths mass drug administration programme. This finding is particularly relevant to because of the nature of the costs of mass drug administration—many of which are fixed.					
Verguet, 2015	The analysis also broadly suggests the kind of fi nancial resources needed to enable surgery scale-up and health system strengthening in those countries, with the objective of mobilising country policymakers and the global health community towards committing such necessary investments. Target date of 2030 refers to the internationally adopted end date for the SDGs.	Estimation of financial resources needed for a large sample (88 LMIC countries) based on target of 5000 surgical operations per 100 000 population per year by	Intended use - estimate resource needs	Scope of analysis - multi-country, global targets for scale-up	Transparent - encourage policy makers and global health		

	Our analysis highlights the signifi cant fi nancial investments that scale-up of surgical services represents. Despite these required large investments, improving surgical capacity is a critical component of health system development, especially in the context of UHC. According to our analysis, a large number of low-income and middle-income countries will not be able to reach the target of 5000 surgical operations per 100 000 population per year by 2030 based on current rates of improvements. Hence, increased attention and commitment from the international community is essential for improving surgical services, a critical step for increasing access to basic health-care services. Unit cost per operating room construction*number of operating rooms to be built + unit cost per surgical procedure as given per income grouping*target (5000 surgical operations per 100 000) for the period.	2030 - format of the study objectives might have guided the choice of deterministic approach: unit cost per operating room construction*number of operating rooms to be built + unit cost per surgical procedure as given per income grouping*target (5000 surgical operations per 100 000) for the period Objective of mobilising country policymakers and the global health community towards committing such necessary investments - transparency might play a role in the choice of projection method.			communit ies towards committin g investmen ts		
Weaver, 2004	Big and representative sample of hopsitals in Vietnam - 654 out of 815 public hospitals in Vietnam. The question about scope is whether or not it is efficient to combine outpatient and inpatient care at the same facility. Physicians often need to see patients on both an inpatient and an outpatient basis; an outpatient who receives diagnostic exams may later be admitted or an inpatient that is discharged may need follow-up visits. In some cases, it may be more efficient for physicians to provide both types of care from a single office at the hospital. In other cases, it may be more	Big and representative sample of hopsitals in Vietnam - 654 out of 815 public hospitals in Vietnam. The study objectives are to measure economies of scale and scope for the six categories of hospitals in Vietnam -	Intended use - determina nts of costs, scale/sco pe efficiencie s	Data-related - big and represent ative sample			

	efficient to reduce the daily flow of a large volume of outpatients at the hospital by having separate facilities. These questions may be answered with estimates of a hospital cost function that shows the relationship between cost and output.	These questions can be answered with estimates of a hospital cost function that shows the relationship between cost and output.					
Winskill, 2017	In areas in which coverage of these interventions is not yet universal, it is important to understand the relative cost-effectiveness of the full suite of interventions and where the RTS,S malaria vaccine could contribute. Importantly, this needs to take into account the diminishing marginal returns associated with the scale-up of interventions that may lead to a higher unit cost at high levels of coverage. In the absence of detailed country-level data for all interventions, we adopted a unit costing approach. These were derived from the literature. The total cost (P) of delivering an intervention to an individual is assumed to consist of two components: the commodity cost (U) and the delivery cost (D): P = U + D. The commodity cost remains fixed per person (under the assumption that economies of scale have been reached) with respect to coverage (C). The delivery cost per person is fixed at a baseline amount, N, until coverage reaches a given threshold, Cτ, above which the delivery costs increase logarithmically. fixed + variable costs.	The study objective is to estimate the cost and impact of different malaria prevention intervention packages at varying levels of scale-up. In particular, to understand the relative cost-effectiveness of the full suite of interventions and where the RTS,S malaria vaccine could contribute. It needs to take into account the diminishing marginal returns associated with the scale-up of interventions that may lead to a higher unit cost at high levels of coverage. In the absence of detailed country-level data for all interventions, we adopted a unit costing approach (identifying	Intended use - CEA at scale	Complexity - accounting for diminishing marginal returns associated with scale-up	Data-related - source of data: absence of detailed country-level data - sourced from the literature and used cost multiplier approach		

		fixed/variable costs). These were derived from the literature.					

Appendix Table A4. Classification of study objectives – Data extraction and classification of intended use of cost estimates

First author, year	Full text extractions – Study objectives	Classification following the GHCC reference case	Study primary objective
Abdullah, 2012	to develop a simple and transparent costing tool that enables health planners to calculate the unit costs of providing basic health services to estimate additional budgets required to deliver services in accordance with national targets.	Financial planning	Inform national budget for medium-term planning
Adam, 2003	The purpose of the work described in this paper, a modelling exercise, was to use the data collected across countries to predict unit costs in countries for which data are not yet available, with the appropriate uncertainty intervals The specific objectives of this paper are to: • explain the observed differences in hospital inpatient cost per bed-day across and within countries; and • use the results to predict cost per bed-day for countries for which these data are not yet available.	Financial planning	Inform national budget for medium-term planning
Ahanhanzoa, 2015	Existing tools to assess routine immunization (RI) costs (such as the comprehensive multi-year plan) do not capture heterogeneity in facility costs. This is an important limitation as previous studies have demonstrated wide variation in facility cost that would contribute to national program costs and performance. The current manuscript seeks to address this issue by analyzing determinants of RI costs at facility level.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites

Ameli, 2008	To research the effects of changes in health service utilization and quality on the costs of the Basic Package of Health Services (BPHS) in 13 provinces of Afghanistan. The main study questions were: • How can NGO expenditure on the BPHS be explained by health service delivery inputs? • How do the local security situation and the geographical remoteness of the health facilities in the contract area of operation affect NGO expenditure? • What factors are related to patient satisfaction? • What does the evidence tell us about service delivery contracts with NGOs?	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Barasa, 2012	We also present an assessment of the costs of scaling up the intervention to the national level.	Financial planning	Inform national budget for medium-term planning
Bautista-Arredondo, 2018	1) to estimate the average annual cost per patient on antiretroviral treatment (unit cost) per facility in Nigeria, and 2) to describe the variation in costs across facilities and identify factors associated with this variation. We are particularly interested in exploring the relationship between cost variation and supply-side and service delivery model characteristics.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Bautista-Arredondo, 2018	Examine unit cost variation across facilities, and investigate key facility-level characteristics associated with cost variation using an econometric approach.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Berman, 2018	To explore the implications of future trends in external funding on Ethiopia's primary health care spending and the potential for domestic resources to sustain the growth of Ethiopia's primary health care system.	Financial planning	Support long-term financial planning
Bollinger, 2014	Estimating a cost function for HIV prevention services to calculate the potential economies of scale associated with VMMC as well as the impact of other factors. With the increasing importance of and investment in VMMC, it is important to understand the main cost drivers associated with providing VMMC services, and also any possible efficiency gains that might be achieved by adapting the service provision to each country setting. Results of this analysis could assist countries in planning scale-up of VMMC service delivery.	Technical efficiency analysis	Identify efficient scale of operation
Cantelmo, 2018	describe how the health ministry used the tool to inform development and prioritization of the strategy and its targets, how much it will cost to implement the plan, and if there are sufficient financial resources available to cover costs.	Financial planning	Inform national budget for medium-term planning

Castaneda-Orjuela, 2013	describes the ProVac CostVac Tool and presents results from a pilot exercise with the tool to estimate the total costs of the Expanded Program on Immunization (EPI) in Colombia. The tool described here is intended to help countries carry out immunization program costing consistent with WHO guidelines, and to provide a transparent framework for collecting and analyzing the cost data. The tool is particularly useful for measuring costs that generally are not visualized in EPI budgets at the central level, for example shared labor costs across public health programs at the service provision level. In addition, it will help countries develop standardized program costing estimates for the WHO-UNICEF Joint Reporting Form on Immunization, among other reporting purposes. Finally, the tool aims to provide countries with up-to-date costing data by allowing updates for part of the data in subsequent years while carrying over other data.	Financial planning	Inform national budget for medium-term planning
Castro, 2016	In our study, we move a step forward and analyse whether the increase in sugar availability/intake is causing health care expenditure to rise. To proceed with this study, we build our analysis upon the standard literature on the determinants of health care expenditure and estimate a dynamic panel data model over a sample of 156 countries for the period 1995–2014. Accounting for the traditional determinants of health care expenditure – income, population structure, medical/technological progress, urbanization, female participation in the labor force, share of public health expenditure, hospital beds, air pollution, among others – we find that an increase in sugar availability leads to a significant rise in diabetes expenditure (per capita and per diabetic) and in the growth rate of total health care expenditure per capita. This trend is observed in both developed and developing countries.	Financial planning	Support long-term financial planning
Chandrashekar, 2010	This paper explores the cost of Avahan activities during the first 2 years of its activity (financial years 2004/ 2005 and 2005/2006) as it moves from start-up to rapid scale-up. It documents the costs of implementation of HIV prevention for female sex workers, men who have sex with men and transgenders in 62 districts of the four Southern states where Avahan was operational, calculates the cost per person registered and the cost per sexually transmitted infection clinic visit and analyses the causes of cost variation across the NGO projects.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites

Dandona, 2005	As part of a study to assess the cost-efficiency of various HIV prevention strategies in Andhra Pradesh, we report data on the outputs, cost and efficiency of HIV prevention programmes for female sex workers.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Deghaye, 2006	This study aims to provide a comprehensive costing of highly active antiretroviral therapy (HAART) to health care workers, which goes beyond the estimation of drug and testing costs.	Financial planning	Inform national budget for medium-term planning
Deo, 2019	A critical success factor to ensure the scale-up ofsuch pilots and their successful integration into Revised National TB Control Program is to ensure that their cost is not significantly higher than the cost of providing TB care in the public sector, as is typically assumed. In this paper, we address this issue and estimate the operating costs of these pilots at various levels of population coverage and estimate the budget required to scale them at a national level.	Financial planning	Inform national budget for medium-term planning
Ensor, 2012	The focus of the study is on the estimation of the funding required in order to achieve the minimum SPM (minimum package of health services) coverage level defined politically for each service across different regions of the country taking into account variations in demography and epidemiology.	Financial planning	Inform national budget for medium-term planning
Galarraga, 2017	Lastly, the methods to measure cost and scale have developed slowly in the HIV field over the past decade with innovations still necessary to optimize program scale and economic efficiency (Kumaranayake 2008). Mathematical modelling in costing has played an important role, but the mathematical models can only predict accurately if there is empirical measurement of costs at various scales. Most of the literature has explored costs and scale in HIV prevention relying on modelling, with only few recent exceptions (Lepine et al. 2015); thus, the technical issues of documenting costs and their relationship with scale of HIV prevention services production remain as fertile areas of research with important policy implications.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Global Burden of Disease Health Financing Collaborator Network, 2018	We used historical health financing data for 188 countries from 1995 to 2015 to estimate future scenarios of health spending and pooled health spending through to 2040. Additionally, we assessed past relationships between pooled health spending and performance on a measure of universal health care service coverage. Last, we quantified the magnitude by which changes in health financing, as projected into the future, could lead to changes in universal health care by 2030 and 2040.	Financial planning	Support long-term financial planning

Guinness, 2007	The paper presented here goes beyond the simple regressions used in this previous research to estimate an econometric cost function for HIV prevention services. It uses the commercial sex worker cost data presented in Guinness et al [28] and a new set of data from 78 HIV prevention projects for vulnerable groups collected for the present analysis. Marginal costs for different levels of coverage are calculated to measure the degree of scale economies in HIV prevention projects targeted at high risk populations. The impact of other key contextual factors on total and average costs is also assessed.	Technical efficiency analysis	Identify efficient scale of operation
Johns, 2013	In this paper, we examine the costs of delivering child health services in 4 districts of Malawi at the start of the community-based case management programme for U5s. Also explore determinants of costs with cost functions.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Kerr, 2015	Optima can be used to (1) estimate epidemiological trends to produce long-term forecasts, including for counterfactual scenarios; (2) calculate program cost-effectiveness, returns on investment, and other economic and HIV-related health outcomes; (3) determine the allocation of resources and associated coverage levels that minimize any of several objectives, including the number of new infections, HIV-related deaths and disease burdens, current and future HIV-related costs, or combinations thereof; and (4) determine the minimal resources required to achieve specific targets regarding those objectives.	Economic evaluation	Optimisation
Lepine, 2015	This study aims to investigate the causal effect of scale on average cost and to estimate unbiased economies of scale (for the reasons of endogeneity described in the paper).	Technical efficiency analysis	Identify efficient scale of operation
Lepine, 2016	We therefore present here an investigation into the drivers of cost of the Avahan programme during scale-up in order to inform programme managers to design economically efficient HIV prevention services and to inform the design of HIV programmes that provide grants to NGOs more generally.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Marschall, 2008	We would like to demonstrate the impact of increased access to primary care on total and average costs in the rural health district of Nouna, Burkina Faso.	Financial planning	Inform national budget for medium-term planning
Marseille, 2012	In this article, we assess the cost and cost-effectiveness of the program for individual health centers and as a whole. Additionally, we examine the	Economic evaluation	Conduct a cost-effectiveness analysis at scale

	correlates of variation in unit-costs and cost-effectiveness across the 45 health centers.		
Menzies, 2012	Understanding the determinants of HIV treatment costs will help improve efficiency and provide greater certainty about future resource needs.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Meyer-Rath, 2012	PLoS Medicine Collection, ‘‘Investigating the Impact of Treatment on New HIV Infections’’ analyse the sensitivity of the projected population-level incidence reductions to the structure and assumptions of an epidemiological projection model [7–9]. This paper focuses on the cost side of such projection models. We begin with a general discussion of cost accounting identities versus flexible cost functions. Then we review the available literature on modelled estimates of the projected cost of ART provision, including ART for prevention, with a focus on identifying determinants authors have included, implicitly or explicitly, in their assumed cost function for ART service delivery. We then discuss the evidence for a number of such cost determinants. Finally, we present an example of a flexible cost function used to explore how economies of scale might affect the costs of scaling up ART in South Africa.	Technical efficiency analysis	Identify efficient scale of operation
Mujasi, 2015	Using regression analysis, this paper examines various models to explain observed variations in pharmaceutical expenditure at the district level in Uganda; with recommendations for models to be used for rough national pharmaceutical budget estimation, setting and allocation to the districts.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Obure, 2016	The objective of this study is therefore to estimate a multi-output cost function for integrated HIV and sexual and reproductive health service delivery to evaluate the existence of economies of scale and scope in a sample of health facilities in Kenya and Swaziland.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Parthan, 2012	The objective of this paper was to arrive at cost functions for a typical developing country dataset while stepping through the method previously used to arrive at cost functions for developed countries.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Pitt, 2017	We provide an economic analysis of the costs of administering three monthly courses of seasonal malaria chemoprevention in 2010 to a population of over 180,000 children aged 3 months to 10 years in central Senegal in the context of the step-wedge trial previously described. Extending the preliminary findings reviewed by WHO, we provide a	Technical efficiency analysis	Analyse drivers of technical efficiency between sites

	comprehensive analysis of cost drivers, the distribution of costs across the 3 months of administration and across health system levels, variation in costs between health posts, and economies of scale. We aim to inform decisions on whether to extend the recommended age range for seasonal malaria chemoprevention and draw conclusions of wider relevance to the implementation of other large scale health campaigns and the organization of the health system.		
Prinja, 2018	In this paper, we specifically report the cost of ReMiND program in district Kaushambi. Also, we estimated the scale up cost of this program in Uttar Pradesh state which is relevant from the fiscal planning point of view.	Financial planning	Inform national budget for medium-term planning
Rodrigues, 2014	In this paper, we present the costs that the National AIDS Control Programme in India would incur to deploy mHealth interventions on a national scale for antiretroviral treatment-adherence support.	Financial planning	Inform national budget for medium-term planning
Schneider, 2007	The analysis employs an econometric cost function to compare the effect of user fees and micro health insurance with capitation payment plus a small co-payment on provider cost and efficiency in health centres. Payer-specific marginal and average costs are estimated. Scale measures are derived to identify resource capacity in health centres.	Technical efficiency analysis	Analyse drivers of technical efficiency between sites
Terris-Prestholt, 2006	This paper presents the annual costs of implementing the Mema kwa Vijana trial intervention by project phase (development, startup, implementation), by component, by nature of inputs (capital and recurrent costs), and by year (1997–2001); unit costs are presented over 3 years. Estimates of the additional budget required to fund the 4-district scale-up of Mema kwa Vijana within an integrated public sector model are presented.	Financial planning	Inform national budget for medium-term planning
Turner, 2016	We aimed to use a soil-transmitted helminths transmission model to compare use of a cost function to take into account economies of scale to the standard method of assuming a constant cost per treatment when investigating the cost and cost effectiveness of scaling up a soil-transmitted helminths mass drug administration programme targeting Ascaris lumbricoides.	Economic evaluation	Conduct a cost-effectiveness analysis at scale
Verguet, 2015	We aimed to model what volume of surgical services could potentially be achieved in low-income and middle-income countries by the year 2030, at various rates of scale-up, and to estimate the associated costs.	Financial planning	Support long-term financial planning

Weaver, 2004	After a brief background section on hospital reforms in Vietnam, we report estimates of the hospital variable cost function using the data from the survey of hospitals in Vietnam. These estimates were used to calculate marginal costs, short-run returns to the variable factor, economies of scale, and economies of scope for the six categories of hospitals.	Technical efficiency analysis	Identify efficient scale of operation
Winskill, 2017	Here, we use a well-established transmission model for Plasmodium falciparum malaria and its associated interventions to estimate the cost and impact of different intervention packages at varying levels of scale-up. We evaluate these packages over a wide range of transmission settings and use the estimates to derive the most cost-effective pathways for scaling-up malaria interventions in order to inform decisions about the introduction of the RTS,S malaria vaccine.	Economic evaluation	Conduct a cost-effectiveness analysis at scale

Appendix Table A5. Summary of study characteristics by year, outlet of publication, world region/country, and intervention sector (N=40)

	Frequency	%
Year of publication		
2003-2008 [6 years]	9	22%
2009-2014 [6 years]	12	30%
2015-2019 [5 years]	19	48%
Publication outlet – research areas and journals		
Health Economics	7	19%
Cost Effectiveness and Resource Allocation	4	11%
Health Economics	2	5%
The European Journal of Health Economics	1	3%

Health Management, Policy, and Planning	5	13%
Health Policy and Planning	3	7%
Journal of Health Systems & Reform	1	3%
The International Journal of Health Planning and Management	1	3%
Health Service Delivery	27	65%
BMC Health Services Research	1	3%
BMC Pregnancy and Childbirth	1	3%
BMC Public Health	1	3%
BMJ Global Health	1	3%
Bulletin of the World Health Organization	2	5%
Journal of the International AIDS Society	2	5%
PLoS medicine	2	5%
PloS one	6	12%
Sexually Transmitted Diseases	1	3%
Sexually Transmitted Infections	2	5%
Social Science & Medicine	2	5%
South African Medical Journal	1	3%
The Lancet	1	3%
The Lancet Global Health	1	3%
The Lancet Infectious Diseases	1	3%
Vaccine	2	5%
Waste Management	1	3%
Waste Management & Research	1	3%
World region and countries		
East Asia & Pacific	4	11%
Cambodia	1	3%
Indonesia	2	5%
Vietnam	1	3%
Latin America & Caribbean	1	3%
Colombia	1	3%

South Asia	10	23%
Afghanistan	1	3%
India	9	20%
Sub-Saharan Africa	19	48%
Burkina Faso	1	3%
Ethiopia	1	3%
Kenya	2	5%
Malawi	1	3%
Nigeria	1	3%
Rwanda	1	3%
Senegal	1	3%
South Africa	2	5%
Tanzania	1	3%
Uganda	2	5%
Zambia	1	3%
6 countries	1	3%
4 countries	1	3%
2 countries	2	5%
Unknown	1	3%
Multiple regions	6	15%
188 countries	1	3%
156 countries	1	3%
88 countries	1	3%
6 countries	2	5%
Unknown	1	3%
Intervention sector		
Health	39	97%
Adolescent Health	1	3%
Basic Package of Health Services	6	14%
Health Care Expenditures	2	5%

Health Insurance	1	3%
HIV	16	38%
Hospital Expenditures	2	5%
Malaria	2	5%
Maternal and Child Care	3	7%
Parasitology - Helminthiasis	1	3%
Pharmaceutical Expenditures	1	3%
Surgery	1	3%
Tuberculosis	1	3%
Vaccination	2	5%
Waste Management	1	3%
Solid Waste Management	1	3%

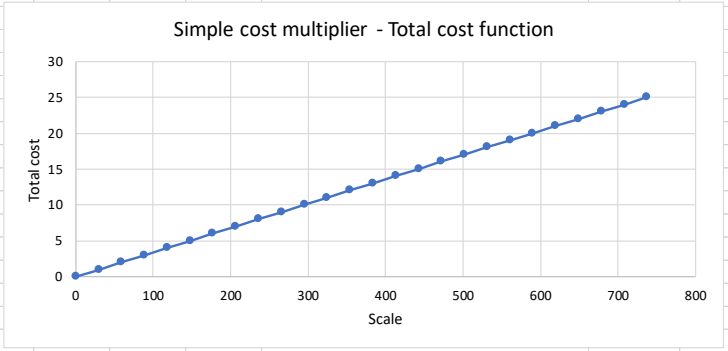
Appendix Table A6. Cost function mathematical notations: Applied examples

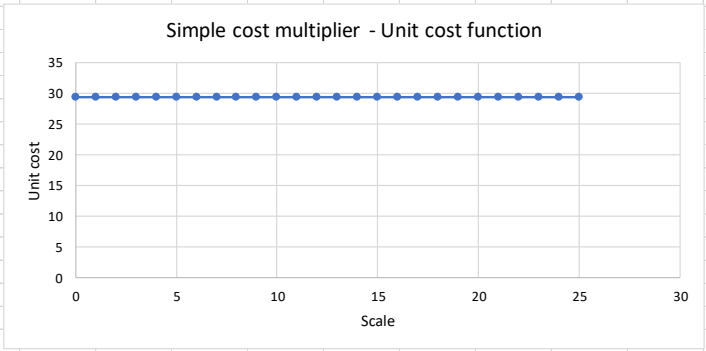
Simple cost multiplier

C:	Total costs of the HIV testing programme to reach desired scale
s:	Number of HIV test to conduct
UC:	Unit cost per HIV test conducted
i:	Building such as HIV testing centre, equipment such as laptop, personnel at health facility such as a nurse, HIV test supply
Pi:	Cost for conducting one HIV test corresponding to building, equipment, nurse time, price of one HIV testing kit
Qi:	Quantity of building and equipment allocated to one HIV testing session, nurse time for conducting one HIV test, one HIV testing kit

i	Pi (in US$)	Qi
Building: HIV testing centre	100	0.1
Equipment: laptop	20	0.75
Personnel: Nurse at HIV testing centre	5	0.3
Supply: HIV testing kit	3	1
UC	**29.5**	

C	s	UC
0	0	29.5
29.5	1	29.5
59	2	29.5
88.5	3	29.5
118	4	29.5
147.5	5	29.5
177	6	29.5
206.5	7	29.5
236	8	29.5
265.5	9	29.5
295	10	29.5
324.5	11	29.5
354	12	29.5
383.5	13	29.5
413	14	29.5
442.5	15	29.5
472	16	29.5
501.5	17	29.5
531	18	29.5
560.5	19	29.5
590	20	29.5
619.5	21	29.5
649	22	29.5
678.5	23	29.5
708	24	29.5
737.5	25	29.5



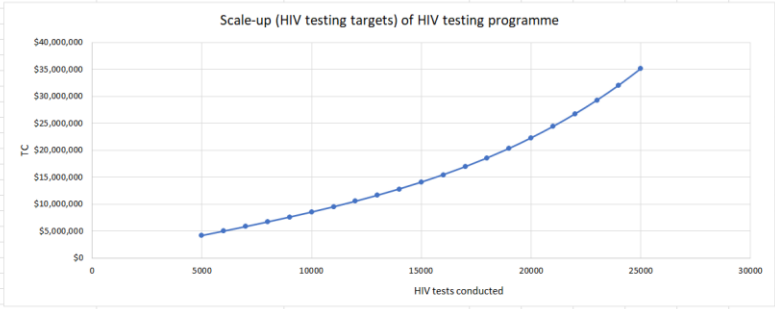


Accounting cost function

Example 1

cj	sk	Dk	ck	sl	cl	sm	Sfullm	cm	Cfullm	$\left(\frac{s_m}{S_m^{full}}\right)^x \cdot (C_m^{full} - c_m) + c_m$
central $	number of HIV tests to conduct	maximum number of test conducted per local facility per year	Yearly $ of running a local facility	number of HIV tests to conduct	$ of HIV test	number of HIV tests to conduct	number of HIV tests to conduct at full scale-up	average $ of reaching rural site	average $ of reaching rural site at full scale-up	
	5000			5000		5000				$305
	6000			6000		6000				$308
	7000			7000		7000				$313
	8000			8000		8000				$320
	9000			9000		9000				$328
	10000			10000		10000				$338
	11000			11000		11000				$351
	12000			12000		12000				$366
	13000			13000		13000				$384
	14000			14000		14000				$405
$100,000	15000	1000	$300,000	15000	$200	15000	25000	$300	$900	$430
	16000			16000		16000				$457
	17000			17000		17000				$489
	18000			18000		18000				$524
	19000			19000		19000				$563
	20000			20000		20000				$607
	21000			21000		21000				$656
	22000			22000		22000				$709
	23000			23000		23000				$767
	24000			24000		24000				$831
	25000			25000		25000				$900

Year	SCALE-UP = increase # of HIV tests conducted	total $								
2021	5000	$4,124,000	$100,000	2%	$1,500,000	36%	$1,000,000	24%	$1,524,000	37%
2022	6000	$4,949,766	$100,000	2%	$1,800,000	36%	$1,200,000	24%	$1,849,766	37%
2023	7000	$5,792,198	$100,000	2%	$2,100,000	36%	$1,400,000	24%	$2,192,198	38%
2024	8000	$6,657,286	$100,000	2%	$2,400,000	36%	$1,600,000	24%	$2,557,286	38%
2025	9000	$7,551,942	$100,000	1%	$2,700,000	36%	$1,800,000	24%	$2,951,942	39%
2026	10000	$8,484,000	$100,000	1%	$3,000,000	35%	$2,000,000	24%	$3,384,000	40%
2027	11000	$9,462,214	$100,000	1%	$3,300,000	35%	$2,200,000	23%	$3,862,214	41%
2028	12000	$10,496,262	$100,000	1%	$3,600,000	34%	$2,400,000	23%	$4,396,262	42%
2029	13000	$11,596,742	$100,000	1%	$3,900,000	34%	$2,600,000	22%	$4,996,742	43%
2030	14000	$12,775,174	$100,000	1%	$4,200,000	33%	$2,800,000	22%	$5,675,174	44%
2031	15000	$14,044,000	$100,000	1%	$4,500,000	32%	$3,000,000	21%	$6,444,000	46%
2032	16000	$15,416,582	$100,000	1%	$4,800,000	31%	$3,200,000	21%	$7,316,582	47%
2033	17000	$16,907,206	$100,000	1%	$5,100,000	30%	$3,400,000	20%	$8,307,206	49%
2034	18000	$18,531,078	$100,000	1%	$5,400,000	29%	$3,600,000	19%	$9,431,078	51%
2035	19000	$20,304,326	$100,000	0%	$5,700,000	28%	$3,800,000	19%	$10,704,326	53%
2036	20000	$22,244,000	$100,000	0%	$6,000,000	27%	$4,000,000	18%	$12,144,000	55%
2037	21000	$24,368,070	$100,000	0%	$6,300,000	26%	$4,200,000	17%	$13,768,070	57%
2038	22000	$26,695,430	$100,000	0%	$6,600,000	25%	$4,400,000	16%	$15,595,430	58%
2039	23000	$29,245,894	$100,000	0%	$6,900,000	24%	$4,600,000	16%	$17,645,894	60%
2040	24000	$32,040,198	$100,000	0%	$7,200,000	22%	$4,800,000	15%	$19,940,198	62%
2041	25000	$35,100,000	$100,000	0%	$7,500,000	21%	$5,000,000	14%	$22,500,000	64%

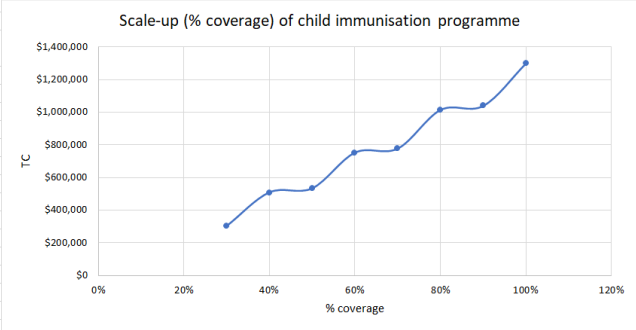


Accounting cost function

Example 2

% coverage	cj central $	sk number of new district office required for scale-up	Dk maximum number of district office per district	ck Yearly $ of running a district office	sl number of child to vaccine	cl $ of one vaccination session	sm number of new vaccine centre to build (~5/district)	Sfullm number of new vaccine centre to build for full scale-up (~5/district)	cm average $ of building a vaccine centre	Cfullm average $ of building a vaccine centre in the most remote setting (assuming increasing building $ between urban and rural settings)	$\left(\frac{s_m}{s_m^{full}}\right)^x \cdot (C_m^{full} - c_m) + c_m$
30%	$100,000	5	1	$30,000	25000	$1	25	125	$1,000	$2,000	$1,040
40%		10			50000		50				$1,160
50%		10			75000		50				$1,160
60%		15			100000		75				$1,360
70%		15			125000		75				$1,360
80%		20			150000		100				$1,640
90%		20			175000		100				$1,640
100%		25			200000		125				$2,000

Year	SCALE-UP = increase in % pop coverage	total $								
2021	30%	$301,000	$100,000	33%	$150,000	50%	$25,000	8%	$26,000	9%
2022	40%	$508,000	$100,000	20%	$300,000	59%	$50,000	10%	$58,000	11%
2023	50%	$533,000	$100,000	19%	$300,000	56%	$75,000	14%	$58,000	11%
2024	60%	$752,000	$100,000	13%	$450,000	60%	$100,000	13%	$102,000	14%
2025	70%	$777,000	$100,000	13%	$450,000	58%	$125,000	16%	$102,000	13%
2026	80%	$1,014,000	$100,000	10%	$600,000	59%	$150,000	15%	$164,000	16%
2027	90%	$1,039,000	$100,000	10%	$600,000	58%	$175,000	17%	$164,000	16%
2028	100%	$1,300,000	$100,000	8%	$750,000	58%	$200,000	15%	$250,000	19%



Econometric cost function

Adapted from d'Elbée et al. *BMJ Global Health* , 2021

HIVST: HIV self-testing kits

We assume the same UC across all sites v

$$C = \sum_{v} UC_v \cdot s_v \quad with \quad UC_v = \beta_0 + \sum_{w} \beta_{vw} \cdot X_{vw}$$

C: Total costs of the HIV self-testing programme to reach desired scale

v: community-based HIV self-testing kit distribution site

UCv: Unit cost per HIV self-testing kit distributed at the site

sv: Target number of HIV self-testing kits to distribute

Table - **Xvw:** Regressors introduced in the model

Variable category	Variable name
Quantities	Scale
Site organisational characteristics	HIVST distributors
	Campaign-style
	Efficiency
Characteristics of population targeted	% HIVST kits distributed to men
	% never tested for HIV
Environmental characteristics	Distance
	Catchment population
	% positivity at health facility
	HTS average cost at health facility
Input price level	Price level

$C = \sum_v UC_v \cdot s_v \quad with \quad Log(UC_v) = \beta_0 + \beta_1 *Scale_v + \beta_2 *Scale^2_v + \beta_3 *Scale^3_v + \beta_4 *Distributor\_site_v + \beta_5 *Campaign_v + \beta_6 *Log(Efficiency_v) + \beta_7 *Perc\_men_v + \beta_8 *Perc\_never\_tested_v + \beta_9 *Distance_v + \beta_{10} *Population_v + \beta_{11} *Positivity_v + \beta_{12} *Cost\_facility_v + \beta_{13} *Price\_level_v$

Where:

C: Total programme cost

v: Unit of analysis: community-based site

Log(UC_v): Natural logarithm of the unit cost per scale variable s_v for unit v

Scale: Average number of HIVST kits distributed per month

Distributor_site: Average number of distributors per site

Campaign: Type of intervention (campaign style (= 0) versus fixed distributors (= 1))

Log(Efficiency): Natural logarithm of the number of HIVST kits distributed per agent monthly

Perc_men: Percentage of HIVST kits distributed to men out of total distribution volumes

Perc_never_tested: Percentage of HIVST kits distributed to people who never tested before out of total distribution volumes

Distance: Distance of site from implementer's central warehouse (in kilometres)

Population: Size of total population at the site

Positivity: Positivity of rapid HIV testing (number of HIV-positive case found out of total number of persons tested) at nearby health facilities

Cost_facility: Unit cost per facility-based HIV testing session at nearby health facilities

Price_level: Proxy for input price level variation across countries based on per capita GDP

β_0: Model intercept

β_1-β_{13}: Model coefficients computed using empirical dataset

s_v: scale target: number of HIVST kits to distribute

		Values		
Parameters	**Estimate (parameters Beta)**	**2021**	**2022**	**2023**
Constant	3.153			
Scale (in thousands)	-1.578	2820	2079	4184
Scale^2 (in millions)	0.553	7952400	4322241	17505856
Scale^3 (in billions)	-0.056	22425768000	8985939039	73244501504
Campaign-style	0.174	0	0	0
Efficiency (log)	-0.049	16.4	9.2	15.4
% HIVST kits distributed to men	0.511	0.57	0.57	0.57
% HIVST kits distributed to people who	-0.097	0.02	0.02	0.02
Distance (in thousands)	0.603	381.5	381.5	381.5
% Positivity	0.177	0.03	0.03	0.03
HTS average cost	-0.004	4.3	4.3	4.3
Price_level (in thousands)	0.139	1118.1	1118.1	1118.1
	log(UC)	**2.45**	**2.37**	**2.73**
	UC	**$12**	**$11**	**$15**

Year	SCALE-UP: Number of HIVST kits to distribute across all units v	SCALE-UP: Number of HIVST kits to distribute monthly	UCv	C
2021	33840	2820	$12	$32,622
2022	24948	2079	$11	$22,351
2023	50208	4184	$15	$64,436

Appendix Table A7. Synthesis of estimators based on healthcare cost data features (adapted from Mihaylova et al, 2011)

Analytical approach	Normal distribution-based methods	Alternative distributions models	Transformations.	Generalised linear models	Two-part or hurdle models (out of scope?)	Panel data models
Type of analysis	Cross sectional	Cross sectional	Cross sectional	Cross sectional	Cross sectional	Longitudinal
Sample size	> hundreds to thousands	< hundreds to thousands	< hundreds to thousands	< hundreds to thousands	< hundreds to thousands	
Skewness	Yes	Yes +++	Yes +++	Yes +++	Yes +++	
Heavy tails	Yes	Yes +++	Yes +++	Yes +++	Yes +++	
Excess zeros	NA	NA	NA	NA	Yes	
Multimodality	Yes	Yes +++	Yes +++	Yes +++	Yes +++	
Estimator	linear regression approaches - Ordinary Least Squares	Ordinary Least Squares with Inverse gamma or lognormal (Cobb–Douglas) distributions	Ordinary Least Squares with log transformation of cost variable	Generalized linear models (Gamma, Poisson or negative binomial specification)	1/ Logit or probit model to estimate the probability of incurring any resource use or costs 2/ (a) Log-linear, GLM or OLS models to evaluate mean costs, and (b) truncated-at-zero Poisson, negative binomial , or truncated Poisson-lognormal models to evaluate resource use	Generalized method of moments linear mixed models Panel data fixed effects model Generalized least squares random effects model
Quotes	1/ assumption of near-normality of sample means depends on the	Sensitivity to alternative choices of distribution should be	Essential that an appropriate 'back transformation' is used to produce	Attractive approach when we have covariates. GLMs offer some of the benefits of alternative distributions and/or transformation without the		The overall goal is to control for unobservable (longitudinal)

	degree of skewness and also on the complexity of the covariate adjustment or subgroup analysis that is to be performed 2/ number of large costs should be sufficient for the answers not to be unduly influenced by a few very large outlying costs	assessed (Nixon and Thompson, 2004). In the case of the lognormal distribution the results may be non-robust to outliers in the data. The log-logistic distribution may be too heavy tailed to often be realistic in practice.	inferences on the original cost scale, rather than on the transformed scale. Checking sensitivity to the choice of transformation is recommended. In the case of the lognormal distribution the results may be non-robust to outliers in the data.	need to back transform. Limitations of GLMs is that they are based implicitly on assuming a particular distributional form (and so there is again a recommendation to check for sensitivity to this choice), and that the frequentist inferences involve approximation. Also, unless the identity link function is used (which may not always be realistic) there is still a back transformation issue that can lead to substantial loss of precision from ignoring the fuller characteristics of the data generating process.		individual effects constant over time. A Hausman test should be conducted to choose between a panel estimator with fixed effects and random effects. Should be further developed - these are examples found papers included in the review
Sources	Mihaylova, 2011	Mihaylova, 2011	Mihaylova, 2011	Mihaylova, 2011	Mihaylova, 2011	Lepine, 2015; Castro, 2016; Arellano & Bond, 1991; Windmeijer, 2005 Global Burden of Disease Health Financing Collaborator Network, 2018 Lepine, 2016 Obure, 2016

Appendix Text A1. Other factors considered when fitting a cost function

1. Scope of analysis (geography, type of intervention, intervention levels, time frame)

The scope of analysis also guide the choice of the method for both accounting [30, 34, 39, 40, 46, 51, 62, 65, 66] and econometric approaches [35, 48, 95].

It considers whether the evaluation is for a multi-country analysis, world region, country selection by income groups or adjusted to country-specific characteristics (e.g. Indonesia archipelago), or a single country [30, 34, 35, 39, 40, 46, 62, 65].

The scope of analysis can be related to the type of intervention, whether it is disease specific or not [35, 62, 95], related to a health area (e.g. vaccination, maternal health) [34, 40] or for an entire health package of basic universal health coverage (e.g. World Health Organization OneHealth tool) [39, 46].

It assesses whether the analysis can differentiate costs at different levels of the intervention (e.g. central, district, health facility, community, etc.) [30, 39, 40], estimate total versus incremental costs [62], can include additional health system costs (either lacking or double-counted when estimated separately by programmes and then summed across programmes) [39, 40], be carried out within a framework of overall health system capacity assessment (financial sustainability, identification of financial gap, etc.) [39, 51], differentiate between public and private sector health provision [39, 48], or account for environmental factors [48].

Finally, the possibility to include a time frame (for medium- or long-term projections) [30, 39, 62, 65, 66], application to longitudinal data to answer specific research questions also matters [48].

2. Complexity of cost function (flexibility in the treatment of cost data, inclusion of complex measure and economic concepts, measure of uncertainty)

The level of complexity that can be achieved with a specific method also influences the choice of cost projection method. For instance, the method can use real-world and country specific data to provide realistic cost estimates [39, 45]. The treatment of costs as fixed or variable, whether overhead costs at various health system levels are permitted to vary, the possibility of inclusion/exclusion of specific cost categories or focus on a specific one (e.g. human resource needs) [34, 39, 44-46, 64, 65, 68]. The method can account for local sources of funding as well as development assistance for health [37].

The method can explore measures traditionally difficult to include in the analysis: supply and demand side constraints such as availability of skilled workers [44, 96], quality of services [39], economies of scale or scope and can be flexible regarding choice of functional form of output variables [37, 65, 68], geographic factors impacting costs (e.g. distance to health facilities) [46, 64], or provide an analysis adjusting for different target groups with various health-related risks [46].

The method can include additional economic concepts such as the diminishing marginal returns associated with the scale-up of interventions (e.g. higher costs at high level of coverage for hard-to-reach groups) [68].

A measure of uncertainty can be included (standard deviation, confidence interval, etc.). The method can assess assumptions of the error variance distribution and allow the application of standard tests for heteroscedasticity and multicollinearity (regression models) [21, 31].

3. Data-related (data source and collection method, sample representativeness)

Specific sample characteristics influence the choice of the cost projection method. The source of data and collection method matters, for example whether data is empirical or modelled, country-specific or not, cost data collected through bottom-up or top-down costing approaches, and whether data collection and analysis methods are standardized across sites/countries [21, 41, 56, 60, 68, 97].

Additional consideration is on sample representativeness, whether the method can handle significant amount of missing data or omitted variables in regression analysis, provide a proxy when specific data is missing (e.g. variable to assess quality of service delivery), work effectively on small study samples or if the effect of the sampling strategy can be varied to assess the risk of bias of estimated costs [21, 40, 41, 56, 61, 67].

4. Other themes identified – Method being easy to use, transparent, replicable, and the analysis tool is available online

Emphasis is sometimes put on using a method that is simple enough to allow for non-experienced researchers to use the method and conduct the cost projection exercise in a short time period. In this case, the authors report a participatory approach with health service planners and experts from central and local governments, capacity building from the research team members, the possibility of training through workshops, on a user-friendly interface (e.g. Excel, OneHealth) [39]. Some studies report the development of handbook to guide users, therefore, facilitating adoption [40]. In one case, the authors choose a simplified method on purpose to remain as closely aligned with the assumptions in national health plans as possible [54]. Other themes identified less frequently but important nonetheless are method transparency and the possibility of replicating results [30, 40, 64, 66]. Lastly, the use of a tool freely available on the internet or from the authors, validated by international organization such as the WHO influences the choice of method [39].

Appendix Text A2. Application of cost functions to economic evaluations – A few examples

3.1. Econometric cost function used for cost-effectiveness analysis

Marseille and colleagues estimate the costs of providing antiretroviral treatment provision in forty-five health facilities in Zambia and fitted a cost function to assess predictors of costs and cost per DALY averted at health facility level. The authors apply a simple linear model using normal and log transformed average total cost per DALY averted as dependent variables, and use dummy predictors to indicate whether a facility falls above or below a threshold of cost-effectiveness [55].

3.2. Accounting cost functions used in dynamic transmission models for cost-effectiveness analysis applying a comparative approach with simple cost multiplier

To describe how the total cost per year of mass drug administration for the control of soil-transmitted helminths changes with the number of person treated, Turner and colleagues use a accounting cost function and compare with using the standard method assuming constant returns to scale [65]. They identify fixed costs at above service delivery level, invariant with scale, and incremental cost per treatment (variable cost), accounting for some economies of scale. They find that the accounting approach account well for the noted patterns in the cost data compared to the standard method and increase the cost-effectiveness in terms of preventing infections by over 70%, highlighting the limitation of using constant cost per treatment in dynamic transmission models.

Going further, Winskill and colleagues consider two approaches for costing increasing coverage of four interventions for Malaria prevention [68]. The first approach assume increases in coverage are associated with linear increases in cost. The second approach identifies: the commodity cost (fixed per person with respect to coverage) and the delivery cost fixed at a baseline amount, until coverage reaches a given threshold above which the delivery costs increase logarithmically therefore accounting for diminishing marginal returns when increasing the coverage leading to a closer picture (according to economic theory) of the cost-effective scale-up pathway.

3.3. Accounting cost functions used in software package for optimisation, CEA, etc. (Optima)

Kerr and colleagues developed Optima, a software designed to assist national decision-makers, programme managers, and funding partners to achieve maximum impact with the funding available for the country's HIV response [51]. Optima uses cost functions, which associates program expenditure with coverage levels using a logistic function to model cost–coverage curves. Whilst results are sensitive to uncertainty in the slopes of the cost– coverage–outcome relationships, relying on often sparse data available, this model present an innovative approach to the application of cost functions.

3.4. Combination of accounting and econometric approaches for range estimate (Berman)

To estimate future resource needs of the Ethiopia government primary care, Berman and colleagues develop an average cost function using the natural log of annual spending per capita in primary health care units at district level. The model specification are primary care per capita costs, key coverage indicators, socioeconomic status, and control for regional variations. This model is used to project future costs based on changes in key parameters forecasted over 20 years.

The cost function estimates for primary care are compared to a recent government costing exercise that was produced for Ethiopia's 2015–2020 Health Sector Transformation Plan, developed using the WHO's OneHealth costing tool. The accounting cost function projections are about 58% higher on average than econometric cost estimates for primary care between 2015–2016 and 2019–2020.

Because they are based on normative costs and standards to provide primary care, the OneHealth cost estimates are potentially overestimating the resource need. On the other hand, the econometric cost function approach might underestimate the resources needed due to limited inclusion of capital investments for instance. Consequently, the authors suggest that the two approaches likely represent high or low estimates of future resources needed to deliver primary care services. Although a

accounting approach is indeed likely to project higher estimates than an econometric one, it does not necessarily mean these are low and high estimates of the true value, nevertheless, the innovative approach taken can provide an informative range of cost projections. The distinction between normative and positive approaches to cost estimation is further explained by Scitovsky and Over [98].

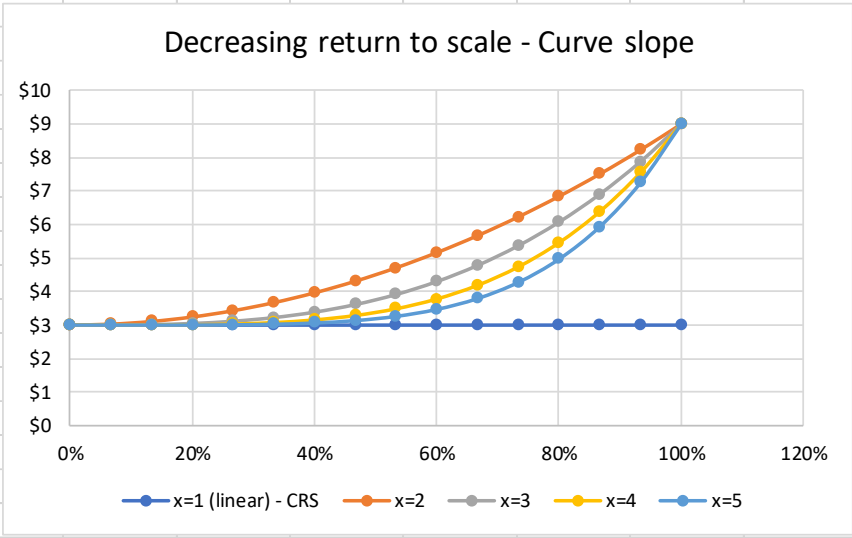
Appendix Text A3. Choice of statistical method for cost data analysis

Basically, the more flexible the function is, the more accurate it becomes, but the more statistically complex it is to specify, and the choice of the appropriate estimator will need to balance this. Challenges in finding the right specifications for regression models are well documented in the literature in high income countries and choosing the best estimator for health care cost analysis is not simple [74-84]. Several literature reviews and comparative studies exist to guide the choice and specification of a regression model [85-91], we find the review by Mihaylova and colleagues particularly useful [92]. The authors propose a selection of analytical approach based on four features of cost data: skewness, heavy tails, excess zeros, and multimodality. They recommend using simple methods in large samples (hundreds to thousands of observations) where the assumption of near-normality of sample means hold. In smaller samples, simple methods able to deal with one or two of the four criteria, are preferred but checking sensitivity to assumptions is necessary. For more complex dataset, some methods exist, but are not always validated and require good statistical knowledge [92]. We summarise in Appendix Table A6 the different estimators that can be used based on Mihaylova' review and empirical applications from our study sample [92].

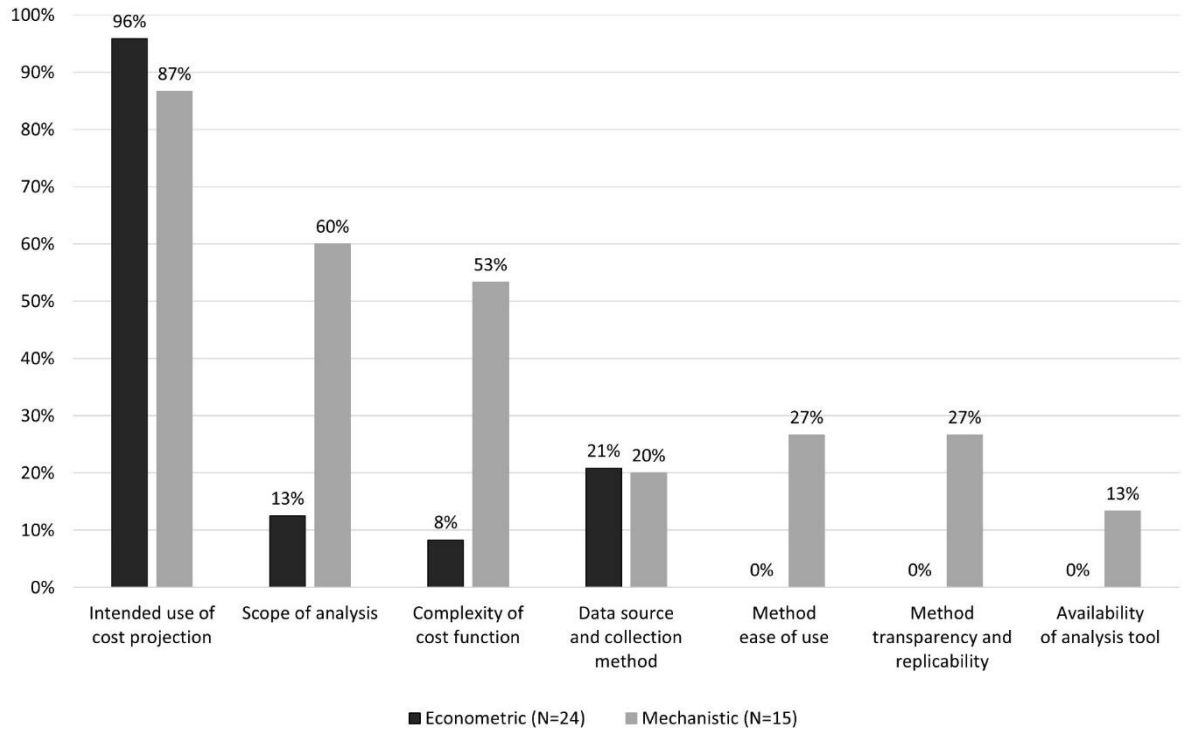
Appendix Figure A1. Implication of powers for the scale factor x applied to cost inputs m

Cm	$3
Cmfull	$9

Scale (#)	Scale (%)	x=1 (linear) - CRS	x=2	x=3	x=4	x=5
0	0%	$3	$3	$3	$3	$3
2000	7%	$3	$3	$3	$3	$3
4000	13%	$3	$3	$3	$3	$3
6000	20%	$3	$3	$3	$3	$3
8000	27%	$3	$3	$3	$3	$3
10000	33%	$3	$4	$3	$3	$3
12000	40%	$3	$4	$3	$3	$3
14000	47%	$3	$4	$4	$3	$3
16000	53%	$3	$5	$4	$3	$3
18000	60%	$3	$5	$4	$4	$3
20000	67%	$3	$6	$5	$4	$4
22000	73%	$3	$6	$5	$5	$4
24000	80%	$3	$7	$6	$5	$5
26000	87%	$3	$8	$7	$6	$6
28000	93%	$3	$8	$8	$8	$7
30000	100%	$3	$9	$9	$9	$9



Appendix Figure A2. Factors considered when fitting a cost function by type of cost function



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Conclusions from Paper 1

The results presented in this paper can guide the more consistent use of cost functions in LMIC using the relevant approach based on the intended use of the cost estimate. In particular, it can help the analysts' decision process of balancing simplicity versus accuracy when critical, and increase the overall transparency in the reporting of methods.

Research gaps

I presented in chapter 1 that HIVST can play a crucial role in the HIV response and attainment of the first UNAIDS 95 target. However, some important research gaps still exist related to operational considerations for effectively implementing and scaling up HIVST. These include the need to assess whether the addition of HIVST to existing community-based HTS can potentially generate economies of scope regarding HIV-positive case finding, as clients are encouraged to self-test for HIV, allowing HTS providers to conduct other HIV prevention activities. This question is explored in the Paper 2.

Another important consideration relates to the approach taken to integrate HIVST into existing HTS services. More specifically, some HTS provision channels targeting traditionally hard-to-reach criminalised and/or stigmatised groups such as FSW, MSM, PWUD and their sexual partners, are often run by civil society organisations (CSO) as we have seen with the ATLAS project. CSO working with these populations have an established relationship based on trust and years of experience working with these vulnerable groups. Implementing and scaling up a promising new technology such as HIVST requires an operational approach tailored to this context. With the ATLAS project, the non-governmental organisation Solthis was working with an umbrella of CSO differing regarding the scale of operation, the key populations they work with and the approach taken to respond to their specific needs, the challenges encountered including social stigma, or sometimes, CSO functioning with restricted administrative capacity, etc. The international partner organisation Solthis did require

progressive development and start-up phases to create and strengthen their collaboration with these CSO in Côte d'Ivoire, Senegal, and Mali. Paper 4 aims to explore the impact of developing sustainable approaches for adding HIVST to existing CSO activities, and to shed light on the potential long term economic benefits of fully integrating HIVST capacity into local CSO-led HTS programmes in these countries.

In addition, this thesis aims to fill research gaps, discussed in chapter 2, related to economic considerations of implementing and scaling up a new technology in LMIC using the case of HIVST implementation and scale-up in southern and western Africa. First, this thesis will cover some of the gaps related to costing community-based HIVST and HTS programmes for the general population in Lesotho, as well as for key populations and their sexual partners in Côte d'Ivoire, Senegal and Mali (Papers 2 and 4).

As previously mentioned, I will estimate potential efficiency gains from adding HIVST to HTS programmes by comparing the unit cost per HIV-positive case identified before and after the addition of HIVST to community-based HTS programmes in Lesotho over an observation period of two years. This analysis of efficiency gain will also raise important questions regarding costing methods, more specifically on adopting a full versus an incremental costing approach and its implications on the estimation of HIVST costs (Paper 2).

Beyond costing the observed interventions, there is a need to inform HIVST scale-up by further understanding how average cost per HIVST kit distributed are likely to vary when the programme is being scaled up from pilot evaluations to national programmes. I will conduct in Lesotho a cost analysis observing HIVST programme scale-up over two years of implementation (Paper 2). Using both accounting and econometric scale-up cost methods, I will estimate cost functions based on empirical data to estimate HIVST costs at scale. These cost functions will be applied for community-based provision of HIV self-testing services in five countries (Malawi, Zambia, Zimbabwe, South Africa, and

Lesotho) in southern Africa (Paper 3), and three countries (Côte d'Ivoire, Senegal, and Mali) in western Africa (Paper 4).

Finally, another important consideration is the application of our empirical econometric cost function to inform HIVST implementation and scale-up in southern African countries where there were no costing studies conducted (non-STAR countries). Paper 3 will aim to fit an econometric cost function with potential application to out-of-sample countries for the budgeting and financial planning of HIVST provision to the general population in southern Africa.

Chapter 4 – Paper 2: Using HIV self-testing to increase the affordability of community-based HIV testing services: A longitudinal analysis in Lesotho

Overview of Paper 2

As presented in chapters 1 and 2, there are economic and operational considerations for implementing and scaling up HIVST. This paper estimates the costs of implementing HIVST and explores potential efficiency gains arising from the addition of HIVST to conventional community-based HTS programmes in Lesotho.

This work was reviewed and approved by the National Health Research Ethics Committee of Lesotho and the London School of Hygiene and Tropical Medicine Ethics Committee (**Appendix IV**). Full informed consent was obtained from all participants for the time and motion study data collection.

Further information on the study methods and findings can be found in the supplementary material. Appendix figures A1 and A2 provide an overview of the client flow on the community-based HTS model (mobile outreach and index model). Appendix text A1 provide additional information on the allocation of personnel costs between HTS and HIVST activities. Appendix table A1 describes the composition of economic costs for the full costing of HTS and HIVST and assumptions on HIVST costs composition for an incremental cost analysis. Appendix tables A2 and A3 provide additional information on the time and motion study methods and findings. Finally, Appendix table A4 presents the detailed HTS and HIVST cost analysis over the two-year implementation period.

I conducted a micro-costing study alongside programme implementation between May 2017 and April 2019 from a provider's perspective following the Global Health Cost Consortium guidelines.

This paper is presented as accepted in the *AIDS* journal in August 2020. This paper fulfils the research objective 2 to carry out a cost analysis of the community-based programme for HTS and HIVST with the highest level of testing coverage in Lesotho over a two-year observation period. These results are

also used in the paper 3 to compare observed versus projected costs at scale using an econometric cost function analysis in Lesotho, so this paper also contribute to the research objective 3.

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Student ID Number	1805320	**Title**	Mr
First Name(s)	Marc		
Surname/Family Name	d'Elbée		
Thesis Title	Estimating healthcare costs at scale in low- and middle-income countries – the case of community-based HIV self-testing scale-up in southern and western Africa		
Primary Supervisor	Prof 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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When was the work published?	August 2020		
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SECTION E

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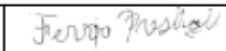
Supervisor Signature	
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Using HIV self-testing to increase the affordability of community-based HIV testing services: A longitudinal analysis in Lesotho

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Running head – Costs of HIV testing in Lesotho

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Authors' contributions - MD and FTP were responsible for the conceptual design of the study. MD, MM, MJ, MTA, AM contributed to the initial design of the study. MD and MTA collected data. MD cleaned and analysed data. AM, CN, MJ, MT, MTA, LS, EC, CJ, KH, GMR, FTP provided guidance throughout data collection, cleaning and analysis. MD drafted the paper; all authors revised and approved the final manuscript.

Compliance with Ethical Standards - All procedures performed involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The research project has been approved by the National Health Research Ethics Committee of Lesotho and the Research Ethics Committee of the London School of Hygiene and Tropical Medicine.

Informed consent was obtained from all individual participants included in the time and motion study.

Keywords: HIV testing services; HIV self-testing; Community-based; Costs and Cost Analysis; Longitudinal Studies; Efficiency, Organizational; Africa, Southern; Lesotho

Word count: 3,487/3,500

Abstract (250 words max)

Objectives: This study estimates the costs of community-based HIV testing services (HTS) in Lesotho and assesses the potential efficiency gains achieved by adding HIV self-testing (HIVST) and then self-testing booths.

Design: Micro-costing analysis using longitudinal data from a real-world intervention.

Methods: We collected data prospectively on provider's costs and programmatic outcomes over three time periods of approximately eight months each, between May 2017 and April 2019. The scope of services was extended during each period as follows: 1) HTS only, 2) HTS and HIVST, 3) HTS and HIVST with individual HIVST booths where clients were encouraged to self-test on-site followed by on-site confirmative testing for those with reactive self-test. For each implementation period, we estimated the full financial and economic implementation costs, the incremental costs of adding HIVST onto conventional HTS and the cost per HIV positive case identified.

Results: Costs per HIV-positive case identified increased between period 1 (US$956) and period 2 (US$1,249) then dropped in period 3 (US$813). Full versus incremental cost analyses resulted in large differences in the magnitude of costs, attributable to methods rather than resource use: e.g. in period 3, the average full and incremental cost estimates for HTS were US$34.3 and US$23.5 per person tested, and for HIVST were US$37.7 and US$14.0 per kit provided, respectively.

Conclusions: In Lesotho, adding HIVST to community-based HTS improves its overall affordability regarding HIV-positive case finding. The reporting of both full and incremental cost estimates increase transparency for use in priority setting, budgeting and financial planning for scale-up.

Introduction

Lesotho has the second highest HIV burden in the world at a prevalence of 25.6% (30.4% among women and 20.8% among men) and an annual incidence of 1.1% among adults in 2017 [1]. In recent years, the country made considerable progress towards the United Nation's 90-90-90 targets (by 2020, 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral treatment (ART), and 90% of all people receiving ART will have viral suppression) [2]. In 2017, among the estimated 306,000 people living with HIV (PLHIV), 81% reporting knowledge of status, 92% of those are on ART, and of those who are on ART, 88% are virally suppressed [1].

Nationally, the total number of people tested for HIV increased from 221,616 in 2009 to 1,109,345 in 2017, while the proportion of new HIV-positive diagnosed out of all those tested (HIV yield rate) decreased from 18% to 4% over the same period [3]. Population Services International (PSI), a global non-governmental health organisation (NGO), provides most community-based HIV testing services (HTS) in Lesotho [4], including door-to-door and mobile outreach services. In 2015, community-based index testing, which is HTS for sexual partners and biological children of people diagnosed with HIV, was added to PSI services under the CID-LINK project, achieving an average HIV yield rate of 4.2% with 79% of linkage to care among those diagnosed between May 2015 and November 2017 [5].

Yet, reaching the first 90 target called for innovative methods to reach undertested groups, notably men and young people (aged 15-24) among whom awareness of HIV positive status was only 76.6% and 67.6% respectively [1, 3, 6, 7]. Following demonstrated success elsewhere in southern Africa, the Lesotho Ministry of Health (MOH) added HIV self-testing (HIVST) to the HTS strategy in 2017 with technical support and funding provided by the STAR (HIV Self-Testing AfRica) Initiative [8-13].

Provision of multiple services delivered jointly alongside conventional HTS has the theoretical potential to achieve economies of scope [14, 15], through efficiency gains that reflect sharing of overheads, common fixed costs or through joint learning by staff for services provision or demand

creation[16, 17]. In particular, HIV self-testing can increase total testing numbers, but may also increase the programme's technical efficiency when provided alongside standard testing services if more people are diagnosed at a given cost [18]. However, relatively few data exist on how costs change over time during implementation of national HTS [12, 19] or whether new testing modalities have succeeded in increasing a programme's efficiency.

The objective of this study was to estimate the costs of community-based HTS implementation in Lesotho before and after integration of HIVST. We aim to investigate potential efficiency gains from the addition of self-testing and from continuous programme development.

Methods

Setting and intervention

In Lesotho, the community-based HTS programme was expanded in five districts over two years starting in May 2017 [4]. The programme was offering community-based HTS. HIVST was added as an alternative option to conventional HTS in December 2017. Finally, from September 2018, individual HIVST booths were introduced at mobile outreach sites and clients were encouraged to self-test on-site (Figure 1). These are defined as period 1, 2 and 3, respectively.

Two community-based HTS interventions were assessed: 1) mobile outreach with tents providing HTS, and 2) index testing where counsellors travel to the index case household and offer testing door-to-door to all those in the area, so avoiding stigmatisation. At the mobile outreach site, the client was offered the option to receive HTS or to self-test on-site at the HTS tent (with or without the HTS provider supervision) with immediate confirmatory testing available, or to take the kit away for use off-site. All HIV-positive clients were offered a home visit by a counsellor for index testing. If the client refused a home visit, HIVST kits were offered to their sexual partner(s). If the client accepted a home visit, the contact details of the sexual partners (index cases) were recorded. The index cases were

contacted by the provider by telephone and offered HIV testing either at the nearby health facility, or during a home visit by the providers. During home visits, index cases who refused conventional testing by the providers could opt for HIVST. A more detailed presentation of the community-based HTS is published elsewhere [4]. Client flows for the mobile outreach and index testing models are presented in **Appendix Figures S1 & S2**. When individual HIVST booths were introduced, the revised strategy allowed multiple clients to self-test at the same time and encouraged clients with a reactive self-test to get immediate confirmatory testing and referral for linkage to care. Because the same team and resources are used to provide these two HTS interventions (single provider potentially conducting these two activities in the same day), we analyse costs of this intervention as one and use the term "community-based HTS" to cover the two testing approaches.

The analysis is divided in three time periods corresponding to major changes in the HTS strategy presented in **Figure 1**.

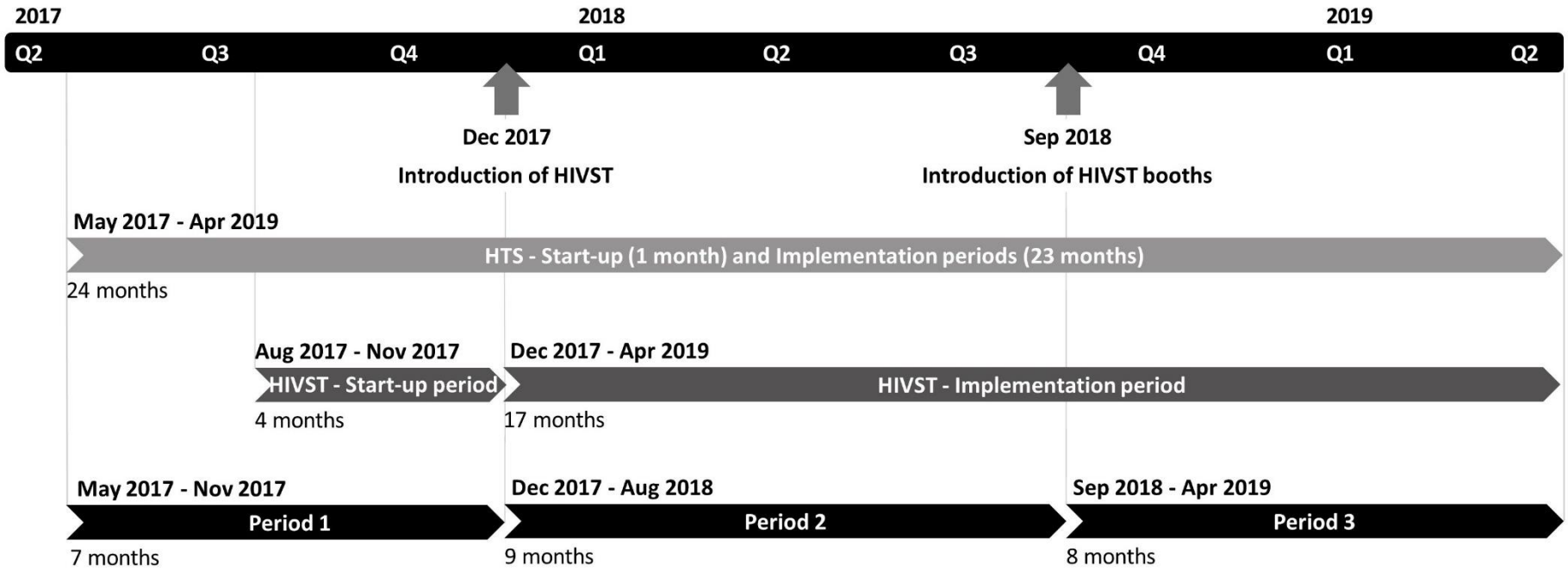

Figure 1. Timelines of the community-based HIV testing services, major changes in strategy and analysis periods

Study design and data collection

We conducted a micro-costing study alongside programme implementation over two years (May 2017 – April 2019) from a provider's perspective (PSI). We collected data on costs and programmatic outcomes prospectively following guidelines [14, 20, 21].

We conducted two types of cost analysis for HTS and HIVST. A full cost analysis where we estimated the financial and economic (e.g. donated goods and services) costs of all resources used in running the HTS and HIVST programmes independently from each other, including PSI Lesotho headquarter costs [14]. Because HIVST is added onto the existing HTS as an alternative option within community-based HTS, we also estimated incremental costs where shared costs (such as operational costs) are fully allocated to the full package of community-based HTS, thus accounting only for the new inputs that were required by the new intervention [21]. The composition of cost categories in the full versus incremental cost analysis for each activity is presented in **Appendix Table S1**.

Firstly, we analysed PSI financial reports, referred as top-down costing, collating all financial expenditures from financial reports and categorising each line item by cost category allocating them to distribution model [22]. Based on these reports, the average purchasing cost per HIVST kit, including freight costs, was US$2.71. Costs were allocated to community-based activities following predefined allocation factors. A more detailed description of this costing method is described elsewhere [23]. We estimated quarterly cost averages to allow for comparison between periods. Secondly, a time and motion study (TMS) was conducted to observe staff providing both HTS/index testing and HIVST services and allocate personnel costs based on the time spent on each activity [24, 25]. The TMS differentiates between supervised and unsupervised (provider is absent at least while the client waits for the self-test results) HIVST episodes on-site. This study also estimates provider's indirect time which corresponds to the personnel time spent not seeing any clients, travel time and administrative work. In the case of the incremental HIVST costing analysis, providers' indirect time is allocated fully to conventional HTS, while in the full HIVST cost analysis, indirect time is shared between HTS and

HIVST, following time allocations from the TMS. Methods and results for the TMS are presented in **Appendix text document S1 and Table S3**. Thirdly, we used a bottom-up costing approach through site observations and interviews with senior staff to include the economic costs not captured in financial reports. All local goods costs were adjusted for inflation over time using the gross domestic product deflators in the local currency, then all costs were converted to 2019 United States dollars (US$) using the Central Bank of Lesotho exchange rate for each year[14]. Start-up, training and other capital costs were annualized over the assumed years of useful life of each item using a 3% discount rate, which was varied in sensitivity analysis [14]. Research costs were excluded. We calculated the average costs per person tested with HTS, per HIVST kit distributed, and per HIV-positive identified as the conventional HTS and HIVST costs respectively, by dividing the relevant total costs by the relevant outcomes for each period.

Output data were collected from paper-based monitoring and evaluation (M&E) forms filled by HTS providers, compiled in an excel database, cleaned using consistency checks, and analysed by PSI M&E officers. Confirmed yield rate was defined as the proportion of new HIV-positive cases out of all clients tested with HTS, including confirmatory testing following a reactive self-test.

Sensitivity and scenario analysis

We conducted a series of univariate sensitivity analyses to assess the impact of key cost assumptions on the average incremental costs per HIVST kit distributed and costs per HIV-positive case identified for the latest costs data (period 3). For the costs per HIVST kit distributed and per HIV-positive case identified, the sensitivity analysis assessed the impact of the discount rate used to annualize capital costs to capture the influence of not discounting or using a higher local central bank discount rate (base: 3%; 0%; 15%), the years of useful life of start-up costs (base: 2 years; 1 year; 3 years). For the costs per HIVST kit distributed only, the durations of sessions for providing HTS and HIVST services estimated from the TMS (+/-20%) – TMS results were not affecting costs per HIV-positive case

identified because all personnel members were involved in HIV testing only and the TMS only affects the allocation between the types of testing. For the costs per HIV-positive case only, we also assessed the years of useful life of vehicles (base: 15 years; 10; 20) – absent for the incremental cost per HIVST kit distributed.

We also added a scenario analysis to inform the scale-up of the programme to the other districts. In the scenario analysis, we assessed headquarter and field-based personnel costs (+/-10%) reflecting variation of headquarter costs and the shift of HIVST distribution by lay providers rather than professional counsellors; the volume of HIVST kits distributed (+/-10%) which could vary according to the personnel capacity to provide unsupervised on-site HIVST or to the effect of HIVST stock-outs; the market price of HIVST kits to reflect a hypothetical price approximately equal to the current cost of a rapid kit (US$1) [26]. For HIVST costs only, we also varied the proportion of unsupervised HIVST session on-site, allowing for more clients to self-test with the same number of staff available. For costs per HIV-positive case detected only, we varied the number of HIV-positive test to reflect the variation of yield (+/-10%). Variations in individual parameter values informed our best/ worst case scenario in which all the parameters were combined to yield the lowest/ highest average costs.

Ethical approval was obtained from the National Health Research Ethics Committee of Lesotho and the London School of Hygiene and Tropical Medicine Ethics Committee (protocol numbers: ID64-2018 and 14887 respectively).

Results

Outcomes of the community-based HTS and HIVST activities

In period 1, HTS activities are gradually increasing and reach a peak of 11,000 tests conducted monthly (**Figure 2. a.**). In period 2, mainly on-site HIVST is provided by HTS counsellors who, consequently, reduce their HTS activities both at the mobile outreach and index testing. In period 3, we observe an increase of the number of HIVST kits used on-site, and kits provided for off-site use, with the addition of individual booths. The number of HIV-positive case finding is increasing and is driven by index testing activities (**Figure 2.b.**). Yield is constant in periods 1 and 2 (at 3%), until the introduction of HIVST booth in period 3 where it gradually increases to an average of 5%.

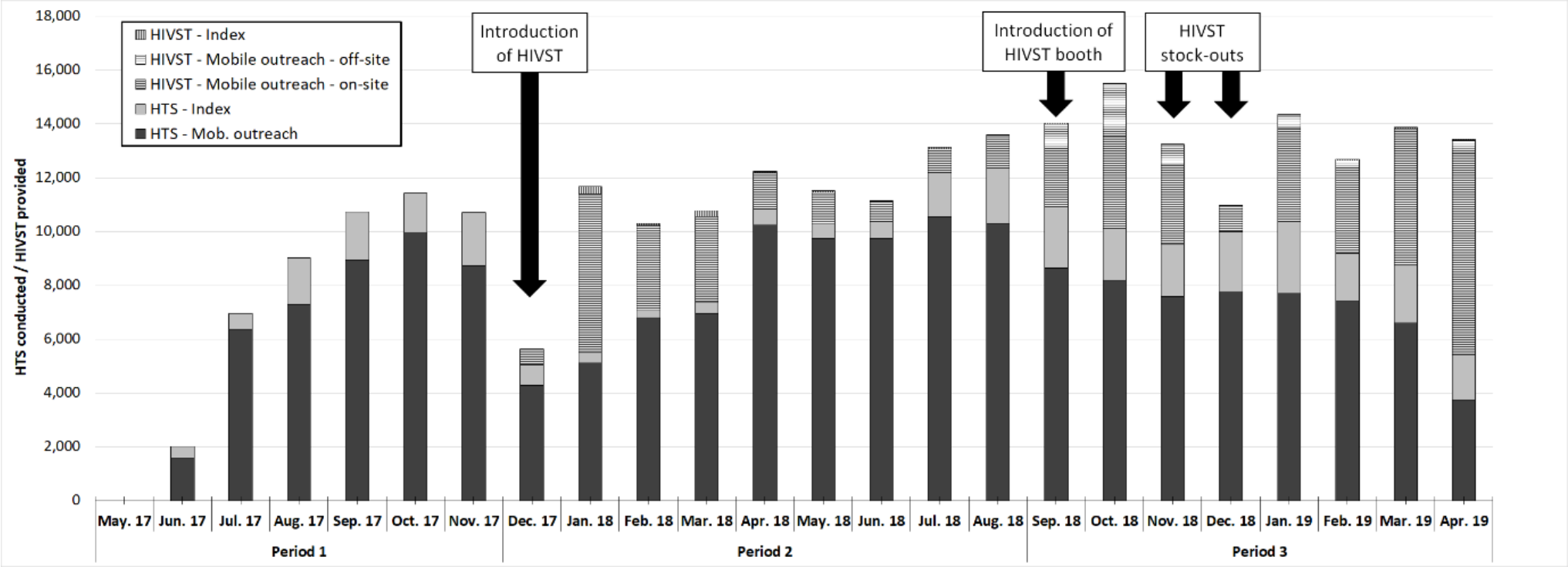

Figure 2.a. Outcomes of the community-based HTS and HIVST provision between May 2017 and April 2019: Volume of HTS and HIVST

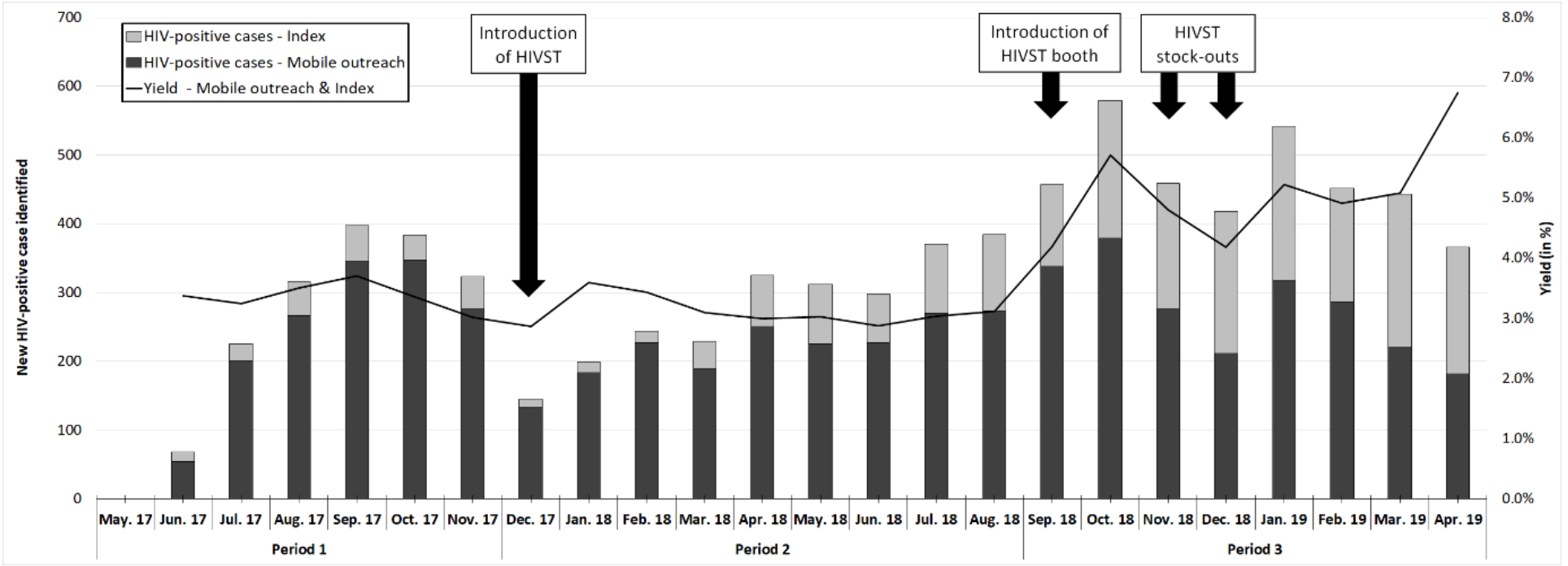

Figure 2.b. Outcomes of the community-based HTS and HIVST provision between May 2017 and April 2019: Number of new HIV-positive case identified and yield

Results from the time and motion study and implication for the estimation of full versus incremental HIVST costs

There are two central findings from using the TMS to allocate shared costs (**Appendix Table S3**). First, indirect time accounts for a significant proportion of the daily working hours of a provider. The way this time is allocated in the calculation of personnel costs has a significant impact on total costs in both the full and incremental costs analysis. Second, the difference between average observed time spent on-site by counsellors to provide unsupervised and supervised HIVST services is important (mean (standard deviation): 10.4 (3.2) minutes versus 24.1(5.2) minutes, respectively – $t(53)=-8.6$, $p<0.01$).

