Health and economic impact of decentralized health interventions in sub-Saharan Africa

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Abstract

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In most low- and middle-income country (LMIC) settings, including Eastern and Southern Africa (ESA), health systems face persistent challenges in delivering accessible, quality care due to limited healthcare infrastructure, workforce shortages, and logistical constraints. Funding for critical health responses, such as HIV and TB, remains insufficient; UNAIDS estimates a shortfall of $9.8 billion to meet HIV targets in 2025, and 62 LMICs reported a combined funding gap of $1.5 billion for TB programs in 2022. Although innovative solutions such as decentralized service delivery models show promise in expanding healthcare access with a patient- and provider-centered lens, governments remain uncertain about the affordability and economic sustainability of these approaches. Economic evaluations are essential to help policymakers understand the health and economic implications of adopting decentralized models, which could increase coverage more efficiently and may reduce funding requirements in LMIC settings where health budget allocation is critical. This dissertation applies economic evaluation to assess the health and economic impact of decentralized care interventions across tuberculosis (TB), HIV, and cardiovascular disease among people living with HIV (PLHIV) in real world settings.

Aim 1 evaluates the cost and cost-effectiveness of decentralized TB diagnostic testing using the Molbio Truenat MTB Plus and MTB-RIF Dx assays compared to hub-and-spoke GeneXpert MTB/RIF Ultra testing in Mozambique and Tanzania, using primary cost and effectiveness data from a pragmatic cluster-randomized trial. Facility-based diagnostic costs per participant tested

were higher in the decentralized arm ($51 vs $40 in Mozambique; $46 vs $31 in Tanzania) from a modified societal perspective. However, the diagnostic cost per participant initiating TB treatment within seven days was comparable or lower with decentralized testing ($703 vs $853 in Mozambique; $592 vs $596 in Tanzania). The incremental cost per incremental seven-day treatment initiation was $422 (95% uncertainty range: –$114, $1,019) in Mozambique and $580 ($167, $1,638) in Tanzania. Cost-effectiveness was highly sensitive to testing volume, with per-test costs stabilizing when instruments were utilized at three or more tests per day. These findings demonstrate that decentralized molecular TB testing can be cost-effective when deployed in settings with sufficient demand and appropriate integration into service delivery.

Aim 2 assesses the health and economic impact of hypertension screening, treatment, and an associated implementation strategy (Systems Analysis and Improvement Approach, "SAIA") among PLHIV in Mozambique using a decision-analytic state-transition model informed by trial data. Scaling up hypertension screening and pharmacological treatment reduced acute myocardial infarction and stroke events by 25–31% over ten years and yielded an incremental cost-effectiveness ratio (ICER) of $212 per disability-adjusted life year (DALY) averted, at an additional cost of $4.61 per person per year. Incremental to the clinical intervention, the SAIA implementation strategy further reduced cardiovascular events by approximately 15% and had an ICER of $44 per DALY averted, at an additional cost of $0.79 per person per year. Average ten-year cardiovascular risk was reduced by 29.3% with the intervention alone and by 40.3% when the SAIA strategy was co-introduced. These results show that implementation strategies can generate substantial additional health gains at low incremental cost, but only when a minimum level of health system readiness is present.

Aim 3 evaluates the cost-effectiveness of delivering HIV pre- and post-exposure prophylaxis (PrEP and PEP) through online pharmacies in Kenya using an agent-based HIV transmission model parameterized with empiric utilization data from an online PrEP/PEP pilot study. Online PrEP/PEP achieved low population coverage (0.7% for PEP and 0.3% for PrEP) but was projected to avert 13.9% of HIV infections over ten years. From the Ministry of Health perspective, the intervention was cost-effective with an ICER of $212 per DALY averted. In a scenario with online PEP only, 11.6% of infections were averted with a similar ICER of $210 per DALY averted, indicating that PEP accounted for the majority of health benefits due to high observed demand.

The intervention remained cost-effective across sensitivity analyses and became cost-saving under scenarios of reduced HIV testing and treatment coverage.

Across chronic and infection diseases, this dissertation demonstrates that decentralized care models can deliver substantial health benefits and represent good value for money in sub-Saharan Africa, but that their efficiency depends critically on implementation context, utilization, and system readiness. By embedding economic evaluation within implementation science, this work provides policy-relevant evidence to guide decisions about scaling, sustaining, and adapting decentralized health interventions in resource-constrained settings.

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Dedication

To my wife, Xian, and my son, Rohan.

CHAPTER 1 – INTRODUCTION

In most low- and middle-income countries (LMIC), including in Eastern and Southern Africa (ESA), health systems face persistent challenges in delivering accessible, quality care due to limited healthcare infrastructure, workforce shortages, and logistical constraints[1]. Funding for critical health responses, such as HIV and TB, remains insufficient; UNAIDS estimated a shortfall of $9.8 billion to meet HIV targets in 2025, and 62 LMICs reported a combined funding gap of $1.5 billion for TB programs in 2022[2,3]. Although innovative solutions such as decentralized service delivery models show promise in expanding healthcare access with a patient- and provider-centered lens, governments remain uncertain about the affordability and economic sustainability of these approaches[4]. Economic evaluations are essential to help policymakers understand the health and economic implications and value for money of adopting decentralized models, which could increase coverage more efficiently and may reduce funding requirements in LMIC settings where health budget allocation is critical. This dissertation assesses the health and economic impact of decentralized care interventions across tuberculosis (TB), cardiovascular disease among people living with HIV (PLHIV), and HIV prevention in real world settings.

Decentralized and differentiated models of care have emerged as a central strategy to expand access to essential health services. These models shift services closer to patients by moving diagnostics, treatment initiation, and follow-up away from centralized facilities and into primary care, community, or private-sector settings. Examples include near point-of-care diagnostics, community-based treatment delivery, task-shifting to lower-cadre providers, telehealth, and private-sector engagement[4–6]. Decentralized models aim to reduce structural barriers such as distance, long wait times, stigma, and opportunity costs while improving patient-centeredness and system efficiency.

This dissertation is grounded in implementation science, which seeks to understand not only whether interventions work, but how they can be delivered effectively, equitably, and sustainably in real-world contexts. Within implementation science, economic evaluation plays a crucial role by quantifying the resources required to implement interventions and the health

gains achieved. Economic evaluation helps bridge the "know–do gap" by identifying whether effective interventions can be feasibly implemented within existing system constraints and at what cost.

Economic evaluation, including costing and cost-effectiveness analysis, is increasingly recognized as a core component of implementation science[7]. Traditional economic evaluations often focus on the cost-effectiveness of clinical interventions in isolation, such as medications or diagnostic tests[8]. However, real-world impact depends not only on the availability of effective technologies, but also on the strategies used to implement them, including training, supervision, workflow redesign, data systems, and quality improvement processes. Distinguishing the cost and impact of evidence-based interventions, from the implementation strategies used to deliver them, is essential for understanding why interventions succeed or fail and what resources are required to replicate success in new settings. Without this distinction, policymakers may underestimate the true costs of implementation or misattribute health gains to clinical interventions alone.

Mathematical modeling is often an essential component of economic evaluation, particularly when assessing interventions in real-world implementation contexts. Most economic evaluations extend beyond observed data and therefore rely on modeling to project long-term costs and health outcomes, synthesize evidence from multiple sources, and evaluate alternative implementation scenarios[9]. In the context of decentralized care, modeling enables the assessment of how variations in delivery strategies, coverage, adherence, and system capacity influence both costs and effectiveness over time. By linking epidemiologic, behavioral, and cost data, modeling-supported economic evaluations provide a more complete understanding of value for money under different implementation conditions. This is especially important in resource-constrained settings, where decisions about scale-up must account not only for effectiveness, but also for feasibility, sustainability, and efficient use of limited resources.

Decentralized approaches to service delivery are not new. Many programs in LMIC settings have long operated in community-based models without explicitly labeling them as such. While economic evaluations of decentralized health interventions exist, they are relatively limited in

number and often vary in scope and methodological approach[10]. In particular, few studies explicitly integrate implementation considerations into economic evaluation or assess how differences in delivery influence value for money. This dissertation builds on existing work by applying consistent economic evaluation frameworks across multiple decentralized interventions and explicitly incorporating implementation context into the analysis.

The overarching objective of this dissertation is to assess the health and economic impact of decentralized care interventions in sub-Saharan Africa, with a focus on generating evidence for policymakers and implementers. The dissertation has three specific aims, each applying economic evaluation and each addressing a different component of decentralized service delivery:

I. Decentralized diagnostics (Aim 1)

II. Decentralized decision-making and quality improvement (Aim 2)

III. Decentralized delivery of preventive services through e-pharmacy channels (Aim 3)

Aim 1: Evaluate the cost and cost-effectiveness of the Truenat MTB assay in Tanzania and Mozambique

Aim 1 evaluates the cost and cost-effectiveness of deploying the Truenat MTB molecular diagnostic platform at decentralized health facilities in Tanzania and Mozambique, compared to centralized testing using standard-of-care GeneXpert-based and sputum smear testing models.

In low-and middle-income countries, missed or delayed tuberculosis (TB) diagnoses contribute to avoidable morbidity, mortality, and transmission. Decentralized testing platforms, such as the Molbio Truenat, may offer solutions by providing accurate point-of-care testing, improving access, and lowering out-of-pocket costs. Despite these advantages, the overall cost and cost-effectiveness of identifying additional TB cases using the Truenat MTB assays remain inadequately explored and understood.

We collected economic data from a multicentre randomized controlled trial of TB testing using decentralized Molbio Truenat platform with MTB Plus and MTB-RIF Dx assays (Truenat MTB assays) versus hub-and-spoke Xpert MTB/RIF Ultra (standard of care) in Tanzania and Mozambique (TB-CAPT Core trial). We estimated facility-based diagnostic cost per participant tested and incremental facility-based diagnostic cost per incremental participant initiating TB treatment within seven and sixty days from enrolment. We used the societal perspective and conducted sensitivity analyses to determine key drivers of cost-effectiveness.

Aim 2: Develop a mathematical modeling framework to assess hypertension interventions and implementation strategies among people living with HIV (PLHIV) in African countries

Aim 2 develops and applies a mathematical modeling framework to evaluate the health and economic impact of cardiovascular interventions and implementation strategies among people living with HIV (PLHIV), using the SAIA-HTN trial in Mozambique as a test case.

Few economic evaluations distinguish between the cost and impact of evidence-based interventions and the strategies used to improve their implementation. This distinction is essential for understanding whether a strategy is cost-effective, why it works, and the resources required to replicate its success. The Systems Analysis and Improvement Approach Hypertension (SAIA-HTN) trial evaluated a decentralized implementation strategy ("SAIA") designed to improve hypertension care among people living with HIV (PLHIV) in Mozambique. We developed a mathematical model to estimate the cost-effectiveness of both the evidence-based intervention (including hypertension screening, pharmacological treatment and follow up, and lifestyle modifications such as diet and exercise) and the SAIA implementation strategy.

We constructed a state-transition model that simulated cardiovascular risk, outcomes, and associated costs for PLHIV receiving hypertension care in Mozambique. Model inputs came from published epidemiological studies and primary data from the SAIA-HTN trial on effectiveness and costs of both the intervention and implementation strategy. We estimated the incremental

cost-effectiveness of rolling out both components, compared to a “status quo” scenario where screening and treatment of hypertension remained at their current (very low) levels.

Aim 3: Assess the health and economic impact of online pharmacy distribution of pre and post-exposure prophylaxis (PrEP and PEP) in Kenya

Aim 3 assesses the health and economic impact of delivering HIV pre- and post-exposure prophylaxis (PrEP and PEP) through online pharmacies in Kenya, using an agent-based HIV transmission model informed by primary data from an e-Pharmacy PrEP/PEP pilot study.

Despite the availability of effective biomedical prevention tools, uptake and persistence of PrEP remain low in many facility-based programs, and PEP remains underutilized. Barriers such as stigma, clinic wait times, limited operating hours, and privacy concerns limit access to prevention services. Online pharmacies offer a differentiated delivery model that leverages telehealth, private-sector logistics, and extended hours to provide discreet and timely access to PrEP and PEP. However, the health impact and economic impact of this intervention are unknown. We modeled the health and economic impact of online PrEP/PEP scale-up in western Kenya.

We adapted an agent-based network model, EMOD-HIV, to simulate online PrEP/PEP implementation from 2026-2036. Estimates of costs and PrEP/PEP utilization, according to client demographics and sexual behavior, were informed by the ePrEP pilot study which implemented and online PrEP/PEP in Nairobi and Mombasa, Kenya. We assumed online PrEP/PEP delivery was implemented through a public/private partnership in which the Kenya Ministry of Health (MOH) provides PrEP/PEP drugs while service delivery costs are paid by the online pharmacy (and charged to clients).

Taken together, this dissertation demonstrates how economic evaluation can provide evidence on the value for money of decentralized care delivery in low resource settings. Across TB diagnostics, integrated chronic disease care, and HIV prevention, the findings illustrate that decentralized models can be cost-effective, but their value depends on context, implementation strategy, and system readiness.

This work provides an understanding how governments can allocate limited resources efficiently to expand access to care. The dissertation contributes methodological tools, empirical evidence, and policy-relevant insights that can guide future investments in decentralized and differentiated care models in LMIC settings.

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CHAPTER 2 – AIM 1

Decentralized TB diagnostic testing with Truenat MTB Plus and MTB-RIF Dx vs. hub-and-spoke GeneXpert MTB/RIF Ultra in Mozambique and Tanzania: a cost and cost-effectiveness analysis

Short Title: Cost-effectiveness of decentralized TB testing with Truenat vs. GeneXpert

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ABSTRACT

Background

In low-and middle-income countries, missed or delayed tuberculosis (TB) diagnoses contribute to avoidable morbidity, mortality, and transmission. Decentralized testing platforms, such as the Molbio Truenat, may offer solutions by providing accurate point-of-care testing, improving access, and lowering out-of-pocket costs. Despite these advantages, the overall cost and cost-effectiveness of identifying additional TB cases using the Truenat MTB assays remain inadequately explored and understood.

Methods

We collected economic data from a multicentre randomized controlled trial of TB testing using decentralized Molbio Truenat platform with MTB Plus and MTB-RIF Dx assays (Truenat MTB assays) versus hub-and-spoke Xpert MTB/RIF Ultra (standard of care) in Tanzania and Mozambique (TB-CAPT Core trial). We estimated facility-based diagnostic cost per participant tested and incremental facility-based diagnostic cost per incremental participant initiating TB treatment within seven and sixty days from enrolment. We used the societal perspective and conducted sensitivity analyses to determine key drivers of cost-effectiveness.

Findings

The facility-based diagnostic cost per participant initiating treatment within seven days from enrolment in Mozambique was $853(95% uncertainty range: $707, $1072) for hub-and-spoke testing and $690($588, $823) for decentralized testing; in Tanzania costs were $596($485, $746) for hub-and-spoke testing and $592($495, $715) for decentralized testing. At sixty days, costs per treatment initiation were $581($493, $706) for hub-and-spoke vs. $678($576, $811) for decentralized testing in Mozambique, and $391($324, $476) vs. $591($494, $716) in Tanzania. Comparing decentralized to hub-and-spoke testing, the incremental cost per incremental seven-day treatment initiation was $403(-$103, $941) in Mozambique and $580($167, $1638) in Tanzania, and $805(-$10107, $10560) and -$353(-$20299, $20802) for sixty-day treatment initiation, respectively. Utilization (i.e., testing volume) of decentralized equipment was the strongest driver of cost-effectiveness.

Interpretation

Decentralized TB testing with Truenat MTB assays is cost-effective relative to hub-and-spoke testing in Mozambique and Tanzania.

Funding

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INTRODUCTION

Tuberculosis (TB) kills more than 1.3 million people globally each year, with a case fatality rate of 12%[1]. Approximately one-third of all people with TB, have a missed or inaccurate diagnosis[2]. Lack of access to diagnostic testing and participant loss to follow up during the TB care cascade contribute to missed diagnoses, leading to TB morbidity, mortality, and transmission[3]. Diagnostic testing for TB needs to optimize access, turnaround time, and thus time to treatment initiation and cost[4].

"Hub-and-spoke" Xpert MTB/RIF Ultra ("Xpert"; Cepheid, Sunnyvale, CA, USA) testing with specimen transport to centralized laboratories is standard practice for TB diagnosis in many low-and-middle-income countries (LMICs)[5]. While the approach allows for GeneXpert

instruments to be placed in central locations, it also results in missed diagnosis and losses to follow up while participants wait for their Xpert results[6,7].

Previous economic evaluations have demonstrated that decentralized testing for TB can be implemented with only a slight increase in per-test cost compared to centralized testing[6]. For example, in peripheral clinics in Uganda, a multicomponent strategy focused on decentralized molecular testing incurred only a 10% increase in per-test cost relative to the standard of care ($20·46 *vs* $18·20)[6]. Modeling studies have similarly suggested that decentralized Xpert testing can be cost-effective in settings characterized by high loss to follow-up, moderate-to-high peripheral testing volumes, and inability to distribute specimen transport costs among other disease entities[8].

More accurate point of care (PoC) testing may increase access and reduce participant out-of-pocket costs[6]. Options for PoC TB testing include Xpert EDGE[9] and the Molbio Truenat MTB Plus and MTB-RIF Dx assays ("Truenat MTB assays"; Molbio Diagnostics, Verna, Goa, India)[10].

The TB-CAPT Core randomized clinical trial assessed the effectiveness of PoC Truenat MTB assays in improving the TB diagnostic pathway in primary health clinics in Mozambique and Tanzania using a pragmatic design[1]. The primary study outcome was the absolute number and proportion of participants with microbiologically confirmed pulmonary TB starting TB treatment within seven days of enrolment, accounting for potential delays in receiving a diagnostic test due to clinic workflow, patient follow-up, and access barriers. In both Mozambique and Tanzania, a higher proportion of individuals achieved the primary outcome in the Truenat arm vs. the hub-and-spoke standard of care: 7.08% (5.60%, 8.81%) vs. 4.44% (3.16%, 6.05%) in Mozambique, and 7.59% (5.99%, 9.45%) vs. 5.07% (3.86%, 6.51%) in Tanzania[1].

Decentralized testing with Molbio Truenat at peripheral health facilities allows for accurate and rapid, same-visit results, contrasting with the traditional hub-and-spoke model at centralized hospitals or laboratories, thereby improving access and lowering out-of-pocket costs[7]. Despite these advantages, there is a lack of costing studies that evaluate the difference in incremental

costs between facility and decentralized testing strategies, which are necessary for decision-makers and budgetary planning.

As part of the TB-CAPT Core study, we collected economic data from the societal perspective to assess facility-based diagnostic costs per participant tested and facility-based diagnostic costs per participant initiating treatment for confirmed TB within seven days of enrolment.

METHODS

Study design and participants

Cost data were collected within the TB-CAPT Core, a pragmatic, cluster-randomized trial recruiting participants from 26 August 2022, to 16 June 2023, at 29 peripheral health facilities across four sites in Tanzania and Mozambique. The unit of randomization was the clinic. Clinics were eligible for inclusion if they offered TB treatment, did not have a GeneXpert laboratory on-site, and were selected in coordination with the respective National TB Programs. Selection was based on TB notification data from 2018–2019, and clinics were stratified by location and estimated TB testing volume before randomization. Adults presenting with symptoms suggestive of tuberculosis were enrolled across the 29 health facilities, of which 15 were grouped under the Truenat arm where samples were tested using the Molbio Truenat platform and MTB assays (Truenat MTB Plus and MTB-RIF Dx) capable of processing two samples simultaneously on site. The remaining 14 health facilities tested samples according to the hub-and-spoke standard of care strategy, which included Xpert MTB/RIF Ultra testing off-site in all health facilities and additionally in some health facilities sputum smear microscopy on site. The protocol and trial results have been published previously[1].

At intervention clinics, microscopists were trained to use the Truenat platform, and ensure rapid result communication for same-day treatment initiation, with repeat or reflex testing conducted as needed. At control clinics, staff received refresher training on national TB guidelines, with sputum samples processed via smear microscopy on-site or Xpert testing off-site, while operational bottlenecks like sample transport delays and stockouts were addressed through logistical provisions[1].

The study was approved by regulatory and ethical committees in Mozambique (National IRB approval #131/CNBS/22) and Tanzania (National IRB approval #NIMR/HQ/R.8c/Vol.I/2323 and TMDA approval #BD.59/62/46/05). Voluntary written informed consent was sought for enrolment into the study and extraction of participant data.

Inclusivity in global research

Additional information regarding the ethical, cultural, and scientific considerations specific to inclusivity in global research is included in the Supporting Information (S1 Checklist).

Procedures

We estimated the facility-based diagnostic costs of the intervention from the societal (primary) and health system (secondary) perspectives. Across the 29 clinics, we evaluated participant costs from a systematic sample of approximately every 10th study participant enrolled, including both direct and indirect costs of TB testing. Participant costs were captured through a structured participant cost survey, with interviews directly administered to participants by study staff. To capture health system costs, we conducted project staff interviews, facility assessments, and analysis of trial expense reports.

A bottom-up, ingredients-based, micro-costing approach was used for the cost analysis. Direct participant costs included all medical (consultation fees and any out-of-pocket payment for medicines, X-rays, and diagnostics) and non-medical expenses (travel costs for participants and caregivers, food costs incurred while in-hospital, money spent buying any special foods, etc.). Indirect costs were estimated as the opportunity cost of time spent seeking care (from the time of symptom onset to the time of treatment initiation). The Gross National Income (GNI) per capita at current prices for 2022 were converted to an average hourly wage to estimate economic losses to participants owing to missed work[11].

We estimated the health system costs from a subset (19 out of 29) of intervention and standard of care clinics across the four study sites. Data on TB and HIV testing capacity, sample transportation, testing procedures, testing infrastructure, and related implementation

procedures was captured[12]. We classified costs as cartridge, other consumables, communication and monitoring & evaluation (CME), health system staffing, equipment, and warranty and maintenance. Training costs were grouped under CME, while other consumables included sample preparation kits, fuel, personnel protective equipment, and other medical consumables. Capital assets (such as testing equipment) were annuitized and depreciated linearly based on ten expected life-years at a 3% annual discount rate[13]. Costs of equipment were estimated using product catalogues and trial expense reports[14].

Analysis was conducted separately for Mozambique and Tanzania. Facility-based diagnostic costs were captured in the respective local currencies, MZN for Mozambique and TZS for Tanzania, and were converted to 2022 USD using the average exchange rate during the study period (1 USD = 2334 TZS = 63.9 MZN), from August 2022 to June 2023[15]. The cost analysis used a time horizon corresponding to the trial period, capturing costs incurred during the study.

Outcomes

The primary effectiveness outcome in the parent TB-CAPT Core trial was the number of participants with microbiologically confirmed pulmonary TB initiating treatment within one week of enrolment. As cost outcomes, we estimated the facility-based diagnostic cost per participant tested, as well as the diagnostic cost per participant starting treatment within seven days and sixty days of enrolment. Our primary cost-effectiveness outcome was the incremental facility-based diagnostic cost per incremental microbiologically positive participant initiating treatment within seven days of enrolment, comparing the Truenat and standard of care arms. The secondary cost-effectiveness outcome was the incremental facility-based societal diagnostic cost per incremental microbiologically positive participant receiving treatment within 60 days of enrolment.