Costs analysis

For both HTS and HIVST, the main drivers of costs are personnel costs at headquarters and in the field, followed by testing supplies and vehicle operation and maintenance (**Figure 3**). The average HTS cost per test conducted is US$32.2 in period 1. In period 2 and 3, when an incremental costing method is applied to HIVST, HTS average costs are US$35.0 and US$34.3, and HIVST average costs are US$15.4 and US$14.0. In the case of a full costing approach, where joint costs are shared, HTS average costs are US$28.5 and US$23.5, and HIVST average costs are US$43.3 and US$37.7, in period 2 and 3, respectively. HIVST incremental financial costs, which includes only directly STAR project financial contributions for HIVST, were US$6.0 and US$5.6 in period 2 and 3, respectively. Total costs are increasing over time and are driven by increasing personnel costs (**Figure 3**). Cost per HIV-positive case identified increases between period 1 (US$956) and period 2 (US$1,249), in the transition to distributing HIVST, but is the lowest in period 3 (US$813), when booths allowed onsite self-testing and immediate confirmatory testing, (**Table 1**). Detailed total and average costs for all three periods for the full and incremental costs analysis are presented in **Appendix Tables S4.a, S4.b and S4.c**.

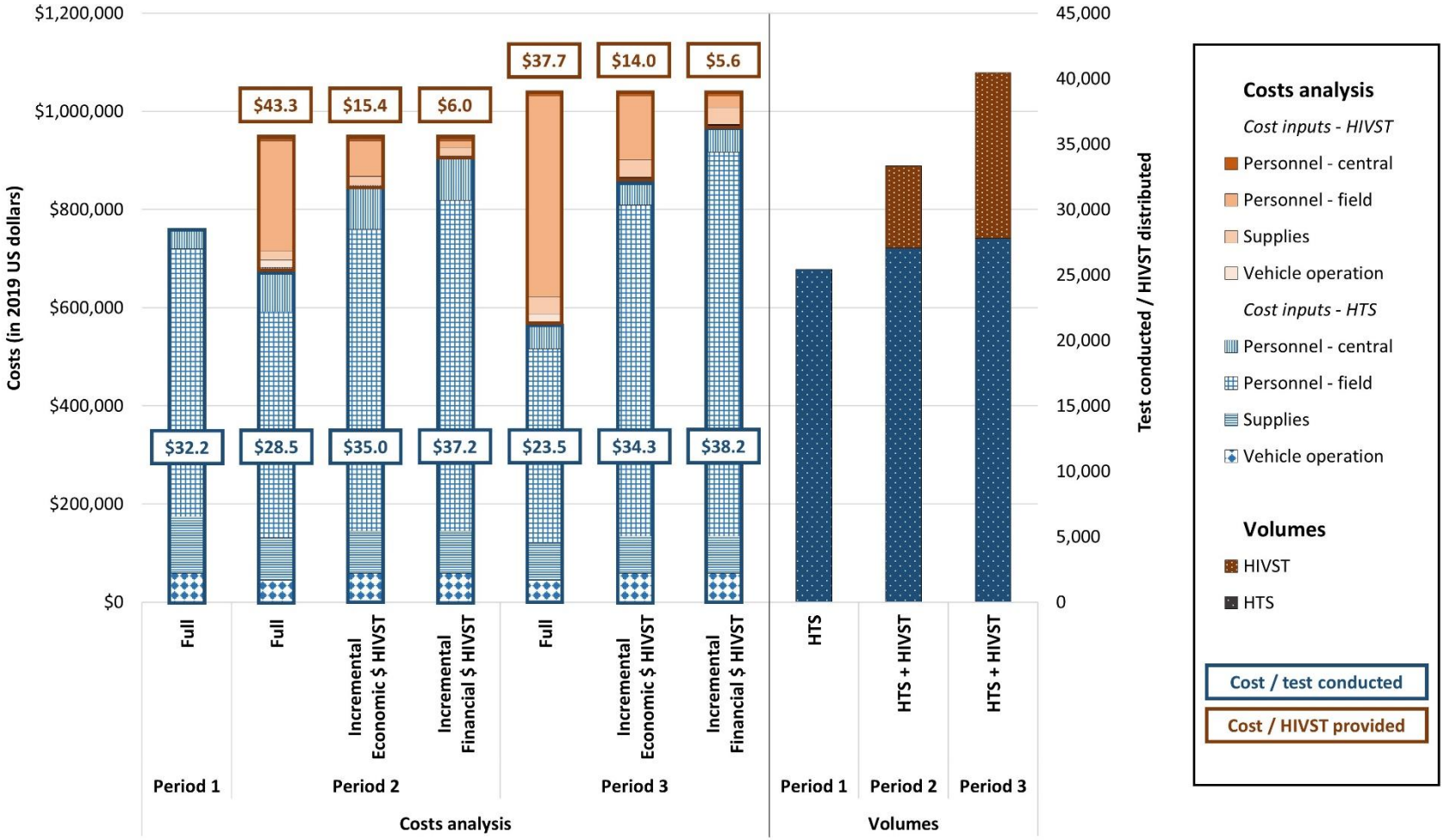

Figure 3. HTS and HIVST costs drivers, average costs and volumes per analysis period (in 2019 US$)

Table 1. Quarterly averages of total and average costs per HIV-positive case identified with community-based HTS during the period May 2017 – April 2019 (in 2019 US$)

	Period 1	**Period 2**	**Period 3**
Total costs (HTS and HIVST services)	819,640	1,043,448	1,131,003
HIV-positive cases identified	858	836	1392
Yield (%)	3.4	3.1	5.0
Cost per HIV-positive case identified	956	1,249	813

Sensitivity and scenario analysis

Average costs per HIVST kit distributed and per HIV-positive case identified remained robust when key cost parameters were varied (**Figure 4.a.** and **Figure 4.b.**). Start-up and capital costs account for a small proportion of the community-based HTS, therefore, our assumptions on the life years of start-up costs, vehicle life and discount rate applied have only a small impact on our results (ranges from US$14.0 - US$14.1 and US$808.6 - US$825.6 for cost per kit and cost per HIV-positive respectively). The variation by 20% of the length of observed testing episodes used for personnel costs allocation has a slightly stronger effect on average cost per kit (range: US$12.3 - US$15.7).

For both scenario analyses, we looked at factors potentially reducing average costs. The variation of headquarter-based personnel costs only has a minor effect (ranges from US$14.0 - US$14.1 and US$808.0 - US$817.0) on cost per kit and cost per HIV-positive respectively. The reduction of the HIVST kit price and increase of distribution volumes reduced average cost per kit distributed (US$12.3 and US$12.8 respectively) but only had a minor effect on cost per HIV-positive (US$796.9 and US$810.0 respectively). As expected, a reduction of field-based personnel costs impacts on the average costs

per HIV-positive (US$754.7) but the effect is less important on cost per kit (US$13.0). The yield strongly affects cost per positive (US$738.6). A 50% reduction of the level of supervision by PSI staff for on-site HIVST can also reduce costs per kit distributed (US$12.0) but is likely also to have effects on impact. Finally, the best-worst case scenarios show ranges of US$8.5 - US$16.9 and US$668.6 - US$969.3 for cost per kit and cost per HIV-positive respectively.

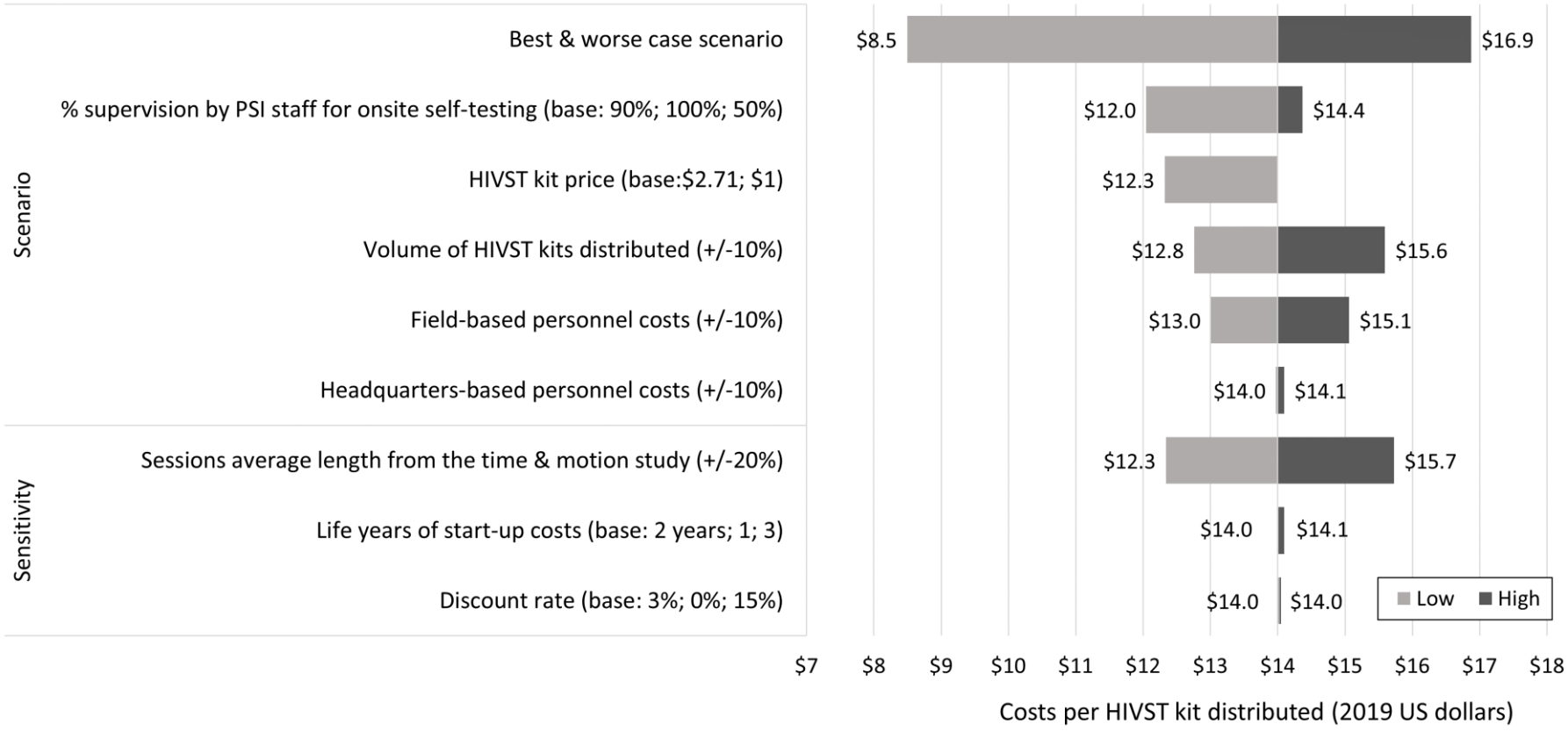

Figure 4.a. Results from the sensitivity and scenario analysis on the costs per HIVST kit distributed in period 3 (in 2019 US$)

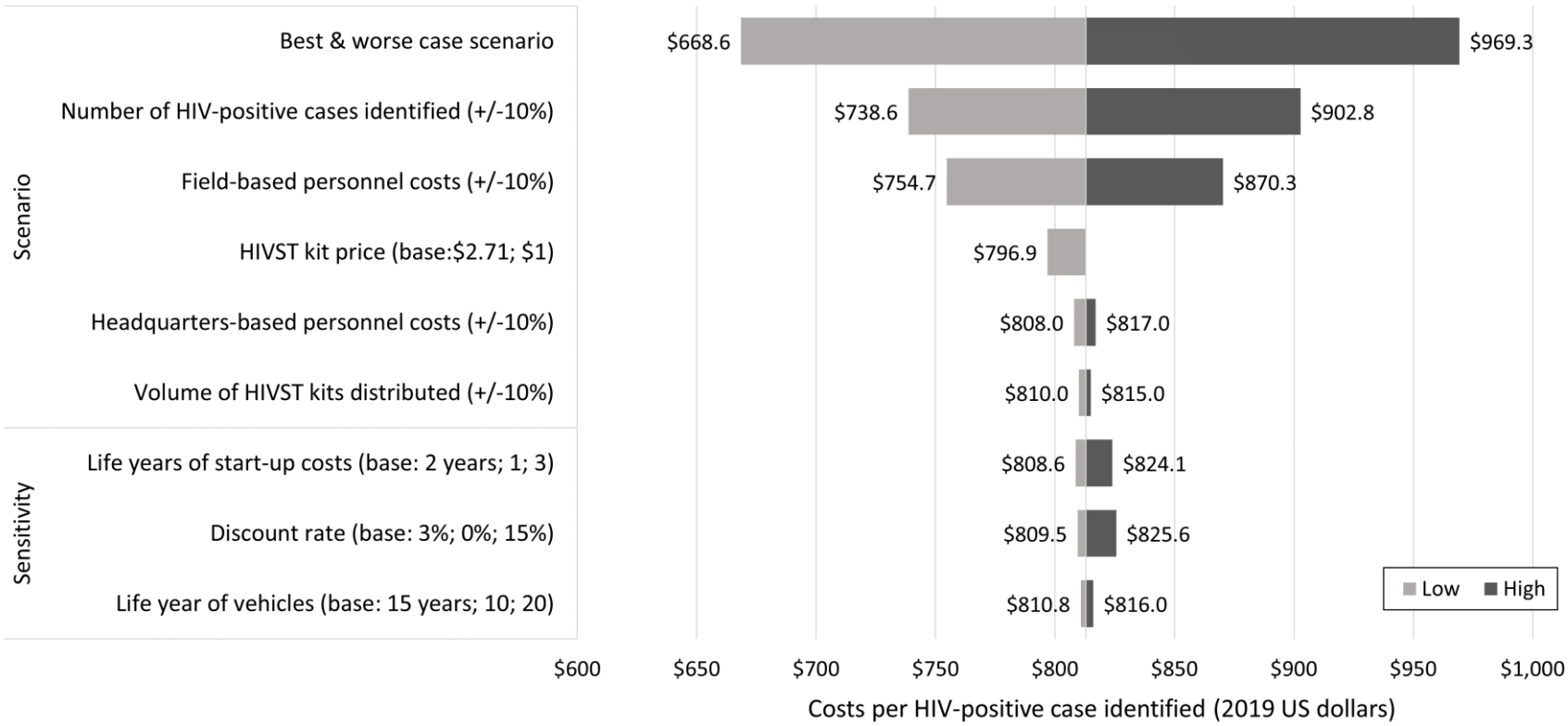

Figure 4.b. Results from the sensitivity and scenario analysis on the costs per HIV-positive case identified in period 3 (in 2019 US$)

Discussion

We found that the addition of HIVST increases the overall programme's affordability for HIV-positive case finding. The increase of HIV-positive case finding, and yield is driven by an increase in index testing activities, thanks to the efficient introduction of self-testing and booths in period 3, allowing more staff to conduct index testing instead of being mobilized at the mobile outreach. TMS data were also used to value potential impact on costs of efficiency gains in services provision, particularly regarding high personnel costs. As suggested by the scenario analysis, an increase of unsupervised on-site HIVST could have a significant impact on HIVST average costs, allowing more staff to focus on index testing or other activities.

Recent best practice guidelines on cost-effectiveness analysis recommend the use of quality-adjusted life years gained (QALYs) and disability-adjusted life year averted (DALYs) for valuing health outcomes [27]. Previous work suggests that cost-per-diagnosis is strongly correlated with cost per disability-adjusted life year averted when evaluating HTS and that it can be used as a metric to assess an intervention's cost-effectiveness [28]. Our micro-costing study, within its scope and timeframe, does not capture all individual and population-based costs and benefit of the intervention, therefore, these results should not be interpreted for cost-effectiveness analysis.

Our HIVST full economic average costs estimates are higher than recently published estimates by Mangenah et al [23]. The authors published a full economic average cost per HIVST kit distributed at US$8.15, US$16.42 and US$13.84 in Malawi, Zambia and Zimbabwe, respectively. The HIVST model was door-to-door only, where community-based agents were offering HIVST kits directly to households without immediate confirmatory testing and the costs reported per HIVST kit distributed. HIVST full costs are higher in Lesotho because HIVST volumes distributed were lower potentially leading to diseconomies of scale, and HIVST kits were distributed in the communities by either professional or lay counsellors resulting in higher field personnel costs. Because the test results were not reported, results from Mangenah et al. are not comparable with average cost per positive case

identified. In addition, our costs are higher to those reported in a recent studies on costs of HIV testing in sub-Saharan Africa including Lesotho [29-32]. This difference may be explained by several factors. We included above service level costs, and our intervention is managed by an international NGO with high quality of services and M&E reporting relative to public sector. Furthermore, HIV-positive case finding in communities require additional staff time and equipment such as vehicles [4]. Finally, the number of positive cases identified was relatively low in a context where 81% of PLHIV already know their status with a yield of 3% [1]. The differences in personnel cost allocation between full (personnel costs associated with travel and administrative activities is shared between HTS and HIVST based on the volume of activities[21]) and incremental (personnel costs of time spent on indirect client activities is allocated to the existing intervention HIVST is being added to) costing approaches have a significant impact on costs. This is particularly relevant for community-based interventions in remote areas where provider's indirect time is significant [33, 34]. Budgeting of HIVST using incremental costs risks to underestimate needs if HTS is not running well. Incremental HIVST costing, only considering financial costs, assumes that the existing intervention has the capacity (particularly human resources) to absorb the new intervention. They may be applicable in a case of low HIVST distribution where the staff has the capacity to absorb the added testing modality and the effect on the services it is being added to is minor. This was not the case in Lesotho but is shown to highlight how incremental costs can potentially vary between interventions.

Programme costs and cost per HIV-positive identified tend to increase over time [29]. The increase in total costs over time is mainly explained by an increase of the team size in the field. Integration of HIVST improved the HTS efficiency as defined by increased rates of HIV positive case finding which is a great achievement in the current HIV testing landscape, where increasing HIV testing coverage makes it increasing harder to identify new HIV positive cases.

Cost and cost-effectiveness studies for HIVST need to account for capacity to improvement over time in order to avoid over-estimating costs (period 2 to 3). New programmes should encourage

implementation research and use early results to inform programme strategy. For instance, we applied this strategy with the ATLAS project on HIV self-testing in West Africa to identify opportunities for task shifting from medical doctors to less scarce health care workers [35].

As well as guiding sustainable national scale-up for Lesotho, these data have relevance to other countries considering the addition of self-testing to community-based HTS [36]. First, HIVST can be added to improve community-based program efficiency and allow a reallocation of scarce human resources to other key activities in the HIV response. Second, community-based interventions can incur important indirect personnel costs such as travel time to sites, other costing analyses should be transparent and report their inclusion/exclusion. Third, full and incremental costing approaches can provide a range to estimate health system needs for scale-up. The risks of using costs not fit for purpose or setting can lead to under-budgeting and depleting health system through cross-subsidization from core health services, or rejecting potentially cost-effective intervention seen as too expensive.

Our study has limitations. First, because HIVST was introduced in all sites of the intervention at the same time, there were no control sites against which to evaluate the effect of HIVST introduction. Second, only new positive cases detected are reported, the volume of known seropositive clients retesting was not reported and cannot be estimated. Third, stock-outs happened in period 3, limiting the number of kits distributed and potentially impacting on our costs, this might overestimate our average costs per kit distributed and per positive case identified.

To our knowledge, this is the first cost analysis using longitudinal data from a real-world intervention on HTS efficiency gains before and after introduction of HIVST. We showed that adding HIVST to community-based HTS can improve its overall affordability regarding HIV-positive case finding. We also highlighted the importance of transparency in reporting methods for priority setting, budgeting and financial planning.

Acknowledgements - The study was undertaken in collaboration with Unitaid, PSI, WHO and the HIV Self-Testing Africa Research Consortium institutions. The authors would like to thank all their partners and study participants in Lesotho.

Figures and Tables

Figure 1. Timelines of the community-based HIV testing services, major changes in strategy and analysis periods

Figure 2. Outcomes of the community-based HTS and HIVST provision between May 2017 and April 2019: Volume of HTS and HIVST (**2.a.**), number of new HIV-positive case identified and yield (**2.b.**)

Figure 3. HTS and HIVST costs drivers, average costs and volumes per analysis period (in 2019 US$)

Figure 4. Results from the sensitivity and scenario analysis on (**4.a.**) the costs per HIVST kit distributed in period 3 and (**4.b.**) on the costs per HIV-positive case identified in period 3 (in 2019 US$)

Table 1. Quarterly averages of total and average costs per HIV-positive case identified with community-based HTS during the period May 2017 – April 2019 (in 2019 US$)

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Chapter 4 - Supplemental Digital Content – List of items

Figure S1. Client Flow at the "New Start" mobile outreach model with the option of HIV self-testing

Figure S2. Client Flow for the community-based index testing model with the option of HIV self-testing

Text document S1. Estimation of personnel costs allocation factors between HTS and HIVST activities for periods 2 & 3

Table S1. Composition of economic costs for the full costing of HTS and HIVST and assumptions on HIVST costs composition for an incremental cost analysis

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Supplemental Digital Content

Figure S1. Client Flow at the "New Start" mobile outreach model with the option of HIV self-testing

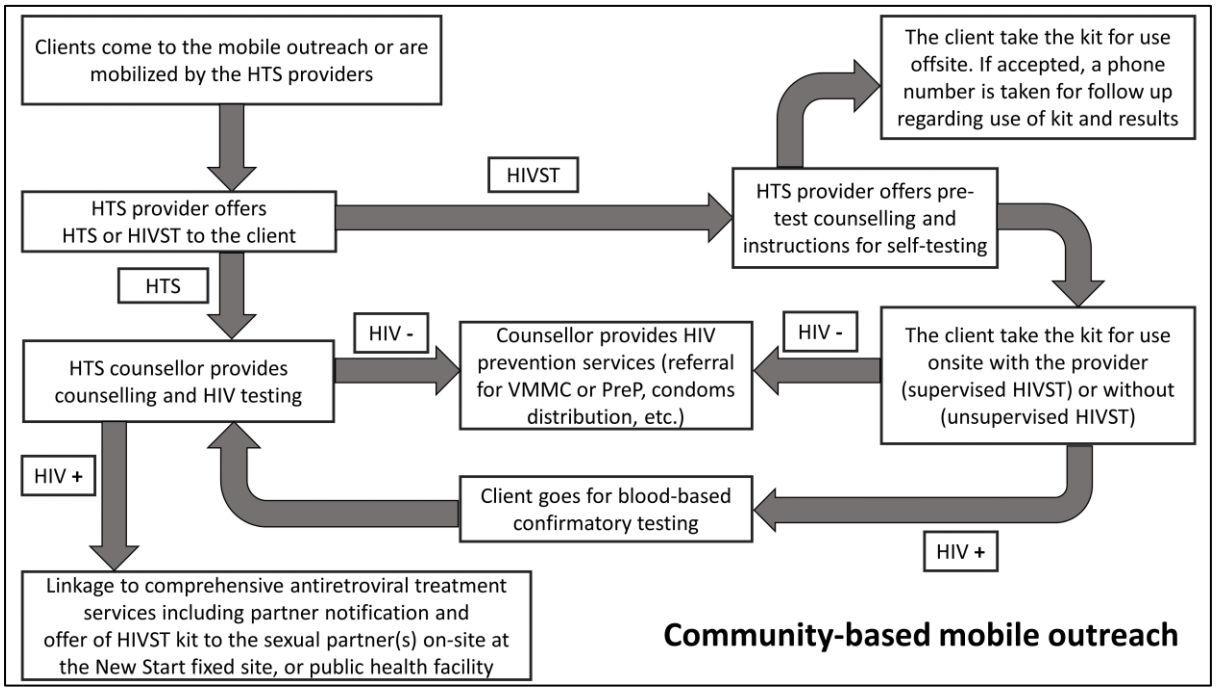
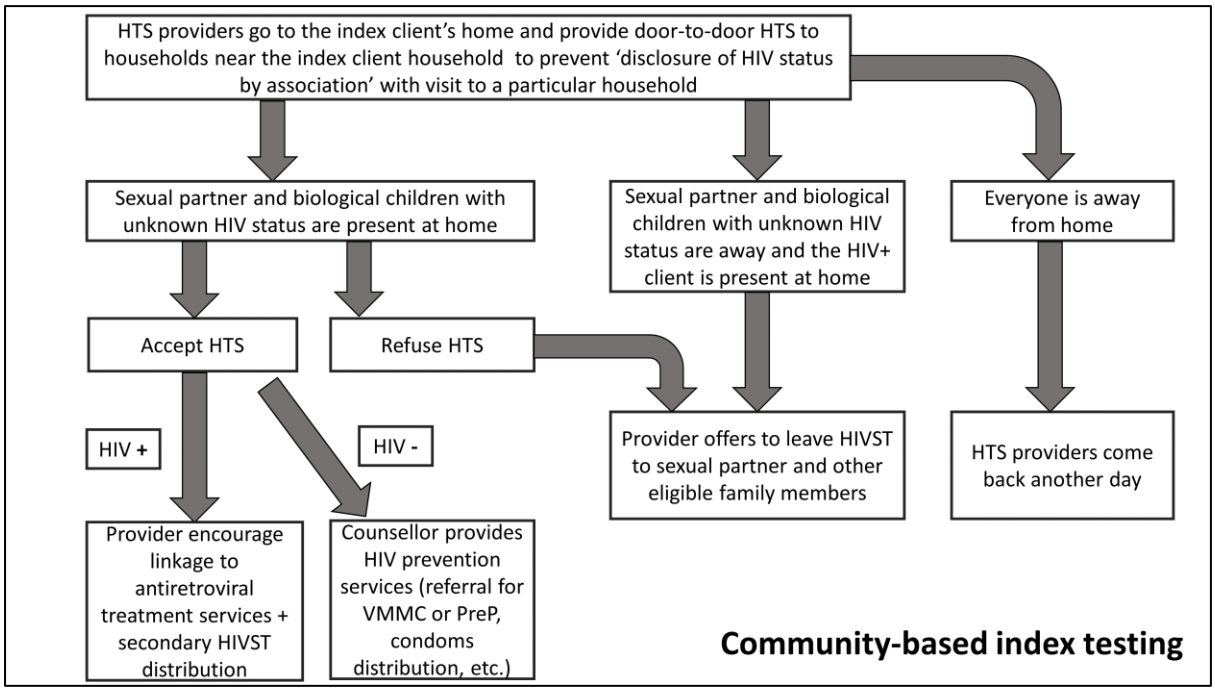


Figure S2. Client Flow for the community-based index testing model with the option of HIV self-testing



Text document S1. Estimation of personnel costs allocation factors between HTS and HIVST activities for periods 2 & 3

a. Description of the intervention

The first HIVST distribution started in December 2017 (period 2) promoting HIVST for use off-site or on-site using the HTS gazebos. These gazebos were specifically designed to provide HTS, and if a HIVST session was conducted in it, it led to the incapacity of a counsellor to conduct HTS. It is worth noting that a HTS session takes much less time than a HIVST session when the HIV test result is negative.

In period 3, individual booths were introduced in addition to the HTS gazebos. Consequently, people wanting to self-test in private could use these booths while the gazebos were reserved for counsellor who could provide HTS and confirm results of a reactive or inconclusive self-test. As a result, the outreach team could reorganize their activities where some counsellors or interpersonal communication agents could conduct community mobilization or provide support as needed to client self-testing in the booths while the rest of the counsellors were based in the gazebos to provide conventional HTS and confirm HIVST reactive test.

This change meant that TMS data collected in period 2 allocated an important percentage of staff time to HIVST activities while the period 3 allowed to better use the staff time and provide services more efficiently, rebalancing the allocation of staff time between activities.

b. Time and Motion study (TMS) - Methodology

A time and motion study (TMS) was conducted to observe staff providing both HTS/index testing and HIVST services and allocate personnel costs based on the time spent on each activity [24, 25]. The TMS differentiates between supervised and unsupervised HIVST episodes on-site. An HIVST episode is defined as supervised when the provider is with the client during the entire testing process (pre-test counselling, instruction for self-testing, oral sampling, waiting for results and post-test counselling) and unsupervised if the provider is absent at least while the client waits for the self-test results. This study also estimates provider's indirect time which corresponds to the personnel time spent not seeing any clients, travel time and administrative work. In the case of the incremental HIVST costing analysis, providers' indirect time is allocated fully to conventional HTS, while in the full HIVST cost analysis, indirect time is shared between HTS and HIVST, following time allocations from the TMS. M&E, administrative, and programme level staff were charging either CIDLINK or STAR projects and the allocation of costs between projects was based on their timesheets or with individual interviews for senior staff. Field based personnel costs providing both HTS and HIVST services were only charging CIDLINK project. The TMS was conducted as part of the costing exercise to observe staff providing both HTS and HIVST services and allocate personnel costs based on the time spent on each activity. The TMS only used results from observations at the mobile outreach and not the index testing activities which were provided alongside and accounted for 4% to 7% of total community-based HTS and for 2% to 4% of total HIVST index activities. The TMS results also helped to value efficiency gains with the introduction of on-site HIVST.

The TMS used external observers conducting continuous observations of health providers during their normal working day which is considered as the gold standard method [24]. We conducted continuous observation with paper-based tools to record the start and stop times of observed tasks with a detail of minutes. We used a duration measurement for a series of pre-defined episodes based on our

understanding of the intervention. We also aimed to capture the effect of the HIV test results and the supervision level by the provider (for self-testing) on the length of the conventional and self-testing episodes.

The TMS was conducted between September-November 2018 by two data collectors. In total, 16 providers (interpersonal communication agent, lay counsellors, professional counsellors or nurses) gave written consent and were observed either the morning or afternoon, in a rural or urban setting. Some days of observation, provision of HTS/HIVST could be as low as two episodes or up to eighteen per provider in more busy areas.

Data collected included: date, district, name of site, data collector ID, distributor ID, distributor grade, direct patient time (time at the outreach and available to provide HIV testing), driving time to get to the outreach, time to provide HTS to a client, information on HIVST without distribution, HIVST distribution for off-site testing (differentiated between primary and secondary distribution), supervised and unsupervised on-site HIVST, test result for HTS and HIVST. The categories are presented in **Table S2**.

Since the time of the day and the type of provider, did not affect the length of the testing session, we estimated average time for each episode on the overall sample.

c. Application of results from the TMS to estimation field-based personnel costs allocation factors

Because direct client time was varying significantly between mobile outreach (e.g. outreaches in rural setting could have very low direct client time because of travel time), we did not use the results from the TMS.

Instead, we estimated the average number of episode per provider, per day and per mobile outreach for each episode of HTS (with a positive or negative test result) and HIVST (off-site, on-site/supervised and on-site/unsupervised) based on the M&E data. The method to estimate the % of unsupervised HIVST episodes in period 3 is described in the section c.

We then multiplied the average number of episodes with the corresponding times from the TMS to estimate a proportion of time spent on HTS and on HIVST then used to allocate personnel costs.

For a full costing approach, the denominator was the direct client time estimated as the sum of total HTS and HIVST activities [21]. For an incremental costing approach, the costs of time spent on activities such as travel, administrative activities, and any other activities with provider's indirect time should not be included as they are indirect costs. Therefore, the denominator was the average total daily working hours of the employees.

d. Estimation of on-site supervised and unsupervised HIVST episodes in period 3

While efficiency gains were observed during the TMS with the introduction of individual booths in period 3 allowing for more episodes of unsupervised on-site HIVST sessions, the M&E data reported whether the client self-tested on-site or off-site, but the information on whether it was a supervised or unsupervised on-site HIVST episode could not be used.

The M&E results shows an increase of direct client time (expressed by the number of testing/self-testing episodes provided) between period 2 and 3, even after adjusting for the field-based team size over time. We assumed that the team was working at full capacity in period 2, therefore, the estimated

total direct client time per provider per day per outreach should be the same between period 2 and 3. The increase of direct client time is due to unsupervised on-site HIVST activities.

Based on the above assumptions and the following algebraic equations with two unknowns, we estimated that 7% of on-site HIVST were unsupervised and that 93% were supervised by a health provider.

Algebraic equation with two unknowns:

$\mathbf{x_3} + \mathbf{y_3} = z_3$

$\mathbf{x_3} * Tx + \mathbf{y_3} * Ty = Tz_3$

$\mathbf{x_3}$: Average number of on-site *supervised* HIVST per provider per day in period 3 (**unknown**)

$\mathbf{y_3}$: Average number of on-site *unsupervised* HIVST per provider per day in period 3 (**unknown**)

z_3: Average number of on-site HIVST per provider per day in period 3

*T*x: Average time spent by a provider on an on-site *supervised* HIVST episode

*T*y: Average time spent by a provider on an on-site *unsupervised* HIVST episode

Tz_3: Average total time spent on on-site HIVST per provider per day in period 3

The results from these exercises are presented in **Table S3**.

Table S1. Composition of economic costs for the full costing of HTS and HIVST and assumptions on HIVST costs composition for an incremental cost analysis

Cost category	Composition of conventional HIV testing (HTS) costs	Composition of full HIVST costs	Incremental HIVST costs - Assumptions
Start-up			
S1: Training	Fin.: Expenditure report for training venue and per diems, catering, etc. (annualised costs) Eco.: Annualised and discounted financial costs	Fin.: Expenditure report for training venue and per diems, catering, etc. (annualised costs) Eco.: Annualised and discounted financial costs	All start-up costs are included in the incremental costs
S2: Sensitisation	Fin.: Advert production, printing of flyers, sensitization meetings with stakeholders (annualised costs) Eco.: Annualised and discounted financial costs	Fin.: Advert production, printing of flyers, sensitization meetings with stakeholders (annualised costs) Eco.: Annualised and discounted financial costs	All start-up costs are included in the incremental costs
S3: Start-up other	Fin.: Expenditure reports for all other costs incurred during the start-up period (annualised costs) Eco.: Annualised and discounted financial costs	Fin.: Expenditure reports for all other costs incurred during the start-up period (annualised costs) Eco.: Annualised and discounted financial costs	All start-up costs are included in the incremental costs
Capital			
A: Building & storage	Fin.: Proportion of the rent of PSI HQ office, storage warehouse and New Start fixed sites where the staff is based for activities not in the field (planning outreaches, storage of equipment, etc.) (annualised costs) Eco.: Annualised and discounted financial costs	Fin.: Programme costs allocated to rent of PSI central warehouse for storage of HIVST kits only. Storage costs at New Start fixed site are negligible. (annualised costs) Eco.: Annualised and discounted financial costs	Except for HIVST kits storage, all other building costs are excluded.
B: Equipment	Fin.: Furniture purchase and other equipment at PSI headquarters and New Start sites (tables, gazebos, chairs, booth,	Fin.: individual booth only (annualised costs) Eco.: Include donated goods such as a proportion of equipment used for HTS allocated to HIVST programme	Except for the individual booth, all other equipment costs are excluded.

Cost category	Composition of conventional HIV testing (HTS) costs	Composition of full HIVST costs	Incremental HIVST costs - Assumptions
	etc.) (annualised costs) Eco.: Annualised and discounted financial costs	based on programmes' activities, then, all costs are annualised and discounted	
C: Vehicles	Fin.: New vehicle bought in period 1 (annualised costs) Eco.: Includes donated goods such as costs of older vehicles then, all costs are annualised and discounted	Fin.: None since all HIVST activities are attached to existing HTS Eco.: Includes donated goods such as costs of vehicles allocated to HIVST based on programmes' activities, then all costs are annualised and discounted	Excluded since all HIVST activities are added to existing HTS activities. However, at scale-up, supply chain costs will be considered
Recurrent			
E: Personnel & Per diems - HQ	Fin.: Proportion of personnel costs at HQ in Maseru (M&E, finance, admin, etc.) under PSI common costs allocation Eco.: Financial costs	Fin.: Proportion of personnel costs at HQ in Maseru (M&E, finance, admin, etc.) under PSI common costs allocation Eco.: Financial costs	Included in the incremental cost analysis
E: Personnel & Per diems	Fin.: Personnel at New Start fixed site (senior HTS counsellor, M&E assistant, team leader, drivers) based on time tracking reports, and field-based professional, assistant and lay HTS counsellors 100% on CIDLINK Eco.: Financial costs	Fin.: Costs of personnel at New Start fixed site (senior HTS counsellor, M&E assistant, team leader, drivers) based on time tracking reports. Interpersonal communication agents (HIVST distributors) 100% on STAR Eco.: Includes donated services such as field-based professional, assistant and lay HTS counsellors working for CIDLINK and providing HIVST, and financial costs	Costs allocation based on the results of the time and motion study. Incremental HIVST costs exclude indirect costs of staff spent on travel time, time spent on administrative tasks, etc. One should consider the potential effect of significant HIVST kits shortages on field-based activities (HIVST kit shortages lead to reduced field-based HIVST activities and reduced % allocation of personnel costs to HIVST activities - but this can be justified with a task shifting back to conventional HTS in the situation of HIVST shortages. Additional M&E and management charges (directly charged to STAR are

Cost category	Composition of conventional HIV testing (HTS) costs	Composition of full HIVST costs	Incremental HIVST costs - Assumptions
			kept to STAR in the incremental costing analysis to reflect this additional charge)
F: Supplies	Fin.: PSI office supplies such as stationery (under common costs allocation) Eco.: Includes donated goods such as HTS supplies (e.g. rapid test kits Determine, Unigold, etc.) and financial costs	Fin.: PSI office supplies such as stationery (under common costs allocation) + HIVST kits costs Eco.: Financial costs	Included in the incremental cost analysis
G: Vehicle operation, maintenance & transport	Fin.: Costs such as fuel, insurance, repair and maintenance (oil, etc.) allocated to the programme under PSI common costs allocation Eco.: Financial costs	Fin.: Costs such as fuel, insurance, repair and maintenance (oil, etc.) allocated to the programme under PSI common costs allocation Eco.: Financial costs	Excluded since all HIVST activities are added to existing HTS activities. However, at scale-up, supply chain costs will be considered
H: Building operation/maintenance	Fin.: Costs such as office/warehouse reparation and maintenance, utilities, equipment repair/maintenance, and insurance allocated to the programme under PSI common costs allocation Eco.: Financial costs	Fin.: Costs such as office/warehouse reparation and maintenance, utilities, equipment repair/maintenance, and insurance allocated to the programme under PSI common costs allocation Eco.: Financial costs	Included in the incremental cost analysis
I: Recurrent training	Fin.: Hiring of venue, hotel, per diem for participants. Training every 2 years so the costs were annualised Eco.: Annualised and discounted financial costs	N/A	N/A
J: Waste management	Fin.: Contracting with an external company. Costs allocated to the programmes under PSI common costs allocation Eco.: Financial costs	Fin.: Contracting with an external company. Costs allocated to the programmes under PSI common costs allocation Eco.: Financial costs	Included in the incremental cost analysis

Cost category	Composition of conventional HIV testing (HTS) costs	Composition of full HIVST costs	Incremental HIVST costs - Assumptions
K: Other recurrent	Fin.: Bank fees, subscriptions, postage, etc. Costs allocated to the programmes under PSI common costs allocation Eco.: Financial costs	Fin.: Bank fees, subscriptions, postage, etc. Costs allocated to the programmes under PSI common costs allocation Eco.: Financial costs	Included in the incremental cost analysis

Table S2. Description of the pre-defined activities used in the time and motion study

Code	Activity description
HTS_negative	HIV testing episode which can include individual, couple or group pre-test counselling; individual HIV rapid testing with a negative result and post-test counselling
HTS_positive	HIV testing episode which can include individual, couple or group pre-test counselling; individual HIV rapid testing with a positive result and post-test counselling
On-site HIVST_supervised	HIV self-testing kit primary distribution, which can include pre-test counselling, demonstration on how to self-test, self-testing, waiting for the results and post-test counselling. This account for the time spent by the provider with the client during the entire session
On-site HIVST_unsupervised	HIV self-testing kit primary distribution, which can includes pre-test counselling, demonstration on how to self-test, self-testing, waiting for the results and post-test counselling. The provider is not with the client during the session, in particular when waiting for and reading the test result and this time is not included
Off-site_HIVST	HIV self-testing kit secondary distribution which can include pre-test counselling and demonstration on how to self-test
Other_DPS	Other Direct Patient Services: time allocated to services that are not related to HTS and HIVST (e.g. family planning, PrEP, ART initiation etc.) provided by the health care worker to a client
Non_DPS	Any time spent not facing clients (breaks, lunch, waiting for clients, etc.)
Weekly_average_working_hours	Regular working hours reported by the study participant

Table S3. Results from the time and motion study and allocation factors of personnel costs between HTS and HIVST activities by period

Activities	**HTS**		**HIVST**		
Sessions	HTS-negative	HTS-positive	Off-site HIVST	On-site HIVST - supervised	On-site HIVST - unsupervised
Results - Time and Motion Study[a]					
Average time per session- Mean(StD[b]) - min	17.3(5.5)	32.3(10.7)	8.1(4.0)	24.1(5.2)	10.4(3.2)
# of observations	35	7	9	46	12
Daily working hours - min	480				
Period 2 - M&E data and personnel costs allocation factors					
Average # of session/provider/day	5.2	0.2	2.2	1.1	0.0
Total session time/provider/day - min	89.1	5.4	17.9	25.5	0.0
Total activity time/provider/day - min	94.6		43.3		
Total direct client time/provider/day - min	137.9				
HTS & HIVST - Full costs analysis (=Total activity time/Total direct client time)	**68.6%**		**31.4%**		
HIVST - Incremental costs analysis (=Total activity time/Working hours)*	**91.0%**		**9.0%**		
Period 3 - M&E data and personnel costs allocation factors					
Average # of session/provider/day	3.6	0.1	0.6	2.6	0.4
Total session time/provider/day - min	61.6	4.7	5.1	62.0	4.5

Total activity time/provider/day - min	66.3	71.6
Total direct client time/provider/day - min	137.9	
HTS & HIVST - Full costs analysis (=Total activity time/Total direct client time)	**48.0%**	**52.0%**
HIVST - Incremental costs analysis (=Total activity time/Working hours)[c]	**85.1%**	**14.9%**

[a]In total, 16 health providers and 109 episodes were observed [b]StD: Standard Deviation, [c]Formula applied to HIVST activities, the remaining % is allocated to the existing HTS.

Table S4.a. Quarterly averages of the full economic cost of HTS and ST during the period May 2017 – April 2019 (in 2019 US$)

Cost category	**Period 1**		**Period 2**				**Period 3**			
	Full analysis		**Full analysis**				**Full analysis**			
	HTS		**HTS**		**HIVST**		**HTS**		**HIVST**	
	Full costs	**%**	**Full costs**	**%**	**Full costs**	**%**	**Full costs**	**%**	**Full costs**	**%**
Start-up										
S1: Training	-	-	-	-	120	0%	-	-	120	0%
S2: Sensitisation	-	-	-	-	14	0%	-	-	14	0%
S3: Start-up other	15,807	2%	15,807	2%	756	0%	15,807	2%	756	0%
Start-up - sub-total	***15,807***	***2%***	***15,807***	***2%***	***890***	***0%***	***15,807***	***2%***	***890***	***0%***
Capital										
A: Building & storage	5,168	1%	16,544	2%	274	0%	18,526	3%	553	0%
B: Equipment	1,374	0%	4,400	1%	2,026	1%	1,446	0%	1,921	0%
C: Vehicles	12,470	2%	6,187	1%	6,187	2%	6,135	1%	6,135	1%
Capital - sub-total	***19,012***	***2%***	***27,131***	***4%***	***8,486***	***3%***	***26,107***	***4%***	***8,609***	***2%***
Recurrent										
E: Personnel & Per diems - HQ	37,139	5%	90,166	12%	4,509	2%	55,303	8%	7,761	2%
E: Personnel & Per diems	546,031	67%	461,434	60%	225,273	83%	396,200	61%	408,716	85%
F: Supplies	115,657	14%	86,126	11%	17,396	6%	75,490	12%	34,510	7%

G: Vehicle operation, maintenance & transport	59,099	7%	44,325	6%	15,056	6%	44,325	7%	16,119	3%
H: Building operation/maintenance	6,477	1%	12,326	2%	201	0%	9,830	2%	456	0%
I: Recurrent training	9,715	1%	9,715	1%	0	0%	9,715	1%	0	0%
J: Waste management	1,947	0%	1,932	0%	133	0%	1,915	0%	162	0%
K: Other recurrent	8,756	1%	21,977	3%	699	0%	17,522	3%	1,700	0%
Recurrent - sub-total	***784,822***	***96%***	***728,001***	***94%***	***263,267***	***97%***	***610,300***	***94%***	***469,424***	***98%***
Total costs	**819,640**		**770,939**		**272,509**		**652,213**		**478,790**	
HTS session / HIVST kit distributed per quarter	**25,433**		**27,045**		**6,300**		**27,780**		**12,687**	
Cost per HTS conducted / HIVST kit distributed	**32.2**		**28.5**		**43.3**		**23.5**		**37.7**	

Table S4.b. Quarterly averages of the full economic cost of HTS and incremental economic costs of HIVST during the period May 2017 – April 2019 (in 2019 US$)

Cost category	**Period 2**				**Period 3**			
	Incremental analysis				**Incremental analysis**			
	HTS		**HIVST**		**HTS**		**HIVST**	
	Full costs	**%**	**Incr. costs**	**%**	**Full costs**	**%**	**Incr. costs**	**%**
Start-up								
S1: Training	-	-	120	0%	-	-	120	0%
S2: Sensitisation	-	-	14	0%	-	-	14	0%
S3: Start-up other	15,807	2%	756	1%	15,807	2%	756	0%
Start-up - sub-total	***15,807***	***2%***	***890***	***1%***	***15,807***	***2%***	***890***	***1%***
Capital								
A: Building & storage	16,570	2%	247	0%	18,832	2%	247	0%
B: Equipment	5,857	1%	569	1%	2,463	0%	905	1%
C: Vehicles	12,374	1%	0	0%	12,270	1%	0	0%
Capital - sub-total	***34,802***	***4%***	***816***	***1%***	***33,564***	***4%***	***1,152***	***1%***
Recurrent								
E: Personnel & Per diems - HQ	90,166	10%	4,509	5%	55,303	6%	7,761	4%
E: Personnel & Per diems	614,262	65%	72,445	75%	674,713	71%	130,203	73%
F: Supplies	86,126	9%	17,396	18%	75,490	8%	34,510	19%

G: Vehicle operation, maintenance & transport	59,099	6%	281	0%	59,099	6%	1,344	1%
H: Building operation/maintenance	12,326	1%	201	0%	9,830	1%	456	0%
I: Recurrent training	9,715	1%	0	0%	9,715	1%	0	0%
J: Waste management	1,932	0%	133	0%	1,915	0%	162	0%
K: Other recurrent	21,977	2%	699	1%	17,522	2%	1,700	1%
Recurrent - sub-total	***895,604***	***95%***	***95,664***	***98%***	***903,588***	***95%***	***176,136***	***99%***
Total costs	**946,212**		**97,236**		**952,958**		**178,045**	
HTS session / HIVST kit distributed per quarter	**27,045**		**6,300**		**27,780**		**12,687**	
Cost per HTS conducted / HIVST kit distributed	**35.0**		**15.4**		**34.3**		**14.0**	

Table S4.c. Quarterly averages of the full economic cost of HTS and incremental financial costs of HIVST during the period May 2017 – April 2019 (in 2019 US$)

Cost category	**Period 2**				**Period 3**			
	Incremental analysis				**Incremental analysis**			
	HTS		**HIVST**		**HTS**		**HIVST**	
	Full costs	**%**	**Incr. costs**	**%**	**Full costs**	**%**	**Incr. costs**	**%**
Start-up								
S1: Training	-	-	120	0%	-	-	120	0%
S2: Sensitisation	-	-	14	0%	-	-	14	0%
S3: Start-up other	15,807	2%	756	2%	15,807	1%	756	1%

Start-up - sub-total	***15,807***	***2%***	***890***	***2%***	***15,807***	***1%***	***890***	***1%***
Capital								
A: Building & storage	16,570	2%	247	1%	18,832	2%	247	0%
B: Equipment	6,417	1%	8	0%	2,853	0%	514	1%
C: Vehicles	12,374	1%	0	0%	12,270	1%	0	0%
Capital - sub-total	***35,362***	***4%***	***256***	***1%***	***33,955***	***3%***	***762***	***1%***
Recurrent								
E: Personnel & Per diems - HQ	90,166	9%	4,509	12%	55,303	5%	7,761	11%
E: Personnel & Per diems	673,021	67%	13,686	36%	781,795	74%	23,121	33%
F: Supplies	86,126	9%	17,396	46%	75,490	7%	34,510	49%
G: Vehicle operation, maintenance & transport	59,099	6%	281	1%	59,099	6%	1,344	2%
H: Building operation/maintenance	12,326	1%	201	1%	9,830	1%	456	1%
I: Recurrent training	9,715	1%	0	0%	9,715	1%	0	0%
J: Waste management	1,932	0%	133	0%	1,915	0%	162	0%
K: Other recurrent	21,977	2%	699	2%	17,522	2%	1,700	2%
Recurrent - sub-total	***954,363***	***95%***	***36,905***	***97%***	***1,010,669***	***95%***	***69,055***	***98%***
Total costs	**1,005,531**		**37,917**		**1,060,430**		**70,573**	
HTS session / HIVST kit distributed per quarter	**27,045**		**6,300**		**27,780**		**12,687**	
Cost per HTS conducted / HIVST kit distributed	**37.2**		**6.0**		**38.2**		**5.6**	

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Conclusions from Paper 2

The results presented in this paper offer important insights into efficiency considerations with the addition of a new technology such as HIVST, to existing HTS programme. This longitudinal analysis suggests that the addition of HIVST increases the overall programme's affordability for HIV-positive case finding. Another important finding relates to the scope of incremental and full costing methods. This analysis highlights that budgeting of HIVST using incremental costs risks to underestimate needs if the HTS programme is not running well. These two findings are particularly relevant when costing the implementation of a new technology and estimating the costs of scaling up this programme.

The next paper presents an empirical econometric cost function analysis to estimate the drivers of HIVST costs, including scale and efficiency, and uses this function to model costs at scale in the region.

Chapter 5 – Paper 3: Modelling costs of community-based HIV self-testing programmes in Southern Africa at scale: An econometric cost function analysis across five countries

Overview of Paper 3

The economic analyses from paper 2 and from Mangenah et al (**Appendix I**), provide insights into the implementation costs of community-based HIVST programmes in various settings. An analysis of HIVST cost drivers can inform programme planners for the scale-up of HIVST in the southern African region.

Paper 3 uses costs and programme data from Malawi, Zambia, Zimbabwe, and South Africa to fit a cost function with determinants related to scale, locales organisational and environmental characteristics, target populations, and per capita Growth Domestic Product. I then use this model to project HIVST costs at scale. I also explore various models differing in data intensity for cost predictions and compare projected costs with observed costs estimated in paper 2 over two years of implementation in Lesotho.

This work was reviewed and approved by the local ethics committees in each country, as well as the London School of Hygiene and Tropical Medicine Ethics Committee, University College London Ethics Committee, and the Institutional Review Board of Boston University School of Public Health (**Appendix IV**). Informed consent was obtained from all individual participants included in the time and motion study.

The Appendix text presents a narrative description of the community-based HIVST distribution models across countries. Appendix figure presents a correlation matrix of HIVST cost drivers considered for the analysis. I include additional details on the costing methodology with a table of the factors used to allocate costs from STAR expenditures to models, and from models to districts. Finally, I present the findings from the observed incremental HIVST costs for each scale-up period in Lesotho.

This paper is presented as accepted in the journal *BMJ Global Health* in May 2021. This paper fulfil research objective 3 by estimating the costs drivers of community-based HIVST distribution in Malawi, Zambia, Zimbabwe and South Africa, using econometric methods and, based on the model outputs, projecting costs at scale using community-based HIVST national scale-up in Lesotho as a case study.

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Thesis Title	Estimating healthcare costs at scale in low- and middle-income countries – the case of community-based HIV self-testing scale-up in southern and western Africa		
Primary Supervisor	Prof Fern Terris-Prestholt		

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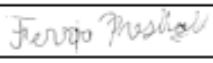
Supervisor Signature	
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Modelling costs of community-based HIV self-testing programmes in Southern Africa at scale: An econometric cost function analysis across five countries

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Abstract (300/300 words max)

Background: Following success demonstrated with the STAR (HIV Self-Testing AfRica) Initiative, HIV self-testing (HIVST) is being added to national HIV testing strategies in southern Africa. An analysis of the costs of scaling up HIVST is needed to inform national plans, but there is a dearth of evidence on methods for forecasting costs at scale from pilot projects. Econometric cost functions (ECF) apply statistical inference to predict costs; however we often do not have the luxury of collecting large amounts of location-specific data. We fit an ECF to identify key drivers of costs, then use a simpler model to guide cost projections at scale.

Methods: We estimated the full economic costs of community-based HIVST distribution in 92 locales across Malawi, Zambia, Zimbabwe, South Africa, and Lesotho between June 2016 and June 2019. We fitted a cost function with determinants related to scale, locales organisational and environmental characteristics, target populations, and per capita Growth Domestic Product (GDP). We used models differing in data intensity to predict costs at scale. We compared predicted estimates with scale-up costs in Lesotho observed over a two-year period.

Results: The scale of distribution, type of community-based intervention, percentage of kits distributed to men, distance from implementer's warehouse, and per capita GDP predicted average costs per HIVST kit distributed. Our model simplification approach showed that a parsimonious model could predict costs without losing accuracy. Overall, ECF showed a good predictive capacity, i.e. forecast costs were close to observed costs. However, at larger scale, variations of programme efficiency over time (number of kits distributed per agent monthly) could potentially influence cost predictions.

Discussion: Our empirical cost function can inform community-based HIVST scale-up in southern African countries. Our findings suggest that a parsimonious ECF can be used to forecast costs at scale in the context of financial planning and budgeting.

Summary box

What is already known?

Following success demonstrated with the STAR (HIV Self-Testing AfRica) Initiative, HIV self-testing is being added to national HIV testing strategies in southern Africa.

Community-based models delivering HIV self-testing either at people's homes or within the community setting with mobile outreach are a convenient approach for reaching under-tested groups such as young people (16-25 years old) and men.

There is little guidance or empirical evidence on methods for forecasting costs at scale for programming and planning.

What are the new findings?

Our study developed an econometric cost function for scaling up community-based HIV self-testing programmes for the general population in southern Africa, using data from five countries.

Our model simplification approach showed that we could use a more parsimonious model, including scale, type of community-based intervention, percentage of men reached by the programme, distance from implementer's warehouse, and per capita Growth Domestic Product, to predict costs without significantly losing accuracy.

What do the new findings imply?

The extrapolation of cost predictions to inform community-based HIV self-testing scale-up in southern African countries is possible with our empirical cost function.

Our analysis adds to the literature on the trade-off between simplicity versus accuracy in cost projection methods.

Introduction

The HIV burden remains concentrated in southern Africa, with estimated adult prevalence ranging between 10.6% in Malawi and 25.6% in Lesotho in 2018 [1]. Expanding access to HIV testing services (HTS) and ensuring linkage to prevention or timely antiretroviral therapy (ART) initiation for people living with HIV (PLHIV) is vital to achieving epidemic control. HIV self-testing (HIVST) is an additional testing modality where an individual collects his/her own oral fluid or blood sample, conducts the test, and interprets results. HIVST has increased the uptake and frequency of testing among individuals who would not test otherwise [2, 3]. The Unitaid-funded Self-Testing AfRica (STAR) Initiative led by Population Services International (PSI) started implementing HIVST delivery models in southern Africa in 2016 [4]. Many HIVST distribution models were evaluated, including community-based, workplace, public and private sector facility-based primary distribution strategies, and secondary distribution strategies to sexual partners and peers among key populations[5].

Community-based models delivering HIVST either at people's homes or within the community setting with mobile outreach were shown to be a convenient approach for reaching under-tested groups such as young people (16-25 years old) and men [6-10]. Although community-based approaches are expensive from a provider perspective, they decrease users' costs in accessing HIV testing, in particular among working men whose time might be more expensive [9, 11, 12]. Following the success demonstrated in the STAR Initiative, the Lesotho Ministry of Health added HIVST to its revised national HTS strategic plan for 2018-2023[13]. An analysis of the costs of scaling-up HIVST (increasing the provision of HIVST kits) was needed by country planners to inform the HIVST national scale-up plans and budget in Lesotho. However, there is little guidance or empirical evidence on methods for projecting costs at scale for programming and planning [14, 15].

Cost functions can be derived from a production function to estimate the total cost of production given a specific output produced. The simplest cost function multiplies a single unit cost by a quantity - the commonly used "simple cost multiplier" (SCM). It is a practical costing method used for high level

budgeting [15]. Accounting cost functions (ACF) identify all the cost inputs to a production process (equipment, personnel, etc.) over a defined costing period (usually one year), and categorize them as fixed, semi-fixed, or variable costs in the short run, or all variable in the long run [14-17]. Econometric cost functions (ECF) do not follow the production process but rather apply statistical inference to predict costs. The challenge of ECF is to reflect the complexity of real-world production process with a mathematical model of inputs and outputs [14, 16]. In most studies, we do not have the luxury of collecting large amounts of location-specific cost data, and applications of ECF for cost predictions are rare [14, 18]. In the absence of detailed data, SCM is commonly used.

This study aims to fit an ECF to estimate the cost drivers of the community-based HIVST programmes in Southern Africa using data from Malawi, Zambia, Zimbabwe, and South Africa. We then inform the use of ECF to predict costs at scale by comparing ECF models with different level of data requirements. Finally, we assess the validity of our empirical ECF by comparing projected costs with observed costs at scale in Lesotho. We select Lesotho as our case study because we conducted in this country a longitudinal micro-costing analysis of HIVST scale-up from a real-world intervention over two years of implementation [19].

Methods

Setting – Data sources

We estimated the full economic costs of community-based HIVST distribution in 92 sites across Malawi, Zambia, Zimbabwe, South Africa, and Lesotho (**Table 1**) [12, 19, 20]. We collaboratively developed cost analysis methods following standard guidelines and analysed data, ensuring consistency of methods across countries [15, 21]. Programme expenditures supplemented by on-site observation and monitoring and evaluation data were used to estimate HIVST distribution costs [22]. Costing studies in Malawi, Zambia, Zimbabwe were conducted as part of larger randomized controlled trials [12]. We also

conducted time and motion studies. Cost data collection and analysis methods are described in detail elsewhere [12, 23, 24]. Some variations of the "community-based" intervention were observed between countries and are described in **Appendix Text S1**. For resources shared across different services, models, or levels, we allocated expenditure using allocation factors summarised in **Appendix Table S1**. Costs were adjusted for inflation using each country's Consumer Price Index and presented in 2019 US$ [15, 25].

For cost determinants (or cost drivers) presented in **Table 2**, data on scale, number of HIVST distributors per site, efficiency, type of community-based intervention, percentages of HIVST kits distributed to men and to those who never tested for HIV were collected through the PSI M&E programme. Distance between distribution site and PSI headquarters, size of catchment population, HTS costs and positivity rates at nearby health facilities, per capita Growth Domestic Product (GDP) in 2019 US$, were collected as part of the STAR costing studies [12, 24].

Study timelines

Cost data were collected between June 2016 and June 2019 across all countries (**Figure 1**). For the analysis of observed costs at scale in Lesotho, costs were collected between August 2017 and April 2019 (17 months) in five districts (Berea, Leribe, Mafeteng, Maseru, Mohale's Hoek) where HIVST kits were distributed. We observed three scale-up phases of approximately 6 months each in Lesotho (period 1: December 2017-April 2018; period 2: May 2018-October 2018; period 3: November 2018-April 2019).

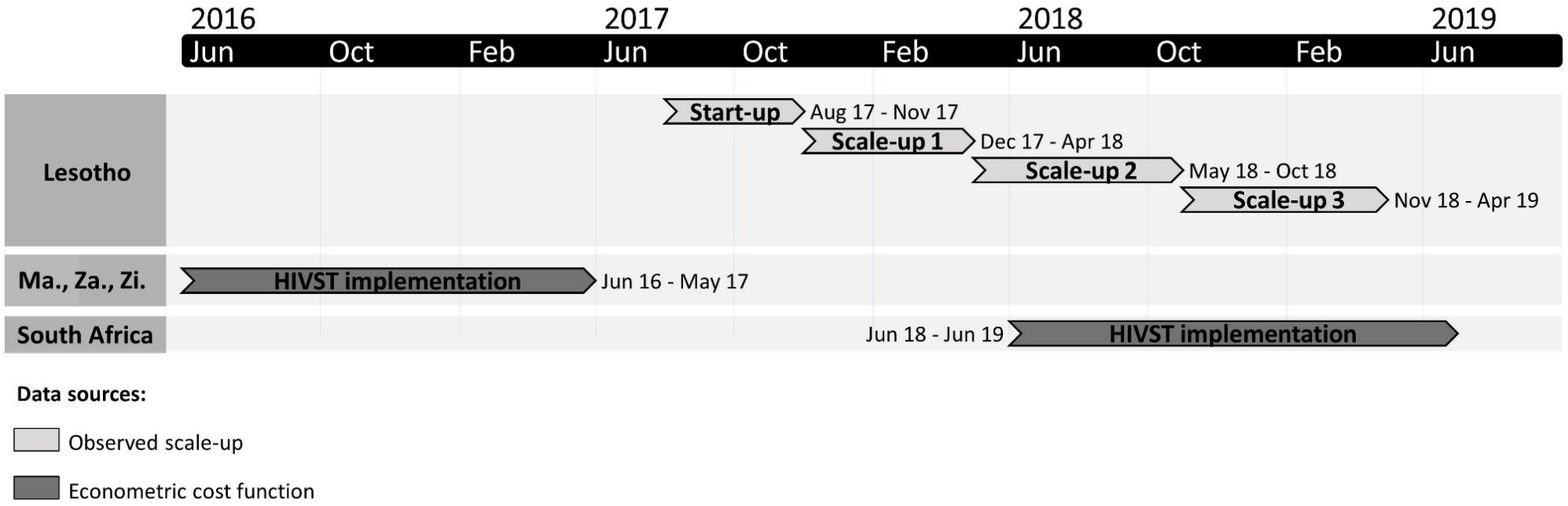


Figure 1. STAR costing period and data sources by country for each cost analysis (Ma.: Malawi, Za.: Zambia, Zi: Zimbabwe)

Table 1. Overview of interventions by countries

	Malawi	Zambia	Zimbabwe	South Africa	Lesotho	Source
Per Capita Gross Domestic Product (2019 US$)	$412	$1,305	$1,464	$6,001	$1,118	[26]
National HIV prevalence among adults 15 to 59 years (%) - 2018	10.6	12.0	14.6	20.4	25.6	[27-31]
Intervention district	Blantyre, Machinga, Mwanza, Neno	Choma, Lusaka, Ndola, Kapiri	Mberengwa, Buhera Masvingo, Chivi, Gweru, Bulilima, Gutu, Mazowe	City of Tshwane, City of Johannesburg	Maseru, Berea, Leribe Mohale, Mafeteng	[32]
Definition of site	Catchment area of a rural public primary health clinic	Catchment area of a rural public primary health clinic	Ward (subdivision of a district)	District	Catchment area of a PSI fixed site (~one per district) i.e. a district and across all five districts, for each period 1-3	[12]

Number of sites	11	16	44	3	18	[32]
Location: rural; urban or peri-urban	11; 0	8; 8	44; 0	0; 3	4; 1	[32]
Analysis period	June 2016 – May 2017 (12 months)	June 2016 – May 2017 (12 months)	June 2016 – May 2017 (12 months)	June 2018 – June 2019 (13 months)	August 2017 – April 2019 (17 months)	[32]
Total number of HIVST kits distributed in included sites during observation period	152,671	103,589	92,559	154,111	51,676	[12, 19, 32]

Econometric analysis

Econometric model specification using data from Malawi, Zambia, Zimbabwe, and South Africa

We start our analysis with the conventional cost function where total costs are a function of quantity and prices [17]. We use a linear regression approach (Ordinary Least Squares) and use average cost per HIVST kit distributed (arithmetic mean) as the dependent variable [33]. We use average costs instead of total costs as our sample is composed of sites at various administrative levels between countries (district, catchment area of health facility), thus making comparison more intuitive, and because the unit of output (HIVST kits distributed) is clearly defined (**Equation 1**). We included PSI central costs (country and regional offices) in the average cost estimates to allow for comparison with observed costs at scale. Because the cost data were highly skewed to the right with a heavy tail, we log-transformed the dependent variable[33].

Cost determinants were selected based on the economic theory of production function, through programme observation, and the literature on cost functions for HIV care services [14, 34-47]. Cost drivers' description, expected effect on costs and justification for inclusion in the model are presented in **Table 2,** following Lepine and colleagues' approach for the categorisation of determinants [42]. We used multiple imputation for missing data although overall missingness was low, mean and standard deviation were comparable before/after imputation. We checked model robustness with the addition/removal of single regressors. The cost function was fitted using the R package [48].

Equation 1:

$$C = \sum_k AC_k \cdot Q_k \quad with \quad Log(AC_k) = \beta_0 + \beta_1 * Scale_k + \beta_2 * Scale^2_k + \beta_3 * Scale^3_k + \beta_4 * Distributor\_site_k + \beta_5 * Campaign_k + \beta_6 * Log(Efficiency_k) + \beta_7 * Perc\_men_k + \beta_8 * Perc\_never\_tested_k + \beta_9 * Distance_k + \beta_{10} * Population_k + \beta_{11} * Positivity_k + \beta_{12} * Cost\_facility_k + \beta_{13} * Price\_level_k$$

Where:

C: Total programme cost

k: Level of analysis: district, catchment area of health facility

Log(AC_k): Natural logarithm of the average cost per scale variable Q_k for level k

Scale: Average number of HIVST kits distributed per month

Distributor_site: Average number of distributors per site

Campaign: Type of intervention (campaign style versus fixed distributors)

Log(Efficiency): Natural logarithm of the number of HIVST kits distributed per agent monthly

Perc_men: Percentage of HIVST kits distributed to men out of total distribution volumes

Perc_never_tested: Percentage of HIVST kits distributed to people who never tested before out of total distribution volumes

Distance: Distance of site from implementer's central warehouse (in kilometres)

Population: Size of total population at the site

Positivity: Positivity of rapid HIV testing (number of HIV-positive case found out of total number of persons tested) at nearby health facilities

Cost_facility: Average cost per facility-based HIV testing session at nearby health facilities

Price_level: Proxy for input price level variation across countries based on per capita GDP

β_0: Model intercept

β_1-β_{13}: Model coefficients computed using empirical dataset

Q_k: Quantity of units for level k: number of HIVST kits distributed

Using the model to predict costs at scale in Lesotho

Coefficients in a log-linear model are the estimated percentage change – elasticity – in the dependent variable for a unit change in the independent variable [49, 50]. We used the 'predict' function in R package to estimate average cost for various scale values. We used exponential function to back transform estimated average costs as our error terms are normally distributed [51]. We compare total costs at "national" (all five districts) and district level to allow for comparison between observed costs (scale-up periods 1,2 and 3) and predicted costs. The Likelihood Ratio test (LRT), comparing the goodness of fit of two statistical models, was used to assess whether we could simplify the model (i.e. reduce the number of parameters in our regression model) for cost projections.

Patient and Public Involvement

To conduct our costing study from a provider perspective, it was not appropriate to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Ethical approvals

Ethical approvals for the parent studies 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. Ethical approval was obtained from the National Health Research Ethics Committee of Lesotho and the London School of Hygiene and Tropical Medicine Ethics Committee (Ref. # ID64-2018 and 14887, respectively). Ethics approvals for the costing work in South Africa were obtained from research ethics committees of the London School of Hygiene and Tropical Medicine (Ref. # 15408), the Human Research Ethics Committee (Medical) of the University of Witwatersrand (Ref. # M180379), and the Institutional Review Board of Boston University School of Public Health (Ref. # H-37713). Informed consent was obtained from all individual participants included in the time and motion study.

Table 2. Variable categories, description, expected effect on costs and justification

Variable category	Variable name	Description	Expected effect on costs	Justification	Source
Dependent variable	Average costs per HIVST kit distributed including central costs	Unit costs per HIVST kit distributed including in-country central costs and start-up costs in 2019 USD	NA	NA	[12]
Quantities	Scale	Number of HIVST kit distributed by site during the observation period	+/-	(Dis)Economies of scale	PSI
Site organisational characteristics	HIVST distributors	Number of full time equivalent HIVST distributor in each site	+/-	Increase your coverage and # of HIVST kits distributed (so lower average costs per kit distributed), but also increase personnel costs	PSI

	Campaign-style	Variable coded 1 if the same distributors travel from sites to sites (campaign style distribution) or 0 if they live within the community	+	In some countries, HIVST kits distribution was more conservative and restricted by campaign duration in each site, so this approach could drive costs higher due to lower volumes of kits distributed and travel costs	PSI
	Efficiency	Number of HIVST kits distributed per agent per month	-	The higher the number of HIVST kits distributed per agent, the more efficient they are, and the lower is the cost per kit distributed	PSI
Characteristics of population targeted	% HIVST kits distributed to men	Number of kits distributed to men – Also measure if programme is targeting well (proxy for quality)	+	Men might be harder to reach and to convince to take a kit, might lead to higher costs of provision	PSI
	% never tested for HIV	% of people who never tested for HIV	-	Higher knowledge of HIV status might lead to lower demand for testing, including HIVST, leading to increased average cost per kit distributed	STAR household surveys

	Distance	Distance from central warehouse to site in kilometres	+	Longer distance from the PSI headquarters and warehouse might lead to high costs of service provision	PSI, Google Maps
	Catchment population	Size of the catchment population of the site regardless of eligibility	-	Number of potential HIVST recipients affect levels of distribution potentially leading to economies of scale	PSI, MoH
Environmental characteristics	Positivity at health facility	Annual new HIV-positive identified over total tested at nearby health facility (positivity rate)	+	If the health facilities experience high positivity rates, the demand for HIVST might be lower leading to increased average costs (higher costs to reach the last % of target population)	PSI, MoH
	HTS average cost at health facility	Average cost per person tested with HTS at the nearest health facility	+	Although not a determinant, a significant correlation might suggest the effect of other unobserved environmental characteristics on costs	[12, 24]
Input price level	Price level	Per Capita Growth Domestic Product in 2019 US$	+	Proxy for input price level variation across countries	[26]

Results

Descriptive statistics

Descriptive statistics (mean, standard deviation, min, max) of data are presented for the full sample and for each country in **Table 3**. Sample mean of average cost per kit distributed was $14.58 (median: $13.54). On average, each site had 26 (range: 2-272) distributors and distributed 993 (range: 160-5,904) kits. Part of the strategy was to reach men, and those who had never tested before, these groups made up, on average, 48%, and 12%, respectively of kit recipients. Average distance of site to warehouse was 162 kilometres, population size of 672,429 inhabitants, finally, positivity rate of 8% and the cost of provider-delivered HIV testing was $6.22 per person tested at nearby health facilities.

Determinants of HIVST average costs at programme level and model simplification

We retained a combination of three scale variables, normally distributed, quadratic and cubic, because they explained the largest share of the variance (R^2 was the highest) [52, 53]. We explored several functional forms for other cost determinants, only efficiency was log-transformed as it improved model fit. Other determinants were kept with a normal distribution. The correlation matrix showed high correlation between *population* and *scale*, between *distributors* and *campaign-style*, and low or no correlation otherwise (**Appendix Figure S1**); therefore, the variables *population* and *distributors* were excluded. Multicollinearity was assessed on the remaining cost drivers using the variance inflation factor (VIF) test and was acceptable (mean VIF: 2.94). We tested for heteroscedasticity using the Breusch-Pagan test and failed to reject the null hypothesis ($p>0.05$), therefore heteroscedasticity was not present in the model.

We progressively added cost determinants to our model starting with scale, followed by organizational characteristics, characteristics of the population reached, environmental factors, and price level (**Table 4**). Major cost determinants were *scale*, *campaign-style* distribution, *% of kits distributed to men*, *distance* from the implementer's warehouse, and *price level* (*Model 5*). We found a negative association between scale and average cost. If scale increases by 100 HIVST kits distributed, average cost decreases by 0.16%. Campaign-style distribution increased costs by 19%. An increase in one percent of kits distributed to men increased average cost by 0.67%. An increase of the distance between the implementer's warehouse and HIVST distribution areas by one kilometre increased costs by 0.01%. Finally, an increase of per capita GDP (*price_level*) by $10, led to an increase of average cost by 0.01%.

For the model simplification analysis, we removed *% never tested*, *positivity* and *HTS costs at health facility* in *Model 6*, as these determinants were not significant (**Table 5**). *Model 5* did not significantly improve fit to the data than *Model 6* (LRT: p-value: 0.82). Additionally, *Model 7*, where *efficiency* was removed, did not significantly reduced goodness of fit than *Model 6* (LRT: p-value: 0.67).

Table 3. Descriptive statistics

	Total sample				**Malawi**				**Zambia**			
Number of sites (N)	**92**				**11**				**16**			
Variables	**Mean**	**Std**	**Min**	**Max**	**Mean**	**Std**	**Min**	**Max**	**Mean**	**Std**	**Min**	**Max**
Average cost per HIVST kit distributed (including central costs)	14.58	2.8	7.2	54.44	10.65	2.93	7.20	17.04	21.11	10.73	7.91	50.01
Average cost per HIVST kit distributed (excluding central costs)	10.73	1.7	4.52	41.49	5.56	1.03	4.52	7.52	12.39	5.36	6.40	26.50
Scale	1,319	819	160	5,904	1,045	1,005	380	3,511	589	398	160	1,859
HIVST distributors	26	26	2	40	13	8	6	31	9	3	5	18
Campaign-style	0.56	0.5	0	1	0	0	0	0	0	0	0	0
Efficiency	109	56	13	486	75	22	48	113	64	23	27	103
% HIVST kits distributed to men	48	8	31	76	50	3	45	55	56	25	33	76
% HIVST kits distributed to people who never tested for HIV	12	2	0	22	18	3	11	22	18	3	13	21
Distance	162	35	3	647	85	55	20	180	210	122	11	348
Catchment population	672,429	824,163	549	4,949,347	24,007	21,804	4,452	82,581	48,379	50,924	10,096	172,753

Positivity	0.08	0.03	0	0.62	0.09	0.04	0.03	0.14	0.09	0.07	0.00	0.27
HTS average cost	6.22	2.5	2.3	34.78	3.97	1.09	2.64	5.81	4.45	1.41	2.49	7.17
	Zimbabwe				**South Africa**				**Lesotho**			
Number of sites (N)	**44**				**3**				**18**			
Variables	**Mean**	**Std**	**Min**	**Max**	**Mean**	**Std**	**Min**	**Max**	**Mean**	**Std**	**Min**	**Max**
Average cost per HIVST kit distributed (including central costs)	15.79	7.32	10.19	54.44	13.54	5.36	9.69	19.67	11.79	3.79	6.97	22.81
Average cost per HIVST kit distributed (excluding central costs)	11.65	5.66	7.44	41.49	12.59	5.38	8.76	18.74	11.45	3.64	6.80	21.96
Scale	1,052	401	160	2,101	2,901	2,636	971	5,904	1,009	1,007	188	4,184
HIVST distributors	23	7	5	40	10	7	2	14	75	71	10	272
Campaign-style	1	0	1	1	0	0	0	0	0	0	0	0
Efficiency	47	14	13	80	346	155	130	486	15	7	5	40
% HIVST kits distributed to men	44	4	38	55	51	12	37	60	38	9	31	56
% HIVST kits distributed to people who never tested for HIV	12	4	5	21	11	8	3	18	2	1	0	2
Distance	349	141	33	647	90	85	17	184	76	54	3	130

Catchment population	8,023	24,453	549	165,590	2,989,107	2,117,801	742,822	4,949,347	292,627	144,458	165,590	519,186
Positivity	0.07	0.10	0.00	0.62	0.13	0.05	0.10	0.18	0.03	0.01	0.03	0.04
HTS average cost	7.15	5.74	2.30	34.78	11.21	6.94	5.02	18.71	4.30	1.32	2.49	6.15

Std: Standard deviation

Table 4. Determinants of HIVST average costs at programme level

	Model 1			Model 2			Model 3			Model 4			Model 5		
Parameters	**Estimate**		***Std. Error***	**Estimate**		***Std. Error***	**Estimate**		***Std. Error***	**Estimate**		***Std. Error***	**Estimate**		***Std. Error***
Constant	3.501	***	*0.125*	3.428	***	*0.335*	3.135	***	*0.390*	2.395	***	*0.405*	3.153	***	*0.437*
Scale (in thousands)	-1.261	***	*0.250*	-1.935	***	*0.316*	-1.889	***	*0.319*	-1.529	***	*0.314*	-1.578	***	*0.291*
Scale^2 (in millions)	0.388	***	*0.132*	0.684	***	*0.149*	0.656	***	*0.150*	0.492	***	*0.146*	0.553	***	*0.137*
Scale^3 (in billions)	-0.036	**	*0.016*	-0.068	***	*0.018*	-0.064	***	*0.018*	-0.046	***	*0.017*	-0.056	***	*0.016*
Campaign-style				0.364	***	*0.101*	0.392	***	*0.104*	0.169		*0.108*	0.174	*	*0.100*
Efficiency				0.050		*0.095*	0.071		*0.093*	0.171	*	*0.095*	-0.049		*0.109*
% HIVST kits distributed to men							0.533	**	*0.246*	0.737	***	*0.228*	0.511	**	*0.221*
% HIVST kits distributed to							-0.557		*0.769*	-1.236	*	*0.722*	-0.097		*0.748*

people who never tested for HIV									
Distance (in thousands)				1.062	***	*0.279*	0.603	**	*0.292*
Positivity				0.071		*0.352*	0.177		*0.327*
HTS average cost				-0.001		*0.006*	-0.004		*0.006*
Price_level (in thousands)							0.139	***	*0.041*
No. of obs.	74	74	74	74			74		
R2	0.51	0.63	0.66	0.74			0.78		
R2-adjusted	0.49	0.60	0.62	0.69			0.74		

***p<0.01, **p<0.05, *p<0.10

Table 5. Model simplification approach

	Model 5			Model 6			Model 7		
Parameters	**Estimate**		***Std. Error***	**Estimate**		***Std. Error***	**Estimate**		***Std. Error***
Constant	3.153	***	*0.437*	3.110	***	*0.418*	2.963	***	*0.191*
Scale (in thousands)	-1.578	***	*0.291*	-1.630	***	*0.271*	-1.662	***	*0.257*
Scale^2 (in millions)	0.553	***	*0.137*	0.575	***	*0.129*	0.585	***	*0.126*
Scale^3 (in billions)	-0.056	***	*0.016*	-0.059	***	*0.015*	-0.060	***	*0.015*
Campaign-style	0.174	*	*0.100*	0.187	**	*0.093*	0.205	**	*0.080*
Efficiency	-0.049		*0.109*	-0.037		*0.092*			
% HIVST kits distributed to men	0.511	**	*0.221*	0.519	**	*0.216*	0.542	**	*0.208*
% HIVST kits distributed to people who never tested for HIV	-0.097		*0.748*						
Distance (in thousands)	0.603	**	*0.292*	0.582	**	*0.245*	0.623	***	*0.222*

Positivity	0.177		*0.327*						
HTS average cost	-0.004		*0.006*						
Price_level (in thousands)	0.139	***	*0.041*	0.133	***	*0.035*	0.126	***	*0.029*
No. of obs.	74			74			74		
R2	0.78			0.77			0.77		
R2-adjusted	0.74			0.75			0.75		
Likelihood ratio test: Model 5 vs. Model 6, and Model 6 vs. Model 7									
Difference of chi-squared values									
(degrees of freedom)				0.93 (3)			0.18 (1)		
p-value				0.82			0.67		

***p<0.01, **p<0.05, *p<0.10; degrees of freedom calculations: Model 5 vs. Model 6: 13-10=3, Model 6 vs. Model 7: 10-9=1

Observed costs at scale in Lesotho

The cost analysis (**Appendix Table S2**) was conducted for each of the three costing periods at national and district level. The main cost drivers identified were personnel costs at national level (9%, 12%, and 9% for period 1, 2, and 3 respectively), district level (29%, 29%, and 31%), and community outreach (27%, 28%, and 21%), as well as HIVST kits costs (25%, 20% and 30%). Overall, HIVST distribution volumes were decreasing between periods 1 and 2 (14,099 and 12,471 kits), then increasing between period 2 and 3 (12,471 and 25,106 kits). Between districts, we observed wide variation in HIVST kit distribution volumes ranging from 1,130 kits (Mohale's Hoek, period 2) to 7,958 kits (Leribe, period 3). At national level, average cost per kit distributed varied between periods: $10.69, $13.71, and $9.12 in period 1, 2, and 3, respectively. At district level, wide variation was observed with average cost ranging from $6.97 (Leribe, period 3) to $22.81 (Berea, period 2).

Predicting costs at scale in Lesotho using the ECF with varying levels of complexity and comparison with observed costs at scale

We present observed total costs for each scale-up period at national and district level in Lesotho, against projected costs from *Models 5-7* (**Figure 2**). Overall cost projections at given scale were close to observed costs at district level and at national level in period 1, whereas we report some discrepancies at national level in periods 2 and 3. The comparison of projected total costs also showed that more parsimonious ECF (*Model* 7) were not less accurate than more data hungry ECF (*Model 5*). Simplified models were more precise due to narrower 95% confidence intervals, but would sometimes not include the observed costs in their range (*Model 5* versus *Model 7*: all districts – period 2).

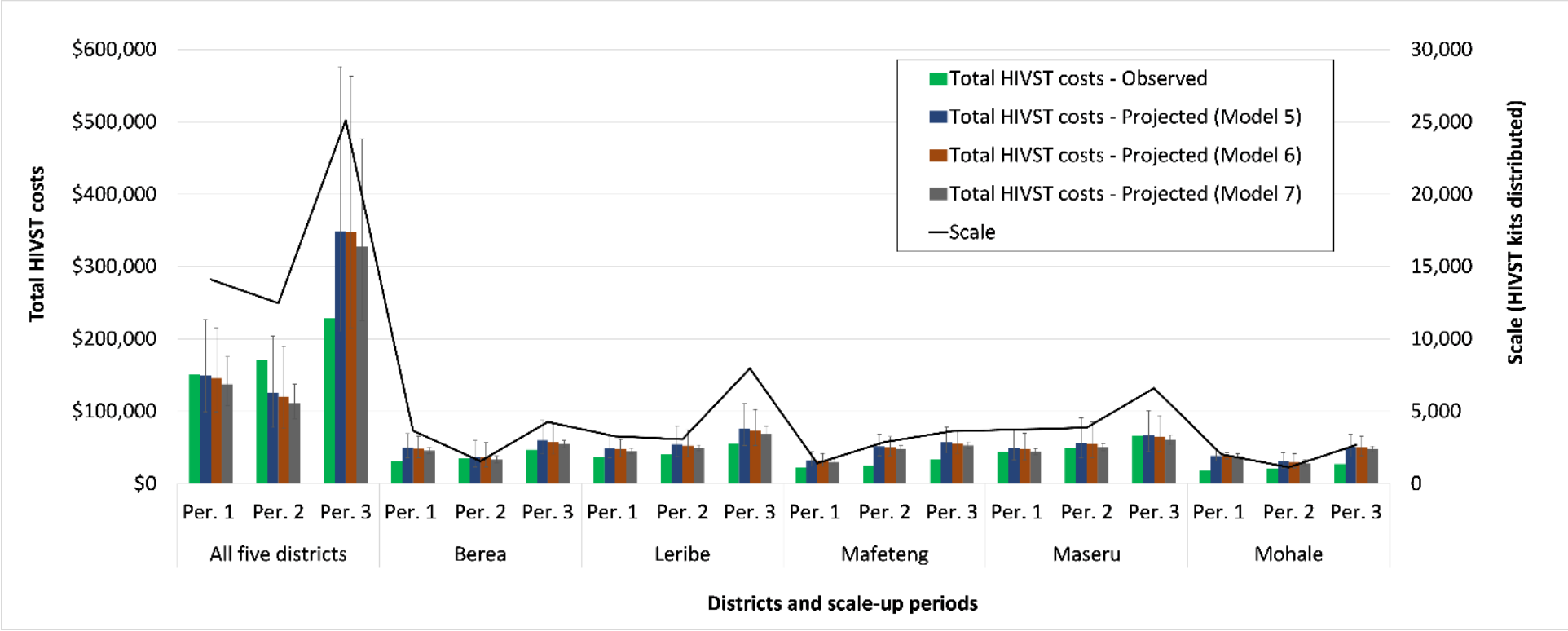


Figure 2. National and district level observed and projected (*Models 5-7*) HIVST total costs by scale-up period in Lesotho (error bars: 95% Confidence intervals)

Discussion

Our study developed an econometric cost function for scaling up community-based HIVST programmes for the general population in southern Africa, using data from five countries. Our results suggest that programme design characteristics, including the scale of HIVST distribution, type of community-based intervention, characteristics of the population targeted with HIVST (men), distance from implementer's headquarter, and per capita GDP can be used to predict average costs. These findings are consistent with previous studies on HIV prevention cost functions highlighting the role of scale as the major cost determinant among other cost drivers [42, 43, 47, 54]. We also found that reaching men was associated with higher average HIVST distribution costs. Previous studies have shown that men's uptake of community HIV testing is often lower than uptake in women, as men are less likely to be present when mobile testing teams visit households, or might be more reluctant to take a kit, therefore increasing provision costs [5, 55, 56]. In addition, it is increasingly relevant to account for decreasing returns to scale for epidemics such as HIV or malaria where testing efforts have increased over decades, making it more expensive to reach the last percentage of the target population – due to the last remaining untested living in remote areas, or being part of harder to reach population groups, etc.

Our model simplification approach showed that we could use a more parsimonious model to predict costs without significantly losing accuracy. This is particularly relevant as in most studies, we have scant opportunity to collect large amounts of location-specific cost data, and the necessary background information (e.g. percentage of population who never tested at the community level) might not exist. The per capita GDP variable showed that our cost function could potentially be applied to other countries. This is in line with the study by Cerecero-Garcia and colleagues that used per capita GDP as a determinant to predict HIV treatment average costs in out-of-sample countries [57]. The extrapolation of cost projections to other southern African countries seems possible with our parsimonious empirical cost function, however it would probably require additional or different

variables in other settings such as in West Africa. The use of ECF to predict costs at scale in the context of financial planning and budgeting is limited in the development economics literature [14, 18, 58, 59]. In a study from 2018, Berman and colleagues used a combination of ECF and ACF (using the normative costing approach incorporated in the World Health Organization's OneHealth tool) to provide low and high estimates of financial needs to plan Ethiopia's primary health care system. The authors suggested that ECF could provide a low estimate of resource needs due to limited inclusion of capital investments, future changes in services offered to meet changes in health needs, and future improvements potentially required for the quality of services provided [18]. Their findings suggest that our cost projections based on ECF could potentially underestimate the amount of resources needed.

Our findings in Lesotho for the observed cost analysis across scale-up periods are consistent, in terms of average costs and cost composition, with the existing literature on HIVST costs in the region, ranging from US$8.15 per kit distributed in Malawi to US$16.42 in Zambia [12, 19]. This suggests that they can be used as comparators with forecast costs analysis. Overall, ECF gave highly accurate and consistent scale-up cost estimates compared to observed costs at district level, suggesting a good predictive capacity of our empirical cost function. At higher scale (national level), cost predictions were close to observed costs in period 1, but were slightly below observed costs in period 2, and above in period 3. HIVST implementation and scale-up in Lesotho went through varying levels of efficiency (i.e. number of HIVST kits distributed by agents monthly), and was explained by an HIVST implementation strategy maturing over time with important impact on programme costs[19]. HIVST scale-up went through an inefficient phase in period 2 with limited HIVST distribution volumes because of the time spent by providers to offer individual onsite counselling and supervision for self-testing at the mobile outreach. Period 2 was then followed by a more efficient phase, when self-testing booth were introduced at the mobile outreach (period 3) allowing staff to supervise onsite self-testing of many clients at the same time. Although we account for efficiency as a cost determinant in our models 5-7, it was not significant, maybe related to our relatively small sample size or the small role that distributor salaries play in overall costs. Additionally, our ECF is highly sensitive to scale (strongest cost driver), explained by

observed large economies of scale in our country sample (Malawi, Zambia, Zimbabwe)[12], which is why the 'efficiency' effect is only observed at larger scale (national and not district level). Consequently, during the inefficient period 2, our projected costs are underestimating observed costs (predicting higher economies of scale than actually observed), and vice versa in period 3.

Our study has several limitations. First, although we use primary data and standardised cost data collection and analysis methods, we have an unbalanced sample of sites. While some countries contributed with a large sample of sites, others only included a few observations. We assume that because the same implementer (PSI) is working in the region with similar financial reporting system, this unbalance would not affect our modelling approach. Second, we use an observed scale-up period in Lesotho which evolved over time as programme matures, limiting our assessment of cost projections' accuracy. Third, we do not have country-specific panel data, therefore, time-dependent unobserved cost determinants are ignored for the econometric analysis. Fourth, while these estimates provide some likely key drivers of costs and their direction, we do expect our cost projections to be more accurate within settings where the main change relates to variations in scale. Fifth, our cost analysis is limited to average 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, limiting the applications of our findings by policymakers and programme planners.

Our empirical analysis adds to the discussion on the trade-off between simplicity versus accuracy in cost projection method. Further research should estimate health intervention costs at scale using the three different cost function methods (SCM, ECF and ACF), and compare cost predictions at various scales, ultimately to inform the choice of a cost projection method based on the intended use of the cost estimates.

Tables and figures

Appendix – Chapter 5

Appendix Text - Narrative description of the community-based HIVST distribution models across countries – PSI New Start programme in all countries (adapted from Mangenah et al., 2019; d'Elbée et al., 2020)

Appendix Figure S1. Correlation matrix

Appendix Table S1. Allocation factors from STAR expenditures to model, and model to districts

Appendix Table S2. Observed incremental HIVST costs for each of the three costing periods (period 1: December 2017 – April 2018, period 2: May 2018 – October 2018, period 3: November 2018 – April 2019) at national and district levels in Lesotho

Appendix Text - Narrative description of the community-based HIVST distribution models across countries – PSI New Start programme in all countries (adapted from Mangenah et al., 2019; d'Elbée et al., 2020)

Malawi

In Malawi, a randomised controlled trial (RCT) was conducted in rural areas of Blantyre, Machinga, Mwanza and Neno districts in Southern Malawi and comprised a total trial population of approximately 62,500 residents. Catchment populations of 22 public rural primary health clinics (PHCs) were randomized 1:1 to either HIVST or standard of care. In the 11 HIVST intervention communities, residents had access to community-based distribution agent's (CBDA) delivered HIVST (door-to-door) or the option to go to the CBDA's home over a continuous 1-year period (June 2016 to May 2017). CBDAs were paid an incentive of United States Dollar (US) $0.15 [100 Malawi Kwacha (MWK)] per kit distributed. This was integrated into their regular activities distributing contraceptives and other health products. In all sites, residents could access free HTS and ART if HIV-positive, through the PHCs.

Zambia

In Zambia, residents across 16 rural community sites had access to CBDA delivered HIVST or the option to go to the CBDA's home over a continuous 1-year period (July 2016 to June 2017), reaching a total target adult population of 416,294 across Ndola, Kapiri, Lusaka and Choma districts. In this hub and spoke model CBDAs were linked to specific clinics and worked in their surrounding catchment populations. CBDAs were initially paid a monthly allowance of US$78 [750 Zambia Kwacha (ZMK)] independent of performance; this was later supplemented by a US$0.21 (2 ZMK) incentive per used kit returned. Though only six sites were included in the RCT, costs were evaluated for all 16 sites.

Zimbabwe

In Zimbabwe, the RCT was conducted across eight rural district sites with a total trial population of approximately 224,116 residents. Forty-four geographically defined wards were randomized 1:1 to either linkage intervention (HIVST plus distributor incentive for linkage events) or control (HIVST with fixed distributor allowance) clusters. HIVST was delivered across sites through one-off 4-6 week campaigns, moving sequentially from one district to the other between August 2016, and May 2017. In each district, new CBDAs were recruited and trained for three days. CBDAs then each distributed a specific number of tests proportional to their confined catchment area. Each CBDA was equipped with a tablet to demonstrate how to conduct a self-test through a video and to collate data on each self-tester.

At one to two weeks following HIVST distribution, the routine PSI mobile outreach service offered HIV confirmatory testing for individuals with reactive HIVST test result and HIV treatment referral to public sector health facilities for individuals with confirmed HIV positive results, including other services such as family planning and screening for non-communicable diseases. All CBDAs received a fixed allowance

of USD$50, with an additional US$0.20 incentive for those in the linkage intervention arm per HIVST positive tester who linked for post-test services at PSI mobile outreach services. There was no compensation given to HIV negatives linking to post-test services. We estimated the cost of HIVST distribution in both intervention and –control sites. The cost of providing confirmatory testing at outreach services is not included in this study, for consistency across countries.

Lesotho

HIVST provision was done through PSI mobile outreaches or mobile team conducting door-to-door HTS and HIVST distribution in five priority districts of Lesotho (Maseru, Berea, Leribe, Mafeteng, and Mohale's Hoek).

In the case of outreach based activities, the client is offered the option to self-test or to receive provider delivered HTS at the mobile outreach. The HTS provider collects client data based on the HIVST register. Clients who opt for self-testing have the choice of testing on site or taking the kit away for testing at their convenience. Clients are encouraged to test at mobile outreach where possible to maximize review of test result with HTS provider.

Clients who choose to self-test on-site are given a self-test package and access to testing tent where they can self-test in private. If the result is positive, the client is offered confirmatory HIV Testing by the HTS provider at the site. If confirmatory results are positive, the client is referred to the preferred nearby health facility. All confirmed clients living with HIV are offered HIV self-test kit for secondary distribution to their sexual partner(s) or home visit for index HIV testing.

If HIV self-test is negative, the client is counselled on HIV prevention and offered preventive methods including VMMC for males, PrEP if eligible according to guidelines and consistent & correct condom use. The clients with a negative HIV status are also counselled on need for subsequent repeat testing according to risk profile outlined in the national guidelines. Clients who opt to do self-test off site also follow similar processes for clients who test off site at New Start.

South Africa

Between Jan 2018 and Oct 2019, 158,997 HIVST kits were distributed by Society for Family Health - SFH (PSI affiliate) in community-based models through fixed-point distribution in the districts of City of Tshwane, City of Johannesburg, and Dr Kenneth Kaunda.

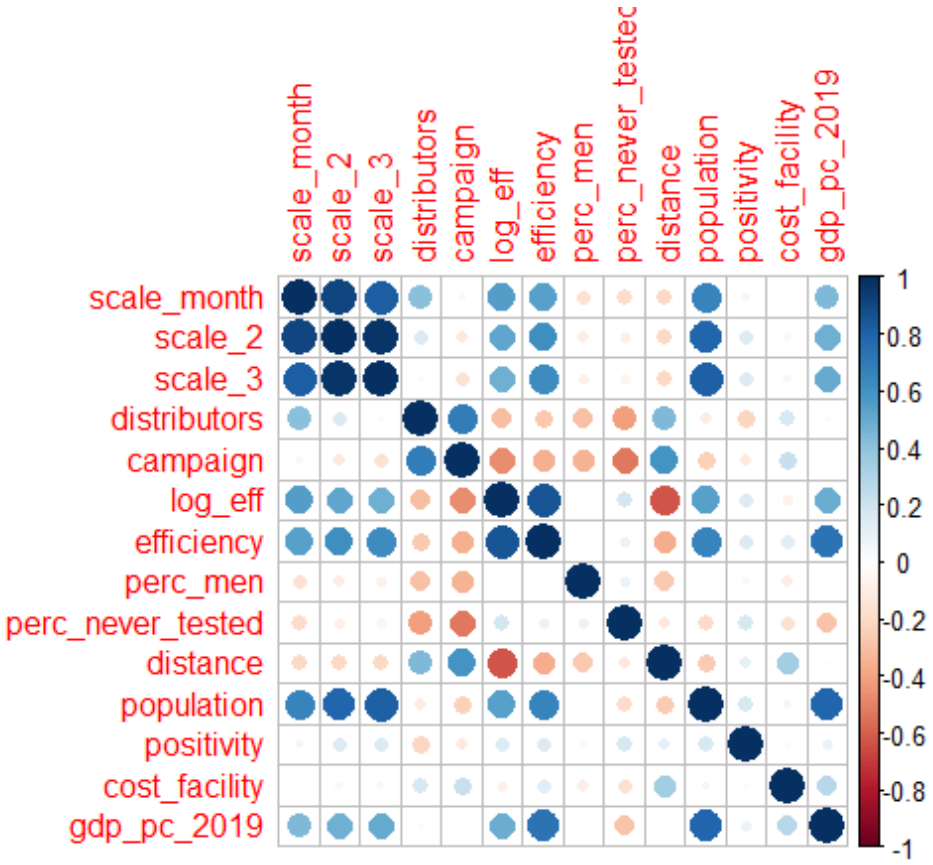
HIVST was integrated with existing community-based HTS activity platforms where HIVST was offered to individual clients after demonstration of how to use it as an HTS screening option. At the time of receiving the package clients were shown an instructional video on a tablet or smartphone. Basic information were collected from the client, including demographics and history of HIV testing; using REDCap™. Clients could choose to self-test themselves onsite or with assistance of the counsellor. Clients who chose to self-test onsite were given a HIVST kit with validated instructions and access to a private space. Clients were encouraged to disclose their HIVST results to the counsellor. Clients who self-tested negative were referred for prevention services and clients who had a reactive self-test were confirmed and referred for further managed health care.

Appendix Table S1. Allocation factors from STAR expenditures to model, and model to districts

Input types	STAR expenditure - Allocation of incremental HIVST costs	STAR expenditure - Allocation factors - Model to districts
Start-up		
S1: Training	Not applicable	% of participants to the training
S2: Sensitisation	Not applicable	Equally across districts
S3: Start-up other	Not applicable	% of HIVST kits distributed
Capital		
A: Building & storage	Full: Direct expenditures Incremental: Direct expenditure	% of direct expenditure
B: Equipment	Full: % of HTS versus HIVST activities Incremental: Direct expenditure	% of direct expenditure
Recurrent		
E: Personnel & Per diems – HQ (international and national)	Full: Direct expenditures Incremental: Direct expenditures	Equally across districts
E: Personnel & Per diems – HQ (district)		% of HIVST distributors
E: Personnel & Per diems – HQ (field)		% of HIVST distributors
F: Supplies (including HIVST kits)	Full: Direct expenditures Incremental: Direct expenditures	% of HIVST kits distributed

G: Vehicle operation, maintenance & transport	Full: Direct expenditures	% of mileage (HQ to district HQ) and # of cars per site
H: Building operation/maintenance	Full: Direct expenditures	% of direct expenditure
K: Other recurrent	Full: Direct expenditures Incremental: Direct expenditures	% of HIVST kits distributed

Appendix Figure S1. Correlation matrix



Appendix Table S2. Observed incremental HIVST costs for each of the three costing periods (period 1: December 2017 – April 2018, period 2: May 2018 – October 2018, period 3: November 2018 – April 2019) at national and district levels in Lesotho (1/3)

	5 districts						**Berea**					
	Dec 17 – Apr 18		May 18 - Oct 18		Nov 18 – Apr 19		Dec 17 - Apr 18		May 18 - Oct 18		Nov 18 – Apr 19	
# of implementation month	**5**		**6**		**6**		**5**		**6**		**6**	
Input types	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**
Start-up												
S1: Training	$574.57	0%	$574.57	0%	$574.57	0%	$68.31	0%	$68.31	0%	$68.31	0%
S2: Sensitisation	$188.75	0%	$188.75	0%	$188.75	0%	$37.75	0%	$37.75	0%	$37.75	0%
S3: Start-up other	$4,039.27	3%	$4,039.27	2%	$4,039.27	2%	$786.35	3%	$786.35	2%	$786.35	2%
Start-up - sub-total	***$4,802.59***	***3%***	***$4,802.59***	***3%***	***$4,802.59***	***2%***	***$892.41***	***3%***	***$892.41***	***3%***	***$892.41***	***2%***
Capital												
A: Building & storage	$64.75	0%	$1,374.58	1%	$1,367.43	1%	$11.51	0%	$244.25	1%	$242.98	1%
B1: Equipment - National	$0.00	0%	$32.43	0%	$0.00	0%	$0.00	0%	$5.76	0%	$0.00	0%
B2: Equipment - District	$315.96	0%	$588.52	0%	$2,373.13	1%	$56.15	0%	$104.58	0%	$421.69	1%
Capital - sub-total	***$380.71***	***0%***	***$1,995.53***	***1%***	***$3,740.57***	***2%***	***$67.65***	***0%***	***$354.59***	***1%***	***$664.68***	***1%***
Recurrent												
E1: Personnel & Per diems - HQ - International	$7,623.82	5%	$7,166.08	4%	$3,502.23	2%	$1,524.76	5%	$1,433.22	4%	$700.45	1%
E2: Personnel & Per diems - HQ - National	$13,966.18	9%	$20,438.02	12%	$20,469.76	9%	$2,793.24	9%	$4,087.60	12%	$4,093.95	9%
E3: Personnel & Per diems - HQ - District	$43,608.84	29%	$50,170.86	29%	$70,638.18	31%	$9,344.75	30%	$10,750.90	31%	$15,136.75	32%

E4: Personnel & Per diems - Field	$40,247.13	27%	$48,296.56	28%	$48,296.56	21%	$8,624.39	28%	$10,349.26	29%	$10,349.26	22%
F1: Supplies	$465.80	0%	$165.28	0%	$173.01	0%	$90.68	0%	$32.18	0%	$33.68	0%
F2: HIVST kits	$38,255.60	25%	$33,838.26	20%	$68,121.51	30%	$7,447.51	24%	$6,587.55	19%	$13,261.74	28%
G: Vehicle operation, maintenance & transport	$422.02	0%	$1,311.18	1%	$3,802.08	2%	$67.17	0%	$208.68	1%	$605.11	1%
H: Building operation/maintenance	$284.57	0%	$656.66	0%	$1,282.08	1%	$50.57	0%	$116.68	0%	$227.82	0%
K: Other recurrent costs	$664.84	0%	$2,080.78	1%	$4,250.60	2%	$129.43	0%	$405.08	1%	$827.50	2%
Recurrent - sub-total	***$145,538.81***	***97%***	***$164,123.68***	***96%***	***$220,536.00***	***96%***	***$30,072.49***	***97%***	***$33,971.16***	***96%***	***$45,236.26***	***97%***
Total HIVST costs	**$150,722.11**		**$170,921.79**		**$229,079.16**		**$31,032.55**		**$35,218.16**		**$46,793.34**	
HIVST kits distributed	**14,099**		**12,471**		**25,106**		**3,656**		**1,544**		**4,258**	
Average HIVST costs	**$10.69**		**$13.71**		**$9.12**		**$8.49**		**$22.81**		**$10.99**	

Appendix Table S2. Observed incremental HIVST costs for each of the three costing periods (period 1: December 2017 – April 2018, period 2: May 2018 – October 2018, period 3: November 2018 – April 2019) at national and district levels in Lesotho (2/3)

	Leribe						Mafeteng					
	Dec 17 - Apr 18		May 18 - Oct 18		Nov 18 - Apr 19		Dec 17 - Apr 18		May 18 - Oct 18		Nov 18 - Apr 19	
# of implementation month	**5**		**6**		**6**		**5**		**6**		**6**	
Input types	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**
Start-up												
S1: Training	$130.58	0%	$130.58	0%	$130.58	0%	$88.40	0%	$88.40	0%	$88.40	0%
S2: Sensitisation	$37.75	0%	$37.75	0%	$37.75	0%	$37.75	0%	$37.75	0%	$37.75	0%
S3: Start-up other	$987.18	3%	$987.18	2%	$987.18	2%	$639.74	3%	$639.74	3%	$639.74	2%
Start-up - sub-total	***$1,155.52***	***3%***	***$1,155.52***	***3%***	***$1,155.52***	***2%***	***$765.89***	***4%***	***$765.89***	***3%***	***$765.89***	***2%***
Capital												
A: Building & storage	$16.16	0%	$343.00	1%	$341.22	1%	$10.03	0%	$212.98	1%	$211.87	1%
B1: Equipment - National	$0.00	0%	$8.09	0%	$0.00	0%	$0.00	0%	$5.02	0%	$0.00	0%
B2: Equipment - District	$78.84	0%	$146.86	0%	$592.18	1%	$48.96	0%	$91.19	0%	$367.70	1%
Capital - sub-total	***$95.00***	***0%***	***$497.95***	***1%***	***$933.40***	***2%***	***$58.99***	***0%***	***$309.19***	***1%***	***$579.58***	***2%***
Recurrent												
E1: Personnel & Per diems - HQ - International	$1,524.76	4%	$1,433.22	4%	$700.45	1%	$1,524.76	7%	$1,433.22	6%	$700.45	2%
E2: Personnel & Per diems - HQ - National	$2,793.24	8%	$4,087.60	10%	$4,093.95	7%	$2,793.24	13%	$4,087.60	16%	$4,093.95	12%
E3: Personnel & Per diems - HQ - District	$10,760.62	30%	$12,379.82	30%	$17,430.20	31%	$5,380.31	25%	$6,189.91	25%	$8,715.10	26%

E4: Personnel & Per diems - Field	$9,931.11	28%	$11,917.33	29%	$11,917.33	21%	$4,965.56	23%	$5,958.67	24%	$5,958.67	18%
F1: Supplies	$113.84	0%	$40.39	0%	$42.28	0%	$73.77	0%	$26.18	0%	$27.40	0%
F2: HIVST kits	$9,349.54	26%	$8,269.96	20%	$16,648.67	30%	$6,058.93	28%	$5,359.31	22%	$10,789.10	32%
G: Vehicle operation, maintenance & transport	$129.41	0%	$402.08	1%	$1,165.92	2%	$82.81	0%	$257.29	1%	$746.08	2%
H: Building operation/maintenance	$71.01	0%	$163.86	0%	$319.92	1%	$44.09	0%	$101.75	0%	$198.65	1%
K: Other recurrent costs	$162.48	0%	$508.53	1%	$1,038.83	2%	$105.30	0%	$329.55	1%	$673.21	2%
Recurrent - sub-total	***$34,836.02***	***97%***	***$39,202.80***	***96%***	***$53,357.56***	***96%***	***$21,028.77***	***96%***	***$23,743.47***	***96%***	***$31,902.60***	***96%***
Total HIVST costs	**$36,086.54**		**$40,856.27**		**$55,446.47**		**$21,853.65**		**$24,818.55**		**$33,248.06**	
HIVST kits distributed	**3,270**		**3,064**		**7,958**		**1,411**		**2,866**		**3,625**	
Average HIVST costs	**$11.04**		**$13.33**		**$6.97**		**$15.49**		**$8.66**		**$9.17**	

Appendix Table S2. Observed incremental HIVST costs for each of the three costing periods (period 1: December 2017 – April 2018, period 2: May 2018 – October 2018, period 3: November 2018 – April 2019) at national and district levels in Lesotho (3/3)

	Maseru						**Mohale**					
	Dec 17 - Apr 18		May 18 - Oct 18		Nov 18 - Apr 19		Dec 17 - Apr 18		May 18 - Oct 18		Nov 18 - Apr 19	
# of implementation month	**5**		**6**		**6**		**5**		**6**		**6**	
Input types	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**	**Costs**	**%**
Start-up												
S1: Training	$245.10	1%	$245.10	0%	$245.10	0%	$42.19	0%	$42.19	0%	$42.19	0%
S2: Sensitisation	$37.75	0%	$37.75	0%	$37.75	0%	$37.75	0%	$37.75	0%	$37.75	0%
S3: Start-up other	$1,150.76	3%	$1,150.76	2%	$1,150.76	2%	$475.23	3%	$475.23	2%	$475.23	2%
Start-up - sub-total	***$1,433.60***	***3%***	***$1,433.60***	***3%***	***$1,433.60***	***2%***	***$555.17***	***3%***	***$555.17***	***3%***	***$555.17***	***2%***
Capital												
A: Building & storage	$20.41	0%	$433.30	1%	$431.05	1%	$6.64	0%	$141.03	1%	$140.30	1%
B1: Equipment - National	$0.00	0%	$10.22	0%	$0.00	0%	$0.00	0%	$3.33	0%	$0.00	0%
B2: Equipment - District	$99.60	0%	$185.52	0%	$748.08	1%	$32.42	0%	$60.38	0%	$243.49	1%
Capital - sub-total	***$120.01***	***0%***	***$629.04***	***1%***	***$1,179.13***	***2%***	***$39.06***	***0%***	***$204.74***	***1%***	***$383.79***	***1%***
Recurrent												
E1: Personnel & Per diems - HQ - International	$1,524.76	3%	$1,433.22	3%	$700.45	1%	$1,524.76	9%	$1,433.22	7%	$700.45	3%
E2: Personnel & Per diems - HQ - National	$2,793.24	6%	$4,087.60	8%	$4,093.95	6%	$2,793.24	16%	$4,087.60	20%	$4,093.95	15%
E3: Personnel & Per diems - HQ - District	$13,875.54	32%	$15,963.46	32%	$22,475.78	34%	$4,247.61	24%	$4,886.77	24%	$6,880.34	25%

E4: Personnel & Per diems - Field	$12,805.91	29%	$15,367.09	31%	$15,367.09	23%	$3,920.18	22%	$4,704.21	23%	$4,704.21	17%
F1: Supplies	$132.70	0%	$47.09	0%	$49.29	0%	$54.80	0%	$19.45	0%	$20.35	0%
F2: HIVST kits	$10,898.74	25%	$9,640.27	19%	$19,407.31	29%	$4,500.88	25%	$3,981.17	19%	$8,014.69	30%
G: Vehicle operation, maintenance & transport	$16.20	0%	$50.34	0%	$145.96	0%	$126.43	1%	$392.80	2%	$1,139.01	4%
H: Building operation/maintenance	$89.70	0%	$207.00	0%	$404.14	1%	$29.20	0%	$67.37	0%	$131.54	0%
K: Other recurrent costs	$189.41	0%	$592.80	1%	$1,210.96	2%	$78.22	0%	$244.81	1%	$500.10	2%
Recurrent - sub-total	***$42,326.20***	***96%***	***$47,388.85***	***96%***	***$63,854.94***	***96%***	***$17,275.32***	***97%***	***$19,817.40***	***96%***	***$26,184.65***	***97%***
Total HIVST costs	**$43,879.81**		**$49,451.50**		**$66,467.67**		**$17,869.55**		**$20,577.31**		**$27,123.61**	
HIVST kits distributed	**3,739**		**3,867**		**6,598**		**2,023**		**1,130**		**2,667**	
Average HIVST costs	**$11.74**		**$12.79**		**$10.07**		**$8.83**		**$18.21**		**$10.17**	

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Conclusions from Paper 3

The results presented in this paper offer important insights into key costs drivers of HIVST implementation such as programme design characteristics, including the scale of HIVST distribution, type of community-based intervention, characteristics of the population targeted with HIVST (men), distance from implementer's headquarter, and per capita GDP. The model simplification approach suggests that I could use a more parsimonious model to predict costs and adds to the discussion on the trade-off between simplicity versus accuracy in cost projection method. Finally, my comparative study with observed scale-up costs in Lesotho suggests that this cost function could potentially inform analyses of scale-up costs in other countries of the region.

The next paper presents the costs of implementing and scaling-up community-based HIVST programmes in western Africa with a different epidemiology of HIV, using accounting cost function methods.

Chapter 6 – Paper 4: Costs and scale-up costs of integrating HIV self-testing into civil society organisation-led programmes for key populations in Côte d'Ivoire, Senegal, and Mali

Overview of Paper 4

As presented in chapter 1, in response to the concentrated HIV epidemic on key populations in western Africa, HIVST is being added to HTS programme in Côte d'Ivoire, Senegal and Mali with the ATLAS research project.

This paper estimates the costs of implementing HIVST through civil society organisations-led models for KP in Côte d'Ivoire, Senegal, and Mali. A simple accounting cost function is also proposed to model the costs of scaling up this intervention based on national country targets.

This work was reviewed and approved by the ethics committees from the London School of Hygiene and Tropical Medicine, WHO Ethic Research Committee, Comité National d'Ethique des Sciences de la vie et de la Santé de Côte d'Ivoire, Comité National d'Ethique pour la Recherche en santé du Sénégal, Comité d'Ethique de la Faculté de Médecine de Pharmacie et d'Odonto-Stomatologie de l'Université des Sciences et des Techniques de Bamako in Mali (Appendix IV).

Appendix table A1 contains additional details on the methods taken regarding the selected allocation factors for the top-down costing analysis by input types. Appendix table A2 presents the full observed total and average intervention costs by CSO and key groups for all countries. Appendix table A3 reports total and average intervention costs in transition and at scale-up by key group and scale-up year for all countries. Finally, Appendix figures A1 and A2 reports the tornado diagrams of findings from the deterministic sensitivity analysis by country, and the estimated average cost at scale per HIVST kit distributed by key group and scale-up year from the scenario analysis, respectively.

Cost data analysis was conducted following the Global Health Cost Consortium guidelines. The accounting cost function used a simple model with the identification of fixed and variable costs at various intervention levels.

This paper is presented as accepted in the journal *Frontiers in Public Health* in May 2021.

This paper fulfils research objective 4 by applying accounting approaches to estimate costs at scale using the case of community-based HIVST national scale-up in Côte d'Ivoire, Senegal, and Mali.

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SECTION A – Student Details

Student ID Number	1805320	**Title**	Mr
First Name(s)	Marc		
Surname/Family Name	d'Elbée		
Thesis Title	Estimating healthcare costs at scale in low- and middle-income countries – the case of community-based HIV self-testing scale-up in southern and western Africa		
Primary Supervisor	Prof 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?	Frontiers in Public Health		
When was the work published?	May 2021		
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Have you retained the copyright for the work?*	No	Was the work subject to academic peer review?	Yes

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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 designed and supervised the study, co-conducted data collection with MT and KB, co-analysed the cost data and led the scale-up modelling work. I wrote the first draft and incorporated co-authors comments.

SECTION E

Student Signature	
Date	24/08/2021

Supervisor Signature	
Date	19/08/21

Costs and scale-up costs of integrating HIV self-testing into civil society organisation-led programmes for key populations in Côte d'Ivoire, Senegal, and Mali

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Keywords: Costs and cost analysis, Scale-up, HIV self-testing, Key populations, Men who have sex with men, Female sex workers, People who use drugs, Knowledge of HIV status, diagnosis, screening, West Africa, Côte d'Ivoire, Senegal, Mali

Running title: Costs of HIV self-testing provision to key populations in Côte d'Ivoire, Senegal, and Mali

Abstract (350/350 words)

Despite significant progress on the proportion of individuals who know their HIV status in 2020, Côte d'Ivoire (76%), Senegal (78%), and Mali (48%) remain far below, and key populations (KP) including female sex workers (FSW), men who have sex with men (MSM), and people who use drugs (PWUD) are the most vulnerable groups with a HIV prevalence at 5%-30%. HIV self-testing (HIVST), a process where a person collects his/her own specimen, performs a test, and interprets the result, was introduced in 2019 as a new testing modality through the ATLAS project coordinated by the international partner organisation Solthis (IPO).

We estimate the costs of implementing HIVST through twenty-three civil society organisations (CSO)-led models for KP in Côte d'Ivoire (N=7), Senegal (N=11), and Mali (N=5). We modelled costs for programme transition (2021) and early scale-up (2022-2023). Between July 2019 and September 2020, a total of 51,028, 14,472 and 34,353 HIVST kits were distributed in Côte d'Ivoire, Senegal, and Mali, respectively. Across countries, 64%-80% of HIVST kits were distributed to FSW, 20%-31% to MSM, and 5%-8% to PWUD.

Average costs per HIVST kit distributed were $15 for FSW (Côte d'Ivoire: $13, Senegal: $17, Mali: $16), $23 for MSM (Côte d'Ivoire: $15, Senegal: $27, Mali: $28), and $80 for PWUD (Côte d'Ivoire: $16, Senegal: $144), driven by personnel costs (47%-78% of total costs), and HIVST kits costs (2%-20%). Average costs at scale-up were $11 for FSW (Côte d'Ivoire: $9, Senegal: $13, Mali: $10), $16 for MSM (Côte d'Ivoire: $9, Senegal: $23, Mali: $17), and $32 for PWUD (Côte d'Ivoire: $14, Senegal: $50). Cost reductions were mainly explained by the spreading of IPO costs over higher HIVST distribution volumes and progressive IPO withdrawal at scale-up.

In all countries, CSO-led HIVST kit provision to KP showed relatively high costs during the study period related to the progressive integration of the programme to CSO activities and contextual challenges (COVID-19 pandemic, country safety concerns). In transition to scale-up and integration of the HIVST programme into CSO activities, this model shows large potential for substantial economies of scale. Further research will assess the overall cost-effectiveness of this model.

Introduction

In Western and Central Africa, 5 million people are living with HIV, representing a prevalence of 1.4% in 2019 [1]. As in most countries of the region, the epidemic is mixed in Côte d'Ivoire, Senegal, and Mali, with national prevalence in 2018 ranging between 0.4% and 2.6% and much higher prevalence at 5% to 30% in hard-to-reach key populations (KP) including female sex workers (FSW), men who have sex with men (MSM), and people who use drugs (PWUD) [1]. In 2019 in Western and Central Africa, HIV prevalence was 10% for FSW, 14% for MSM, and 5% for PWUD [1]. Because of the HIV prevention gap among these groups, KP contribute mostly to HIV transmission [2-4].

UNAIDS has set targets for 95% of people living with HIV to know their status, 95% of known HIV-positive individuals to be on antiretroviral therapy (ART), and 95% of those on ART to have their viral load suppressed by 2030 [5]. Despite significant progress on the proportion of individuals who know their HIV status (increase from 4% in 2000 to 67% in 2020), Western Africa remains far below the first 90 UNAIDS target, with disparities observed between Côte d'Ivoire (76%), Senegal (78%), and Mali (48%) in 2020 [6].

Conventional facility-based HIV testing services (HTS) does not adequately reach those KP due to stigma, discrimination and health services not responding to needs specific to each group. Local civil society organisations (CSO) providing mostly community-based HIV testing services using peer educators have proven successful in reaching the core members of these populations, linking, and retaining them into care [7, 8].

HIV self-testing (HIVST) is defined as a process where a person collects his/her own specimen (oral fluid or blood), performs an HIV test and interprets the result, often in private[9]. Following promising demonstration projects in Eastern and Southern Africa [10-15], HIVST was introduced in 2019 as a new testing modality in West Africa with the ATLAS project (*Auto Test VIH, Libre d'Accéder à la connaissance de son Statut*) [16]. The project is led by the French non-governmental organisation Solthis - namely international partner organisation (IPO) in this study - in consortium with the Institut de Recherche pour le Développement, Ministries of Health, and

local implementing CSO in Côte d'Ivoire, Senegal, and Mali. HIVST has the potential to overcome some of the existing structural barriers to testing and to increase diagnosis coverage among KP (primary distribution) and their peers, sexual partners and clients (secondary distribution) not reached by conventional HTS [17, 18].

OraQuick® HIV self-tests have been subsidised by the Bill and Melinda Gates Foundation, then proposed by Orasure Inc. at US$2 per kit in 50 low- and middle-income countries for public sector distribution [19]. However, HIVST is still around twice the price of standard HIV rapid diagnostic tests currently used for HIV testing in Africa. In southern Africa, HIVST increased diagnosis coverage and showed potential value for money for key populations as a complement to current testing approaches [9, 10, 20].

In this study, we estimate the costs of implementing HIVST through CSO for KP in Côte d'Ivoire, Senegal, and Mali. We also assess the costs of scaling up this model to guide project national scale-up, propose costed operational plans, and inform on the sustainability of this distribution model.

Material and methods

2.1. Intervention setting

HIVST kits were distributed through twenty-three CSO across Côte d'Ivoire (N=7), Senegal (N=11), and Mali (N=5) from July 2019 to September 2020. Implementing partners' key characteristics are presented in Table 1. The deployment strategy identified three sequential intervention phases: 1) *development phase (June 2018 – March 2019)*: all activities that identify sustainable distribution models for each country, to fully integrate HIVST into existing programmes; 2) *start-up phase (April 2019 – July 2019 (Senegal/Mali), - October 2019 (Côte d'Ivoire))*: adaptation of self-testing information materials to the local context, development of training manuals, training of HIVST providers, sensitisation of key actors and building partnerships with local partners (regardless of when the costs were incurred), and other start-up costs; and 3) *early implementation phase (up to September 2020)*: demand creation, HIVST kits distribution, and project supervision (Figure 1). In each

country, all CSO did not start HIVST kits distribution at the same time, and this was accounted for in the cost analysis by adjusting the length of the implementation period by distribution channel. We costed community-based activities used by CSO for reaching KP and excluded facility-based costs corresponding to HIVST kits provision through index testing and sexual health consultations, accounting for a small proportion of CSO activities and outside the scope of this analysis. CSO1 (Senegal) is not technically a CSO but a public facility included in the analysis because they provide community-based services to PWUD.

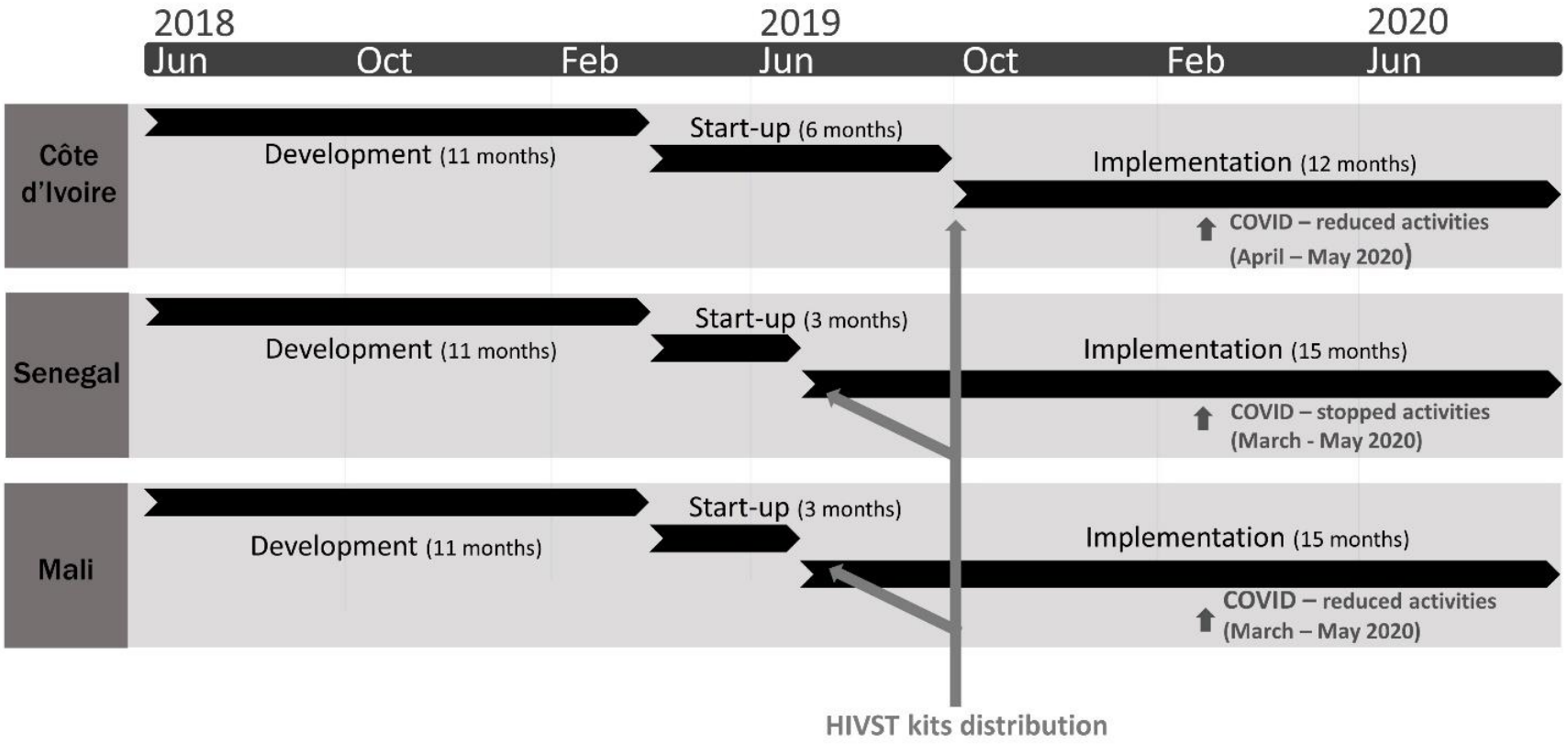

Figure 1. Description of the ATLAS project's three HIV self-testing (HIVST) deployment phases in Côte d'Ivoire, Senegal, and Mali over 2018-2020

Table 1. Overview of the ATLAS project's implementing partners in Côte d'Ivoire, Senegal, and Mali

Country	Administrative region	Number of districts covered	Civil society organisation	Distribution channel	Number of trained HIVST providers	HIVST kits distribution target
Côte d'Ivoire	Gbôklé, Nawa, San-Pédro	2	CSO1	FSW	13	9,605
				MSM	4	4,172
	Abidjan 1	2	CSO2	FSW	29	9,175
	Abidjan 2	2	CSO3	FSW	20	15,944
				MSM	6	6,812
				PWUD	9	4,230
	Mé, Abidjan 1	2	CSO4	MSM	7	2,177
	Sud Comoé	1	CSO5	FSW	6	2,261
				MSM	5	1,370
	Mé, Sud Comoé	2	CSO6	FSW	13	5,181
				MSM	8	2,511
	Gbôklé, Nawa, San-Pédro	2	CSO7	FSW	8	7,044
				MSM	3	4,406
Sub-total					131	74,888
Senegal	Dakar, Thiès	11	CSO1	PWUD	22	1,862

	Dakar, Thiès, Ziguinchor	18	CSO-Associations	FSW	25	1,540
				MSM	33	2,933
	Dakar, Thiès	9	CSO-mobile clinics	FSW	4	810
	Dakar, Thiès, Ziguinchor	17	CSO-independent distributors	FSW	16	4,320
				MSM	12	2,400
				PWUD	4	160
Sub-total					116	14,025
Mali	Bamako, Sikasso, Koulikoro, Kayes, Segou	7	CSO1	FSW	15	11,250
				MSM	14	4,813
	Bamako, Segou, Sikasso, Kayes, Koulikoro	11	CSO2	FSW	78	22,400
				MSM	20	3,360
	Bamako, Segou, Sikasso	5	CSO3	FSW	31	20,910
	Kayes, Koulikoro	12	CSO4	MSM	19	12,321
	Sikasso	2	CSO5	FSW	7	4,623
				MSM	7	2,139
Sub-total					191	81,816
TOTAL					438	170,729

HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

2.2. Cost data collection and analysis

The costing teams followed the Global Health Cost Consortium guidelines and collaboratively analysed data, ensuring consistency of methods across countries [21-23]. We used the provider's perspective. We conducted an incremental cost analysis, where only additional resources needed to introduce HIVST to existing service provision were considered. These incremental costs were collated from the IPO and implementing partners' financial expenditures and each line item was categorised by input type and distribution model (top-down costing approach) [24]. Inputs were categorised into start-up, capital, and recurrent costs. Inputs were allocated to distribution sites following predefined allocation factors, based on project monitoring and evaluation data, including the percentage of HIVST distributors in each site, estimated cohort size of HIV-positive patients followed by the CSO, percentage of kits distributed, and percentage of direct expenditures, which is a weighted average of the preceding allocation factors. Further details on the methods and allocation factors can be found in Appendix Table 1, and elsewhere [25-27]. To estimate economic costs, the expenditure analysis was complemented by a valuation, with market prices or financial data provided by the implementers, of all other resources used in the delivery model (donated services such as personnel time at the CSO headquarters and in the field, not paid by the ATLAS project). Finally, a time-motion study was conducted to observe staff providing HIVST alongside other services and allocate personnel costs based on the time spent on each activity [28, 29]. The HIVST kit cost was US$2.68 for Côte d'Ivoire and US$3.08 for Senegal and Mali. Start-up, training, and all other capital costs were annualised using a discount rate of 3%. All costs were estimated in 2020 USD dollars using annual exchange rates. Total costs and average cost per kit distributed were estimated at the country level, at the CSO level and per channel.

2.3. Sensitivity analysis of costs

We conducted a series of one-way sensitivity analyses, using tornado diagrams, to assess the impact of key cost assumptions on the average cost per HIVST kit distributed. We varied the discount rate used to annualised costs to 0% and 16% (base case is 3%) to capture the impact of not discounting or using a higher local central

bank discount rate such as in Mali [30]. We evaluated the impact of applying alternative allocation factors that is swapping percentage trained distributors to percentage cohort size for IPO expenditures. We varied annualisation (economic life years) time frames: training & sensitisation were varied between 1 and 3 years (base: 2 years), project development life between 5 and 15 years (base: 10 years), and start-up life (training, sensitisation and other costs incurred during this phase) between 2.5 and 7.5 years (base: 5 years) to assess the impact of the assumed project life years on costs. For Senegal only due to data availability, we swapped the allocation of field-based personnel costs from using percentage HIVST time observed during the time-motion study to using percentage HIVST time reported by study participants. Finally, episodes of violence against MSM occurred during the study period, and CSO had to suspend their activities in Senegal and Mali. The COVID-19 pandemic also led to reduced/suspended activities (Figure 1), therefore we also estimated the average cost per target HIVST distribution volumes.

2.4. Scale-up cost model and scenario analysis

We also modelled costs at scale-up when HIVST kit distribution volumes would increase following each country's National Strategic Plan for HIV testing to predict the variation of average cost between the implementation and scale-up phases. The production function, developed by Cobb and Douglas, describes the relationship between outputs and factors of productions (inputs)[31]. Accounting cost functions follow step-by-step the intervention production process as close as possible to reality [22, 32]. They identify fixed and variable costs, typically assumed to vary linearly with the scale such as that used in input-output analysis as originally developed by Leontief [33, 34]. It should be noted that with the exception of training costs (variable cost) and sensitisation costs (fixed cost) considered in the scale-up model, all other costs incurred during the development and start-up phases are considered one-off costs incurred at the start of the programme and therefore, are excluded from the costs of scaling-up. The model algebra is presented here, the detailed model structure listing fixed and variable costs is presented in Table 2.

$$\mathbf{C} = \sum_{\mathbf{j}} (\mathbf{FC_j} + \mathbf{VC_j})$$

$$\text{with } \mathbf{VC_j} = \mathbf{UC_j} \cdot \mathbf{S_j}$$

Where:

C: Total cost

j: inputs differentiating intervention levels – international, national, district, and community

FC_j: Fixed cost (independent of S_j) for fixed input *j* (e.g. building, personnel at central level)

VC_j: Variable cost for input *j* (e.g. field personnel, HIVST kits)

UC_j: Unit cost per variable inputs *j* for one output (the type of unit depends of each category): new staff to train, HIVST kits to distribute, etc.

S_j: Scale variable for input *j* to reach desired number of outputs: number of new providers required for scale-up, total number of providers at scale-up, number of HIVST kits to distribute

Table 2. Model structure – Accounting cost function

Intervention level	Type of costs	Cost inputs	Scale variable*
International	Fixed costs	S2. Sensitisation – Coordination R1. Personnel & Per diems – Headquarters IPO coordination	
	Variable costs	None	
National	Fixed costs	C1. Buildings and storage C2. Equipment C3. Vehicles	

		C4. Other capital costs S2. Sensitisation – IPO country R2. Personnel & Per diems – Headquarters IPO country	
	Variable costs	S1. Trainings (start-up phase only)	Number of <u>new</u> providers to train
		R6. Vehicle operation and maintenance/transportation	Total number of HIVST providers
		R7. Building operation and maintenance	Total number of HIVST providers
		R8. Other recurrent costs	Total number of HIVST providers
Sub-national - Implementing partners	Fixed costs	None	
	Variable costs	R3. Personnel & Per diems – Headquarters Implementing partner	Total number of HIVST providers
Local - HIVST distribution areas	Fixed costs	None	
	Variable costs	R4. Personnel & Per diems – Field (HIVST distributors)	Total number of HIVST providers
		R5. HIV self-testing kits (implementation phase only)	Number of HIVST kits to distribute

*The selection of scale variables was done in a way to account for the fact that the project is in early implementation phase (HIVST kits distribution targets not always reached by CSO in early phase) and the COVID-19 pandemic impact (reduced field activities), meaning CSO were not working at full capacity during the observed costing period. Therefore, the model uses predominantly the number of providers as scale up variable rather than the number of HIVST kits distributed during our observed period to limit the risks of bias.

The number of kits to distribute is used to estimate projected costs based on HIVST volume distribution targets for each year 2021-2023.

IPO: International Partner Organisation

In anticipation of planned project scale-up by respective country ministries of health and post-ATLAS transition, we conducted a series of scenario analyses varying some of the key model parameters by country and by scale-up year, considering 2021 as a transition year, 2022 partial scale-up, and 2023 as full scale-up. Four potential scenarios are presented in Table 3. Logistical and contextual challenges with CSO-led delivery channels to criminalised KP, and current donors' commitments for funding, were noted to cause challenges leading to uncertainty related to the timely attainment of targets. We therefore anticipate that those programmatic objectives might not be reached. Accounting for this would provide more nuanced scale economies, and we applied different percentages for reaching targets – higher percentages in Mali, where more funding is already secured (*scenario 1*). IPO's goal to progressively disengage to promote local project ownership overtime was considered. Note that we still account for 15% of international costs in 2023 because we assume another coordination component will still exist (and incur costs) within the local health system at central level. Year 2023 would then represent what it costs for the country to support HIVST post-ATLAS (*scenario 2*). We also assessed the impact of optimising delivery channels by simplifying the model of partners/sub-partners and decreased CSO headquarter costs by 20%, which is reasonable to assume when evaluating interventions transitioning from pilot (ATLAS) to routine implementation phase (*scenario 3*) [35]. Finally, we conducted country-specific simulations to account for varying HIVST kit cost for each year considering factors such as bulk buying, maritime provision instead of airways (except Mali), and integrating HIVST delivery chain with other health supplies (*scenario 4*). Finally, we combined all scenarios above to assess the global impact on average costs at scale per KP and scale-up year.

This study was approved by the London School of Hygiene and Tropical Medicine (n° 17141/RR/13198, 31st March 2019) WHO Ethic Research Committee (n°ERC0003181, 7th August 2019), and by three national ethic

committees: Comité National d'Ethique des Sciences de la vie et de la Santé de Côte d'Ivoire (n°049-19/MSHP/CNESVS-kp, 28th May 2019), Comité National d'Ethique pour la Recherche en santé du Sénégal (n°SEN19/32, 26th July 2019), and Comité d'Ethique de la Faculté de Médecine de Pharmacie et d'Odonto-Stomatologie de l'Université des Sciences et des Techniques de Bamako au Mali (n°2019/88/CE/FMPOS, 14th August 2019).

Table 3. Selected parameters for the scenario analysis of costs at scale-up in Côte d'Ivoire, Senegal, and Mali (baseline: all parameters at 100%)

	Scenario 1			Scenario 2			Scenario 3			Scenario 4		
	Reaching HIVST distribution volume targets (% of target achieved)			Progressive disengagement of IPO (% reduction of IPO costs)			Implementing partners headquarter costs (% reduction of IP costs)			HIVST kit cost based on volumes (% reduction of original kit cost)		
	2021	2022	2023	2021	2022	2023	2021	2022	2023	2021	2022	2023
Côte d'Ivoire	-25%	-25%	-30%	As in baseline	-50%	-85%	-20%	-20%	-20%	-9%	-9%	-9%
Senegal	-25%	-25%	-30%	As in baseline	-50%	-85%	-20%	-20%	-20%	-17%	-17%	-17%
Mali	-20%	-20%	-25%	As in baseline	-50%	-85%	-20%	-20%	-20%	-13%	-13%	-13%

IPO: International Partner Organisation, IP: Implementing Partner

Results

3.1. Programme outcomes in Côte d'Ivoire, Senegal, and Mali

During the costing period, 51,028, 14,472 and 34,353 HIVST kits were distributed in Côte d'Ivoire, Senegal, and Mali through a total of 161, 48, and 191 peer educators, respectively. These volumes corresponded to 68% (Côte d'Ivoire), 103% (Senegal), and 42% (Mali) of planned targets. The average number of HIVST kits distributed was 7,290 (range: 1,295 to 16,513) across 7 CSO in Côte d'Ivoire, 3,618 (range: 422 to 7,193) across the main four models composed of 11 CSO in Senegal (CSO-Associations, CSO-Mobile clinics, CSO-independent distributors, and the public partner working with PWUD only), and 6,871 (range: 2,688 to 17,891) across 5 CSO in Mali. In Côte d'Ivoire, 66% of kits (n=33,647) were distributed to FSW, 26% (n=13,250) to MSM, and 8% (n=4,131) to PWUD. In Senegal, 64% of kits (n=9,338) were distributed to FSW, 31% (n=4,472) to MSM, and 5% (n=662) to PWUD. In Mali, 80% of kits (n=27,528) were distributed to FSW, and 20% (n=6,825) to MSM.

3.2. Project total costs and average costs per kit distributed, distribution target

In Côte d'Ivoire, the total distribution costs were calculated as $440,648, $201,910, and $65,691 for FSW, MSM and PWUD respectively (Table 4). Start-up phase accounted for 25%, 23%, and 26% of total costs for FSW, MSM, and PWUD respectively, while the development phase only accounted for 2% across key groups. Personnel costs at various intervention levels accounted for a substantial portion of total costs, at 47% for FSW, and 50% for MSM and PWUD, followed by HIVST kits costs at 20%, 18%, and 17% (Figure 2). Average cost per HIVST kit distributed were $13, $15, and $16 for FSW, MSM, and PWUD.

For Senegal, total intervention costs were $159,393, $120,374, and $95,091 for FSW, MSM, and PWUD (Table 4). Start-up phase costs were 17% for FSW and MSM, and 5% for PWUD, and at a mean of 5% for development phase costs across groups. Personnel costs were 51%, 57%, and 78% of total costs while HIVST kits costs were 18%, 11%, and 2% for FSW, MSM, and PWUD, respectively (Figure 2). Average costs per kit were $17, $27, and $144 for FSW, MSM, and PWUD.

Finally, in Mali, total costs were $438,553 and $188,159 for FSW, and MSM (Table 4). Start-up phase and development phase costs accounted on average for 13% and 3% of total costs across groups. Personnel costs were 53%, and 61% of total costs, while HIVST kits costs were at 19% and 11% for FSW and MSM, respectively (Figure 2). Average cost per kit were $16 and $28 for FSW and MSM.

While the share of start-up costs as percentage of total costs was comparable between target groups in Côte d'Ivoire and in Mali, it differed in Senegal because the CSO delivering to PWUD were small organisations, hence being allocated a low share of start-up costs. Because the start-up period was longer in Côte d'Ivoire (6 months) compared to the one in Senegal and Mali (3 months), start-up costs as percentage of total costs were higher in Côte d'Ivoire.

Wide variations of average costs per HIVST kit distributed were found between CSO (Appendix Tables 2.a.b.c). In Côte d'Ivoire, average cost per kit distributed ranged $9-$27 for FSW, $10-$29 for MSM, and only one CSO worked with PWUD. In Senegal, average costs were $13-$32 for FSW, $25-$28 for MSM, and $121-$156 for PWUD. In Mali, average cost per kit distributed ranged $15-$27 for FSW, and $17-$59 for MSM. In Senegal, CSO-Associations had lower average costs than CSO-Independent distributors (mean: $19 versus $23), but overall distributed less HIVST kits (5,834 kits versus 6,953 kits) to FSW and MSM.

The major driver of these cost differences both between and within key groups for all countries was the number of kits distributed per dispensing agent, except in Côte d'Ivoire where the average number of kits distributed per dispensing agent was comparable between groups. Another important driver of cost variation between and within groups for all countries was the total number of HIVST kits distributed by a CSO. An increase of any of these two drivers would lead to a reduction in average costs.

Table 4. Observed total and average intervention costs by intervention phase and key group – Côte d'Ivoire, Senegal, and Mali

	Côte d'Ivoire - Global estimates					
	FSW		MSM		PWUD	
	$	%	$	%	$	%
INTERVENTION PHASES						
Development	7,612	*2%*	3,518	*2%*	1,118	*2%*
Start-up (start-up and other costs)	120,874	*27%*	52,238	*26%*	18,687	*28%*
Implementation	312,162	*71%*	146,153	*72%*	45,887	*70%*
TOTAL ANNUAL COSTS	440,648		201,910		65,691	
HIVST kits distributed	33,647		13,250		4,131	
Average cost per HIVST kit distributed	13		15		16	
	Senegal - Global estimates					
	FSW		MSM		PWUD	
	$	%	$	%	$	%
INTERVENTION PHASES						
Development	8,262	*5%*	5,684	*5%*	4,754	*5%*
Start-up (start-up and other costs)	35,628	*22%*	25,579	*21%*	9,648	*10%*
Implementation	115,502	*72%*	89,111	*74%*	80,689	*85%*
TOTAL ANNUAL COSTS	159,393		120,374		95,091	
HIVST kits distributed	9,338		4,472		662	
Average cost per HIVST kit distributed	17		27		144	
	Mali - Global estimates					

	FSW		MSM	
	$	%	$	%
INTERVENTION PHASES				
Development	11,544	*3%*	5,434	*3%*
Start-up (start-up and other costs)	74,345	*17%*	29,633	*16%*
Implementation	352,664	*80%*	153,093	*81%*
TOTAL ANNUAL COSTS	438,553		188,159	
HIVST kits distributed	27,528		6,825	
Average cost per HIVST kit distributed	16		28	

HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

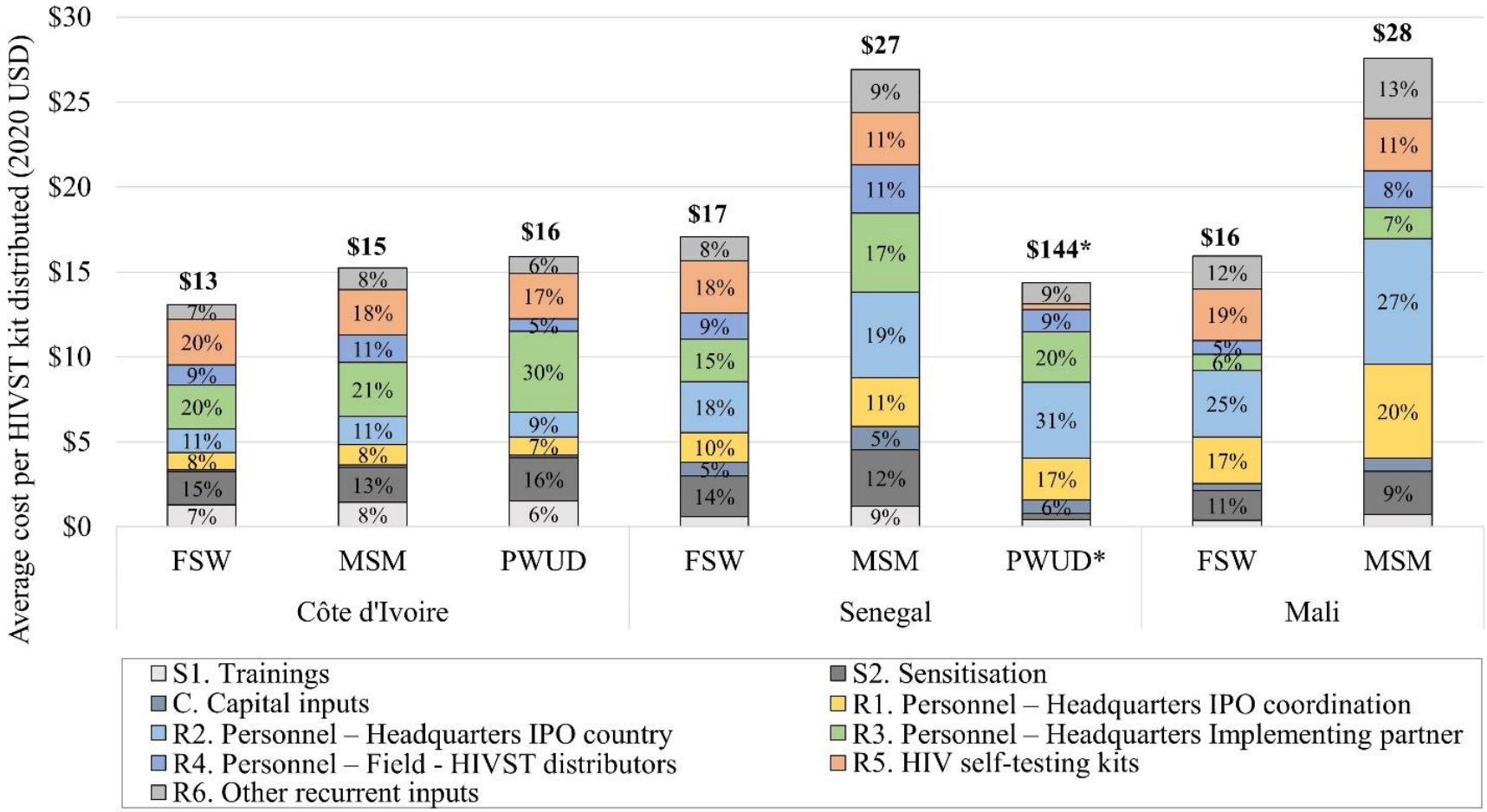

Figure 2. Average intervention costs by inputs for each key group – Côte d'Ivoire, Senegal, and Mali

*For PWUD in Senegal, costs are presented on this figure divided by ten for scale purpose

3.3. Sensitivity analysis of costs results

Appendix Figure 1. presents results from the univariate sensitivity analyses by key groups for Côte d'Ivoire (1.a.), Senegal (1.b.), and Mali (1.c.). Our unit costs per HIVST kit distributed remained robust when key cost parameters were varied. In Côte d'Ivoire, varying life of start-up sensitisation and training between one and three years had the strongest effect on costs ranging between $12-$17, $14-$19, and $14-$20 for FSW, MSM and PWUD, respectively. The life year of development and start-up phases, allocation factor swapping (for FSW and MSM) had a moderate effect with less than a dollar variation. The variation of discount rate almost had no effect on costs. In Senegal, the discount rate applied had the strongest effect with average costs varying between $17-$19, $26-$30, and $141-$163 for FSW, MSM and PWUD respectively due to higher proportion of capital costs compared to Côte d'Ivoire. Allocation factor swapping from trained distributors had an effect on average costs for PWUD (reduction to $127), while swapping from time-motion study results had no effect. In Mali, swapping of allocation factors has the strongest effect, but overall, average costs only varied by less than two dollars suggesting our average costs were quite robust.

Reaching HIVST distribution targets greatly reduced costs (not presented in Appendix Figure 1). Average cost per HIVST kit distributed were $9, $9, and $16 for FSW, MSM, and PWUD, assuming distribution targets were reached in Côte d'Ivoire. In Senegal, average costs per kit were $24, $23, and $47 for FSW, MSM, and PWUD assuming distribution targets were reached. Finally, in Mali, average cost per kit would be much lower if targets were reached, at $7 and $8 for FSW and MSM, respectively.

3.4. Cost at scale-up following National Strategic Plans

Costs at scale-up for each year of the National Strategic Plans are presented by country, year, and key groups in Figure 3, with details in Appendix Tables 3.a.b.c.

Over the period 2021-2023, costs per kit distributed are on average at $9 (FSW and MSM), and $14 (PWUD) in Côte d'Ivoire; $13 (FSW), $23 (MSM) and $50 (PWUD) in Senegal; and $10 (FSW), and $17 (MSM) in Mali. We note the significant reduction of average costs at scale-up versus observed average costs for FSW and MSM in

Côte d'Ivoire, PWUD in Senegal, and all groups in Mali. Across countries, years, and key groups, the trend is an overall increase in total costs as expected. Although we estimate variation between countries and key groups, in transition and scale-up, overall cost drivers are fixed costs such as sensitisation activities, and headquarter-based personnel costs at national and sub-national level, and variable costs such as training and HIVST kits costs (varying with HIVST distribution targets). In Senegal, we estimate higher personnel costs at CSO level (headquarter- and field-based).

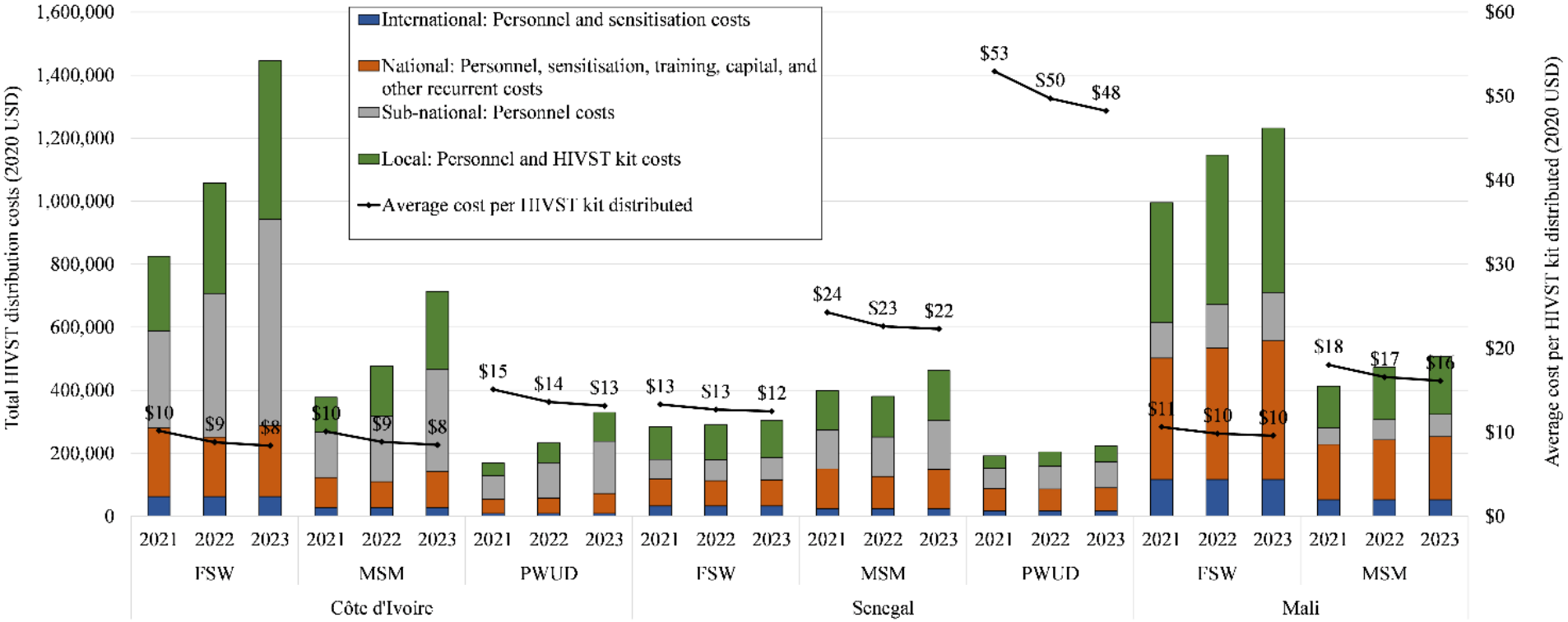

Figure 3. Total and average intervention costs in transition (2021) and at scale-up (2022-2023) by country and key population

3.5. Scenario analysis of scale-up costs

As the scale-up model does not account for other contextual factors related to the transition post-ATLAS, analyses of plausible scale-up scenario are presented in Appendix Figures 2.a.b.c..