Analysis

Empirical cost inputs from clinics across the four sites were used to estimate the primary, lower, and upper bound values of each health system cost category. The mean facility-based diagnostic cost per participant tested was calculated from the health system perspective as the total monthly testing cost divided by the number of monthly tests performed at the health facility,

assuming 16 tests per month (see supplementary material S1.3) in the reference case. Participant cost surveys were used to estimate uncertainty ranges of costs from the participant perspective.

We performed a one-way deterministic sensitivity analysis for both Tanzania and Mozambique to evaluate the influence of key assumptions on the incremental facility-based diagnostic cost per incremental microbiologically positive participant initiating treatment within seven days of enrolment. We varied the monthly TB testing frequency from 12 tests per month (one test every other workday) to 125 tests per month (more than five tests per workday). Additionally, we adjusted TB prevalence and modified all input cost categories, each by 25%.

We also conducted a probabilistic sensitivity analysis by sampling each cost and effectiveness value from a corresponding distribution 10,000 times; 95% uncertainty ranges were defined as the 2.5^{th} and 97.5^{th} percentiles of results across these simulations. In addition to costs, effectiveness values were varied to account for differences in TB prevalence, which influence the number of individuals testing positive and subsequently impact cost-effectiveness estimates. For each parameter, we constructed a beta distribution around the empirically observed point estimate, with the weighted mean serving as the mode of the distribution and range based on the minimum and maximum observed values for each parameter in the trial. We assumed alpha = 4 for all parameters (which corresponds to a 95% confidence interval covering 63% of the width of the full distribution, when the beta distribution was symmetric).

Lastly, we assessed the facility-based diagnostic cost per participant tested at different testing volumes to inform placement and utilization strategies for the dual module Truenat machine. We estimated this cost, from the societal perspective, for both the intervention and standard of care at hypothetical testing volumes assuming a Poisson distribution (ranging from <1% to 100% utilization, see supplementary material S2).

All analyses were performed in Microsoft Excel (version 2311) and R (version 4.3.2).

Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

RESULTS

Of 3987 participants in the TB-CAPT Core trial, 388 (9.7%) were enrolled in the participant cost survey. Survey participants were similar to the full study population in most measured characteristics (Table 1). Survey respondents were more likely to be female in Mozambique.

Table 1. **Participant characteristics for the TB-CAPT Core study and the participant cost survey.**

	Mozambique				**Tanzania**			
	Extended participant cost survey* (cost data collected)		TB CAPT Core full study population		Extended participant cost survey* (cost data collected)		TB CAPT Core full study population	
	Standard of care	**Truenat**	**Standard of care**	**Truenat**	**Standard of care**	**Truenat**	**Standard of care**	**Truenat**
Participants enrolled	85	99	855	1045	110	94	1125	962
Sex								
Female	58 (68%)	65 (66%)	489 (57%)	600 (57%)	55 (50%)	44 (47%)	559 (50%)	488 (51%)
Age, years								
Median	44	44	43	43	40	40.5	42	41
18-30	18 (21%)	20 (20%)	206 (24%)	249 (24%)	23 (21%)	18 (19%)	258 (23%)	210 (22%)

31-40	19 (22%)	21 (21%)	179 (21%)	222 (21%)	33 (30%)	29 (31%)	274 (24%)	254 (26%)
41-50	23 (27%)	19 (19%)	180 (21%)	193 (18%)	17 (15%)	28 (30%)	258 (23%)	240 (25%)
>50	25 (29%)	39 (39%)	290 (34%)	381 (36%)	37 (34%)	19 (20%)	335 (30%)	258 (27%)
HIV Status								
Positive	43 (51%)	29 (29%)	350 (41%)	288 (28%)	31 (28%)	28 (30%)	358 (32%)	272 (28%)
Negative	34 (40%)	42 (42%)	412 (48%)	474 (45%)	64 (58%)	46 (49%)	583 (52%)	509 (53%)
Unknown / not tested	8 (9%)	28 (28%)	93 (11%)	283 (27%)	15 (14%)	20 (21%)	184 (16%)	181 (19%)

Cost and cost-effectiveness outcomes

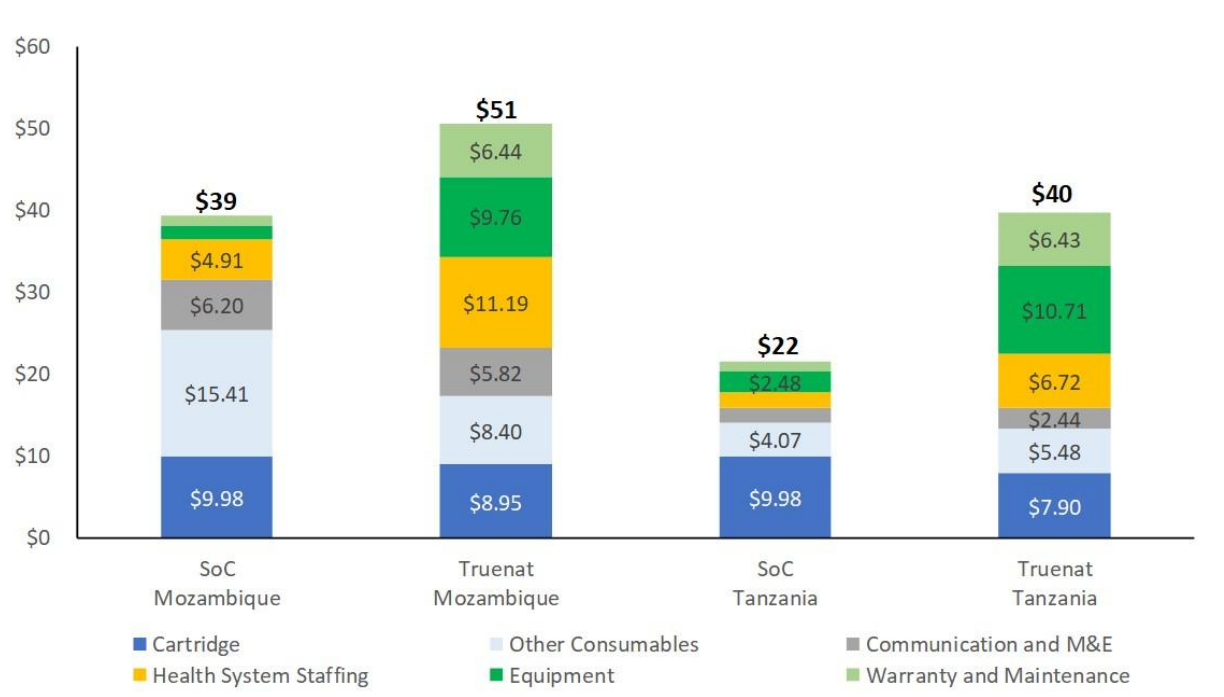


Fig 1. Health system facility-based cost per participant tested for tuberculosis, comparing point-of-care Truenat MTB assays versus hub-and-spoke Xpert Ultra MTB assays (standard of care, SoC) testing in the TB-CAPT Core Trial. Each segment within each stacked bar corresponds to a distinct cost category, illustrating its proportionate contribution to the total health system expenses for diagnostic testing in each arm of the trial. Training costs were grouped under communication and monitoring & evaluation (CME), while other consumables included sample preparation kits, fuel, personnel protective equipment, and other medical consumables. All costs are reported in 2022 US dollars. For legibility, costs labels are presented for only those categories where the cost is higher than $2.

Table 2. **Cost and cost-effectiveness of decentralized vs. hub-and-spoke testing for tuberculosis in the TB-CAPT CORE trial.**

	Mozambique		Tanzania	
	Standard of care	Truenat	Standard of care	Truenat
Number of participants tested for TB*	855	1045	1125	962
Societal facility-based diagnostic cost per participant tested**^	$40 ($37, $44)	$51 ($47, $56)	$31 ($27, $36)	$46 ($41, $52)
Total cost	$34,520	$53,439	$35,264	$44,504

Number of 7-day treatment initiations	38 (27, 52)	74 (59, 92)	57 (43, 73)	73 (58, 91)
Cost per 7-day treatment initiation	$853 ($707, 1072)	$703 ($599, $838)	$596 ($485,$746)	$592 ($495, $715)
Incremental cost per incremental 7-day treatment initiation		$422 (-$114, $1019)		$580 ($167, 1638)
Number of 60-day treatment initiations	57 (44, 73)	77(61, 95)	88 (71, 107)	73 (58, 91)
Cost per 60-day treatment initiation	$581 ($493, $706)	$678 ($576, $811)	$391($324, $476)	$591 ($494, $716)
Incremental cost per 60-day treatment initiation^^		$805 (-$10107, $10560)		-$353(-$20299, $20802)

*Number of participants who were offered a test. See supplementary materials for details.

**includes both health system and participant level costs

^95% uncertainty ranges are mentioned in parenthesis

^^Scenarios with negative incremental cost per treatment estimates indicate that the Truenat arm is dominated by the standard of care after the 60-day window, meaning that in some

simulations, the Truenat arm is more expensive and less effective. This quantity is highly sensitive for the 60-day treatment initiation scenario because when the difference in the number of participants treated is nearly zero, the variability of the estimate is significantly amplified.

From the health system perspective, for the standard of care (hub-and-spoke) arm, the facility-based diagnostic cost per participant tested was $39 (95% credible interval: $36, $43) in Mozambique, and $22 ($19, $24) in Tanzania. The estimated facility-based diagnostic cost per participant tested using on-site Truenat MTB assays was $51 ($46, $56) in Mozambique and $40 ($35, $45) in Tanzania. Figure 1 presents a breakdown of these facility-based diagnostic costs per participant tested.

As presented in Table 1, from a societal perspective, the facility-based diagnostic cost per participant testing microbiologically positive for TB within seven days of enrolment in the intervention arm was $703 ($599, $838) in Mozambique and $592 ($495, $715) in Tanzania. For the standard of care arm, this facility-based diagnostic cost per participant was $853 ($707, $1072) in Mozambique, and $596 ($485, $746) in Tanzania. The incremental facility-based diagnostic cost per incremental participant initiating treatment within seven days of enrolment was $422 (-$114, $1019) for Mozambique and $580 ($167, $1638) for Tanzania. The incremental facility-based diagnostic cost per incremental 60-day treatment initiation was $805 (-$10107, $10560) for Mozambique and -$353 (-$20299, $20802) for Tanzania.

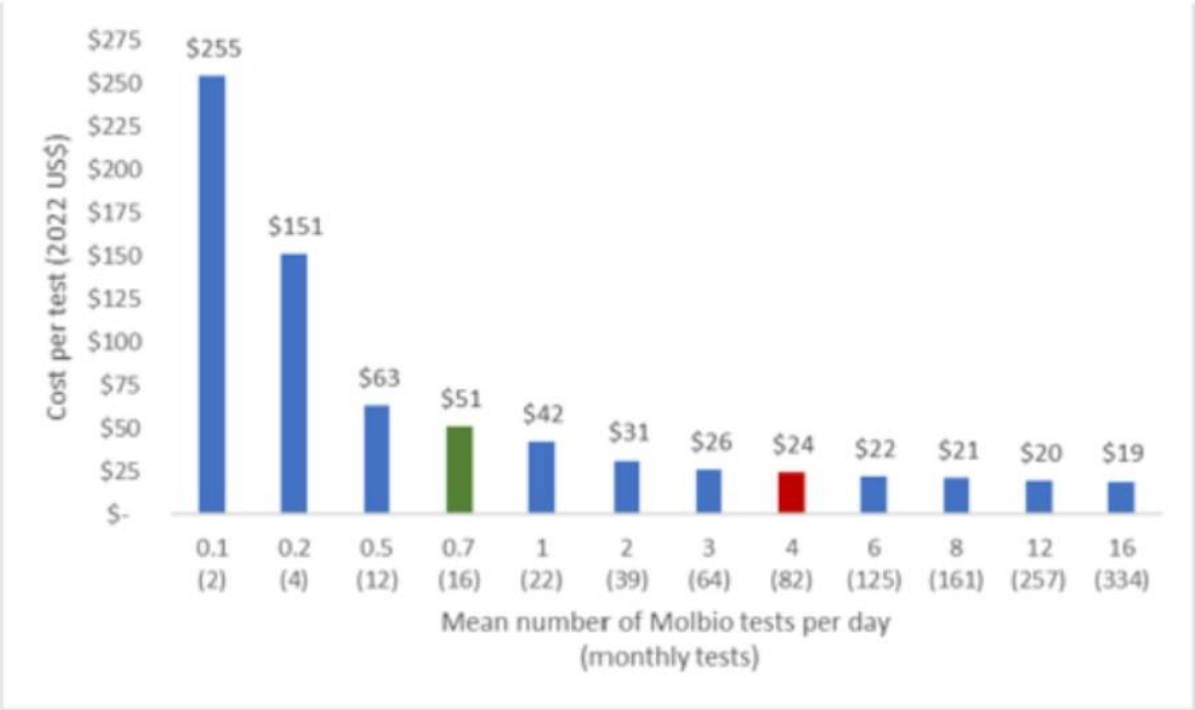
Sensitivity analysis

The incremental cost per 7-day treatment initiation (“ICER”) was most sensitive to changes in monthly TB testing frequency and equipment and warranty, across both Mozambique and Tanzania. In Mozambique, staffing and monitoring and evaluation (M&E) were also significant cost drivers, while in Tanzania, TB prevalence played a crucial role in affecting the cost-effectiveness. A visual representation of the analysis is presented in the supplementary materials (Figure S1).

Varying Testing Utilization

Figure 2 illustrates the societal facility-based diagnostic cost per participant tested at varying testing volumes, a key determinant of cost-effectiveness. Comparing different scenarios of testing volume (from theoretically achievable but not practically feasible 16 samples per day to two samples per month), per-test costs stabilized at a volume of ≥3 tests per day, whereas observed testing volumes were 16 per month (0.7 per day) across Tanzania and Mozambique[10]. The supplementary material (section S2) lists the calculated monthly testing volumes at different utilization scenarios.

A. Mozambique



B. Tanzania

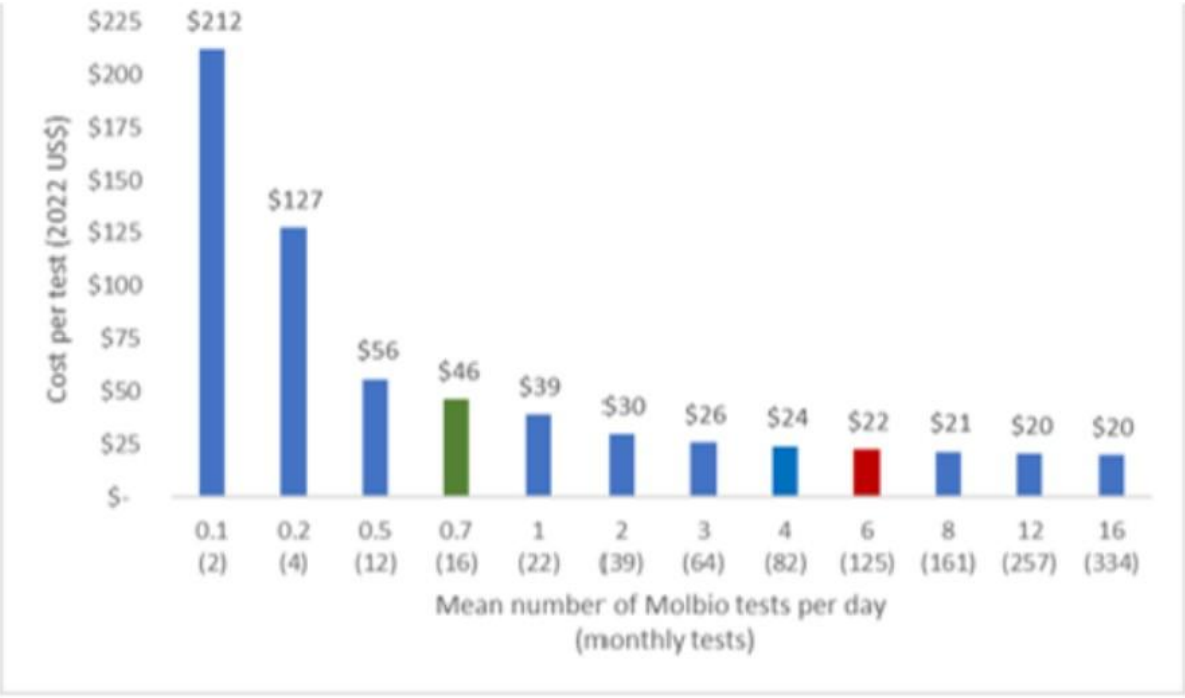


Fig 2. Unit cost of decentralized testing using Truenat MTB assays for tuberculosis. Bars show the estimated unit cost (in 2022 US dollars) of decentralized Molbio testing as a function of the

mean daily (monthly) number of tests performed (*x*-axis). The green bar indicates the testing volumes observed during the trial. The red bar for each country corresponds to the average number of tests per health facility required to test everyone in the country presenting with symptoms of TB. Maximum capacity for the Molbio MTB/RIF instrument is approximately 16 tests per day. Costs were derived by assuming a Poisson distribution of daily test volumes. Above mean daily volumes of approximately three tests per day, the unit cost remains relatively stable (between $20 and $26 per test).

On probabilistic sensitivity analysis, the probability of cost-effectiveness at a threshold of $500 per incremental seven-day diagnosis was 0.65 in Mozambique and 0.35 in Tanzania (as presented in a cost-effectiveness acceptability curve, Figure 3). Cost-effectiveness was enhanced under assumptions of higher testing volumes.

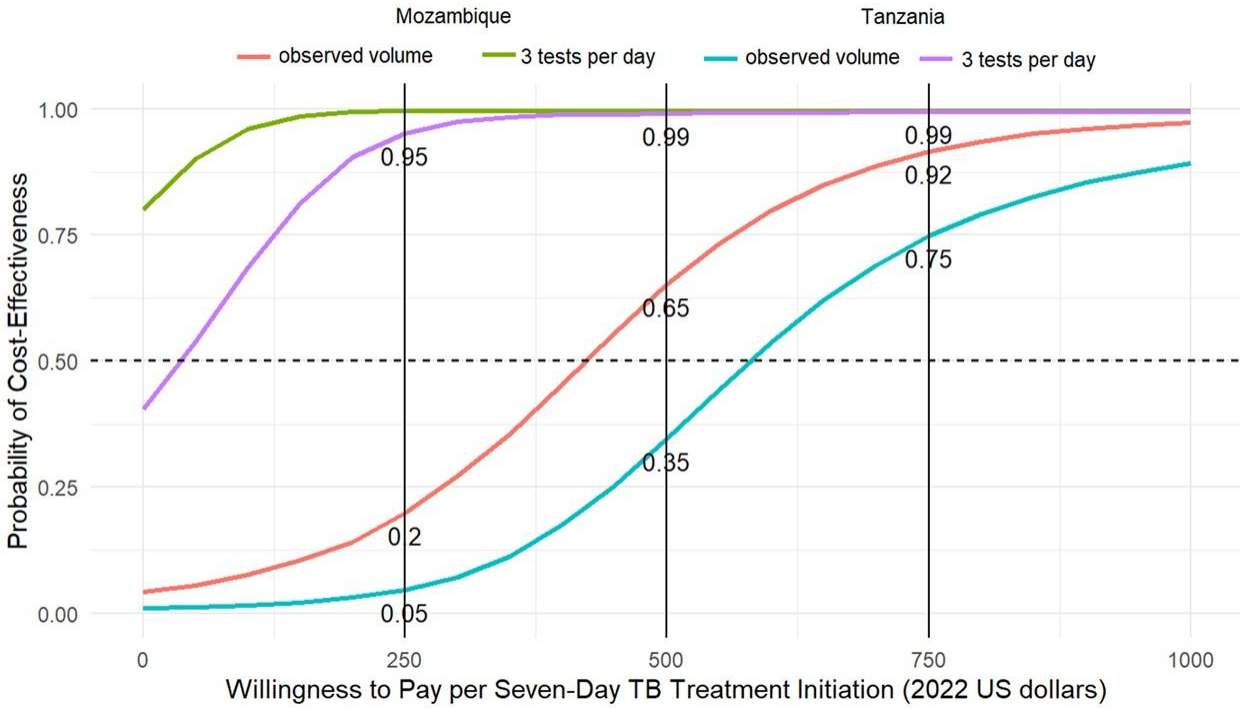


Fig 3. Cost-effectiveness acceptability curves. Cost-effectiveness acceptability curves comparing the incremental facility-based diagnostic cost per incremental participant initiating treatment

within seven days of enrolment, comparing point-of-care Truenat arm to the hub-and-spoke standard of care. Solid vertical lines represent alternative thresholds for evaluating cost-effectiveness.

DISCUSSION

The TB CAPT Core study demonstrated that decentralized TB testing via the dual module Molbio Truenat with MTB assays is effective in certain low-resource settings; this analysis complements those results by estimating costs and cost-effectiveness. Across both countries, while the facility-based diagnostic cost per participant tested was higher in the intervention arm ($46 vs $31 in Tanzania; $51 vs $39 in Mozambique), the diagnostic cost per seven-day treatment initiation for confirmed TB was comparable or lower ($592 vs $596 in Tanzania; $703 vs $853 in Mozambique). These results suggest that, in settings where hub-and-spoke molecular testing for TB is currently the standard of care, decentralized testing with Truenat assays is at least similar in cost on a per-rapid-treatment-initiation basis and is associated with better diagnostic outcomes. Decentralized TB testing is most cost-effective at higher testing volumes, in settings with higher prevalence of TB, and in settings with affordable staffing and monitoring and evaluation.

Cost per patient tested provides a useful measure of resource use and efficiency, especially in settings where diagnostic capacity and budget constraints shape decision-making. In decentralized testing models, understanding the cost per test helps guide optimal placement of diagnostic platforms to balance accessibility, affordability, and impact.

At higher testing volumes, our findings of a per test cost of $20-$25 for Molbio Truenat in both countries are consistent with a recent analysis from Uganda, in which the estimated cost of decentralized Xpert testing was $20.46 (in 2022 USD), and of centralized testing was $18.20[4]. At a willingness-to-pay threshold of $500, the cost-effectiveness of implementing Molbio Truenat improves markedly with increased testing volumes. Specifically, in Mozambique, at a higher testing frequency of three tests per day, the probability of cost-effectiveness reaches 100%,

compared to 65% at the currently observed testing volume of 16 tests per month. In Tanzania, the probability of cost-effectiveness at three tests per day is 99%, higher than the 35% probability observed at the lower testing volume of 16 tests per month.

When considering placement strategies for testing equipment, cost-effectiveness and logistical feasibility may be greatest in areas with higher testing volumes. However, the clinical impact of same-day testing might be most significant in remote clinics with lower testing volumes. As the distance from a clinic to a testing hub increases, as observed with the varying distances to off-site Xpert testing locations in this trial, the cost of transporting samples can become prohibitively expensive. While centralized testing in high-volume areas offers logistical ease and cost-effectiveness, it's essential to recognize the trade-offs between impact and feasibility. In regions with lower testing demand, a decentralized testing model could be crucial in ensuring equitable access to timely care, thereby reducing the burden of multiple trips for testing and results[7].