For all countries and key groups, we find that HIVST volumes are the major determinants of costs per HIVST kit distributed (economies of scale), followed by IPO withdrawal starting in 2022, reduction of implementers' central costs, and the estimated reduction of HIVST kit price. Accounting for all these factors together would increase estimated scale-up average costs between $9 (FSW – 2023) and $18 (PWUD – 2021) in Côte d'Ivoire, from $12 (FSW – 2023) to $65 (PWUD – 2021) in Senegal, and from $9 (FSW – 2023) to $21 (MSM – 2021) in Mali.

Discussion

In this study, we estimated the cost of implementing HIVST for KP and their partners in three West African countries. Across countries, we found that costs ranged between $13-$17 for FSW, $15-$28 for MSM and $16-$144 for PWUD. Note that PWUD channels distribute small quantities of HIVST kits, and average costs are therefore highly sensitive to scale of operation between CSO. Major cost contributors were personnel costs at central and regional intervention levels. Start-up costs across countries, corresponding to sensitisation of CSO and other partners, and training costs contributed to 10%-28% of total costs. This is due to the complexity and lengthy process of building partnerships with numerous local CSO and involving key stakeholders in an intervention fully integrated with existing health care delivery services for KP. Costs per kit distributed were lowest in Côte d'Ivoire and highest in Senegal. Across countries, average costs per HIVST were lowest for FSW, followed by MSM, then PWUD. These differences could be explained by HIVST volumes by channels with a total of 70,513 kits distributed to FSW, 24,547 kits to MSM, and 4,793 kits to PWUD during our costing period. However, it is likely that other factors played a role. For instance, in Senegal and Mali, several episodes of violence against MSM were reported at different time points (unrelated to the programme), and CSO had to

suspend their field activities for security reasons, contributing to an unstable, and therefore costly, delivery system of kits for this group. In Mali, there were safety concerns due to the country's *Coup d'Etat* in August 2020, and ongoing armed conflict with intermittent suspension of fieldwork activities. Indeed, estimated average costs per kit would be as low as $7 (FSW) and $8 (MSM) assuming targets were reached in Mali. Finally, the COVID-19 pandemic also led to reduced (Côte d'Ivoire and Mali) or suspended (Senegal) activities during two to three months, leading to high observed costs, although self-testing was shown to be a timely alternative to provider-delivered HIV testing during periods of lockdown and reduced social interactions [36].

Important average costs variations between CSO were observed. High number of kits distributed per dispensing agent led to a reduction in average costs and depended on the type of HIVST distribution activity with high distribution in bars and brothels, and low distribution in small gatherings at KP's house. CSO-specific policy with monthly maximum targets of kits distribution per agent could potentially lead to higher average costs. Small number of HIVST kits distributed per CSO was also driving average costs high and was explained by the type of population reached (e.g. CSO working with PWUD only deliver small HIVST volumes), and the CSO size. To a lesser extent in Mali, numerous HIVST delivery models per CSO (some not presented here such as Index and STI services) could lead to higher spreading of central costs across models, and therefore, a reduction of average costs.

Our costs were comparable to other community-based HIVST costing studies, many of them arising from the STAR (*HIV Self-Testing AfRica*) project [37-39]. Across six southern Africa countries (Malawi, Zambia, Zimbabwe, South Africa, Lesotho, eSwatini), costs per kit distributed ranged from $8 for door-to-door distribution in Malawi to $18 for mobile integration (more similar to the ATLAS programme) in South Africa [25, 26, 40, 41]. Although HIVST volumes were generally higher as targeting the general population and benefiting from economies of scale, many of these models were highly vertical incurring significant above service level costs. However, cost per kit distributed to South African FSW and MSM were lower than our observed costs at $4 and $6 respectively for 19,901 and 12,218 kits distributed. This is partly explained by the high number of HIVST delivery models in South Africa and sharing of central costs across models [40]. Additionally, our costs were

comparable to one study in Côte d'Ivoire reporting HTS unit costs from the Ivorian *Programme National de Lutte contre le Sida (PNLS)* for FSW and MSM at $16 and $21 respectively [42]. However, one should consider the reduced costs to the kit user (in terms of transportation cost or opportunity cost for example), and therefore to society, when comparing community-based HIVST distribution and facility-based provider-delivered HTS costs [43, 44].

The scale-up model suggests that these early-stage CSO-led community-based HIVST distribution programmes can exhibit economies of scale. When comparing year 2023 with observed costs, we estimated variable scale economies between groups and countries, with about 56% (FSW), 63% (MSM), and 10% (PWUD) of average cost reduction in Côte d'Ivoire, 19% (FSW), 12% (MSM) and 66% (PWUD) in Senegal, and 35% (FSW), 41% (MSM) in Mali. Beyond scale economies, other contextual factors were considered, such as accounting for progressive integration of the ATLAS project to existing CSO and withdrawal of the IPO. The scenario analysis suggests that, overall, even if target were not reached, costs at scale would decrease in Côte d'Ivoire (except PWUD) and Mali. However, results are more nuanced for Senegal with constant (FSW) or increasing average costs (MSM, PWUD) due to high fixed costs at sub-national level.

Our study has several limitations. First, our outcome metric "per HIVST kit distributed" does not fully capture the HIVST cascade. For example, there remain uncertainties related to the true percentage of kits use, the actual final users of the kit (e.g. HIVST distribution through a FSW model could also be used by their clients), and among those with a reactive HIVST the linkage rate to confirmatory testing. However, there is now large evidence on high acceptability of HIVST kits in the general population and among KP [11, 13, 14, 17, 18, 45-48]. Moreover, the ATLAS programme is currently trying to evaluate the impact of HIVST on HIV case finding and ART initiation, these data will then feed in a modelling analysis to estimate cost-effectiveness. Second, total and average costs are estimated across a diverse range of CSO for each country leading to inevitable cost variation by distribution channel. Third, the COVID-19 pandemic led to reduced/suspended activities during a trimester for some CSO, but also encouraged the use of HIVST by other actors as a timely alternative to HTS in response to lockdown and social distancing, therefore, its impact on costs and project outcomes is difficult to

assess [36]. Fourth, scale-up costs and scenario analysis were conducted in collaboration with the implementer to ensure model assumptions were close to reality, but these remain arbitrary and should be interpreted with caution.

In three countries of West Africa, HIVST kit provision to KP through CSO had higher initial costs during the study period, related to the progressive integration of HIVST to CSO activities, and a challenging implementing environment (criminalised KP, pandemic COVID-19, security concerns). The analysis of costs at scale suggests that, in transition to scale-up and further integration of the ATLAS project, this model shows large potential for substantial economies of scale as programmes scale-up and mature.

Recent modelling studies in Cameroon, Senegal, Côte d'Ivoire, and South Africa show that key populations and their sexual partners, particularly FSW and their clients, can play an important role in HIV transmission in both low and high HIV prevalence settings due to prevention gaps [3, 4, 49]. HIV prevention and treatment strategies targeting these groups are essential for controlling the HIV epidemic and are likely to provide good value for money. The CSO-led HIVST delivery model is particularly relevant as it remains today the most promising strategy for reaching KP, their sexual partners and clients of FSW not accessing HIV testing, so-called "hidden populations". Further research will assess the overall cost-effectiveness of the CSO-led HIVST delivery programme.

List of Tables and Figures

Appendix Figure 2.a. Average cost at scale per HIVST kit distributed by key group and scale-up year - Scenario analysis – Côte d'Ivoire (2.a.), Senegal (2.b.), and Mali (2.c.)

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Chapter 6 - Supplementary Material

Appendix Table 1. Allocation factors for the top-down costing analysis by input type

	Allocation factors to site level		
Input type	Côte d'Ivoire	Senegal	Mali
Start-up costs			
S1. Trainings	% trained distributors	% trained distributors	% trained distributors
S2. Sensitisation	% of cohort size	% of cohort size	% of cohort size
Capital costs			
C1. Buildings and storage	% direct expenditure	% direct expenditure	% direct expenditure
C2. Equipment	% direct expenditure	% direct expenditure	% direct expenditure
C3. Vehicles	% HIVST kits distributed	% HIVST kits distributed	% HIVST kits distributed
C4. Other capital costs	% direct expenditure	% direct expenditure	% direct expenditure
Recurrent costs			
R1. Personnel & Per diems – Headquarters IPO coordination	% trained distributors	Equally shared across sites	% trained distributors
R2. Personnel & Per diems – Headquarters IPO country	% trained distributors	Equally shared across sites	% trained distributors
R3. Personnel & Per diems – Headquarters Implementing partner	% trained distributors	% HIVST distributors	% trained distributors
R4. Personnel & Per diems – Field - HIVST distributors	% trained distributors	% HIVST distributors	% trained distributors
R5. HIV self-testing kits	% HIVST kits distributed	% HIVST kits distributed	% HIVST kits distributed
R6. Vehicle operation and maintenance/transportation	% HIVST kits distributed	% HIVST kits distributed	% HIVST kits distributed
R7. Building operation and maintenance	% direct expenditure	% direct expenditure	% direct expenditure
R8. Other recurrent costs	% direct expenditure	% direct expenditure	% direct expenditure

IPO: International Partner Organisation

Appendix Table 2.a. Observed total and average intervention costs by CSO and key groups – Côte d'Ivoire (1/2)

	CSO1				CSO2		CSO3						CSO4	
	FSW		MSM		FSW		FSW		PWUD		MSM		MSM	
	$	%	$	%	$	%	$	%	$	%	$	%	$	%
INTERVENTION PHASES														
Development	1,327	*2%*	543	*2%*	1,766	*2%*	1,941	*2%*	1,118	*2%*	721	*1%*	634	*3%*
Start-up (start-up and other costs)	21,890	*27%*	8,887	*31%*	24,169	*24%*	33,812	*33%*	18,687	*28%*	13,436	*26%*	5,581	*23%*
Implementation	58,166	*71%*	19,497	*67%*	74,030	*74%*	67,769	*65%*	45,887	*70%*	37,774	*73%*	18,337	*75%*
COST CATEGORIES														
Start-up														
S1. Trainings	7,379	9%	2,635	9%	10,541	11%	11,068	11%	6,324	10%	3,689	7%	3,689	15%
S2. Sensitisation	12,256	15%	5,290	18%	10,684	11%	19,479	19%	10,475	16%	8,493	16%	816	3%
Total Start-up	*19,634*	*24%*	*7,925*	*27%*	*21,225*	*21%*	*30,547*	*30%*	*16,799*	*26%*	*12,183*	*23%*	*4,505*	*18%*
Capital														
C1. Buildings and storage	576	1%	187	1%	971	1%	462	0%	426	1%	239	0%	372	2%
C2. Equipment	145	0%	54	0%	285	0%	198	0%	147	0%	72	0%	86	0%
C3. Vehicles	34	0%	34	0%	11	0%	34	0%	23	0%	34	0%	11	0%
C4. Other capital costs	10	0%	4	0%	22	0%	14	0%	11	0%	5	0%	7	0%
Total Capital	*766*	*1%*	*278*	*1%*	*1,289*	*1%*	*708*	*1%*	*606*	*1%*	*350*	*1%*	*476*	*2%*

Recurrent														
R1. Personnel – Headquarters IPO coordination	4,408	5%	1,574	5%	9,347	9%	5,946	6%	4,455	7%	2,021	4%	3,128	13%
R2. Personnel – Headquarters IPO country	5,862	7%	2,093	7%	12,704	13%	7,845	8%	5,984	9%	2,671	5%	4,243	17%
R3. Personnel – Headquarters IP	15,686	19%	4,886	17%	19,094	19%	28,644	28%	19,665	30%	19,101	37%	3,826	16%
R4. Personnel – Field - HIVST distributors	5,599	7%	1,756	6%	7,243	7%	3,230	3%	3,055	5%	1,638	3%	2,424	10%
R5. HIV self-testing kits	25,296	31%	8,076	28%	22,166	22%	21,730	21%	11,068	17%	11,446	22%	3,470	14%
R6. Vehicle operation and maintenance	1,276	2%	1,276	4%	653	1%	1,134	1%	1,019	2%	1,159	2%	622	3%
R7. Building operation and maintenance	2,080	3%	774	3%	4,586	5%	2,716	3%	2,224	3%	990	2%	1,364	6%
R8. Other recurrent costs	775	1%	288	1%	1,657	2%	1,024	1%	816	1%	372	1%	494	2%
Total Recurrent	*60,983*	*75%*	*20,724*	*72%*	*77,450*	*77%*	*72,268*	*70%*	*48,286*	*74%*	*39,399*	*76%*	*19,571*	*80%*
TOTAL ANNUAL COSTS	81,383		28,928		99,964		103,523		65,691		51,931		24,552	
HIVST kits distributed	9,441		3,014		8,273		8,110		4,131		4,272		1,295	
Average cost per HIVST kit distributed	9		10		12		13		16		12		19	

CSO: Civil Society Organisation, IPO: International Partner Organisation, IP: Implementing Partner, HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Table 2.a. Observed total and average intervention costs by CSO and key groups – Côte d'Ivoire (2/2)

	CSO5				CSO6				CSO7			
	FSW		MSM		FSW		MSM		FSW		MSM	
	$	%	$	%	$	%	$	%	$	%	$	%
INTERVENTION PHASES												
Development	554	*1%*	466	*2%*	1,166	*2%*	729	*2%*	858	*2%*	424	*2%*
Start-up (start-up and other costs)	7,090	*18%*	5,240	*17%*	18,641	*27%*	10,576	*25%*	15,271	*33%*	8,518	*35%*
Implementation	31,650	*81%*	24,402	*81%*	50,042	*72%*	31,008	*73%*	30,505	*65%*	15,135	*63%*
COST CATEGORIES												
Start-up												
S1. Trainings	3,162	8%	2,635	9%	6,852	10%	4,216	10%	4,743	10%	2,108	9%
S2. Sensitisation	2,990	8%	1,811	6%	9,842	14%	5,133	12%	9,070	19%	5,670	24%
Total Start-up	*6,152*	*16%*	*4,447*	*15%*	*16,694*	*24%*	*9,349*	*22%*	*13,813*	*30%*	*7,778*	*32%*
Capital												
C1. Buildings and storage	163	0%	130	0%	364	1%	219	1%	302	1%	146	1%
C2. Equipment	105	0%	84	0%	241	0%	144	0%	143	0%	69	0%
C3. Vehicles	11	0%	11	0%	11	0%	11	0%	23	0%	23	0%
C4. Other capital costs	9	0%	7	0%	20	0%	12	0%	11	0%	5	0%
Total Capital	*287*	*1%*	*232*	*1%*	*636*	*1%*	*387*	*1%*	*479*	*1%*	*243*	*1%*

Recurrent												
R1. Personnel – Headquarters IPO coordination	3,464	9%	2,887	10%	7,506	11%	4,619	11%	4,206	9%	1,869	8%
R2. Personnel – Headquarters IPO country	4,749	12%	3,957	13%	10,289	15%	6,332	15%	5,717	12%	2,541	11%
R3. Personnel – Headquarters IP	6,451	16%	4,938	16%	10,096	14%	6,306	15%	6,566	14%	3,017	13%
R4. Personnel – Field - HIVST distributors	9,682	25%	6,918	23%	11,359	16%	7,252	17%	2,710	6%	1,244	5%
R5. HIV self-testing kits	5,305	14%	3,990	13%	6,950	10%	3,957	9%	8,705	19%	4,563	19%
R6. Vehicle operation and maintenance	816	2%	816	3%	816	1%	816	2%	1,305	3%	1,305	5%
R7. Building operation and maintenance	1,759	4%	1,417	5%	4,054	6%	2,428	6%	2,302	5%	1,115	5%
R8. Other recurrent costs	629	2%	507	2%	1,450	2%	868	2%	832	2%	403	2%
Total Recurrent	*32,855*	*84%*	*25,429*	*84%*	*52,520*	*75%*	*32,578*	*77%*	*32,343*	*69%*	*16,057*	*67%*
TOTAL ANNUAL COSTS	39,294		30,108		69,850		42,314		46,635		24,078	
HIVST kits distributed	1,980		1,489		2,594		1,477		3,249		1,703	
Average cost per HIVST kit distributed	20		20		27		29		14		14	

CSO: Civil Society Organisation, IPO: International Partner Organisation, IP: Implementing Partner, HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Table 2.b. Observed total and average intervention costs by CSO and key groups – Senegal

	CSO - Associations				CSO – Mobile clinic		CSO – Independent distributors						Public partner	
	MSM		FSW		FSW		MSM		FSW		PWUD		PWUD	
	$	%	$	%	$	%	$	%	$	%	$	%	$	%
INTERVENTION PHASES														
Development	2,689	*5%*	2,644	*5%*	2,575	*8%*	2,996	*5%*	3,043	*4%*	2,176	*7%*	2,578	*4%*
Start-up (start-up and other costs)	12,097	*22%*	9,437	*19%*	7,154	*22%*	13,482	*21%*	19,037	*24%*	3,295	*11%*	6,353	*10%*
Implementation	41,122	*74%*	36,705	*75%*	23,056	*70%*	47,989	*74%*	55,742	*72%*	23,585	*81%*	57,104	*86%*
COST CATEGORIES														
Start-up														
S1. Trainings	3,890	7%	2,947	6%	1,022	3%	1,532	2%	1,532	2%	511	2%	2,240	3%
S2. Sensitisation	5,628	10%	3,939	8%	3,684	11%	9,209	14%	14,734	19%	614	2%	1,663	3%
Total Start-up	*9,517*	*17%*	*6,886*	*14%*	*4,705*	*14%*	*10,741*	*17%*	*16,267*	*21%*	*1,125*	*4%*	*3,902*	*6%*
Capital														
C1. Buildings and storage	1,990	4%	1,450	3%	1,758	5%	3,886	6%	4,077	5%	1,211	4%	4,024	6%
C2. Equipment	64	0%	48	0%	59	0%	125	0%	131	0%	39	0%	124	0%
C3. Vehicles	61	0%	53	0%	19	0%	36	0%	36	0%	12	0%	34	0%
C4. Other capital costs	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Total Capital	*2,115*	*4%*	*1,551*	*3%*	*1,836*	*6%*	*4,048*	*6%*	*4,244*	*5%*	*1,262*	*4%*	*4,183*	*6%*

Recurrent														
R1. Personnel – Headquarters IPO coordination	6,414	11%	5,231	11%	4,639	14%	6,414	10%	6,414	8%	6,414	22%	9,963	15%
R2. Personnel – Headquarters IPO country	11,275	20%	8,962	18%	7,805	24%	11,275	17%	11,275	14%	11,275	39%	18,216	28%
R3. Personnel – Headquarters IP	9,012	16%	6,759	14%	4,882	15%	11,716	18%	11,716	15%	3,905	13%	15,578	24%
R4. Personnel – Field - HIVST distributors	5,512	10%	4,134	8%	2,986	9%	7,166	11%	7,166	9%	2,389	8%	6,475	10%
R5. HIV self-testing kits	6,776	12%	11,176	23%	3,148	10%	6,985	11%	14,410	19%	739	3%	1,299	2%
R6. Vehicle operation and maintenance	3,105	6%	2,511	5%	885	3%	1,863	3%	1,863	2%	621	2%	1,955	3%
R7. Building operation and maintenance	788	1%	580	1%	707	2%	1,540	2%	1,615	2%	480	2%	1,572	2%
R8. Other recurrent costs	1,392	2%	996	2%	1,191	4%	2,719	4%	2,852	4%	847	3%	2,893	4%
Total Recurrent	*44,275*	*79%*	*40,349*	*83%*	*26,243*	*80%*	*49,677*	*77%*	*57,311*	*74%*	*26,669*	*92%*	*57,951*	*88%*
TOTAL ANNUAL COSTS	55,908		48,786		32,785		64,466		77,822		29,056		66,036	
HIVST kits distributed	2,202		3,632		1,023		2,270		4,683		240		422	
Average cost per HIVST kit distributed	25		13		32		28		17		121		156	

CSO: Civil Society Organisation, IPO: International Partner Organisation, IP: Implementing Partner, HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Table 2.c. Observed total and average intervention costs by CSO and key groups – Mali (1/2)

	CSO1				CSO2			
	MSM		FSW		MSM		FSW	
	$	%	$	%	$	%	$	%
INTERVENTION PHASES								
Development	1,245	*3%*	1,330	*2%*	1,702	*3%*	6,813	*3%*
Start-up (start-up and other costs)	6,719	*16%*	11,499	*20%*	6,558	*13%*	33,270	*14%*
Implementation	34,512	*81%*	46,105	*78%*	42,588	*84%*	199,997	*83%*
COST CATEGORIES								
Start-up								
S1. Trainings	1,170	3%	1,253	2%	1,601	3%	6,243	3%
S2. Sensitisation	3,879	9%	8,462	14%	2,680	5%	17,865	7%
Total Start-up	*5,049*	*12%*	*9,716*	*16%*	*4,280*	*8%*	*24,108*	*10%*
Capital								
C1. Buildings and storage	1,131	3%	1,311	2%	1,561	3%	6,002	3%
C2. Equipment	34	0%	38	0%	47	0%	179	0%
C3. Vehicles	9	0%	9	0%	20	0%	36	0%
C4. Other capital costs	0	0%	0	0%	0	0%	0	0%
Total Capital	*1,174*	*3%*	*1,359*	*2%*	*1,627*	*3%*	*6,218*	*3%*

Recurrent								
R1. Personnel – Headquarters IPO coordination	8,440	20%	9,724	16%	11,547	23%	45,035	19%
R2. Personnel – Headquarters IPO country	11,845	28%	13,748	23%	16,207	32%	63,206	26%
R3. Personnel – Headquarters IP	2,897	7%	3,386	6%	3,963	8%	15,456	6%
R4. Personnel – Field - HIVST distributors	6,073	14%	7,099	12%	1,643	3%	6,409	3%
R5. HIV self-testing kits	2,193	5%	8,444	14%	5,033	10%	49,840	21%
R6. Vehicle operation and maintenance	1,606	4%	1,739	3%	1,541	3%	15,257	6%
R7. Building operation and maintenance	1,264	3%	1,469	2%	2,335	5%	4,280	2%
R8. Other recurrent costs	1,935	5%	2,252	4%	2,671	5%	10,271	4%
Total Recurrent	*36,253*	*85%*	*47,859*	*81%*	*44,940*	*88%*	*209,754*	*87%*
TOTAL ANNUAL COSTS	42,476		58,933		50,848		240,080	
HIVST kits distributed	715		2,753		1,641		16,250	
Average cost per HIVST kit distributed	59		21		31		15	

CSO: Civil Society Organisation, IPO: International Partner Organisation, IP: Implementing Partner, HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

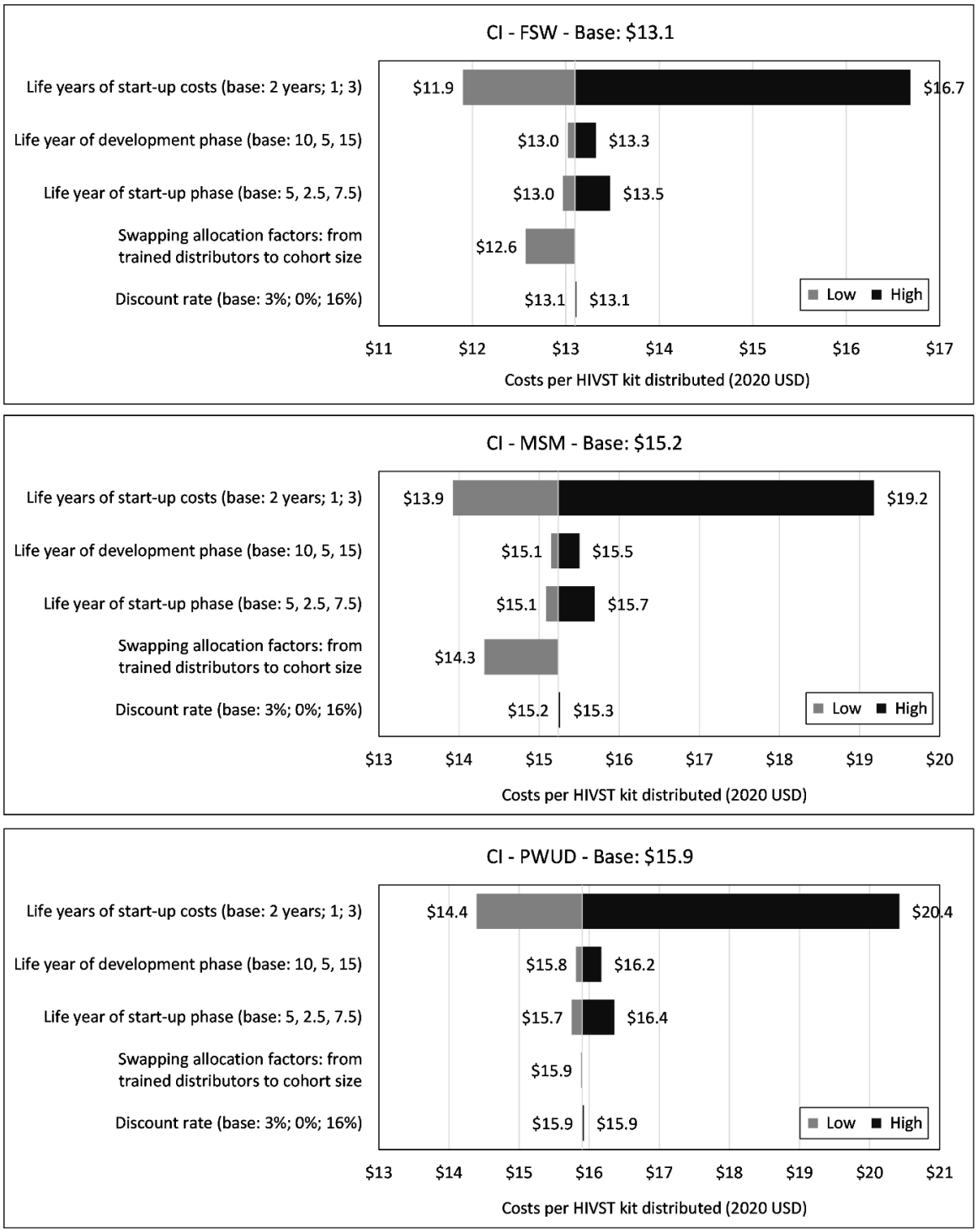
Appendix Table 2.c. Observed total and average intervention costs by CSO and key groups – Mali (2/2)

	CSO3		CSO4		CSO5			
	FSW		MSM		MSM		FSW	
	$	%	$	%	$	%	$	%
INTERVENTION PHASES								
Development	2,833	*3%*	1,732	*3%*	754	*3%*	568	*2%*
Start-up (start-up and other costs)	24,581	*22%*	13,024	*20%*	3,331	*11%*	4,995	*19%*
Implementation	85,714	*76%*	50,009	*77%*	25,985	*86%*	20,849	*79%*
COST CATEGORIES								
Start-up								
S1. Trainings	2,481	2%	1,521	2%	560	2%	560	2%
S2. Sensitisation	18,285	16%	9,171	14%	1,706	6%	3,687	14%
Total Start-up	*20,766*	*18%*	*10,692*	*17%*	*2,266*	*8%*	*4,247*	*16%*
Capital								
C1. Buildings and storage	2,399	2%	1,591	2%	646	2%	512	2%
C2. Equipment	72	0%	46	0%	19	0%	15	0%
C3. Vehicles	48	0%	29	0%	6	0%	6	0%
C4. Other capital costs	0	0%	0	0%	0	0%	0	0%
Total Capital	*2,518*	*2%*	*1,666*	*3%*	*672*	*2%*	*534*	*2%*

Recurrent								
R1. Personnel – Headquarters IPO coordination	17,899	16%	11,797	18%	6,153	20%	3,441	13%
R2. Personnel – Headquarters IPO country	25,120	22%	16,678	26%	5,672	19%	5,672	21%
R3. Personnel – Headquarters IP	6,143	5%	4,107	6%	1,387	5%	1,387	5%
R4. Personnel – Field - HIVST distributors	2,547	2%	1,703	3%	5,528	18%	5,528	21%
R5. HIV self-testing kits	23,092	20%	8,244	13%	5,462	18%	3,055	12%
R6. Vehicle operation and maintenance	8,258	7%	5,365	8%	1,101	4%	1,101	4%
R7. Building operation and maintenance	2,681	2%	1,782	3%	722	2%	572	2%
R8. Other recurrent costs	4,104	4%	2,732	4%	1,106	4%	876	3%
Total Recurrent	*89,844*	*79%*	*52,408*	*81%*	*27,132*	*90%*	*21,632*	*82%*
TOTAL ANNUAL COSTS	113,128		64,765		30,070		26,413	
HIVST kits distributed	7,529		2,688		1,781		996	
Average cost per HIVST kit distributed	15		24		17		27	

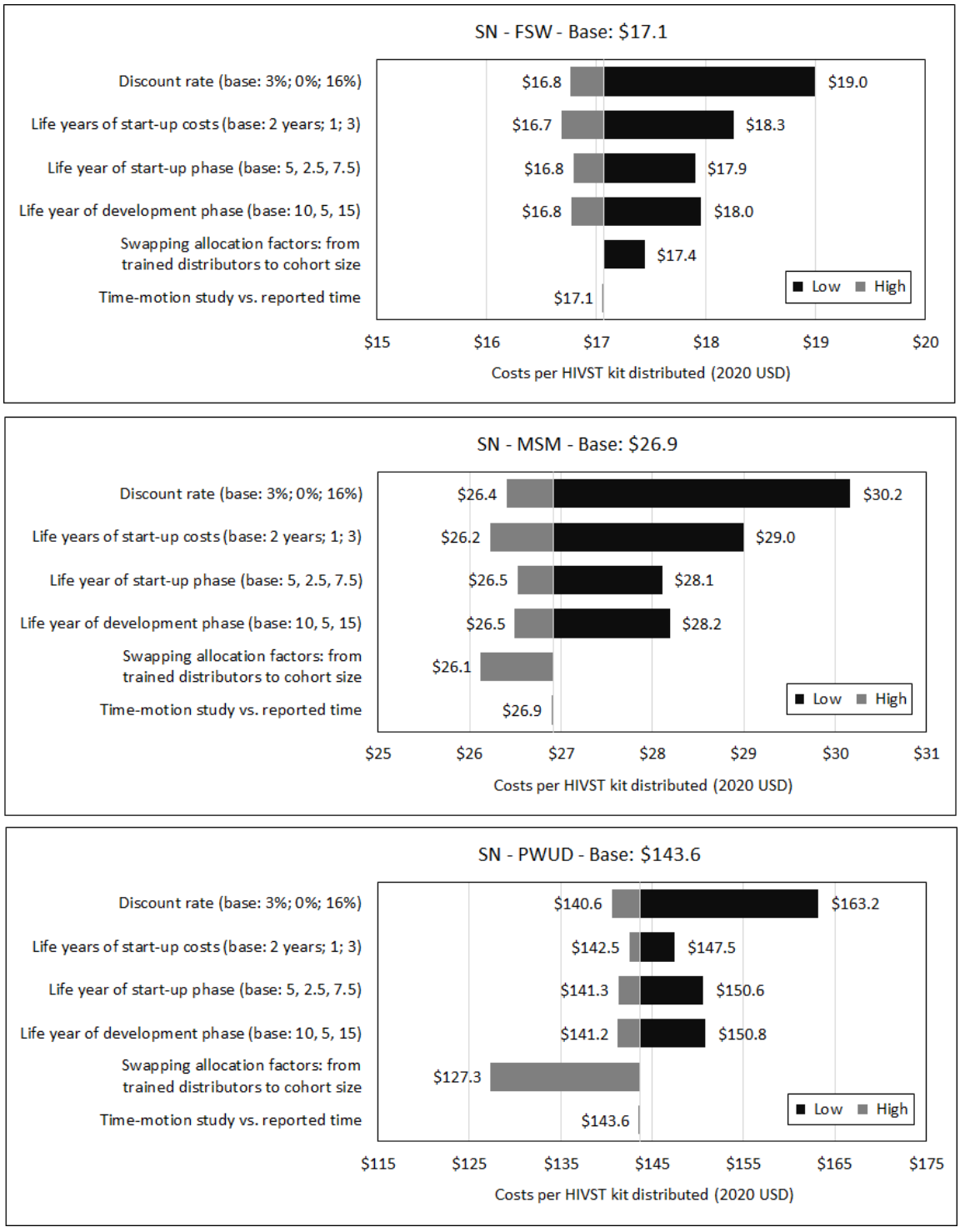
CSO: Civil Society Organisation, IPO: International Partner Organisation, IP: Implementing Partner, HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Figure 1.a. Tornado diagrams of findings from deterministic sensitivity analysis in Côte d'Ivoire



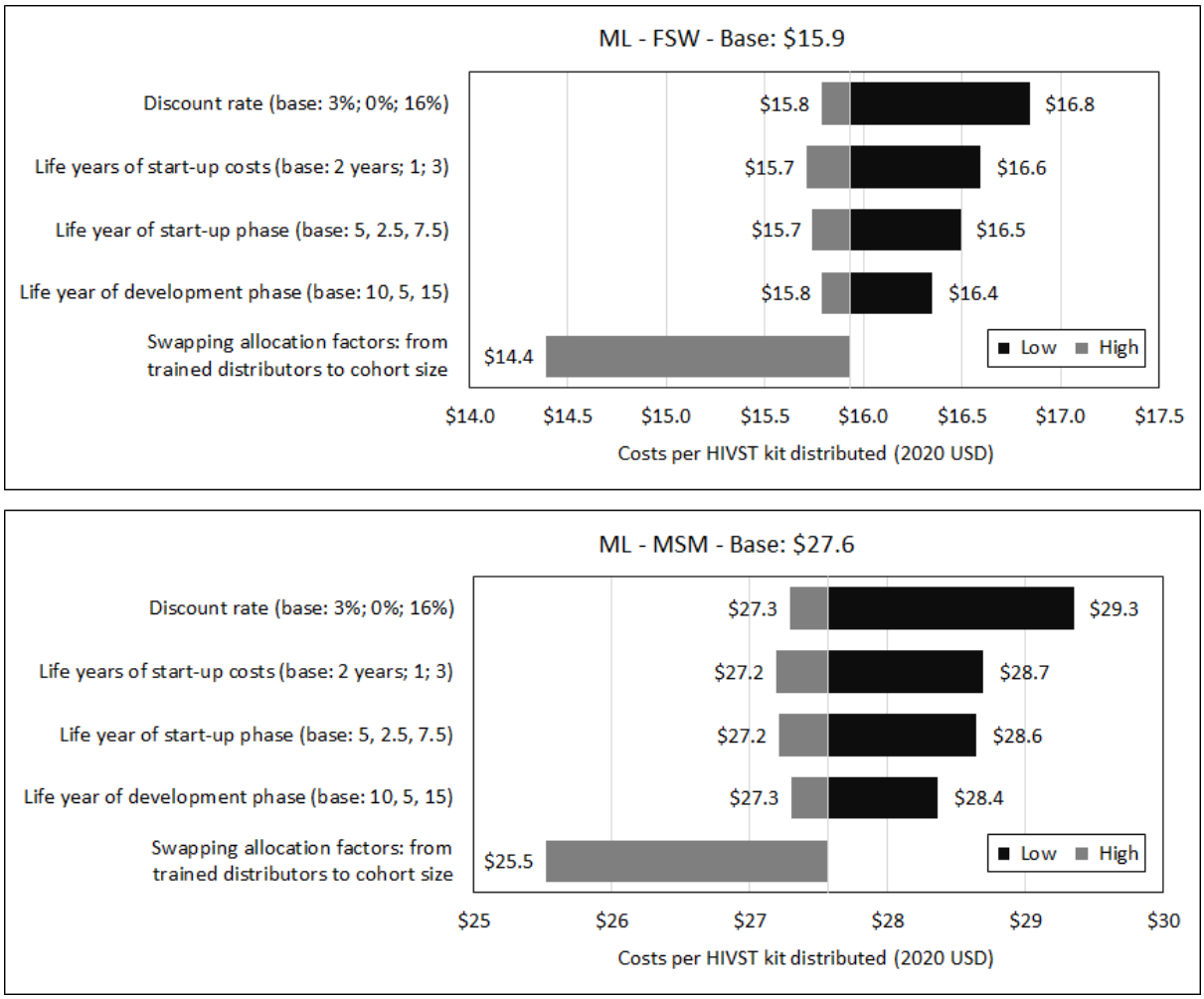
HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Figure 1.b. Tornado diagrams of findings from deterministic sensitivity analysis in Senegal



HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Figure 1.c. Tornado diagrams of findings from deterministic sensitivity analysis in Mali



HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Table 3.a. Total and average intervention costs in transition and at scale-up by key group and scale-up year – Côte d'Ivoire

	Côte d'Ivoire					
	2021					
	FSW		MSM		PWUD	
Intervention level and costs	$	%	$	%	$	%
International level - Fixed costs (S2, R1)	62,455	8%	27,766	7%	8,946	5%
National level - Fixed costs (C1-C4, S2, R2)	88,073	11%	39,347	10%	12,574	7%
National level - Variable costs (S1)	111,930	14%	46,063	12%	17,407	10%
National level - Variable costs (R6-R8)	17,712	2%	9,720	3%	15,232	9%
Sub-national - Implementing partners (R3)	307,960	37%	144,216	38%	73,789	44%
Local - HIVST distribution areas (R4)	23,620	3%	12,130	3%	11,462	7%
Local - HIVST distribution areas (R5)	213,489	26%	98,398	26%	29,419	17%
Total costs	825,239		377,641		168,828	
Scale	81,174		37,414		11,186	
Average costs	10		10		15	
	2022					
	FSW		MSM		PWUD	
Intervention level and costs	$	%	$	%	$	%
International level - Fixed costs (S2, R1)	62,455	6%	27,766	6%	8,946	4%
National level - Fixed costs (C1-C4, S2, R2)	88,073	8%	39,347	8%	12,574	5%
National level - Variable costs (S1)	74,717	7%	28,690	6%	12,528	5%
National level - Variable costs (R6-R8)	26,213	2%	14,008	3%	23,273	10%
Sub-national - Implementing partners (R3)	455,768	43%	207,836	44%	112,741	48%
Local - HIVST distribution areas (R4)	34,956	3%	17,481	4%	17,512	8%
Local - HIVST distribution areas (R5)	315,954	30%	141,806	30%	44,949	19%
Total costs	1,058,137		476,935		232,523	
Scale	120,135		53,919		17,091	
Average costs	9		9		14	
	2023					

	FSW		MSM		PWUD	
Intervention level and costs	$	%	$	%	$	%
International level - Fixed costs (S2, R1)	62,455	4%	27,766	4%	8,946	3%
National level - Fixed costs (C1-C4, S2, R2)	88,073	6%	39,347	6%	12,574	4%
National level - Variable costs (S1)	100,175	7%	52,436	7%	16,958	5%
National level - Variable costs (R6-R8)	37,611	3%	21,845	3%	34,157	10%
Sub-national - Implementing partners (R3)	653,937	45%	324,112	45%	165,468	50%
Local - HIVST distribution areas (R4)	50,155	3%	27,262	4%	25,702	8%
Local - HIVST distribution areas (R5)	453,332	31%	221,140	31%	65,970	20%
Total costs	1,445,738		713,908		329,775	
Scale	172,370		84,084		25,084	
Average costs	8		8		13	

S1: Trainings, S2: Sensitisation, C1: Buildings and storage, C2: Equipment, C3: Vehicles, C4: Other capital costs, R1: Personnel & Per diems – Headquarters International Partner Organisation (IPO) coordination, R2: Personnel & Per diems – Headquarters IPO country, R3: Personnel & Per diems – Headquarters Implementing partner, R4: Personnel & Per diems – Field - HIVST distributors, R5: HIV self-testing kits, R6: Vehicle operation and maintenance, R7: Building operation and maintenance, R8: Other recurrent costs

HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Table 3.b. Total and average intervention costs in transition and at scale-up by key group and scale-up year – Senegal

	Senegal					
	2021					
	FSW		MSM		PWUD	
Intervention level and costs	$	%	$	%	$	%
International level - Fixed costs (S2, R1)	32,639	11%	23,681	6%	18,043	9%
National level - Fixed costs (C1-C4, S2, R2)	41,676	15%	32,696	8%	35,547	19%
National level - Variable costs (S1)	9,092	3%	26,630	7%	6,302	3%
National level - Variable costs (R6-R8)	35,020	12%	67,433	17%	27,543	14%
Sub-national - Implementing partners (R3)	61,964	22%	122,533	31%	64,128	33%
Local - HIVST distribution areas (R4)	37,900	13%	74,946	19%	29,174	15%
Local - HIVST distribution areas (R5)	65,761	23%	50,592	13%	11,165	6%
Total costs	284,051		398,511		191,902	
Scale	21,351		16,426		3,625	
Average costs	13		24		53	
	2022					
	FSW		MSM		PWUD	
Intervention level and costs	$	%	$	%	$	%
International level - Fixed costs (S2, R1)	32,639	11%	23,681	6%	18,043	9%
National level - Fixed costs (C1-C4, S2, R2)	41,676	14%	32,696	9%	35,547	17%
National level - Variable costs (S1)	1,026	0%	796	0%	1,229	1%
National level - Variable costs (R6-R8)	37,482	13%	69,108	18%	31,282	15%
Sub-national - Implementing partners (R3)	66,320	23%	125,577	33%	72,832	36%
Local - HIVST distribution areas (R4)	40,564	14%	76,808	20%	33,134	16%
Local - HIVST distribution areas (R5)	70,384	24%	51,849	14%	12,680	6%
Total costs	290,091		380,514		204,746	
Scale	22,852		16,834		4,117	
Average costs	13		23		50	
	2023					

	FSW		MSM		PWUD	
Intervention level and costs	$	%	$	%	$	%
International level - Fixed costs (S2, R1)	32,639	11%	23,681	5%	18,043	8%
National level - Fixed costs (C1-C4, S2, R2)	41,676	14%	32,696	7%	35,547	16%
National level - Variable costs (S1)	988	0%	7,612	2%	1,299	1%
National level - Variable costs (R6-R8)	39,852	13%	85,122	18%	35,233	16%
Sub-national - Implementing partners (R3)	70,514	23%	154,677	33%	82,031	37%
Local - HIVST distribution areas (R4)	43,129	14%	94,607	20%	37,319	17%
Local - HIVST distribution areas (R5)	74,835	25%	63,864	14%	14,282	6%
Total costs	303,632		462,259		223,752	
Scale	24,297		20,735		4,637	
Average costs	12		22		48	

S1: Trainings, S2: Sensitisation, C1: Buildings and storage, C2: Equipment, C3: Vehicles, C4: Other capital costs, R1: Personnel & Per diems – Headquarters International Partner Organisation (IPO) coordination, R2: Personnel & Per diems – Headquarters IPO country, R3: Personnel & Per diems – Headquarters Implementing partner, R4: Personnel & Per diems – Field - HIVST distributors, R5: HIV self-testing kits, R6: Vehicle operation and maintenance, R7: Building operation and maintenance, R8: Other recurrent costs

HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Table 3.c. Total and average intervention costs in transition and at scale-up by key group and scale-up year – Mali

	Mali			
	2021			
	FSW		MSM	
Intervention level and costs	$	%	$	%
International level - Fixed costs (S2, R1)	116,572	12%	52,548	13%
National level - Fixed costs (C1-C4, S2, R2)	126,200	13%	58,366	14%
National level - Variable costs (S1)	34,350	3%	15,537	4%
National level - Variable costs (R6-R8)	225,175	23%	101,531	25%
Sub-national - Implementing partners (R3)	112,339	11%	51,918	13%
Local - HIVST distribution areas (R4)	91,938	9%	62,817	15%
Local - HIVST distribution areas (R5)	288,941	29%	70,674	17%
Total costs	995,515		413,392	
Scale	93,812		22,946	
Average costs	11		18	
	2022			
	FSW		MSM	
Intervention level and costs	$	%	$	%
International level - Fixed costs (S2, R1)	116,572	10%	52,548	11%
National level - Fixed costs (C1-C4, S2, R2)	126,200	11%	58,366	12%
National level - Variable costs (S1)	10,917	1%	4,959	1%
National level - Variable costs (R6-R8)	279,940	24%	126,226	27%
Sub-national - Implementing partners (R3)	139,661	12%	64,546	14%
Local - HIVST distribution areas (R4)	114,298	10%	78,096	17%
Local - HIVST distribution areas (R5)	359,214	31%	87,863	19%
Total costs	1,146,802		472,604	
Scale	116,628		28,527	
Average costs	10		17	
	2023			

	FSW		MSM	
Intervention level and costs	$	%	$	%
International level - Fixed costs (S2, R1)	116,572	9%	52,548	10%
National level - Fixed costs (C1-C4, S2, R2)	126,200	10%	58,366	12%
National level - Variable costs (S1)	5,622	0%	2,554	1%
National level - Variable costs (R6-R8)	308,143	25%	138,943	27%
Sub-national - Implementing partners (R3)	153,731	12%	71,049	14%
Local - HIVST distribution areas (R4)	125,814	10%	85,964	17%
Local - HIVST distribution areas (R5)	395,404	32%	96,715	19%
Total costs	1,231,486		506,138	
Scale	128,378		31,401	
Average costs	10		16	

S1: Trainings, S2: Sensitisation, C1: Buildings and storage, C2: Equipment, C3: Vehicles, C4: Other capital costs, R1: Personnel & Per diems – Headquarters International Partner Organisation (IPO) coordination, R2: Personnel & Per diems – Headquarters IPO country, R3: Personnel & Per diems – Headquarters Implementing partner, R4: Personnel & Per diems – Field - HIVST distributors, R5: HIV self-testing kits, R6: Vehicle operation and maintenance, R7: Building operation and maintenance, R8: Other recurrent costs

HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Figure 2.a. Average cost at scale per HIVST kit distributed by key group and scale-up year - Scenario analysis in Côte d'Ivoire

Scenario 1: We anticipate that programmatic objectives might not be reached. Accounting for this would provide more nuanced scale economies, and we applied different percentages for reaching targets

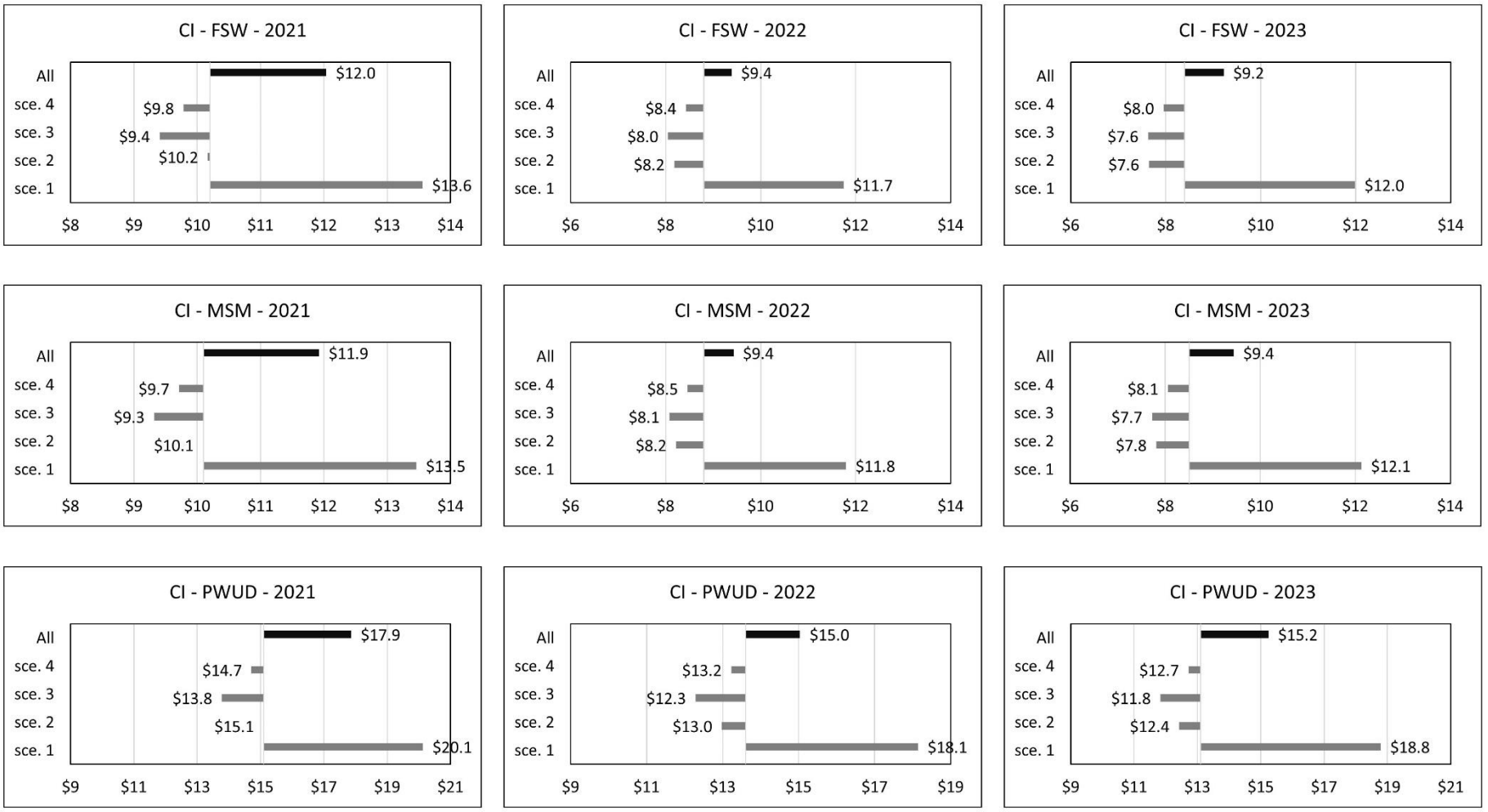
Scenario 2: International Partner Organisation's goal to progressively disengage to promote local programme ownership overtime was considered. Note that we still account for 15% of international costs in 2023 because we assume another coordination component will still exist (and incur costs) within the local health system at central level. Year 2023 would then represent what it costs for the country to support HIVST post-ATLAS

Scenario 3: We assessed the impact of optimising delivery channels by simplifying the model of partners/sub-partners and decreased civil society organisation's headquarter costs by 20%, which is reasonable to assume when evaluating interventions transitioning from pilot (ATLAS) to routine implementation phase

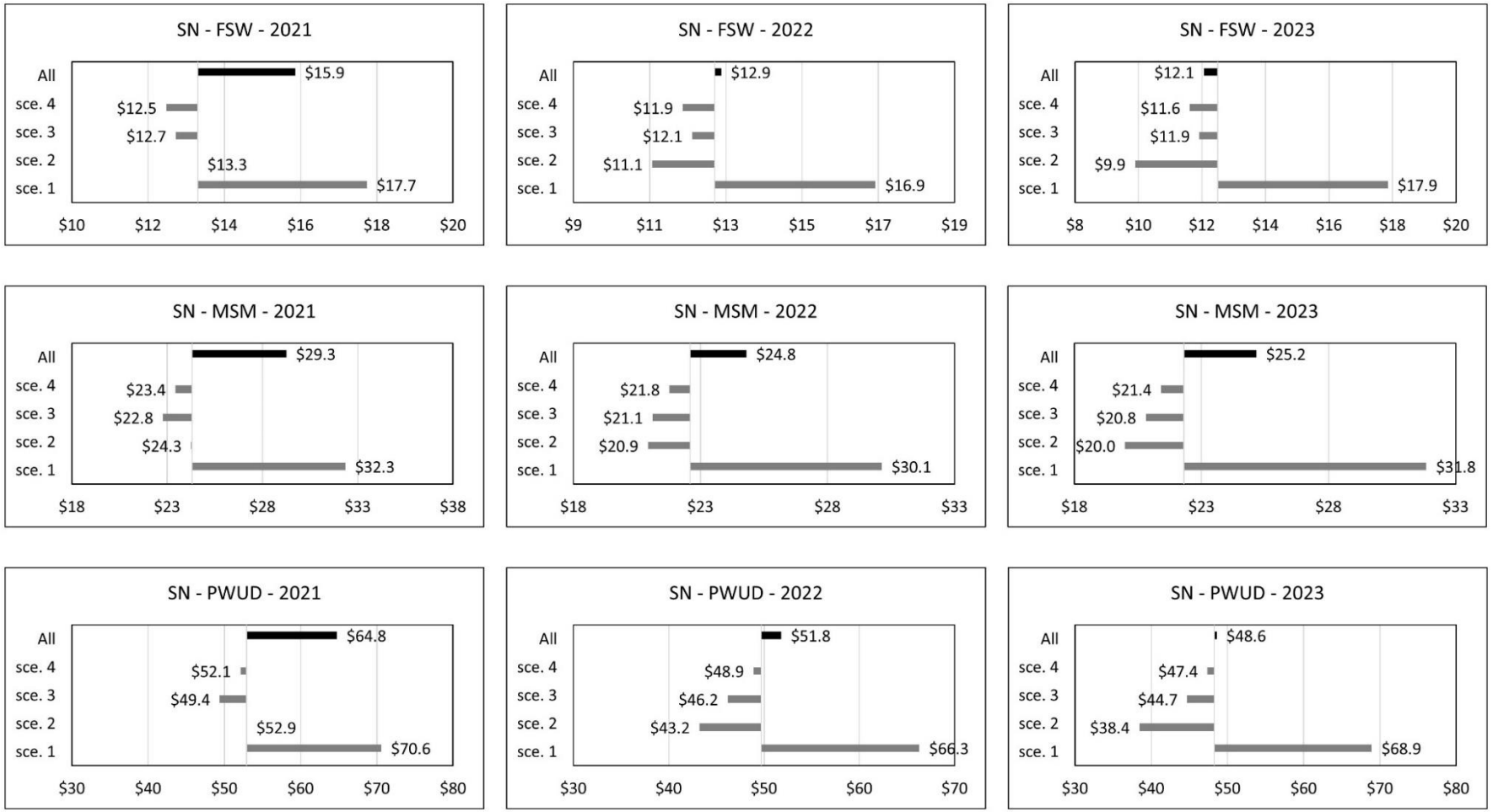
Scenario 4: We conducted country-specific simulations to account for varying HIVST kit cost for each year considering factors such as bulk buying, maritime provision instead of airways (except Mali), and integrating HIVST delivery chain with other health supplies

All: We combined all scenarios (1 to 4) to assess the global impact on average costs at scale per key population and scale-up year

Baseline scenario: All parameters above are unchanged (100% of their original value)



CI: Côte d'Ivoire, SN: Senegal, ML: Mali, HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs



Appendix Figure 2.b. Average cost at scale per HIVST kit distributed by key group and scale-up year - Scenario analysis in Senegal

CI: Côte d'Ivoire, SN: Senegal, ML: Mali, HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

Appendix Figure 2.c. Average cost at scale per HIVST kit distributed by key group and scale-up year - Scenario analysis in Mali

CI: Côte d'Ivoire, SN: Senegal, ML: Mali, HIVST: HIV Self-Testing kit, FSW: Female Sex workers, MSM: Men who have Sex with Men, PWUD: People who use drugs

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Conclusions from Paper 4

The results presented in this paper offer important insights into contextualising the results from a health intervention cost analysis in early phase for informing scale-up. The findings showed relatively high costs during the study period related to the progressive integration of the programme to CSO activities and contextual challenges (COVID-19 pandemic, country safety concerns). In contrast, I also find that in transition to scale-up and integration of the HIVST programme into CSO activities with the removal of the international partner organisation Solthis, the CSO-led model can generate substantial economies of scale.

Chapter 7 – General discussion

1. Key findings

Objective 1 – To conduct a scoping review of methods used to date to estimate the costs at scale of health interventions in LMIC and describe the relationship between the choice of the estimation method and the intended use of the costs projections - *Paper 1*

The first objective was addressed in Paper 1 with a scoping review of cost function applications in LMIC. I reviewed seven databases reporting quantitative analysis of cost for informing the scale up of an intervention between 2003 and 2019. The 40 studies identified were classified following two main families of cost functions – namely accounting and econometric, and by the intended use of cost projections. I conducted a critical review of these studies and reported issues with the current methods used related to sampling approach, reporting of uncertainty measure, and selection of the right estimator based on sample size and cost data features. I also assessed how to better account for variable returns to scale with the application of these cost functions. Finally, applied frameworks were proposed for the fitting of cost functions based on the intended use of these estimates. The development of these frameworks was based on the synthesis of cost function algebra from the study sample, the qualitative analysis of authors' motivators guiding the fitting of a cost function, and it was complemented by the methodological literature on healthcare cost data analysis.

Major limitations of this review are that it is limited to the peer-reviewed literature and might be missing other innovative approaches. I was also unable to assess the validity of cost projection methods from the sampled studies because observed costs at scale-up are almost never reported, therefore the critical assessment of studies is limited to method transparency.

To my knowledge, this is the first study to develop frameworks that can guide the more consistent use of cost functions in LMIC using the relevant approach based on the intended use of the cost estimate and better accounting for variable returns to scale. I hope it can facilitate the analysts' decision process of balancing simplicity versus accuracy when critical, and increase the overall transparency in the reporting of the methodological approach taken.

Objective 2 – To carry out a cost analysis of the community-based programme for HTS and HIVST with the highest level of testing coverage in Lesotho over a two-year observation period - *Paper 2*

The second objective was addressed in paper 2 where I conducted a micro-costing analysis using longitudinal data from a real-world intervention in Lesotho. Costs and outcomes data were collected over two years observing the addition of HIVST, then HIVST booth to the existing HTS programme. I found that costs per HIV-positive case identified increased with the addition of HIVST (from US$956 to US$1,249) then dropped with the addition of HIVST booths (US$813) due to the improvement of the HIVST integration strategy to the existing HTS programme. So, the addition of HIVST increased the overall programme's affordability for HIV-positive case finding. Importantly, I found that full versus incremental cost analyses resulted in large differences in the magnitude of costs, attributable to methods rather than resource use and should be considered with caution. Indeed, incremental HIVST costing, only considering financial costs, assumes that the existing intervention has the capacity (particularly human resources) to absorb the new intervention. So, budgeting of HIVST using incremental costs risks to underestimate needs if HTS is not running well. A major limitation of this work is that HIVST was introduced in all sites of the intervention at the same time, therefore, there were no control sites against which to evaluate the effect of HIVST introduction, and we know that uncontrolled before-after studies are not the most robust approach to evaluate an intervention [1]. However, it is recognised that this national change in HTS strategy would otherwise go unevaluated and the results from this study can provide evidence of proof of concept prior to more robust evaluation.

To my knowledge, this is the first cost analysis using longitudinal data from a real-world intervention on HTS efficiency gains before and after introduction of HIVST. I showed that adding HIVST to community-based HTS can improve its overall affordability regarding HIV-positive case finding. I also highlighted the importance of transparency in reporting methods for priority setting, budgeting and financial planning.

Objective 3 – To estimate the costs drivers of community-based HIVST distribution in Malawi, Zambia, Zimbabwe and South Africa, using econometric methods and, based on the model outputs, project costs at scale using community-based HIVST national scale-up in Lesotho as a case study - *Paper 3*

Paper 3 addresses the third objective. The scale of distribution, type of community-based intervention, percentage of kits distributed to men, distance from implementer's warehouse, and per capita GDP predicted average costs per HIVST kit distributed. In addition, the model simplification approach showed that a parsimonious model could predict costs without losing accuracy. I sought to assess the validity of ECF-based cost projections, comparing them with observed costs at scale in Lesotho. Findings suggest an acceptable predictive capacity to out-of-sample countries of the southern African region. Major limitations are a small magnitude of HIVST scale-up to compare observed and projected costs in Lesotho because of the relatively small operating scale in this country. Since I did not have country-specific panel data, time-dependent unobserved cost determinants were ignored for the analysis. To my knowledge, this is one of the few study to use ECF for cost projections for the purpose of financial planning [2], the first to explore the trade-off between simplicity versus accuracy using ECF-based cost projection methods, and a comparative approach of projected versus observed scale-up costs for validation purpose.

Objective 4 – To apply accounting approaches to estimate costs at scale using the case of community-based HIVST national scale-up in Côte d'Ivoire, Senegal, and Mali - *Paper 4*

The fourth objective is addressed in Paper 4. I estimated the costs of implementing HIVST through civil society organisations (CSO)-led models for KP in Côte d'Ivoire (N=7), Senegal (N=11), and Mali (N=5), and

I modelled costs for programme transition and early scale-up using a relatively simple accounting cost function. Average costs per HIVST kit distributed were ranging between $13 and $80, driven by personnel costs (47%-78% of total costs), and HIVST kits costs (2%-20%). Average costs at scale-up were estimated between $9 and $50 per HIVST kit distributed, and cost reductions were mainly explained by the spreading of IPO fixed costs over higher HIVST distribution volumes (economies of scale) and progressive IPO withdrawal at scale-up. The main study limitation is the impact of the COVID-19 pandemic leading to reduced/suspended activities during a trimester for some CSO, but also encouraged the use of HIVST by other actors as a timely alternative to HTS in response to lockdown and social distancing, therefore, its impact on costs and project outcomes is difficult to assess.

To my knowledge, this is the first large scale economic analysis of CSO-led HIVST distribution programme to KP and their sexual partners in Africa. Interestingly, the findings suggests that the horizontal approach taken by the ATLAS project for the integration of the HIVST programme into existing CSO-led HTS programmes, shows large potential for substantial economies of scale and moderate above service level cost reductions as programmes scale-up nationally and mature.

Objective 5 – To synthetize and critically appraise the above research to discuss recommendations about the choice of methods for estimating scale-up costs, taking into consideration the scope of its application, whether it is priority setting, budgeting, or financial planning.

The fifth objective is met with the discussion on the key findings of Objectives 1-4, the proposed frameworks presented in Paper 1, and the discussion in this chapter.

2. Contribution to knowledge

This thesis provides contribution to both empirical and methodological knowledge.

a. Contribution of empirical findings

A first contribution of this thesis relates to the review of cost function applications in LMIC with paper 1. I report on the use of simple cost multipliers, accounting and econometric cost functions. As expected, I identified that accounting cost functions are usually applied for medium- and long-term financial planning, whereas econometric cost functions tend to be used for technical efficiency analyses. Sometimes, a combination of both approaches could be used for low- and high-estimates of a range of projected costs [2]. I also found gaps in reporting of methods in particular related to the choice of the estimator and reporting of standard statistical tests in econometric analyses. Finally, I present frameworks that can guide how to fit these cost functions and encourage a more consistent use and reporting of these methods. In particular, the proposed mathematical notations aim to inform any type of cost analysis at scale regardless of the type of health intervention and intended use of the cost estimates.

The second contribution of this thesis relates to the generation of cost estimates for community-based HIVST kits provision for the general population in Lesotho through mobile outreaches, and for key populations and their sexual partners through CSO in Côte d'Ivoire, Senegal, and Mali. I present in papers 2 and 4 that these incremental costs are at $15 per kit distributed in Lesotho, and between $13-$17 for FSW, $15-$28 for MSM, and $16-$144 for PWUD in Côte d'Ivoire, Senegal, and Mali. Compared to other costing studies in sub-Saharan Africa for HIV self-testing services with a global estimate at $13 per kit distributed [3], our costs are slightly above. This is particularly true for west Africa costs where CSO work with hard-to-reach criminalised and/or stigmatised key populations making implementation challenging, and with low HIVST distribution volumes, leading to increased provision costs.

In paper 2, I present how HIVST can potentially play a role in improving HTS efficiency (as defined by the cost per HIV-positive case identified). In Lesotho, the introduction of HIVST and onsite self-testing booth increased the capacity of staff to provide more testing services. It allowed staff to reallocate their activities to other strategies, in particular index testing, with known high positivity rate [4]. As a result, the overall costs of the HTS and HIVST programmes combined, led to reduced costs per HIV-positive case identified. Paper 2 is the first study showing that in a high HIV prevalence country such as Lesotho, HIVST, beyond reaching populations who would otherwise not test [5], can potentially play a role in improving HTS efficiency. This is particularly relevant in a context where donors are significantly reducing funding for HIV response in LMIC [6], and it is becoming increasing costly to identify the remaining undiagnosed PLHIV [7].

Another contribution from this thesis relates to the economic analysis of the large scale programme ATLAS working with twenty-three CSO across Côte d'Ivoire, Senegal and Mali presented in paper 4. As opposed to many 'vertical' HIV programme stemming from international aid in Africa [8, 9], the integrated (or 'horizontal') approach taken by the international partner organisation Solthis in coordination with local CSO for full integration of HIVST provision into the local health systems and CSO did result in a lengthy process with development and start-up phases before effective HIVST implementation could start. In paper 4, I attempted to estimate the possible returns on investment of such strategy illustrated by the expected unit cost reductions (between 12% and 63%) from observed study costs to costs at scale-up once the programme is fully integrated into existing services and run nationally. This study also highlight the importance of contextualisation of findings from standard one-year observational costing studies during pilot projects, and suggest that, when relevant, the estimation of costs at scale-up should always be provided in all costing studies.

Beyond results from our costing studies, papers 3 and 4 estimate the costs at scale to inform HIVST scale-up of HIVST programmes in southern and western Africa, using two distinct approaches: accounting cost function (in Côte d'Ivoire, Senegal, and Mali), and econometric cost function (in Malawi, Zambia,

Zimbabwe, South Africa, and Lesotho). These costs can, therefore, be used in national HTS budgeting and financial planning in these countries. In addition, they could potentially feed into mathematical models to better inform cost-effectiveness at scale-up [10].

Finally, the econometric cost functions presented in paper 3 identify key cost drivers of HIVST programmes in southern Africa. Major cost drivers were the scale of HIVST distribution, the type of community-based intervention, the percentage of kits distributed to men, the distance from implementer's warehouse, and the per capita GDP. These findings propose an alternative approach to programme costs estimation methods based on programme characteristics rather than the more conventional input-based calculation method. Although, this type of study will be limited to large scale programmes with a sufficient number of sites to allow for a robust statistical analysis.

b. Contribution to methods

This thesis has also made several important contributions to methods. A first contribution relates to our proposed frameworks for the fitting of cost functions based on the intended use of cost estimates (paper 1). Although these frameworks will go through a peer review before publication, and are therefore likely to evolve, they constitute, to my knowledge, the first attempt to provide a typology, and increase transparency in reporting, of cost functions in LMIC. I hope they can encourage the more consistent use of cost functions for financial planning and priority setting, particularly, related to mathematical modelling of cost-effectiveness, where the commonly used constant unit cost at scale has sometimes be found to be a source of bias in cost-effectiveness predictions [11-13]. Thus, variable returns to scale needs to be accounted for in cost projection methods. I also discuss how this concept can potentially be incorporated into cost functions, guiding the method selection based on the purpose of cost estimates with a focus on whether or not to consider constant or variable returns to scale.

A second contribution from this thesis is about raising the case for transparency related to the estimation of full and incremental costs of implementing HIVST presented in paper 2. Because HIVST is added onto the existing HTS as an alternative option to provider-delivered HTS, we estimated incremental costs where shared costs (such as operational costs) are fully allocated to the HTS programme, thus accounting only for the new inputs that were required by the new intervention [14, 15]. A full cost analysis estimates the costs of all resources used in running the HTS and HIVST programmes independently from each other. As I find significant difference in average HIVST costs (incremental: $14, full: $38), I stress the importance of transparency in reporting and communicating costing methods. Incremental HIVST costing, only considering financial costs, assumes that the existing intervention has the capacity (particularly human resources) to absorb the new intervention, so there is a risk to under budget and deplete the health system. On the other hand, if only presenting full costs, the intervention might be compared with other intervention incremental costs, and potentially be rejected as an efficient intervention. This should be carefully considered in similar studies and the scope of costing clearly presented in research papers and when presenting results to policy makers and financial planners.

Finally, paper 3 assessed the application of econometric cost functions for estimating costs at scale in southern Africa. I derived an empirical cost function for the estimation of HIVST costs at scale in our sample and out-of-sample countries of the region. I tested this function against Lesotho observed HIVST scale-up costs to inform on its external validity, with acceptable results. I also presented simplified models with similar prediction capacity. To my knowledge, this is the first study of the like, assessing the external validity of ECF-based cost projections and exploring simplified models for cost projections. These results have important methodological implications for developing more parsimonious cost prediction models less hungry of data that can, sometimes, be challenging to collect/estimate at site level. The review of cost functions reports that on average across all studies, ECF models use eleven regressors for cost predictions. Although the number of the regressors depends on many factors such as the type of statistical

model, sample size, the availability of data and quality of proxies used, our results suggest that considerations for model simplification can better extend the applicability of ECF findings to out of sample countries. Finally, more studies are needed to assess the external validity of ECF-based cost projections.

3. Limitations of thesis approach

I present in this section the major limitations of this thesis. Research papers limitations are discussed in more details in chapters 5 to 8.

Outcome measure for public health impact - HIVST kits distributed

The first limitation of the cost analyses presented in papers 2 and 4, is reporting unit costs per HIVST kit distributed without (or with partially) observed data linking the unit costs to numbers of new HIV case identified and those linked to care. 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 in paper 4, thus limiting our assessment of the public health impact of HIVST. In paper 2, I costed the entire HTS programme, allowing us to estimate the overall cost per HIV-positive case identified, however there are some gaps in our understanding of the impact of HIVST, e.g. I do not know how many of new HIV-positive identified had self-tested as this data was collected only at a later phase of the programme. This is an inherent challenge with the evaluation of HIVST due to the private nature of this testing modality and the need for confidentiality for specific end users such as key populations and their sexual partners.

Connecting the findings from the scoping review (Paper 1) with accounting cost function applications (Paper 4)

Another limitation of this thesis relates to our accounting cost function presented in paper 4. The development of the cost function review frameworks (paper 1) was not finalised by the time I was estimating and publishing ACF-based costs at scale in paper 4. Thus, the relatively simple ACF model presented in paper 4 could further consider variable returns to scale by cost input to improve the accuracy of model predictions according to the production theory. For example, costs related to vehicle operation and maintenance/transportation could be considered as inputs exhibiting decreasing returns to scale rather than constant returns to scale (currently considered) as the programme is being scaled-up to more remote areas. However, paper 4 found that the two main factors of cost variation at scale are the spreading of fixed costs over higher number of HIVST volumes (economies of scale), and the progressive withdrawal of the international partner organisation over time. Moreover, transport costs accounted for a small proportion of total costs (between 1% and 7%). So, I could assume that, in this case, accounting for decreasing returns to scale would have little impact on cost predictions. If I were to apply mathematical notations from Paper 1, I would first classify cost inputs as fixed/semi-variable/variable and by their expected ability to exhibit constant/variable returns to scale, estimate cost predictions, and run sensitivity analysis on assumed returns to scale. This would need to be assessed in more details in future studies.

Lesotho as a case study for cost projections at scale - Issue for generalisability of our findings to countries outside of sample

A third limitation of our analytical approach relates to using the country of Lesotho as a case study for assessing the external validity of our econometric cost function in paper 3. Lesotho has a geographical area just over 30,000 square kilometres and a total population of about 2 millions [16]. Although it has the

second highest HIV prevalence in the world at 22.3%, its estimated national population of PLHIV is among the smallest in the southern African region with 340,000 adult in 2019[17]. Planned HIVST kits distribution volumes in the country by the MoH National HIV Testing Strategy across all delivery models is around 521,000 kits for the period 2019-2022 [18]. Thus, the magnitude of scale-up might be more important in other countries and lead to higher costs falling above the range of costs that our cost function might be able to project. Although, this limitation is difficult to assess with the data we have, and is only speculative. The complexity of the operational scale-up might also be important to consider. Lesotho is composed of ten districts where the main implementer PSI had one to two fixed sites per districts. This model is, therefore, relatively simple. Other countries, might operate with more complex administrative structures, which might lead to lower or higher costs for HIVST intervention scale-up. As a result, although the cost function from paper 3 showed an acceptable external validity in Lesotho, it should be interpreted with caution if used for countries with radically different HIVST scale-up volumes, and different administrative structures. Nevertheless, Lesotho's relatively simple structure allowed good transparency on how the system was operating and the sources of costs. Moreover, it is the only country where we had the opportunity to observe HIVST scale-up over two years of implementation and access to detailed HIVST and HTS programme data.

Further characterising accounting versus statistical approaches for cost projections

Another limitation is related to not better characterising differences/similarities in cost projections obtained between accounting and econometric cost functions using the same data base. To my knowledge, only one study did use a combination of both projection models to estimate scenarios exploring Ethiopia's ability to finance its primary health care system [2]. One of their major assumption was that accounting cost functions potentially overestimate resource need because they are based on

normative costs and standards to provide primary care. Whereas, econometric cost functions underestimate the resources needed due to limited inclusion of capital investments, future changes in services offered among primary care facilities to meet changes in health needs, and future improvements that may be made in quality of services provided. The authors conclude that the best estimate of projected costs lies between these two projections. Possibly, health system demand side and supply side constraints and absorption capacity to operate efficiency could also have an impact on predicted costs [19]. Further research would be needed to further understand the functional forms for each methods, to better define their respective applications, as well as assessing their external validity. This is an area of further research that could be explored.

Considerations of the HIVST programme's cost-effectiveness

Another limitation might be related to the scope of this thesis. While I focused on methods for projecting costs at scale in LMIC and I used the HIVST intervention scale-up as a case study, I recognise that programme's cost-effectiveness is a prerequisite before scale-up. I report a study on the cost-effectiveness of the community-based HIVST intervention in Malawi, Zambia, and Zimbabwe [10]. In this study, cost-effectiveness was defined by an incremental cost-effectiveness ratio (ICER; cost-per-disability-adjusted life-year (DALY) averted) below US$500 over a time horizon of 50 years. Targeting adult men with HIVST had the greatest impact (averting 1500 HIV infections and 520 deaths per year) in the context of a simulated country with nine million adults, but it was only cost-effective if the programme was limited to five years or with undiagnosed prevalence above 3%. HIVST distribution to women having transactional sex was the most cost-effective. Interestingly, the main drivers of cost-effectiveness were the cost of the HIVST programme and the prevalence of undiagnosed HIV. Whereas a fixed unit cost was used in this study, it would be informative to assess how cost-effectiveness might change if we replaced a fixed unit

cost (used in this study) by a cost function. This is particularly relevant as we have been observing significant economies of scale for HIVST programme implementation in these countries [20].

Multi-country analyses and limited knowledge of the diversity of all local contexts

A challenge with multi-country/multi-region analyses is to ensure their relevance to the local context. I have been conducting field work in all the STAR and ATLAS countries since February 2016, and autonomous for the work in Lesotho. I was mainly based in London but I conducted field work in all countries. In some cases, this data was collected by my colleagues based locally. However, I was always involved in these analyses with different roles between countries - either coordinating the research study or supporting and leading data collection and analysis. All analyses have been conducted in close collaboration with local health economists since 2016, is continuing today, and they are all co-authors of the published work.

Economies of scope and restricted use of our scale-up cost estimates

Finally, it is important to note that the average cost per HIVST kit distributed varies depending on the other services it is delivered with [21]. I explored economies of scope in paper 2 when HTS and HIVST were delivered jointly, and where providers delivered services more cheaply (as defined by the number of HIV-positive case identified) through onsite reorganisation of staff activities. I also presented in this paper, full versus incremental cost and the importance of considering the service (and its costs) that HIVST is being added to, when making cost projections, for the purpose of budgeting for instance. In the econometric cost analysis (paper 3), one sample country delivered HIVST only (Zimbabwe), whereas others added HIVST to existing community-based HTS and/or activities distributing contraceptives and other health

products (Malawi, Zambia, South Africa, Lesotho). In Côte d'Ivoire, Senegal, and Mali, HIVST was added to existing community-based HTS programmes (paper 4). As a result, estimated costs at scale from papers 3 and 4 are only good HIVST cost estimates of a specific combination of services, i.e. when HIVST is being added to existing community-based sexual and reproductive health programmes. HIVST implementation and scale-up through radically different delivery channels such as public health facilities, or drugstores, should not use my cost estimates. This issue could be further explored if I expanded our data set to cost estimates through other delivery models and included a variables reflecting the type of model and the service that HIVST is delivered with, to account for potential economies of scope. But this would have brought important heterogeneity in my sample because of cross-country variation between delivery models – for example, facility-based models existed across various units for each site (OPD, VMMC, HTS, ART, TB, MNCH, etc.) in all countries. My sample of sites would also become too small for such analysis.

4. Strength of thesis approach

Research embedded in projects across southern and western African regions with the same coordinating team for six years

One of the strength of this thesis is that it was embedded into two research projects across southern and western African regions with the same coordinating team between 2015 and 2021 where the candidate was the field coordinator.

This unique opportunity ensured harmonised methods for data collection and analysis across all countries, reviewing and improving the analytical approach over the years, and gaining experience and perspective around HIVST implementation and scale-up in sub-Saharan Africa in strong partnership with various local collaborators. Multi-year and multi-country analyses allowed me to further explore research questions beyond costs and cost-effectiveness, such as programme maturing over time and implications for scale-

up cost projections, returns on investment of an integrated approach for HIVST, or empirical cost function application to out-of-project countries.

Moreover, research studies were conducted in the two world regions most affected by the HIV epidemic with diversity of HIV epidemiological settings – southern Africa with a generalised epidemic, whereas it is a concentrated epidemic among key populations in western Africa, ensuring the relevance of our empirical findings and expanding the application of scale-up cost projection methods to diverse epidemiological settings.

As I was extremely lucky to do this PhD degree part-time as a research fellow and field coordinator, a significant added value to this thesis is my learning experience in large scale research project management and coordination of field work, as a complement to more academic skills.

Use of cost estimates and cost projection methods in the National HTS Operational Plan in Lesotho 2018-2023

Another strength to this thesis is the opportunity of the candidate to work as a consultant for The Global Fund and the Ministries of Health and Finance of Lesotho, to cost the National HTS Operational Plan for the revised National HTS Strategy of Lesotho for the period 2018-2023. The consultancy was done in February-March 2019 at the beginning of the PhD research.

In brief, the work consisted in costing the different activities, at national and sub-national levels, required to implement recommended activities from the Operational Plan developed by another consultant. In particular, one major activity was the implementation and national scale-up of HIVST as a complementary testing modality.

The consultancy provided to the candidate pragmatic approaches to translate research data from the STAR project into practical information for country financial planning. In particular, I would apply a full costing approach for the HTS programme, and then use a simple cost multiplier method to HIVST incremental costs, ensuring the appropriate cost estimate (incremental versus full) is applied for the relevant implementation strategy (addition of HIVST to existing fully funded HTS programme). In this case, I would account for the spreading of fixed costs at scale-up generating some economies of scale, but I would be cautious when considering variable returns to scale (in particular increasing returns to scale) to ensure I am more at risk of overbudgeting rather than underbudgeting the programme.

This experience also influenced the research approach throughout the thesis when developing methods to project costs at scale with a focus of keeping simplicity and transparency in methods when appropriate and more complex approach when critical, depending on the use of cost estimates for budgeting, financial planning, or for priority setting in a research context.

Considering intervention uptake to inform HIVST programme scale up

Although the focus on this thesis is on methods to inform the supply side of health interventions, there is no successful implementation and scale-up without considering the demand side of it [19].

Before and during the PhD degree, I conducted discrete choice experiments (DCE), a quantitative method for assessing the relative strength of preferences of potential users for various HIVST delivery models and linkage to care/prevention strategies [22]. These DCE were conducted in Malawi, Zambia, and Zimbabwe between 2016 and 2019 [23-25].

In the most recent DCE conducted in Zimbabwe, published in January 2019 presented in Appendix V of this thesis (the candidate is co-first author), I explore the impact of HIVST service characteristics on uptake

along the testing cascade to understand potential users' perspectives [25]. I found that free HIVST distribution by local volunteers and immediately available antiretroviral therapy were the strongest relative preferences identified. Moreover, successful HIVST scale-up should accommodate linkage to confirmatory testing preferences, notably ensuring efficient provision of antiretroviral therapy, could facilitate "resistant testers" to test while maximizing uptake of post-test services.

Although not considered in the current thesis work, this additional piece of research could further inform research on how to include potential users' preferences into models of cost projections to anticipate variation of resource needs and ensure effective scale-up of the HIVST programme, potentially based on specific sub-group preferences such as men, young people, or those who never tested for HIV, or based expected uptake of differentiated HIVST delivery models within a national implementing strategy.

5. Implications for research

Future research on HIV self-testing and the rise of self-care

HIVST is a promising approach to close the first 95 HIV testing gap and, since March 2021, WHO is now urging countries to fast-track implementation and scale-up of HIVST in Asia and the Pacific [26]. Our donor UNITAID with the STAR Initiative and ATLAS project has provided catalytic investment for implementation of HIVST to reach untested populations. Such funding will need to continue and expand, complemented by domestic funding to support the scale-up of effective approaches. In the context of the COVID-19 pandemic, countries also need to modify service delivery models by using online digital platforms and social media tools which may increase demand for HIV testing for key populations. More implementation research will be needed to inform these innovative and integrated service delivery approaches.

Beyond HIVST, self-care is on the rise with WHO first consolidated guidelines on self-care interventions for sexual and reproductive health and rights published in 2019 [27, 28]. Tools currently available are for fertility management, contraception, and diagnosis of sexually transmitted infections [29]. Self-care interventions can help for reaching universal health coverage, however, evidence on their costs, cost-effectiveness and financing is still very limited in LMIC. More research is also needed to inform on the delivery of efficient and equitable self-care interventions [30].

Use of cost functions versus constant unit cost depending on relevance and policymakers' interest

Unit costs are function of inputs and outputs, they vary by the level and the scope of service provision, both time-dependent[21]. Thus, in most cases, the average cost function for a service cannot be characterized using a single unit cost value, and doing so might lead to biased estimates in programme planning and priority setting. Yet, in most cases, because of its simplicity and transparency, single unit costs are commonly used in budgeting, short-, medium-, long-term financial planning, and in economic evaluations for priority setting. Recent studies have raised the importance of further understanding the functional form of the cost function used in transmission dynamic models and its impact on the magnitude and shape of costs when outputs and coverage are increasing [11-13]. My frameworks presented in paper 1 attempt to further inform the choice and fitting of cost functions better accounting for variable returns to scale.

Each cost functions presented in this thesis is different by design, so, the way I can analyse projected cost estimates will also vary. Simple cost multiplier do not provide any insight on cost variation at scale. ACF can show that scaled up programme costs can exhibit high proportion of fixed costs implying that average cost is highly dependent of the level of output, and that unit cost composition will vary at scale. On the contrary, ECF do not inform on the cost composition of the unit cost. The choice of the cost projection

method should account for areas of interest to the policymaker such as the need for additional resources, the impact assessment of programme constraints and enabling factors on scale-up costs. For instance, the choice of regressors for ECF can be based on characteristics of the population reached (men), environmental factors (urban/rural), programme design (provider team size on site) that are of interest for an effective scale-up. If using ACF, the financial impact of programme characteristics of interest for scale-up can be integrated in the model structure, such as transition from international to local governance, re-training of health providers, or supplies bulk purchasing.

In summary, I have shown that the choice of cost functions to project costs should account for the intended use of cost estimates and the characteristics of the intervention being evaluated. Factors to consider for method selection are (1) the policymaker's interest for assessing constant or variable return to scale and whether there is information on the expected functional form of the scale component, (2) the interest for the variation of cost composition during scale-up (fixed/variable and cost inputs), (3) the intervention level of analysis, (4) the determinants of scale-up costs and whether they are related to contextual determinants (e.g. characteristics of the population reached, epidemiological or socio-demographic factors – as presented in paper 3), and/or to programme design (e.g. withdrawal of international organisation as presented in paper 4), and (5) the expected magnitude of scale-up. These considerations should inform costing studies design for cost data collection and analysis with the aim of using cost functions that are the most relevant to the policymaker research questions.

Scaling up and scaling out key HTS programmes

Another area that would warrant further research relate to the concept of *scaling out*. While scaling-up is about expanding the same intervention at bigger scale, scaling-out is about expanding its coverage to new target populations. Typically, a programme is designed on the basis of trials and demonstration

programmes on relatively small scales and then scaled up to cover a large population. The marginal cost of adding an extra place could be compared to the marginal cost of adding another target population or increasing the coverage. My findings from paper 3 suggest that ECF approach works for estimating costs of scaling up, further research would need to assess to which extent it can be applied to scaling out.

Innovative approaches with secondary distribution of HIVST kits by patients attending clinic services to their hard-to-reach partners are promising and could improve the rate of HIV diagnosis [31]. In 2021, they are focusing on women receiving antenatal care, people newly diagnosed with HIV (i.e. index patients), and key populations, but the epidemiological and economic impact of expanding the range of potential recipients for secondary distribution (drugstore, bars, etc.) or designing a more efficient combination of secondary HIVST distribution models still need to be further understood.

Moreover, with limited resources, a global priority is about finding effective ways to diagnose the remaining PLHIV who do not know their status. A study published in the Lancet in 2021, reviewed existing risk-based tools - *a set of criteria to either identify high-risk individuals for HTS who would not otherwise be offered a test ("screen in") or exclude people from a routine offer of a test ("screen out")* – and argue that they could significantly improve the efficiency of HIV testing services [32]. Balancing key interventions scale up and scale out might, therefore, become in the coming years one of the key economic consideration in designing successful and efficient HTS strategies for reaching UNAIDS 95 targets, and achieving HIV epidemic control.

6. Implications for policy

The need for effective strategies for linkage to HIV confirmatory testing and care alongside HIVST implementation models

This thesis demonstrated that HIVST can reach people who would otherwise not test, in particular men, young people, and key populations (FSW, MSM, and PWUD). Paper 2 also highlighted the importance of HIVST integration strategies that enhance linkage to HIV confirmatory testing, prevention and care services in order to measure the impact of HIVST. Indeed, Lesotho is an example of successful promotion of onsite HIVST - facilitating immediate linkage to confirmatory testing and ART initiation - while increasing the overall efficiency of the HTS programme in combination with index testing activities. Although this strategy might not work as effectively elsewhere because of Lesotho unique context of high HIV prevalence, this study suggests that HIVST integrated approaches tailored to specific country HIV testing landscape can implement effective linkage strategies following HIVST.

Although linkage to confirmatory HIV testing and care, and prevention strategies has been a concern since the early HIVST implementation phase [23, 25, 33-36], measuring linkage to HIV treatment, care and prevention services still remain a challenge in LMIC. Concerns about monitoring linkage have kept several national HIV programmes from making HIVST available in some countries. A recent article published in the *Journal of the International AIDS Society* provides some insights into pragmatic measures for assessing linkage to HIV treatment services following HIVST in low-income settings [37]. These include monitoring ART initiations at treatment centres before and during HIVST distribution, including questions in clinic registers to ascertain whether clinic testing was prompted by prior HIVST use, population-based surveys, digital tools, and individual-level follow ups.

Informing country HTS budgets and financial planning

Another policy implication of this thesis is about translating results from research studies into data for country budgeting and financial planning. As highlighted in papers 2 and 4, the project life phase is likely to affect estimated average costs. For instance, it can be related to programme learning and maturing over time as observed in Lesotho (paper 2), or related to the withdrawal of the international partner Solthis following a progressive integrated implementation strategy (paper 4), both having significant effects on average costs. So, contextualising costing study results in pilot phases is necessary for the estimation of unbiased resource needs. I recommend for costing studies to also inform how these costs are likely to change at scale based on country operational plans.

With the example of the budgeting of the Lesotho Operational Plan for the revised HTS National Strategy 2018-2023 using the STAR data from the candidate, most of the cost data produced with this thesis can inform country HTS budget and the economic considerations around HIVST integration into existing HTS delivery services. When considering translating research data into financial information for country planning, I also aimed to propose frameworks in paper 1 that would increase the transparency of the cost function methodologies and adjust the level of complexity in cost estimation methods to the policy need (also discussed in paper 3), in order to facilitate data sharing between different actors.

However, a major challenge that I had throughout both STAR and ATLAS projects was the use of research results by financial planners, mostly related to the timeliness of having this information available from the researchers, and potentially related to a lack of communication between researchers and country planning financial teams. This is an area that might require additional preparation when conducting similar studies, i.e. on how to set up more timely data sharing processes around research results from the beginning, and throughout the project.

7. Conclusions

This thesis expands the existing knowledge on economic considerations for predicting the costs of scaling up promising health interventions in LMIC, by proposing improved methods, using community-based HIVST distribution programmes scale-up in southern and western Africa as a case study. This thesis applied accounting and econometric cost function methods to model the scale-up of STAR and ATLAS interventions. We show that these methods have wide applications for priority setting, budgeting, or financial planning. Our findings also suggest that they can be applied to various settings, that they present acceptable external validity, and that they were successfully applied to guide HIVST scale up in sub-Saharan Africa.

Self-testing for HIV, as well as self-care in sexual and reproductive health more broadly, offers convenience to the users and privacy in dealing with their own health. It also creates the need for better implementing linkage programmes into prevention and care, in particular with the role of digital health. Further research needs to inform the design of equitable, effective, and cost-effective linkage programmes as entry points into the health care system beyond the traditional health facility.

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Appendices to thesis

Appendix I – Economic cost analysis of door-to-door community-based distribution of HIV self-test kits in Malawi, Zambia and Zimbabwe. Mangenah et al.

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Student ID Number	1805320	**Title**	Mr
First Name(s)	Marc		
Surname/Family Name	d'Elbée		
Thesis Title	Estimating healthcare costs at scale in low- and middle-income countries – the case of community-based HIV self-testing scale-up in southern and western Africa		
Primary Supervisor	Prof 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?	Journal of the International AIDS Society		
When was the work published?	January 2019		
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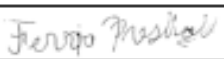
Supervisor Signature	
Date	19/08/21

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 (339 words)

Introduction:

HIV self-testing (HIVST) is recommended by the World Health Organization (WHO) 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 (M&E) data were used to estimate total economic and unit costs of HIVST distribution, by input and site. Inputs were categorised into a start-up, capital and recurrent costs. Sensitivity and scenario analyses were performed to assess the impact of key parameters on unit costs.

Results:

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. Average cost per HIVST kit distributed was US$8.15, US$16.42 and US$13.79 in Malawi, Zambia, and Zimbabwe, respectively, with pronounced inter-site 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 programs show large potential, both for reaching untested populations and for substantial economies of scale as HIVST programs 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.

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.

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 with living with HIV (PLWH) remain undiagnosed (1). UNAIDS has set global targets for 90% of PLWH to know their status, 90% of known HIV-positives to be on ART, and 90% of those on 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, either alone or with someone they trust. The World Health Organization (WHO) 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 (RDTs) currently used for HIV testing in Africa (7). Though 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 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).

Methods

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 Supplement 1. 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 are published elsewhere (11).

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 (5,500– 82,581)	18,266 (7673– 50,094)	3,196 (549– 6,699)	(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	(12)
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-$9.24)	$4.24 ($2.49-$6.24)	$8.79 ($3.38 -$21.51)	(12)

Table 2: Overview of door-to-door community-based HIV self-testing delivery models

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 HIV self-testing 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 4-6 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: enquire whether it had been used, pick up the used kit, and disclosed non-reactive HIVST: referral to *VMMC* 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: enquire whether it had been used, pick up the used kit, and disclosed non-reactive HIVST: referral to *VMMC* 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 1-2 weeks post HIVST kit distribution. confirmatory HTS plus Family planning, Blood Pressure checks, and CD4 count when available 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: at all intervention sites.	Specially designed and locked drop-boxes were used to return used self-test kits, located: at each facility, and local community public areas.	Specially designed and locked drop-boxes, located: at CBDA's homestead, each health facility and 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 (4-6 weeks) US$50 with a maximum of 100 kits per distributor, and Per HIVST client linking to any PSI outreach service: $0.20 in half of the evaluation clusters.

CBDA: community-based distribution agent; MWK: Malawi Kwacha, ZMW: Zambian Kwacha;

Costing Methods

We estimated the full economic cost of delivering HIVST within the CBDA model from the providers perspective, following international costing guidelines (13). 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 $ inflation rate (14-16).

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 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 allocation factors. Table A1 presents how each allocation factor was applied to in input type. Further detail of the definitions of project phase and inputs can be found in Supplement 2.

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 as well as 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.

Sensitivity analysis

We undertook a series of one-way sensitivity analyses to assess the impact of key cost assumptions on the unit cost 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 (14-16). We further evaluated the impact of applying alternative allocation factors, i.e. 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 2.5-7.5 years (base case is five years) to assess impact if the project goes on for shorter or longer than assumed.

Scenario analysis

In anticipation of planned program 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) (12). 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 (12), we also present costs without above site-level costs and start-up.

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, monitoring and evaluation 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.

Results

Community-based distribution model program 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, and 139, and 1,009 CBDAs, respectively. The average number of HIVST kits distributed was 12,538 (range: 4,556-42,134) across 11 sites in Malawi, 7,206 (range: 1,758-20,450) across 16 sites in Zambia and 2,124 (range: 319-4,201) across 44 sites in Zimbabwe, where distribution was intentionally restricted by campaign duration (Appendix table A2). Nearly half (49%, 51% and 43%, respectively) of the HIVST kits were distributed to men.

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, 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. Though 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).

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 (12): 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-$9.24), $4.24 ($2.49-$6.24) and $8.79 ($3.38-$21.51) in Malawi, Zambia and Zimbabwe, respectively.

Figure 1: HIVST costs per HIVST kit distributed by site and quantity in 2017 US$

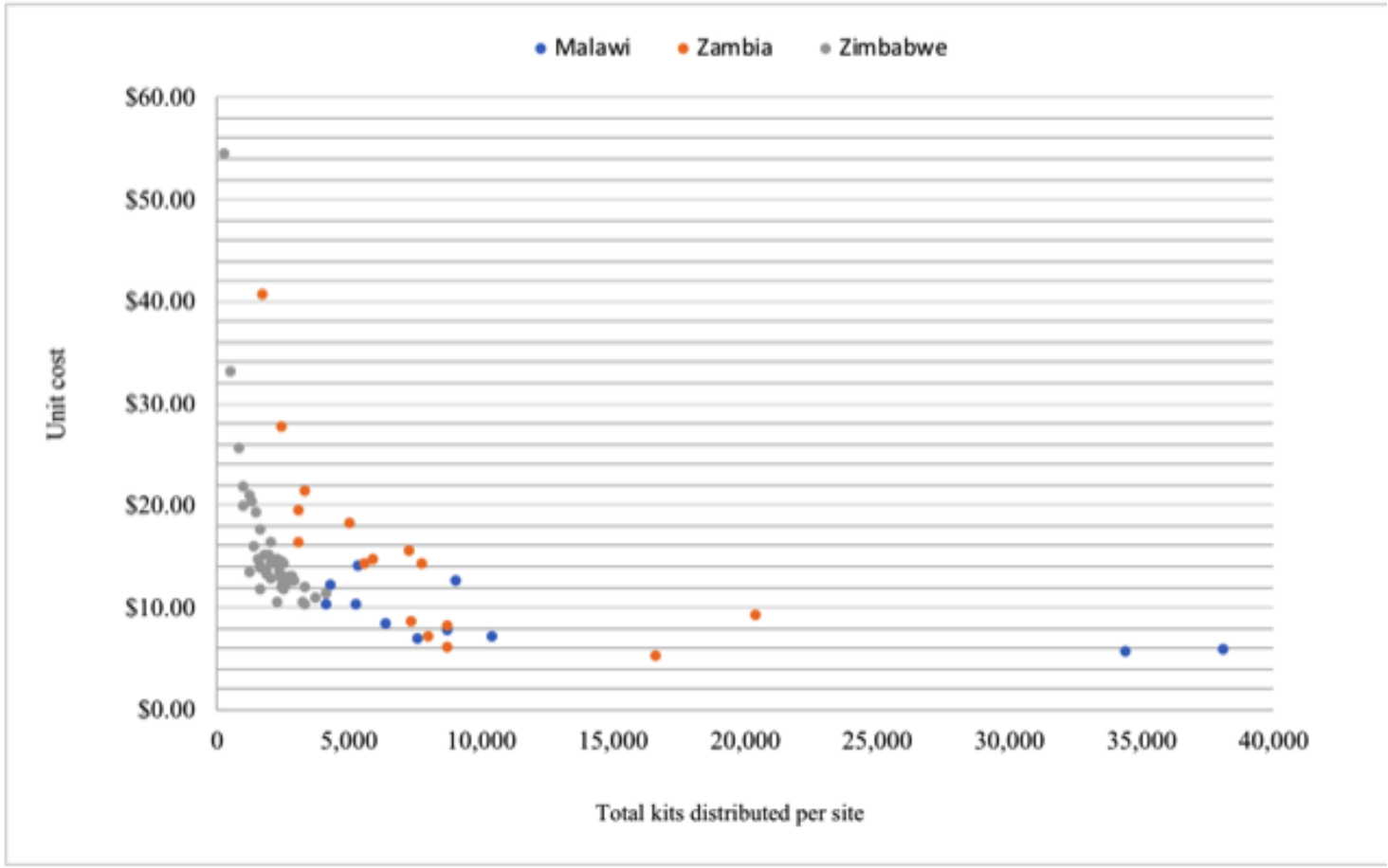


Table 3: HIV self-test kit distribution cost breakdown and key cost contributors (in 2017 US$)

	Malawi **kits distributed: 152,671** 12 months: June 2016 – May 2017		**Zambia** **kits distributed: 103,589** 11 months: July 2016-May 2017		**Zimbabwe** **kits distributed: 93,459** 10 months: August 2016-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%
Sensitisation	$58,485.72	5%	$58306.8	3%	$2,694.30	0%
Start-up other	$108,409.87	9%	$84,745.15	5%	$75,942.83	6%
Capital costs						
Building & storage						
Central	$16,755.33	1%	$54077.43	3%	$3,266.62	0%
Warehouse	$-	0%	$-	0%	$-	0%
Site level	$-	0%	$-	0%	$-	0%
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%	$-	0%	$-	0%
Other Capital	$-	0%	$-	0%	$35.14	0%
Total Costs (capital and start-up)	$226,153	18%	$241727	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 & transport	$109,240.41	9%	$148117.37	9%	$57,396.14	4%
Building operation/maintenance		0%				
Central	$2,204.87		$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	$-	0%	$-	0%	$554.89	0%
Other recurrent	$120,607.08	10%	$75,671.83	4%	$20,414.02	2%
Total costs (recurrent)	$1,017,787	82%	$1,459003	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	

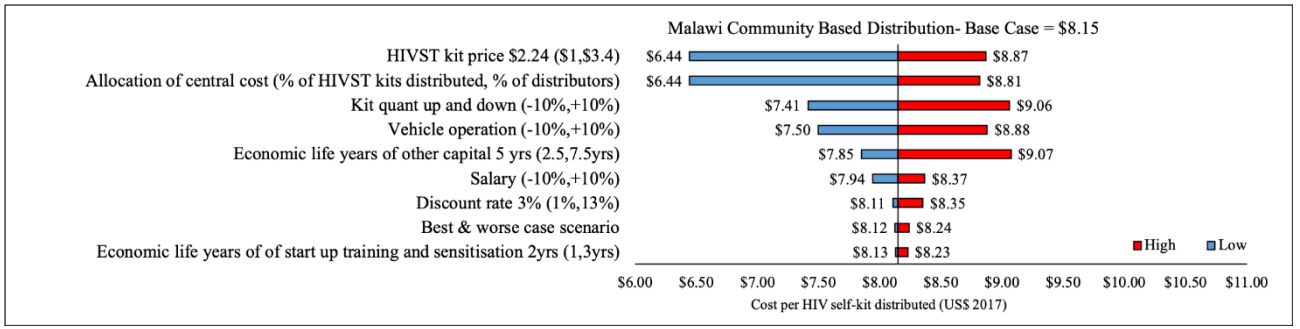
Note that totals have been rounded to the nearest US$.

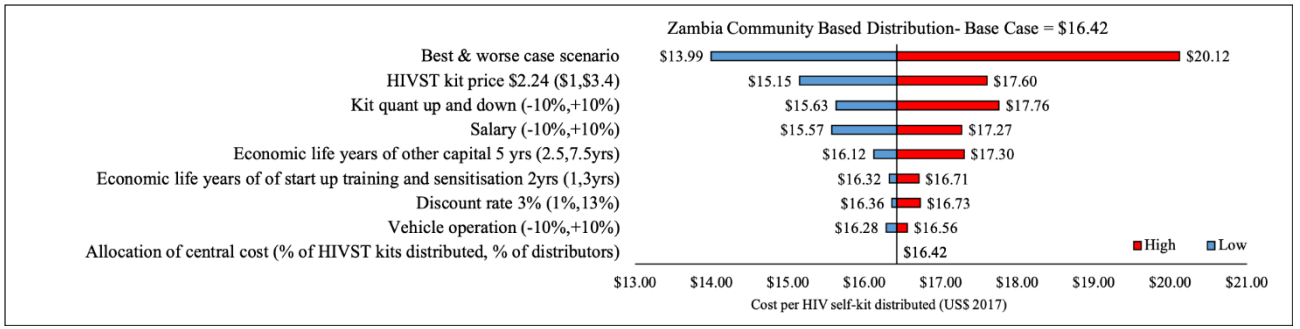
Sensitivity and scenario analysis

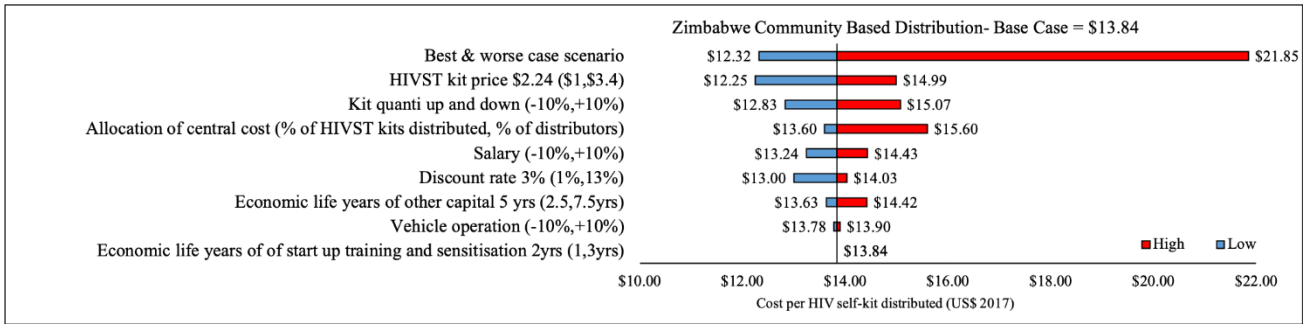
Figures 2a, 2b and 2c show results from the univariate sensitivity and scenario analyses by country. Our unit costs per HIVST kit distributed remained robust when key cost parameters were varied. Varying life of start-up training and sensitization between one and three years resulted in costs of US$7.85 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 4-6 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% 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 $6.14, $13.99 and $12.32 per kit distributed whereas the worst case scenario was $10.27, $20.12 and $21.85 per kit distributed.

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







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 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.

Though 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 $8.84 for men [the user costs reported above and the provider costs as reported by Mwenge et al. (12). This is comparable with our observed HIVST societal costs (excluding start-up and above service level costs: $6.67) in Malawi. Thus, HIVST may provide for unmet testing needs among 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 -US$36.93) (19, 20). While we did find that CBDA delivered HIVST under this early demonstration and research programs were more costly than facility-based HIV testing (12, 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, whilst only 26%-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 programs 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, HIV self-testing. 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. Firstly, 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. Secondly, 10-20% of the costs were start-up and initial capital costs, which would decrease as services mature. Thirdly, 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 sensitisation 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. Further, 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.

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-positives 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 utilisation. However, previous work has not only shown

high uptake of HIVST but also high levels of kit utilisation by recipients (4). Key strengths of this cost analysis are the estimation of costs across 71 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.

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, i.e. 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.

Conclusion

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%-37% for facility HIV testing.

Competing interests

The authors have no conflicts of interest to declare.

Authors' contributions

CM, LM, LS, NA, MD, HM, FTP conceptualised and designed the study.

CM, LM, LS, NA, PC, TC, SK collected and facilitated the collection of data.

CM, LM, LS, NA, PC, TC, SK, MD, JJO, HM, 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, FTP drafted the manuscript and revised it critically.

MM, MN, RC, PI, ELS, MNE, GN, OM, KH, CJ, HA, ELC, FC, HM, 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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List of abbreviations

CBDA	-	Community-based distribution agent
COMREC	-	Malawi College of Medicine Research Ethics Committee
CRT	-	Cluster-randomized trials
HIVST	-	HIV self-testing
LSHTM	-	London School of Hygiene and Tropical Medicine
HTS	-	HIV testing services
M&E	-	Monitoring and evaluation
MRCZ	-	Medical Research Council of Zimbabwe
MWK	-	Malawian Kwacha
PHC	-	Primary health clinics
PSI	-	Population Services International
SFH	-	Society for Family Health
UCL	-	University College London
UNZAREC	-	University of Zambia Biomedical Research Ethics Committee
US$	-	United States Dollar
WHO	-	World Health Organization
ZMW	-	Zambia Kwacha

Supplement 1: Narrative description of the CBDA models across countries

Malawi

In Malawi, the CRT was conducted in rural areas of Blantyre, Machinga, Mwanza and Neno districts in Southern Malawi and comprised a total trial population of approximately 62,500 residents. Catchment populations of 22 public rural primary health clinics (PHCs) were randomized 1:1 to either HIVST or standard of care. In the 11 HIVST intervention communities, residents had access to CBDA delivered HIVST over a continuous 1-year period (June 2016 to May 2017). CBDAs were paid an incentive of United States Dollar (US) $0.15 [100 Malawi Kwacha (MWK)] per kit distributed. This was integrated into their regular activities distributing contraceptives and other health products. In all sites, residents could access free HTS and ART if HIV-positive, through the PHCs.

Zambia

In Zambia, residents across 16 rural community sites had access to CBDA delivered HIVST over a continuous 1-year period (July 2016 to June 2017), reaching a total target adult population of 416,294 across Ndola, Kapiri, Lusaka and Choma districts. In this hub and spoke model CBDAs were linked to specific clinics and worked in their surrounding catchment populations. CBDAs were initially paid a monthly allowance of US$78 [750 Zambia Kwacha (ZMK)] independent of performance; this was later supplemented by a US$0.21 (2 ZMK) incentive per used kit returned. Though only six sites were included in the CRT, costs were evaluated for all 16 sites.

Zimbabwe

In Zimbabwe, the CRT was conducted across eight rural district sites with a total trial population of approximately 224,116 residents. Forty-four geographically defined wards were randomized 1:1 to either linkage intervention (HIVST plus distributor incentive for linkage events) or control (HIVST with fixed distributor allowance) clusters. HIVST was delivered across sites through one-off 4-6 week campaigns, moving sequentially from one district to the other between August 2016, and May 2017. In each district, new CBDAs were recruited and trained for three days. CBDAs then each distributed a specific number of tests proportional to their confined catchment area. Each CBDA was equipped with a tablet to demonstrate how to conduct a self-test through a video and to collate data on each self-tester.

At one to two weeks following HIVST distribution, the routine PSI mobile outreach service offered HIV confirmatory testing for individuals with reactive HIVST test result and HIV treatment referral to public sector health facilities for individuals with confirmed HIV positive results, including other services such as family planning and screening for non-communicable diseases. All CBDAs received a fixed allowance of USD$50, with an additional US$0.20 incentive for those in the linkage intervention arm per HIVST positive tester who linked for post-test services at PSI mobile outreach services. There was no compensation given to HIV negatives linking to post-test services. We estimated the cost of HIVST distribution in both intervention and –control sites. The cost of providing confirmatory testing at outreach services is not included in this study, for consistency across countries.

Supplement 2: Definitions of cost category and cost inputs and allocation factors

Start-up costs, including the costs incurred in providing training and sensitization activities, and all costs incurred during the period of intervention design and preparation to first distribution were treated as a capital cost as benefits of such investments would be expected to accrue to programmes over longer periods. Start-up costs were assumed to have a useful life of two years to reflect the lifespan of the STAR implementation.

Recurrent costs included the cost of personnel, HIVST kits and project operational activities which included vehicle operation costs such as fuel, insurance and maintenance for vehicles, building operations and maintenance, recurrent training, waste management costs and utilities. Building space included provider office space, warehouses and storage space at health facilities within distribution communities. Building operation and maintenance costs included rentals, utilities such as electricity and water, building insurance and security. Supplies included HIVST branded satchels, t-shirts, and hats, surge protectors, laptop bags, and power packs. Other supplies included office stationery such as bond paper, printer cartridges, first aid kits, envelopes, maps and pens, cellphone credit/airtime and internet data as well as utensils and office snacks and teas. Other recurrent costs included indirect expenses such as consultancies, office repairs and office fuel expenses.

Table A1: Cost allocation factors across the interventions by cost input type

Cost input type	Allocation factors to site level		
	Malawi	Zambia	Zimbabwe
Training	% of distributors	% of distributors	% of distributors
Sensitization	% of communities within the site	% of direct expenditure	% of direct expenditure
Other Start-up	NA	% of HIVST kits distributed	% of HIVST kits distributed
Building and storage			
Central	% of direct expenditure	% of direct expenditure	% of direct expenditure
Warehouse	% of HIVST kits distributed	% of HIVST kits distributed	% of HIVST kits distributed
Site level	% of direct site level expenditure	% of direct site level expenditure	% of direct site level expenditure
Equipment			
Central equipment	% of direct expenditure	% of direct expenditure	% of direct expenditure
Site level	% of direct site level expenditure	% of direct site level expenditure	% of direct site level expenditure
Vehicles and bicycles		NA	NA
Other capital	% of HIVST kits distributed	% of HIVST kits distributed	% of HIVST kits distributed
Personnel	% of distributors	% of distributors	% of distributors
HIVST Kits	% of HIVST kits distributed	% of HIVST kits distributed	% of HIVST kits distributed
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			
Central	% of direct expenditure	% of direct expenditure	% of direct expenditure
Warehouse	% of HIVST kits distributed	% of HIVST kits distributed	% of HIVST kits distributed
Site level	% of direct site level expenditure	% of direct site level expenditure	% of direct site level expenditure
Waste management	NA	NA	% of HIVST kits returned
Other recurrent	% of HIVST kits distributed	% of HIVST kits distributed	% of HIVST kits distributed

Table A2: Site level Total & Unit costs of HIVST and Facility based testing

Country	Site number	Total HIVST kits distributed	Total intervention cost (Full)	Full Cost / kit distributed	Recurrent $ / pp tested*	Nearest facility HTS $ / pp tested (12)
Malawi						
	1	9,329	$89, 358.48	$9.58	$5.26	$4.05
	2	4,556	$53,387.87	$11.72	$5.72	$3.86
	3	9,184	$88,055.20	$9.59	$5.15	-
	4	7,731	$66,691.09	$8.63	$4.76	-
	5	42,134	$303,251.49	$7.20	$4.52	$3.16
	6	29,941	$231,897.62	$7.75	$4.61	$4.68
	7	6,292	$107,209.07	$17.04	$7.52	$3.04
	8	9,922	$133,192.52	$13.42	$6.81	$2.96
	9	7,176	$70,874.51	$9.88	$5.19	$5.38
	10	4,608	$61,093.47	$13.26	$6.81	$5.81
	11	7,042	$64,378.23	$9.14	$4.77	
Zambia						
	1	5,587	$105,822.48	$18.9	$11.61	-
	2	7,370	$101,485.07	$13.8	$7.79	-
	3	3,113	$81,341.94	$26.1	$15.71	$6.15
	4	3,090	$61,563.63	$19.9	$12.11	$3.87
	5	20,450	$161,774.90	$7.9	$6.40	-
	6	8,029	$76,522.03	$9.5	$7.38	-
	7	8,759	$93,243.83	$10.6	$8.40	-
	8	8,768	$70,206.19	$8.0	$6.44	-
	9	7,752	$158,721.75	$20.5	$10.17	-
	10	1,758	$87,921.17	$50.0	$26.50	$2.64
	11	5,030	$130,696.73	$26.0	$13.36	-
	12	7,270	$157,551.93	$21.7	$10.88	-
	13	4,902	$116,784.17	$23.8	$13.62	-
	14	2,452	$81,773.42	$33.3	$20.42	$2.49
	15	5,895	$121,294.01	$20.6	$11.70	-
	16	3,364	$90,732.00	$27.0	$15.75	$3.64
Zimbabwe						
	22	3,353	$39,960.07	$11.92	$8.73	$4.95
	23	2,891	$36,484.04	$12.62	$9.27	-
	24	2,197	$31,258.24	$14.23	$10.50	-
	25	1,966	$29,505.61	$15.01	$11.09	-
	26	1,041	$22,542.09	$21.66	$16.17	$6.85
	27	578	$19,065.95	$32.98	$24.81	-

28	2,551	$33,137.68	$12.99	$9.53	$4.97
29	2,123	$30,787.85	$14.50	$10.71	$10.49
30	1,633	$28,669.79	$17.56	$13.10	$4.99
31	2,941	$37,059.67	$12.60	$9.25	$3.87
32	2,791	$36,302.63	$13.01	$9.57	$2.30
33	4,201	$46,958.62	$11.18	$8.16	-
34	2,564	$29,747.30	$11.60	$8.50	$34.78
35	1,646	$22,668.12	$13.77	$10.17	$4.56
36	2,452	$29,125.78	$11.88	$8.71	$6.79
37	2,616	$31,896.61	$12.19	$8.98	$2.74
38	1,647	$23,078.31	$14.01	$10.36	$9.05
39	1,931	$25,845.10	$13.38	$9.89	$8.90
40	3,732	$40,450.67	$10.84	$7.91	$5.52
41	1,403	$22,161.10	$15.80	$11.71	$3.01
42	2,029	$28,873.18	$14.23	$10.55	$7.17
43	1,806	$27,092.58	$15.00	$11.15	$2.54
44	1,002	$19,877.25	$19.84	$14.85	$3.18
45	2,489	$31,729.73	$12.75	$9.39	$3.90
46	1,277	$17,065.84	$13.36	$9.89	$5.25
47	3,388	$34,511.24	$10.19	$7.44	$4.15
48	2,320	$24,299.61	$10.47	$7.64	$11.49
49	1,696	$19,847.36	$11.70	$8.59	$5.11
50	1,332	$27,025.41	$20.29	$15.24	$11.61
51	1,485	$28,640.85	$19.29	$14.47	$12.41
52	1,240	$26,020.07	$20.98	$15.77	$9.29
53	2,030	$33,007.35	$16.26	$12.12	$13.94
54	319	$17,366.19	$54.44	$41.49	$11.97
55	893	$22,739.56	$25.46	$19.21	$20.93
56	3,240	$34,106.23	$10.53	$7.65	$4.06
57	2,521	$30,200.13	$11.98	$8.79	$4.06
58	1,946	$25,541.65	$13.13	$9.66	$5.71
59	2,353	$31,612.65	$13.44	$9.96	$4.28
60	1,613	$23,754.33	$14.73	$10.91	$4.23
61	2,071	$26,507.47	$12.80	$9.41	$4.08
62	2,313	$33,854.68	$14.64	$10.79	$3.97
63	2,448	$35,059.27	$14.32	$10.56	$4.17
64	2,875	$37,380.71	$13.00	$9.54	$4.08
65	2,516	$35,870.54	$14.26	$10.51	$4.22

* (Excludes start-up and training and above site level costs)

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Appendix II – ALTAS Costing Protocol

ATLAS – AutoTest VIH – Libre d'Accéder à la connaissance de son Statut VIH

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SUB-STUDY ON THE COSTS OF IMPLEMENTING HIV SELF-TESTING

IN COTE D'IVOIRE, MALI and SENEGAL

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Abbreviations

AF: Allocation Factor

AHF: AIDS Health Foundation

ANC: Antenatal Clinic

CITC: Client-Initiated HIV Testing & Counselling

DHIS2: District Health Information System 2

FP: Family Planning

HIVST: HIV Self-Testing

HTS: HIV Testing Services

ICER: Incremental Cost-Effectiveness Ratio

IEC: Information, Education and Communication

LOE: Level Of Effort

LOP: Life Of the Project

LSHTM: London School of Hygiene and Tropical Medicine

M&E: Monitoring and Evaluation

MNCH: Maternal Neonatal Child Health Services

MoH: Ministry of Health

NCD: Non-communicable disease

NGO: Non-Governmental Organization

NIAID: National Institute of Allergy and Infectious Diseases

NSF: National Strategic Framework

PITC: Provider-Initiated HIV Testing & Counselling

PMTCT: Prevention of Mother-To-Child Transmission

PreP: Pre-exposure Prophylaxis

PSI: Population Services International

RDT: Rapid Diagnostic Test

STAR: HIV Self-Testing AfRica

TAG: Technical Advisory Group

TB: Tuberculosis

UNAIDS: The Joint United Nations Programme on HIV/AIDS

VMMC: Voluntary Medical Male Circumcision

WHO: World Health Organization

Project summary

Full title: Research components integrated in ATLAS (autotest VIH, libre d'accéder à la connaissance de son statut VIH) program in West Africa

Short title: ATLAS · Research

Funding: Unitaid

Scientific coordination : Joseph Larmarange, Institut de Recherche pour le Développement

Principal investigators :

Marie-Claude Boily, Imperial College London

Alice Desclaux, Institut de Recherche pour le Développement

Joseph Larmarange, Institut de Recherche pour le Développement

Dolorès Pourette, Institut de Recherche pour le Développement

Fern Terris-Prestholt, London School of Hygiene and Tropical Medicine

Countries: Côte d'Ivoire, Mali, Sénégal

Presentation of ATLAS program:

Coordinated by Solthis NGO, the ATLAS programme aims to promote and deploy HIV self-testing in three West African countries (Côte d'Ivoire, Mali, Senegal). Over the period 2019-2021, in close collaboration with the national AIDS programmes/councils of the three countries, ATLAS plans to provide 500,000 HIV self-tests through ten delivery channels combining fixed and advanced strategies and primary and secondary distribution of HIV self-tests.

Taking into account West African epidemiology, the main targets of the ATLAS programme are key populations (sex workers, men who have sex with other men, drug users) and their partners, partners of people living with HIV and patients presenting with sexually transmitted infections.

In parallel with implementation activities, the ATLAS programme includes a research component aimed at supporting implementation and generating knowledge on HIV self-testing scale-up in West Africa. The main protocol specifically addresses the research component of the ATLAS programme. All HIV self-tests distributed through ATLAS will be in routine care. The research component does not provide for any additional self-test distribution (no intervention component). These are exclusively observational surveys.

General objective: Describe, analyse and understand the social, health, epidemiological and economic effects of the introduction of HIV self-testing in Côte d'Ivoire, Mali and Senegal to improve testing offer (accessibility, effectiveness and ethics)

Secondary objectives:

➔ Understand the social, cultural and organisational factors facilitating and limiting the primary and secondary distribution of HIV self-tests and their use/appropriation by the different actors concerned (decision-makers, delivery agents, primary contacts, secondary contacts).

➔ Describe the socio-behavioural profile and HIV testing history of HIV self-tests users and their care history in the event of a reactive self-test.

➔ Analyze the positive and negative social and health consequences of the introduction of HIV self-testing for individuals, communities and the health system.

➔ Estimate the incremental costs of dispensing HIV self-tests per delivery channel.

➔ Model the epidemiological impacts of the ATLAS program and different scaling scenarios on epidemic dynamics.

➔ Estimate the medium- and long-term cost-effectiveness and budgetary impact of different scaling up strategies.

Methods: To meet these various objectives, the research component of the ATLAS programme is organised into five work packages (WP) combining qualitative and quantitative data collection and economic and epidemiological modelling.

WP Key populations

Specific objectives: to identify the factors that promote and limit the integration of HIV self-testing into the health care system and the primary and secondary distribution of HIV self-tests in key populations; to analyse the perceptions, attitudes, ownership, experience and experience of HIV self-testing; to analyse the social effects of HIV self-testing at the individual, collective and health system level.

Methodology: qualitative surveys (individual in-depth interviews and focus group discussions) conducted in the three countries: (i) key actors in screening programs targeting key populations (FSW, MSM, PWuID); (ii) members of the three key population communities; (iii) HIV self-test users recruited either by peer educators or through the Coupons survey (see below).

WP Index testing

Specific objectives: to describe how HIV care services and healthcare professional integrate HIV self-testing for partners of people living with HIV (PLHIV); to study how PLHIV negotiate issues around the HIB self-testing proposal to their partner(s); to analyse perceptions, uses and modalities of use of HIV self-tests by partners; to identify individual, marital and social impacts.

Methodology: ethnographies (three months per ethnography) of three HIV care services (one per country) proposing HIV self-tests for partner testing through ATLAS.

WP Coupons survey

Specific objectives: to document the socio-behavioural profile and screening history of HIV self-tests users; to identify the care trajectories of these HIV self-tests users following a reactive or indeterminate self-test; to provide an empirical estimate of some parameters used by the Modelling WP.

Methodology: anonymous and voluntary telephone survey. Through information on HIV self-test kits, self-test users will be invited to anonymously call a toll-free number to participate in a telephone survey. Those who have declared an indeterminate or reactive self-test will be contacted again three months later for a follow-up questionnaire.

WP Economic surveys (this sub-study is presented in the protocol)

Specific objectives: to estimate the incremental costs of providing HIV self-tests; to compare the costs of HIV self-testing with other HIV testing approaches; to model medium- and long-term scaling costs; to compare costs with expected epidemiological impacts (Modelling WP) to estimate the cost-effectiveness of these scaling scenarios.

Methodology: (i) a top-down costing approach with programmatic cost collection; (ii) a bottom-up costing approach with a sample of HIV self-tests distribution sites; (iii) a time-motion study with a sample of distribution agents.

WP Modelling

Specific objectives: to identify those most likely to acquire and transmit HIV and to identify delays in testing and diagnosis; to estimate the population impact of the introduction of HIV self-testing in the three ATLAS countries, at the scale achieved by the ATLAS programme and under possible scale-up scenarios; to estimate the cost-effectiveness of these scale-up scenarios and conduct a sensitivity analysis.

Methodology: adaptation, parameterization and calibration of a dynamic compartmental model to the three project countries. The model will be adapted to take into account the different populations targeted by the ATLAS program and model different testing approaches including HIV self-testing. Once calibrated, the model will be used to reproduce different hypothetical or observed scenarios.

Timeline: 2019-2021

General information

Title: ATLAS – AutoTest VIH – Libre d'Accéder a la connaissance de son Statut VIH - SUB-STUDY ON THE COSTS OF IMPLEMENTING HIV SELF-TESTING IN COTE D'IVOIRE, MALI and SENEGAL

Date: MARCH 2019

Funder: The funding body for the ATLAS project is UNITAID, a global health initiative housed within WHO that supports the development and optimisation of robust, high-quality and low-cost products specifically intended to meet the diagnostic and pharmaceutical needs of HIV, tuberculosis (TB) and malaria programmes in low-resource countries. The physical address is: Chemin de Blandonnet 10 – BIBC III – 8th Floor, 1214 Vernier, Switzerland.

Global and local investigators' role, institution and contact information are presented in Table 1.

Table 1. Global and local investigators' role and contact information

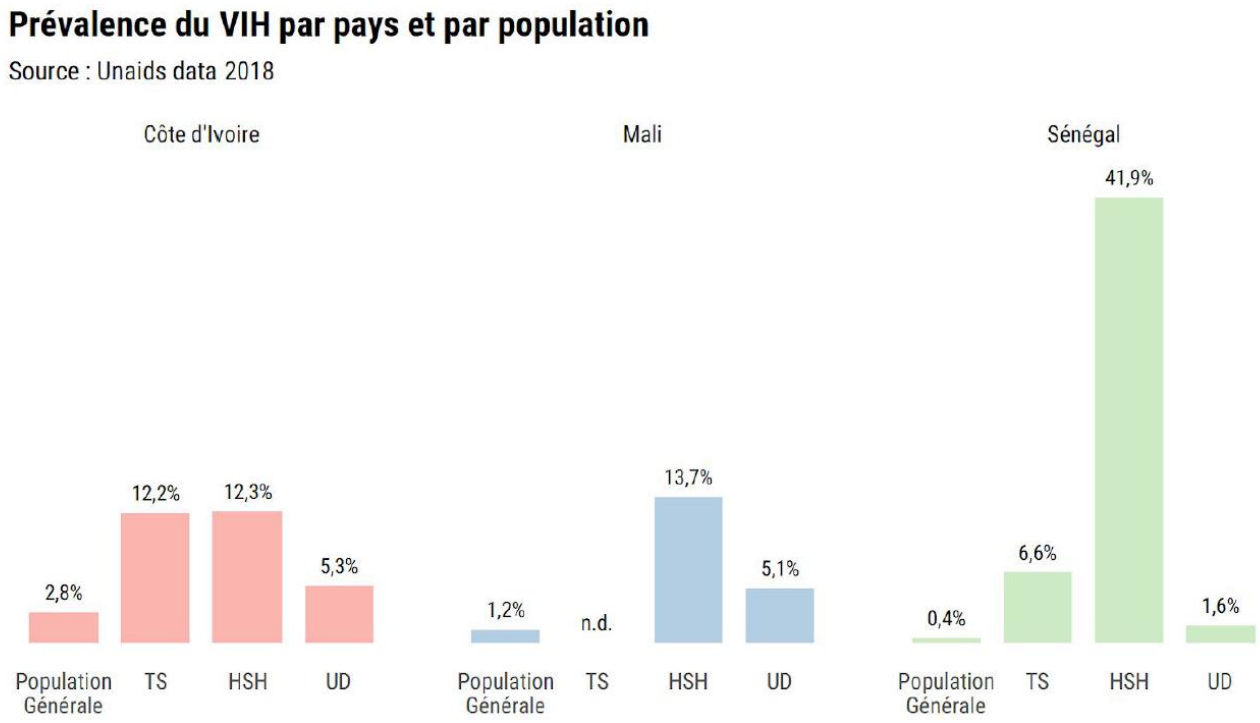
Investigators	Institution	Telephone	Email	Role
Global investigators				
Fern Terris-Prestholt, PhD (Principal Investigator)	London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, Kings Cross, London WC1H 9SH, United Kingdom	+44-7760-399887	fern.terris-prestholt@lshtm.ac.uk	Responsible for the overall design and supervision of cross country cost studies including design, analysis and dissemination of results
Joseph Larmarange, PhD	45 Rue des Saints-Pères, 75006 Paris, France	+33 6 62 06 51 82	joseph.larmarange@gmail.com	ATLAS research director
Marc d'Elbée, Pharm.D.	London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, Kings Cross, London WC1H 9SH, United Kingdom	+44-7490-405594	marc.delbee@lshtm.ac.uk	Developed the research protocol and will coordinate data collection, analysis and dissemination of results.
Anthony Vautier	Solthis, Senegal	+221 77 674 14 46	directeurtech.ATLAS@solthis.org	ATLAS technical director
Clémence Doumenc-Aïdara	Solthis, Senegal	+ 221 78 466 47 20	directriceprojet.ATLAS@solthis.org	ATLAS project director
Local investigators – Cote d'Ivoire				
Olivier Geoffroy	Solthis, Cote d'Ivoire	+225 89 34 49 13	chefdeprojetatlas.rci@solthis.org	Responsible for overall program implementation
Local investigators - Mali				
Odé Kanku Kabemba	Solthis, Mali	+ 223 72 18 69 58	chefdeprojetatlas.mali@solthis.org	Responsible for overall program implementation
Local investigators - Senegal				
Dr Sanata Diallo	Solthis, Senegal	+221 77 674 15 00	sanata.diallo@solthis.org	Responsible for overall program implementation

Rationale & background information

Epidemiological context of HIV in West Africa

The number of people living with HIV (PLHIV) is estimated at 36.9 million worldwide in 2017. The two regions most affected by the epidemic are East and Southern Africa (19.6 million PLHIV) and West and Central Africa (6.1 million PLHIV). (UNAIDS 2018)

In West Africa, HIV epidemics were considered generalized in population in the early 2000s. Following the evolution of estimation techniques and the arrival of first serological surveys in the general population, they are now as concentrated within specific populations. In reality, the situation is more nuanced and the HIV epidemics in West Africa are mixed, widespread with prevalence include between 0.4% and 3% in the general adult population and concentrated in specific groups, that is to say key populations (female sex workers (FSW), men who have sex with men (MSM), injectable drug users (IDU) and vulnerable populations (variable depending on the country: men in uniform, mobile workers, FSW customers ...) (Figure below in French, translation: TS: FSW, HSH:MSM, UD: IDU).



Côte d'Ivoire, Mali and Senegal present contrasting epidemiological contexts. With a prevalence estimated at 2.8% among adults in the general population at the end of 2018, Côte d'Ivoire is the country

most affected by HIV in these three countries, while in Senegal, the least affected country in the sub-region, the epidemic has remained historically low in the general population (prevalence of 0.4% end of 2017).

HIV self-testing

Historically most countries implement a provider-based approach to HTS (1). The provider-based model requires that individuals present at an HIV screening location staffed by a dedicated provider either at the health facility, in the community, or in the home. The provider-based model for HIV testing is therefore costly (2).

HIV self-testing (HIVST), where an individual collects his/her own oral fluid or blood sample, conducts the test and interprets results(3), is an additional testing modality that has increased the uptake and frequency of testing among individuals who would not otherwise test(4, 5). According to World Health Organization (WHO) guidelines(5), a reactive HIVST result should be followed by further confirmatory testing by a trained provider.

The main data we have in sub-Saharan Africa have been collected as part of STAR initiative in Eastern and Southern Africa, funded by UNITAID (6). The first phase (2015-2017) delivered almost 650,000 HIVST kits in three countries: Malawi, Zambia, Zimbabwe, the largest global assessment of HIVST to date. Strategies for distribution were mainly community-based with distribution of HIVST kits at home door-to-door (7). STAR has generated important information about efficient and ethical ways to distribute HIVST kits, including post-test tips to respond to questions about the feasibility, acceptability and impact of interventions in Sub-Saharan Africa. These data were used for the development of news recommendations, and the development of national public policies on self-screening of HIV. The second phase of the STAR initiative (2018-2020) extends this program to three additional countries (South Africa, Eswatini and Lesotho) and plans to distribute 4.8 million HIVST kits on six countries.

Costs and cost-effectiveness of HIV testing and HIV self-testing

The first study on the cost of HIVST in Africa sub-Saharan disease was carried out in a tuberculosis prevention trial in Malawi through a home screening with HIVST versus conventional screening. In this study, the total cost per participant (direct and indirect costs) of screening was, on average, people screened by HIVST (US $ 9.23) than by fixed strategy with conventional screening (US $ 11.84), mainly due to non-medical costs (transportation, lunch) and indirect costs (absence at work) (8). Average costs for initiation of antiretroviral therapy were lower for HIVST patients compared to those using conventional method but the average cost of one year of follow-up treatment was comparable in both groups (8).

Some pilot HIV self-testing experiments have been implemented in West Africa (for instance the SOAR project in Senegal implemented by Enda Santé in partnership with John Hopkins) but they have not yet, to our knowledge, been published in a journal peer-reviewed scientist. However, there is a strong demand for the introduction of new innovative prevention and screening tools, such as HIVST, in the sub region (9, 10).

HIV self-testing is an emerging technology in West Africa, and it is important to determine cost and cost-effectiveness to inform the national strategy and identify potential financial savings and efficiencies. First, it is crucial to assess previous studies' findings on costs and cost-effectiveness analyses of HTS. Multiple studies assessed facility-based HTS and reported cost per person tested and cost per HIV positive case detected. From studies conducted in Nigeria, South Africa, Kenya, Rwanda, Zambia, Malawi, Uganda, Eswatini and Zimbabwe, the facility-based HTS cost per person tested and cost per HIV positive case detected ranged between $7.40 to $12.18 and $22.78 to $1057, respectively (11-20).

Regarding HIVST costs, a cluster randomised trial study in Malawi showed the health provider cost for attending HIV positive individuals for ART initiation were lower for HIV self-testers ($19.92) compared to facility-based HTS ($22.79) (20). A cost analysis study in Malawi showed that though the provider cost per individual HIV self-tested ($8.78) was higher than the regular facility-based HIV testing service ($7.53), the mean societal costs, which includes users' costs, for HIV self-testers ($9.23) was lower than facility-based HTS $11.84 (14). In STAR, economic costs of door-to-door community-based HIVST distribution in 71 sites were collected across Malawi, Zambia and Zimbabwe (21). These costs were estimated at 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.

Cost-effectiveness studies on HIV testing have also been carried out. One study in South Africa applied the costing study in high and low HIV prevalence areas, and findings showed the cost of $522 per person tested and 4 gained QALYs in high HIV prevalence areas, and cost of $635 per person tested and 5 gained QALYS in low HIV prevalence areas (22). A clinical impact study in South Africa showed the incremental cost-effectiveness ratios of $1570/QALY for HIV screening every five years and $1720/QALY for annual screening (23).

One cost-effectiveness modelling studies of the HIVST have been published recently. The ratio cost-effectiveness of an HIVST strategy using the WHO treatment guidelines of 2015 and over a period of 20 years would be US $ 253.90 per QALY (quality-adjusted life year or year quality-weighted earned life) compared to conventional testing. The introduction of HIVST would be therefore cost-effective in Malawi with high HIV prevalence (24). Another model-based study showed 20-year net saving of $75 million from introducing a $3 HIVST in Zimbabwe (25).

These results show that decentralisation of HTS by bringing HIVST to the community has the potential to reduce societal costs for accessing HIV testing, increase efficiency gain by not having to pay for provider costs of conducting the test and to reach people who would otherwise not test. However, there is a need to better understand how estimated costs per person tested for HIV and person identified HIV positive compares between HIVST and HIV standard of care. Provider costs for distributing HIVST need to be evaluated to inform CI, Mali and Senegal national HIV prevention strategy. Our study aims to fill these gaps by estimating incremental costs of providing HIVST in addition to existing HTS services at the various distribution channels in all three countries.

Study goals and objectives

Between 2015 and 2017, the UNITAID/PSI HIV STAR project conducted HIVST implementation research in Malawi, Zambia and Zimbabwe to generate the evidence base required for WHO to introduce its guidelines on HIVST (26). As part of phase 2, the STAR Initiative investigated different models for distributing oral based HIVST kits in South Africa, Eswatini and Lesotho and evaluated their costs.

Coordinated by Solthis NGO, the ATLAS programme aims to promote and deploy HIV self-testing in three West African countries (Côte d'Ivoire, Mali, Senegal). Over the period 2019-2021, in close collaboration with the national AIDS programmes/councils of the three countries, ATLAS plans to provide 500,000 HIV self-tests through ten delivery channels combining fixed and advanced strategies and primary and secondary distribution of HIV self-tests.

The overall ATLAS research objectives are to describe, analyse and understand the social, health, epidemiological and economic effects of the introduction of HIV self-testing in Côte d'Ivoire, Mali and Senegal to improve testing offer (accessibility, effectiveness and ethics).

This protocol presents the costing studies led by LSHTM and which composes a sub-study of the ATLAS research. Other work packages are not presented in this protocol as they do not involve LSHTM staff or students.

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

2. Overall project objectives and research questions

CI, Mali and Senegal are preparing to introduce HIVST to their national HIV prevention strategy in order to reach the UN 90/90/90 and 95/95/95 goals. Cost estimates from program initiation and scale up are needed to increase the evidence base on different implementation options for policymakers. In a context with scarce resources, this costing study aims to present the total and unit costs incurred in routine HTS as compared with various HIVST delivery channels.

Research question

What are the costs of introducing and scaling up different delivery models of oral HIV self-testing compared to the conventional HTS approaches at community-, facility-, sub-national and national levels?

Research objective

The primary objective of this work is to estimate the costs associated with the provision of conventional HTS and the incremental costs of distributing HIV self-testing to all target groups in CI, Mali and Senegal

This secondary objective is to model scale up costs of a combination of cost-effective models of HIVST distribution in the medium term (3 to 5 years) and longer term for purposes of financial planning, based on observed programme costs.

3. Summary of UNITAID/SOLTHIS ATLAS activities

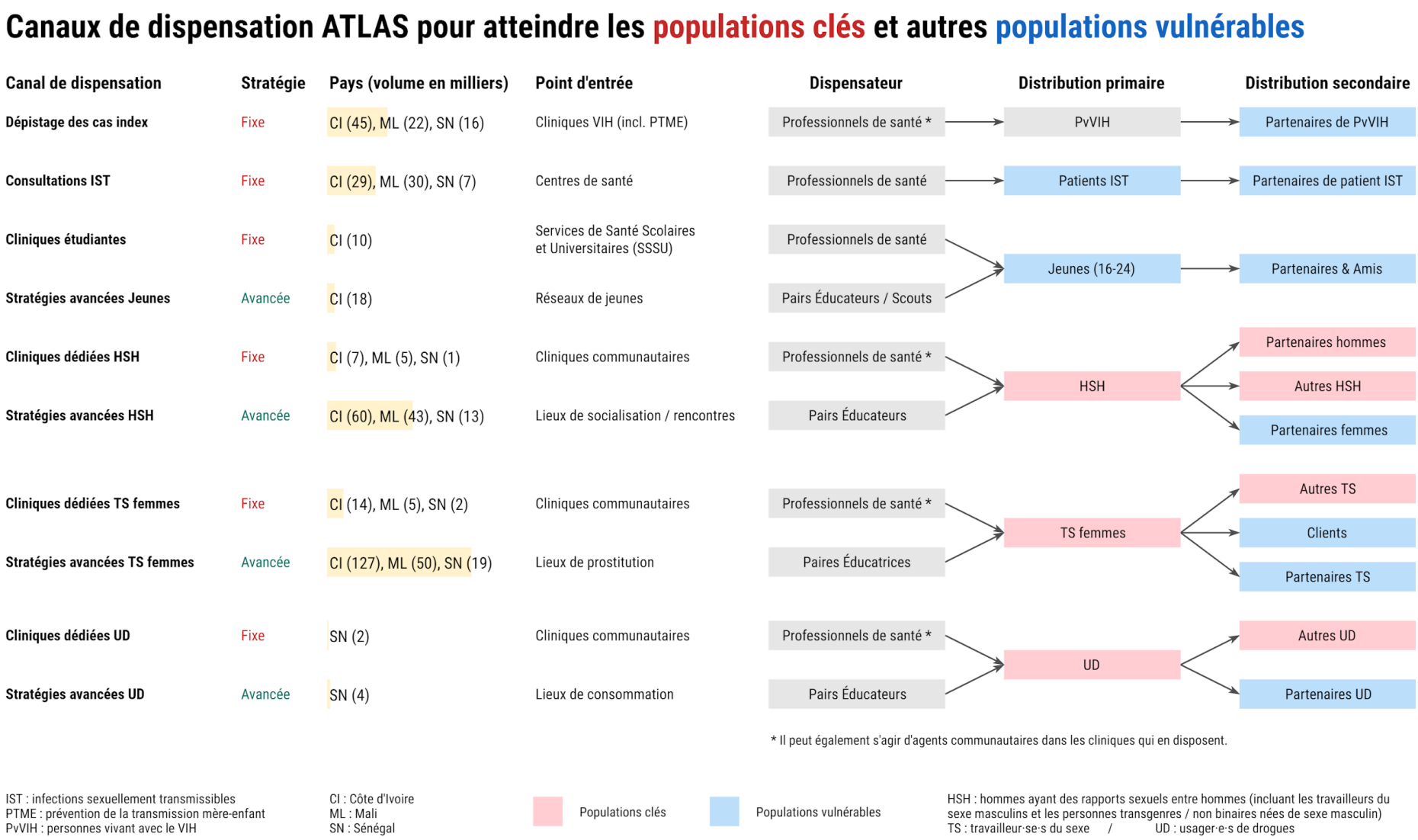
Over the 2019-2021 period, ATLAS plans to dispense 500,000 HIV self-tests; develop contextualized documentation on HIVST (notices, videos, website ...); strengthening of free national HIV information and support telephone lines; setting campaigning campaign to raise awareness and information on HIV self-tests; setting up tools monitoring and evaluation of the activities carried out. In each country, the dispensing of self-tests comes in addition to the strategies.

HIV testing and will be carried out by the field actors already in charge of the activities funded by the Global Fund or PEPFAR. The different channels of dispensation and target populations for each country were developed with country stakeholders (national AIDS programs, international institutions, local actors). The volumes and distribution strategies will be subject to an annual reassessment within the framework of technical working groups set up by each national program/council to fight against AIDS.

At the start of the ATLAS program, only oral self-tests (OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test from OraSure), prequalified by the WHO and validated by the three countries of intervention, will be used. Depending on the qualification of other HIV self-testing devices, blood-based self-tests may be used in 2020 and / or 2021.

The figure 1 below shows the ten dispensing channels selected for the ATLAS program after discussion with the different stakeholders, some channels can only be implemented in only one of the three countries. Six adopt a fixed strategy (dispensing HIVST kits in the framework of a health structure) and four an advanced, community-based strategy in the context of field activities.

Figure 1. Summary of HIVST kits dispensing channels in Cote d'Ivoire, Mali and Senegal



Study processes

Training and study initiation

The LSHTM team will conduct a follow-on visit as soon as IRB approval is obtained to support the local team to pilot instruments and train data collectors. This will be a 2-3 week visit. Thereafter the LSHTM team will start data collection with the local partner. This will include 2 to 3 in country visits to supervise and participate in data collection which may take up to 6 months and 3 months for data cleaning. One local research assistant will be hired by Solthis in collaboration with LSHTM in each country to collect cost data. The research fellow based in London will coordinate and support the data collection between the three countries.

Analysis of results

The analysis of results will be done collaboratively between the local economists and the LSHTM based economist via Skype call and workshops where the LSHTM and local teams will meet and analyse the data together. These workshops will likely be attached to wider ATLAS Consortium meetings expected to happen once or twice a year. Additional workshops will be planned as necessary. Data analysis will be completed at the end of the first year. The scale up cost model will be developed during the second year of the study.

Study Design and Methodology

1. Study design

The cost analysis follows the Global Health Costing Consortium (GHCC) reference case which sets standards for global health costing studies (27). The purpose of this costing is to estimate the incremental economic costs of introducing HIVST to existing health promotion services using alternative delivery model.

Estimated costs will be incremental to existing HIV testing services (PITC and CITC). Full costing will be conducted when no HTS services are in place within the delivery channel. The primary outcome is the total and unit cost per HIVST kit distributed among the various distribution channels.

The perspective describes which payers' costs are included in the estimate. For our analysis, to inform budget consideration, we will estimate the costs that fall on the government as well as civil society organizations' perspective.

Costing period – HIVST kits distribution

The costing study will analyse data expenditures for one year following HIVST kits distribution in each model. We expect the costing study to start on September 1st, 2019.

2. Cost data collection

Scope of the costing

We will estimate financial and economic costs for providing HIVST via the different models with a data analysis of overhead expenditures complemented by an ingredient-based approach (top-down and bottom-up costing).

The costing activities will include the three following activities:

1/ Top down costing (macro-costing) applies to Solthis and partners expenditure data analysis and will ensure:

All financial costs are captured

High comparability with accounts between countries

2/ Bottom up costing (micro-costing) to obtain additional costs data not captured in the financial report, allocation factors across distribution models as well as economic costs (donated goods and services).

3/ Scale up modelling to consider budget impact after scaling up.

Unit costs

For all countries, we will estimate total and unit cost per HIVST kit distributed for each delivery channel. The monitoring & evaluation data will be collected and provided by the implementer Solthis and its partners.

A coupon survey with the objective to track linkage rates of people with a reactive self-test will be run alongside. Depending on the success of this survey, we can expand our outcome measure to unit costs per HIV positive person identified and linked for confirmatory testing. HTS costs data will be used to estimate the cost per confirmatory HIV test.

The coupon survey will be able to track by which delivery model the person received the HIVST kit, therefore, this outcome will be matched with our costs by delivery model.

Based on these cost estimates, we can model the budget impact of scaling up HIVST under the range of the distribution models part of the study. These unit costs will be presented by distribution model to allow for comparison across the distribution strategy. Observed costs will be collected prospectively over year 1 and feed into the scale up cost model.

Time horizon

The time horizon will be of 1 year following HIVST distribution, and will include both start-up and implementation phase of HIVST.

Costs will be disaggregated into those in the 'start-up' phase (all costs incurred before the first service is delivered) and those in the 'implementation' phase. The timeframe for the costs will be annual, with annualization of capital resources that provide benefits for more than one year.

The costing activities will run over 2019 (Year 1) and 2020 (Year 2):

Year 1: We will use short term observed costs of HIVST distribution models, to estimate total and unit costs.

Year 2: Longer term cost analysis for the duration of the project, which will be the full first year plus additional months depending on how long start up took. We will use the latest period of observed costs as input into the scale up cost model.

Identification and measurement of resource use

As a first step, we need to identify all the relevant providers and activities involved in the delivery process of HIVST. For each distribution model, this will include an analysis of expense records of each provider, interviews with key informants and observations of testing distribution. A pilot phase will guide any adaptation of the cost data collection tools. A more generic tool for the development of the adapted data collection tool is presented in Appendix.

An interview of the facility manager will be conducted to explain the purpose of our study and request for financial data. A sensitization sheet will be provided and the facility manager will be asked to sign a consent form to authorize the data collection process. Information sheet and consent form can be found in Appendix.

The research team will combine "top-down" and "bottom-up" costing approaches to estimate the overall costs of distributing HIVST. The main objective of the bottom-up costing is to identify cost allocation factors for PSI delivery systems. For government clinics, we will need to do the full micro-costing. We will also conduct time and motion (TM) studies with health care workers to estimate their allocated time to provide HIVST, where shared across various activities. The TM study is presented later in the section "*ii. Recording of resource use – "bottom-up" costing*" of the protocol.

Extraction of financial data from expenditure reports – "top-down" costing

The data analysis plan aims to ensure that all costs are identified. It will be fully transparent for programmes as all expenditures are tracked and will provide insights into programme budgeting. Due to the timelines, our costs analysis will capture early programme costs, thus requiring modelling to estimate changes attributable to economies of scale and programme learning.

Our expenditure analysis will follow 3 steps: by phase (1), by ingredient (2) by activity (3).

1. Project phase. All expenditures prior to the first training or implementation will be classified as start-up and treated as capital costs with a life span of the project.

2. Expenditure analysis by ingredients. Line items in expenditure data will be categorized by type of input used, e.g. supply, equipment, etc., staff. This is useful to understand the types of resources required for future role out.

3. Activity based costing. This refers to costing by HIVST distribution model disaggregated by cost category at different level ((distribution point and district level). This expenditure analysis will be complemented with the bottom-up costing method to collect quantities and prices of items that were not part of Solthis' and partners' expenditures.

Costs will be allocated across HIVST distribution models, cost category and level using:

Overhead costs

District level costs

Number of HIVST kits distributed

Number of HIVST distributor trained

Geographical distance between storage and distribution points

A summary of the tentative allocation factors is presented in Appendix.

Recording of resource use – "bottom-up" costing

In collaboration with providers at distribution sites, resources quantities and unit costs will be assessed. Data to be collected include capital costs (building, vehicle, start-up (training and others)) and recurrent costs (staff, testing supplies, other supplies, etc.). The generic cost data collection tools presented in Appendix will be used for government facility costing; we will then adapt them for different model.

Capital costs and start up

Land and Buildings

Buildings costs or annual rent equivalent, where applicable, will be estimated by using current replacement values based on Ministry of Health building costs. The information on annual rent equivalent will be obtained from facility managers or partners where applicable. If this information is not available, information will be collected locally about the cost of buildings and land. In addition, the physical space utilised by each department, including specific room allocated for HIVST, will be measured and allocated to HIVST according to use. For government clinics, the cost of building will be obtained from the MoH, private housing agents or estimated based on current housing rates. Specific information includes purchase price or construction cost of each capital good (such as facility buildings, generators, vehicles, etc.). This information will be used to estimate the cost of constructing the facility.

Start up and training

In addition, information on the cost of training of service providers, peer educators, counsellors and other personnel or volunteer involved in HIVST kits delivery will be obtained from Solthis & partners and country MoH supporting the training of service providers at the national and district level. This information will include the number of participants attending the training (opportunity cost of their time will be based on

their salary), the total cost of organising a workshop and the number of workshops held. The cost per person trained should take into account expenses related to refreshments, office supplies, facilitator, etc.

Furniture and Equipment

The furniture, equipment and other asset data will be obtained from the asset register of the service providers. The cost of each piece of equipment, medical and non-medical, will be obtained from the price lists from Solthis, the partner supporting HIVST distribution. Alternatively, the cost of furniture and equipment will be obtained from local markets. The locally appropriate life of each item will be applied to calculate annual costs.

HIVST kits and other supplies

Information on the HIV self-test kits, including kits price, will be obtained from Solthis as actual purchase price. The full list of supplies used for HIVST will be included in the data collection form.

Recurrent Utilities and recurrent transport costs

Utility costs include telephone, water, gas and electricity, maintenance of vehicles, and transport costs. The invoices for each utility will be obtained from the accounts or the in-charge on site where applicable.

Volume of services

Information on volume of kits distributed in different sites will be obtained from the Solthis and from MoH facility outpatient registers.

Personnel and time and motion study

Personnel

Personnel salaries will be obtained from Solthis accounts as well as national salary scales and will be used to value staff time. Any contribution to living allowance, subsidies as well as number of working day per year will be collected during the site visit. Staff time allocated to providing HIVST services will be captured in the time and motion study.

Time and motion (TM) study

Time and motion studies will be completed in all distribution models. The aim of this sub-study is to observe how much time health providers (including a broad range of providers: HTS counsellors, nurses,

peer educators, etc.) spend on delivering HIV testing services to their clients, differentiating time allocated to HIVST and to standard HTS. This usually includes activities such as time to ask previous HIV testing history and last HIV test results, explain how the self-testing device work and other type of counselling on HIV prevention, STI prevention or family planning depending on the provider and distribution model. Results from the TM study will be used to allocate direct personnel costs in settings where HIVST is provided along with other health care services.

The TM data collection form, consent forms and information sheets are presented in Appendix.

Below is an overview of staff directly involved in the provision of HIVST services eligible for inclusion in the TM study.

Cote d'Ivoire:

- Hotline Staff: 16 (for hotline staff, still to confirm whether or not involved in other activities and therefore the need for observation or other method of cost allocation)
- Health professionals: ~ 120
- Peer educators: ~200

Mali:

- Hotline Staff: 8
- Health professionals: ~ 120
- Peer educators: 250

Senegal:

- Hotline staff: 10
- Health professionals: ~100
- Peer educators: ~100

Data on logistics

The costs both within the Solthis supply chain management as well as the government system will be estimated. The following information will be collected from Solthis or from service delivery points when government services are being utilized: cost of transporting the HIVST commodities, cost of storage (warehousing), cost of waste disposal and cost of personnel for supply chain management.

Data collection on demand creation

Information on demand creation will be obtained from Solthis and other partners supporting demand creation and advocacy. The specific information, education and communication (IEC) data to be obtained will include the cost of IEC communication strategy as well as cost of IEC campaigns in the selected sites.

Valuation of resource use

Capital goods

We will take into account depreciation of equipment and building (cost allocation of a tangible asset over its useful life) using a discount rate of 3% following guidelines, while using country specific discount rates in the sensitivity analysis.