Among people diagnosed with confirmed tuberculosis in the TB CAPT Core Trial, 82% started tuberculosis treatment on the day of presentation in the intervention compared to 3.3% under the standard of care. Thus, if the primary outcome of the trial were same-day (rather than seven-day) treatment initiation, both effectiveness and cost-effectiveness would be even more favorable for the intervention. We found that when a single module Truenat machine is utilized at higher levels and exceeding 10% of its maximum testing capacity, it demonstrates notable efficiency, leading to a stabilization and plateauing of per-test facility-based diagnostic costs. This suggests that fixed costs such as equipment costs, which are a significant proportion of per-test facility-based diagnostic cost in the Truenat arm have lesser influence on per test costs at scale.

A key strength of this study is that the pragmatic nature of the trial enabling us to estimate costs under programmatic conditions. Another strength is the provision of same-day test results in the Truenat arm, including those testing negative. This allowed healthcare staff to finalize participant interactions immediately, avoiding the need to retrieve participant records later and ensuring that participants did not need to return to the clinic for results, averting out of pocket

costs. Owing to the quicker negative diagnosis in the Truenat arm, participants presenting with symptoms specific to TB were more likely to receive a faster clinical diagnosis compared to those in the standard of care.

However, this study also has certain limitations. First, in keeping with the primary effectiveness outcome of the trial, our primary cost-effectiveness outcome was the facility-based diagnostic cost per participant initiating treatment for confirmed TB within a seven-day window. However, the clinical and epidemiological importance of 7-day treatment initiation (as opposed to ever-initiation) has not been fully studied. It is reassuring that the cost per 7-day treatment initiation was similar or lower in the intervention compared to the standard of care, but this estimate may nonetheless be difficult to compare to other cost-effectiveness estimates that use measures such as health utility (Disability adjusted life years, DALYs or quality adjusted life years, QALYs). Second, although implementation costs were collected, they were done so retrospectively. Prospective collection of implementation costs, along with routine time and motion exercised and facility assessments by dedicated costing staff would have strengthened the costing estimates and provided a more complete understanding of costs throughout the implementation process. And lastly, even though this was a pragmatic trial, the conditions of the trial may not fully reflect programmatic reality, particularly in countries with other epidemiological and economic contexts.

The findings of this trial offer valuable insights for policymakers aiming to improve diagnostics infrastructure in resource-limited settings. Future research could consider strategies of placement for limited volumes of Truenat Molbio (or Xpert) instruments, as well as multiplexing of existing testing equipment[16,17]. Other use cases for molecular platforms in low resource settings are Human Immunodeficiency Virus (HIV) and hepatitis B (HBV) viral load testing, sexual transmitted infections, febrile diseases and respiratory viruses specifically influenza and covid-19[18]. The dependency of cost-effectiveness on test volume reflects all tests performed on a given instrument – not just tests for TB. Thus, if the same instruments could be used to test for other diseases (e.g., HIV, HBV), the cost-effectiveness of the higher testing volume scenarios presented here could be achieved without the need for higher volumes of people with presumptive TB. Recent World Health Organization (WHO) is exploring ways to enhance access

to integrated multiplex technologies, such as the Truenat Molbio, and translate them into impactful diagnostic policies[19].

CONCLUSION

In conclusion, these results from a pragmatic trial in Tanzania and Mozambique demonstrate that under conditions of high TB prevalence, and high testing demand, decentralized molecular testing for TB using Truenat MTB assays can link more participants to TB treatment within seven days, at a cost per 7-day treatment initiation that is similar to, or lower than, traditional hub-and-spoke testing. Cost-effectiveness could be enhanced further by placing instruments in locations with high TB prevalence and high testing volume – including using the same equipment for diagnosis of multiple diseases. While decentralized testing for TB is likely to be effective and cost-effective, it will require more resources to implement; thus, implementation of this strategy must be accompanied by a careful assessment of existing service volumes, testing infrastructure across disease areas, equity, epidemiology of TB, and budget availability.

ACKNOWLEDGEMENTS

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SUPPORTING INFORMATION CAPTIONS

Fig S1. One-way sensitivity analysis. Bars present the incremental facility-based diagnostic cost per participant initiating TB treatment within seven days of enrolment comparing on-site Truenat and standard of care (hub-and-spoke) testing under the high (orange) and low (blue) values across each parameter's specified range, holding all other parameters constant. The monthly TB testing frequency was varied from 12 tests per month (every other day) to 125 tests per month (more than five tests per day). All other parameters were varied by 25%.The vertical line represents the incremental cost-effectiveness ratio when using base-case estimates of all parameters. Only those parameters for which variation resulted in a change of more than $100 in the incremental cost-effectiveness ratio in at least Tanzania or Mozambique are shown for both countries.

SUPPLEMENTARY MATERIALS

S1 Health system costs

A combination of data collection tools, trial expense reports, and product catalogues were analysed to assess the per test cost component borne by the health system.

S1.1 Data collection tools

We interviewed study teams, primarily the costing coordinator across the four sites. These coordinators were the primary personnel responsible for completing the implementation costing tools, and for providing qualitative inputs on how the trial was implemented across the clinics in their respective sites.

A set of three tools were developed to assess implementation costs across the study sites.

S1.1.1 External laboratory implementation costs

This assessment tool was developed to evaluate the operational characteristics of TB and HIV diagnostics "laboratories" (external laboratories or centralized hospitals) located near the study

sites. We aimed to gather detailed information about the laboratories' processes, costs, and infrastructure, but it was not intended as a performance assessment instrument.

For each type of test, TB or HIV, we aimed to capture details on the testing platform used (e.g., model name) and the number of samples analyzed per month. The sample collection process for both TB sputum and HIV viral load samples was investigated by querying how samples are received from clinics or other collection sites, including the frequency and turnaround time of these collections.

In the laboratory, we aimed to assess total spending on TB sputum and HIV viral load testing over the past month, ideally including an average monthly breakdown of various operational costs. These costs were to include equipment maintenance, technical expertise, building lease, utilities, and staff hours dedicated to leadership and administration. Additionally, the tool queried the cost per test for both TB diagnostics and HIV viral load testing, along with the transportation cost per sample.

We also aimed to explore the detailed steps involved in processing TB sputum and HIV viral load samples. For each testing platform, the steps from initial participant contact to the delivery of results were to be outlined, noting the percentage of specimens lost at each step. The average cost and time for various components, such as cartridge costs, consumables, result delivery, and staff time, were also examined.

Furthermore, we aimed to capture total revenue amassed from participants, clinics, or other facilities for TB sputum and HIV viral load testing in the past month. Finally, information on the laboratory's operational hours was gathered, including the number of days per week and the average number of hours per day the laboratory operates.

The tool has been presented below in grey font.

External laboratory (centralized lab or hospital)

Meet the lab in charge who will guide you to the persons(s) who will best be able to answer these questions.

This assessment form is a tool developed for the TB CAPT study to assess the current operational characteristics of TB and HIV Diagnostics laboratories that are closest to the TB CAPT study sites.

Here, laboratories may mean a.) centralized lab operating machines at high throughput b.) secondary or tertiary hospitals with TB testing capacity.

This tool is not a performance assessment tool. It is an instrument that will help the research team assess how certain practices, from the clinics to the laboratories, can be streamlined to make operational costs more efficient from a societal lens, benefitting both the patients and the health system.

1a. Name of laboratory

1b. Name of town/district

HIV-TB Diagnostic Infrastructure and Status

2a. Does the laboratory test TB sputum samples?

i. Yes

ii. No

2b. If yes to 2a, please also mention the platform (model name) and the number of samples analyzed per month

For example if there are four 16-module Xpert Ultra machines in the lab and in the last month 430 sputum samples have been tested then answer as Xpert Ultra 16 module (4) - 430

_____

_____

_____

_____

3a. Does the laboratory test HIV viral load samples?

i. Yes

ii. No

3b. If yes to 2a, please also mention the platform (model name) and the number of samples analyzed per month

For example if there are four 16-module Xpert machines in the lab and in the last month 430 viral load samples have been tested then answer as Xpert 16 module (4) - 430

_____

_____

4a How do you receive TB sputum samples from a clinic or another site where sample collection takes place. Please mention the frequency in front of the selected option?

For example, staff from clinic may take samples once a week, twice a week, more than once a week or once in two weeks

i. Staff from clinic or other sample collection site bring samples to the laboratory, enter frequency here _____

ii. Staff from laboratory collects samples from the clinic, enter frequency here

_____

iii. An external courier system or external individual (please specify):

_____, enter frequency here

_____

iii. Other method (specify) : _____, enter frequency here

_____

4b How do you receive HIV viral load samples from a clinic or another site where sample collection takes place. Please mention the frequency in front of the selected option?

For example, staff from clinic may take samples once a week, twice a week, more than once a week or once in two weeks

i. Staff from clinic or other sample collection site bring samples to the laboratory, enter frequency here _____

ii. Staff from laboratory collects samples from the clinic, enter frequency here

_____

iii. An external courier system or external individual (please specify):

_____, enter frequency here

_____

iii. Other method (specify) : _____, enter frequency here

_____

5a For each type of test, how much time on an average does it take for a patient to get their TB sputum sample test results, from the day the laboratory received the test to the day the result was reported

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

5b For each type of test, how much time on an average does it take for a patient to get their HIV viral load test results, from the day the laboratory received the test to the day the result was reported

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

Enter test platform _____ Enter number of days_____

6 How much did your lab spend in total on TB sputum and HIV viral load testing in the last month _____

7. Please provide details on how much would you expect to pay for the following per month

Note: We need an average breakdown below. Numbers need not add up to total costs, but should not exceed total cost

If values available in year, please divide by 12

	TB sputum	HIV viral load	Note:
Average equipment maintenance cost per month			cost to outside technical experts and/or their own staff time
% of time equipment not available per month			Rough estimate
Number of staff hours for leadership/ admin per month			How many cumulative hours spent to oversee samples
Building lease per month			Proportionally depending on how much of the facility used for TB sputum or HIV viral load testing
Utilities and other costs such as security per month			

8a For a single average test performed for TB diagnostics samples please provide the cost per test

Enter test platform _____ Enter testing cost _____

Enter test platform _____ Enter testing cost _____

Enter test platform _____ Enter testing cost _____

8b For a single average test performed for HIV viral load samples please provide the cost per test

Enter test platform _____ Enter testing cost _____

Enter test platform _____ Enter testing cost _____

Enter test platform _____ Enter testing cost _____

9a. For TB diagnostics tests, please mention the sample transportation cost per sample

Note: If costs aggregated by batch, then divide the total costs by the total number of samples per batch

_____

_____

9b. For HIV viral load tests , please mention the sample transportation cost per sample

Note: If costs aggregated by batch, then divide the total costs by the total number of samples per batch

_____

_____

10a For the TB sputum tests that are performed please provide the following details

Here platform may be Xpert, Molbio, or any other dealing with TB sputum samples

i.Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

ii. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

iii. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

10b For the HIV viral load tests please provide the following details

i. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

ii. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

iii. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

11a In the past month, how much total money was collected from patient, clinics, or other sample collection facilities testing fee for TB sputum testing? _____

11b In the past month, how much total money was collected from patient, clinics, or other sample collection facilities testing fee for HIV viral load testing? _____

12. For how many days a week does your laboratory run? _____

13. For how many hours per day on average, does your laboratory run?

_____

S1.1.2 Intervention and control clinic implementation costs

The tool aimed to gather detailed information about the clinics' diagnostic infrastructure and operational processes. For a subset of clinics, ideally one large and one small across the four sites, we aimed to determine whether the clinic collects sputum samples for TB sputum and HIV Viral load testing and, if so, where the samples are tested, including the platform and the number of samples analysed per month. Details regarding the testing platform and monthly test volume for both in-clinic and external laboratory testing were captured.

Staffing information for TB sputum and HIV viral load testing was gathered, including the number of staff responsible and the cumulative number of hours spent per month on each type of testing. The number of staff responsible for both TB and HIV testing was also captured. Since equipment is not shared in the Truenat arm, the corresponding per-test cost for equipment, its maintenance and warranty, and its handling and operations via program staff is expected to be higher in the Truenat arm compared to the standard of care.

For samples tested outside the clinic, we aimed to capture information on how TB sputum and HIV viral load samples are sent to the testing facility, including the frequency and method of transportation. We aimed to determine the average time it takes for participants to receive their

TB sputum and HIV viral load test results, from the day of the test to the day the result was reported, for each test platform used.

Cost information for TB sputum and HIV viral load testing was collected, including total spending in the last month, average monthly costs for equipment maintenance, technical expertise, building lease, utilities, and staff hours dedicated to leadership and administration. Additionally, the cost per test for both TB diagnostics and HIV viral load testing, as well as the sample transportation cost per sample for tests not performed at the clinic, was captured.

Detailed steps involved in processing TB sputum and HIV viral load samples at the clinic were explored. For each testing platform, the steps from initial participant contact to the delivery of results were outlined, noting the percentage of specimens lost at each step. The average cost and time for various components, such as cartridge costs, consumables, result delivery, and staff time, were also examined.

Revenue information from participant testing fees for TB and HIV testing in the past month was captured. The tool also aimed to gather information on equipment and consumables used for the TB CAPT study, including those procured by the TB CAPT Core study and those not procured using TB CAPT Core funding but used for the study. Details on training conducted for clinic staff, including the purpose, attendees, and costs associated with the training, were collected.

Monitoring and supervision costs were also captured, including costs incurred during visits made by the site study team to the clinic. A list of clinic staff involved in the TB CAPT Core Study, along with their roles, activities performed, time spent, and estimated salary, was compiled.

Finally, the tool aimed to gather information on miscellaneous costs, including utilities, rent, safety, and security, as well as other operational and transportation costs not categorized elsewhere.

The tool is presented below in grey font:

Intervention and Control Clinic Implementation Costs

First ask the clinic in charge who the best person(s) would be to answer the questions below.

If you do not know the exact answer, use the best estimate along with the source you used or the reasons for your assumption.

Fill the following form once for each intervention clinic.

1. Name of clinic

I.HIV-TB Diagnostic Infrastructure and Status –

2a. Does the clinic collect sputum samples for TB testing?

i. Yes

ii. No

2b. If yes to 2a, where are the TB sputum samples tested? Please also mention the platform and the number of samples analyzed per month

For example, if 20 sputum samples analyzed by Xpert Ultra at a centralized laboratory, and 10 sputum samples tested by Molbio Truenat at the clinic, then answer Xpert ultra (20) for external laboratory, and Truenat (10) for clinic

i. At this clinic, please mention platform(s) and number of monthly test per platform here

>Name of platform _____

>Number of Samples analysed Per month_____

ii. Analyzed offsite at an external laboratory, please mention name of laboratory, platform(s) and number of monthly test per platform here

>Name of the Laboratory_____

> Name of platform(s) _____

>Number of Samples analysed Per month_____

iii. Other location, please mention here, please mention name of location, platform(s) and number of monthly test per platform

>Name of the Location_____

> Name of the platform _____

>Number of Samples analysed Per month_____

3a. Does the clinic collect samples for HIV viral load testing?

i. Yes

ii. No

3b. If yes to 3a, where are the HIV viral load samples tested? Please also mention the platform and the number of samples analyzed per month

For example, if 20 HIV viral load samples analyzed by Xpert at a centralized laboratory, then answer Xpert ultra (20) for external laboratory

i. At this clinic, please mention platform(s) and number of monthly test per platform here

> Name of the platform _____

>Number of Samples analysed Per month_____

ii. Analyzed offsite at an external laboratory, please mention name of laboratory, platform(s) and number of monthly test per platform here

>Name of the Laboratory_____

> Name of platform(s) _____

>Number of Samples analysed Per month_____

iii. Other location, please mention here, please mention name of location, platform(s) and number of monthly test per platform

>Name of the Location_____

> Name of platform(s) _____

>Number of Samples analysed Per month_____

4a. How many staff in your facility are responsible for TB sputum testing. Also mention the cumulative number of hours they spend per month on TB testing

For example, if three staff are involved, with two spending 40 hours per month and the third one spending only 10 hours per month on an average, then answer 3 for staff, and 90 for the number of hours

i. Number of staff _____

ii. Cumulative number of hours _____

4b. How many staff in your facility are responsible for HIV viral load testing . Also mention the cumulative number of hours they spend per month on TB testing

For example, if three staff are involved, with two spending 40 hours per month and the third one spending only 10 hours per month on an average, then answer 3 for staff, and 90 for the number of hours

i. Number of staff _____

ii. Cumulative number of hours _____

4c. How many staff in your facility are responsible for both TB and HIV testing (may be the same people as in 5a or 5b)

For example, if three staff are involved, with two spending 40 hours per month and the third one spending only 10 hours per month on an average, then answer 3 for staff, and 90 for the number of hours

i. Number of staff _____

ii. Cumulative number of hours _____

5a Ask if TB sputum samples tested outside the clinic --> How do you send TB sputum samples to the testing facility. Please mention the frequency in front of the selected option?

For example, staff from clinic may take samples once a week, twice a week, more than once a week or once in two weeks

i. Staff from clinic takes samples from the testing facility, enter frequency here

_____

ii. Staff from testing facility collects samples from the clinic, enter frequency here

_____

iii. An external courier system or external individual (please specify):

_____, enter frequency here _____

iv. Other method (specify) : _____,

enter frequency here _____

5b Ask if HIV viral load samples tested outside the clinic --> How do you send HIV viral load samples to the testing facility

For example, staff from clinic may take samples once a week, twice a week, more than once a week or once in two weeks

i. Staff from clinic takes samples from the testing facility, enter frequency here

_____

ii. Staff from testing facility collects samples from the clinic, enter frequency here

_____

iii. An external courier system or external individual (please specify):

_____, enter frequency here

_____

iv. Other method (specify) : _____, enter frequency here

_____

6a. For each type of test, how much time on an average does it take for a patient to get their TB sputum test results, from the day of the test to the day the result was reported.

Enter test platform _____Enter number of days _____

Enter test platform _____ Enter number of days

_____

Enter test platform _____ Enter number of days

_____

6b How much time on an average does it take for a patient to get their HIV viral load test results, from the day of the test to the day the result was reported.

Enter test platform _____Enter number of days _____

Enter test platform _____ Enter number of days

_____

Enter test platform _____ Enter number of days

_____

7 How much did your site spend in total on TB sputum and HIV viral load testing in the last month _____

8 Please provide details on how much would you expect to pay for the following per month

Note: We need an average breakdown below. Numbers need not add up to total costs, but should not exceed total cost

If values available in year, please divide by 12

	TB sputum	HIV viral load	Note:
Average equipment maintenance cost per month			cost to outside technical experts and/or their own staff time
% of time equipment not available per month			Rough estimate
Number of staff hours for leadership/ admin per month			How many cumulative hours spent to oversee samples
Building lease per month			Proportionally depending on how much of the facility used for TB sputum or HIV viral load testing
Utilities and other costs such as security per month			

9a For a single average test performed for TB diagnostics samples please provide the cost per test

Enter test platform _____Enter testing cost

_____

Enter test platform _____Enter testing cost

_____

Enter test platform _____Enter testing cost

_____

9b For a single average test performed for HIV viral load samples please provide the cost per test

Enter test platform _____Enter testing cost

_____

Enter test platform _____Enter testing cost

_____

Enter test platform _____Enter testing cost

_____

10a For TB sputum tests that are not performed at the clinic, please mention the sample transportation cost per sample

Note: If costs aggregated by batch, then divide the total costs by the total number of samples per batch

_____

10b For HIV viral load tests that are not performed at the clinic, please mention the sample transportation cost per sample

Note: If costs aggregated by batch, then divide the total costs by the total number of samples per batch

_____

_____

11a For the TB sputum tests that are performed at the clinic (and not outside) please provide the following details.

Here platform may be Xpert, Molbio, smear, or any other dealing with TB sputum samples

i. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

ii. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

iii. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

11b For the HIV viral load tests that are performed at the clinic (and not outside) please provide the following details.

Here platform may be Xpert, Molbio, smear, or any other dealing with TB sputum samples

i.Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

ii. Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

Enter test platform _____

For the platform listed above where testing happens at clinic, list out the steps that would be required for processing that specimen, from initial patient contact to returning of results

For each step, mention approximately what percentage of specimens are lost

Step 1:

Step 2:

Step 3:

Step 4:

Step 5:

Step 6:

For the platform listed above, provide the average cost or time for the following components

Cartridge costs

Other consumables

Cost of result delivery

Time from result availability to result delivery

Staff member, their level, and hours they spend

12a In the past month, how much total money was collected from patient testing fee for TB testing? _____

12b In the past month, how much total money was collected from patient testing fee for HIV testing? _____

II. Equipment and consumables that are used for the TB CAPT study

Prepare a list of equipment used at the clinic procured by the TB CAPT Core study

This may include medical equipment such as the TrueNat TB assay, or the Molbio Truenat platform, sputum cups, etc. Or non medical equipment like laptops, filing cabinet, internet router etc.

Consumables may include test cartridges, reagents, etc.

List the quantity, unit and total cost (including fee and taxes)

If known, show service and maintenance costs as a separate line item

Example: If 100 cartridges are procured by the clinic of which 40 are used for the TB CAPT study, enter 40% under % used for TB CAPT

Equipment	Unit cost	Quantity	Total Cost	% Used for TB CAPT core activities	Source
Consumables	Unit cost	Quantity used per month	Total Cost	% Used for TB CAPT core activities	Source

2. Were there any delays in procurement of the above listed equipment and consumables?

If yes, what were the reasons for the delays (customs, COVID-19 related delays)? Were there any other challenges faced, e.g. approval of equipment purchase

Equipment /consumables	Reasons for delay	Duration of delay

3. Please make a list of all equipment and consumables not procured using TB CAPT Core funding but used for the TB CAPT Core study.

Enter the name, quantity, year when purchased (if available) and unit and total cost (if available)

Equipment	Unit cost	Quantity	Total Cost	% Used for TB CAPT core activities	Source
Consumables	Unit cost	Quantity used per month	Total Cost	% Used for TB CAPT core activities	Source

iii. **Training conducted for clinic staff**

1. List out the trainings that have been attended by your clinic along with the purpose for each.

List the team responsible for training, the team attending the training and the number of people at each skill level, and the format of the as given in the example below:

Training Purpose	Month/Year	Attendees (number)	Format	Curriculum Development	Coordinator

2. List any equipment procured or expenses incurred linked to the trainings.

Please make sure these equipment are not listed in the equipment and consumables section above. Mention the unit cost (including taxes and fees), quantitiy, and total cost

Also list the source - e.g. procurement log, expense receipt, finance records, etc.

Some examples may include per diem, stationery, room and projector rental, transport, meals, trainer fee, etc.

Training Equipment /item	Unit cost	Quantity	Total Cost	Source

IV. Monitoring and supervision costs

1. Apart from introductory visits and trainings, list the visits made by the site study team at this clinic E.g., regulatory visits, delivery of materials, etc.

For each visit, list the corresponding costs incurred

Examples of cost may include per diem, transport, meals, etc.