Currency conversion

We will report total costs in USD2019 –i.e. US dollars valued at 2019 prices— and in local currency, using a 3% discount rate where costs need to be adjusted over time. Costs incurred in local currency will be adjusted for local inflation, and converted in USD at the base year (2019) using the current exchange rate.

3. Sampling method

HIVST distribution sites are presented in Appendix. For the costing studies, if the number of clinical sites for the HIVST distribution model is less than six, then all sites will be cost. If a model has more than six sites, then purposive sampling of clinical sites will be done to capture a range of clinical characteristics, including rurality, catchment size, and if large variation in prevalence this will also be considered when developing a sampling frame. A maximum of six health care providers will be included in the time and motion study per HIVST distribution site.

4. Cost data analysis

Cost analysis

We will determine the unit costs per HIVST kit distributed and per HIV positive person linked into treatment or care within each model. This analysis will inform decisions on allocative efficiency for the distribution of the kits among the different models and the investment in HIV testing and HIVST distribution across model. We will report on cost breakdowns by intervention phases, input category, at facility and district level within each distribution model.

Scale up cost model

Once full costs are obtained to estimate value of all resources used for each model, they will feed into the scale-up cost modelling. We will conduct an investigation on the budget impact of the delivery process for in-country policy makers for a scale-up of HIVST distribution.

Cost modelling work will inform on the impact of scaling up, on predicted costs of changes by distribution model. The scale up cost model will capture all costs by level at which they will be fixed. Examples of fixed cost include training costs (start-up phase), supply chain management cost (district level), waste management costs (facility level), etc.

More precisely, this model will aim to capture economies of scale and above service level costs. However this model may still not account for diseconomies of scale due to changes in input prices and demand side considerations such as pent up demand (higher costs for harder to reach populations).

Data Management and Statistical Analysis

Expenditure data will be received from relevant finance departments (Solthis and partners), or collected on site and will be analysed in Microsoft Excel software by the LSHTM and local economists. All expenses will be converted to US dollars 2019 for analysis, capital costs will be annualised. Data will be disaggregated per distribution site and per model.

M&E data will be provided by the coordinator responsible for data processing, analysis and reporting. Data from the M&E plan inform on the number of HIVTS kits distributed by channel.

Further analysis of mean and median costs across sites will be estimated where there are multiple sites implementing the same model. Cross country analysis of unit costs and their drivers will be undertaken.

Data Quality control and storage

Data quality control

Financial and other cost data will be validated on entry through a range of consistency checks. For instance, excel checks will identify where allocation factors do not add up to 100%. Logical and consistency data checks will also be performed across data types, to ensure that the narratives reported in the interviews with the in-charges are consistent with the accounting data and that both form a realistic picture of activities. Errors will be reviewed and corrected on a quarterly basis.

For the TM study, the local research assistant will be timing the health provider. This will ensure there is no reporting bias regarding participants' time allocated to the delivery of HTS and HIVST.

The M&E team will conduct routine visits to sites to supervise data collection and compilation of reports. Data checks are conducted to verify correctness and completeness of data recorded on paper forms against data entered on the database.

ATLAS has also formed a TAG to review data and provide expert opinion on ongoing and planned research studies.

Data storage

Study records (consent forms, cost data spreadsheets, etc.) will be kept in a secure location accessible only to authorised study staff. All records will be archived in a secure storage facility for at least five years after the completion of the study. Security of data access and storage and discussed in more details in the "Ethical considerations" section.

All anonymised cost data will be analysed by a local researcher and a research fellow at LSHTM, under the supervision of the principal investigators on the study. Results will be fed back to local team and discussed before inclusion in the final analyses. However costs will be identifiable by study site.

Dissemination of Results and Publication Policy

The results of this research will be used to guide the formation of national and international policies around HIVST. Findings will also be distributed internationally to global health policy makers, nationally to the country governments, including HTS technical working groups. Research will be published in international journals and presented at international conferences.

ATLAS consortium partners have also established an ATLAS technical websites where updates and outcomes are shared on a regular basis as soon as new evidence is available. Research findings will be discussed with members of the ATLAS Technical Advisory Group (TAG), which brings together public health experts, scientists and policy makers to guide research and programme implementation as well as with the HIVST technical working group established by WHO.

Study timelines

Table 2 describes the expected timelines in all three countries. The study will be implemented in the third quarter of 2019.

Table 2. Study timelines in Cote d'Ivoire, Mali and Senegal

ATLAS costing study timelines - 2019 - 2021	2019						2020												2021					
Quarters (2018-2019)	Q3		Q4				Q1		Q2				Q3			Q4			Q1				Q2	
Month (2019-2021)	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	April	May	June
Ethical approval of the study	x	x																						
Costing: data collection-start up and training			x	x																				
Costing: ongoing prospective data collection			x	x	x	x	x	x	x	x	x	x	x	x	x									
Costing: data cleaning					x	x	x	x	x	x	x	x	x	x	x	x	x							
Costing: expenditure primary analysis						x	x	x	x	x	x	x	x	x	x	x	x	x						
Cost modelling: model scale up & unit costs																			x	x	x	x	x	x
Dissemination at conferences and publications									x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Problems Anticipated

Data collection progress at the various distribution sites can sometimes be delayed due to logistical issues (e.g. planning of the visit, absence of the key staff personnel at the clinic, etc.). In this situation, members of the team (from LSHTM or in-country team) will support each other, for example by providing additional human resources to help with the data collection. Delay in starting of models will reduce the costing follow up period, which may make generalisation from some models less valid. Problems with surveys capturing testing and linkage to care would reduce our ability to estimate cost per person linked and reduce the ability of estimating cost effectiveness.

Ethical considerations

Ethical approval for the study will be sought from the local research ethics boards, the World Health Organization research ethics and the Research Ethics Committees of the London School of Hygiene and Tropical Medicine. The study has been discussed with and has the support of senior staff at the implementing partner organization Solthis.

The study may be subject to audit by UNITAID, the funding body for the ATLAS project, and inspection by regulatory authorities, to ensure compliance to the protocol, and all applicable regulatory requirements.

Confidentiality of data

Sensitive information from individual provider resource use (e.g. salary information) and information collected from the time and motion study will be kept confidential. All hard copies of the records will be stored by the local health economist in locked filing cabinets. Electronic copies data will be stored in password protected computers on the LSHTM secured server. Access to the records will be restricted to the local health economist, and to ATLAS team members as required.

M&E data will be provided by the coordinator responsible for data processing, analysis and reporting. The research team will not have access to individual level patient information and data on linkage to care will be obtained at distribution site level. Therefore, there is no risk for breach of patient anonymity.

Time and motion (TM) study

No incentive will be given to compensate the time of health care workers. Interview forms and TM sheets will be identified using a participants' study number. The names or identities of participants will not be collected, only their professional grade. All electronic documentation (including all electronic versions of the paper documents) will be stored in a password-protected computer server accessible by the local research assistant. The electronic documentation will be transferred to LSHTM and updated regularly (quarterly) via secure methods as per standard school procedures.

An information sheet describing the purpose of the study globally and the TM study will also be provided to the participant. It will be clearly stated why we ask them to participate in the study and what it entails. The consent form clearly states that there will be no consequences if providers decide not to participate in the study and that they can withdraw at any time during the study. The data collector will allow time to answer any questions the participant may have. If the heath provider does not wish to participate in the TM study, the data collector will only proceed to cost data collection at the distribution site.

The patients of the health care worker taking part in the TM study will be informed that their consultation has been timed; the researcher will read a brief information sheet specifying that no other information has been collected. During data collection phase, if the client is requesting for privacy, the data collector will be waiting outside of the room and will time the length of the consultation. If the client is comfortable with the presence of the researcher, the researcher will stay in the room during the testing session but will leave the room when the test result is read to respect confidentiality of the clinical appointment.

Informed consent forms will be obtained from the health providers in order to conduct the TM study. A copy of the consent form, participant and patient information sheets can be found in Appendix. These three documents will be translated into local languages.

Other research activities of the investigators

The principal investigator Fern Terris-Prestholt is currently engaged in the following projects:

Project description	Source of funding	Project dates	Time spent (in person month per calendar year)
1/ Stimulating and shaping the market for HIV self-testing in Africa: two-tier demonstration and evaluation of accuracy and linkage in 4 countries: The major goals of this project are to pilot and formally evaluate multiple distribution models to deliver approximately 2.7 million HIVST episodes across intervention countries (Malawi Zambia, Zimbabwe and South Africa)	Unitaid	2015-2019	7.84
2/ Crowd sourcing a Public Health Campaign	NIAID	2015-2020	1.16
3/ OPTIONS: The major goal of this project is to facilitate access to ARV-based prevention for women in key project countries.	USAID	2015-2020	3.00

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Appendix

I.ATLAS_Facility questionnaire_v1_En.docx

DATA COLLECTION FORM – INGREDIENT BASED COSTING

Date: _____

Interviewer: _____

HIVST distribution model: _____

District: _____

Name of Facility: _____

Section A: Environmental characteristics of the health facility		
Question	Answer	Additional notes
Location of the clinic? *Urban* *Semi-urban* *Rural*		
How many IPC HIVST mobilisers does this clinic have?		
How many counsellors are at the HTC section per day?		
How many days a week does the clinic provide HTC Services?		
Additional notes/issues		

CAPITAL COSTS

A. Buildings and Storage

Sources of data: _____

Annual rent/hire: _____

Spaces	Size of room (Square meters)	% working week room used by HTC team	% working week room used by HIVST team
Entire site			
Reception			
Storage room			
Laboratory			
HTS room			
HIVST room			

Furnishing: can be done at 10%.

B. Equipment

Sources of data: _____

What kind of equipment are used for this programme?

Who funds each piece of equipment?

What is the cost of each piece of equipment?

What is the life expectancy of each piece of equipment?

Equipment (list)	Quantity	Cost		Life expectancy or working life	% allocation
		Fin.	Econ.		

Note: use current cost of similar equipment – not the original price.

C. Vehicles

Sources of data: _____

What kind of vehicles are used for this programme?

Who funds each of the vehicles?

What is the cost of each vehicle?

What is the life expectancy of each vehicle?

Vehicles (list)	Funded by	Cost		Life expectancy or working life	% allocation
		Fin.	Econ.		

Notes: Use current market price, estimate similar working life for similar vehicles,

D. Other capital costs (any residual capital costs>$100)

Sources of data: _____

What other capital costs are incurred for this programme?

Who funds each item?

What is the cost of each item?

What if the life expectancy of each item?

Item (list)	Quantity	Cost		Life expectancy or working life	% allocation
		Fin.	Econ.		

RECURRENT COSTS

E. Personnel

Sources of data: _____

Which categories of personnel are involved in this programme? (Receptionist, HTS counsellor, nurse, doctor, clinic manager, volunteer, community mobiliser, cleaning staff)

Who funds each category of personnel?

What is the cost of each of their gross annual salary?

What is the cost of each of their annual allowance?

Category of personnel	Quantity	Gross annual salary		Cost of annual allowances (specify)		% allocation
		Fin.	Econ.	Fin.	Econ.	

Position or Job Title	Number of full working days in clinic	% of time spent working in:					
		Front Desk	HTS/VCT clinic	Management	HIVST	Demand Creation	Other

Note: Doctor, nurses, HTS counsellor, volunteers, receptionist, cleaning staff, driver, etc.

F. Supplies

Sources of data: _____

What type of supplies are used for this programme?

Who funds each item?

What quantity of each item is consumed annually, including loss and wastage?

What is the unit cost of each item?

Supplies (list)	Annual quantity consumed	Cost		% allocation - HTS	% allocation - HIVST
		Fin.	Econ.		

Note: Supplies (equipment used within a year or <$100) – see allocation aid at end of document. Should include supply chain costs. Include wastage. Quantity: only HIVST that are distributed during the year of costing should be included. But should include wastage at higher levels. No need to annualise small supplies (<$100).

G. Vehicle operation and maintenance and/or transportation

Sources of data: _____

What type of vehicle operation, maintenance, and/or transportation (e.g., petrol/diesel, oil, maintenance, insurance, registration, repairs, spare parts) are used for this programme?

Who funds each item?

What is the unit cost of each item?

Supplies (list)	Quantity	Cost		% allocation
		Fin.	Econ.	

Note: fuel, insurance, registration fee, repairs, etc.

H. Building operation and maintenance

Utility	Telephone/fax	Water	Electricity	Maintenance/ repair	Insurance	Other (please describe)
Source of funds						
January						
February						
March						
April						
May						
June						
July						
August						
September						
October						
November						
December						
Annual cost						

Note: Allocation – use floor space.

I. Recurrent training (HTS & HIVST Related Only) – Also include initial HIVST training cost (to be categorised under start-up costs)

Sources of data: _____

What personnel is involved in recurrent training for this programme?

Who funds this training?

What is the cost of fees, travel, subsistence, and salary for each personnel involved?

Detail personnel involved in training	Funded by	Fees	Travel	Subsistence & misc.	Salary costs	% allocation

Note: Capital overheads costs of other organization with partial involvement in the training should be captured. Training costs incurred by organisers should be included. Allocation - # of participants at site and district level.

J. Waste management

Sources of data: _____

What type of wastage is involved in the programme operations?

Who funds the waste management?

What company is responsible for waste collection, if applicable?

What is the unit cost for waste management of each item?

Type of wastage (list, e.g. incinerator)	Funded by	Company responsible for waste collection	Quantity	Unit cost		% allocation
				Fin.	Econ.	
Incinerator						
Used HIVST kit collection cost (waste management)						

Note: Allocation HTS/HIVST – will depend on the waste management chain.

K. Quality assurance and supervision

K-a. Incoming inspection

How many internal inspections were carried out during the costing period? _____

Supplies	Quantity	Unit price			Allocation to clinic	QA cost per sample set	
		Fin.	Econ.			Fin.	Econ.

Personnel (Project staff)	Funded by	Quantity	# days	Salary costs/day		Allocation to Clinic	QA cost per sample set	
				Fin.	Econ.		Fin.	Econ.

Note: equipment, personnel time (TM study or direct interview), vehicle, etc.

K-b. Confirmatory retesting

Supplies	Quantity	Unit price			Allocation to clinic	QA cost per sample set	
		Fin.	Econ.			Fin.	Econ.

Personnel (Project staff)	Funded by	Quantity	# days	Salary costs/day		Allocation to Clinic	QA cost per sample set	
				Fin.	Econ.		Fin.	Econ.

K-c. Total QA/QC Costs

Quality Assurance	Financial	Economic
Incoming inspection costs		
External quality control		
External quality assurance		
Retesting		

Supervision	Financial	Economic
Vehicle hire costs		
Vehicle maintenance/operation		
Personnel costs		

L. Other recurrent costs

Sources of data: _____

What other recurrent costs are incurred for this programme?

Who funds each item?

What is the cost of each item?

What if the life expectancy of each item?

Item (list)	Funded by	Cost		Life expectancy or working life	% allocation
		Fin.	Econ.		

OUTCOME INDICATORS

Sources of data: _____

Month 2019-2020	Determine®	Unigold®	Total HIV+ client	Total HIV- client	Total HIVST client	Total HTS client	Total client seen at the facility	Notes
September								
October								
November								
December								
January								
February								
March								
April								
May								
June								
July								
August								
Total								

ASSUMPTIONS

Date	Assumption/Decision

Equipment and Consumables Checklist

Consumables Medical and non-medical	Equipment Medical and non-medical
Cotton Wool	Tables (e.g. wooden; plastic; size)
Alcohol swab wipes (small)	Benches (e.g. wooden; plastic; size)
HIV – RDTs (Determine; Unigold)	Chairs (e.g. wooden; plastic; size)
HIV – Oral self-test kits	Filing Cabinet
Blood lancets	Cupboards
Capillary tubes	Bin (e.g. wooden; plastic; size)
Swabs	Fridge (e.g. size; fridge v freezer)
Aprons	Book Shelf
Gloves	Office Computer
Alcohol Spirit	Office Printer
Bin liners – large; medium; small	Patient Examination Bed
Hand sanitizers	Weighing Scale (Patients)
Hand washing soap	
Sharp Bins (Name/Size)	
Syringes - 10mls; 5ml; 2ml	
Gauze Bandages	
Hand Towels	
A4 Paper	
Pens	
Adhesive Labels	
Clinic Registry books (inc M+E)	
A4 Hard Folders (large; small)	
Computer Ribbons for printers	
Staple Machine	
Hole puncture	
Printer Ribbons - ART Computer	
Files - Pocket files	

II.ATLAS_Information leaflet_v1_En.docx

ATLAS costing study – Information leaflet

Version 1.0 - 20th March 2019

Information on the project

We are health economists working for the NGO Solthis and the London School of Hygiene and Tropical Medicine (LSHTM). We conduct HIV research in your country.

Regular HIV testing is very important in your country and around the world because it helps HIV-positive people to get treatment when they are still healthy and can also help reduce the spread of HIV. HIV self-testing is an innovative way to test yourself and is being introduced in your country.

ATLAS is a research project that we hope will help us understand the best way to introduce HIV self-testing. The study we are conducting is part of the ATLAS project, which is an analysis of the costs of conventional HIV testing, and the costs associated with providing HIV self-testing.

Interview with the health facility manager (or other relevant authority)

During this interview, we will ask questions about how the facility operates to provide HIV care services, to identify and estimate the costs associated with conventional HIV testing and HIV self-testing. We will ask to provide us with financial data.

Time and motion study with HIV services providers

The purpose of this study is to estimate the time it takes for providers to offer HIV testing services and to provide HIV self-testing to a patient. We will be able to evaluate the staff costs directly associated with the provision of HIV care by estimating their working time on these activities.

This involves timing sessions for the provision of services for HIV testing and / or self-testing by health providers. We will ask health care providers participating in the study to sign a consent form. The observations will be made on a full day of work.

This can be either for an HIV testing service at a health facility or at mobile outreach, or for the provision of HIV self-testing that the patient will perform on his / her own, or that he / she may suggest to a partner.

We would like to reassure participants that the purpose of this study is not to "control" the quality of care provided, but to better understand the time needed to perform HIV tests / self-tests.

The researcher will be present during the consultation with the agreement of the patient. If the patient wishes to be alone with the health care provider, the researcher will stay outside the consultation room.

Confidentiality of data

All information from the study will be stored securely on paper and in computer files, and only researchers participating in this study will have access to it. We will use a number to identify the participant. For the time and motion study, we will not record any names, only the professional status will be recorded. The data provided will be analysed, and confidentiality will be preserved throughout the process of data processing and storage.

The data we collect will be published in scientific journals and project reports so that others can learn from your experience. The data can also be made available to other researchers via a data repository in the public domain so that it can be used to improve the delivery of HIV services. All data will be anonymised.

Study approval by research ethics committees

The study has been reviewed and approved by the ethics committee of your country, the World Health Organization and the London School of Hygiene and Tropical Medicine.

If you have any questions about this study, do not hesitate to ask them now. If you have any questions after our departure, do not hesitate to contact us by calling the following number and ask (Name, First Name) (Principal Investigator): Tel: XXX.

Additional information on the ATLAS program

If you would like more information about the study, you can contact one of the team members. A website dedicated to the ATLAS program can be found at this address (https://atlas.solthis.org/). You will find there additional information as well as the results of the research at the end of the project.

III.ATLAS_Health facility_Manager_Consent form_v1_En.docx

Interview with the health facility manager (or other relevant authority)

for the provision of costs data on HIV testing services

–

Consent form

The information leaflet, version 1.0 dated March 20th, 2019, describing the purpose of the study was read and explained to me. I had the opportunity to have satisfactory answers to all the questions and I had enough time to think about my participation.

Do you have additional questions about the study?

Do you agree to be interviewed?

☐ I agree to be recorded. ☐ I do not agree to be recorded.

If you have no more questions and if you agree to participate in the study, sign this form, indicating that I have informed you of your rights as a participant and that you have agreed to participate in the research. We thank you for your time.

[PARTICIPANT] I have read the information sheet for this study (or they have been read to me). All my questions about the study and my participation in it have been answered. I freely accept to participate in this study.

_____

Name of participant (in capital letters) Signature Date

_____

Name of researcher (in capital letters) Signature Date

IV. Tentative cost allocation factors for the cost data analysis

Input type	Central (PSI-HQ)level	District Level	Health Facility level	Model level (New Start, VMMC, Public facility)
Training	Costs allocated to training directly from PSI expenditure cost description.	Like at HQ, costs allocated to facilities by number of distributor trained	Like at HQ, costs allocated to facilities by number of distributor trained	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
Sensitisation	Treated as overhead/program shared costs and allocated to districts by district level direct expenditure.	Allocated to facilities by number of HIVST kits distributed.	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
Other Start up	Treated as overhead/program shared costs and allocated to districts by district level direct expenditure.	Allocated to facilities by number of HIVST kits distributed.	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
Building and storage	Treated as overhead/program shared costs and allocated to districts by district level direct expenditure.	Allocated to facilities by number of HIVST kits distributed.	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
Equipment	Treated as overhead/program shared costs and allocated to districts by district level direct expenditure.	Allocated to facilities by number of HIVST kits distributed.	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
Personnel	Treated as overhead and allocated to districts by district level direct expenditure. Program shared costs by distributors.	Allocated to district by number of distributor trained	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care

HIVST Kits	Allocated by kits distributed. Remove % of warehouse remaining stock at end of year.	Allocated to models by number of HIVST kits distributed.	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
T-shirts, bags, flipcharts	Allocated by number of distributors trained	Allocated by number of distributors trained	Allocated by number of distributors trained	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
Other supplies	Allocated to districts by number of HIVST kits distributed.	Allocated to models by number of HIVST kits distributed.	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
Vehicle maintenance and transportation	Allocated by distance (km) to district	Allocated by distance (km) to facilities	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care
Building operations and maintenance	Treated as overhead/shared program costs and allocated to districts by district level direct expenditure.	Allocated to district by number of distributers trained by district	Allocated to models by number of HIVST kits distributed.	Unit costs calculated by dividing cost by HIVST kits distributed or per HIV positive person identified linked to care

V.ATLAS_TM study_Consent form_v1_En.docx

Time and motion study – Consent form

The information leaflet, version 1.0 dated March 20th, 2019, describing the purpose of the study was read and explained to me. I had the opportunity to have satisfactory answers to all the questions and I had enough time to think about my participation.

If you agree to participate in the study, we will record your daily activities throughout the day. We remind you that the objective of this study is not to "control" the quality of care provided, but only to better understand the time needed to perform HIV tests / self-tests.

Do you have questions about the study?

Do you agree to participate in the time and motion study?

If you have no more questions and if you agree to participate in the study, sign this form, indicating that I have informed you of your rights as a participant and that you have agreed to participate in the research. We thank you for your time.

[PARTICIPANT] I have read the information sheet for this study (or they have been read to me). I know that I have the right to withdraw from the study at any time or to refuse to answer any questions. If I do not agree to take part in the study. I understand that I will not be penalized for doing so by the researchers nor by any medical service personnel in the future. All my questions about the study and my participation in it have been answered. I freely accept to participate in this study.

_____

Name of participant (in capital letters) Signature Date

_____

Name of researcher (in capital letters) Signature Date

VI.ATLAS_TM study_Patient information sheet_v1_En.docx

Time and motion study

–

Information for the Patients

of the health care worker taking part in the Time and Motion Study

Version 1.0 - 20th March 2019

Hello I am ……, a health economist part of ATLAS, a research project with the NGO Solthis and the London School of Hygiene & Tropical Medicine.

ATLAS is a research project which will inform on the best way to introduce HIV self-testing in your country. This study that is part of the ATLAS project, its aim is the analysis of the costs of conventional HIV testing, and the costs associated with delivering HIV self-testing.

The purpose of the time and motion study is to estimate the time it takes for providers to provide HIV testing services and to provide HIV self-testing to a patient. We will be able to evaluate the staff costs directly associated with the provision of HIV care by estimating their working time on this activity.

We present this information because we will record the duration of your consultation with the health care provider who has agreed to participate in this study.

The researcher will be present during your consultation or stay out of the consultation room according to your preference. If it suits you, we will attend the consultation until the test is done but we will leave the room when reading the result of the test to respect the confidentiality of your clinical appointment. The data is anonymous, your name is not collected.

Additional information on the ATLAS program

If you would like more information about the study, you can contact one of the team members. A website dedicated to the ATLAS program can be found at this address (https://atlas.solthis.org/). You will find there a notice of information as well as the results of the research at the end of the project.

VII.ATLAS_TM study_Data collection tool_v1_En.docx

DATA COLLECTION FORM - TIME AND MOTION STUDY

STUDY ID:_____

Date: _____

Interviewer: _____

District: _____

Name of site: _____

Participant ID:_____

HIVST DISTRIBUTION MODEL	Check	
Female sex worker mobile outreach		Tick several boxes if the provider works across models during the observation period and report the type of model in the "Note" section for each observation
Female sex worker fixed site		
Men who have sex with Men mobile outreach		
Men who have sex with Men fixed site		
People who inject drugs mobile outreach		
People who inject drugs fixed site		
Consult' STI		
Index testing		
Young (16-24) outreach		
School and university health services		

DID THE PROVIDER GIVE CONSENT FOR THE INTERVIEW? (use the written consent forms)

1 YES		
2 NO	►	STOP THE ADMINISTRATION OF THIS STAFF TIME USE INTERVIEW

GRADE OF HIVST PROVIDER:

STAFF GRADE	Check
Nurse	
HST counsellor	
Lay counsellor	
Interpersonal communication agent	
Peer educator/volunteer	
Other (please specify):	

ENUMERATOR, READ

To begin, I'm going to ask you some background information. This will help us understand how your time is divided across services within a day. Please list your regular work hours during a normal working week. This includes all hours you spend at the facility or distribution site - including travel time (back and forth) to the distribution site if you do community-based distribution - from the time you start working until the time you finish.

WEEKLY AVERAGE WORKING HOURS:

	START TIME		END TIME	
	HH	MM	HH	MM
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				

Sunday							
Public Holidays							

Note: Please specify any particular working pattern (works every third weekend, etc.)

The following section should be filled out by observing one distributor at a single time for the entire working day. Record each activity observed as a separate line. Use one Time & Motion form for one provider. Use back of sheet if necessary.

CODE	ACTIVITY DESCRIPTION
HIVST ADMIN	Pre-drive admin, including decision where to go, stats collection etc. *(if community-based distribution model)*
DRIVE	Driving time for the distributor to reach the site, including time to pitch the tent *(if community-based distribution model)*
HTS	HIV Testing Services (can include individual, couple or group pre-test counselling; HIV rapid testing; individual, couple or group post-test counselling)
HIVST INFO	Information about self-testing before/without distribution. Use this code if the client declines to take test kit
HIVST 1	HIV self-testing kit primary distribution (can include pre-test counselling, demonstration on how to self-test, waiting for test results and post-test counselling) *(if distribution is to group, note no. of people in group under "Notes")*
HIVST 2	HIV self-testing kit secondary distribution includes pre-test counselling and demonstration on how to self-test *(if distribution is to group, note no. of people in group under "Notes")*
HTS/D2	HIV Testing Services that include a secondary distribution
OTHER DPS	Other Direct Patient Services: time allocated to services that are not related to HTS and HIVST (e.g. family planning, PrEP, ART initiation etc.) provided by the health care worker to a client
NON-DPS	Any time spent not facing clients (breaks, waiting, etc)

EXAMPLES:

Observation	*Activity Code*	*Start Time*	*End Time*	*Self-test on site (Yes/No/Not Applicable=NA)*	*Supervised self-test (Yes/No/NA)*	*HIV test result (+/-)*	*Notes*
1	*DRIVE*	*8:50*	*9:35*	*NA*	*NA*	*NA*	
2	*NON-DPS*	*9:35*	*9:45*	*NA*	*NA*	*NA*	
3	*HIVST INFO*	*9:45*	*9:52*	*NA*	*NA*	*NA*	*Client declined to take the kit*
4	*NON-DPS*	*9:52*	*10:04*	*NA*	*NA*	*NA*	
5	*HIVST1*	*10:04*	*10:16*	*No*	*NA*	*NA*	
6	*NON-DPS*	*10:16*	*10:24*	*NA*	*NA*	*NA*	
7	*HIVST1*	*10:24*	*10:52*	*Yes*	*Yes*	*-*	
8	*NON-DPS*	*10:52*	*11:08*	*NA*	*NA*	*NA*	
9	*HIVST2*	*11:08*	*11:20*	*NA*	*NA*	*NA*	
10	*NON-DPS*	*11:20*	*11:35*	*NA*	*NA*	*NA*	
11	*HTS*	*11:35*	*12:22*	*NA*	*NA*	*+*	*A kit is given to the newly identified HIV+ client*
12	*NON-DPS*	*12:22*	*12:38*	*NA*	*NA*	*NA*	
13	*OTHER DPS*	*12:38*	*12:53*	*NA*	*NA*	*NA*	*Family planning*

OBSERVATION				Description of additional data to collect: Self-test on site: the client self-tests on site. Supervised self-test: the provider stays with the client while waiting for the results. HIV test result: result of HIV test (or self-test) if the client tests for HIV.
START TIME		END TIME		
HH	MM	HH	MM	

Observation	*Activity Code*	*Start Time*	*End Time*	*Self-test on site (Yes/No/Not Applicable=NA)*	*Supervised self-test (Yes/No/NA)*	*HIV test result (+/-/NA)*	*Notes*
1							
2							
3							
4							
5							
6							
7							
8							
9							

Observation	*Activity Code*	*Start Time*	*End Time*	*Self-test on site (Yes/No/Not Applicable=NA)*	*Supervised self-test (Yes/No/NA)*	*HIV test result (+/-/NA)*	*Notes*
10							
11							
12							
13							
14							
15							
16							
17							
18							
19							
20							
21							
22							
23							
24							
25							
26							
27							

Observation	*Activity Code*	*Start Time*	*End Time*	*Self-test on site (Yes/No/Not Applicable=NA)*	*Supervised self-test (Yes/No/NA)*	*HIV test result (+/-/NA)*	*Notes*
28							
29							
30							
31							
32							
33							
34							
35							
36							
37							
38							
39							
40							
41							
42							
43							
44							
45							

Observation	*Activity Code*	*Start Time*	*End Time*	*Self-test on site (Yes/No/Not Applicable=NA)*	*Supervised self-test (Yes/No/NA)*	*HIV test result (+/-/NA)*	*Notes*
46							
47							
48							
49							
50							
51							
52							
53							
54							
55							
56							
57							
58							
59							
60							
61							
62							
63							

Observation	*Activity Code*	*Start Time*	*End Time*	*Self-test on site (Yes/No/Not Applicable=NA)*	*Supervised self-test (Yes/No/NA)*	*HIV test result (+/-/NA)*	*Notes*
64							
65							
66							

VIII. ATLAS – HIVST distribution sites – Cote d'Ivoire

Partner		Delivery channel	Region	District	For facility-based distribution - number of health centres	Quantity HIVST Y1	Quantity HIVST Y2	Quantity HIVST Y3	Total quantity (Y1-Y3)
HEARTLAND ALLIANCE	APROSAM	TS Outreach	GNSP	San Pedro	NA	4311	8622	10776	23709
		TS Outreach	GNSP	Tabou	NA	743	1487	1859	4089
		HSH Outreach	GNSP	San Pedro	NA	1633	3265	4082	8980
		HSH Outreach	GNSP	Tabou	NA	549	1098	1373	3020
	FFS	HSH Outreach	GNSP	Sassandra	NA	787	1573	1967	4327
		TS Outreach	GNSP	Sassandra	NA	1152	2304	2880	6336
	Orasur	HSH Outreach	GNSP	Soubré	NA	2338	4676	5846	12860
		HSH Outreach	GNSP	Méagui	NA				
		TS Outreach	GNSP	Soubré	NA	3740	7481	9351	20572
		TS Outreach	GNSP	Méagui	NA				
	BLETY	TS Outreach	Abidjan 1	Youpougon Est		3685	7369	9212	20266
	Espace confiance	TS outreach	Abidjan 2	Treichville- Marcory	NA	3686	7373	9215	20274
		TS Outreach	Abidjan 2	Port Bouët -Koumassi	NA	4347	8694	10868	23909
		TS Outreach	Abidjan 1	Youpougon Ouest	NA	3904	7808	9761	21473
		HSH Outreach	Abidjan 2	Treichville- Marcory	NA	1058	2117	2646	5821
		HSH Outreach	Abidjan 2	Port Bouët -Koumassi	NA	2444	4889	6111	13444
		HSH Outreach	Abidjan 1	Youpougon Ouest	NA	1192	2383	2979	6554
	Ruban Rouge	HSH Outreach	Abidjan 1	Youpougon Est	NA	2065	4129	5162	11356
Fondation Ariel Glaser		Consult°IST (pop° générale)	GNSP	San Pedro	10	2908	2908	2908	8724
		Consult°IST (pop° générale)	GNSP	Tabou	2	212	212	212	636
		Consult°IST (pop° générale)	GNSP	Soubré	14	3936	3936	3936	11808
		Consult°IST (pop° générale)	GNSP	Sassandra	7	1780	1780	1780	5340
		Consult°IST (pop° générale)	Abidjan 2	Treichville-Marcory	6	6118	6203	6091	18412
		Cas Index (pop° générale)	GNSP	San Pedro	12	1304	2173	2521	5998
		Cas Index (pop° générale)	GNSP	Tabou	2	329	549	636	1514
		Cas Index (pop° générale)	GNSP	Soubré	5	497	829	961	2287
		Cas Index (pop° générale)	GNSP	Sassandra	1	50	83	96	229
		Cas Index (pop° générale)	Abidjan 2	Treichville- Marcory	10	4154	6923	8031	19108
		SSSU (jeunes 16-24) Fixe	GNSP	San Pedro	1 site				
		SSSU (jeunes 16-24) Fixe	GNSP	Soubré	1 site	2455	3682	3682	9819
		SSSU (jeunes 16-24) Fixe	GNSP	Sassandra	1 site				
Association des Scouts Catholiques de Côte d'Ivoire		Jeunes (16 -24) Outreach	GNSP	San Pedro	NA				
			GNSP	Soubré	NA	3623	7246	7246	18115
			GNSP	Sassandra	NA				
				Total quantity per year		**65000**	**111792**	**132188**	**308980**

IX. ATLAS – HIVST distribution sites - Mali

Partner	Delivery channel	Region	District	For facility-based distribution - number of health centres	Quantity HIVST Y1	Quantity HIVST Y2	Quantity HIVST Y3	Total quantity (Y1-Y3)
ARCAD SIDA	Cas index (pop° générale)	Bamako	Bamako	6 sites: CESAC, CNAM, USAC CSRef Commune 1, 4, 5 et 6	2,916	5,184	6,481	14,581
		Sikasso	Koutiala	USAC CSRef Koutiala	181	322	403	906
		Koulikoro	Kati, Fana	2 sites: USAC CSRef Kati, UASAC CSRef Fana	272	483	604	1,359
		Kayes	Kayes	USAC CSRef Kayes	222	395	494	1,112
	Consult IST (pop° générale)	Bamako	Bamako	6 sites: CESAC, CNAM, USAC CSRef Commune 1, 4, 5 et 6	1,688	3,780	3,780	9,248
	(USAC intégré public)	Sikasso	Sikasso, Koutiala	2 sites: Unités santé sexuelle sikasso, USAC CSRef Koutiala	563	750	750	2,062
		Koulikoro	Kati, Fana	2 sites: USAC CSRef Kati, UASAC CSRef Fana	563	750	750	2,062
		Kayes	Kayes	USAC CSRef Kayes	563	750	750	2,062
	HSH et TS fixe (Cas index)	Bamako	Bamako	Halles de Bamako	117	208	260	584
	HSH et TS Fixe (Consult° IST	Bamako	Bamako	Halles de Bamako	281	375	375	1,032
	HSH et TS fixe (Consult° IST	Segou	Segou	Unité de santé sexuelle Ségou	281	375	344	1,001
	HSH Outreach	Sikasso	Sikasso, Koutiala	NA	130	230	288	648
		Bamako	Bamako	NA	1,330	2,365	2,957	6,652
		Segou	Ségou	NA	470	835	1,044	2,349
	TS outreach	Sikasso	Sikasso, Koutiala	NA	138	245	306	689
		Bamako	Bamako	NA	638	1,134	1,418	3,189
		Segou	Ségou	NA	203	360	450	1,013
Soutoura	HSH Outreach	Sikasso	Sikasso	NA	354	630	788	1,772
		Bamako	Bamako	NA	3,594	6,390	7,988	17,972
		Segou	Segou	NA	1,268	2,254	2,817	6,338
	TS outreach	Sikasso	Sikasso	NA	840	1,494	1,868	4,202
		Kayes	Kayes	NA	634	1,127	1,409	3,169
		Koulikoro	Koulikoro	NA	812	1,444	1,805	4,060
		Bamako	Bamako	NA	3,746	6,660	8,325	18,731
		Segou	Segou	NA	1,243	2,210	2,763	6,217
	HSH et TS fixe (Consult° IST)	Bamako	Bamako	CCDV Bamako	188	250	250	688
		Segou	Niono	CCDV Niono	188	250	250	688
		Sikasso	Bougouni,Kolondièba, Sélingué, Yanfolila	4 sites: CCDV Bougouni, CCDV Kolondièba, CCDV Sélingué, CCDV Yanfolila	750	1,000	1,000	2,750
		Kayes	Kayes, Kéniéba	2 sites: CCDV Kayes, CCDV Kéniéba	375	500	500	1,376
		Koulikoro	Koulikoro	CCDV Kati, CCDV Ouéléssébougou, CCDV Kangaba (Kourémalé)	562	750	750	2,062

Partner	Delivery channel	Region	District	For facility-based distribution - number of health centres	Quantity HIVST Y1	Quantity HIVST Y2	Quantity HIVST Y3	Total quantity (Y1-Y3)
Danayaso	TS outreach	Bamako	Bamako	NA	601	1,069	1,337	3,007
		Segou	segou	NA	490	871	1,089	2,450
		Sikasso	Sikasso, Koutiala, Koumentou	NA	200	356	446	1,002
AKS	Cas Index (pop° générale)	Sikasso	Sikasso	Sikasso	304	540	675	1,519
	TS Outreach	Sikasso	Sikasso, Koutiala	NA	488	868	1,085	2,440
	HSH Outreach	Sikasso	Sikasso, Koutiala	NA	417	742	927	2,086
AMPRODE SAHEL	HSH Outreach	Kayes	Kayes, Nioro, Diéma, Kita, Bafoulabé, Kéniéba	NA	650	1,156	1,445	3,250
		Koulikoro	Koulikoro, Kati, Kalaban Coro, Fana, Diola	NA	423	752	941	2,116
Cliniques publiques	Consult° IST (pop° générale)	Sikasso	Sikasso	Hopital de Sikasso	1,058	1,411	1,411	3,881
		Kayes	Kayes	Hopital de Kayes	213	284	284	780
		Bamako	Bamako	5 sites : HPG, HGT, HME, Commune 2 et 3	212	283	283	777
		Segou	Segou	Hopital de Ségou	424	565	565	1,554
	Cas Index (pop° générale)	Sikasso	Sikasso	Hopital de Sikasso	106	188	236	530
		Kayes	Kayes	Hopital de Kayes	245	436	545	1,225
		Bamako	Bamako	5 sites : HPG, HGT, HME, Commune 2 et 3	1,404	2,495	3,119	7,018
		Segou	Segou	Hopital de Ségou	113	200	251	564
	Cas Index /Walé	Segou	Ségou	Site de prise en charge Walé	143	254	317	713
		Total quantity per year			**32,601**	**55,970**	**66,913**	**155,485**

X. ATLAS – HIVST distribution sites - Senegal

Partner		Delivery channel	Region	District	For facility-based distribution - number of health centres	Quantity HIVST Y1	Quantity HIVST Y2	Quantity HIVST Y3	Total quantity (Y1-Y3)
ENDA	2 associations (Espoir, Adama)	HSH Outreach	DAKAR	08 (Centre, Ouest, Nord, Sud, Pikine, Guédiawaye, Keur Massar, Mbao)	NA	880	990	990	2860
	2 Associations (Xam Xamlé, Xewu Yéété)	HSH Outreach	THIES	02 (Thies et Mbour)	NA	880	990	990	2860
	1 association (Wer Werle)	HSH Outreach	Ziguinchor	01 Ziguinchor	NA	440	495	495	1430
	5 associations (Kiray, And Sopeku, Kay Bok, Karlene, Moytou)	TS Outreach	DAKAR	08 (Centre, Ouest, Nord, Sud, Pikine, Guédiawaye, Keur Massar, Mbao)	NA	1232	1386	1386	4004
	Enda (cliniques mobiles)	TS Outreach	DAKAR	08 (Centre, Ouest, Nord, Sud, Pikine, Guédiawaye, Keur Massar, Mbao)	NA	576	972	972	2520
		TS Outreach	THIES	01 Mbour	NA	576	972	972	2520
	Enda Distributeurs communautaires	HSH Outreach	DAKAR	11 (centre, ouest, Nord, sud, Diamniadio, Pikine, Guediawaye, Mbao, Keur Massar, Rufisque, Thiaroye)	NA	920	920	920	2760
			THIES	02 (Thies et Mbour)	NA	552	552	552	1656
			Ziguinchor	01 Ziguinchor	NA	368	368	368	1104
		TS Outreach	DAKAR	11 (centre, ouest, Nord, sud, Diamniadio, Pikine, Guediawaye, Mbao, Keur Massar, Rufisque, Thiaroye)	NA	2392	2392	2392	7176
			THIES	02 (Thies et Mbour)	NA	552	552	552	1656
			Ziguinchor	01 Ziguinchor	NA	368	368	368	1104
		UD Outreach	Ziguinchor	01 Ziguinchor	NA	96	128	128	352

Partner	Delivery channel	Region	District	For facility-based distribution - number of health centres	Quantity HIVST Y1	Quantity HIVST Y2	Quantity HIVST Y3	Total quantity (Y1-Y3)
CEPIAD	UD Fixe (Centre dédiée)	DAKAR	Centre	1 centre	419	744	930	2093
	UD Outreach	DAKAR	10 Districts (Centre, Ouest, Nord, Sud, Pikine, Guediawaye, Keur Massar, Mbao, Thiaroye, Rufisque)	NA	450	800	1000	2250
		THIES	Mbour	NA	180	320	400	900
DLSI	niques IST (pop° généra	Dakar	Guediawaye	01 Las palmas	248	359	386	994
		Dakar	Diamniadio	01 Diamniadio		697	751	1448
		Dakar	Diamniadio	01 PS Sébikotane		276	297	573
		Dakar	Rufisque	01 CS Rufisque		676	728	1403
		Dakar	Rufisque	01 EPS Rufisque	813	1174	1264	3251
		Dakar	Pikine	01 CS Baye Talla Diop	342	494	532	1369
		Dakar	Sud	01 IHS	439	634	683	1755
		Dakar	Mbao	01 CS Mbao	506	731	788	2025
		Thies	Mbour	01 CS Mbour	314	453	488	1256
		THIES	Thiès	01 CS de Thiès (10ième)	130	285	307	721
		Ziguinchor	Diouloulou	01 PS Kaffountine	111	258	278	648
		Ziguinchor	Zguinchor	01 PS Collette Senghor	142	303	327	772
	Cas Index (pop° générale	Dakar	Mbao	01 Mbao		125	175	301
		Dakar	Pikine	01 Pikine		103	144	247
		Dakar	Guediawaye	01 Roi Baudouin adulte		115	161	275
		Dakar	Sud	01 IHS		113	158	271
		Dakar	Rufisque	01 EPS Rufisque		93	130	222
		DAKAR	Centre	01 CRCF	192	320	447	959
		DAKAR	Centre	01 CTA	201	335	468	1004
		Thies	EPS1 Mbour	01 EPS1 Mbour	130	217	304	651
		Thies	Thies	01 CHR Thies		145	202	347
		Ziguinchor	Zguinchor	CHR Ziguinchor		167	234	401
		Ziguinchor	Diouloulou	01 CS Diouloulou		132	184	316
		Ziguinchor	CS Ziguinchor	01 CS Ziguinchor	161	268	375	803
		Ziguinchor	CS Bignona	01 CS Bignona	152	253	355	760
	Clinique dediée TS	DAKAR	Sud	Polyclinique	718	778	838	2334
	Clinique dediée HSH	DAKAR	Sud	Polyclinique	263	285	307	854
			Total quantity per year		**15742**	**22736**	**24725**	**63203**

Appendix III – Costs analyses of HIV testing services in sub-Saharan Africa: a systematic literature review. Ahmed et al.

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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

Student ID Number	1805320	**Title**	Mr
First Name(s)	Marc		
Surname/Family Name	d'Elbée		
Thesis Title	Estimating healthcare costs at scale in low- and middle-income countries – the case of community-based HIV self-testing scale-up in southern and western Africa		
Primary Supervisor	Prof 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?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	BMC Infectious Diseases
Please list the paper's authors in the intended authorship order:	Nurilign Ahmed, Jason J. Ong, Kathleen McGee, Marc d'Elbée, Cheryl Johnson, Valentina Cambiano, Karin Hatzold, Elizabeth L Corbett, Fern Terris-Prestholt, Hendramoorthy Maheswaran

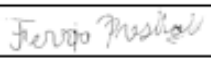
Stage of publication	**Submitted**

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 supported the study design, data extraction and analysis. I provided comments to the manuscript.

SECTION E

Student Signature	
Date	24/08/2021

Supervisor Signature	
Date	19/08/21

Title: Costs analyses of HIV testing services in sub-Saharan Africa: a systematic literature review

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

Abstract

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

Design: A systematic literature review of studies reported from January 2006 to October 2020.

Methods: We searched ten electronic databases for studies that reported estimates for cost per person tested, cost per HIV-positive identified in SSA. We explored variations in incremental cost estimates by different testing modalities (health facility-based, home-based, mobile, self-testing, campaign-style, and stand-alone), by primary or secondary/index HTS and by type of population tested (General population, people living with HIV, antenatal care male partner, antenatal care/postnatal women and key populations). All costs are presented in 2019$.

Results: Sixty-five studies reported estimates for HIV testing modalities. The incremental cost per person tested was lowest with self-testing services $12.75 (median =$11.50, IQR: $9.27-$13.92) followed by mobile-service $16.47 (median = $12.88, IQR: $9.88-$23.94), then home-based testing $19.3 (median = $13.42, IQR: $8.34-$23.36), then facility-based testing $19.45 (median = $9.69, IQR: $6.07-$28.03), then stand along $20.61 (median = $20.52, IQR: $15.10-26.084) and highest with campaign-style $27.64 (median = $26.70, IQR: $12.42-$41.93); lower with primary testing $16.63 (median = $10.68, IQR: $7.29-$18.40) compared with secondary/index testing $27.52,(median = $15.85, IQR: $14.41-$38.88); lowest with the general population $14.06 (median = $10.13, IQR: $7.00-$15.42) and highest with an antenatal male partner $47.94 (median: $55.19, IQR: 13.39-82.28). However, when considering the incremental cost per HIV-positive identified, the lowest cost was with home-based testing services $297.09 (median = $246.75, IQR: $140.50-$381.62), while campaign-style HTS remain the highest $555.91 (median = $388.70, IQR: $258.16-$555.91). In terms of primary versus secondary testing, when considering the incremental cost per HIV-positive identified, primary testing $352.31 (median = $157.03, IQR: $75.86-$393.61) remained lower than secondary/index testing $770.12 (median = $356.22, IQR: $246.75-$1041.58). Similarly, the incremental cost per HIV-positive identified remained lowest with the general population $262.89 (median = $140.13, IQR; $69.85-$338.79) and highest with antenatal and post-natal care $1,172.02 (median = $698.90, IQR: $270.14-$1140.17).

Conclusion: We identified a large number of studies reporting the incremental costs of different HIV testing modalities, but few studies undertook full costing. Although the cost per person tested estimates varied widely, the costs for stand-alone, health facility, home-based, and mobile services were comparable, while substantially higher for campaign-style HTS and the lowest for HIV self-testing. Our review informs policymakers of the affordability of various HTS to ensure universal access to HIV testing.

Research in context

Evidence before this study

Previous systematic reviews (1-3) have assessed either the cost or cost-effectiveness of HIV testing to the latest up to DATE. They reported costs for different HIV testing modalities across different setting, populations, and contexts.

Added-value of this study

Our study systematically reviewed the findings of previous costing studies of HIV testing services in sub-Saharan Africa. We explored how the costs of different HIV testing modalities vary by the costs per person tested and costs per HIV-positive case identified, by primary or secondary/index HTS and by type of population tested. Our study systematically reviewed the cost of HIV testing services to inform HIV testing planning with the most up to date economic evidence by including studies published after 2006. We used the Global Health Cost Consortium (GHCC) reference case to assess cost studies' quality.

Implications of all the available evidence

Our findings add to existing publications reviewing the cost studies of HIV testing services in sub-Saharan Africa. This 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 38 million people, with 1.7 million newly infected in 2019(4). Eastern and Southern Africa (ESA) continue to be disproportionately affected, accounting for 26% of incident HIV infections and 72% of people living with HIV (PLHIV) globally (4). The UNAIDS 95-95-95 targeted recommended that by 2030, 95% of all PLHIV should know their HIV status, 95% of individuals diagnosed with HIV infection should receive antiretroviral therapy (ART), and 95% of those on ART should be virally suppressed to ensure progress towards ending the HIV pandemic (5). At the end of 2017, in ESA, only 81% of PLHIV knew their HIV status (6, 7). Disparities in HIV testing coverage, knowledge of HIV positive status among men and adolescents, and mortality from HIV in men remain a significant concern (8-10). Access to HTS is also essential to ensure HIV-negative people are also referred to effective HIV prevention interventions, including voluntary male medical circumcision (VMMC), condoms, harm reduction and pre-exposure prophylaxis (11-20).

HIV testing is widely available in many sub-Saharan African countries, with testing delivered primarily in health facilities (through the outpatient department, antenatal care, TB., STI department) and various other testing modalities such as home-based workplaces mobile-service, campaign-style, and stand-alone HTS sites. These are delivered by a range of healthcare professionals, lay providers and peers, as well as individuals who may self-test. These strategic mixes of testing approaches have been found acceptable and important for reaching remaining people living with HIV (PLHIV) who do not know their status, including HIV testing provided through more convenient and confidential approaches like HIV self-testing (21-32). Policymakers striving to ensure access to an efficient and effective uptake of HTS in sub-Saharan Africa need to balance these objectives with the financial pressures to ensure cost-efficient spending. In order to achieve this, they urgently need better to understand the costs of different HIV testing modalities.

In this study, we systematically reviewed the findings of previous costing studies of HTS in sub-Saharan Africa. First, we explored how the costs of different testing modalities varied by the outcome, such as the incremental costs per person tested for HIV and the incremental costs per HIV-positive case identified. Second, we reviewed the incremental cost by different testing modalities, by primary or secondary/index HTS and by type of population tested.

Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Supplementary Table S3) (33).

This systematic review was limited to sub-Saharan Africa because most of these countries experienced a generalised epidemic. A description of the various HIV testing modalities in SSA is provided in Table 1 (34). It categorises the costing studies depending on how the results are presented.

Table 1 Definition of model HTS included in the review (34)

HTS model	Description

Health facility-based	Health facility HIV testing includes the provision of pre-test counselling, HIV rapid tests, and post-test counselling offered to clients within the departments of voluntary counselling and testing (VCT), antenatal clinic (ANC), post-natal care (PNC), provider-initiated HIV counselling and testing (PICT) or outpatient department (OPD) or voluntary medical male circumcision (VMMC) centres.
Home-based	Home-based HTS includes pre-test counselling, HIV rapid tests, and post-test counselling by trained HTS provider in the client's home.
Mobile-service	Mobile HTS uses tents and mobile van to provide HIV testing in different community locations such as markets, transport hubs, and open fields. The trained HTS provider selects the specific location on an ad hoc basis.
Self-testing	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 or integrated into mobile services or HIV fixed sites or offered at male-dominated workplaces or integrated with VMMC services.
Campaign-style	HIV testing uses more accessible community spaces that the Ministry of Health or specific organisations. It is more connected to the community, and it is designed to address community needs.
Stand-alone	Static HTS located near transport hubs and markets where it serves community members.
Other	Primary/direct testing providers directly provide HIV testing to individuals who seek HIV testing. Index testing, where providers work with individuals living with HIV (index clients) to list and invite their sexual partners for HIV testing and counselling. Social network testing approaches the recruitment of persons within the same social network for HIV testing and counselling. Workplace HIV testing industries such as military, mining, agriculture, fishing, long-distance drivers many notes have easy access to HTS and workplace HIV testing would be the best approach.

Inclusion and Exclusion Criteria

Costing studies were eligible for inclusion if they reported any cost estimates for HTS in a sub-Saharan African country. This included cost per person tested (US$pptested) and cost per HIV-positive case identified (US$ppositive). Costing studies were included in the analysis more than once if they reported costs for more than one HIV testing model. We included studies that explored HIV testing in all population groups except those that focused on newborn 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) detailing the inclusion and exclusion criteria.

Search strategy and identification of studies

The literature searches were undertaken in December 2019 and updated in October 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 (35). 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 analyses. The search strategy included concepts on cost-effectiveness analyses to capture primary costing data used in the cost-effectiveness modelling studies. Authors and experts in HIV economics were contacted by e-mail for further references, missing outcomes, and clarifications. References of included studies were reviewed for additional relevant articles. The full search strategy is included in Supplementary Table S2.

Study selection and data extraction

According to the inclusion criteria, two independent reviewers (NA and KM) screened the titles and abstracts independently for eligibility. 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 (36) to characterise eligible studies.

We classified the studies by whether they undertook a cost analysis. Studies were deemed to have conducted a cost analysis if they estimated the costs of delivering the HTS related to either the number of HIV tests performed or the number of HIV-positive individuals identified.

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 the person tested HIV negative, and the person tested HIV positive: $\text{US\$pptested} = \frac{total\ costs\ for\ HIV\ testing\ services}{(\text{Person tested HIV}-)+(\text{Person tested HIV}+)}$. For US$ppositive, the total costs for the given HIV testing modality were divided by all individuals that were tested HIV positive (if known those previously tested positive were excluded): $\text{US\$ppositive} = \frac{total\ costs\ \ for\ HIV\ testing\ services}{\text{Person tested HIV}+}$. For studies that reported costs for a package of interventions that included HIV testing and other health services (e.g., family planning or Tuberculosis screening), we excluded the costs for the other health services delivered. We extracted the year the costing exercise was conducted rather than the year the study was published. We assumed it to be the year before the publication date for studies that did not report the costing year. The included studies reported costing perspectives using different terminologies. We categorised the costing perspective as a provider, patient, or societal. A provider perspective captures the costs incurred by the organisation delivering the health intervention, a patient perspective only included the costs incurred by the users, and societal perspective included all the costs incurred by the organisation, the users and possibly second or third parties affected (e.g. a family member) (37).

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 program by reporting the additional capital and recurrent costs incurred without accounting for the cost of the existing infrastructure and overhead costs born by the existing health program. An incremental cost analysis may underestimate the cost of delivering new health interventions or the investment needed to sustain the current provision (38). By contrast, a full cost analysis includes 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 costs estimate the value of all resources used, including donated goods and services such as volunteer time (39). Third, we determined whether the cost represented estimates from primary costing studies (referred to as empirical) or modelled costs. Primary costing studies observe actual resource use to estimate costs, whilst modelled costs are based on assumed or expected resource use (39).

Study quality assessment

Two independent reviewers (NA and MD) assessed the quality of the costing methods using the GHCC reference case (36). The GHCC comprises 17 principles to guide cost estimation; we assessed whether the study had met these guidelines (Table 3). A detailed quality assessment for individual studies is included in Supplementary Tables S4 & S5.

Data analysis

All cost estimates were adjusted for inflation using the World Bank's consumer price index (40) and expressed in 2019 U.S. dollars (US$). First, expenses expressed in US$ 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 cost was inflated using the World Bank's consumer price index and converted back to US$ using the exchange rate of the base year (2019)(41). We did not conduct a meta-analysis on cost estimates due to variation in HTS approaches, populations served, costing perspectives and costing methods.

Results

We identified 65 eligible studies from 26,889 title and abstracts reviewed. The 65 eligible studies reported 169 cost estimates of HIV testing services. Overall, 76 reported costs for facility-based HTS, 32 for home-based testing, 18 for mobile services, 25 for self-testing, 13 for campaign-style, and five for stand-alone HTS (Figure 1). Table 2 summarises the results from studies that undertook a cost analysis. Over half of the studies (54%) were conducted in the Southern African region, 40% from the Eastern African region, and 6% from West Africa. Studies were undertaken in diverse settings, including low (32%), lower-middle (46%) and upper-middle (22%) -income countries, as well as in low to high HIV prevalent countries (1.2% to 27.1%). The majority of cost studies reported incremental (75%), financial (46%), and empirical costs (95%). Cost per person tested was reported by 91% of studies; fewer studies reported cost per person tested HIV-positive (57%), and a minority reported cost per person who never tested before (8%) and cost per ART initiation (14%) (Table 2).

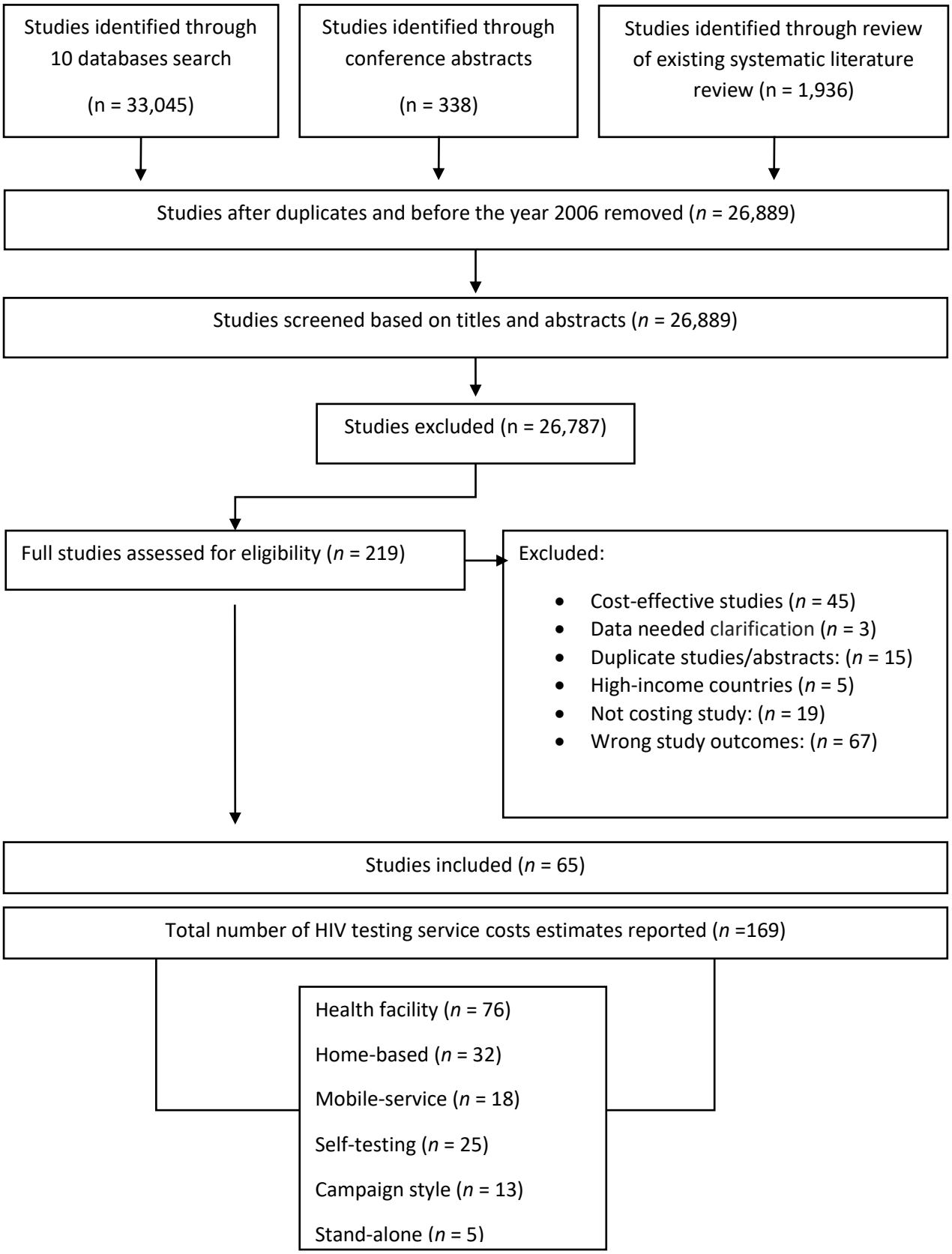

Figure 1 PRISMA flow diagram of the systematic literature review

Table 2 Summary of HTS cost studies included 2006-2020 in 2019 US$ (*N* = 65) in SSA

	Studies (n)	%	Cost Estimates (n)	%
Total	65	100	169	100
African Union (A.U.) Countries				
Kenya	11	17%	29	17%
Malawi	9	14%	20	12%
South Africa	11	17%	23	13%
Uganda	11	17%	31	18%
Zambia	6	9%	20	11%
Other Western AU countries	4	6%	10	6%
Other Southern AU countries	9	14%	26	15%
Other Eastern AU countries	4	6%	10	6%
Country Income Level				
Low Income	21	32%	56	33%
Lower-middle Income	30	46%	85	50%
Upper-middle Income	14	22%	28	17%
Country HIV prevalence (year of costing)				
<5%	5	8%	15	9%
5%-10%	29	45%	71	41%
10%-15%	16	25%	45	27%
15%-20%	9	14%	18	11%
>20%	6	10%	20	12%
Type of Cost Analysis				
Incremental vs. Full	49 vs. 16	75% vs. 25%	132 vs. 37	78% vs. 22%
Financial vs. Economic	30 vs. 35	46% vs. 54%	75 vs. 94	44% vs. 54%
Empirical vs. Modelled	62 vs. 3	95% vs. 5%	163 vs. 6	96% vs. 4%
Reported Costs				
$pptested	59	91%	159	94%
$ppositive	37	57%	89	53%
$new client	5	8%	14	8%
$ART	9	14%	20	12%
Total program costs	18	28%	45	27%

Western A.U. countries (Nigeria) (*n*=4), Southern AU countries (Botswana, Eswatini, Lesotho, Namibia, South Africa, Zambia, Zimbabwe *(n*=35), Eastern A.U. countries (Ethiopia, Kenya, Rwanda, Tanzania, Uganda (n=26).

Cost Analysis

Figure 2a shows the incremental cost estimates for US$pptested by HIV testing modalities from the provider's perspective. For for self-testing $12.75 (median = $11.50, IQR: $9.27-$13.92) (42-44); for mobile-service services $16.47 (median = $12.88, IQR: $9.88-$23.94) (45-54); for home-based testing $19.30 (median = $13.42, IQR: $8.34-$23.36) (49, 50, 52-64); facility-based HTS, the incremental US$pptested was $19.45 (median = $9.69, IQR: $6.07-$28.03) (15, 45, 53, 58-60, 63, 65-79); for stand-alone HTS $20.61 (median = $20.52, IQR: $15.10-26.08) (48, 58), and for campaign-style $27.64 (median = $26.70, IQR: $12.42-$41.93) (51, 80, 81). Most estimatess were for facility-based testing (*n* = 57) with only 13 estimates for campaign-style HTS.

Figure 2b shows the incremental estimates for US$ppositive by testing modality. For stand-alone was $107.15 (range: $107.15-$323.08) (58), for home-based testing $297.09 (median = $246.75, IQR: $140.50-$381.62) (49, 50, 52, 54, 56-58, 60-62, 64); for self-testing $379.40 (median = $113.04, IQR: $78.06-$516.30)(43); for mobile-service services $390.08 (median = $206.71, IQR: $126.321-$387.29) (47-52, 54, 66); facility-based HTS, the incremental US$ppositive was US$412.42 (median = $140.13, IQR: $66.84-$413.81) (58, 60, 66, 67, 69, 71, 77, 79); and for campaign-style $555.91 (median = $388.70, IQR: $258.16-$555.91) (51).

For the primary/direct testing, the incremental US$pptested was $16.63 (median = $10.68, IQR: $7.29-$18.40)(13, 42-45, 47, 49, 50, 52-54, 56-64, 66-71, 73, 74, 77, 82-107), while the secondary/index testing incremental US$pptested was $27.52 (median = $15.85, IQR: $14.41-$38.88)(58, 65, 76, 78, 108-111) (Figure 2c).

Figure 2d shows the incremental US$pptested by type of population tested. For the general population, the incremental US$pptested was $14.06 (median = $10.13, IQR: $7.00-$15.42); for PLHIV partners $20.71 (median = $15.65, IQR: $14.98-$32.20); for key population $20.31 (median = $9.49, IQR: $8.00-$27.21), for ANC/PNC $39.28 (median = $41.32, IQR: $14.08-$62.39); and for ANC partners $47.94 (median: $55.19, IQR: 13.39-82.28.);

Figure 2e shows the incremental US$pptested by country income level. For low-income, the incremental US$pptested was $13.97 (median= $10.43 IQR: $6.18-15.42)); for lower-middle-income $19.40 (median =$13.92 IQR: $8.32-25.42)) and for upper-middle-income $25.91 (median = 13.38 IQR:$7.38-29.96)).

Figure 3a shows the incremental US$pptested by the scale of the HTS costed, so by the number of tests performed. For the scale less than 10,000, the incremental US$pptested was $23.06 (range: $1.82- $111.38), for the scale between 10,000 and 20,000 $25.67 (range: $3.43- $74.63) and for the scale greater than 20,000 $18.22 (range: $4.25- $60.28). Figure 3b shows the incremental US$ppositive by scale. For the scale less than 1,000, the incremental US$ppositive was $428.08 (range: $6.74 $2,979.54). For the scale between 1,000 and 5,000, the incremental US$ppositive was $154.58 (range: $9.69- $691.82). For the scale greater than 5,000, the incremental US$ppositive was $329.93 (range: $45.91-$576.91). The average incremental costs were $17.96 for cost per person tested and

$368.24 for cost per HIV-positive individual identified. The average full costs were $38.18 for cost per person tested, and $351.40 for cost per HIV-positive person identified (

Supplementary Table S5). Table 3 shows the quality assessment of the cost studies and their compliance with the 17 principles of the GHCC reference case. Most cost studies complied with principles 1 to 13 and 17 and did not fully comply with principles 14 to 16 of the GHCC reference case (Supplementary Tables S4, & S5).

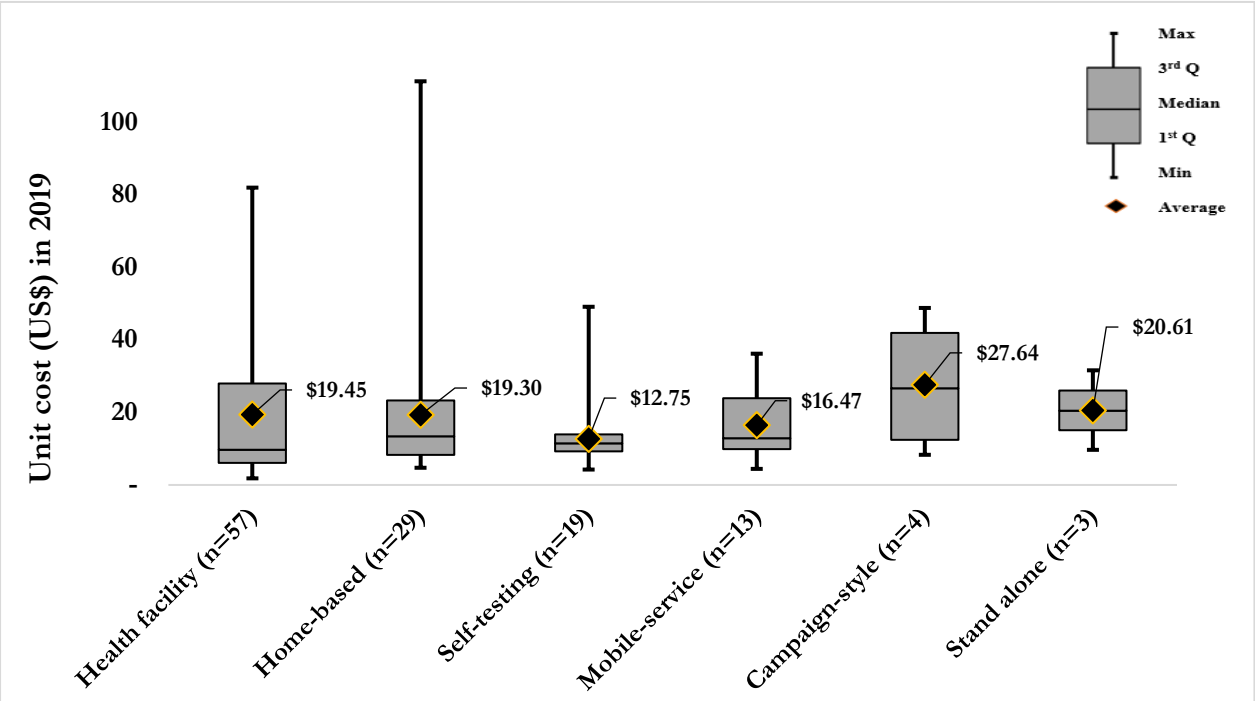

Figure 2a. Average incremental cost per person tested by mode of HIV testing services in 2019 US$

Facility-based testing: Median = $9.69 (IQR: $6.07-$28.03), Home-based testing: Median = $13.42 (IQR: $8.34-$23.36), Self-testing Median = $11.50 (IQR: $9.27-$13.92), Mobile services: Median = $12.88 (IQR: $9.88-$23.94), Campaign-style: Median = $26.70, (IQR: $12.42-$41.93), Stand alone testing: Median = $20.52, (IQR: $15.10-26.08)

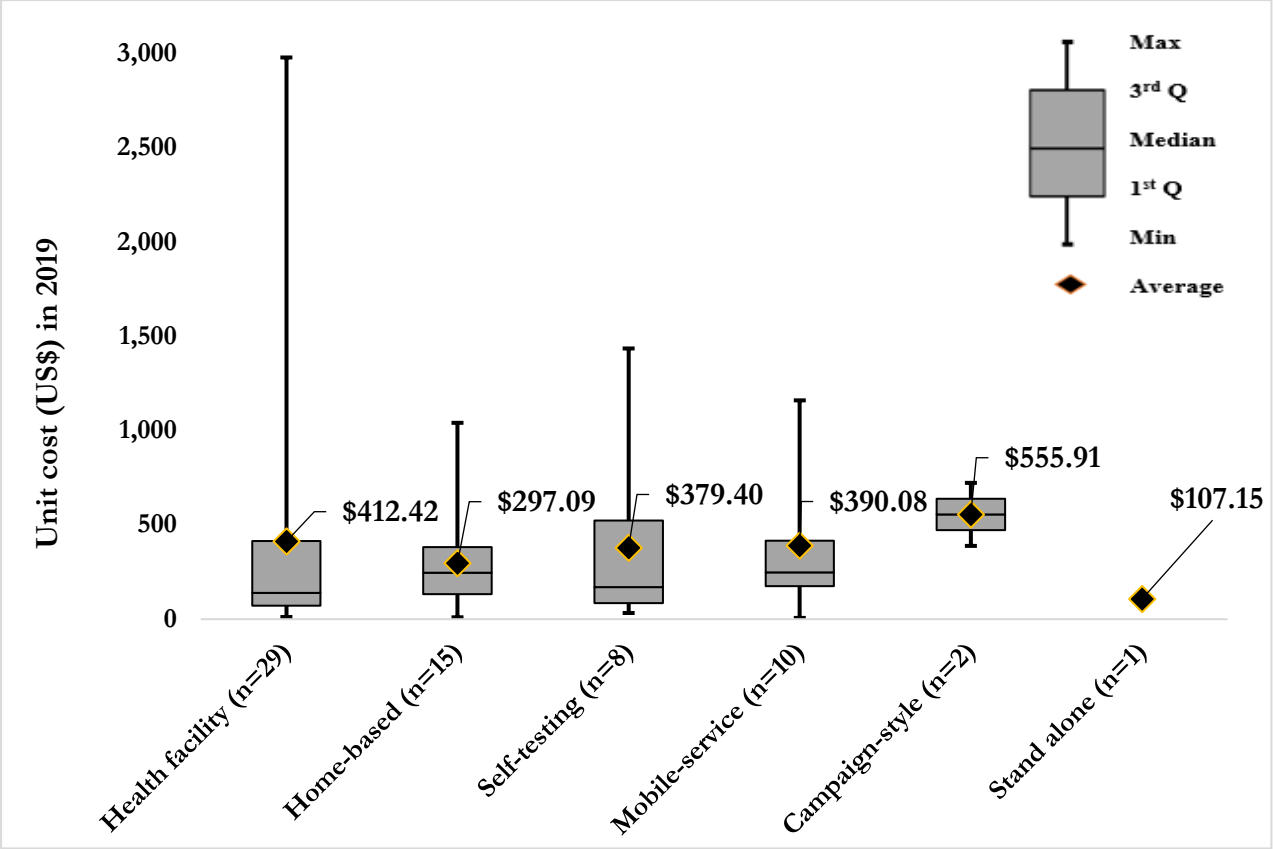

Figure 2b Average incremental cost per person tested positive by mode of HIV testing services in 2019 US$

Facility-based testing: Median = $140.13 (IQR: $66.84-$413.81), Home-based testing: Median = $246.75 (IQR: $140.50-$381.62), Self-testing services: Median = $113.04 (IQR: $78.06-$516.30), Mobile services: Median = $206.71 (IQR: $126.321-$387.29), Campaign-style: Median = $388.70 (IQR: $258.16-$555.91) and Stand alone testing: Only one value: $107.15.