One row for each cost item. For multiple cost items per visit we will use multiple rows

Visit Month/Year	Visit Type	Cost Item	Cost incurred

V. **Clinic costs and admin**

1. Provide a list of the names of all clinic staff involved in the TB CAPT Core Study.

2. For each staff member, list the TB CAPT core study activity conducted by them and the estimated time spent on each activity in a typical week

Note: Use one row per activity. So if staff member has done 3 activities, use 3 rows for that staff member

Staff Name or Staff No	Role/Title	Activities Performed	Time Spent	Estimated saalry based on Government salary scale

VI. **Miscellaneous costs**

1. List the cost paid for utilities including electricity, internet, etc. and other operational costs such as rent, safety and security that is incurred for the study.

If not available by utility item, list the aggregate utility costs or aggregate operational expenses for running the clinic if available

Operational cost item	Total Cost	Duration	% Used for TB CAPT core activities	Source

2. List other miscellaneous costs part of the implementation that are not categorized before.

E.g., transportation costs not linked to training and site visits, etc

Other item	Total Cost	Duration	% Used for TB CAPT core activities	Source

S1.1.3 General Questions for study sites: Implementation Costs

This tool aimed to gather best estimates on several key aspects of trial implementation from the perspective of the central office of each site. The tool aimed to capture information on:

a. Introductory Visits and Site Finalization: This includes documenting the timeline of initial clinic selection, roles of central team members involved, and any challenges causing delays in clinic finalization.

b. Equipment and Consumables: Detailed information on procurement of equipment and consumables, including quantities, unit costs, total costs, and reasons for any procurement delays.
c. Training Conducted for Each Site: Documentation of training sessions attended, purpose of each training, responsible teams, attendees' skill levels, and associated costs not already accounted for in equipment procurement.
d. Main Office Costs and Admin: Listing all staff involved in the trial, their roles, specific trial activities performed, and estimated time spent on each activity.
e. Miscellaneous Costs: Including operational expenses such as utilities, rent, and security, as well as other miscellaneous costs not covered elsewhere in the tool.

The tool has been presented below in grey font.

General Questions – Site HQ

For the economic evaluation of the TB CAPT Core trial, we would like to understand the resources, and corresponding costs, required by the respective clinics which are a part of the study, and the corresponding laboratories that serve these clinics.

In addition, we would like to understand the upfront time investment in kickstarting the trial for your respective site.

If you do not know the exact answer, use the best estimate along with the source you used or the reasons for your assumption.

I. <u>Introductory visits and site finalization</u>

1. When did the initial clinic selection process occur?

This includes time spent on identifying clinics, gauging interest of clinic participation, preparing and finalizing Memorandum of Understanding and subcontracts with clinics, if any.

a. Mention start and end month/year.

b. List the roles/titles of central team members involved

Clinic Name	Start (Month/Year)	End (Month/Year)	Central Team Members Involved

2. Were there any challenges faced by the central team that caused delays in the clinic finalization process?

If yes, indicate the reason for the delay (e.g. COVID-19 related delays) and also indicate by how many weeks/months was the clinic finalization delayed as a result.

Clinic Name	Reasons for delay	Duration of delay

3. Were there any challenges faced by the central team that caused delays in the overall trial start date?

If yes, indicate the reason for the delay (e.g. COVID-19 related delays) and also indicate by how many weeks/months was the trial start delayed as a result.

Reasons for delay	Duration of delay

II. <u>Equipment and Consumables</u>

1. For each item procured for the central site office or the site headquarters, indicate the quantity, unit cost (including taxes and fee), total cost (including taxes and fee).

Please also list the source for each - e.g. procurement logs, finance records, etc.

Please note: equipment also includes furniture or other tangible items

Equipment /item	Unit cost	Quantity	Total Cost	% Used for TB CAPT core activities	Source

2. Were there any delays in procurement of the above listed equipment and consumables?

If yes, what were the reasons for the delays (customs, COVID-19 related delays)? Were there any other challenges faced, e.g. approval of equipment purchase

Equipment /item	Reasons for delay	Duration of delay

3. Please make a list of all equipment not procured using TB CAPT Core funding but used for the TB CAPT Core study.

Enter the equipment name, quantity, year when purchased (if available) and unit and total cost (if available)

Equipment /item	Unit cost	Quantity	Total Cost	% Used for TB CAPT core activities	Source

III. Training conducted for members of each site

1. List out the trainings that have been attended by your site along with the purpose for each.

List the team responsible for training, the team attending the training and the number of people at each skill level, and the format of the as given in the example below:

Training Purpose	Month/Year	Attendees (number)	Format	Curriculum Development	Coordinator

2. List any equipment procured or expenses incurred linked to the trainings.

Please make sure these equipment are not listed in the equipment and consumables section above. Mention the unit cost (including taxes and fees), quantity, and total cost

Also list the source - e.g. procurement log, expense receipt, finance records, etc.

Some examples may include per diem, stationery, room and projector rental, transport, meals, trainer fee, etc.

Training Equipment /item	Unit cost	Quantity	Total Cost	Source

IV. Main Office Costs and Admin

1. Provide a list of the names of all central and field staff involved in the TB CAPT Core Study.

2. For each staff member, list the TB CAPT core study activity conducted by them and the estimated time spent on each activity in days/weeks/months

Note: Use one row per activity. So if staff member has done 3 activities, use 3 rows for that staff member

Staff Name	Role/Title	Activities Performed	Time Spent

IV. Miscellaneous

1. List the cost paid for utilities including electricity, internet, etc. and other operational costs such as rent, safety and security that is incurred for the study.

If not available by utility item, list the aggregate utility costs or aggregate operational expenses for running the site HQ if available

Operational cost item	Total Cost	Duration	% Used for TB CAPT core activities	Source

2. List other miscellaneous costs part of the implementation that are not categorized before.

E.g., IRB related costs, transportation costs not linked to training and site visits, etc

Other item	Total Cost	Duration	% Used for TB CAPT core activities	Source

S1.2 Product Catalogues

To triangulate the prices of testing equipment and consumables, we referred to the Global Drug Facility's (GDF) product catalogue 2022.

S1.3 Data analysis

For each of the clinics where data was collected, we recorded the monthly costs and per test costs (where possible to record) as separate line items and tagged them as either consumables, equipment, monitoring & evaluation and communication, staffing, testing, training, warranty & maintenance, and miscellaneous. The monthly costs were then divided by the estimated number of persons tested each month to get the contribution of that specific cost item to the total cost per test. The table below lists the various cost items reported by the clinics, how they were categorized, and how they were captured calculated.

Table S1

Cost category	Cost items included	Calculation
Consumables	Sample prep kit, pre treatment pack	Per test
	Medical consumables	Captured either in an aggregate manner monthly, or linked to each test
	Reagents	Per test
Testing (also a consumable)	cartridge	Per test
Equipment	Truenat machine	Annualized assuming an expected life of 10 years and then divided by 12 to determine monthly costs.

	Furniture	Annualized assuming an expected life of 10 years and then divided by 12 to determine monthly costs.
	GX machine 4 module	Annualized assuming a expected life of 10 years and then divided by 12 to determine monthly costs.
	Electrical equipment	Annualized assuming a expected life of 5 years and then divided by 12 to determine monthly costs.
	Medical equipment	Annualized assuming a expected life of 10 years and then divided by 12 to determine monthly costs.
M&E and communication	Internal and external monitoring	Monthly
	Internet and communication	Monthly
	Transportation for study monitoring	Monthly
	Supervision	Monthly
Staffing	Salaries	Monthly
Training	SIV core training	Training costs averaged across participating clinics. Assumed training every 2 years.
	Training materials	Monthly: Hardware with an estimated life of 10 years whereas

		stationery with a life of 2 years. Certain costs attributed per test.
	Per diems, conference room, and transport	Training costs averaged across participating clinics. Assumed training every 2 years.
Warranty and Maintenance	Maintenance	Monthly
	Truenat warranty	Monthly
	GeneXpert warranty	Monthly
Miscellaneous	Sample Transport	Per test
	Stationery	Monthly
	IRB/ethics	Monthly: IRB is a one time activity, assuming impact lasts for 10 years
	Results Delivery	Per sample

In both Tanzania and Mozambique, the average number of tests conducted per month per clinic ranged from 14.8 to 15.7. For the deterministic calculation of the cost per participant tested, we standardized this value to 16 tests across all arms to maintain consistency. This figure was then adjusted by 25% to establish minimum and maximum test numbers per month, resulting in 12 and 18 tests, respectively. In Table S2, "PE" represents the point estimate of each cost component per participant tested. Data were collected from 19 clinics across the four sites, reported either monthly or per sample (as detailed in Table 1 above). Monthly costs were converted to per-sample costs by dividing the monthly costs by the number of samples per month, thereby determining the point estimate cost by category. The maximum and minimum values for each cost category in both countries were derived from the range of values reported by the clinics within the respective countries.

Table S2

	TANZANIA			MOZAMBIQUE		
	PE	Min	Max	PE	Min	Max
Testing	7.90	7.89	7.91	8.95	7.89	10.01
Consumables	3.75	3.00	5.41	7.00	3.00	11.00
Equipment	10.57	7.66	15.11	9.64	7.15	13.78
Warranty and maintenance	6.37	5.10	8.49	6.37	5.10	8.49
Training	1.53	0.00	4.53	0.23	0.05	0.50
M&E and comm	2.27	0.77	6.89	5.71	3.46	9.44
Staffing	4.81	0.00	13.42	10.67	6.89	18.71
Miscellaneous	1.64	0.06	3.75	1.41	0.25	2.66
COST PER PARTICIPANT TESTED	59.10	37.52	92.10	49.97	33.80	74.60

	TANZANIA			MOZAMBIQUE		
	PE	Min	Max	PE	Min	Max
Testing	9.98	9.97	9.99	9.98	9.97	9.99
Consumables	1.67	0.00	3.47	13.35	10.02	20.02
Equipment	2.42	1.40	4.39	1.63	0.98	2.44
Warranty and maintenance	1.26	1.01	1.68	1.26	1.01	1.68
Training	0.91	0.00	2.41	0.24	0.05	0.47
M&E and comm	1.75	0.90	3.22	6.08	4.47	9.44
Staffing	0.96	0.00	2.68	4.52	2.76	8.89
Miscellaneous	2.31	0.34	5.49	1.77	0.24	4.66
COST PER PARTICIPANT TESTED	21.26	13.61	33.35	38.83	29.49	57.59

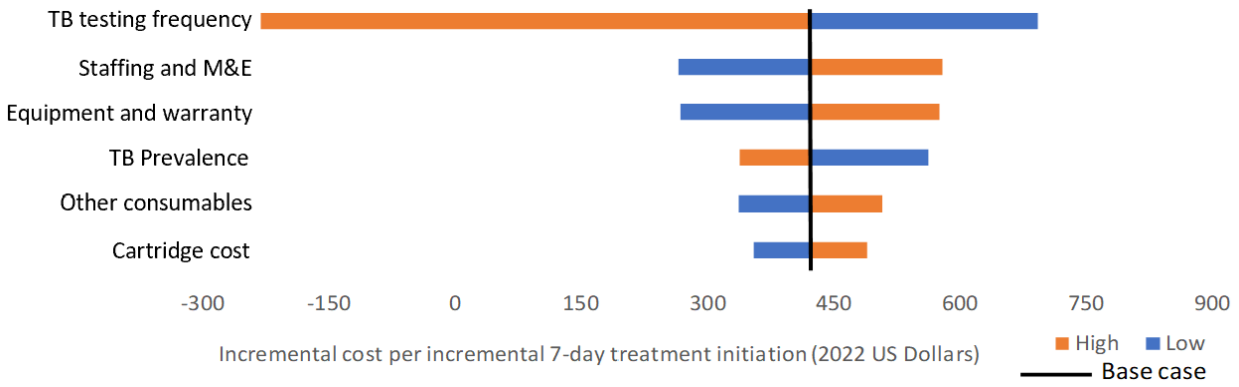
The R code and corresponding input files to the code, can be found on this repository:

https://github.com/akash210593/tbcaptcosting .

S1.3.1 Number of participants tested and number of tests

To calculate the facility based diagnostic cost per participant tested, we took the number of persons tested as the denominator for the calculation of the point estimate. A person may have multiple tests (if one of the tests is invalid), or may have different tests (Xpert/Truenat only or smear only or combination of smear+Xpert/Truenat or any other combination), both of which will impact the true cost per test. To address this, we added uncertainty to the number of people tested (± 25% variation), so that the range of values also encompass the actual number of tests. Across both scenarios, more than 98% of the participants received their test results via Xpert (in the standard of care) or Truenat (in the intervention arm).

A. Mozambique



B. Tanzania

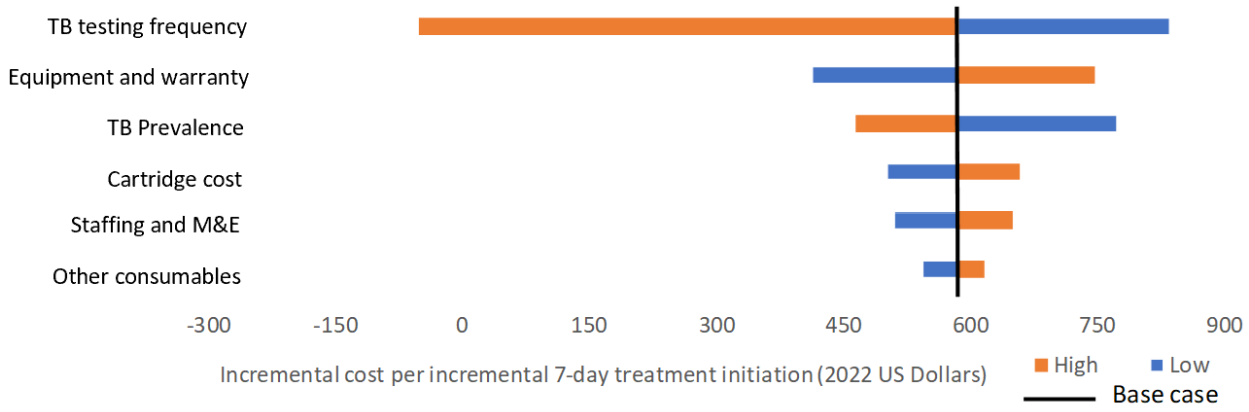


Fig S1. One-way sensitivity analysis.

S2 RESULTS ACROSS DIFFERENT TEST UTILIZATION

S2.1 Distribution of daily test volume and calculating mean facility based cost per participant tested

S2.1.1 Supply side

To assess annual average facility-based diagnostic cost per participant tested based on dynamic daily test volumes laboratories, we generated a set of 250 unique random numbers (representing 1 year of laboratory operations) for each laboratory representing average daily workload (λ = lambda) using a Poisson distribution. We evaluated scenarios of λ ranging between 0.1 to 16 where each λ scenario represents a unique laboratory. Based on the distribution of the daily workloads, we then calculated the number of monthly tests using the Truenat MTB assays, to effectively arrive at a per test cost for each scenario. We assumed a maximum of 8 test cycles a day, resulting in 16 tests per facility per day for a two-module machine. Then, for each random number (representing number of participant samples tested for a given day), we assigned the corresponding index per-test cost of Truenat MTB assays referenced from Table S1 (for example, if a random number generated was 4, we assigned index a per-test unit cost that represented a mean workload of 4 tests for decentralized or centralized testing in that simulated facility).

Table S3. Tanzania: Per test cost in 2022 USD, Truenat MTB assays

Lambda (daily tests)	Monthly tests	Lower bound	Median	Upper bound
0.1	2	178.93	212.01	247.21
0.2	4	108.69	127.49	147.35
0.5	12	48.98	55.78	63.06
0.7	16	40.97	46.26	51.83
1	22	34.66	38.85	43.38
2	39	26.87	29.85	33.18
3	64	23.11	25.61	28.60
4	82	21.72	24.10	26.97
6	125	19.94	22.27	25.00
8	161	19.17	21.46	24.17
12	257	18.28	20.44	23.17
16	334	17.88	20.04	22.76

Table S4. Mozambique: Per test cost in 2022 USD, Truenat MTB assays.

Lambda (daily tests)	Monthly tests	Percentile_2.5	Percentile_50	Percentile_97.5
0.1	2	227.08	254.74	285.58
0.2	4	135.41	150.99	168.89
0.5	12	57.04	63.05	69.62
0.7	16	46.5137	51.33015	56.48
1	22	38.22293	42.25337	46.53012
2	39	27.99189	31.24433	34.46048
3	64	23.11711	26.01444	28.90755
4	82	21.32085	24.16024	26.96848

6	125	19.18679	21.89414	24.62663
8	161	18.20808	20.91681	23.63941
12	257	17.01286	19.66693	22.40117
16	334	16.53492	19.19953	21.88681

Base case: Across both Tanzania and Mozambique, the average number of monthly tests was 15.4 and 15.3 respectively. This roughly corresponded to lambda=0.7, or 16 monthly tests for our base case calculations. Since certain components of the per test cost are sensitive to volume, while conducting a probabilistic sensitivity analysis we varied the monthly number of tests by increasing and decreasing by 20%.

S2.1.2 Demand side

To estimate the number of people at an average health facility, we multiplied the mean number of notifications by 15, or the assumed number of tests for every positive TB test. We divided this quantity by the total number of facilities, across varying capacities and service offering type. We then divided the quantity by 12 to estimate the monthly number of TB tests at an average health facility. We performed separate calculations for both Tanzania and Mozambique, as can be seen in the table below.

Table S5. Estimate of monthly number of tests per facility.

	Tanzania	Mozambique
Annual TB notifications	133000	115000
Estimated number needed to test	15	15
Annual number of tests	1995000	1725000
Number of health facilities	1334	1770

Monthly number of tests	111	81

As a result, assuming 21 working days a month, a single 2-module Molbio Truenat machine, processing six tests daily in Tanzania, and 4 tests daily in Mozambique.

CHAPTER 3 – Aim 2

Title: Mathematical modeling to assess health and economic impact of cardiovascular interventions and implementation strategies among people living with HIV: SAIA HTN

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ABSTRACT

Background: Few economic evaluations distinguish between the cost and impact of evidence-based interventions and the strategies used to improve their implementation. This distinction is essential for understanding whether a strategy is cost-effective, why it works, and the resources required to replicate its success. The Systems Analysis and Improvement Approach Hypertension (SAIA-HTN) trial evaluated an implementation strategy ("SAIA") designed to improve hypertension care among people living with HIV (PLHIV) in Mozambique. We developed a mathematical model to estimate the cost-effectiveness of both the evidence-based intervention (including hypertension screening, pharmacological treatment and follow up, and lifestyle modifications such as diet and exercise) and the SAIA implementation strategy.

Methods: We constructed a decision-analytic, state-transition model that simulated cardiovascular risk, outcomes, and associated costs for PLHIV receiving hypertension care in Mozambique using a health systems perspective. Model inputs came from published

epidemiological studies and primary data from the SAIA-HTN trial on intervention and implementation strategy effectiveness and costs. We estimated the incremental cost-effectiveness (willingness to pay $647/DALY averted, GDP per capita in Mozambique) of rolling out both components, compared to a "status quo" scenario where screening and treatment of hypertension remained at their current (very low) levels. Costs were reported in 2023 US dollars, and costs and outcomes were discounted at 3% over a ten-year time horizon.

Results: Scaling up screening and pharmacological treatment of hypertension in Mozambique would have an incremental cost-effectiveness ratio (ICER) of around $212 per disability-adjusted life year (DALY) averted and cost an additional $4.61 per person per year. Incremental to the intervention, the SAIA implementation strategy would have an ICER of $44 per DALY averted and cost an additional $0.79 per person per year. The average reduction in ten-year cardiovascular risk would be 29.3% for the intervention and 40.3% if the SAIA implementation strategy were co-introduced.

Conclusions: Our model is a tool for implementation scientists, policymakers, and researchers aiming to assess cardiovascular interventions and associated implementation strategies among PLHIV. Its application to SAIA-HTN suggests that this is a cost-effective strategy for improving hypertension care, but only in the presence of adequate blood pressure equipment, training, and medications. Our study shows how implementation strategies require a minimum threshold of health system readiness to generate meaningful health impact.

Trial Registration: ClinicalTrials.gov (NCT04088656).

CONTRIBUTIONS TO THE LITERATURE

- Studies rarely separate the cost and impact of evidence-based interventions from the strategies used to implement them. This study distinguishes both components using a decision-analytic modeling approach.
- The study demonstrates how economic evaluation can be embedded within implementation science to assess the value of a systems engineering–based implementation strategy (SAIA) alongside clinical hypertension care for people living with HIV.

- The findings show that implementation strategies can be highly cost-effective but require a minimum level of health system readiness to achieve impact.
- The framework offers a practical approach for evaluating and adapting implementation strategies in other diseases and low-resource settings.

KEYWORDS: Hypertension; HIV; cardiovascular disease; sub-Saharan Africa; Mozambique; implementation strategy; mathematical modeling; decision-analytic model; cost-effectiveness; economic evaluation

BACKGROUND

Cardiovascular (CV) illness is the leading cause of morbidity and mortality amongst non-communicable diseases (NCDs) in Mozambique, accounting for over 40% of NCD deaths, and about 11% of death from all causes[1]. In 2021 in Mozambique, ischemic heart disease and stroke had prevalences of 0.84% and 0.73%, respectively, with an estimated 35,337 and 29,336 new cases that year[1]. Hypertension (HTN) is one of the major and modifiable risk factors for CV illness, especially amongst people living with HIV (PLHIV) [2]. In Mozambique, two in five adults are hypertensive, though only 14.5% know of their diagnosis, and only half of those are treated[3]. With the provision of antiretroviral therapy (ART), PLHIV are living longer and face a substantially higher risk of CV illness, estimated to be approximately 50% greater than in HIV-negative populations [4,5]. As HIV has become a chronic, manageable condition, especially in countries with high ART coverage, the clinical and public health agenda has expanded to address emerging chronic comorbidities such as cardiovascular disease alongside continued HIV care[6]. Importantly, access to specialized interventions such as cardiac stents or thrombolytics remains very limited in Mozambique, underscoring the need for prevention through early detection and treatment of hypertension[7].

For patients with HIV and hypertension, co-management of both chronic conditions presents unique challenges and opportunities[8]. Existing resources like equipment and trained personnel are underutilized due to limited quality assurance across care points, resulting in

suboptimal care integration[9]. For example, while clinics may have blood pressure measurement devices and staff trained to manage hypertension, these resources are not consistently integrated into routine HIV care[10]. This disconnect results in missed opportunities to identify and treat hypertension in HIV patients.

The Systems Analysis and Improvement Approach (SAIA) provides a structured, scalable framework to standardize and improve quality across service points, ensuring consistent, integrated care along the HTN care cascade and ultimately improving health outcomes for individuals with HIV and HTN[9]. SAIA's iterative, facility-based implementation strategy leverages process mapping and continuous quality improvement tools to address systemic inefficiencies. A simplified logic model for SAIA-HTN is presented in Figure 1. The SAIA HTN trial, conducted in the Manica and Sofala provinces of Mozambique, between July 2020 and September 2023, demonstrated an increase in screening rates (37% at baseline vs. 99% post intervention roll out) and in process outcomes in the HTN care cascade such as treatment eligibility and medication pick up among PLHIV [11]. Additionally, compared to the control arm, clients in the intervention arm were 2.22 times more likely to achieve hypertension control.