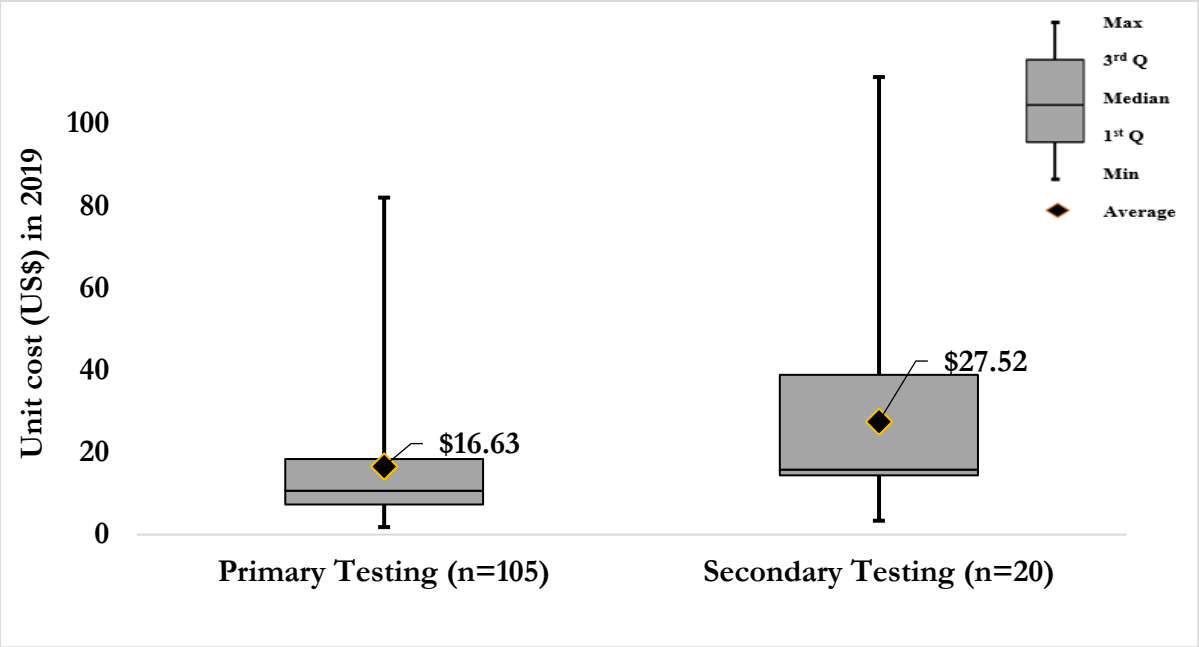

Figure 2c. Average incremental cost per person tested by primary/direct or secondary/index HIV testing services in 2019 US$

Primary/direct testing: Median = $10.68 (IQR: $7.29-$18.40) Secondary/index testing: Median = $15.85 (IQR: $14.41-$38.88)

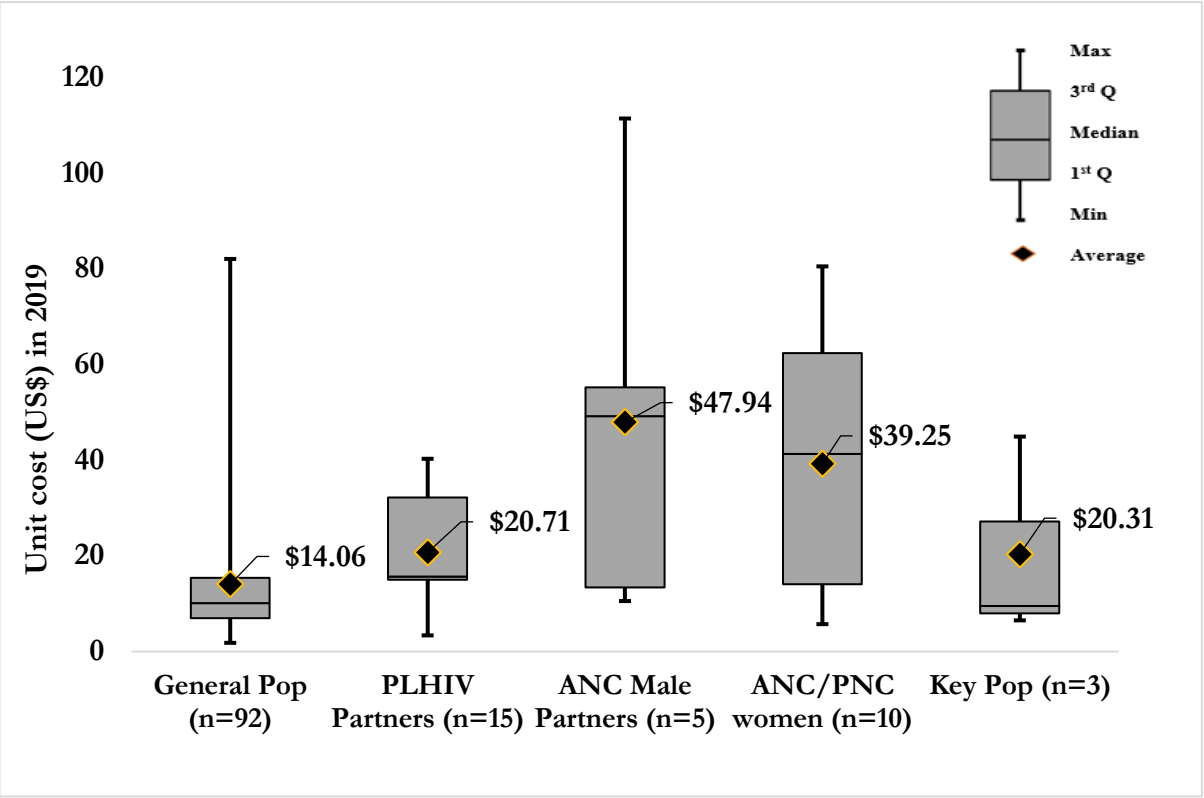

Figure 2d. Average incremental cost per person tested by population tested in 2019 US$

General population: Median = $10.13 (IQR: $7.00-$15.42), PLHIV Partners: Median = $15.65 (IQR: $14.98-$32.20), ANC Male partners: Median: $55.19 (IQR: 13.39-82.28), Pregnant women, or women breastfeed: Median = $41.32, (IQR: $14.08-$62.39), and Key populations: Median = $9.49 (IQR: $8.00-$27.21)

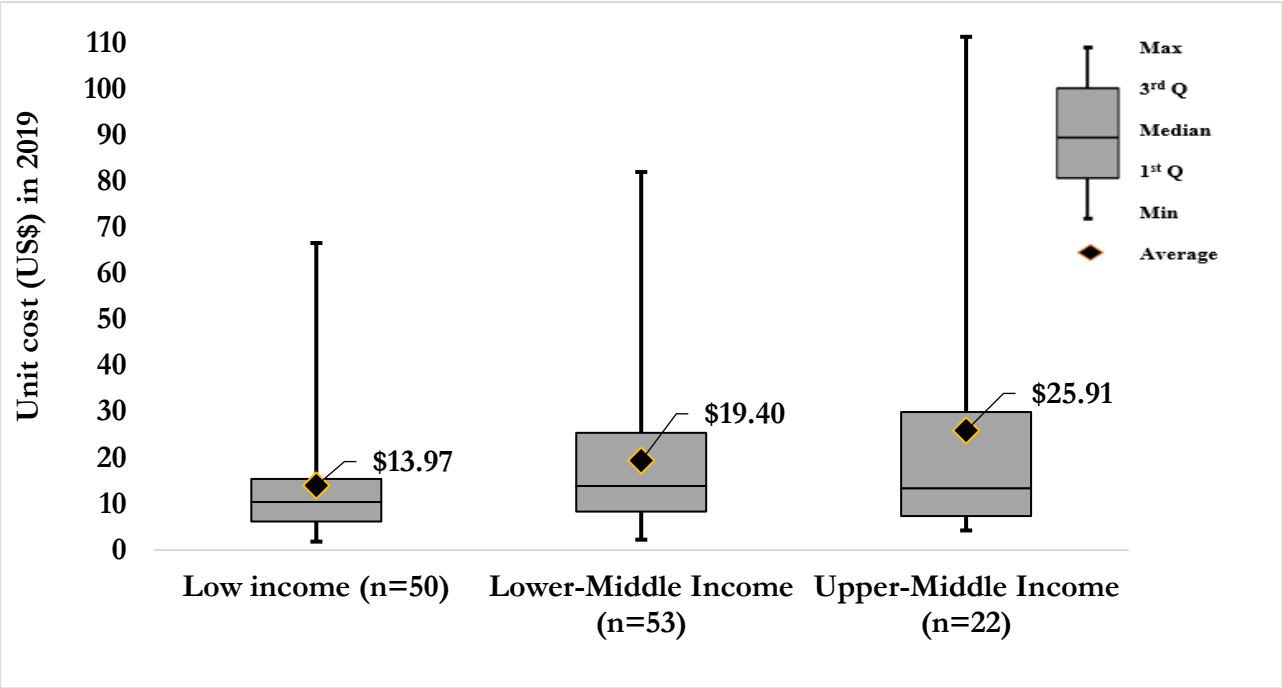

Figure 2e. Average incremental cost per person tested by country income level in 2019 US$

Low income: Median= $10.43 (IQR: $6.18-15.42), Lower-Middle Icome: Median =$13.92 (IQR: $8.32-25.42) Upper-Middle Income: Median = 13.38 (IQR:$7.38-29.96)

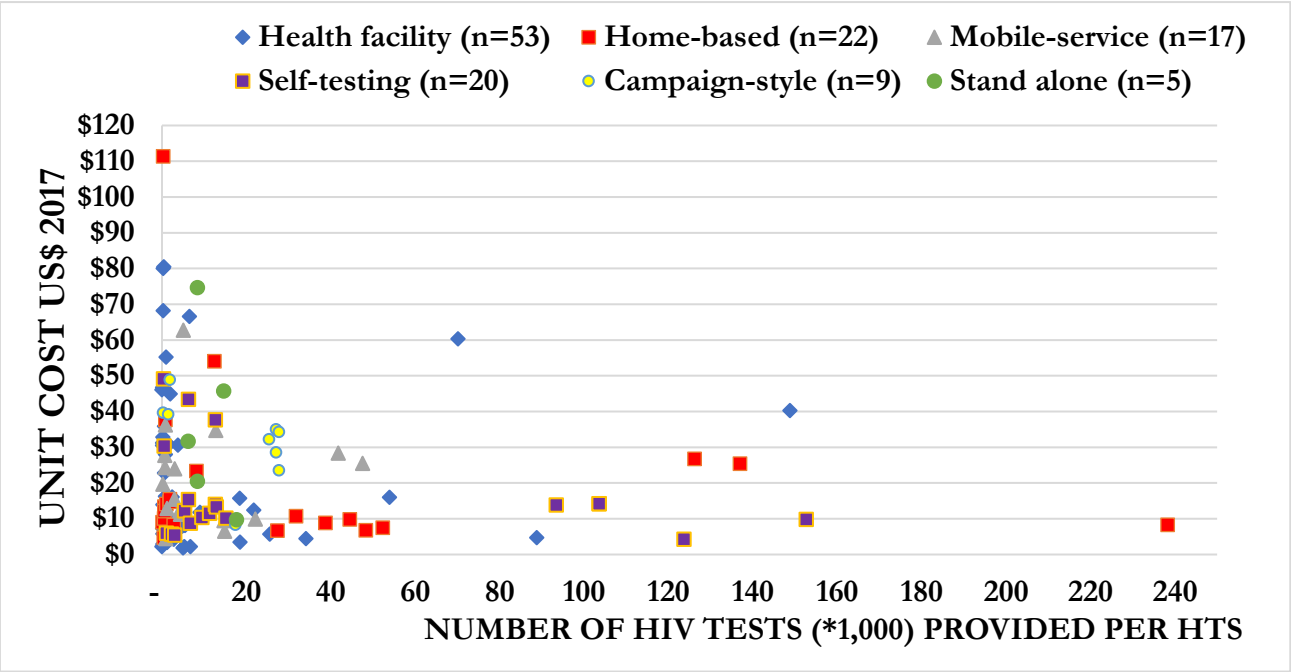

Figure 3a. Incremental unit cost per person tested by the number of persons tested by mode of HIV testing services in 2019 US$

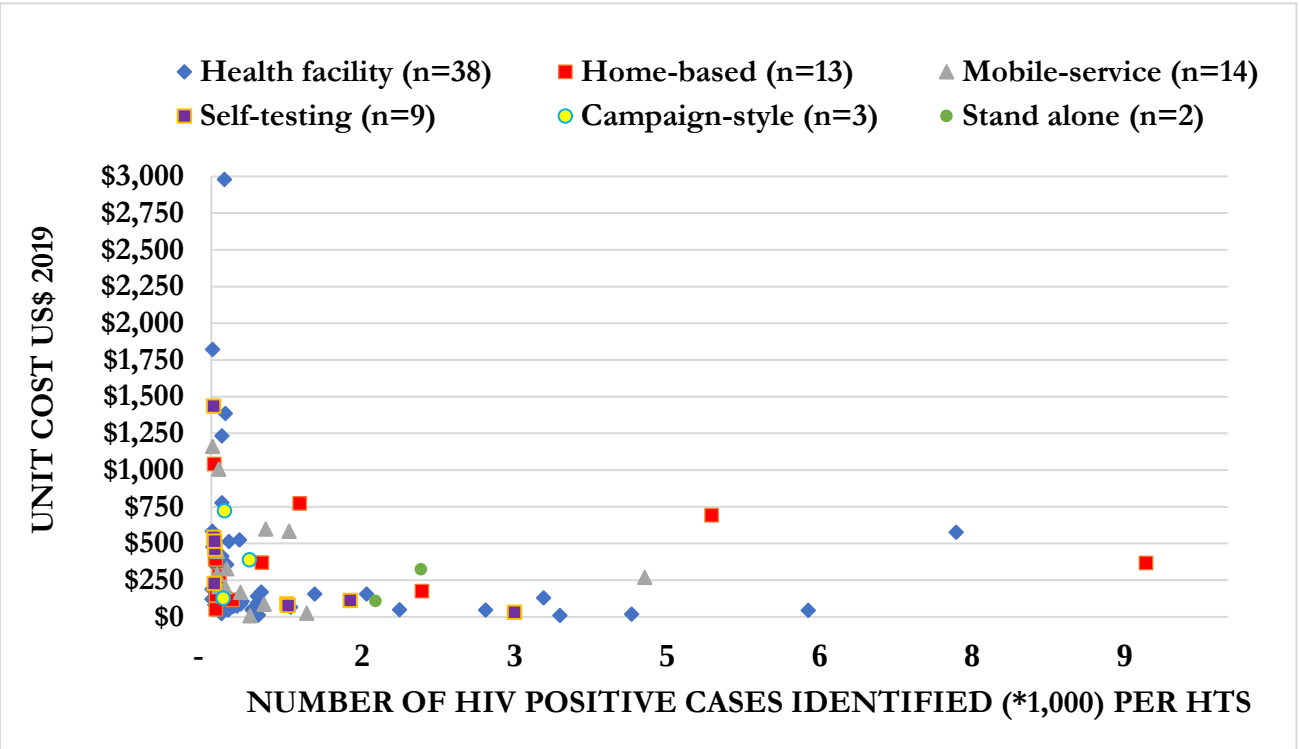

Figure 3b. Incremental unit cost per person tested positive by the number of persons tested positive by mode of HIV testing services in 2019 US$

Table 3 Quality assessment: Percentage of the cost studies compliant with GHCC Reference Case[a]

Quality assessment of cost studies (*n* = 65) following the GHCC principles (112) 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)	Characterising heterogeneity (P15)	Characterising uncertainty (P16)	Communicated limitations, conflicts of interest (P17)
Health facility (*n* = 76)	100%	80%	73%	87%	87%	22%	26%	17%	91%
Home-based (*n* = 32)	100%	85%	77%	88%	77%	8%	8%	31%	100%
Mobile-services (*n* = 18)	100%	93%	91%	100%	86%	0%	14%	71%	100%
Self-testing (*n* = 25)	100%	100%	100%	100%	100%	33%	33%	100%	100%
Campaign style (*n* = 13)	100%	100%	100%	100%	100%	0%	50%	50%	100%
Stand-alone (*n* = 5)	100%	100%	83%	50%	100%	0%	0%	0%	100%

[a] Data are presented as % unless otherwise indicated.

Table 5. Findings from a quality assessment using the GHCC's principles and methods reporting checklist for cost studies included in the review (112) (n=65)

Author, year (Ref)	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13[1]	P14	P15	P16	P17	Source	Score[1]
Adebajo, 2013(44)	Y	N	N	N	N	N	N	N	N	N	N	N/A	N/A	N	N	N	N	Slides	3/17
Ahmed, 2018(79)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	Poster	15/17
Aliyu, 2012(84)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	Y	N	Y	PRP	15/17
Allen, 2014(45)	Y	Y	N	N	Y	N	N	N	N	N	Y	N	N/A	N	N	N	N	Abstract	5/17
Armbruster, 2010(65)	Y	Y	N	Y	N	N	N	N	Y	Y	N	N	N	N	N	N	Y	PRP	6/17
Bassett, 2007(46)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N/A	N	N	N	N	Y	PRP	12/17
Bassett, 2014(75)	Y	Y	N	Y	Y	Y	Y	Y	N	Y	Y	N/A	Y	N	N	Y	Y	PRP	13/17
Bautista-Arredondo, 2016(47)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	N	Y	PRP	16/17
Bogart, 2017 (85)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	N	Y	PRP	16/17
Chang, 2016(76)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	14/17
Grabbe, 2010(77)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	PRP	14/17
Hauck, 2018(66)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	Slides	15/17
Hausler, 2006(48)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	PRP	14/17
Helleringer, 2013(67)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	14/17
Ibekwe, 2017(49)	Y	N	N	Y	N	N	N	N	N	N	N	N/A	N/A	N	N	N	N	Abstract	4/17
Kahn, 2011(82)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	PRP	14/17

Kahwa, 2008(86)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N	N	N	Y	PRP	14/17
Labhardt, 2014(68)	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	12/17
Lasry, 2019(69)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	PRP	15/17
Liambila, 2008(50)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	Y	N	Y	Report	15/17
Maheswaran, 2016(80)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	PRP	17/17
Meehan, 2009(78)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	PRP	13/17
Mangenah, 2019 (81)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	PRP	15/17
Menzies, 2009(51)	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	N/A	N/A	N	N	N	Y	PRP	12/17
Muhumuza, 2012(52)	Y	N	N	Y	Y	N	N	N	N	Y	N	N	N	N	N	N	Y	Abstract	5/17
Mulogo, 2013(53)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	14/17
Mwenge, 2017(54)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	PRP	15/17
Negin, 2009(70)	Y	N	Y	Y	Y	Y	N	Y	N	Y	Y	N/A	N/A	N	N	N	Y	PRP	11/17
Obure, 2015(55)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N	N	Y	PRP	16/17
Obure, 2012(56)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N	N	Y	PRP	15/17
Orlando, 2010(87)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N	N	Y	Y	PRP	15/17
Parker, 2015(71)	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	N	N	N	N	N	Y	PRP	10/17
Perchal, 2006(57)	Y	N	Y	Y	Y	N	Y	N	Y	Y	Y	N/A	N/A	N	N	N	Y	Slides	11/17
Perez, 2016(58)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	Poster	14/17
Pinto, 2013(59)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	N	Y	PRP	16/17

Rutstein, 2013(60)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	N	Y	PRP	14/17
Shade, 2013(61)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	Y	N	Y	PRP	15/17
Sharma, 2016(62)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	PRP	16/17
Sharma, 2014(72)	Y	Y	N	Y	N	Y	N	Y	Y	Y	N	N	N	N	N	N	Y	Abstract	8/17
Smith, 2015(73)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	N	Y	Y	PRP	15/17
Tabana, 2015(63)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	PRP	15/17
Terris-Prestholt, 2006(88)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	PRP	16/17
Terris-Prestholt, 2008(64)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PRP	14/17
Tumwesigye, 2010(74)	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

Discussion

This review adds to existing systematic literature reviews of HIV testing (1, 2, 22, 113) by exploring the costs of HIV testing strategies in SSA until the end of 2019. We identified cost estimates for six different HIV testing modalities. We found the incremental costs to test individuals through stand-alone, health facility, home-based, and mobile services were comparable: $20.61 (median = $20.52, IQR: $15.10-26.08), $19.45 (median = $9.69, IQR: $6.07-$28.03), $19.30 (median = $13.42, IQR: $8.34-$23.36) , and $16.47 (median = $12.88, IQR: $9.88-$23.94), respectively. In contrast, the incremental costs were substantially higher for campaign-style at $27.64(median = $26.70, IQR: $12.42-$41.93) and lower for HIV self-testing: $12.75 (median = $11.50, IQR: $9.27-$13.92) per person tested. Despite differentiating between full and incremental costs, cost variances across studies are significant, particularly for facility-based HTS (range: $1.82- $82.04), for home-based (range $4.75- $111.38), and self-testing (range: $4.25-$49.17) due to the heterogeneity of the scope of the costing study.

The average and the median incremental costs per person tested by secondary/index testing (median = $15.85, IQR: $14.41-$38.88) are higher than the average and median incremental costs per person tested by primary/direct testing (median = $10.68, IQR: $7.29-$18.40). The average number of persons tested in primary/direct testing is 20,250 compared with 1,347 in secondary/index testing across all studies and testing modalities, and this is a potential reason for the discrepancy in cost per person tested. When looking at the cost studies by type of population tested, the incremental cost per person tested was lowest amongst the general population at $14.06 (median = $10.13, IQR: $7.00-$15.42) and the highest for more targeted populations, especially for ANC male partners $47.94(median: $55.19, IQR: 13.39-82.28) and women in antenatal or postnatal care $39.25 (median = $41.32, IQR: $14.08-$62.39). ANC male partners and secondary/index testing are more targeted testing approaches that achieve greater yield than testing volume. These were also the most affordable based on the studies reviewed in consideration of greater yield. One of the limitations of secondary/index testing is that positivity and cost are higher when following up child index cases of PLHIV 0-14 vs partners. The effect of this would be higher costs without parsing out the impact of strategies that included a much larger sample of children and those that were adults (KP or GP). However, it was not feasible to address these in our analysis due to data scarcity and exclusion criteria.

When looking at the cost studies by country income level, the average incremental cost per person tested increased along with countries income ranking from $13.97 for low income to $19.40 for lower-middle-income and $25.91 for upper-middle-income. The higher wages could drive this in higher-income countries.

The cost per HIV-positive individual identified varied across the six HIV testing modalities. The incremental mean cost per HIV-positive identified at the health facility, home-based, self-testing, and mobile services were $412.42, $297.09, $379.40, and $390.08, respectively. Although there were a small number of cost studies for campaign-style (*n*=13) and stand-alone (*n*=5) HIV testing modalities, the mean costs were $555.91 and $107.15 per HIV-positive identified, respectively. Interpreting these cost estimates should be done with caution. Some of the differences observed in cost estimates were likely to be explained by variation in HIV prevalence and positivity in the population being tested across settings. For example, low HIV prevalence and high HIV testing rates in Rwanda led to low yields, and higher cost per HIV-positive person identified (67). One study presented cost estimates for

two rounds of home-based HIV testing and reported the cost per HIV-positive person identified nearly doubled between the two rounds (first round $366.97 vs second-round $691.82), and a reduction in HIV positivity rate partly explained this. The authors also stated costs were sensitive to community-specific factors such as service delivery and population characteristics (56). Thus, HIVST and door-to-door testing every 3-5 years may be a key opportunity to maximise limited resources in low prevalence settings.

Additionally, we observed variation in costing methods that reported incremental vs full cost or financial vs economic cost estimates. The average incremental costs were $17.96 for cost per person tested and $368.24 for cost per HIV-positive individual identified. The average full costs were $38.18 for cost per person tested, and $351.40 for cost per HIV-positive person identified (

Supplementary Table S5). Studies that used incremental costing methods will likely underestimate costs as they did not include the existing infrastructure and overhead costs borne by the existing health program. 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 utilised 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. 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 used the GHCC reference case to assess cost studies' quality, respectively (36, 114) (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-standardised definition of unit cost and approaches to data collection, cost analysis reporting. The included cost components varied considerably. Cost components and 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.

Limitations

This review has several limitations. We acknowledge the diversity and complexity of healthcare systems in sub-Saharan Africa. Thus, the review presented the cost studies 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 single country were all six HIV testing modalities assessed, which made the comparison of different testing modalities difficult. The shadow price for goods and opportunity costs of time, characterising heterogeneity and uncertainty, were poorly reported. Thus, it was challenging to identify economic or financial costing methods accurately. The methods used to undertake the economic analysis were not always

comprehensive or comparable, limiting the findings' generalizability. Some studies proposed checklists of transferability of economic evaluations (115-118). Moreover, we extracted data from diverse published sources, such as peer-reviewed papers, posters, abstracts, and presentations, limiting the quality assessment and comparison between studies.

Conclusion

We identified a large number of studies reporting the incremental costs of different HIV testing modalities, but few studies undertook full costing. Although the cost per person tested estimates varied widely, this study presented the different HIV testing approaches for different population or setting that would be informative for SSA. Targetted testing approaches such as ANC male partners and secondary index testing achieve greater yield-especially as countries achieve 95-95-95.

. Acknowledgements

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Authors' contributions

N.A. and FTP planned the study. N.A. and K.M. conducted the search. N.A. and K.M. extracted, analysed, interpreted the data, and produced a draft manuscript. N.A. K.M. and M.D. conducted study appraisals. FTP, J.O. and H.M. 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 studies compliant with GHCC Reference case.

Supplementary Table S1 to Table S6 and Figure S1 to Figure S8

Supplementary document

Title: Costs analyses of HIV testing services in sub-Saharan Africa: a systematic literature review

Authors: Nurilign Ahmed, Jason J. Ong, Kathleen McGee, Marc d'Elbée , Cheryl Johnson, Valentina Cambiano, Karin Hatzold, Elizabeth L Corbett, Fern Terris-Prestholt, Hendramoorthy Maheswaran

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.	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 no new primary costs data are presented.

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 analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	980
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	256,689

	(deficiency virus)) OR acquired immunodeficiency syndrome OR acquired immunedeficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immune$) AND (deficiency syndrome)) OR Sexually Transmitted Diseases	
Concept 2	Counselling OR Counseling OR Counse*OR Testing OR Test*	495,348
Concept 3	Cost OR Costs OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives* OR Cost*	2,320,362
C1 AND C2 AND C3		569
Concept 4	hiv self-testing OR hiv self-test OR hivst OR home test* OR rapid test*	1993
Popline		
C1 AND C2 AND C3	HIV Infections* OR HIV OR human immunodeficiency virus* OR acquired immunodeficiency syndrome* OR AIDS And Counselling OR Counseling OR Counse*OR Testing OR Test* AND Cost OR Costing OR Cost-effectiveness OR Cost-effectiveness analysis OR Cost effectiveness analysis OR Effec* OR effectives*	175
Concept 4	hiv self-test* OR hiv self-testing	68
SCOPUS*		
C1 AND C2 AND C3	HIV Infections OR HIV OR hiv OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect$ 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	5,138

	((acquired immun*) AND (deficiency syndrome)) OR Sexually Transmitted Diseases	
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	Summarise 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 (112)

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 generalisable.
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 minimise.
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 minimise 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 annuitised 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 subsidised goods).
Principle 15	P15	Variation in the cost of the intervention by site size/organisation, 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 characterised (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 Summary of incremental and full cost estimates

	Average Incremental Costs		**Average Full Costs**	
	$pptested	$ppositive	$pptested	$ppositive
Total (n=175)	$17.96	$368.24	$38.18	$351.40
Countries				
Botswana *(n=2)*			$44.40	$678.77
Eswatini *(n=5)*	$11.58	$205.48	$31.13	$121.42
Ethiopia *(n=2)*	$31.53			
Kenya *(n=29)*	$25.11	$178.56	$32.77	$139.41
Lesotho *(n=13)*	$14.11	$300.13	$29.33	$670.08
Malawi *(n=26)*	$10.79	$149.00		
Namibia *(n=3)*			$48.03	$587.80
Nigeria *(n=10)*	$22.55	$1,297.86		
Rwanda *(n=3)*	$10.09	$1,528.00		
South Africa *(n=23)*	$27.41	$480.72		
Tanzania *(n=5)*	$8.30	$353.08		
Uganda *(n=31)*	$3.76	$226.26	$33.56	$522.45
Zambia *(n=20)*	$20.29	$312.66	$52.34	$79.04
Zimbabwe *(n=3)*	$11.35	$180.55	$80.00	
Income Level				
Low income *(n=62)*	$12.87	$293.71	$ 33.56	$522.45
Lower-middle income *(n=85)*	$19.40	$382.65	$37.10	$217.80
Upper-middle income *(n=28)*	$27.41	$480.72	$46.58	$633.29
Country HIV prevalence (year of costing*)*				
1%-5% *(n=15)*	$21.05	$1,374.57		
5%-10% *(n=71)*	$15.59	$217.52	$32.95	$248.85
10%-15% *(n=51)*	$15.18	$215.81	$53.98	$282.54
15%-20% *(n=18)*	$31.94	$565.08		
20%-25% *(n=15)*	$14.11	$300.13	$32.07	$674.43

25%-30% *(n=5)*	$11.58	$205.48	$31.13	$121.42
HTS Type				
Campaign style *(n=13)*	$27.64	$413.14	$36.88	
Facility based *(n=76)*	$19.45	$388.33	$42.26	$180.39
Facility - ANC/PMTCT *(n=13)*	$42.74	$967.23	$44.09	$582.60
Facility - HTC stand-alone *(n=36)*	$14.68	$276.35	$48.91	$48.53
Facility – Integrated *(n=12)*	$30.69	$33.83	$23.34	$89.95
Facility – OPD *(n=15)*	$6.91	$83.96	$60.28	$576.91
Home based *(n=38)*	$16.63	$297.09	$27.83	$704.62
Mobile *(n=18)*	$16.47	$356.93	$37.81	$483.69
Self-testing *(n=25)*	$14.49	$441.03	$28.18	$462.30
ST- Community *(n=8)*	$9.83	$529.59	$40.55	
ST- Facility *(n=12)*	$10.70	$92.00	$14.75	
ST- Home *(n=5)*	$30.04	$2,358.10	$30.30	$462.30
Stand-alone *(n=2)*	$20.61	$107.15	$60.16	$323.08
Primary vs Secondary Testing				
Primary/Direct testing *(n=144)*	$16.63	$335.80	$38.64	$375.16
Secondary/Index testing *(n=31)*	$23.30	$802.91	$30.75	$274.19

Table S6 Summary of HTS cost studies included 2006-2019 in 2019 USD (*n*=65)

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
Adebajo, 2013(45)	Nigeria	Health facility, HTC	Key population	Inc/Fin/Emp	$44.92	-	1,988	177	NS
		Mobile service, referred			$9.49	-	14,726	480	
		Mobile service peer-lead			$6.51	-	14,895	1,853	
Ahmed, 2018(42)	Zambia	Self-testing, Facility-based	General population	Inc/Fin/Emp	$13.34	-	12,885	NA	TRNG, SNST BLDG, STOR, EQP, SUPL, VEH PER, TEST, REC
		Self-testing, VMMC			$11.50	-	11,330	NA	
		Self-testing, community- based			$14.23	-	103,589	NA	
Aliyu, 2012(82)	Nigeria	Health facility	General population	Inc/Fin/Emp	$9.69	-	N.S.	NA	TRNG, FURN EQP, PER, EST, ARV
					$24.23	-	N.S.	NA	
					$8.28	-	N.S.	NA	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
Allen, 2014(65)	Zambia	Health facility (CHCT)	General population	Inc/Fin/Emp	$40.28	-	148,839	NA	TRNG, SNST, EQP, SUPL, VEH, PER, OVHD ADMN, M&E, TEST
Bassett, 2007(66)	South Africa	Health facility OPD	General population	Inc/Fin/Emp	$7.29	$21.98	137	102	BLDG, PER, TEST
					$7.66	$11.47	1,414	463	
Bassett, 2014(46)	South Africa	Mobile service	General population	Inc/Fin/Mod	-	$25.46	18,870	939	VEH, PER
Bautista-Arredondo, 2016(67)	Kenya	Health facility HTC	General population	Inc/Eco/Emp	$8.09	$168.80	1,270	491	TRNG, PER, SUPV
		Health facility ANC/PMTCT	Pregnant women, or women breastfeeding		$68.21	$778.11	288	105	
	Rwanda	Health facility	General population		$4.51	$1233.10	2,340	106	
			Pregnant women, or women breastfeeding		$16.24	$1823.04	812	14	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
	South Africa	Health facility	General population		$28.03	$156.45	808	1,019	
			Pregnant women, or women breastfeeding		$80.48	$512.75	426	172	
	Zambia	Health facility	General population		$13.92	$89.35	242	291	
			Pregnant women, or women breastfeeding		$35.89	$413.81	618	104	
Bautista-Arredondo, (2018) (119)	Nigeria	Health facility	General population	Inc/Eco/Emp	$30.49	$1,386.12	141	139	TRNG, EQP. VEH PER, SUPV
			Pregnant women, or women breastfeeding		$46.75	$2,979.54	137	131	
Bogart, 2017 (83)	Uganda	Home-based	General population	Inc/Eco/Emp	$37.63	-	822	-82	TNSP, PER, TEST
		Campaign style			$39.62	-	344	-41	
Bulterys, (2020)(108)	Uganda	Self-testing Facility-based PWLHW	ANC Male partners	Inc/Eco/Emp	$13.39	-	-	-	TRNG SNST, BLDG, EQP SUPL, TNSP PER,

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
		Self-testing Facility-based positive partner test			-	$11.89	NS	NA	OVHD, TEST, WST, REC
		Self-testing Facility-based negative partner test			$10.55	-	N.S.	NA	
Cham, (2019)(84)	Tanzania	Health facility OPD	General population	Inc/Eco/Emp	$4.75	$128.98	88,813.	3,270	TRNG, EQP SUPL, TNSP, PER
		Home-based			$6.73	$369.69	27,407	499	
		Campaign style			$8.32	$388.70	17,475	374	
Change, 2016(47)	Uganda (West)	Mobile service	General population	Inc/Eco/Emp	$11.22	$166.17	4,417	287	BLDG, EQP SUPL, PER
					$24.36	$288.84	771	57	
	Uganda (East)	Mobile service	General population		$12.27	$329.38	4,260	153	
					$27.75	$1,160.67	675	14	
	Kenya	Mobile service	General population		$15.46	$86.47	2,969	519	
					$36.22	$203.97	832	136	
Grabbe, 2010(48)	Kenya	Mobile service	General population	Ful/Eco/Emp	$25.47	$268.54	47,539	4,265	BLDG , EQP ,SUPL ,VEH ,PER ,OVHD
					$28.32	-	41,829	3,782	
		Stand-alone			$45.69	$323.08	14,634	2,063	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
			General population		$74.63	-	8,415	1,612	
Cherutich, (2018)(109)	Kenya	Health facility - index	PLHIV Partners	Ful/Eco/Emp	-	$30.42	NA	NS	BLDG, EQP SUPL, TNSP, OVHD, M&E, STRT
		Health facility - index			-	$21.43	NA	NS	
DeBeer, (2015)(120)	Namibia	Health facility	General population	Ful/Eco/Emp	$ 60.28	$576.91	70,143.	7,329	TRNG, BLDG, FURN, TNSP PER, TEST
		Mobile service			$62.75	5$98.69	5,124.	537	
d'Elbée,(2020) (85)	Lesotho	Campaign style	General population	Ful/Eco/Emp	$32.20	-	25,433	NA	TRNG, SNST BLDG ,STOR EQP ,SUPL ,TNSP ,VEH ,PER ,WST STRT
		Campaign style			$28.50	-	27,045	NA	
		Self-testing community-based			$43.40	-	6,300	NA	
		Campaign style			$23.50	-	27,780	NA	
		Self-testing community- based			$37.70	-	12,687	NA	
		Campaign style			$35.00	-	27,045	NA	
		Self-testing community-based			$15.40	-	6,300	NA	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
		Campaign style			$34.30	-	27,780	NA	
		Self-testing community-based			$14.00	-	12,687	NA	
George, (2018) (86)	Kenya	Self-testing	Key population	Ful/Eco/Emp	$15.90	-	N.S.	NA	TRNG, BLDG, EQP, SUPL, COMM, PER OVHD, SUPV
		Self-testing			$13.59	-	N.S.	NA	
		Health facility			$5.64	-	N.S.	NA	
Golovaty, (2018) (87)	South Africa	Home-based	General population	Inc/Eco/Emp	$10.08	-	570.00	NA	TRNG, MTG BLDG, EQP SUPL, COMM TNSP, PER OVHD, M&E TEST, STRT
Grabbe, (2010)(88)	Kenya	Mobile service	General population	Ful/Eco/Emp	$25.47	$268.54	47,539	4,265	BLDG, EQP SUPL, VEH. PER OVHD
		Mobile service			$28.32	-	41,829	3,782	
		Stand-alone			$45.69	$323.08	14,634	2,063	
		Stand-alone			$74.63	-	8,415	1,612	
Hauck, 2018(56)	Zambia	Home-based	General population	Inc/Fin/Emp	$26.77	$366.97	126,208	9,196	EQP, SUPL ,TNSP ,PER ,ADMN
					$25.42	$691.82	136,966	4,921	
Hausler, 2006(68)	South Africa	Health facility	General population	Ful/Eco/Emp	$15.05	-	NS	NA	
					$18.40	-	N.S.	NA	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
					$11.71	-	N.S.	NA	TRNG ,BLDG ,FURN EQP ,VEH , PER ,SUPV ,TEST
Helleringer, 2013(57)	Malawi	Home-based	General population	Inc/Fin/Emp	$12.13	$150.45	597	48	TRNG, SNST, TNSP
					$13.42	$393.67	586	45	
Hewett, (2016) (89)	Zmabia	Health facility	General population	Ful/Eco/Emp	$88.63	-	N.R.	NA	N.R.
					$86.44	-	N.R.	NA	
					$82.04	-	N.R.	NA	
Ibekwe, 2017(69)	Nigeria	Health facility	General population	Inc/Eco/Mod	-	$476.26	NA	15	N.R.
			Pregnant women or women breastfeeding		-	$349.54	NA	44	
Kabami ,(2017) (90)	Uganda	Campaign style	General population	Ful/Eco/Emp	-	$127.61	2,119	116	TRNG, SNST ,EQP ,SUPL , TNSP ,PER OVHD ,ADMN M&E ,TEST
Kahn, 2011(80)	Kenya	Campaign style	General population	Ful/Eco/Emp	$13.78	-	N.S.	NA	TRNG, SNST, SUPL ,TNSP ,PER
					$57.93	-	N.S.	NA	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
					$44.47	-	N.S.	NA	
Kahwa, 2008(121)	Tanzania	Health facility	General population	Inc/Eco/Emp	$15.97	-	53,926	NA	BLDG, FURN EQP, SUPL ,VEH ,PER ,TEST
Korte, (2020) (110)	Uganda	Health facility ANC/PMTCT	ANC Male partners	Ful/Fin/Emp	$31.20	$582.60	187	10	TRNG, EQP, SUPL, PER
		Self-testing, home-based			$30.30	$462.30	519	34	
Labhardt, 2014(49)	Lesotho	Home-based	General population	Inc/Fin/Emp	14.14	393.33	1,083	39	SUPL TNSP, PER, TEST
		Mobile service			12.87	206.60	1,207	75	
Labhardt, (2019) (93)	Lesotho	Home-based - weekdays	General population	Inc/Fin/Emp	$10.12	$322.76	NS	NS	TRNG, MTG, EQP, SUPL ,TNSP ,PER ,TEST
Labhardt, (2019)(93)	Lesotho	Home-based-weekends	General population	Inc/Fin/Emp	$19.27	$1017.41	NS	NS	NS
Lasry, 2019(50)	Botswana	Home-based	General population	Ful/Eco/Emp	$54.10	$773.70	12,415	870	SNT, EQP, SUPL, TNSP ,PER ,ADMN ,TEST
		Mobile service			$34.70	$583.85	12,820	766	
Liambila, 2008(70)	Kenya	Health facility	General population	Inc/Fin/Emp	$46.12	-	27	NA	TRNG, SNT ,MTG ,SUPL ,PER ,SUPV TEST

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
Maheswaran, 2016(43)	Malawi	Self-testing	General population at health facility-1	Inc/Eco/Emp	$8.73	$78.06	6,759	756	TRNG, EQP, PER, OVHD, M&E
		Self-testing	General population at health facility-2		$12.25	$88.57	5,372	743	
		Self-testing	General population at health facility-3		$10.32	$32.81	9,488	2,984	
		Self-testing	General population at the health facility		$10.18	$113.04	15,190	1,367	
Maheswaran, (2017)(122)	Malawi	Health facility	General population	Ful/Fin/Emp	-	$508.74	NA	NS	TRNG, EQP, PER, OVHD ,M&E
Meehan, 2017(51)	South Africa	Campaign-style	General population	Inc/Fin/Emp	$48.85	$723.11	1,909	128	BLDG, UTL, COMM, OVHD, M&E
		Mobile service			$23.94	$1006.61	3,057	74	
	Malawi			Ful/Eco/Emp	$9.82	-	152,671	-	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
Mangenah, 2019 (44)	Zambia	Self-test, home-based	General population		$14.23	-	103,589	-	TRNG, SNST, BLDG ,STOR ,EQP ,SUPL , TNSP ,VEH ,PER ,TEST ,WST ,REC
	Zimbabwe				$13.84	-	93,459	-	
Medley, (2019)(123)	South Africa	Health facility	ANC Male partners	Inc/Fin/Emp	$55.19	$356.22	966	150	NS
		Home-based			$111.38	$1,041.58	280	30	
		Self-testing			$49.17	$1,435.94	401	23	
Menzies, 2009(58)	Uganda	Stand-alone	General population	Inc/Fin/Emp	20.52	107.15	8,391	1,616	TRNG, BLDG, EQP ,SUPL ,UTL ,VEH ,PER ,TEST
		Health facility	General population		12.44	45.91	21,755	5,872	
		Home-based	PLHIV Partners		14.75	246.75	1,861	80	
		Home-based	General population		8.83	174.62	38,799	2,072	
		Stand-alone	General population		31.64	-	6,227	1,511	
		Health facility	General population		15.69	-	18,428	5,807	
		Home-based	PLHIV Partners		15.49	-	1,916	101	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
		Home-based	General population		9.81	-	44,523	2,350	
Mostert ,(2020) (96)	South Africa	Self-testing	General population	Inc/Eco/Emp	$4.25	-	123,727	NA	SNST, EQP, SUPL ,TNSP ,VEH PER ,M&E, TEST,WST
Muhumuza, 2012(59)	Uganda	Health facility	General population	Inc/Fin/Emp	$4.49	-	34,119	3,753	NS
		Home-based			$10.68	-	31,770	953	
Mulogo, 2013(60)	Uganda	Health facility	General population	Inc/Fin/Emp	$6.07	$82.10	454	36	TRNG, BLDG, FURN, SUPL, TNSP, PER
		Home-based			$4.75	$51.92	444	45	
Mwenge, 2017(71)	Malawi	Health facility	General population	Inc/Eco/Emp	$6.50	$105.11	3,404	304	TRNG, BLDG, STOR, EQP, SUPL, VEH, PER, TEST, WST
	Zambia				$4.24	$73.66	2,789	251	
	Zimbabwe				$8.87	$180.55	1,542	93	
Negin, 2009(61)	Kenya	Home-based	General population	Inc/Fin/Emp	8.18	116.80	2,780	209	TRNG, TNSP, TEST
Nichols, (2020)(99)	Malawi	Health facility	General population	Inc/Fin/Emp	$2.94	$121.64	248.00	6	TRNG, SNST, EQP, PER, OVHD
		Health facility			$5.77	$187.88	261.00	8	
		Self-testing			$6.01	$227.63	1,063	28	
	Zambia	Health facility		Inc/Fin/Emp	$2.25	$70.85	6,728	214	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
Nichols, (2019) (124)		Self-testing	General population		$5.41	$516.30	3,059.	32	TRNG, SNST, EQP, PER, OVHD, TEST
		Self-testing			$5.68	$542.87	2,294	24	
Obure, 2012(73)	Kenya	Health facility OPD	General population	Inc/Eco/Emp	$8.13	$66.84	5,486	780	TRNG, BLDG, FURN EQP SUPL, COMM, PER, TEST
		Health facility HTC			$11.77	$157.03	9,005	1,527	
	Eswatini	Health facility OPD	General population		$7.96	$48.92	4,872	1,851	
		Health facility HTC			$9.65	$46.58	6,061	2,698	
Obure, 2015(72)	Kenya	Health facility	General population	Ful/Eco/Emp	$16.08	$53.58	NS	NS	BLDG, SUPL, PER, OVHD ADMN, TEST
	Eswatini				$31.13	$121.42	NS	NS	
Ochoa-Moreno, (2020)(100)	Zimbabwe	Health facility	Pregnant women or women breastfeeding	Ful/Eco/Emp	$80.00	-	305.00		PER, TEST, ARV REC
Orlando, 2010(101)	Malawi	Health facility	Pregnant women or women breastfeeding	Inc/Fin/Emp	$66.62	-	6,500	1,371	BLDG, FURN, VEH, PER, TEST ARV
Parker, 2015(52)	Eswatini	Home-based	General population	Inc/Fin/Emp	$9.02	$281.22	170	75	SNT, FURN, EQP, COMM, TNSP, PER, TEST
		Mobile service			$19.68	$445.20	228	60	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
Perchal, 2006(74)	Ethiopia	Health facility	Pregnant women or women breastfeeding	Inc/Fin/Emp	$49.69	-	N.S.	NA	SUPL, PER, TEST, OTH
					$13.36	-	N.S.	NA	
Perez, 2016(53)	South Africa	Mobile service	General population	Inc/Fin/Emp	$9.88	-	22,152	699	SNST, EQP, COMM, TNSP, PER, TEST
		Health facility			$9.69	-	17,678	807	
		Home-based			$6.78	-	48,330	896	
Rutstein, 2013(76)	Malawi	Health facility	PLHIV Partners	Inc/Fin/Emp	$16.04	-	2,436	NA	TNSP, PER, M&E, TEST
					$7.60	-	2,537	NA	
					$3.38	-	1,207	NA	
					$30.40	-	1,267	NA	
					$15.20	-	1,320	NA	
					$6.76	-	627	NA	
Settumba (2015), (102)	Uganda	Health facility	General population	Inc/Eco/Emp	$2.22	-	5296	NA	TRNG, BLDG, EQP, SUPL, UTL TNSP, PER, ARV
					$1.82	-	4983	NA	
					$3.72	-	746	NA	
					$2.18	-	7	N.A.	
Shade, 2013(77)	Kenya	Health facility		Inc/Fin/Emp	-	$19.31	NA	4,135	

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
			General population		-	$9.69	NA	3,429	TRNG, BLDG, SUPL, SUPV OTH
Sharma, 2014(54)	South Africa	Mobile service	General population	Inc/Eco/Emp	$4.43	$6.74	890	381	NS
		Home-based			$6.69	$9.87	NS	NS	
Sharma, 2016(78)	Kenya	Home-based	PLHIV Partners	Inc/Eco/Emp	$33.99	-	N.S.	NA	BLDG, EQP, SUPL, TNSP, PER, OVHD, M&E, STRT
					$38.43	-	N.S.	NA	
					$40.23	-	N.S.	NA	
					$15.25	-	N.S.	NA	
					$15.65	-	N.S.	NA	
					$17.17	-	N.S.	NA	
Smith, 2015(62)	South Africa	Home-based	General population	Inc/Fin/Emp	$7.08	$19.01	NA	NA	MTG, BLDG, EQP, SUPL, TNSP, PER, OVHD, M&E, STRT
Tabana, 2015(63)	South Africa	Health facility	General population	Inc/Eco/Emp	$30.60	-	3,818	NA	TRNG, BLDG, EQP, VEH, PER, TEST
		Home-based			$23.35	-	8,177	NA	
Terris-Prestholt, 2006(103)	Uganda	Campaign-style	General population	Ful/Eco/Emp	$39.18	-	1,526	NS	BLDG, EQP, SUPL, VEH, PER, OVH, STR

Author, year, ref	Country	HTS approach	Population	Costing method[1]	($pptested)	($ppositive)	Number of HIV tests provided	Number of HIV+ cases identified	Explicitly named cost inputs[2]
Terris-Prestholt, 2008(79)	Zambia	Health facility	General population	Ful/Eco/Emp	$31.01	$95.76	1,381	455	TRNG, SNST, BLDG, EQP SUPL, VEH, PER STRT, OTH
					$32.83	$46.51	239	166	
					$9.12	$48.34	2,115	399	
					$22.80	$94.85	638	154	
Toure,(2013)(105)	Namibia	Health facility	Pregnant women or women breastfeeding	Ful/Eco/Emp	$21.07	-	NS	NS	TRNG, MTG, SUPL, TNSP, PER, OVHD, SUPV, TEST ARV
	Rwanda	Health facility			$9.51	-	NS	NS	
Tumwesigye, 2010(64)	Uganda	Home-based	General population	Inc/Eco/Emp	$7.51	$148.40	52,342	NS	SUPL, TNSP, PER, TEST
					$8.34S	-	238,290	NS	
Vyas, (2020a),(106)	Tanzania	Health facility		Inc/Eco/Emp	$5.73	$524.94	25,593	279	TRNG, BLDG, EQP, SUPL, PER, OVHD, TEST
Vyas (2020B), (107)	Malawi	Health facility	General population	Inc/Eco/Emp	$3.43	$140.13	18,509	453	TRNG, BLDG, EQP, SUPL, PER, OVHD, SUPV, TEST

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

[2]Training, workshops= TRNG, Sensitization, Events, Opening Ceremony, Outreach= SNST, Meeting=MTG, Building, Space, Building operation and maintenance, office rental= BLDG, Storage=STOR, Furniture= FURN Equipment, assets= EQP, Supplies= SUPL, Utilities= UTL, Communication, airtime, cell phones= COMM, Transport, travel= TNSP, Vehicle, bicycle, VEH operation and maintenance=VEH, Personnel, salaries, staff, labour, food/per diem=PER, Overhead, Central support costs=OVHD, Administration=ADMN, Monitoring & Evaluation, follow up, census, tracing=M&E, Supervision, auditing=SUPV, Test kits, viral load tests, testing commodities, diagnostics=TEST, Drugs, ARV, treatment commodities, medications=ARV, Waste Management=WST, Other start-up=STRT, Other recurrent=REC, Other (No specification)=OTH, and Not specified=NS

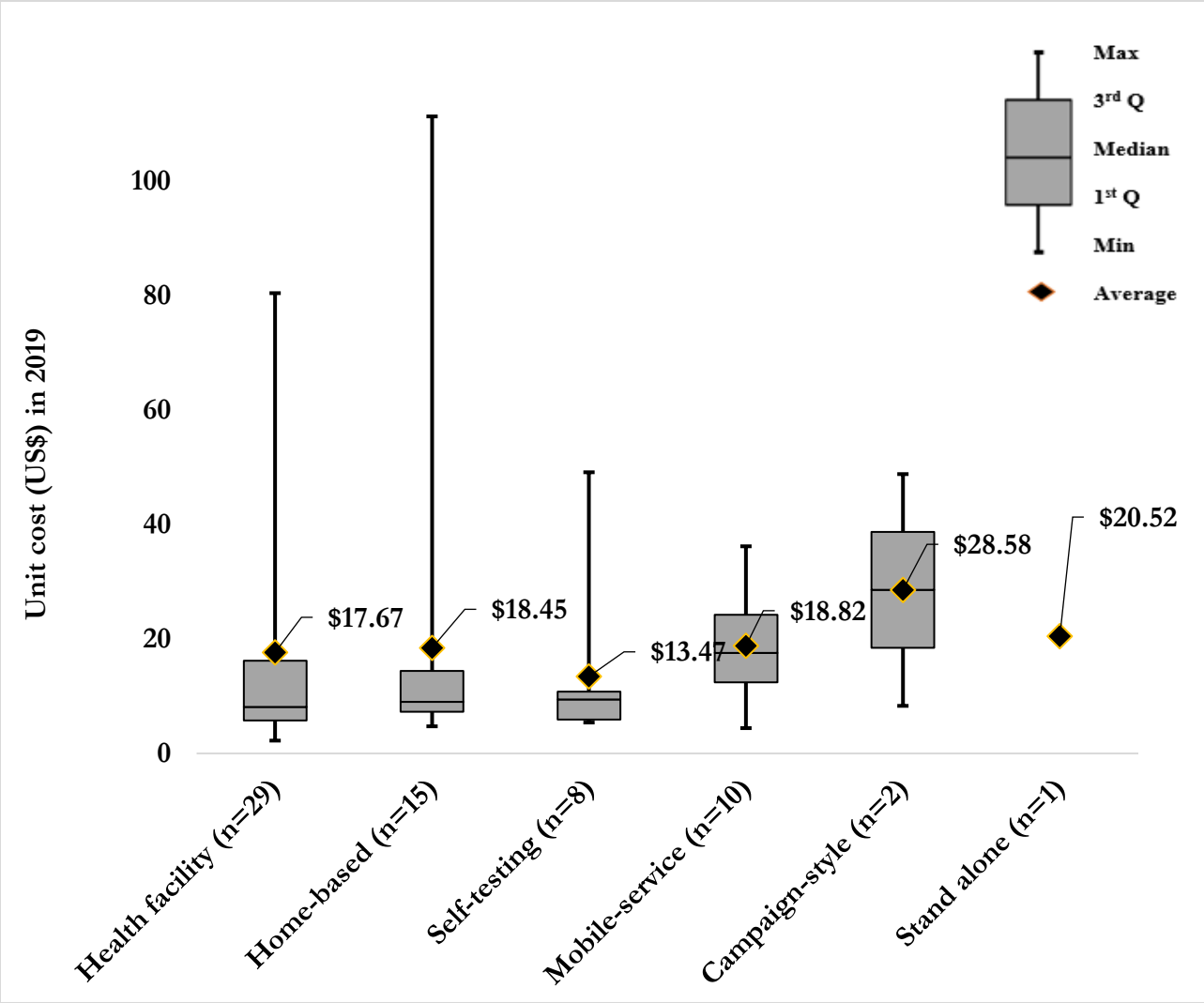

Figure S1 Average incremental cost per person tested by mode of HIV testing services in 2019 US$

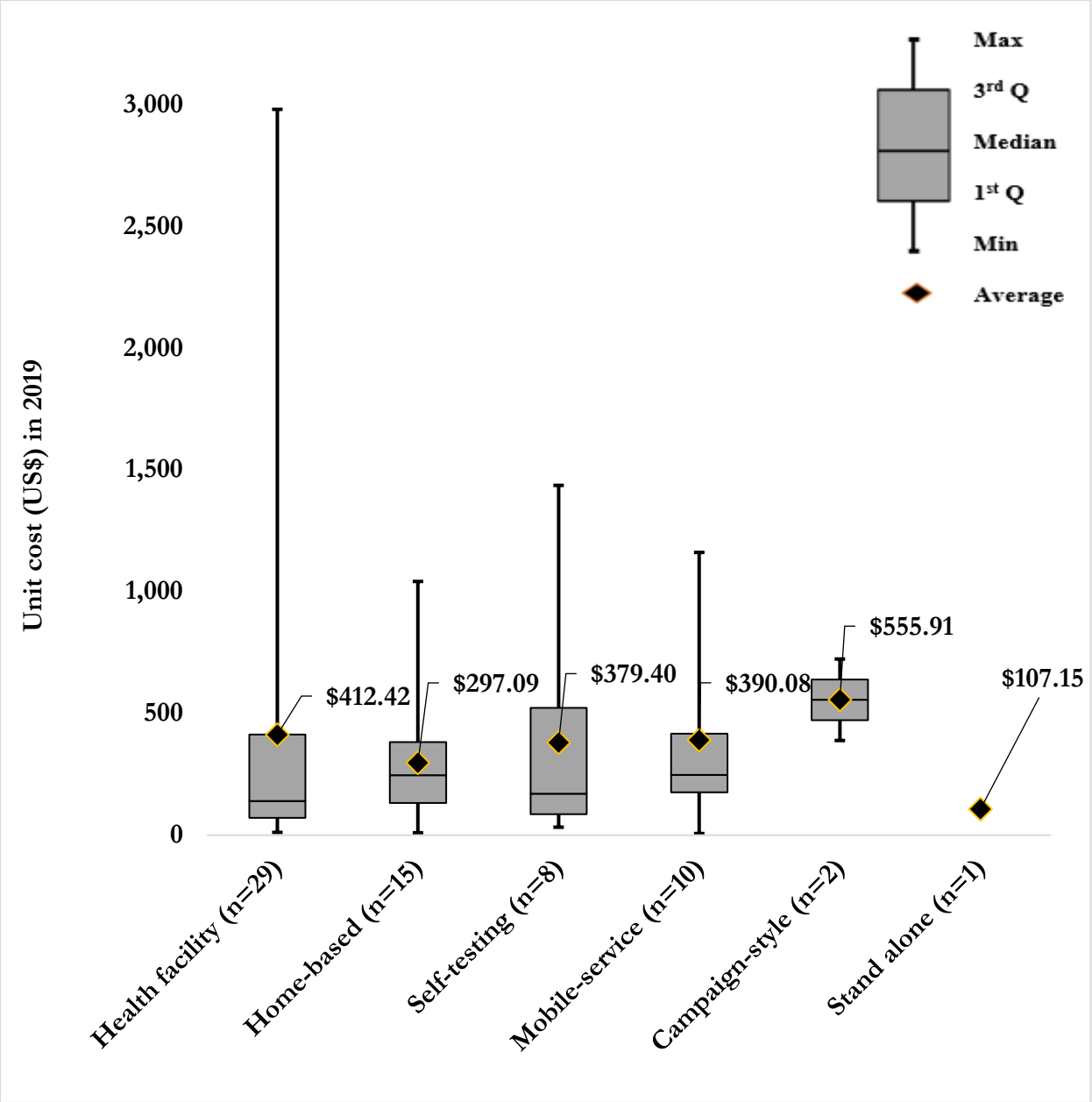

Figure S2 Average incremental cost per person tested positive by mode of HIV testing services in 2019 US$

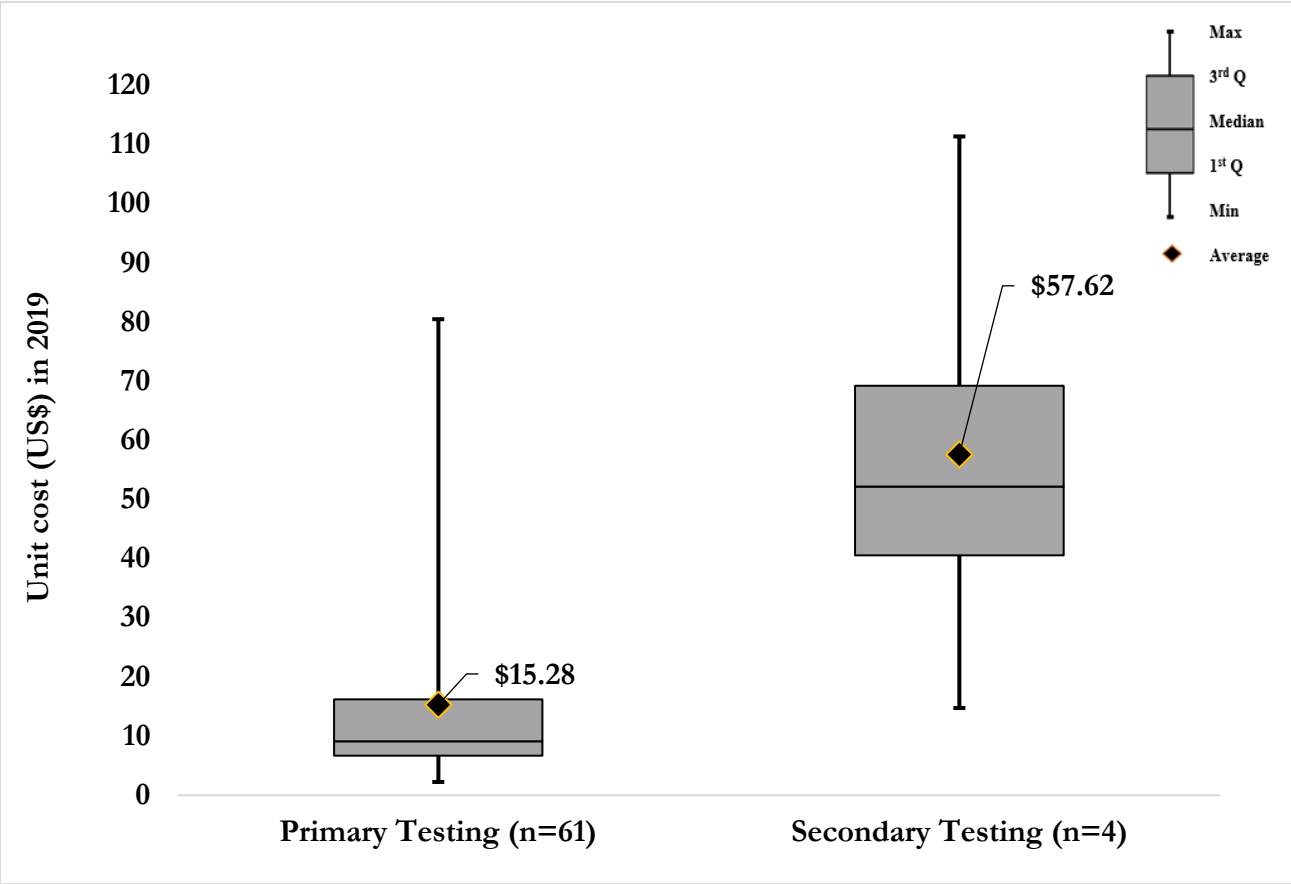

Figure S3 Average incremental cost per person tested by primary/direct or secondary/index HIV testing services in 2019 US$

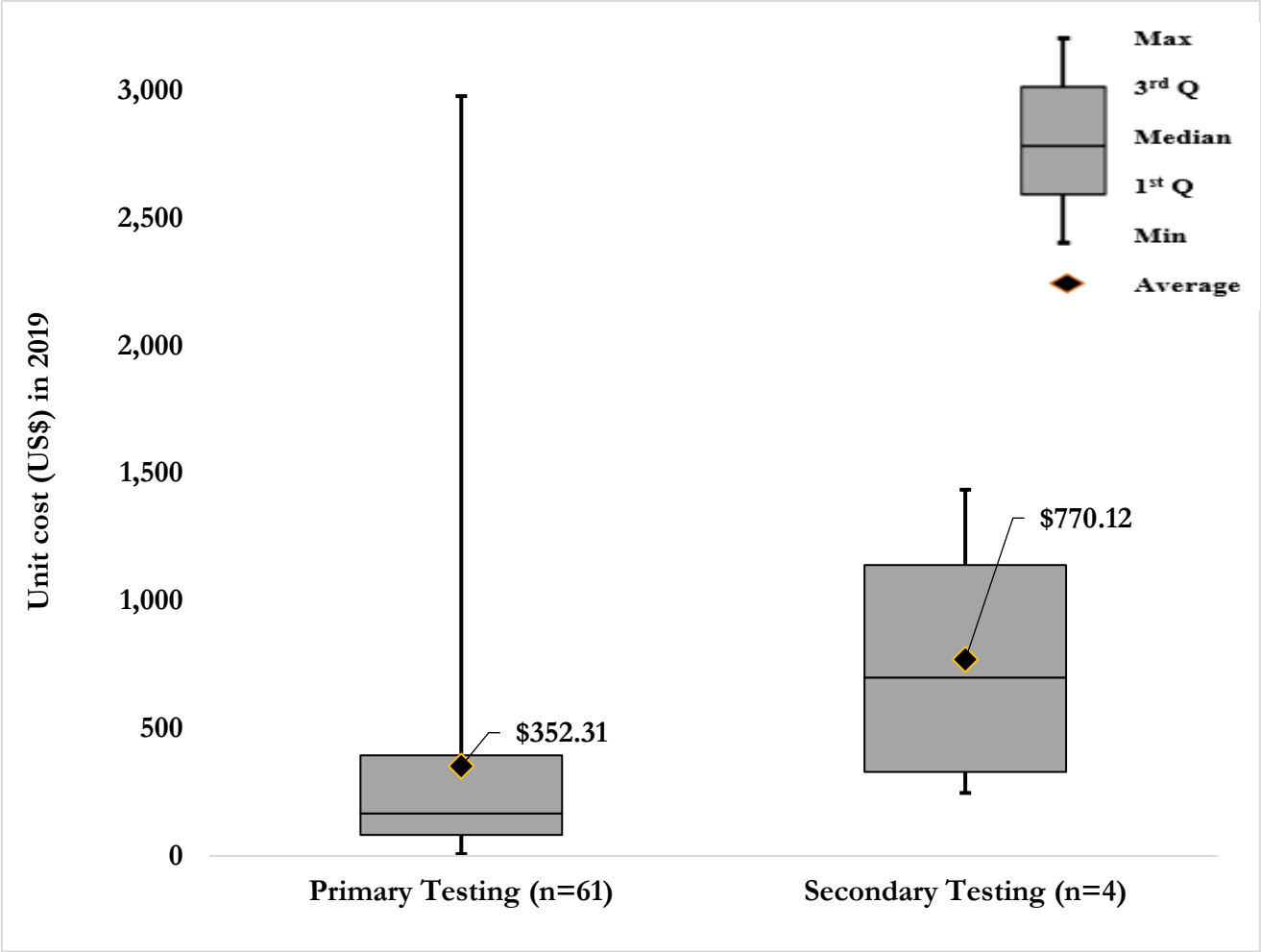

Figure S4 Average incremental cost per person tested positive by primary/direct or secondary/index HIV testing services in 2019 US$

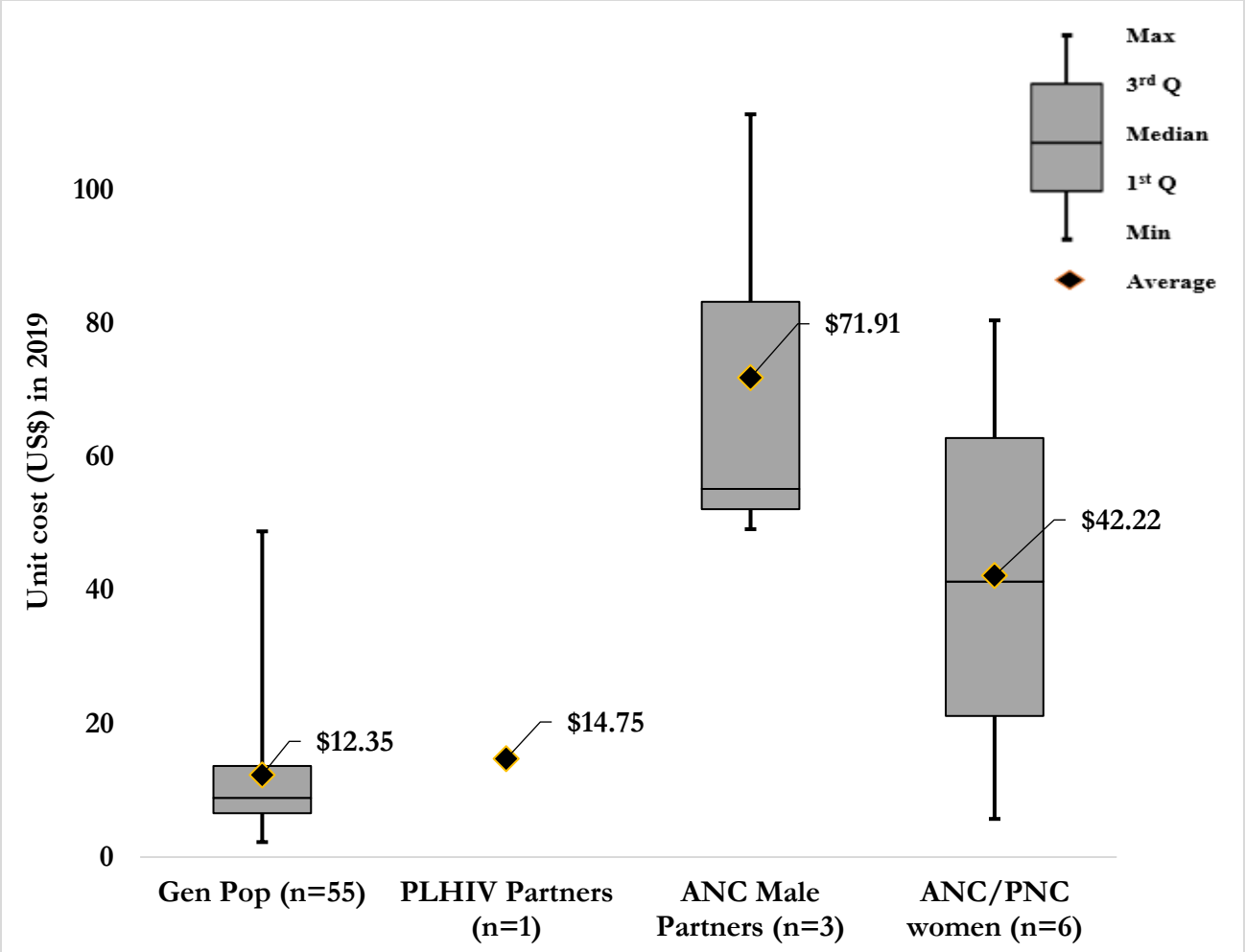

Figure S5 Average incremental cost per person tested by population tested in 2019 US$

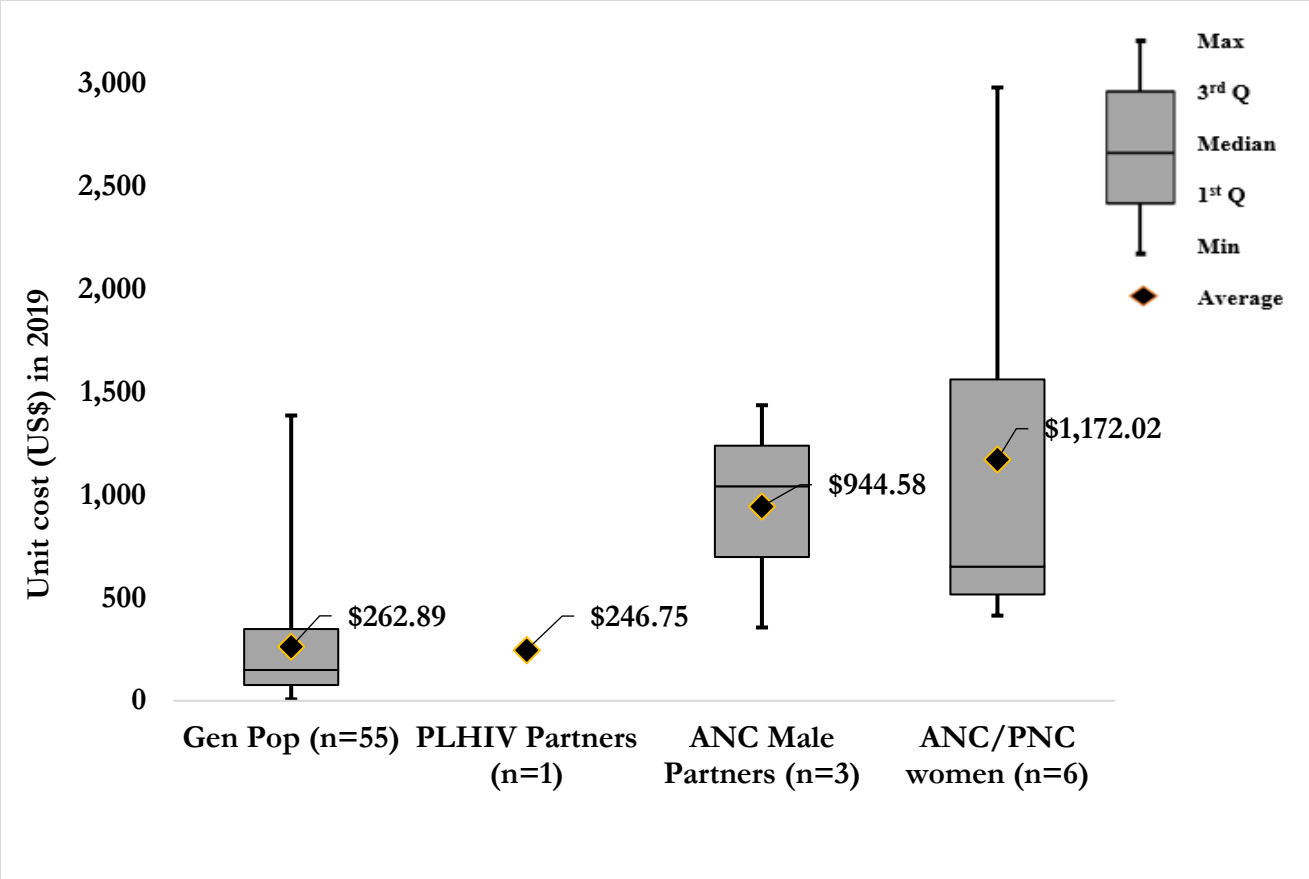

Figure S6 Average incremental cost per person tested positive by population tested in 2019 US$

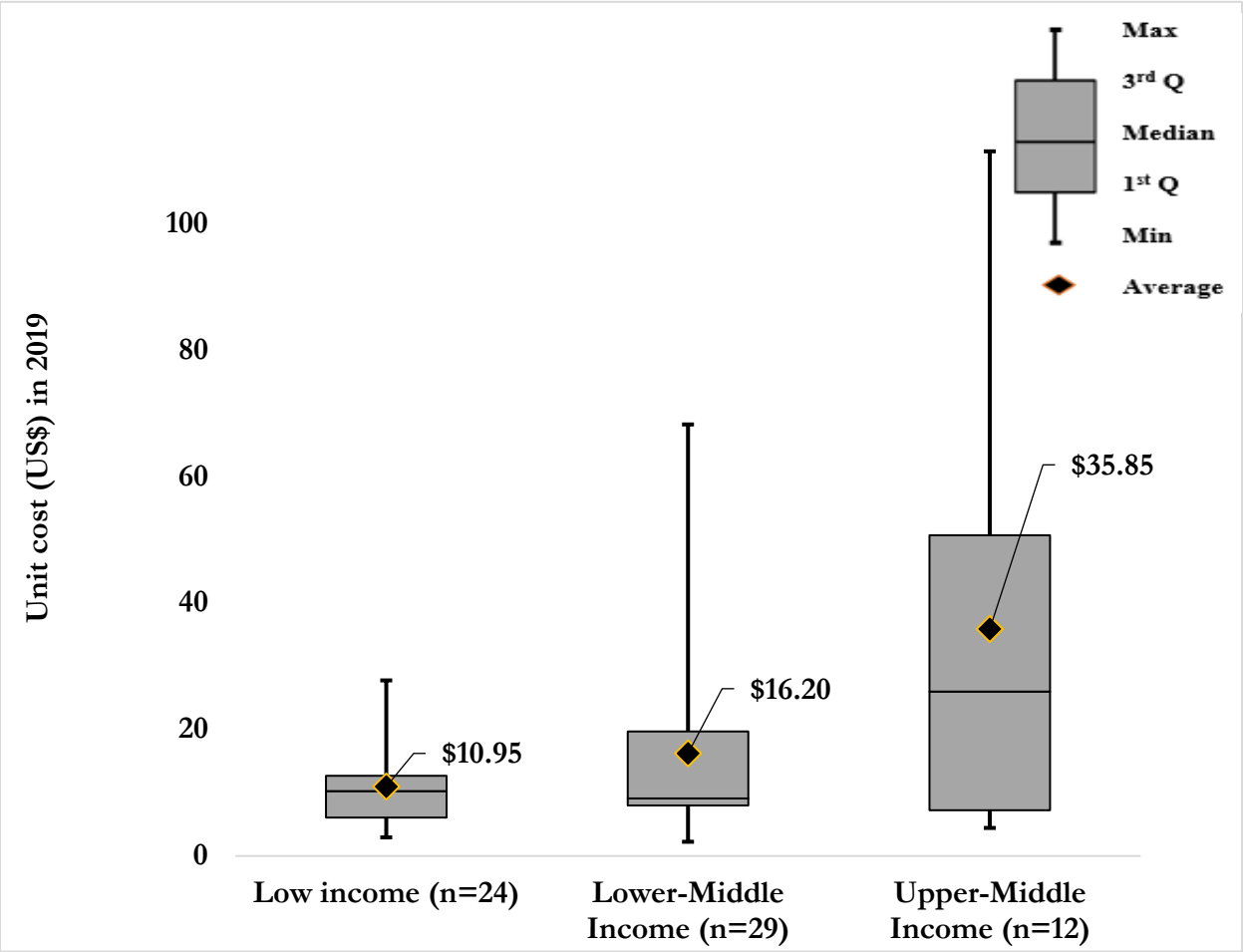

Figure S7 Average incremental cost per person tested by population tested in 2019 US$

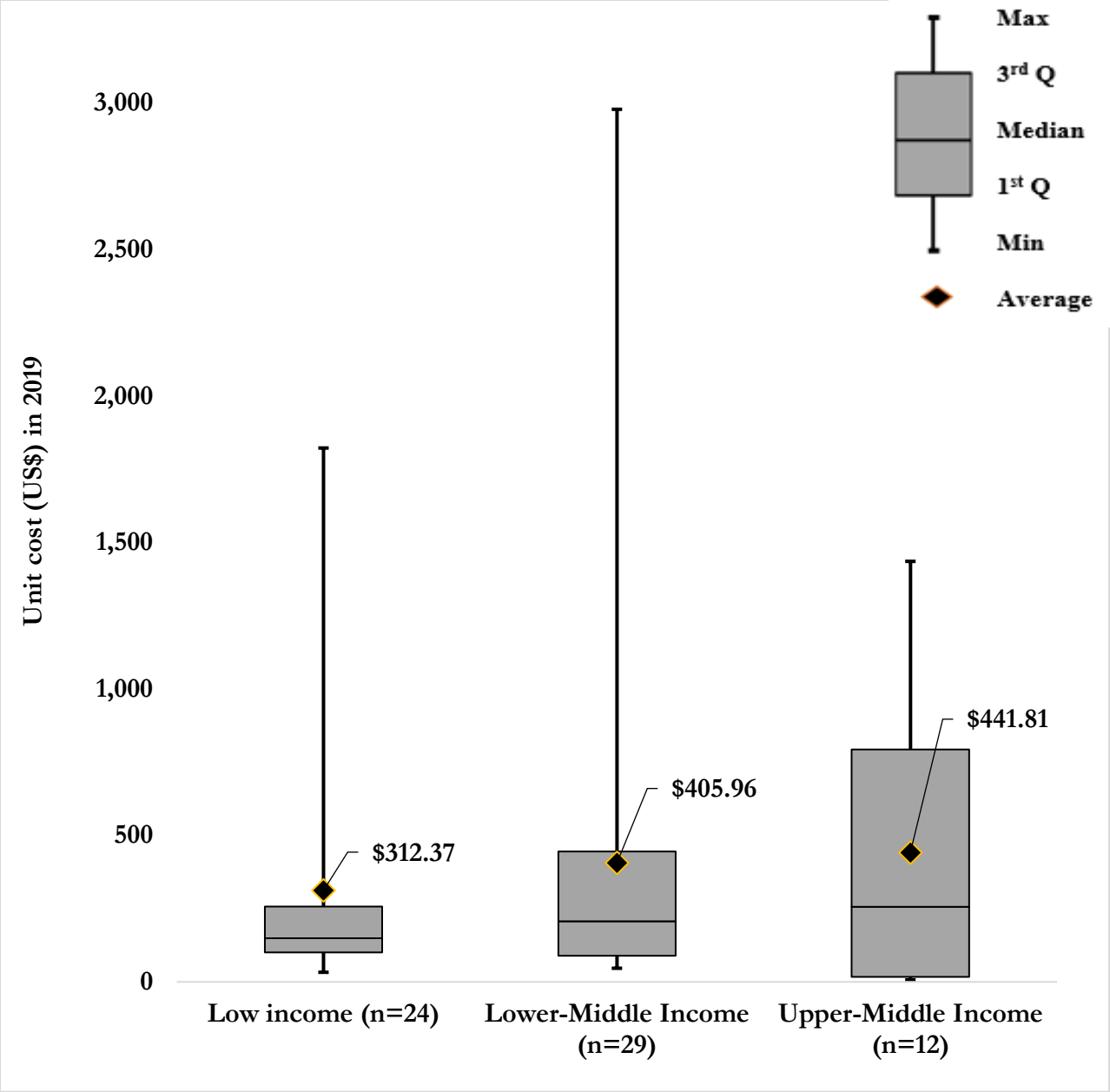

Figure S8 Average incremental cost per person tested positive by population tested in 2019 US$

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Appendix IV – Study ethical approval letters

CERTIFICATE OF ETHICS APPROVAL

This is to certify that the College of Medicine Research and Ethics Committee (COMREC) has reviewed and approved a study entitled:

P.01/16/1861 – HIV self-testing Africa (STAR) Malawi: General population – A duster randomized trial of providing HIV and self-testing kits through community-based distribution agents by Dr. Nicola Desmond

On 29th February 2016

As you proceed with the implementation of your study, we would like you to adhere to international ethical guidelines, national guidelines and all requirements by COMREC as indicated on the next page

Dr. C. Dzamalala- Chairperson (COMREC)

Approved by
College of Medicine
29 FEB 2016
(COMREC)
Research and Ethics Committee

29/02/2016
Date

Observational / Interventions Research Ethics Committee

Prof Liz Corbett
Professor of Clinical Epidemiology
Department of Clinical Research (CRD)
LSHTM

19 April 2016

Dear Prof Liz Corbett ,

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

LSHTM ethics ref: 10566

Thank you for your application for the above research, which has now been considered by the Interventions Committee.