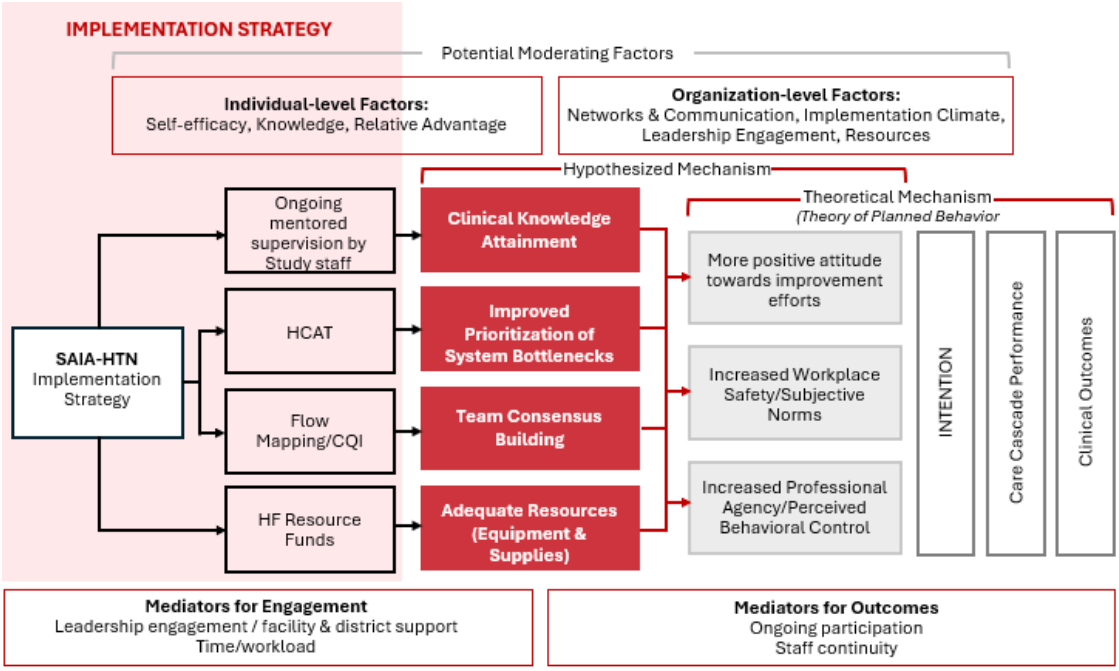

Figure 1. SAIA HTN logic model. Core SAIA components such as cascade analysis, process mapping, continuous quality improvement cycles, and mentored supervision, are mapped to proximal system-level changes, including improved identification of care bottlenecks, enhanced team coordination, clinical knowledge attainment, and adequate resources. These changes are expected to improve hypertension screening, treatment continuity, and blood pressure control, which ultimately reduce long-term CVD risk.

Few economic evaluations distinguish between the cost and impact of evidence-based interventions (EBIs) and the strategies used to improve their implementation[12]. This distinction is essential for understanding whether a strategy is cost-effective, why it works, and the resources required to replicate its success, thus helping understand the know-do gap from an economic standpoint. From a health economics perspective, the case for integrating hypertension screening and treatment into HIV care is strong. Models have demonstrated the cost-effectiveness of pharmacologic management of hypertension among PLHIV[13]. However, the feasibility and impact of real-world scale-up depend not just on clinical effectiveness or cost per pill, but on how these services are implemented. The presence of antihypertensive medications or blood pressure cuffs alone does not translate into health gains without accompanying strategies to support uptake, adherence, and system-level delivery improvements[14].

The objective of this analysis was twofold: to conduct a cost-effectiveness analysis of the SAIA-HTN trial in Mozambique, and to demonstrate how economic evaluation methods can be applied in an implementation science context to distinguish the contributions of evidence-based clinical interventions from those of implementation strategies. We developed a mathematical model to estimate the cost-effectiveness of both the evidence-based intervention (including hypertension screening, pharmacological treatment and follow-up, and lifestyle modifications such as diet and exercise) and the SAIA implementation strategy among people living with HIV. We use the SAIA-HTN trial as an applied case example to illustrate this modeling approach using real-world data. We introduce a flexible modeling framework that can be adapted by other

settings to assess the value of implementation strategies using routine data and inform hypertension intervention strategies across diverse African healthcare settings. Our goal is to bridge the gap between economic evaluation and implementation science, to provide tools that help not only determine what works, but how to make it work better, and at what cost.

METHODS

Study design

This cost-effectiveness analysis leverages a decision-analytical-model informed by the SAIA-HTN trial. The parent study design, protocol, and results have been reported elsewhere[9,11]. The trial compared HTN care among PLHIV against the SAIA implementation strategy across three sequential phases, i.e., baseline, intensive, and sustainment. The present analysis uses observed patient data and trial-based effectiveness estimates to simulate CV outcomes and costs across four modeled scenarios. A schematic of the two arms and three phases, along with the relative reduction in CV risk in each phase-arm combination is presented in Figure 2.

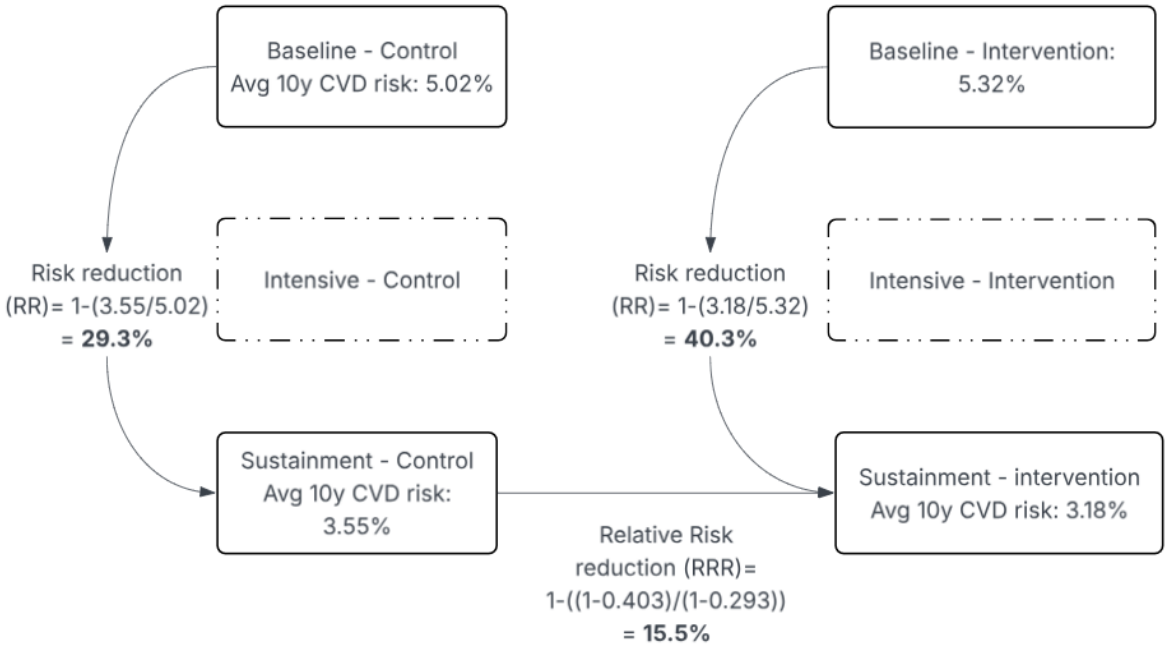

Figure 2. Change in 10-year CVD risk by arm and derivation of relative risk reduction. Solid boxes show baseline and sustainment mean 10-year cardiovascular risk for control and intervention arms; arrows indicate within-arm risk reduction and the cross-arm relative risk reduction (RRR). The intensive phase is shown for context.

Model Structure

The structure of the decision-analytic model was informed by standard cardiovascular disease modeling approaches and comprised two distinct pathways: one for ischemic heart disease (IHD) and another for stroke (Figure 3). In each pathway, individuals begin in the "No CVD" state and may experience an initial acute event (acute myocardial infarction [MI] or acute stroke). Transitions between states occur in monthly cycles and are time- and risk-dependent. Patients could only experience one major CVD event (MI or stroke) during the simulation. Tunnel states for acute MI or stroke lasted one cycle. A small proportion of patients experiencing an event were assumed to access treatment. If they survive, patients who experienced an acute condition enter a chronic post-event state (chronic IHD or post-stroke), where they remain at risk for disease-specific mortality, background mortality, or remain stable.

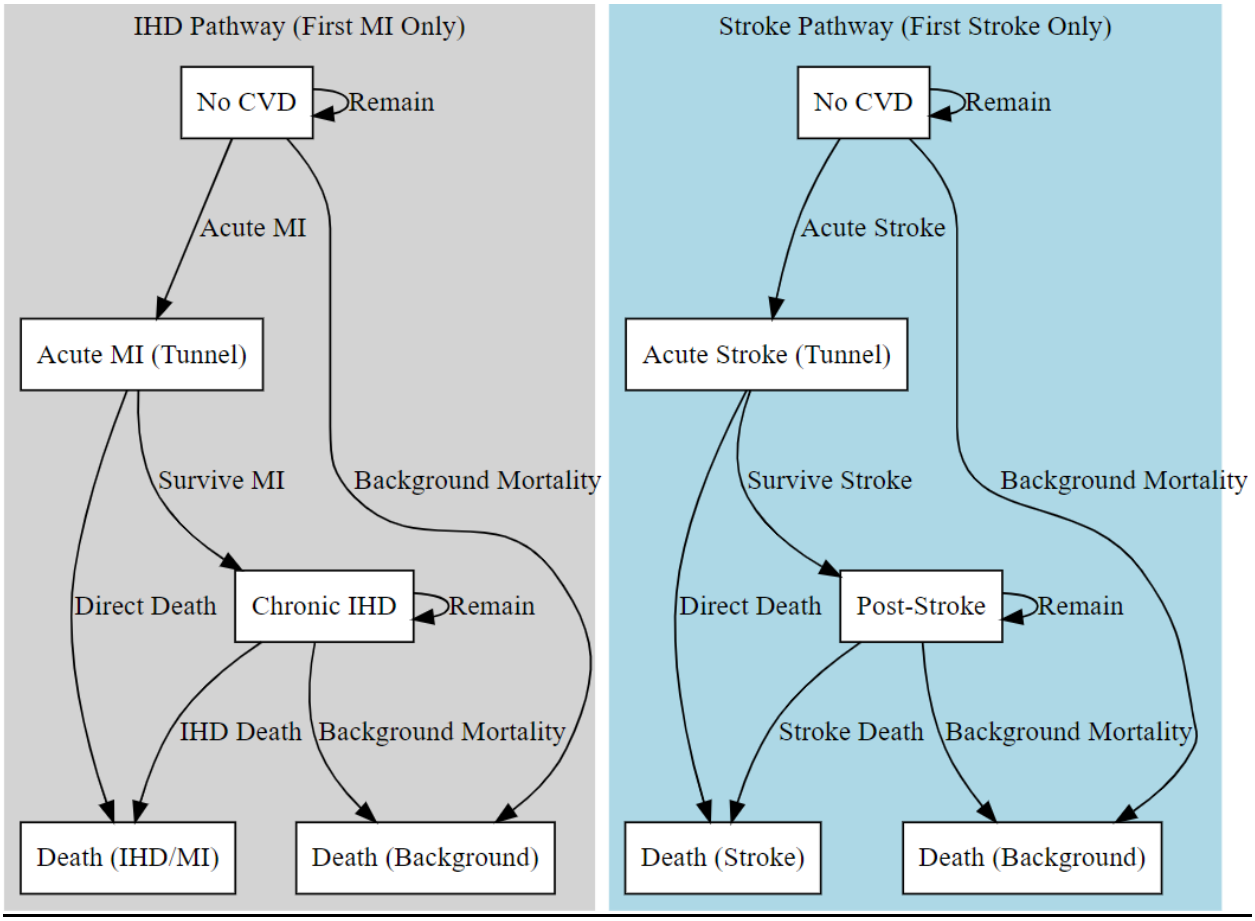

Figure 3. Decision-analytical model structure. Left panel: Ischemic Heart Disease/Myocardial Infarction (IHD/MI) pathway; right panel: stroke pathway. Individuals start in the no cardiovascular disease (CVD) state, may experience a first acute event (tunnel state), and either die acutely or survive to chronic IHD/post-stroke, with ongoing background and cause-specific mortality each monthly cycle. Only the first MI/stroke is modeled.

A hybrid modeling structure was used. A subset of patients who appeared in all three phases of the SAIA-HTN trial formed the simulation cohort (S1 Table in Supplementary Text). Baseline cardiovascular risk for each patient was estimated using the WHO non-laboratory CVD risk charts[15].

Four scenarios were modeled (S1 Figure in Supplementary Text). The status quo, across both the intervention and control arm, assumed minimal to no screening or treatment for HTN and no

change in cardiovascular risk. The sustainment phase in the control arm reflected potential improvements in hypertension care delivery. The fourth scenario included both the intervention and the SAIA strategy, with potentially additional gains in blood pressure control.
Implementation costs were assigned based on facility, arm, and phase, with minimal "standard of care" costs in the baseline phase and additional labor and system strengthening costs attributed to the intensive and sustainment phases.
The model was implemented in R and simulated a 10-year time horizon from a health system perspective, with both costs (in 2023 US dollars) and health outcomes discounted at 3% annually[16].

Data sources

Individual-level demographic and clinical data were extracted from the SAIA-HTN REDCap database, including age, sex, blood pressure (BP) measurements, body mass index (BMI), and smoking status. These characteristics were captured at every patient visit across all three study phases, i.e., baseline, intensive implementation, and sustainment, for both intervention and control arms. This information was used to estimate each patient's 10-year cardiovascular risk as described previously. Observed reductions in systolic BP across the phases and arms were translated into changes in cardiovascular risk using evidence from a large meta-analysis, which found that a 5 mm Hg reduction in systolic BP reduced the risk of major cardiovascular events by approximately 10%, irrespective of prior CVD history or baseline BP level[17].

Transition probabilities, background mortality rates, disability weights, and life expectancy assumptions were sourced from the Global Burden of Disease (GBD) study, the WHO, and peer-reviewed literature[1,18–22]. Mortality risk and life-years lost were applied depending on the specific age and sex of the patient using Mozambican life tables. Disability-adjusted life years (DALYs) were calculated by summing years of life lost (YLL) due to premature mortality and years lived with disability (YLD) from post-MI and post-stroke states. Model inputs are presented below in Table 1.
Table 1. Key model inputs

Parameter	Value	Source
Average 10-year cardiovascular risk reduction		
From control baseline to control sustainment (A)	29.3%	Primary data analysis
From intervention baseline to intervention sustainment (B)	40.3%	Primary data analysis
Relative risk reduction (1-(1-B)/(1-A))	15.5%	Primary data analysis
Relative proportion of CVD events that are MI	55%	[1]
Relative proportion of CVD events that are stroke	45%	[1]
Transition probabilities (Monthly)		
Acute MI to death	0.65	[19–21]
Chronic IHD to death	0.0034	[18]
Stroke to death	0.38	[18]
Post-stroke to death	0.0043	[18]
Background mortality	0.0018	[1]
Disability weights (Annual)		
Acute MI	0.439 (0.405, 0.477)	[18]
Chronic IHD	0.101 (0.093, 0.103)	[18]
Stroke	0.920 (0.782, 0.990)	[18]
Post-stroke	0.266 (0.228, 0.295)	[18]
Costs		
SAIA HTN trial expenditure		
Control arm	$355,448	Primary data analysis
Intervention arm	$468,126	Primary data analysis
Hypertension medication (per patient)		

Average annual per patient costs	$17.50	[23], calculated
% participants accessing treatment in baseline phase	2.1%	[11]
% participants accessing treatment in sustainment phase	8.2%	[11]
Cardiovascular outcomes		
Acute MI (one time)	$547 ($465, $629)	[24]
Chronic IHD (annual)	$12 ($10, $14)	[24]
Stroke (one time)	$317 ($265, $365)	[24]
Post-stroke (annual)	$14 ($12, $16)	[24]
CV illness treatment access for acute/emergency care	20% (0%, 80%)	Expert input

Input costs

To estimate cost per patient-year of hypertension care and SAIA implementation, we combined both bottom-up and top-down costing approaches (Figure 4). Primary cost data were collected during the trial using time and motion studies, provider-reported REDCap activity logs, Ministry of Health salary bands, facility and project budgets, and staff interviews. Costs were categorized as: provider salary, consumables/travel/equipment, SAIA implementation costs (e.g., coaching, dashboards, training), treatment costs (e.g., medication, clinical visits), and indirect/overhead costs. Costs were further tagged as research or program costs, with the latter used for the analysis[25].

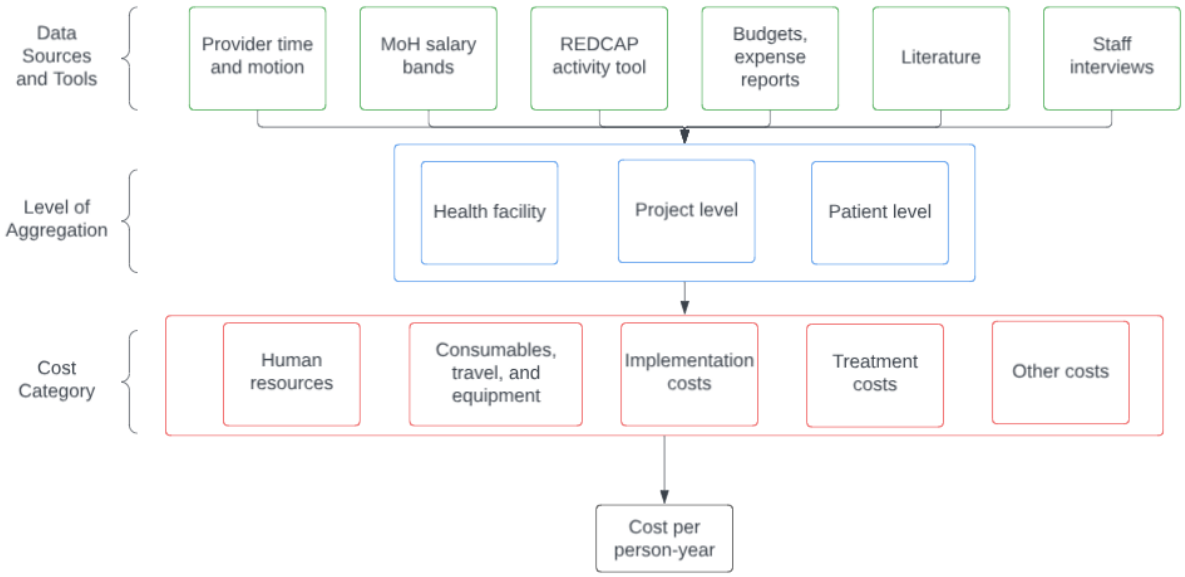

Figure 4. Costing framework and data flow. Primary inputs (provider time-and-motion, Ministry of Health salary bands, REDCap activity logs, budgets/expense reports, literature, staff interviews) are aggregated at health-facility, project, and patient levels and classified as human resources, consumables/travel/equipment, implementation, treatment, and other costs to derive cost per person-year.

Costs were aggregated at the facility, project, and patient levels, and then assigned to patients based on their utilization of services. Program costs which included human resources, consumables, travel, and other implementation costs were shared across all patients receiving screening in the respective arms, while treatment costs were assigned only to patients eligible for and initiated on HTN treatment. A proportion of the human resources costs were assigned for patient visits at baseline, to account for low levels of HTN screening at baseline. In the sustainment phase, total costs were converted to cost per person-year by dividing expenditures across each category by the number of patient-years observed per arm. Detailed breakdowns of inputs and cost calculations are available in the supplementary text (S2, S3, and S4 Tables).

Cost-effectiveness analyses

We further classified and presented cost per person per year into three categories, i.e. direct costs of hypertension care (treatment of HTN and downstream CV illness, consumables, human resources); facility indirect costs, estimated using a markup of 7.4% for outpatient services and 27% for inpatient care[26]; and system strengthening costs, including the cost of implementing SAIA. Primary outcomes included incidence and mortality due to cardiovascular events, DALYs averted, total health system costs, and the incremental cost-effectiveness ratio (ICER). The primary outcomes have been modeled per 100,000 PLHIV seeking HTN care. Two ICERs were estimated based on the modeled scenarios (S1 Figure in supplementary text), one for the hypertension intervention (control sustainment vs. control baseline), and the other for the implementation strategy (intervention sustainment vs. control sustainment).

Sensitivity Analyses

We conducted both deterministic and probabilistic sensitivity analyses to assess how uncertainty in key inputs influenced model results.

For deterministic sensitivity analysis, we varied parameters one at a time. These included the cost of treating acute and chronic cardiovascular conditions, cost of antihypertensive medication, cost of implementing SAIA, the proportion of individuals receiving care after an event, the probability of death following MI or stroke, and the disability weights assigned to each cardiovascular state.

In addition, we implemented probabilistic sensitivity analysis (PSA) by drawing values from defined parameter distributions. We sampled cost and disability weight values using triangular and beta distributions, respectively, based on minimum, mean, and maximum values. Transition probabilities were also varied within plausible ranges.

For the intervention ICER, we also retained patient-level simulation in our model to reflect heterogeneity in baseline characteristics and disease risk. We simulated 334 individuals, for

whom we had data across the three phases, under 100 distinct parameter sets (334 × 3 × 100 = >100,000 draws). The risk reduction estimates in this simulation were informed from a larger dataset (n=7,385). While the PSA captures parameter uncertainty (i.e., how model results vary due to inputs like cost or disability weight), the individual-level simulation allows us to account for heterogeneity across patients, including variation in baseline cardiovascular risk. This hybrid approach allowed us to represent both types of uncertainty in our cost-effectiveness results.

The study received ethical approval from Eduardo Mondlane University/Maputo Central Hospital and the University of Washington (CIBS FM&HCM/96/2018; STUDY00006694), and was registered on ClinicalTrials.gov (NCT04088656). This analysis fulfils the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist, which is attached as a supplementary file[27].

RESULTS

Detailed characteristics of the trial population and the subset used in our model are provided in the Supplementary Text (Section 2)

Implementation cost: Per person per year

When expressed as average annual cost per person, the baseline phase of the control arm cost approximately $2.46 per patient-year (Figure 5). This increased to $7.07 in the control sustainment phase, reflecting higher uptake of hypertension screening and treatment. In the intervention sustainment phase, per-patient costs increased further to $7.86, primarily due to the addition of SAIA program costs. At sustainment, human resource costs were slightly lower in the intervention arm because patients had fewer visits and hence lower apportioned costs for healthcare worker time. The incremental cost per patient-year of control sustainment compared with baseline was $4.61, and of intervention sustainment compared with control sustainment was $0.79.

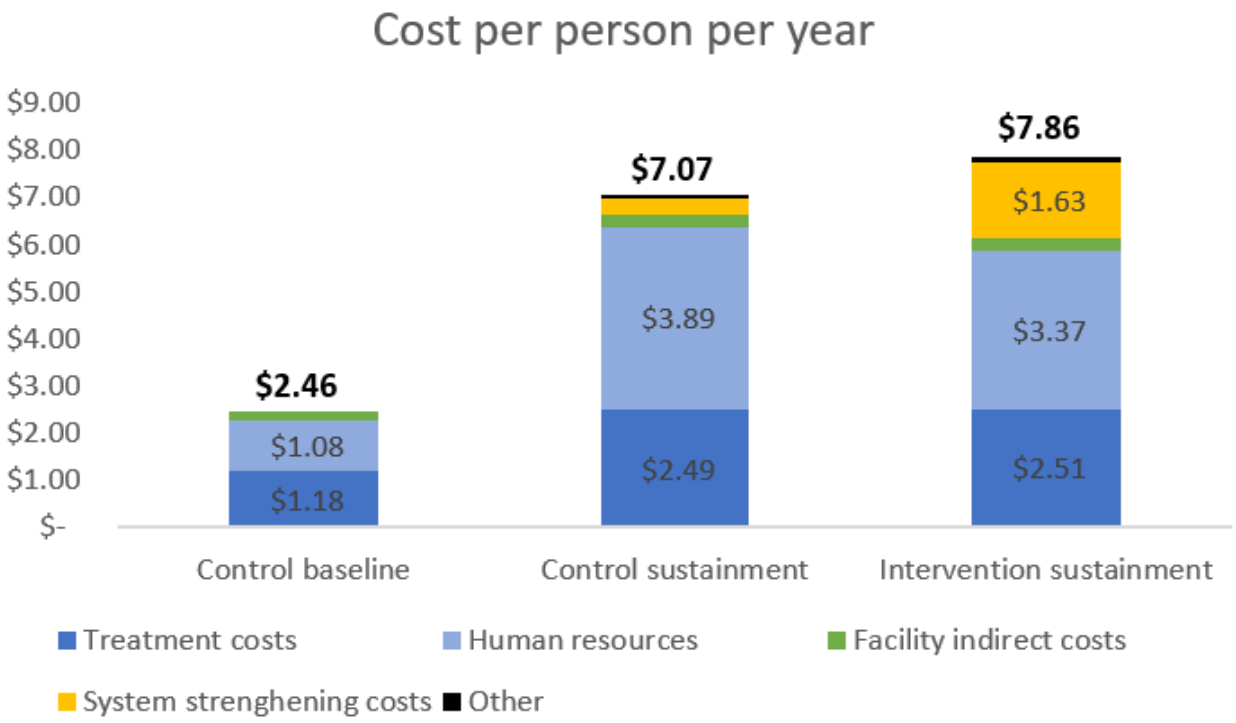

Figure 5. Cost per patient per year in control and intervention arms, by cost category. Each colored stack represents a unique cost category. The height of each stack is the contribution of that particular category to the overall cost per patient per year across both arms. The bars are stacked from bottom to top in the descending order of their relative contribution to the total cost in the control baseline. Treatment costs and human resources costs constitute direct healthcare costs. Treatment costs include costs of outpatient (HTN) and inpatient (MI and stroke) treatment, and related consumables. System strengthening costs including capacity building, meetings, and visits supporting the intervention and the SAIA implementation strategy. Labels are shown only for cost categories with values of at least $0.50 per patient-year.

Modeled costs and DALYs

Both the intervention and the SAIA implementation strategy substantially reduced cardiovascular events and deaths, while remaining highly cost-effective. Modeled results for 100,000 patients over the 10-year time horizon are presented in Table 2. Compared to the

baseline phase of the control arm, the intervention reduced acute MI and stroke cases by 25% and 31%, and both MI and stroke deaths by 31% each. Compared to the sustainment phase of the control arm, the implementation strategy further reduced acute MI and stroke cases by 15.3% each, and deaths by 15% each. The intervention averted DALYs by 5.8%, leading to an ICER of $212 (95% UI: $48, $440) per DALY averted. The implementation strategy had an ICER of $44 (95% UI $42, $46) per DALY averted.

Table 2. 10-year model outcomes (per 100,000 PLHIV population)

	Control Baseline	Control Sustainment	Intervention Sustainment
Patient with acute MI	4,389	3,048	2,582
Patients with stroke	3,591	2,494	2,113
Deaths due to MI	2,853	1,981	1,678
Deaths due to stroke	1,365	948	803
Total DALYs	265,015	239,983	224,736
Total costs	$2.37M	$6.16M	$6.83M
Intervention ICER	$212/DALY averted		-
Implementation strategy ICER	-	$44/DALY averted	

Sensitivity Analyses

One-way deterministic sensitivity analyses are shown in Figure 6.

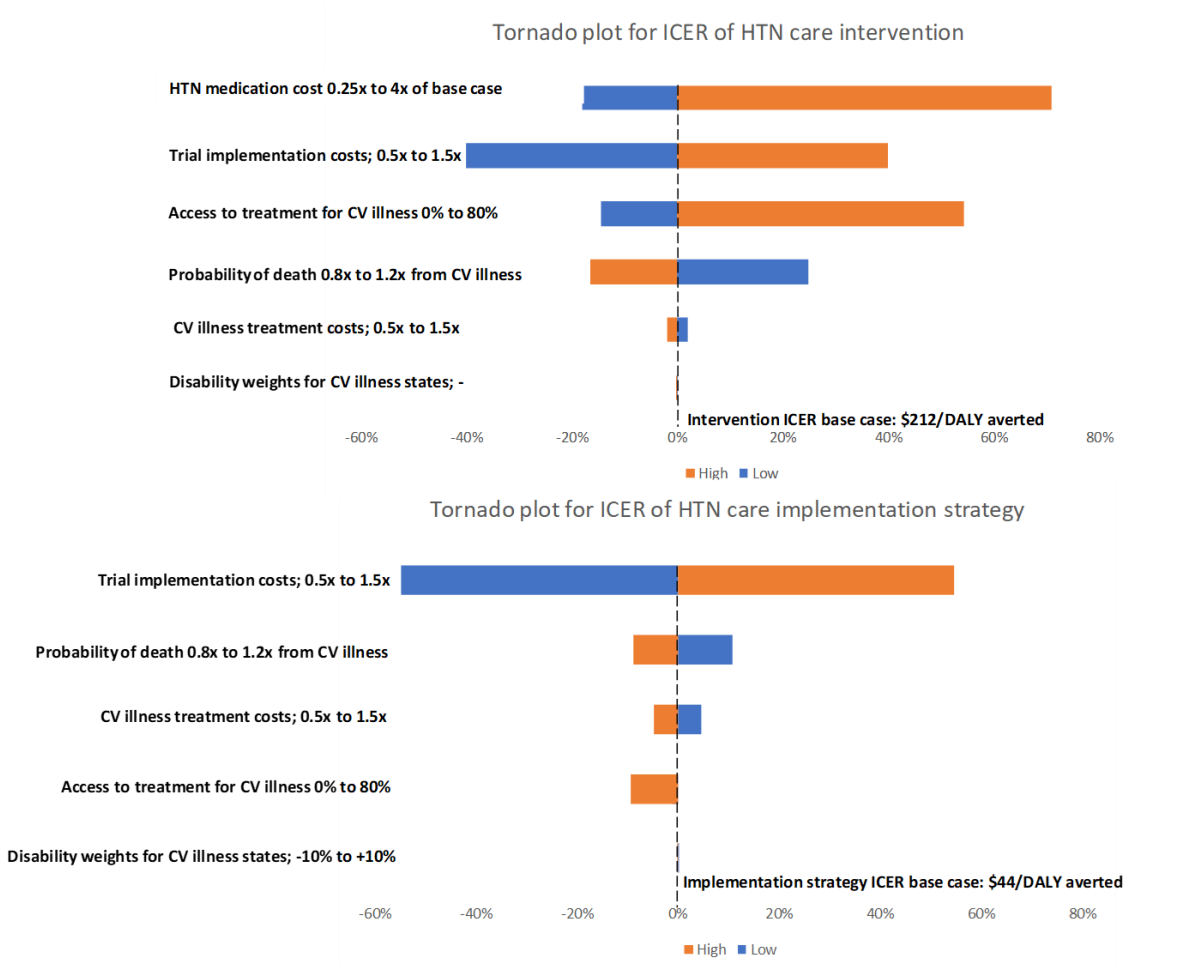

Figure 6A and 6B. ICER Tornado plots. The reference vertical dashed line in both the plots represent the base case incremental cost effectiveness ratio (ICER) when all the parameters were set to their primary estimate values. The width of the bar indicates the relative change in the ICER with change in the value of the respective parameter. The blue bars indicate change in ICER when the value of the respective parameter is less than the primary estimate. The orange bars indicate change in ICER when the value of the respective parameter is more than the primary estimate. The drivers of cost are arranged in descending order of their influence on the ICER.

For the intervention ICER (control sustainment vs control baseline), results were most sensitive to variability in HTN medication costs, trial implementation costs, and access to treatment for CV illness. Variation in probability of death for acute CV conditions also had meaningful effects,

while CV illness treatment costs and disability weights had limited impact. For the implementation strategy ICER (intervention sustainment vs control sustainment), the largest drivers of variation were trial implementation costs. Probability of death from CV illness, CV illness treatment costs, and access to CV illness treatment had little but meaningful impact, and as was the case with the intervention ICER, the disability weights has limited to no impact. Within a willingness to pay threshold of $647/DALY averted (Mozambique's Gross Domestic Product or GDP per capita[28,29]), the intervention and the implementation strategy remained cost-effective across all plausible parameter ranges.

In the probabilistic sensitivity analyses, both the intervention and the SAIA strategy were found to be consistently cost-effective, both being consistently more effective and more costly than the comparator across all simulation runs. At a willingness-to-pay threshold of $162.5 per DALY averted (0.25x per capita GDP), the SAIA implementation strategy was cost-effective in 100% of simulations, while the intervention was cost-effective in 40%. At $325 (0.5x per capita GDP), the probability of cost-effectiveness for the intervention was 85%, and at $647 (1x per capita GDP), it exceeded 99%. The cost-effectiveness acceptability curve (CEAC) is shown in Figure 7.

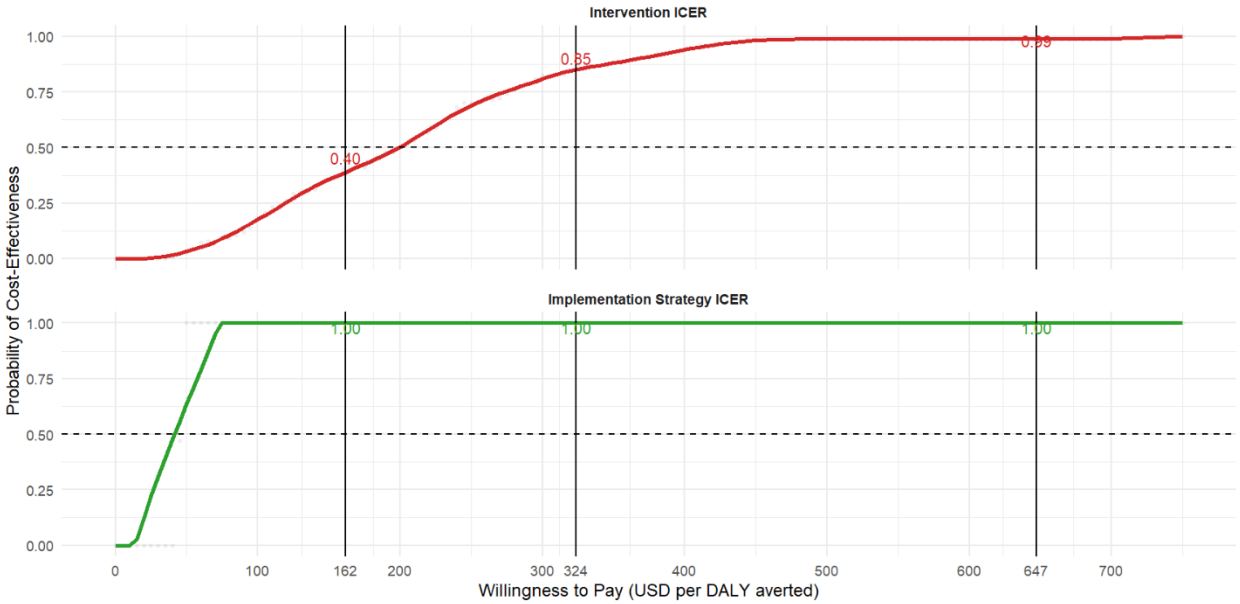

Figure 7A and 7B. Cost-effectiveness acceptability curves. Cost-effectiveness acceptability curves for the SAIA-HTN intervention (Panel A in red) and the SAIA-HTN implementation strategy (Panel

B in green). The intervention incremental cost-effectiveness ratio (ICER) is computed comparing the sustainment phase to the baseline phase in the control arm. The implementation strategy ICER is computed comparing the sustainment phase in the intervention arm to the control arm. Solid vertical lines represent alternative thresholds for evaluating cost-effectiveness, which include standard thresholds of 0.25x, 0.5x, and 1x of the GDP per capita in Mozambique, $647, per DALY averted.

DISCUSSION

This analysis showed substantial improvements in 10-year cardiovascular risk outcomes among PLHIV receiving care for Hypertension under the SAIA-HTN trial in central Mozambique. Average annual cost per patient rose from $2.46 in the baseline phase to $7.07 in control sustainment, with a further increase to $7.86 in intervention sustainment due to added SAIA program costs. These investments translated into a 25–31% reduction in acute cardiovascular events and deaths over ten years. The intervention alone yielded an ICER of $212 per DALY averted, while adding SAIA reduced the ICER to just $44 per DALY averted, confirming that both strategies are highly cost-effective.

Strengthening basic hypertension care produced the largest reductions in cardiovascular risk, confirming the value of even modest improvements in diagnosis and treatment in high-prevalence settings. Adding SAIA on top of this foundation provided further health gains at low incremental cost, underscoring the role of implementation strategies in closing quality gaps. Taken together, these findings suggest that investments in both EBIs and the strategies to deliver them can work in tandem to generate health impact at scale.

Hypertension is highly prevalent in Mozambique, with two in five people (among those 25-64 years old) having high hypertension, yet awareness, treatment, and control rates remain low[3]. Several descriptive studies have emphasized the need for improved screening and sustained treatment. Economic evaluations of hypertension care in Mozambique are scarce. Evidence

from other African settings shows that using existing health systems for population-level hypertension screening by community health workers, and treatment through integrated chronic care clinics, can reduce cardiovascular illness and is likely to be cost-effective[13]. Integrated six-month multi-month dispensing of HIV and hypertension medicines has also been shown to improve outcomes for patients already in care, reducing loss to follow-up and deaths by ensuring more reliable services[30]. These studies focused on the cost of medication and long-term health gains, with less attention to how services are delivered in practice. One of the few comparable economic evaluations is by Sando et al. (2020), who modeled the cost-effectiveness of integrating hypertension, diabetes, and high cholesterol screening and treatment into HIV care in Uganda and reported ICERs ranging from approximately $1,400 to $3,250 per DALY averted among older adults receiving ART (lower reduction in CVD risk compared to our intervention)[31]. While their analysis differs in scope and does not explicitly separate implementation strategies from clinical interventions, the magnitude of their cost-effectiveness estimates provides a relevant benchmark. Other studies in this area, such as evaluations of integrated HIV–NCD care in Malawi, have primarily focused on costs and clinical outcomes rather than cost-effectiveness[32].

By integrating individual-level trial data with a pragmatic modeling framework, we captured heterogeneity in baseline risk and simulated patient pathways under real-world conditions. We also explicitly separated the cost-effectiveness of the clinical intervention (hypertension treatment) from the cost-effectiveness of the implementation strategy (SAIA). This distinction has rarely been made in the literature, despite its policy relevance. By showing how delivery systems influence health outcomes, we add value by providing stronger evidence for how interventions can be implemented effectively in resource-limited health systems.

From a policy perspective, our findings suggest that investing in hypertension control should be a priority for Mozambique's health system. Hypertension treatment is highly cost-effective, with major implications for reducing the burden of cardiovascular disease, which accounts for a large share of NCD mortality in the country. At the same time, SAIA provides an effective approach to

improving quality of care where blood pressure control rates remain low. The SAIA strategy has been specified in prior work, which outlines its core components and intended pathways of effect and this analysis builds on that foundation by translating those system-level processes into health and economic outcomes[33]. The sequence of investments matters; Mozambique must first ensure that primary health centers can screen and treat hypertension reliably. Once this foundation is in place, SAIA can be deployed to strengthen quality of care and close implementation gaps.

Beyond Mozambique, other low- and middle-income countries facing similar challenges can adapt our model with local parameters, generating context-specific evidence to guide scale-up. The structure is flexible and can be applied across diverse settings. The underlying message is consistent, i.e., hypertension treatment is cost-effective, and quality improvement strategies like SAIA help ensure these benefits are realized.

From a research perspective, our study demonstrates the importance of evaluating both EBIs and the strategies used to deliver them. Implementation strategies often require additional resources, such as training, supervision, or workflow redesign, but their incremental costs are modest relative to the health gains they unlock. By modeling the contributions of both components, we show how routine care and quality improvement approaches can work in tandem. This provides a framework for future evaluations of implementation science interventions, which are often overlooked in economic analyses.

Further, it must be noted that the EBI reflects hypertension screening and treatment as delivered under existing standard-of-care conditions, which necessarily embed a baseline level of implementation activities and constraints. The SAIA strategy represents an explicit, theory-informed approach to strengthening and optimizing delivery beyond this baseline. Our broader motivation is to highlight that when implementation strategies are evaluated only in combination with clinical interventions, their incremental contribution may be obscured. By

separating these components analytically, we aim to better characterize the added value of SAIA as an implementation strategy.

This study also has certain limitations. First, the disease structure was simplified. We modeled only one major CVD event (MI or stroke) per patient and assumed fixed probabilities for accessing acute and chronic care. We did not model hypertensive heart disease as an independent condition, even though it accounts for approximately 16% of cardiovascular deaths in Mozambique[1]. This omission, along with the lack of modeling of recurrent events, likely led to an underestimation of the total disease burden averted, correspondingly leading to an underestimation of the ICER. In addition, indirect societal costs such as lost productivity were not included, meaning our estimates may be conservative from a societal perspective. Secondly, cardiovascular risk was estimated using WHO non-laboratory risk charts parameterized for Eastern sub-Saharan Africa, which includes Mozambique and neighboring countries, and represent the closest available regionally relevant inputs. However, to our knowledge, these risk scores have not been formally validated among people living with HIV in Mozambique. Additionally, the generalizability of cost data and care patterns may be limited. Still, the model was designed to be flexible. Other settings can adapt it using their own parameters and choose between a simple cohort model or a more detailed patient-level simulation, depending on data availability. Lastly, the modeling cohort was relatively small (n=334), restricted to patients who participated in all three phases of the trial. While this allowed for detailed tagging of costs and risk changes, it may not represent the broader population. We addressed this by applying risk reduction estimates from a larger dataset (n=7,385), though assuming uniform effects across patients may not hold everywhere.

For future directions, rollout of SAIA is already underway and being evaluated through the SCALE-SAIA HTN study, a scaled up and scaled out expansion of the SAIA HTN trial[3]. This provides an opportunity to collect prospective data on costs including societal costs, data on quality improvements, on detailed health outcomes, and cost per cascade outcomes, enabling a more robust economic evaluation, including facility-level cost-effectiveness heterogeneity. This

heterogeneity may even encompass variations in drug availability and workforce capacity. A cost-effectiveness analysis of SCALE-SAIA HTN will help refine parameter estimates and improve model accuracy. SCALE-SAIA HTN also creates an opportunity to examine equity-relevant dimensions, including whether SAIA reduces geographic and system-level disparities in access to hypertension care. Beyond Mozambique, the framework can be extended to other settings, adapted for general adult populations at risk of cardiovascular disease, and tailored to other NCD programs. These extensions will strengthen our understanding of how to maximize the value of both interventions and implementation strategies in diverse health systems.

CONCLUSIONS

Our model is a tool for implementation scientists, policymakers, and researchers aiming to assess cardiovascular interventions and associated implementation strategies among PLHIV. Its application to SAIA-HTN in Mozambique suggests that this is a cost-effective strategy for improving hypertension care, but only in the presence of adequate blood pressure equipment, training, and medications. Our study illustrates how implementation strategies require a minimum threshold of health system readiness to generate meaningful health impact, and how economic evaluation methods can be applied to assess the added value of delivery strategies for chronic disease care in resource-limited settings.

LIST OF ABBREVIATIONS

i. CV: Cardiovascular
ii. NCD: non-communicable diseases
iii. HTN: Hypertension
iv. PLHIV: people living with HIV
v. ART: antiretroviral treatment
vi. SAIA: Systems Analysis and Improvement Approach
vii. IHD: ischemic heart disease
viii. MI: myocardial infarction
ix. BP: blood pressure

x. BMI: body mass index
xi. GBD: Global Burden of Disease
xii. DALYs: Disability-adjusted life years
xiii. YLL: years of life lost
xiv. YLD: years lived with disability
xv. ICER: incremental cost-effectiveness ratio
xvi. PSA: probabilistic sensitivity analysis
xvii. CHEERS: Consolidated Health Economic Evaluation Reporting Standards
xviii. CEAC: cost-effectiveness acceptability curve
xix. GDP: Gross Domestic Product

DECLARATIONS

Ethics approval and consent to participate

The study received ethical approval from Eduardo Mondlane University/Maputo Central Hospital and the University of Washington (CIBS FM&HCM/96/2018; STUDY00006694).

Consent for publication

Not applicable

Availability of data and materials

Costing data and model results generated or analysed during this study are included in this published article and/or the supplementary text.

De-identified client data underlying the results reported in the parent study (which informed the effectiveness outcomes used in this article) and the respective data dictionary will be made available at the request of investigators whose proposed use of the data has been approved by an independent review committee identified for this purpose. Request submissions should be submitted to **saiastrategy@uw.edu**, and a data access agreement will need to be signed per the procedures of the University of Washington.

Competing Interests

The authors report no competing interests.

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Authors' contribution

DW conceptualized the economic evaluation study. AOM, KS, and SG conceptualized the parent study. AM conducted the costing and mathematical modeling analysis. MJC, MJFC, AC, OAU, AOM, SG, KS, CH, AM and IR supported study implementation. AM and OAU analyzed the parent study data. DW and AM drafted the manuscript. All authors reviewed the manuscript. AOM, SG, DW, and AM had final responsibility for the decision to submit for publication.

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SUPPLEMENTARY TEXT

1. Additional Model Overview

Mortality in the acute MI state

To parameterize the probability of 30-day mortality after acute MI in Mozambique, where we assume that 80% of patients do not reach the hospital and only 20% are hospitalized, we drew on three complementary data sources. A clinical description of early MI mortality suggested that at least one-third of patients die before reaching hospital, and that 40–50% of those who arrive die rapidly upon admission[1]. This corresponds to an estimated non-hospitalized mortality of 75–83% and an overall mortality of roughly 63–76% under our assumed 80/20 split. Findings from another study, which reported 28-day case fatality rates across 29 populations, indicated a median of 50% overall mortality, with 25% among hospitalized patients. Back-calculating under the 80/20 split implied a non-hospitalized mortality of about 56%, with reported ranges suggesting overall mortality between 34% and 70%[2]. Finally, registry data from the Chinese Acute Stent Study (CASS) provided detailed case counts, reporting 79% 30-day mortality among non-hospitalized patients (239/302) and 19% among hospitalized patients (197/1,052), which translates into an overall 67% mortality under the 80/20 split[3].