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, 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	Malawi CVs	13/01/2016	1
Protocol / Proposal	Gen pop - questionnaires	19/01/2016	1
Information Sheet	Gen pop - updated consent and info 27 Jan	27/01/2016	2
Sponsor Letter	QA786_HIVST_Sponsor Confirmation	27/01/2016	1
Protocol / Proposal	STAR Malawi - General Population V2.0	24/02/2016	2

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.

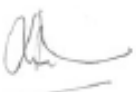
An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

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,



Professor John DH Porter
Chair

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

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636

www.lshtm.ac.uk

Observational / Interventions Research Ethics Committee

Prof. Liz Corbett
Professor of Tropical Epidemiology
Department of Clinical Research (CRD)
LSHTM

19 July 2016

Dear Dr Corbett

Study Title: STAR-ZW: A cluster randomised trial of interventions to improve linkage to care following community-based distribution of HIV self-test kits in rural Zimbabwean communities

LSHTM Ethics Ref: 11738

Thank you for your application for the above research project which has now been considered by the Interventions Committee via Chair's Action.

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, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant. Please provide the full local ethics approval as soon as it is available.

Approved documents

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

Document Type	File Name	Date	Version
Local Approval	Zimbabwe-Ministry-of-Health_STAR-Letter-of-Support	01/02/2016	1
Local Approval	PSI-Zimbabwe_STAR-Letter-of-Support	09/05/2016	1
Investigator CV	biosketch_Euphemia Sibanda	22/06/2016	1
Investigator CV	Cowan CV Jan 2016 short	22/06/2016	1
Local Approval	APPROVED ethics application 6084.004	22/06/2016	1
Local Approval	MRCZ-conditional-approval_STAR-Zimbabwe	23/06/2016	1
Protocol / Proposal	List of contents for baseline survey MN 23 May	23/06/2016	1
Investigator CV	CV Elizabeth Corbett	04/07/2016	1
Sponsor Letter	QA893_HIV STAR Zimbabwe	05/07/2016	1
Protocol / Proposal	Zimbabwe-STAR-trial-protocol_30 Jun CLEAN	05/07/2016	1
Information Sheet	Informed-consent-form_CBD-interviews_English_March2016 LSHTM version	05/07/2016	2
Information Sheet	Informed-consent-form_Client-interviews _English_08March16_LSHTMchanges	05/07/2016	2
Information Sheet	Informed-consent-form_healthcare-worker-interviews_March2016 LSHTM version	05/07/2016	2
Information Sheet	Informed-consent-form_Household-survey_English_Jan2016 LSHTM version	05/07/2016	2

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.

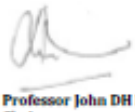
An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

At the end of the study, the CI or delegate must notify the committee using the 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.

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

Yours sincerely,



Professor John DH Porter
Chair

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

Improving health worldwide

UCL RESEARCH ETHICS COMMITTEE
ACADEMIC SERVICES

9 June 2016

Professor Frances Cowan
Centre for Sexual Health and HIV Research
UCL

Dear Dr Cowan

Notification of Ethical Approval
Re: Ethics Application 6084/004: A cluster randomised trial of interventions to improve linkage to care following community-based distribution of HIV self-test kits in rural Zimbabwean communities

I am pleased to confirm in my capacity as Chair of the UCL Research Ethics Committee (REC) that your study has been ethically approved by the REC until 31st August 2018 on condition that recruitment does not commence until local ethical approval through the Medical Research Council of Zimbabwe (MRCZ) has been secured. Approval is also subject to the following conditions.

1. You must seek Chair's approval for proposed amendments to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing the 'Amendment Approval Request Form': http://ethics.grad.ucl.ac.uk/responsibilities.php

2. It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator (ethics@ucl.ac.uk) immediately the incident occurs. Where the adverse incident is unexpected and serious, the Chair or Vice-Chair will decide whether the study should be terminated pending the opinion of an independent expert. The adverse event will be considered at the next Committee meeting and a decision will be made on the need to change the information leaflet and/or study protocol.

3. For non-serious adverse events the Chair or Vice-Chair of the Ethics Committee should again be notified via the Ethics Committee Administrator (ethics@ucl.ac.uk) within ten days of an adverse incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Chair or Vice-Chair will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

On completion of the research you must submit a brief report of your findings/concluding comments to the Committee, which includes in particular issues relating to the ethical implications of the research.

Yours sincerely

Professor John Foreman
Chair of the UCL Research Ethics Committee

Academic Services, 1-19 Torrington Place (9th Floor),
University College London
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Email: ethics@ucl.ac.uk
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Telephone: 791792/791193
Telefax: (263) - 4 - 790715
E-mail: mrcz@mrcz.org.zw
Website: http://www.mrcz.org.zw

Medical Research Council of Zimbabwe
Josiah Tongogara / Mazoe Street
P. O. Box CY 573
Causeway
Harare

APPROVAL

Ref: -MRCZ/A/2038 **14 July, 2016**

Prof. F. M. Cowan
CeSHHAR Zimbabwe
9 Monmouth Road
Avondale West
Harare

RE:-Application For Approval Of Study Entitled :-A Cluster Randomized trial of interventions to improve linkage to care following community-based distribution of HIV self-test kits in rural Zimbabwe Communities

Thank you for the application for review of Research Activity that you submitted to the Medical Research Council of Zimbabwe (MRCZ). Please be advised that the Medical Research Council of Zimbabwe has **reviewed**and **approved**your application to conduct the above titled study.

This approval is based on the review and approval of the following documents that were submitted to MRCZ for review:-

a) Research Proposal v 1.1 dated 03 March, 2016
b) Informed Consent Forms Household Survey (English, Shona and Ndebele)
c) Informed Consent Forms In-depth-Interview Clients (English, Shona and Ndebele)
d) Informed Consent Forms In-depth-Interview CBDs (English, Shona and Ndebele)
e) Informed Consent Forms In-depth-Interview HCWs (English, Shona and Ndebele)
f) In-depth-Interview guides CBDs (English, Shona and Ndebele)
g) In-depth-Interview guides HCWs (English, Shona and Ndebele)
h) In-depth-Interview guides Clients (English, Shona and Ndebele)
i) Household questionnaire (English, Shona and Ndebele)

- **APPROVAL NUMBER : MRCZ/A/2038**

This number should be used on all correspondence, consent forms and documents as appropriate.

- **TYPE OF MEETING : Full Board**
- **EFFECTIVE APPROVAL DATE : 14 July, 2016**
- **EXPIRATION DATE : 13 July, 2017**

After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the MRCZ Offices should be submitted three months before the expiration date for continuing review.

- **SERIOUS ADVERSE EVENT REPORTING**: All serious problems having to do with subject safety must be reported to the Institutional Ethical Review Committee (IERC) as well as the MRCZ within 3 working days using standard forms obtainable from the MRCZ Offices or website.
- **MODIFICATIONS**: Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the MRCZ using standard forms obtainable from the MRCZ Offices or website.
- **QUESTIONS**: Please contact the MRCZ on Telephone No. (04) 791792, 791193 or by e-mail on mrcz@mrcz.org.zw

Other

- Please be reminded to send in copies of your research results for our records as well as for Health Research Database.
- You're also encouraged to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study.

Yours Faithfully

.....

MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE

MEDICAL RESEARCH COUNCIL OF ZIMBABWE
2016 -07- 14
APPROVED
P.O. BOX CY 573 CAUSEWAY, HARARE

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Switchboard: +44 (0)20 7636 8636

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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.

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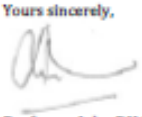
All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

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

Yours sincerely,



Professor John DH Porter
Chair

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

THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
E-mail: unzarec@unza.zm

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,

M.C Maimbolwa PhD
CHAIRPERSON

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

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636

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Observational / Interventions Research Ethics Committee

Dr Fern Terris-Prestholt
Associate Professor
Department of Global Health and Development (GHD)
Public Health and Policy (PHP)
LSHTM

13 March 2018

Dear Fern

Study Title: STAR Initiative - Costing HIV Self-test distribution in Swaziland and Lesotho

LSHTM Ethics Ref: 14887

Thank you for responding to the Observational 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	CV_Terris-Prestholt	31/01/2018	1
Investigator CV	CV_Sikhondze	31/01/2018	1
Investigator CV	CV_Chipango	31/01/2018	1
Protocol / Proposal	STAR_Initiative_Swaziland_Lesotho_Facility cost questionaire_v1.0	31/01/2018	1
Protocol / Proposal	STAR_Initiative_Swaziland_Time and motion_questionnaire_v1.0	31/01/2018	1
Protocol / Proposal	STAR_Initiative_Lesotho_Time and motion_questionnaire_v1.0	31/01/2018	1
Information Sheet	STAR_Initiative_ Swaziland_Time and Motion Study_Participant Information Sheet_v1.0	31/01/2018	1
Information Sheet	STAR_Initiative_Lesotho_Time and Motion Study_Participant Information Sheet_v1.0	31/01/2018	1
Covering Letter	Cover letter_STAR_Initiative_HIVST Costing studies_Swaziland_Lesotho	27/02/2018	1
Protocol / Proposal	STAR_Initiative_Protocol_HIVST Costing studies_Swaziland_Lesotho_v2.0	27/02/2018	2
Information Sheet	STAR_Initiative_Lesotho_Time and Motion Study_Consent Form_v2.0	27/02/2018	2
Information Sheet	STAR_Initiative_Swaziland_Time and Motion Study_Consent Form_v2.0	27/02/2018	2
Information Sheet	STAR_Initiative_Lesotho_Time and Motion Study_Patient Information Sheet_v1.0	27/02/2018	1
Information Sheet	STAR_Initiative_Swaziland_Time and Motion Study_Patient Information Sheet_v1.0	27/02/2018	1

After ethical review

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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,

Professor John DH Porter
Chair

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

LESOTHO

Ministry of Health
P.O. Box 514
Maseru 100

April 17, 2018

To
Albert Machinda (Dr.)
Country Representative
PSI, Lesotho

Dear Dr. Albert,

Re: STAR initiative-Costing of HIV Self-test kits distribution in Lesotho & Swaziland (ID64-2018)

Thank you for submitting the above mentioned proposal. The Ministry of Health Research and Ethics Committee having reviewed your protocol hereby decides that it has the criteria "The study is conducted for Health Economics for a public benefit programme". The committee exempts the proposal from research and ethics review and authorizes you to conduct the study with the understanding that you agree on the following conditions:

- In the event of changes in material or design or execution of the activity, the Research and Ethics Committee must be consulted through the Research Coordination Unit, MOH.
- The study is conducted among the specified population.
- The study protocol will be followed as stated.

Departure from the stipulated conditions will constitute a breach of the permission. We are looking forward to have a progress report and final report at the end of your study.

Yours sincerely,

Dr. Nyane Letsie
Director General of Health Services

Dr. Jill Sanders
Co-chairperson
National Health
Research & Ethics
Committee (NH-REC)

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636

www.lshtm.ac.uk

Observational / Interventions Research Ethics Committee

Dr Fern Terris-Prestholt
LSHTM

25 April 2019

Dear Dr Fern Terris-Prestholt ,

Study Title: ATLAS - SUB-STUDY ON THE COSTS OF IMPLEMENTING HIV SELF-TESTING IN COTE D'IVOIRE, MALI and SENEGAL

LSHTM ethics ref: 17141

Thank you for your application for the above research, which has now been considered by the Observational Committee.

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, 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	CV_Terris-Prestholt	30/03/2019	1
Information Sheet	III.ATLAS_Health facility_Manager_Consent form_v1_En	30/03/2019	1
Information Sheet	VI.ATLAS_TM study_Patient information sheet_v1_En	30/03/2019	1
Protocol / Proposal	ATLAS_Costing Protocol_v1	30/03/2019	1
Protocol / Proposal	VII.ATLAS_TM study_Data collection tool_v1_En	30/03/2019	1
Protocol / Proposal	I.ATLAS_Facility questionnaire_v1_En	31/03/2019	1
Information Sheet	II.ATLAS_Information leaflet_v1_En	31/03/2019	1
Information Sheet	V.ATLAS_TM study_Consent form_v1_En	31/03/2019	1

After ethical review

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

Yours sincerely,

Professor John DH Porter
Chair

MINISTERE DE LA SANTE
ET DE L'HYGIENE PUBLIQUE

COMITE NATIONAL D'ETHIQUE
DES SCIENCES DE LA VIE ET DE
LA SANTE (CNESVS)

US DPT OF HHS REGISTRATION #2 : IRB00011917

Le Président

REPUBLIQUE DE COTE D'IVOIRE
UNION–DISCIPLINE-TRAVAIL

N/Réf : 049-19/MSHP/CNESVS-kp

Abidjan, le 28 MAI 2019

A
Monsieur Joseph Larmarange
Investigateur Principal Projet
Programme ATLAS / ABIDJAN

OBJET : Autorisation de mise en œuvre du protocole de recherche intitulé :
« Décrire, analyser et comprendre les effets de l'introduction de l'autodépistage du VIH en Afrique de l'Ouest ».

Monsieur,

Le Comité National d'Ethique des Sciences de la Vie et de la Santé (CNESVS) a examiné votre demande d'autorisation de mise en œuvre du projet cité en objet.

Sous cette perspective, il a été émis **un avis favorable** à l'utilisation de ce protocole.

Par conséquent, je vous autorise à mettre en œuvre votre étude telle que soumise au Comité National d'Ethique.

Toutefois, il faut noter que la validité de cette autorisation est **d'un an (1) à compter de la date de signature.** Par ailleurs, je vous saurai gré de bien vouloir transmettre au CNESVS une copie du rapport de cette étude dès la fin de sa mise en œuvre.

Je vous prie d'agréer, **Monsieur,** l'expression de mes salutations distinguées.

MINISTÈRE DE LA SANTÉ ET DE L'HYGIÈNE PUBLIQUE
COMITÉ NATIONAL D'ÉTHIQUE DES SCIENCES DE LA VIE ET DE LA SANTÉ
Le Président
CNESVS
CÔTE D'IVOIRE

Dr Louis PENALI

REPUBLIQUE DU SENEGAL
Un Peuple-Un But-Une Foi

N° 00000008 MSAS/CNERS/Sec

Ministère de la Santé et de l'Action sociale

Dakar, le 26 JAN 2021

CNERS Sénégal

La Présidente

AVIS ETHIQUE ET SCIENTIFIQUE

***Référence* : Amendement Protocole SEN19/32 « Décrire, analyser et comprendre les effets de l'introduction de l'autodépistage du VIH en Afrique de l'Ouest »**

Docteur,

J'accuse réception de vos réponses aux questions relatives au protocole en référence ci-dessus. À l'analyse, le Comité National d'Ethique pour la Recherche en Santé les trouve globalement satisfaisantes. En conséquence, le comité émet un avis éthique et scientifique favorable pour permettre la mise en œuvre dudit protocole.

Cet avis a une durée d'une année à compter de sa date de signature. Son renouvellement reste assujetti à la présentation d'un rapport d'étape permettant d'être informé sur le niveau de mise en œuvre de l'étude.

Je vous prie de croire, ***Docteur***, à l'assurance de ma considération distinguée et de mes encouragements renouvelés.

COMITE NATIONAL D'ETHIQUE POUR LA RECHERCHE EN SANTE
Pr Anta Tal DIA
La Présidente

Dr Joseph Larmarange
Démographe, chargé de recherche IRD
Coordinateur scientifique du volet recherche du programme ATLAS

UNIVERSITE DES SCIENCES,
DES TECHNIQUES ET DES TECHNOLOGIES DE BAMAKO
FACULTE DE MEDECINE ET D'ODONTO-STOMATOLOGIE
FACULTE DE PHARMACIE/ BP 1805, *BAMAKO – MALI*
☎ : (223) 20 22 52 77
🖷 : (223) 20 22 96 58

N°2020/ 254 /CE/FMOS/FAPH
Le Président du Comité
D'Ethique de la FMOS/FAPH

Bamako, le 16 novembre 2020

/-)u Docteur KANKU KADEMBA ODE
Chef de Projet ATLAS Mali

Cher Professeur,

J'ai le plaisir de vous informer que votre projet de recherche intitulé : **«Décrire, analyser et comprendre les effets de l'introduction de l'autodépistage du VIH en Afrique de l'Ouest à travers l'exemple du programme ATLAS en Côte d'Ivoire, au Mali et au Sénégal»** version 3.0 du 08 octobre 2020 et les annexes du protocole version 3.0 a été examiné en comité restreint par le comité d'éthique de la Faculté de Médecine, de Pharmacie et d'Odonto-Stomatologie de l'USTTB.

Le comité d'éthique a décidé d'accepter les changements proposés qui permettront d'améliorer la qualité des résultats attendus et par conséquent, vous donne son accord pour la poursuite de vos travaux cependant vous recommande de:

- Fournir le CV de Graham Medley
- Veiller au Counseling lors de la sous-enquête exploratoire portant sur la diffusion de l'ADVIH à travers les consultations IST Eviter toute stigmatisation.

Le comité d'éthique de la FMOS/FAPH approuve les amendements et vous souhaite plein succès dans vos recherches.

P/LE PRESIDENT DU COMITE P.O
LE SECRETAIRE PERMANENT

Faculté de Médecine et de Pharmacie
Le Président
Comité d'Ethique

Pr. Mahamadou DIAKITE

WHO ERC
Review Summary - Continuing Review

Protocol ID: ERC.0003181
Protocol Title: Volet recherche du programme ATLAS : Décrire, analyser et comprendre les effets de l'introduction de l'autodépistage du VIH en Afrique de l'Ouest (Côte d'Ivoire, Mali, Sénégal)
Version : 2.1 **Dated:** 05.08.2019
WHO Responsible Staff Member: Heather Leigh INGOLD
Responsible Unit: Unitaid

The complete documentation for approval of amendments to this project was submitted to the Secretariat on 04/08/2020. This was last approved by ERC on 06.08.2020. Proposed amendments have been reviewed by the secretariat and the Chairperson. The outcome of the review is as follows:

1. Modifications to improve clarify and provide specificity were made to the protocol.
2. Proposed changes were made based on the results of the pilot phase of the study. The main modifications are:
    a. An exploratory sub-survey on HIVST distribution in STI consultations is being proposed. The survey will be conducted among STI patients in STI consultations offering HIVST distribution to patients and their partners and will be run during a period of three months. Please specify the criteria that will be used to select clinics for study purposes.
    b. As result on the pilot phase, it was considered necessary to provide incentives to patients to participate in the survey. Participants will be credited 2000 FCFA on the phone number used to participate in the survey. Please confirm that the amount of the incentive is appropriate for the different sites.

Based on these considerations, **protocol Version 3 Dated 08.10.2020** is approved as submitted.

Chairperson…… Date. 12.01.2021

Name: Peter Olumese

NOTE
Any changes to the proposal or to the attachments (informed consent/ questionnaires etc.) should be approved by ERC before being implemented. **The approval for this proposal is valid for a period of one year only**. Please resubmit this proposal for a Continuing Review at least 2 months before the next re-approval period.

Appendix V – Applying user preferences to optimise the contribution of HIV self-testing to reaching the “first 90” target of UNAIDS Fast-track strategy: results from discrete choice experiments in Zimbabwe. Sibanda, et al.

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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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

Student ID Number	1805320	**Title**	Mr
First Name(s)	Marc		
Surname/Family Name	d'Elbée		
Thesis Title	Estimating healthcare costs at scale in low- and middle-income countries – the case of community-based HIV self-testing scale-up in southern and western Africa		
Primary Supervisor	Prof 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?	Journal of the International AIDS Society		
When was the work published?	January 2019		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	NA		
Have you retained the copyright for the work?*	No	Was the work subject to academic peer review?	Yes

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	

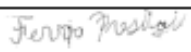
Stage of publication	Choose an item.

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 supported the study design and led DCE data analysis. I co-wrote the first draft and incorporated co-authors comments.

SECTION E

Student Signature	
Date	24/08/2021

Supervisor Signature	Type text here 
Date	19/08/21

Applying user preferences to optimise the contribution of HIV self-testing to reaching the "first 90" target of UNAIDS Fast-track strategy: results from discrete choice experiments in Zimbabwe

Euphemia L Sibanda[1,2§*], Marc d'Elbée[3*], Galven Maringwa[1], Nancy Ruhode[1], Mary Tumushime[1], Claudius Madanhire[1], Jason J. Ong[3,4], Pitchaya Indravudh[5], Constancia Watadzaushe[1], Cheryl C Johnson[4,6], Karin Hatzold[7], Miriam Taegtmeyer[2], James R Hargreaves[3], Elizabeth L Corbett[4,5], Frances M Cowan[1,2], Fern Terris-Prestholt[3]

[1]Centre for Sexual Health & HIV AIDS Research (CeSHHAR) Zimbabwe, Harare, Zimbabwe

[2]Department of International Public Health, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

[3]Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, United Kingdom

[4]Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom

[5]Malawi-Liverpool Wellcome Trust Clinical Research Programme, Blantyre, Malawi

[6]Department of HIV/AIDS, World Health Organization, Geneva, Switzerland

[7]Population Services International, Johannesburg, South Africa

[§]Corresponding first author: Euphemia L Sibanda

CeSHHAR Zimbabwe

9 Monmouth Rd

Avondale

Harare

Zimbabwe

Phone +2634333393

Email: euphemia@ceshhar.co.zw

*These authors have contributed equally to the work

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Key words

Discrete choice experiments, HIV self-testing, HIV testing, Zimbabwe, HIV, preferences

Abstract

Introduction

New HIV testing strategies are needed to reach the United Nations' 90-90-90 target. HIV self-testing (HIVST) can increase uptake, but users' perspectives on optimal models of distribution and post-test services are uncertain. We used discrete choice experiments (DCEs) to explore the impact of service characteristics on uptake along the testing cascade.

Methods

DCEs are a quantitative survey method that present respondents with repeated choices between packages of service characteristics, and estimate *relative* strengths of preferences for service characteristics. From June-October 2016, we embedded DCEs within a population-based survey following door-to-door HIVST distribution by community volunteers in two rural Zimbabwean districts: one DCE addressed HIVST distribution preferences; the other preferences for linkage to confirmatory testing (LCT) following self-testing. Using preference coefficients/utilities, we identified key drivers of uptake for each service and simulated the effect of changes of outreach and static/public clinics' characteristics on LCT.

Results

Distribution and LCT DCEs surveyed 296/329 (90.0%) and 496/594 (83.5%) participants; 81.8% and 84.9% had ever-tested, respectively. The strongest distribution preferences were for i) free kits – a $1 increase in kit price was associated with a *dis*utility (U) of -2.017; ii) door-to-door kit delivery (U=+1.029) relative to collection from public/outreach clinic; iii) telephone helpline for pre-test support relative to in-person or no support (U=+0.415); iv) distributors from own/local village (U=+0.145) versus those from external communities. Participants who had never HIV tested valued phone helplines more than those previously tested.

The strongest LCT preferences were i) immediate antiretroviral therapy (ART) availability: U=+0.614 and U=+1.052 for public and outreach clinics, respectively; ii) free services: a $1 user fee increase decreased utility at public (U=-0.381) and outreach clinics (U=-0.761); iii) proximity of clinic (U=-0.38 per hour walking). Participants reported willingness to link to either location; but never-testers were more averse to LCT. Simulations showed importance of availability of ART: ART unavailability at public clinics would reduce LCT by 24%.

Conclusions

Free HIVST distribution by local volunteers and immediate available ART were the strongest relative preferences identified. Accommodating LCT preferences, notably ensuring efficient provision of ART, could facilitate "resistant testers" to test while maximising uptake of post-test services.

Introduction

HIV testing is an important entry point for uptake of prevention, treatment and care services. United Nations 90-90-90 targets are that by 2020, 90% of people living with HIV should be diagnosed, of whom 90% are on treatment, and 90% of those on treatment are virally suppressed[1]. Although achievement of the "first 90" has already occurred for some countries, many countries have not yet attained these targets, with particularly sub-optimal uptake of testing among men and young people[2, 3]. HIV self-testing (HIVST), where an individual collects his/her own oral fluid or blood sample, conducts the test and interprets results[4], is an additional testing modality that has increased the uptake and frequency of testing among individuals who would not otherwise test[5, 6]. According to World Health Organization (WHO) guidelines[6], a reactive HIVST result should be followed by further confirmatory testing by a trained provider. There are several HIVST delivery models, including community-based, workplace, public and private sector facility-based, and secondary distribution strategies to sexual partners and peers[4].

Optimal models for distributing HIVST, which facilitate both uptake of testing and linkage to confirmatory testing (LCT), to reach those who are undiagnosed are unclear. Uncertainties around ideal service configurations include who should distribute kits, where and when they distribute them, how potential users should be engaged, and what strategies facilitate LCT. A limited number of papers have reported on preferences for service delivery characteristics that facilitate uptake of testing[7, 8], and LCT[9]. Here we report on two discrete choice experiments (DCEs) that were conducted to elicit the strength of users' preferences for both HIVST uptake and LCT to provide recommendations on how self-testing models can be optimised. DCEs are a quantitative survey method that elicit respondents' preferences for attributes of goods/services/programs[10]. We also present the simulated impact of changing existing services to better support uptake of confirmatory testing.

Methods

Setting, model of HIVST kit distribution and support for LCT

This study is part of the Unitaid-funded Self-Test AfRica (STAR) project that aimed to evaluate models of distributing HIVST kits in three countries, Malawi, Zambia and Zimbabwe[11]. In Zimbabwe, HIVST distribution was implemented by Population Services International (PSI), which conducts more than 20% of HIV tests in the country. PSI recruited and trained volunteers (community-based distribution agents: CBDA) to distribute HIVST kits door-to-door. Each CBDA was a resident of the same community - a defined geographic area (all or part of a village) in which he/she distributed kits for four to six weeks. According to Ministry of Health and Child Care guidelines[12], kits were offered to all residents ≥16 years old. CBDAs each received a one-off payment of US$50 at the end of the distribution period. To enable LCT, PSI conducted outreach visits at one and three weeks after commencement of distribution. During distribution, participants were told that they could access confirmatory testing either at PSI outreach, public clinics or any other HIV testing service. We evaluated the distribution strategy using a population-representative survey which was conducted in one in four randomly selected households approximately eight weeks after distribution ended. We nested the distribution and LCT DCEs within the survey in two rural districts, Mazowe and Mberengwa in Mashonaland Central and Midlands provinces, respectively. Participants were eligible for the survey if they were aged ≥16 years and had lived in the community for at least three months. All eligible participants in a household were recruited.

Defining DCE attributes and levels

To design the DCE, we used focus group discussions (FGDs) to identify key design attributes or service characteristics and levels (service options within a characteristic) that were most salient in driving decision-making on willingness to self-test for HIV and LCT[10]. FGDs were also used to inform pictorial illustrations of attributes and their levels.

FGDs were conducted by trained social scientists; eligible participants were aged ≥16 years and had lived in the community during HIVST distribution. We based our FGD sample sizes on standard practice that would enable theoretical saturation[13]. Discussions were held in the local language and were digitally recorded, transcribed and translated. Data analysis started soon after data collection began – field notes were written with view to emerging themes, followed by analytic summaries capturing both descriptive and analytic themes. These informed development of a coding framework. Coding was done using NVIVO 10.

We conducted 16 FGDs to inform the distribution DCE (n=150) and four FGDs for the LCT DCE (n=33). The final attributes and levels are presented in Table 1. FGD guides and illustrations of attributes and attribute levels are presented in Appendix 1 and 2.

Table 1. Attributes, levels and regression coding for the HIVST distribution and LCT DCE

Distribution DCE	
Attribute	Attribute level and
Distribution method	*Only directly to individuals willing to test (-1)*
	Deliver tests for whole household (1)
Kit price	*Free (0)*
	US$0.50 (0.5)
	US$1 (1)
Pre-test support*	*Information leaflet (-1)*
	Telephone helpline (1 or 0)
	Face to face from distributor (1 or 0)
Time of operation	*Monday to Friday 8am -4pm (-1)*
	All days, including evenings and weekends (1)
Distributor age	*Below 30 years old (-1)*
	Above 30 years old (1)
Distributor residence	*From the same village as participant (-1)*
	From outside participant village (1)
Location of kit collection*	*Collection from local clinic (-1)*
	Distributed door-to-door (1 or 0)
	Collection from mobile testing outreach sites (1 or 0)

LCT DCE - labelled design: Public clinic and PSI "New Start" outreach site	
Attribute	Attribute level and regression coding
Proximity from clinic	*Less than 30 minutes' walk from home (0)*
	About 1 hours' walk from home (1)
	More than two hours' walk from home (2)
Busyness of clinic	*Few people (-1)*
	Many people (1)
Time of operation	*Open weekdays 8am-5pm (-1)*
	Open weekdays and weekends 8am – 5pm (1)
Antiretroviral treatment available immediately	*Yes (-1)*
	No (1)
User fee	*None (0)*
	$1 (1)
	$2 (2)
Post-test support*	*None (-1)*
	SMS reminder (1 or 0)
	Call reminder (1 or 0)
	In person follow up (1 or 0)
Time between kit distribution and PSI visit (applied only to PSI outreach)	*Within 1 week (-1)*
	From 2-3 weeks (1)

* Since this attribute has *n* levels and was not treated as a continuous variable, *n-1* variables indicating the level were created for that attribute. For each of these variables, where the variable takes on the omitted reference category, included categories are coded -1, otherwise the non-reference categories take on conventional codes of 0 or 1. To retrieve the parameter for the reference category one must take: -1* sum (parameters of non-reference categories).

Designing the DCE questionnaire

The DCE questionnaire, i.e. the specific set of repeated choices where participants choose between alternative service provision for HIVST distribution or for LCT, was generated using a d-efficient design created in NGENE 1.0 software[14]. A statistically generated experimental design ensures that the parameter or utility coefficient of each level can be retrieved with the least number of choice sets presented to the participant. DCEs assume that choices are made according to the utility maximization principle, where the best choice provides the highest utility/satisfaction to the decision maker.

For the HIVST distribution DCE, the questionnaire presented nine choice situations, each presenting two alternatives composed of seven attributes. Participants were asked to choose their preferred program from each pair of alternatives, (Appendix 3a). For the LCT DCE, we used a design with three labelled alternatives, namely public clinic, PSI outreach testing facilities (New Start), and an opt-out presented as "I would not confirm my reactive HIV self-test result if these were the only two options available". Labels are generally used when the service has multiple dimensions, which cannot be fully described, often illustrated by brand names, while the attributes and levels are objective categories that can be fully described. We considered a labelled experiment suitable for the LCT DCE as the image and status of PSI outreach versus public clinics encompasses a vast range of attitudes and preferences and are not changeable. The LCT DCE questionnaire presented twelve choice situations with three alternatives (Appendix 3b).

Sample size, data collection and analysis

There is no consensus on minimum sample size requirements for stated choice data[15]. We employed the commonly-used rule of thumb by Johnson and Orme to ensure that we were able to estimate parameters for the full sample as well as analyse preference heterogeneity between sub-groups[16]. We aimed to recruit 300 and 500 consecutive household survey participants in Mazowe and Mberengwa, respectively.

Paper-based questionnaires were translated into local languages, colour-printed and administered by trained research assistants from June to October 2016.

We estimated the parameters (utility coefficients) using discrete choice models in NLOGIT 5 software[17]. All categorical attribute levels were effects coded, therefore, the parameter for the omitted level was retrieved using this formula: -1*∑coefficient of non-omitted levels[18]. According to common practice, the multinomial logistic model (MNL) was first estimated, followed by iterations of more complex models including the nested logit (NL) and the random parameter logit (RPL) to capture more complex patterns of preference heterogeneity (i.e. variation in tastes across individuals). To estimate preferences for LCT, the NL model was first tested against the MNL model because of the three-alternative design: two LCT programmes and an opt-out, and its relative simplicity, while allowing for some scale heterogeneity. Model fit was assessed using the Akaike information criterion (AIC); the model with the lowest AIC indicates a better statistical fit[19].

We investigated interactions with age, sex, history of HIV testing and apostolic religion. We explored age and sex since both young people and men have sub-optimal uptake of testing in Zimbabwe and elsewhere in Africa[3, 20]. We explored religion because the largest religious group in Zimbabwe, the Apostolic sect[21], preaches faith-cure and discourages the uptake of health services[22]. The above characteristics were interacted with selected attribute levels based on our literature review. All main

effects (estimated on the full sample) and interaction effects (estimated by sub-groups) were included simultaneously in all models.

A manual decision support system (DSS) using the nested logit model estimates was used to simulate LCT under varying service characteristics[19]. Simulation was not done for the HIVST distribution DCE because we did not have an opt-out alternative to capture a choice not to test. Simulated scenarios compared uptake of new service configurations to the base case scenario, as observed during implementation. Only attributes actionable by policy-makers were included in the simulation exercise: approaches for supporting LCT, clinic operating time, HIV treatment availability and user fees. LCT simulations were run on the full sample and by sex and HIV testing history sub-groups. We tested for statistical differences using two-sample t-tests.

Additional information on the formative qualitative phase, the DCE design, data collection and analysis methods is presented in the supplemental material.

Ethical considerations

The study received ethical approval from Medical Research Council of Zimbabwe (MRCZ/A/2038) and London School of Hygiene & Tropical Medicine Ethics Committee (reference 11738). Written informed consent was obtained from all participants before study activities were conducted.

Results

Of 329 survey participants who were invited to participate in the distribution DCE, 296 (90%) were recruited. For the LCT DCE, an administrative challenge in the field caused a two-day break in DCE completion by survey participants. Out of 747 survey participants seen when DCE recruitment was open, 594 were offered participation. Of these, 496 (83.5%) participated in the DCE. There were no differences between those not offered DCE participation and those who were offered by sex and marital status: 39.9% and 38.7% (p=0.8) were male, and 58.8% and 60.6% (p=0.7) were married, respectively, (results not shown).

Participants' characteristics are presented in Table 2. More than half were women and a third were aged 16-25 years. Among distribution DCE participants, 54 (18.2%) had never tested for HIV, compared with 75 (15.1%) among LCT DCE participants. Across samples, we observed similar levels of education and marital status whereas the LCT DCE sample had higher employment rates than the distribution DCE sample (22.6% versus 10.5%).

Table 2. Sample Characteristics

	Distribution DCE		Linkage DCE	
Sample size	296		496	
	n	%	n	%
Sex				
Male	128	43.2	189	38.1
Female	168	56.8	307	61.9
Age mean (standard deviation)	37.10 (16.68)		38.61 (18.08)	
Age Groups				
16 to 25 years old	96	32.4	148	29.8
26-40 years old	89	30.1	136	27.4
>40 years old	111	37.5	211	42.5
Education level				

O level incomplete	192	64.9	312	62.9
At least O level completed	104	35.1	184	37.1
Participants' religion				
Apostolic	134	45.3	176	35.5
Non-Apostolic	162	54.7	320	64.5
HIV testing experience				
Never tested	54	18.2	75	15.1
Self-tested	136	45.9	260	52.4
Tested but never self-tested	106	35.8	161	32.5
Marital status				
Married	194	65.5	297	59.9
Never married	64	21.6	113	22.8
Divorced/widowed/separated	38	12.8	86	17.3
Employment status-receive regular salary				
No	265	89.5	384	77.4
Yes	31	10.5	112	22.6

Preference for distribution of kits

Table 3 reports findings from the MNL (Model 1) and RPL (Model 2), which both show similar results, providing some reassurance regarding the robustness of the analysis. Positive utilities show relative preference for the attribute level; a negative sign shows relative dislike. The AIC for the RPL model (AIC=3260.9) is lower than the MNL model (AIC=3488.3), therefore we focus on the RPL model outputs.

The strongest relative preference was against paying for kits, where every one-dollar increase in price to users was associated with a disutility U=-2.017, p<0.01. Participants strongly preferred door-to-door delivery of kits (U=1.029, p<0.01), over collection from public/mobile facilities (U=-0.970, p<0.01). For pre-test support, participants strongly preferred the availability of a telephone helpline (U=0.415, p<0.01) relative to face-to-face support from a distributor (U=-0.201, p<0.10) or an information leaflet alone (U=-0.214, p: not available).

There were significant differences in preferences for the mode of distribution of HIVST kits. Batch distribution (distribution to whole households) was preferred among non-testers (U=0.055+0.102=0.157, p<0.10) and older participants (U=0.055+0.004=0.059 per year increment, p<0.05) while men (0.055-0.078=-0.023, p<0.01) and self-testers (U=0.055-0.130=-0.075, p<0.05) valued individual kit distribution. Conventional testers slightly preferred the batch distribution method (U=0.055+(-1*(0.102-0.130)) =0.083, p<0.10).

On interactions, we found variation related to the mode of distribution of HIVST kits. Batch distribution of HIVST was preferred among non-testers (U=0.055+0.102=0.157, p<0.10) and older participants (U=0.055+0.004=0.059 per year increment, p<0.05) while men (0.055-0.078=-0.023, p<0.01) and self-testers (U=0.055-0.130=-0.075, p<0.05) valued individual kit distribution. Conventional testers slightly preferred the batch distribution method (U=0.055+(-1*(0.102-0.130))=0.083, p<0.10).

The RPL model presents unobserved preference heterogeneity (variation in preferences not captured by the participants' characteristics included in the analysis) as shown by a significant standard deviation of utility coefficients (right two columns in Table 3). For example, there was significant unobserved heterogeneity across individuals in the effect of price on their choices.

Table 3. Model 1 and 2 estimation of preferences for HIVST distribution among the general population and by sex, age, HIV testing history and religion

	Model 1 (Multinomial logit)			Model 2 (Random parameter logit)				
Attribute *(base case)**	β		SE	β		SE	StdD	SE
Main effects				*Random parameters*				
Distribution method *(Only directly to individuals)*								
Deliver tests for whole household	0.008		0.051	0.055		0.115	0.632 ***	0.054
Kit price (per $1 increase)	-1.273	***	0.272	-2.017	***	0.400	1.577 ***	0.214
Pre-test support *(Information leaflet)*								
Telephone helpline	0.290	***	0.108	0.415	***	0.152	0.048	0.158
Face-to-face from distributor	-0.131		0.088	-0.201	*	0.120	0.069	0.202
Time of operation *(Monday to Friday 8am -4pm)*								
Monday to Friday 8am -4pm + evenings and weekends	-0.008		0.040	-0.032		0.059	0.036	0.130
Distributor age *(Below 30 years old)*								
Above 30 years old	0.008		0.020	-0.016		0.036	0.258 ***	0.063
Distributor residence *(From the same village)*								
From another village	-0.116	***	0.031	-0.145	***	0.052	0.462 ***	0.061
Location kit collection *(Collection from local clinic)*								
Distributed door-to-door	0.698	***	0.219	1.029	***	0.335	0.007	0.179
Collection from mobile testing outreach sites	-0.648	***	0.199	-0.970	***	0.309	0.404 ***	0.100
Interaction effects				*Non-random parameters*				
*Household distribution*Male*	-0.057	***	0.021	-0.078	***	0.047		
*Household distribution*Age*	0.003	**	0.001	0.004	**	0.003		
*Household distribution*Non-tester*	0.066	*	0.037	0.102	*	0.082		
*Household distribution*Self-tester*	-0.080	***	0.028	-0.130	**	0.064		
Model fit statistics								
Number of participants	296			296				
Number of observations	2641			2641				
AIC	3488.3			3260.9				
AIC/N	1.321			1.235				

SE = Standard Error, StdD = Standard Deviation. *10%, ** 5%, ***1% level of significance with *p* value. *Since effects coding was applied, within each attribute, utility coefficients add up to zero, i.e. for 2-level attributes the coefficient of the omitted level is the same magnitude with opposite sign.

Preferences for LCT

The AIC shows that the NL has a better statistical fit (AIC=8175.2) than the MNL (AIC=8191.4 – not reported in this paper), but the RPL model (AIC=7277.4) provided the best fit. The main and interaction effects estimated by the NL (Model 3) and RPL (Model 4) models are presented in Table 4.

There was no significant difference in preference between LCT at PSI outreach or the public clinic (i.e. the constant was not statistically significant between the two locations); what mattered were the specific service characteristics.

For both clinic types lack of immediate antiretroviral treatment (ART) (public clinic: U=-0.614, p<0.01; PSI outreach: U=-1.052, p<0.01) was the biggest driver of choice. Consistent with the distribution DCE, participants were strongly averse to paying for services (public clinic: U=-0.380, p<0.05; PSI outreach: U=-0.761, p<0.01; per one-dollar increase). The attribute of third relative importance for both locations was proximity to the health facility. Regarding post-test support, call reminders were strongly preferred for PSI outreach. Although post-test support options were generally not significant for the public clinic, no support at all was disliked at both locations (local clinic: U=-0.337; PSI outreach: U=-0.826; p: not available).

While the preference above informs drivers of where people choose to go for LCT, the opt-out provides insights into loss-to-follow-up. While most people showed a strong preference to link following a positive HIVST, the opt-out was more often chosen among those who had never tested for HIV (U=-3.722+0.717=-3.005, p<0.01) or identified as apostolic (U=-3.722+0.144=-3.628, p<0.05). Those who had self-tested chose the opt-out option less often (U=-3.722-0.243=-3.965, p<0.05) i.e. were more likely to link for confirmatory testing at either location. This effect was stronger for those who had previously had a conventional HIV test (U=-3.722+(-1*(0.717-0.243) =-4.196, p<0.05). Non-testers had significantly different preferences in favour of receiving SMS reminders to support uptake of linkage at a public clinic (U=0.065+0.295=0.360, p<0.01) relative to those who have previously tested.

Table 4. Model 3 and 4 estimation of preferences for LCT among the general population and by sex, age, HIV testing history and religion

	Model 3 (Nested logit)			Model 4 (Random parameter logit)					
Attribute *(base case)**	β		SE	β		SE	StdD		SE
Main effects				*Random parameters*					
PUBLIC CLINIC									
Proximity of clinic *(per hour walking from home)*	-0.222	***	0.043	-0.348	***	0.075	0.644	***	0.077
Busyness of clinic *(Few people)*									
Many people	-0.062		0.047	-0.017		0.083	0.101		0.193
Opening/operating hours *(Open weekdays 8am-5pm)*									
Open weekdays and weekends 8am – 5pm	0.065		0.046	0.091		0.082	0.285	**	0.122
Treatment available immediately *(Yes)*									
No	-0.565	***	0.060	-0.614	***	0.093	0.513	***	0.162
User fee *(per $1 increase)*	-0.361	***	0.075	-0.380	**	0.166	1.015	***	0.078
Post-test support *(None)*									
Sms reminder	0.037		0.058	0.065		0.094	0.213		0.252
Call reminder	0.110	*	0.060	0.129		0.097	0.415	***	0.151
In person follow up	0.112	**	0.055	0.143		0.090	0.336	*	0.178
PSI OUTREACH									
Proximity of clinic *(per hour walking from home)*	-0.301	***	0.071	-0.328	***	0.081	0.735	***	0.077
Busyness of clinic *(Few people)*									
Many people	-0.188	***	0.069	-0.347	***	0.091	0.708	***	0.097
Opening/operating hours *(Open weekdays 8am-5pm)*									
Open weekdays and weekends 8am – 5pm	0.000		0.069	-0.034		0.086	0.254		0.187
Treatment available immediately *(Yes)*									
No	-0.614	***	0.070	-1.052	***	0.120	1.664	***	0.131
User fee *(per $1 increase)*	-0.454	***	0.114	-0.761	***	0.185	1.094	***	0.081
Post-test support *(None)*									

SMS reminder	0.054		0.084	0.054		0.097	0.413	**	0.189
Call reminder	0.561	***	0.172	0.654	***	0.185	0.209		0.177
In person follow up	-0.031		0.082	0.118		0.095	0.214		0.281
Time between kit distribution and PSI visit *(Within 1 week)*									
From 2-3 weeks	-0.084		0.057	-0.015		0.065	0.352	***	0.098
Constant *(PSI outreach relative to public clinic)*	-0.218		0.188	0.194		0.155			
				Non-random parameters					
NEITHER *(NOT LINK TO CARE, OPT-OUT)*	-3.479	***	0.256	-3.722	***	0.237			
Interaction effects									
PUBLIC CLINIC									
*SMS reminder*Non-tester*	0.152	**	0.063	0.295	***	0.103			
NEITHER *(NOT LINK TO CARE, OPT-OUT)*									
*Neither*Non-tester*	0.655	***	0.104	0.717	***	0.134			
*Neither*Self-tester*	-0.239	**	0.100	-0.243	**	0.114			
*Neither*Apostolic*	0.145	**	0.070	0.144	**	0.090			
Model fit statistics									
Number of participants	496			496					
Number of observations	5940			5940					
AIC	8175.2			7277.4					
AIC/N	1.376			1.225					
IV parameter (Nested logit)	0.569	***	0.071						

SE = Standard Error, StdD = Standard Deviation. *10%, ** 5%, ***1% level of significance with *p* value.

*Since effects coding was applied, within each attribute, utility coefficients add up to zero, i.e. for 2-level attributes the coefficient of the omitted level is the same magnitude with opposite sign.

Results of simulated linkage programmes compared to the base case scenario

Table 5 presents a summary of the simulation exercise, see Appendix 5 and 6 for full model output and simulated uptake at public clinic and PSI outreach and Figure 1 for illustration. We found that availability of ART had the most significant effect on LCT. Shortages of ART at public clinics (scenario 5) would lead to 24.3% of respondents no longer linking. Similarly, availability of ART at outreach facilities (scenario 6) would result in improved LCT (+3.7%) with a notable shift from public sector clinic (-6.3%) to PSI outreach (+10.0%) (Appendix 6). Introducing user fees would decrease LCT, with user fees of $1 associated with a 15.8% reduction in LCT. Analysis by sex and HIV testing history did not reveal significant differences between these sub-groups.

Table 5. Change in uptake of simulated linkage programmes compared to base case for the full sample, by sex and HIV testing history (%)

Scenario	Scenario description	Full sample (n=496)	Female (n=307)	Male (n=189)	*t-test by Sex*	Testers (n=421)	Non-testers (n=75)	*t-test by Testing History*
1	linkage support: SMS at public clinic and PSI outreach	4.9%	6.8%	1.8%	-	3.5%	12.4%	-
2	linkage support: call at public clinic and PSI outreach	6.5%	7.4%	5.4%	-	6.9%	7.8%	-
3	linkage support: in person at public clinic and PSI outreach	6.7%	7.9%	4.6%	-	6.3%	10.0%	-
4	extended hours at public clinic and PSI outreach	2.5%	1.6%	4.0%	-	2.9%	0.4%	-
5	ART shortage at public clinic	-24.3%*	-25.0%*	-23.6%*	*NS*	-25.2%*	-22.0%*	*NS*
6	ART available at PSI outreach	3.7%*	3.9%*	3.1%*	*NS*	3.7%*	4.0%*	*NS*
7	Service fee: $1 at public clinic and PSI outreach	-15.8%*	-17.4%*	-13.4%*	*NS*	-16.0%*	-15.7%*	*NS*

Significant at α=5%. NS: t-test not statistically significant

Discussion

We found that individuals from two rural Zimbabwe districts prefer HIVST kits to be delivered door-to-door, free of charge, and by locally-based distributors. Males, young people, and individuals who had already self-tested preferred individual kit distribution rather than have kits delivered to whole households. Availability of ART was important for linkage to confirmatory testing: immediate ART initiation was most preferred while simulations showed that unstable supplies at public clinics would reduce LCT by 24.3% and introducing ART at PSI outreach would decongest public clinics as 6.3% of testers would shift to PSI outreach. People also strongly disliked payment for LCT and preferred close proximity of facilities providing confirmatory testing. Importantly, participants would rather link to either public clinic or PSI outreach than not link. Groups that were resistant to testing were also resistant to LCT. To our knowledge this is the first paper that presents preferences related to the full HIV self-testing cascade among participants previously exposed to community-based HIVST.

When comparing our results with findings from other DCEs, it is important to note that differences in context typically result in exploration of different attributes. The importance of user costs is apparent: they were universally reported in three papers: one by our group reporting preference for HIVST distribution among young people in Malawi, Zambia and Zimbabwe[8], one investigating preferences for HIV testing services in Zambia[7], and the last investigating preferences for LCT following HIVST in Zambia and Malawi[9]. All three reported a strong dis-preference for paying for test kits or services. The DCE among young people had other similar findings that we report here, including preference for home delivery of kits by lay distributors [of note, the young people aged 16-25 in the distribution DCE contributed to that analysis]. In contrast to our findings on preference for door-to-door distribution, the study that was conducted in Zambia found no significant preferences for location of HIVST distribution, although they notably did not offer participants the option for door-to-door delivery of kits[7]. Important attributes that we report here that were not explored in other studies include immediate availability of ART and type of health facility for the LCT DCE.

Our findings show preference for the existing community-based HIVST distribution model, with one exception: some participants wanted kits distributed to whole households (i.e. family-based approaches). Our findings aligned with previous research; participants believed distribution to whole household would maximise testing uptake, including individuals who may not be at home during working hours[8]. Also, they felt it would encourage testing among reluctant testers such as men[8]. However, it was the men and young people who were opposed to household distribution of test kits, as it could potentially undermine their autonomy to decide whether they would self-test[8]. Coerced self-testing by partners has been reported by 3% of self-testers in Malawi, although none subsequently regretted testing[8]. Incorporating distribution of kits to whole households would require concerted efforts for mitigating the potential risk of coercive testing. Men and young people have the lowest uptake of HIV testing, hence special consideration should be given to their needs, including alternative targeted models, such as provision at workplaces, internet and VMMC programs.

The LCT DCE showed the importance of both immediate ART initiation and continued reliable drug stocks. This has implications for national policies relating to outreach and home-based ART provision, which has been found to improve linkage to ART[23], and underscores the importance of ensuring reliable drug supplies. Individuals who had not previously tested preferred support through SMS reminders. This is a relatively low-cost intervention that can be implemented to support LCT in this

group, and is likely to be feasible given that Zimbabweans have good access to mobile phones[24]. Notably, apostolic participants and those who had never tested for HIV were hesitant to link even if they did test, suggesting that "resistant testers" may also be "resistant linkers" for whom known status may not be enough to ensure engagement with the rest of the care cascade. In the overall survey in which the DCEs were nested, we found that 12% of participants had never tested for HIV. Interventions among this group may need to focus on shifting attitudes towards health seeking in general.

Before scale-up of both HIVST distribution and linkage models, it is important to consider their cost and sustainability. Although the community-based models have high impact in terms of testing groups that would not otherwise test, such as men and young people, we found that they cost more than standard provider-delivered testing[25]. Low-cost models of ensuring door-to-door HIVST distribution may be important: our group is presently evaluating the feasibility and cost of community-led HIVST distribution approaches.

The strengths of this study include use of simulations of how LCT could be affected by changes to program attributes. We also present preferences for the full HIVST cascade. Although DCE preferences are hypothetical, our study was conducted in communities previously exposed to HIVST, so that participant preferences were shaped by their actual experiences. Using the simulation based RPL to account for unobserved heterogeneity improves the model fit. However, its complex structure is not well suited for use in simple excel based decision support systems, where the utilities are manually entered to predict uptake. We rather used the output from the simpler NL model to simulate the impact of variations in LCT services. Table 3 shows that although the RPL has a better statistical fit, the NL is a good approximation. Nevertheless there are some small differences in relative utilities between the two estimators which lead to minor variations observed between the utility ranking and the simulation exercise. Another limitation is the possibility that people's preferences were shaped by current practice and experiences of self-testing and linkage to prevention and treatment services: we did not look at how preferences varied by linkage status. Also, LCT DCE participants included those who had tested HIV negative and those who had never tested; their views could be different from those with reactive HIVST results. For the LCT DCE, labels can sometimes take away attention from other service characteristics, nevertheless, many attributes had statistically significant findings while the location was not, suggesting that choices made by participants considered the full scenario. Notwithstanding this, we did not have information on people's familiarity or use of post-test services, which has potential to influence the choice of location of LCT services. Data were collected from only two districts, which may not be generalisable, although we do not expect that other Zimbabwe rural communities will be significantly different. Lastly, as is common with hypothetical choices, there may be a higher report of willingness to test and link.

Conclusions

We found practical insights into how HIVST could be optimised, including the needs of specific population groups such as non-testers and those following the apostolic religion. Individuals who have resisted testing may also be resistant to linkage to confirmatory testing. Importantly, efficient provision of ART is central to engagement in post-test services. This study contributes clients' perspectives on how best to scale up HIVST services.

Competing interests

No competing interests are declared

Authors' contributions

Formulated the research study and design - ELS, FMC, FTP, MDE, ELC, MT, MT, KH

Collected data and informed design of data collection methods – NR, MT, CM, CW

Analysed data or contributed to analysis – MDE, GM, FTP, PI

Wrote the first draft of the manuscript - ELS; MDE

Substantial intellectual input to manuscript – ELC, FMC, CJ, JJO, KH, JRH, FTP

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Additional files

Additional file 1: Appendix 3a

Additional file 2: Appendix 3b

Additional file 3: Appendix tables

Additional file 4: Supplemental material

Appendices

Appendix 1. Focus Group Discussion (FGD) guides – HIVST distribution and LCT DCE

FGD guide – HIVST distribution DCE

Opening statements: Thank you for taking time to have this discussion with us. As you may remember, my name is _____, and my colleague here is ____. Today we will have a discussion on your views on how we can detect harms that could result from HIV self-testing, which will give us important information on how we can design a good self-testing program. This discussion will take between one and a half to two hours to complete. Before we start on the questions, we would like to all agree on small rules that will help us have a fruitful discussion. (Moderator to ensure a participatory approach to setting the ground rules, which should be written on flip chart).

1. Have you ever heard of self-testing?

a. What is it and how does it differ from testing that is done by a health care worker?

b. Where did you get this information from?

c. Do you know anyone who has tested themselves for HIV?

d. What does self-testing involve?

i. Procedures

1. Processes for sample collection, analysis, and interpretation of results

2. What to do after self-testing

a. If results are negative

b. If results are positive

2. What are your views on HIV self-testing?

a. Is it a good thing? Why?

b. Will it increase uptake of HIV testing (compared to testing that is done by health care workers)?

i. What sorts of people are likely to take up self-testing?

c. Research that we have done has shown that people can test themselves and produce accurate results. What do you think about this? Do you agree that people can accurately test themselves for HIV? Why?

d. What are your views on how well people will take up prevention and care services after self-testing? Do you think people will link as well, or better, or worse than if they were tested by health care workers?

i. Uptake of medical male circumcision for HIV negative males

ii. Uptake of HIV treatment/care for those who test HIV positive

e. What are your views on social harms due to self-testing?

i. Do you think self-testing will have higher rates of social harms compared to provider-delivered testing? What sorts of harms do you think could result?

1. Forced testing? Is this likely?

a. In what types of relationship is it likely?

i. How likely is it among couples

ii. How likely is it among family e.g. parent forcing child or brother forcing sister

iii. How likely is it in the workplace e.g. employer forcing employee? Domestic helpers?

iv. Religious relationships

v. Community leadership

vi. Any other relationship types?

b. In what type of communities is it likely?

i. General communities?

ii. Institutions e.g. schools, colleges, churches?

iii. Other communities?

2. Gender based violence?

a. How likely is it for each of the above relationship types?

b. How likely is it for each of the above communities?

3. Aside from forced testing and gender based violence, are there other harms that could result from self-testing?

a. Would victims of such harms feel able to report 1) forced testing; 2) gender based violence, 3) other harms?

3. In the past few weeks, community based distributors have been in your community distributing HIV self-test kits in households. What are your views on community-based distribution of self-test kits?

a. Probe: Individual and community feelings about community-based distribution

i. What is good about community-based distribution of kits?

ii. What is not so good about it?

b. What are your views on whether people who were offered self-test kits accepted them?

i. If there is view that some people did not accept the kits:

ii. What sorts of people accepted the kits?

iii. What sorts of people did not accept them?

1. What were the reasons for not accepting the kits?

c. Do you feel the distribution that happened in your community ensured equitable access to the self-test kits?

i. Probe: Are there any sorts of people who were at a greater advantage in terms of access to kits?

ii. Are there any sorts of people who were at a disadvantage in terms of access to kits?

iii. Do you think there are people who wanted self-test kits but did not get them? Please explain

d. Do you think there are people who were given test kits yet they did not want them? Please explain.

i. What may have caused someone to take a test kit if they did not want it?

ii. What sorts of people were more likely to take kits that they did not want?

e. What are your views on whether people who got self-test kits used them?

i. If there is view that some people did not use the kits:

ii. What sorts of people used their kits? What sorts of people did not?

iii. What happened to the kits that were not used?

f. Who should distribute HIV self-test kits?

i. Existing community health workers (vanaMbuya/sekuru utsanana)?

ii. Kit distributors who were specifically appointed for the study – CBDs

iii. Others?

g. What are the preferred characteristics of a person who distributes self-test kits in the community?

i. Is age important? Why?

ii. Is gender important? Why?

iii. Is there preference on where he/she lives?

1. Within your community

2. From outside your community

h. Should distributors leave a kit for every member of the household (even those who are not home at the time of distribution) or should distribution be made only to a person who is physically present and expresses willingness to test? Please explain.

i. Are there precautions that a CBD must take when they are approaching a household to offer test kits?

i. Who to speak to

ii. Anything they should avoid saying or doing?

j. What are your views on what sorts of people should be offered self-test kits?

i. Any age restrictions?

k. How do you suggest that self-test kits be distributed?

i. The same system of using community-based distributors

1. Should they come to people's homes or should those who want kits go to theirs?

ii. Collection from clinics

iii. Buying from pharmacies or other establishments

1. How much would people be willing to pay?

4. Before one begins the self-testing process, what are your suggestions about how he/she should be educated about the process?

5. What sort of support do you think is important before and after self-testing?

6. If self-testing were to be provided widely,

a. Would you be supportive of it? Why?

b. Would communities be supportive of it?

i. What can be done to maximise support/acceptance from the community?

7. It is possible that self-testing could result in social harms such as forced testing and gender based violence. If this were to happen, it would likely happen in secret and would be difficult to detect.

a. How could we detect episodes of forced testing in communities?

i. How could we detect forced testing in the following types of relationship

1. Forced testing between couples

2. Forced testing in families e.g. parent forcing child or brother forcing sister

3. Forced testing in employer/employee relationships

4. Forced testing in other types of relationship that were discussed earlier

ii. How would we detect episodes of gender based violence in each of the types of relationship that we have discussed?

iii. How would we detect episodes of other harms (discuss other harms aside from forced testing and GBV that participants mentioned)

8. How could we prevent these harms from occurring in our communities

a. Forced testing

b. Gender based violence

c. Other harms

9. If you could design a new service for HIV self-testing in your community, what are the components that you feel would be important to include in order prevent or minimise chances of forced testing, gender based violence or other harms?

10. The self-test kits that were distributed in your community make use of oral fluids for testing. It is also possible to do self-testing using blood, where one can do a finger prick, collect their own small sample of blood and test themselves for HIV. Which one do you think is better, using oral fluids or a blood based test?

a. Advantages of using oral fluids

b. Disadvantages of using oral fluids

c. Advantages of using a blood-based test

d. Disadvantages of using a blood based test

What do you think would be your community's preference?

11. Do you have any questions or are there other things which are related to this topic that you would like to talk about?

FGD guide – LCT DCE

General HIV testing questions

Aside from HIV self-testing that was recently offered to you, what current options for HIV testing in your community are you aware of?

How are these HIV testing options viewed in the community?

Probes:

Review each listed option & briefly discuss views on the advantages and disadvantages of the service [focus on access – location, transportation, quality of staff & treatment of clients, cost of services, ability to influence service provision through complaints system/feedback]

In general what do you think are the main reasons why people choose to go for HIV testing in your community?

In general what do you think are the main reasons why people don't go for HIV testing in your community?

Probes:

Mean to but just don't get round to it?

Barriers to access including time & opportunity costs

Reluctance of individuals to acknowledge risk

Not knowing how to include their partner in the decision to test (or leave for below?)

Fear of stigma, discrimination & violence

Confidentiality & trust in service providers

Provider-client interactions (how users are treated)

Personal relationships between providers and clients

How often, in your opinion, should Zimbabweans in general be testing for HIV? Why?

Under what circumstances, if any, should this level of frequency of testing be different? Why?

Probes:

Relationship circumstances (e.g. new vs. established relationships)

Environment circumstances (e.g. high risk locations)

Occupational circumstances

Gender or age (e.g. male vs. female)

Potential for self-testing

If you could choose to design a new service for HIV testing in your community, what are the components that you feel would be important to include?

Probes:

Level of supervision

Role of counsellors

Type of testing

Control of testing environment

Issues surrounding confidentiality

Issues surrounding accessibility

Would you like self-testing to be regularly available to you?

Do you think people in the community would find self-testing acceptable? (Why/why not)

What specific conditions do you think would need to be in place in order to introduce self- testing in your community?

If self-testing becomes available in your community, how do you think people should be able to access the self-test kits?

Probes:

Who should distribute self-test kits in the community

What role/linkages should there be with formal health services (health centres/community health workers/counsellors/VCT centres/referral services)

if self-testing becomes available in your community, what are your views on the level of supervision that would be required to ensure it was conducted properly

Do you think that the level of supervision should be the same for everybody choosing to self-test or should this differ according to different types of people? How?

If self-testing becomes available in your community, who should this be targeted at individuals or couples? Should there be any age restrictions e.g. should the kits be distributed in high schools or universities? Why?

How important do you feel counselling is in currently available HIV testing services?

The self-test kit

What did you think of the self-test kit in general?

Probes

Clarity of instructions

Clarity of reading results

Packaging

Presentation and user friendliness in general

What in your opinion are the potential advantages and disadvantages of self-testing using this test kit if it was introduced into the community?

If it was not provided for free, how much would you be prepared to pay for a self-test kit?

Please indicate how many of you would be willing to test yourselves again using this self-test kit? Why or why not?

What are the most important differences between self-testing and having ordinary VCT at a facility?

What are the most important differences that make it easier to test at home compared to testing at a facility?

Self-testing and counselling

If self-testing becomes available in your community, what kind of role do you think there would need to be for counselling?

What kind of counselling do you think might be possible in the context of self-testing?

Probes:

Telephone counselling

Referral for counselling

No counselling

Locally available community-based counselling with neighbours/strangers

What, if any, differences should there be for counselling strategies amongst different types of people in the community?

Self-testing and linkage to care

If self-testing becomes available in your community, what would be needed to help people to link to support and care services after they self-tested, for example if they tested positive?

Probes:

- Information on where to go provided with the test kit
- A help line number in order to call and ask where to go
- A telephone call from a counsellor to help them to understand where to go
- A home visit from a clinician to provide post-test services in the home
- Post-test services made available locally in the community
- Other ideas about how to help people link to services after self-testing?

What, if any, differences should there be for strategies to link people to care amongst different types of people in the community?

Safety concerns around self-testing

If self-testing were available in your community, how do you think people would self-test?

Probe:

- Alone
- With a partner or friend
- At home
- elsewhere

Do you think, in general, people who self-test will tell someone about their test result?

Did you hear of anyone giving the self-test kit to someone else to use, rather than using it themselves?

What concerns would you have if self-testing was made available in your community?

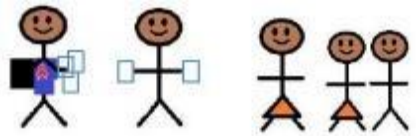
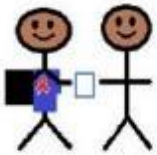
Do you think people who self-test will be prepared for the results?

What could be done to help prepare people for, or help them cope with, their self-test result?

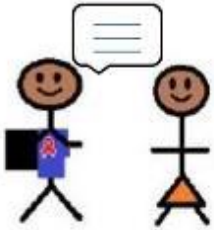
Did you hear of anyone forcing someone else to self-test?

If self-testing was available in your community, do you think forcing people to self-test might be a concern, for example a partner or employer? If so, how do you think this could be prevented?

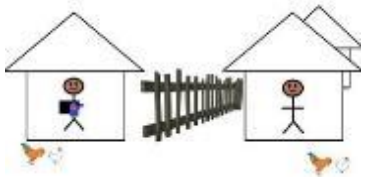
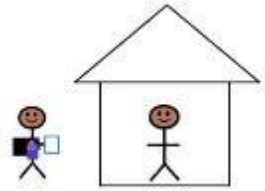
Appendix 2. Attributes, levels and pictorial illustrations for the HIVST distribution and LCT DCE

Distribution DCE		
Attribute	Levels	
Distribution method	*Deliver tests for whole household*	
	Only directly to individuals willing to test	
Kit price	*Free*	
	US$0.50	
	US$1	

Linkage DCE - labelled design: Public clinic and PSI “New Start” outreach site		
Attribute	Levels	
Proximity from clinic	*Less than 30 minutes’ walk from home*	
	About 1 hours’ walk from home	
	More than two hours’ walk from home	
Time between kit distribution and PSI visit (applied only to PSI outreach)	*Within 1 week*	
	From 2-3 weeks	

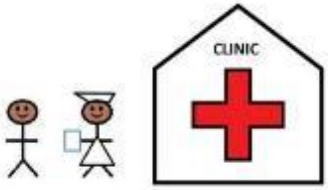
Pre-test support	*Information leaflet*	
	Telephone helpline	
	Face to face from distributor	
Time of operation	*Monday to Friday 8am -4pm*	
	All days, including evenings and weekends	

Busyness of clinic	*Few people*	
	Many people	
Time of operation	*Open weekdays 8am-5pm*	
	Open weekdays and weekends 8am – 5pm	
Antiretroviral treatment available immediately	*Yes*	

Distributor age	*Below 30 years old*	
	Above 30 years old	
Distributor residence	*From the same village as participant*	
	From outside participant village	
Location of kit collection	*Distributed door-to-door*	
	No	
User fee	*None*	
	$1	
	$2	
Post-test support	*None*	

Collection from mobile testing outreach sites

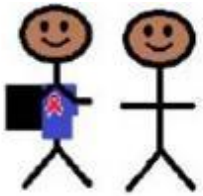
Collection from local clinic



SMS reminder

Call reminder

In person follow up



Appendix 3.a. Distribution DCE questionnaire – Sample of one choice situation (image file)

Appendix 3.b. LCT DCE questionnaire – Sample of one choice situation (image file)

Appendix 4. Selected participants' characteristics - Spearman correlation matrices at significance level 5% (*).

Distribution DCE									
	Age		Male		Non-tester		Self-tester		Apostolic
Age	1								
Male	-0.05		1						
Non-tester	-0.07		0.17	*	1				
Self-tester	-0.03		-0.04		-0.44	*	1		
Apostolic	0.02		-0.22	*	-0.17	*	0.10		1
Linkage DCE									
	Age		Male		Non-tester		Self-tester		Apostolic
Age	1								
Male	-0.07		1						
Non-tester	-0.07		0.07		1				
Self-tester	-0.05		-0.03		-0.44	*	1		
Apostolic	-0.09	*	-0.12	*	0.06		-0.02		1

Appendix 5. Nested logit models on the LCT DCE for the simulations among the full sample, men, women, testers and non-testers

	Full sample (*N*=496)			Men (*N*=189)			Women (*N*=307)			Testers (*N*=421)			Non-testers (*N*=75)		
Main effects	β		SE	β		SE	β		SE	β		SE	β		SE
PUBLIC CLINIC															
Proximity of clinic *(per hour walking from home)*	-0.216	***	*0.043*	-0.304	***	*0.07*	-0.164	***	*0.055*	-0.231	***	*0.047*	-0.139		*0.101*
Busyness of clinic *(Few people)*															
Many people	-0.067		*0.047*	-0.108		*0.078*	-0.04		*0.06*	-0.001		*0.057*	-0.226	**	*0.096*
Opening/operating hours *(Open weekdays 8am-5pm)*															
Open weekdays and weekends 8am – 5pm	0.061		*0.046*	0.097		*0.075*	0.04		*0.058*	0.069		*0.052*	0.011		*0.096*
Treatment available immediately *(Yes)*															
No	-0.576	***	*0.06*	-0.56	***	*0.092*	-0.589	***	*0.08*	-0.598	***	*0.068*	-0.516	***	*0.125*
User fee *(per $1 increase)*	-0.632	***	*0.047*	-0.526	***	*0.077*	-0.702	***	*0.061*	-0.641	***	*0.052*	-0.621	***	*0.114*
Post-test support *(None)*															
Sms reminder	0.014		*0.056*	-0.054		*0.09*	0.055		*0.072*	-0.038		*0.062*	0.264	*	*0.14*
Call reminder	0.1	*	*0.06*	0.114		*0.097*	0.095		*0.076*	0.14	**	*0.066*	-0.026		*0.142*
In person follow up	0.109	**	*0.055*	0.08		*0.088*	0.124	*	*0.07*	0.108	*	*0.06*	0.124		*0.135*
PSI OUTREACH															
Constant *(PSI outreach relative to public clinic)*	-0.218		*0.188*	-0.312		*0.3*	-0.157		*0.24*	-0.292		*0.217*	0.034		*0.467*

Proximity of clinic *(per hour walking from home)*	-0.292	***	*0.07*	-0.2	*	*0.112*	-0.351	***	*0.09*	-0.308	***	*0.083*	-0.248	*0.152*
Time between kit distribution and PSI visit *(Within 1 week)*														
From 2-3 weeks	-0.097	*	*0.057*	-0.087		*0.088*	-0.102		*0.074*	-0.064		*0.065*	-0.235 *	*0.132*
Busyness of clinic *(Few people)*														
Many people	-0.177	***	*0.068*	-0.177		*0.111*	-0.176	**	*0.086*	-0.321	***	*0.082*	0.225	*0.139*
Opening/operating hours *(Open weekdays 8am-5pm)*														
Open weekdays and weekends 8am – 5pm	0.005		*0.068*	0.014		*0.112*	-0.005		*0.087*	0.009		*0.08*	-0.021	*0.138*
Treatment available immediately *(Yes)*														
No	-0.601	***	*0.069*	-0.528	***	*0.112*	-0.644	***	*0.088*	-0.606	***	*0.081*	-0.631 ***	*0.14*
User fee *(per $1 increase)*	-0.929	***	*0.09*	-0.96	***	*0.147*	-0.908	***	*0.115*	-0.942	***	*0.107*	-1.03 ***	*0.184*
Post-test support *(None)*														
Sms reminder	0.038		*0.083*	-0.048		*0.132*	0.094		*0.107*	0.037		*0.095*	0.085	*0.194*
Call reminder	0.012		*0.086*	0.09		*0.137*	-0.042		*0.11*	-0.057		*0.098*	0.285	*0.223*
In person follow up	-0.025		*0.08*	0.01		*0.129*	-0.046		*0.103*	-0.035		*0.091*	-0.007	*0.192*
NEITHER (NOT LINK TO CARE, OPT-OUT)	-3.766	***	*0.249*	-3.784	***	0.402	-3.757	***	0.318	-4.089	***	0.303	-2.908 ***	0.517
Model fit statistics														
Number of participants	496			189			307			421			75	
Number of observations	5952			2268			3684			5052			900	
AIC	8282.8			3217.3			5091			6835.4			1428.1	

AIC/N	1.392			1.419			1.382			1.353			1.587			
IV parameter	0.577	***	0.075	0.587	***	0.124	0.574	***	0.097	0.56	***	0.083	0.529	***	0.161	

SE = Standard Error. *10%, ** 5%, ***1% level of significance with *p* value.

Appendix 6. Change in uptake of simulated linkage programmes compared to base case (%) differentiated by testing facility, sex and HIV testing history

	Full sample (n=496)			Female (n=307)			Male (n=189)			Testers (n=421)			Non-testers (n=75)		
Scenario	Public clinic	PSI outreach	None	Public clinic	PSI outreach	None	Public clinic	PSI outreach	None	Public clinic	PSI outreach	None	Public clinic	PSI outreach	None
1	5.3	-0.4	-4.9	7.3	-0.5	-6.8	2.0	-0.2	-1.8	4.1	-0.6	-3.5	12.4	0.1	-12.4
2	7.3	-0.8	-6.5	8.5	-1.1	-7.4	5.5	-0.1	-5.4	8.3	-1.4	-6.9	5.3	2.5	-7.8
3	7.6	-1.0	-6.7	9.1	-1.2	-7.9	5.0	-0.4	-4.6	7.6	-1.3	-6.3	9.9	0.1	-10.0
4	2.9	-0.3	-2.5	1.9	-0.3	-1.6	4.5	-0.5	-4.0	3.2	-0.3	-2.9	0.6	-0.3	-0.4
5	-27.8	3.5	24.3	-28.4	3.4	25.0	-27.1	3.5	23.6	-28.8	3.6	25.2	-25.2	3.2	22.0
6	-6.3	10.0	-3.7	-6.7	10.6	-3.9	-5.3	8.4	-3.1	-6.3	10.0	-3.7	-6.8	10.8	-4.0
7	-13.7	-2.1	15.8	-15.5	-1.9	17.4	-10.9	-2.4	13.4	-13.9	-2.2	16.0	-13.3	-2.4	15.7

Scenario	Scenario description

1	linkage support: SMS at public clinic and PSI outreach
2	linkage support: call at public clinic and PSI outreach
3	linkage support: in person at public clinic and PSI outreach
4	extended hours at public clinic and PSI outreach
5	ART shortage at public clinic
6	ART available at PSI outreach
7	Service fee: $1 at public clinic and PSI outreach

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