Taken together, these sources converge on high early mortality when access to hospital care is limited. Using pathway-specific base values of approximately 79% for non-hospitalized patients and 25% for hospitalized patients, the overall 30-day mortality varies depending on the assumed distribution: about 79% if all patients are non-hospitalized (100/0 split), 65% under the Mozambique base case assumption of 80/20, and 37% if the majority are hospitalized (20/80 split). For modeling, we adopt a pooled base-case value of 65% overall 30-day mortality for Mozambique.

Stroke events

All stroke types were modeled together in a single acute stroke state, also a one-month tunnel. The case-fatality rate for stroke was taken directly from another modeling paper and applied uniformly[4]. Survivors entered the post-stroke state, where they faced elevated risk of death from stroke as well as background mortality.

Relative distribution of first events (IHD vs. stroke)

Once individuals were in the "No CVD" state, they faced a risk of experiencing their first cardiovascular event. When such an event occurred, 55% of the time it was modeled as an acute IHD event and 45% of the time as an acute stroke. This split was based on the relative incidence of stroke versus IHD in Mozambique in 2021, which reported 29,336 stroke cases and 35,337 IHD cases[5]. These numbers translate to just over half of all events being IHD [35,337/(35,337 + 29,336) ≈ 55%].

Background mortality

Background (non-CVD) mortality was applied to the No CVD, chronic IHD, and post-stroke states. Since the acute states (acute IHD and acute stroke) were one-month tunnel states, background mortality was not applied during those months. This ensured that deaths in the acute phase were attributed only to the cardiovascular event itself.

2. Model Population and CV Risk Reduction

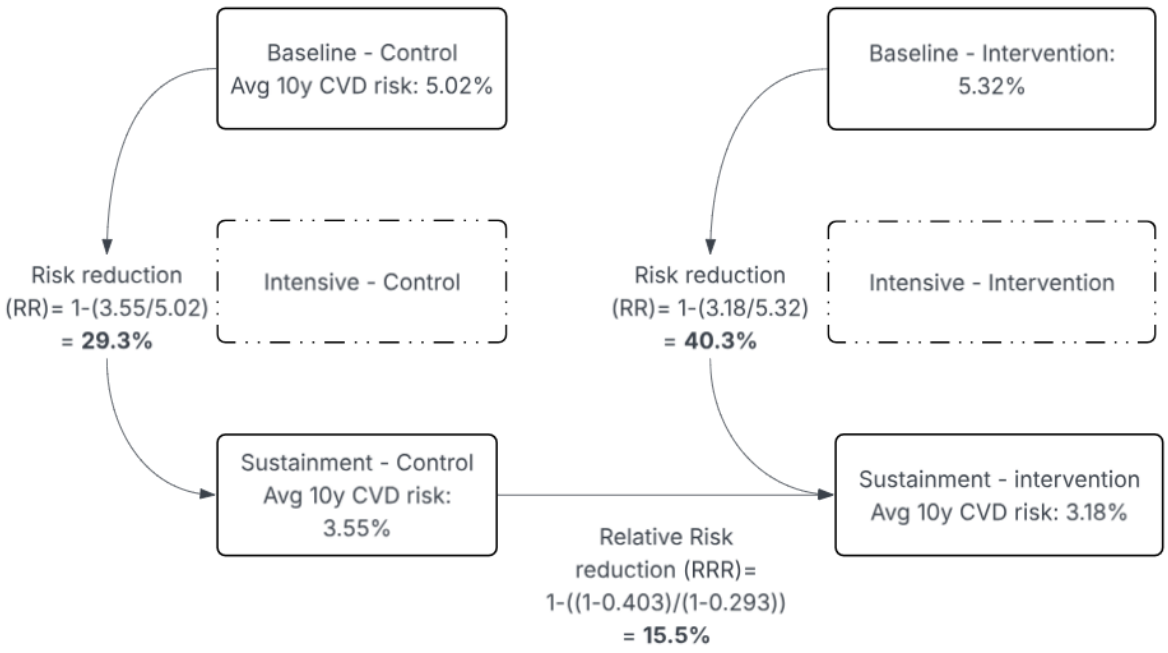
The SAIA-HTN trial enrolled 65,151 individuals receiving ambulatory HIV care across 16 public health facilities in central Mozambique[6]. For the purposes of modeling, we restricted to the subset of 7,385 patients who had complete data on age, sex, systolic blood pressure (SBP), body mass index (BMI), and smoking status, since these are the variables required to calculate 10-year cardiovascular disease (CVD) risk.

A further restricted subset of 334 individuals formed the individual-level simulation cohort. These were patients who appeared across all three phases of the trial (baseline, intensive, and sustainment), comprising 151 individuals in the control arm and 183 in the intervention arm. For each of these patients, baseline CVD risk was calculated, and the intervention effect was applied by scaling risk downward according to the arm-specific reductions derived from the larger 7,385-patient dataset. S1 Table below shows baseline characteristics for this analytic sample.

S1 Table. Patient characteristics at baseline (for simulation cohort)

	Intervention	Control
Number of patients	183	151
Median age (IQR or 95% UI)	48 (40 – 55)	46 (37-55)
Female Sex (%)	38%	44%
Mean BMI (IQR or 95% UI)	24.51 (21.72-26.67)	25.11 (21.78 – 27.62)
Mean SBP (IQR or 95% UI)	168.1 (154.0–179.5)	166.6 (150.0–180.0)
Smokers (%)	2.7%	2.0%
10-year CVD risk	5.07 (3.00–7.00)	5.02 (2.00–6.00)

S1 Figure illustrates the cardiovascular risk reduction and the relative risk reduction between the arms.



S1 Figure. Change in 10-year CVD risk by arm and derivation of relative risk reduction. Solid boxes show baseline and sustainment mean 10-year cardiovascular risk for control and intervention arms; arrows indicate within-arm risk reduction and the cross-arm relative risk reduction (RRR). The intensive phase is shown for context.

In the intermediary dataset with 7385 patients, at baseline, the mean 10-year CVD risk was 5.02% in the control arm and 5.32% in the intervention arm. By the sustainment phase, average risk declined to 3.55% in the control arm and 3.18% in the intervention arm (S1 Figure). This corresponded to a within-arm relative reduction of 29.3% in the control arm (1 – 3.55/5.02) and 40.3% in the intervention arm (1 – 3.18/5.32). When comparing across arms at sustainment, the intervention arm achieved an additional 15.5% relative risk reduction compared with the control arm.

Other Key Model Parameters

Costs

In the main text, we report actual program costs and hypertension treatment costs for the baseline and sustainment phases, also presented in Figure 3. S2 Table below presents the program costs calculated from project expense sheets and activity-based costing tools.

S2 Table. SAIA HTN Programmatic expenses*

	Intervention	Control
Human resources	$ 297,502.07	$ 297,502.07
Other	$ 9,517.01	$ 6,036.15
Consumables	$ 49,614.84	$ 44,113.43
Support	$ 108,504.78	$ 7,601.46
Training	$ 2,987.80	$ 195.15
TOTAL	**$ 468,126.49**	**$ 355,448.25**

These costs were first calculated per visit (with the number of visits later shown in S4 Table). The number of visits per patient in each arm was obtained from the main study: 4.25 visits per client in the intervention arm and 4.79 in the control arm. Because the trial lasted approximately 30 months, we converted these to effective annual visits by multiplying the total visits by 12/30 for each arm. We then added annualized activity costs, annual hypertension and CV treatment costs, and facility indirect costs, to obtain the cost per person-year across arms (as summarized in Figure 3 of the main text). Human resources costs in the baseline were determined by taking a proportion of the costs in the sustainment phase, i.e. the number of people seeking HTN treatment in the baseline vs sustainment arms (simplified assumption where staff involvement increased proportionally with patients seeking care when it comes to HTN access)

S3 Table. Breakdown of costs per person per year.

	Control baseline	Control sustainment	Intervention sustainment
Treatment costs	$ 1.18	$ 2.49	$ 2.51
Human resources	$ 1.08	$ 3.89	$ 3.37
Facility indirect costs	$ 0.20	$ 0.23	$ 0.24
System strenghening costs	$ -	$ 0.38	$ 1.63
Other	$ -	$ 0.08	$ 0.11

In the activity costing tool, we estimated the average meeting time for each SAIA visit, along with office supply and transportation costs associated with these meetings at the cluster level. For a post-trial scenario, we assumed each meeting would include one supervisor and one staff member, with monthly salaries of 50,000 MZN and 30,000 MZN, respectively, giving a combined monthly salary of 80,000 MZN. Assuming 22 working days per month and an 8-hour workday, this translated into an effective salary of 7.58 MZN per minute. The average meeting time (in

minutes) was multiplied by the number of meetings and the effective salary per minute of attendees to calculate indirect HR costs per cluster.

Office supply costs were taken directly from reported expenses. For transportation, we assumed that in a post-trial scenario the Ministry of Health vehicle would be used for SAIA meetings. At a fuel price of 85 MZN per liter and a vehicle mileage of 11.11 km per liter, the effective cost was 7.65 MZN per km. Distances traveled for each visit were recorded and multiplied by mileage to generate transportation costs.

Indirect HR costs, office supplies, and transportation were then combined to calculate the effective activity cost per cluster. While some of these components may overlap with program expenses, our program expense sheets did not capture salaries of government staff or use of government vehicles. In addition, reporting costs by cluster helps capture the heterogeneity in SAIA implementation. S4 Table presents the effective activity costs per visit. The number of visits per cluster was taken from the main effectiveness study, and these costs were incorporated into the "system strengthening costs" category in Figure 3.

S4 Table. Activity costs per client visit

	Cluster	Arm	Phase	Visits	Cost (MZN)	Cost per visit (MZN)	Cost per visit (USD)
HR Buzi	11	int	baseline	312	-	-	-
CS Dondo	12	int	baseline	1017	-	-	-
CS Macurungo	13	con	baseline	2934	-	-	-
CS Mafambisse	14	con	baseline	1080	-	-	-

CS Mascarenhas	15	int	baseline	1458	-	-	-
CS Nhanconjo	16	int	baseline	2713	-	-	-
HR Nhamatanda	17	con	baseline	992	-	-	-
CS Ponte Gea	18	con	baseline	1584	-	-	-
HR Catandica	21	int	baseline	467	-	-	-
CS Eduardo Mondlane	22	int	baseline	2900	-	-	-
HD Manica	23	con	baseline	1885	-	-	-
CS Nhamahoanha	24	con	baseline	1222	-	-	-
CS 1 de Maio	25	int	baseline	3056	-	-	-
CS 7 de Abril	26	int	baseline	2036	-	-	-
CS Sussundenga	27	con	baseline	1084	-	-	-
CS Vanduzi	28	con	baseline	888	-	-	-
HR Buzi	11	int	intensive	6756	135,477	20.05	0.31
CS Dondo	12	int	intensive	9168	90,791	9.90	0.15

CS Macurungo	13	con	intensive	27651	89,549	3.24	0.05
CS Mafambisse	14	con	intensive	10937	78,001	7.13	0.11
CS Mascarenhas	15	int	intensive	10347	36,239	3.50	0.05
CS Nhanconjo	16	int	intensive	17390	74,538	4.29	0.07
HR Nhamatanda	17	con	intensive	10331	86,496	8.37	0.13
CS Ponte Gea	18	con	intensive	7064	43,711	6.19	0.10
HR Catandica	21	int	intensive	5951	100,830	16.94	0.26
CS Eduardo Mondlane	22	int	intensive	17530	38,282	2.18	0.03
HD Manica	23	con	intensive	8145	70,456	8.65	0.14
CS Nhamahoanha	24	con	intensive	9762	17,436	1.79	0.03
CS 1 de Maio	25	int	intensive	13303	41,800	3.14	0.05
CS 7 de Abril	26	int	intensive	15385	12,559	0.82	0.01
CS Sussundenga	27	con	intensive	10278	33,982	3.31	0.05
CS Vanduzi	28	con	intensive	11463	27,740	2.42	0.04

HR Buzi	11	int	sustainment	3024	99,080	32.76	0.51
CS Dondo	12	int	sustainment	5694	87,475	15.36	0.24
CS Macurungo	13	con	sustainment	13858	55,251	3.99	0.06
CS Mafambisse	14	con	sustainment	3709	32,595	8.79	0.14
CS Mascarenhas	15	int	sustainment	4483	15,049	3.36	0.05
CS Nhanconjo	16	int	sustainment	7782	54,189	6.96	0.11
HR Nhamatanda	17	con	sustainment	2879	51,041	17.73	0.28
CS Ponte Gea	18	con	sustainment	3522	17,927	5.09	0.08
HR Catandica	21	int	sustainment	1513	62,111	41.05	0.64
CS Eduardo Mondlane	22	int	sustainment	5715	19,749	3.46	0.05
HD Manica	23	con	sustainment	3244	46,964	14.48	0.23
CS Nhamahoanha	24	con	sustainment	2978	25,671	8.62	0.13
CS 1 de Maio	25	int	sustainment	5170	20,907	4.04	0.06
CS 7 de Abril	26	int	sustainment	6547	20,397	3.12	0.05

CS Sussundenga	27	con	sustainment	4164	35,778	8.59	0.13
CS Vanduzi	28	con	sustainment	5093	33,951	6.67	0.10

From the literature, we estimated the per capita cost of hypertension medication in Mozambique to be $3.50 per year for adults aged 40–64[7]. Assuming 20% of the population is hypertensive, this translates to $17.50 per hypertensive patient per year. Using SAIA-HTN cascade data, we estimated that in the baseline phase, approximately 2.03% of participants were prescribed hypertension medication, while in the sustainment phase this proportion increased to 8.19%. Accordingly, we assumed an average annual per-patient cost of $0.40 in the baseline phase (17.5 × 2%) and $1.44 in the sustainment phase (17.5 × 8%).

Data availability

Spreadsheets with the raw data for these calculations, and the model code, are available in the GitHub repository: https://github.com/akash210593/saiahtn .

Uncertainty Analysis

We incorporated parameter uncertainty through a probabilistic sensitivity analysis. Transition probabilities for mortality were varied within prespecified ranges, including acute deaths from myocardial infarction and stroke, deaths in the chronic IHD and post-stroke states, and background mortality. For each of these, values were drawn from beta distributions parameterized using the mean values and plausible bounds identified in the literature. Program costs per patient were varied within observed ranges using triangular distributions defined by minimum, maximum, and mean values. Acute and chronic cardiovascular care costs were modeled in the same way, with triangular distributions reflecting their lower and upper bounds.

Disability weights for acute myocardial infarction, chronic IHD, acute stroke, and post-stroke sequelae were also varied. Beta distributions were constructed from the reported mean values and plausible ranges, ensuring that each draw remained bounded between zero and one.
A total of one hundred probabilistic draws were implemented. For each draw, costs, years lived with disability, and years of life lost were calculated over the ten-year horizon and then averaged by trial arm and phase. Results are reported as mean values with 95% uncertainty intervals, and incremental cost-effectiveness ratios were calculated for each probabilistic sample.

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CHAPTER 4 – Aim 3

Cost-effectiveness of providing pre- and post-exposure prophylaxis via online pharmacies in Kenya: a modeling analysis

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SUMMARY

Background: Oral pre- and post-exposure prophylaxis (PrEP/PEP) provision via online pharmacies (online PrEP/PEP) offers promise in increasing biomedical prevention coverage. We modeled the impact of online PrEP/PEP scale-up in western Kenya.

Methods: We adapted an agent-based model, EMOD-HIV, to simulate online PrEP/PEP implementation from 2026-2036; costs and PrEP/PEP utilization by client characteristics were informed by the ePrEP pilot which evaluated online PrEP/PEP provision in Nairobi and Mombasa, Kenya. Eligible clients were aged 15-49 reporting condomless sex with non-marital partners. We assumed PrEP/PEP provision was implemented through public/private partnership with the Kenya Ministry of Health (MOH) providing PrEP/PEP drugs and service delivery costs paid by the online pharmacy (and charged to clients). We calculated incremental cost-effectiveness ratios (ICERs) assessing costs incurred by MOH and over 35-years .

Findings: Online PrEP/PEP was projected to achieve population coverage of 0.7% for PEP and 0.3% for PrEP and avert 13.9% of HIV infections over 10 years. The intervention was cost-effective from the MOH perspective (ICER: $212/DALY averted). In a scenario assuming only online PEP availability (to isolate the impact of PEP), 11.6% of infections were averted (ICER: $210/DALY averted). The intervention remained cost-effective when varying PrEP/PEP effectiveness and assuming HIV testing and treatment disruptions.

Interpretation: Online PrEP/PEP can avert substantial HIV infections with low population coverage. PEP was responsible for most intervention health benefits due to high observed demand for PEP vs. PrEP in the pilot. Leveraging private retailers can be efficient for scaling up HIV prevention in an era of shrinking donor funding.

Funding: The Gates Foundation (INV-038274 and INV-037646)

RESEARCH IN CONTEXT

Evidence before this study

We searched PubMed for articles published from January 1, 2016 - September 15, 2025, assessing the health or economic impact of pre- and post-exposure prophylaxis in sub-Saharan Africa using the terms: (("HIV"[tiab]) AND "Africa" AND ("pre-exposure prophylaxis"[tiab] OR "PrEP"[tiab] OR "post-exposure prophylaxis"[tiab] OR "PEP"[tiab]) AND ("economic evaluation"[tiab] OR "cost*"[tiab] OR "budget impact"[tiab])). Our search identified 181 articles: 23 modeled the cost-effectiveness of PrEP in Africa, and two modeled PEP. Among the PEP studies, one study explored the cost-effectiveness of broad community availability of tenofovir, lamivudine, and dolutegravir across Africa assuming self-selection among those at HIV risk, and the other conducted a back-of-the-envelope analysis of PEP cost-effectiveness in Eastern and Southern Africa (ESA) using theoretical assumptions. We did not find studies modeling the cost-effectiveness of PEP using utilization data from real-world studies.

Added value of this study

To our knowledge, this is the first study to evaluate the health and economic impact of PEP provision in Africa using empirical data on client utilization and the first to evaluate the cost-effectiveness of PrEP/PEP provision via online pharmacy. We find that online PrEP/PEP can avert substantial HIV incidence with low population coverage and is cost-effective from the MOH perspective. Online PEP accounts for most of the intervention health benefits, due to the high observed PEP demand in empirical data.

Implications of all the available evidence

Online PrEP/PEP provision has the potential to efficiently increase coverage of biomedical prevention in Kenya and similar settings. PEP is an underused prevention tool at high demand that can complement PrEP scale-up. Policymakers could consider integrating PEP and PrEP in differentiated delivery models and consider public/private partnerships to maximize reach of HIV prevention in the context of constrained budgets and donor transition.

INTRODUCTION

Both oral pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) are promising HIV prevention strategies that can be scaled up to reduce HIV incidence in ESA. Daily oral PrEP is >90% effective when used with high adherence and PEP is 90-95% effective if initiated ≤48 hours after potential HIV exposure[1]. Oral PrEP has been recommended by the World Health Organization (WHO) for persons at substantial HIV risk since 2015 and many ESA countries have rolled out PrEP in clinics. However, clinic-based PrEP uptake and continuation is low in ESA, with clients citing barriers including travel distance, wait times, stigma, privacy concerns, and limited operating hours[2]. Similarly, PEP availability is generally limited to clinics and uptake is low. The WHO recommends differentiated, community-centered delivery of HIV biomedical prevention with task-shifting to increase accessibility. Studies show PrEP provision in community-based settings including pharmacies achieves high uptake and reaches individuals not accessing clinic-based services[3,4]. Modeling studies have found community-based PrEP and PEP is cost-effective in ESA.[5,6]

Leveraging online pharmacies for oral PrEP/PEP provision (online PrEP/PEP) is a novel strategy that can expand HIV prevention coverage by providing convenient and discreet community-based services. Online pharmacies offer direct-to-consumer delivery of medications, health products, health information, and telehealth consultations. Telehealth services have grown rapidly in ESA with increasing internet availability and cell phone ownership; growth was expedited by the COVID-19 pandemic during which HIV services were successfully delivered remotely. The ePrEP Kenya pilot study recently evaluated the first model of online pharmacy-based PrEP/PEP delivery in ESA[7,8]. The model entails clients having remote consultations with clinical providers to ensure PrEP/PEP eligibility/safety, ordering courier-delivered HIV self-test (HIVST) or provider-administered HIV test (to verify HIV-negative status), receiving HIV drugs delivered at home/convenient location, and having access to virtual user support. The pilot found online pharmacy-based PrEP/PEP was feasible and acceptable to clients and providers and reached PrEP naïve populations at HIV risk[9,10]. Additionally, clients were willing to pay (WTP) for PrEP/PEP services[11]. Online PEP was particularly in demand, with 5 times as many clients accessing PEP compared to PrEP, and clients choosing repeat PEP over transitioning to PrEP[9]. The

observed preference for PEP over PrEP may be due to its event-driven nature, which is easier to align with potential HIV exposures compared to PrEP which necessitates anticipation of future condomless sex. Given the importance of timely PEP initiation, online pharmacies may be particularly well suited to delivering PEP within the effectiveness window due to longer operating hours (including evenings and weekends); in the pilot, 96% of clients received drugs ≤72 hours of potential exposure[9]. Online pharmacies can also be leveraged to provide long-acting products in the pipeline including monthly oral PrEP.

Estimating the health and economic impact of online PrEP/PEP provision is essential to informing policy decisions regarding scale-up. Online PrEP/PEP service delivery will likely require partnerships between private and government sector agencies since PrEP/PEP drugs are often provided by Ministries of Health (MOH) while service delivery costs are generally paid by the pharmacy (and charged to clients). Private/public partnerships to distribute government commodities (i.e. PrEP/PEP drugs) are likely efficient strategies, particularly in an era of reduced HIV donor funding. In this analysis, we estimate cost-effectiveness of online PrEP/PEP from the Kenya MOH perspective utilizing costs and PEP/PrEP uptake by demographics and sexual behavior from the ePrEP Kenya pilot. To our knowledge, this is the first study to estimate online PrEP/PEP cost-effectiveness and the first to assess PEP cost-effectiveness using primary data on client characteristics.

METHODS

ePrEP Kenya Pilot

We utilized costs and PrEP/PEP uptake data from the ePrEP pilot conducted in Nairobi and Mombasa counties[9,12]. Briefly, this single arm pilot was conducted from 10/2022-12/2023 in collaboration with MYDAWA, Kenya's first online pharmacy. Eligible clients were ≥18 years, identified at HIV risk, and willing to pay for HIV testing (~US$2 for HIVST or ~US$1 for provider-administered testing) and courier delivery of HIV testing and PrEP/PEP drugs (~US$1/delivery)[11]. Online PrEP/PEP was advertised on MYDAWA's website on the sexual wellness page; interested individuals clicked the ad and self-screened for HIV risk. Eligible clients attended telehealth visits with online pharmacy healthcare providers and received counseling and screening for PrEP/PEP. Clients were prescribed PEP if they reported potential HIV exposure ≤72 hours, or PrEP if reporting

ongoing HIV risk. Clients had HIV testing courier-delivered to their setting of choice to verify HIV-negative status and received courier-delivered PEP (28-day supply) or PrEP (30-day supply at initiation, 90-day at follow-up).

Overall, 88% of enrolled individuals (N=1,757) received online PEP and 12% received PrEP. Most clients were male (64%) and ≥25 years old (72%)[9] **(Table 1)**. Clients reported high prevalence of behaviors associated with HIV acquisition: 65% of PrEP and 46% of PEP clients reported multiple concurrent sexual partners in the past three months and 74% of PrEP and 89% of PEP clients reported partners with unknown HIV status. PrEP continuation was 47%; just 6% of PEP clients transitioned to PrEP and 6% of PrEP clients initiated PEP after discontinuing PrEP[9].

Mathematical model

We adapted a network-based model, EMOD-HIV,[13] which incorporates population demographics, HIV natural history, and heterosexual HIV transmission, configured to match age- and sex-specific sexual relationship patterns. The model includes an HIV care cascade with HIV testing, linkage and retention in care, and a PrEP cascade with uptake, adherence, persistence, and re-initiation.[14] We modified the model to incorporate a PEP cascade and assumed individuals can seek PEP after condomless sex with non-marital partners.[5] The model, parameterized with empiric data from western Kenya, included fertility, mortality, voluntary male circumcision coverage, and number of persons on oral PrEP (Tables S3a-S9b) and calibrated to data on HIV prevalence and ART coverage. We conducted the modeling using 100 good-fitting model parameter sets over monthly time-steps.

Scenarios

In the baseline (no online PrEP/PEP) scenario, we assumed background daily oral PrEP use at currently observed levels among individuals age 15-49 years with HIV risk indication[15]. We assumed oral PrEP decreased HIV acquisition risk by 75% based on clinical trials accounting for average adherence and assumed three-month PrEP persistence based on real-world studies[16]. In intervention scenarios, online PrEP and PEP was implemented from 2026-2036 to evaluate the impact of a ten-year delivery; we utilized a 35-year time horizon (2026-2060) to estimate long-term outcomes and cost-effectiveness.

For intervention scenarios, we calibrated the model to fit primary data from online PrEP and PEP clients separately by age, sex, and sexual behavior in each subgroup (multiple partners, concurrent partners, serodiscordant relationships) (Table S1c and S1d). We parameterized the model with PrEP continuation, PEP-to-PrEP transition, and relative uptake of PEP vs. PrEP from the pilot.

For the online PrEP cascade, eligible individuals first completed HIVST to verify negative status; those testing HIV-positive were assumed to link to ART at background rates. Persons testing HIV-negative received one-month supply of PrEP and had 30% probability of returning for three-monthly PrEP refills thereafter, (resulting in mean PrEP duration of 2.2 months, consistent with the pilot). Individuals completed HIVST at each refill visit. PrEP discontinuation occurred due to loss-to-follow-up or if eligibility criteria were no longer met. We assumed online PrEP had the same adherence-adjusted PrEP effectiveness as background PrEP (75%).

For the online PEP cascade, persons had a probability of initiating PEP after condomless sex with a non-marital partner (based on their age-sex-risk behavior). We assumed 95% PEP effectiveness based on a modeling study using pharmacokinetic and viral dynamics which estimated that three drug PEP regimen (tenofovir, lamivudine, and dolutegravir) was >95% effective if taken daily for ≥28 days within 48 hours of exposure. Based on the pilot, we assumed 6% of PrEP eligible PEP users transitioned to PrEP[9]. Individuals who discontinued PrEP or PEP could re-initiate at the same rate if they met eligibility criteria.

Sensitivity analyses

To isolate the health and economic impact of PEP, we ran a scenario of only online PEP provision (without PrEP). We also lowered PEP efficacy to 75% to assess impact of reduced adherence or initiation ≤72 hours after exposure (instead of <48 hours in main scenario). To understand impacts of anticipated novel long-acting PrEP/PEP products, we evaluated scenarios replacing daily oral PrEP with MK-8527 (monthly oral pill in clinical trials) for both online PrEP and PEP. We also assessed impacts of potential future PEPFAR funding disruptions: we evaluated one scenario in which HIV testing was reduced by 41% and a second in which both HIV testing and ART coverage was reduced by 41%, based on assumptions from a previous modeling analysis

(PEPFAR accounts for 41% of Kenya's HIV budget)[17]; we evaluated a third scenario in which the MOH covers 50% of funding gaps from PEPFAR interruptions, resulting in 20.5% reduction in HIV testing and ART. Finally, to assess impacts of our targeting assumptions, we conducted sensitivity analyses assuming all individuals with non-marital partners were eligible for PrEP and PEP and had the same initiation probability. We varied PEP coverage from low to high levels to assess the relationship between targeting and coverage on health benefits and cost-effectiveness.

Model outcomes

For intervention scenarios, we estimated HIV infections, HIV-related deaths, DALYs averted compared to counterfactual of background oral PrEP only. PrEP and PEP coverage was calculated as the number of person-months on PrEP or PEP divided by the population person-months during the analysis period. We also assess repeat PEP use by client characteristics. We calculated 95% uncertainty intervals across 100 parameter sets to assess uncertainty. Model outputs were analyzed in R version 4.5.1.

Cost-effectiveness and budget impact analysis

We conducted the economic evaluation from the Ministry of Health (MOH) perspective, assuming online pharmacy PrEP/PEP provision was implemented via public/private partnership in which the MOH provides PrEP/PEP drugs while the online pharmacy charges clients to cover HIV testing and service delivery costs. This is consistent with the current online pharmacy PrEP/PEP delivery model via MYDAWA in which clients are charged ~US$6 for services[18]; client volume remained stable after the end of the online PrEP/PEP pilot study and implementation of the payment model (Supplement Section 1.3)[18]. In addition to PrEP/PEP drugs, we assumed the MOH incurred costs of background HIV testing, ART, and HIV-related hospitalizations. Due to uncertainty in future MK-8527 costs, we varied per-pill costs from $2.88, $5.76, and $11.52, which accounts for pill price plus 15% supply chain mark-up. For cost-effectiveness analyses, we discounted costs and health outcomes by 3% annually and utilized a commonly referenced supply-side threshold of US$500/DALY averted[20]. We also estimated the undiscounted ten-year budget impact of online PrEP/PEP from the MOH perspective.

Role of the funding source

The funders had no role in study design, data collection, data analysis, interpretation, or writing of this paper.

RESULTS

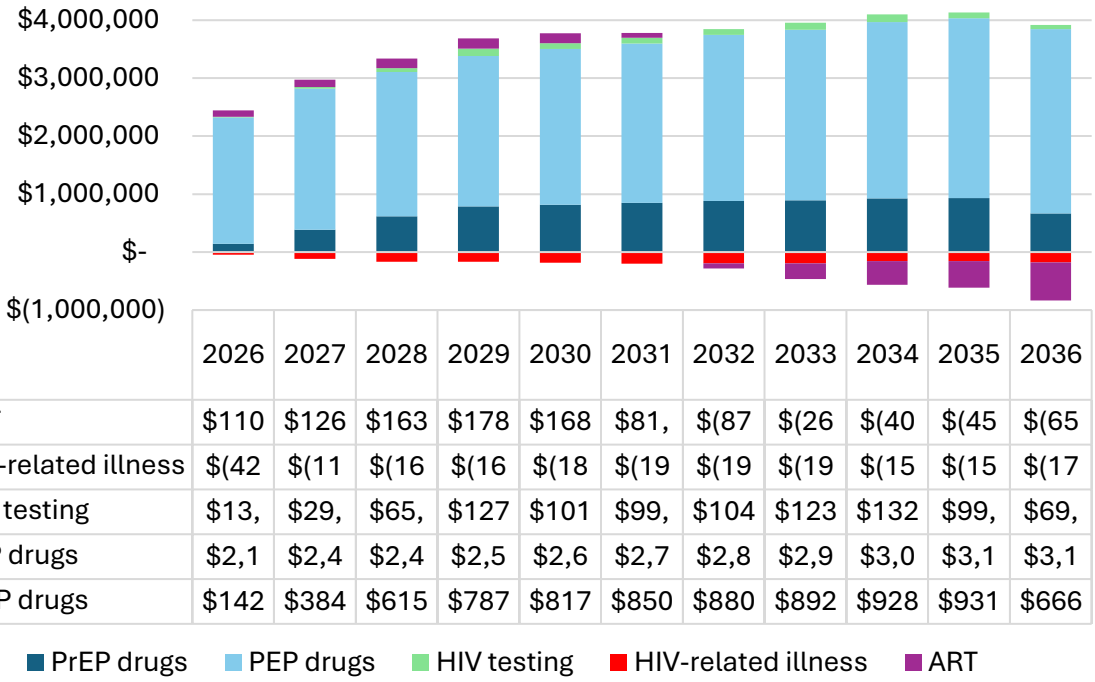
Modeled intervention scale-up to the eligible target population resulted in population coverage of 0.7% for online PEP and 0.3% for online PrEP (Table 3). In the main scenario, online PEP/PrEP provision was projected to reduce HIV infections by 13.9% over ten years of implementation. HIV related deaths were reduced by 4.3% over the 35-year time horizon. The intervention resulted in 4.4 and 1.62 million doses of PEP and PrEP, respectively. Most modeled online PEP clients used PEP once (51-82%) while a smaller proportion initiated twice (16-27%). Repeat PEP use was most common in women aged 25-49 years (Table S13c). The main scenario had an ICER of $212/DALY averted from the MOH perspective (i.e. only including intervention costs of PrEP/PEP drugs and supply chain). When isolating the impact of PEP (scenario with only online PEP availability), coverage of biomedical prevention was reduced by 30% compared to the main scenario (i.e. 0.7% PEP and 0.3% PrEP in the main scenario vs. 0.7% in PEP only) but health benefits were reduced by only 12-15% (e.g. HIV infections 13.9% in main scenario vs 11.6% in PEP only); the ICER was similar to the main scenario ($210/DALY averted).

Most sensitivity analyses yielded findings consistent with the main scenario. Assuming higher PrEP adherence-based effectiveness (95% vs. 75%), resulted in slightly higher health benefits (14.2% of HIV infections averted) and lower ICER: $178/DALY averted. Conversely, assuming lower PEP effectiveness (75% vs. 95%), slightly reduced health benefits (12.5% infections averted) and increased the ICER to $260/DALY averted. In PEPFAR funding reduction scenarios, the intervention had greater health benefits and more favorable ICERs, particularly assuming 41% reduction in both HIV testing and ART; online PrEP/PEP averted 5-times more DALYs than the main scenario and was cost-saving; the intervention remained cost-saving assuming the MOH would cover 50% of funding gaps (Table S10). Evaluating a theoretical full payer scenario which includes all costs (incurred by MOH, online pharmacy, and client) resulted in a higher ICER of $771/DALY averted. Assuming online pharmacies replaced daily oral PrEP and PEP with monthly oral MK-8527 resulted in similar health impacts as the scenario with PrEP at 95% effectiveness and was cost-

saving at MK-8527 costs of $2.88/pill. MK-8527 remained cost-effective at per-pill costs of $5.76 (ICER: $269/DALY averted) but exceeded the cost-effectiveness threshold at higher costs of $11.52/pill (ICER: $1231/DALY averted) (Table S12). Assuming uniform PrEP/PEP uptake among all individuals with a non-marital partner resulted in lower health benefits and higher ICER than the main scenario; for example, at online PrEP and PEP coverages of 0.3% and 0.6% respectively, the intervention averted 8.8% of HIV infections and had an ICER of $440/DALY averted. Higher coverages of uniform targeting increased health benefits but had higher ICERs (Table S11b). Additional results (number of HIV infections and deaths averted, 35-year incremental costs, etc.) are presented in Tables S13a-S13d, and Figures S5-S8.

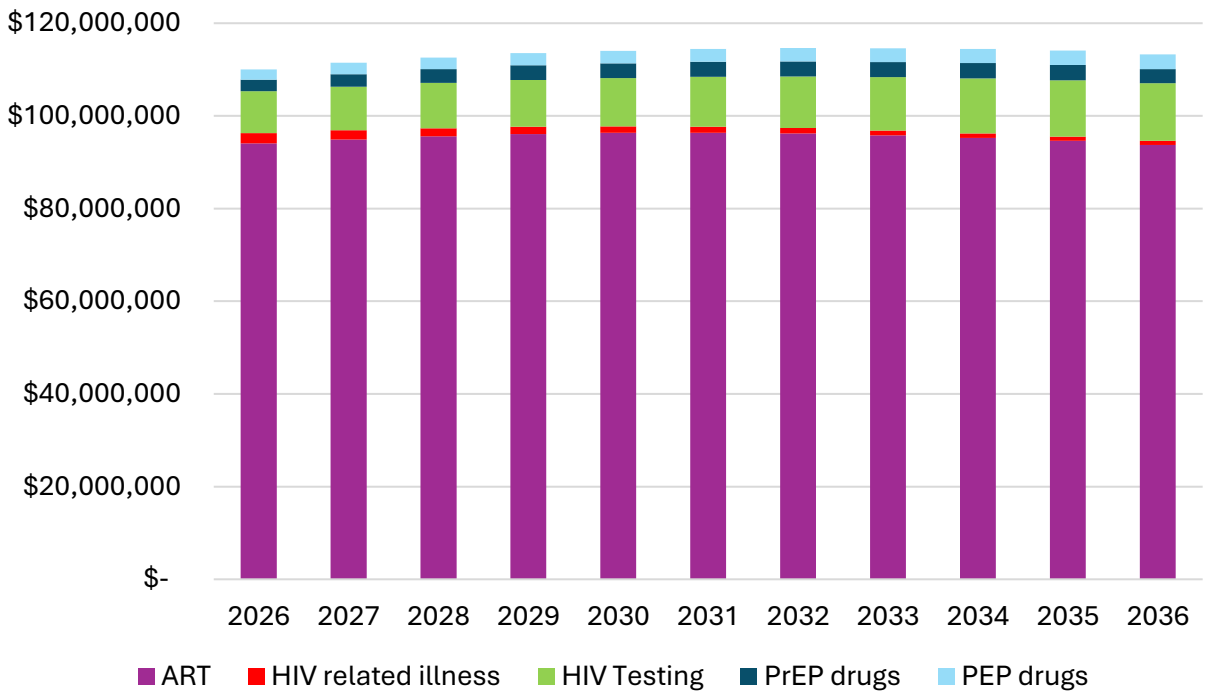
From the MOH perspective, the annual budget impact of implementing online PrEP/PEP ranged from $2.5-3.5 million assuming a modeled population of 6.3 million adults (**Figure 1**). Costs increased in the first 3 years as the intervention was scaled up; PEP drugs made up most costs (77%) with PrEP drugs accounting for 20%. In initial years, the intervention increased ART costs as persons with HIV were identified through HIV testing for PrEP/PEP initiation and linked to care; however, in later years (2032 onwards) cost savings in ART and HIV related illness increased due to averted HIV infections and increased over time. Although PEP drugs were the largest contributor to budget impact, the highest total costs were attributable to ART provision (~84% of total) (**Figure 2**).

Figure 1.



	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036
ART	$110	$126	$163	$178	$168	$81,	$(87	$(26	$(40	$(45	$(65
HIV-related illness	$(42	$(11	$(16	$(16	$(18	$(19	$(19	$(19	$(15	$(15	$(17
HIV testing	$13,	$29,	$65,	$127	$101	$99,	$104	$123	$132	$99,	$69,
PEP drugs	$2,1	$2,4	$2,4	$2,5	$2,6	$2,7	$2,8	$2,9	$3,0	$3,1	$3,1
PrEP drugs	$142	$384	$615	$787	$817	$850	$880	$892	$928	$931	$666

Figure 2.



DISCUSSION

In this analysis, we evaluated the health and economic impact of providing PrEP/PEP via online pharmacies in western Kenya. We find that low coverage of biomedical prevention (1%) can have substantial impact on HIV incidence and is cost-effective from the MOH perspective. Online PEP was responsible for the majority of intervention health benefits, due in part to high observed demand for PEP compared to PrEP from the pilot data used for model parameterization. Further, online PrEP continuation and PEP-to-PrEP transition were low in the pilot, with some clients with ongoing HIV risk opting for repeat PEP rather than PrEP. These findings are consistent with the PrEP literature which demonstrates low uptake and continuation of PrEP in both facility and community settings, despite considerable efforts to expand PrEP coverage[21,22]. One reason may be that PrEP uptake relies on anticipating potential future risks and engaging in proactive prevention while PEP is sought reactively after a risk has occurred. Motivation for seeking HIV prevention may be higher after potential HIV exposure compared to future hypothetical risks. Additionally, the cost-effectiveness of PrEP depends on its alignment with HIV risk, which may be more difficult for individuals to predict, while PEP use is, by definition, aligned with potential HIV exposure. Our findings are consistent with previous modeling analyses that find community-

based PEP provision is cost-effective[5]. Further research is needed to evaluate impacts of repeat PEP use and identify contexts in which it may be more appropriate than PrEP. Our results suggest that repeat PEP use may be beneficial to a substantial minority of clients, particularly women ≥25 years old.

Online PrEP/PEP remained cost-effective from the MOH perspective across sensitivity analyses. In PEPFAR funding reduction scenarios, online PrEP/PEP became more cost-effective due to higher background HIV incidence and lower ART coverage; assuming PEPFAR disruptions to both HIV testing and ART resulted in the intervention being cost-saving and averting substantially more HIV burden than the main scenario. Introduction of low-cost monthly oral MK-8527 increased intervention health benefits and cost-effectiveness. Anticipated long-acting formulations can overcome barriers associated with daily pill taking including stigma and adherence issues. Studies show a strong preference for long-acting PrEP over daily pills in both the general and key populations in ESA[23].

Telehealth is a promising strategy to increase biomedical prevention coverage in ESA. Online PrEP/PEP can provide greater convenience, privacy, and autonomy; longer operating hours and weekend availability make online pharmacies well-suited for PEP delivery, which requires timely provision to maximize effectiveness. Online pharmacies are rapidly growing in ESA and reach clients seeking discreet access to sexual health products, including emergency contraception and HIVST, who may be at risk for HIV. The online PrEP/PEP pilot found that clients had a high prevalence of sexual behaviors associated with HIV risk, indicating that the intervention reached those at substantial HIV risk.

PrEP/PEP delivery via online pharmacies has two important caveats. One, it largely reaches individuals at higher socioeconomic status with computer/smartphone literacy and internet access. While this platform can expand PrEP/PEP coverage to Kenya's growing middle class, other community-based modalities are needed to serve individuals with lower socioeconomic status. However, we found that the intervention can achieve cost-effective reductions on HIV burden with low population coverage and therefore may be used alongside other strategies to optimize biomedical prevention coverage. The second caveat is that online PrEP/PEP is cost-effective to the MOH when delivered through a private/public partnership in

which the MOH pays for drugs and supply chain while remaining costs are borne by the online pharmacy and clients. In a full theoretical payer perspective, the intervention exceeded the cost-effectiveness threshold. However, we observed high demand for online PrEP/PEP in the pilot in which clients were charged for HIVST and delivery of testing and drugs. Additionally, MYDAWA has continued online PrEP/PEP provision outside of the pilot and did not experience reductions in client volume after implementing a client fee of US$7.[18] This amount is consistent with client reported WTP in the pilot as well as another large survey (N=772) among individuals with HIV risk reporting interest in online PrEP/PEP recruited via MYDAWA's website. With the changing global HIV funding landscape, innovative strategies are needed that maximize shrinking health budgets to effectively deliver treatment and prevention. Leveraging private retailers, including online pharmacies, can reach clients who are willing to pay for greater discretion and convenience while freeing up funds for higher cost community-based strategies to reach those at lower socioeconomic status. These partnerships can also benefit online pharmacies by expanding their customer base to clients who may purchase other products. However, additional studies outside of Kenya are needed to understand the uptake and performance of online PrEP/PEP in other ESA countries. Financial and market analyses are also warranted to assess feasibility, demand, and financial costs in diverse contexts. Further, the health and cost impact of online PrEP/PEP is contingent on the scale achieved; if demand is lower than projected, health impacts will likely be smaller and relative costs higher per client since fixed costs would be spread over a lower client volume.

Our analysis has several limitations. We utilized data from a single pilot conducted in Nairobi and Mombasa, so our results may not be generalizable outside urban areas of Kenya. Additionally, data from one study may not be representative of online PrEP/PEP utilization patterns. Similar to previous modeling analyses, our results are sensitive to assumptions regarding PrEP/PEP uptake among those at substantial HIV risk. However, results from brick-and-mortar pharmacy-based PrEP/PEP studies in Kenya show similar sexual behavior and high demand for PEP relative to PrEP[24]. Additionally, prior studies from ESA find that making biomedical prevention widely available results in substantial population-level HIV incidence reduction despite low coverage, suggesting that individuals aligned PrEP use with periods of HIV risk.

Second, our model only simulates heterosexual HIV transmission; therefore, we cannot evaluate online PrEP/PEP's impact on men who have sex with men (MSM) or persons who inject drugs. Indeed, the pilot study showed a considerable number of PrEP users were MSM (28%), although only 3% of PEP users reported being MSM; our analysis likely underestimates the intervention's health impact and cost-effectiveness by not including this subgroup. Third, we do not have empiric data on online PrEP adherence, so we utilized estimates from PrEP implementation studies. However, results were robust to sensitivity analyses. Further, findings were mainly driven by PEP assumptions since it reached substantially higher coverage than PrEP. Additionally, most clients accessing online PEP in the pilot study reported potential HIV exposure through consensual condomless sex; few reported sexual assault or occupational exposure—which has historically been the focus of clinic-based PEP provision in ESA. Therefore, other PEP delivery modalities remain important for these indications.

Strengths of this analysis include using a network model and assessing uncertainty across 100 parameter sets. To our knowledge, this is the first modeling analysis to evaluate PEP scale-up using monthly time steps to align with HIV risk exposure and empiric data on PEP use by age-sex and sexual behavior from a real-world implementation study.

Overall, we found that PrEP/PEP provision via online pharmacies in Kenya can achieve substantial HIV incidence reductions at low population coverage and is cost-effective from the MOH perspective. Our findings can inform policy decisions regarding scale-up of biomedical prevention in an era of shrinking donor funding.

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AUTHOR CONTRIBUTIONS

All authors contributed to the conceptualisation of the analysis, provided substantive input into the modeling plan, advised on relevant data, interpreted results, and commented on manuscript drafts. YC, AS, CP, TK, KN, and KO collected and analysed the empiric data utilised for model inputs. AM, NP, CA, and DK conducting the modeling analysis. MS wrote the first draft of the manuscript with input from all the authors. AM, CA, and NP accessed and verified the data. All authors had full access to the data, read and approved the manuscript, and had final responsibility for the decision to submit for publication.

CONFLICT OF INTEREST

DK reports consulting fees from University College London and Massachusetts General Hospital. KN reports receiving support to attend International AIDS Society (IAS) conferences and meetings and is a member of the Executive Board and President-Elect of the IAS. All other authors report no conflicting interests.

DATA SHARING

Data used for the modeling can be found in the supplementary text. EMOD-HIV is open-source and publicly available: https://docs.idmod.org/projects/emod-hiv/en/2.20_a/.

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Fig 1. Budget impact analysis. Budget impact of implementing online PrEP/PEP from the Ministry of Health perspective. Categories falling below the y = 0 line indicate cost savings. Values in parenthesis indicate cost-savings.

Fig 2. Total costs. ART: antiretroviral therapy; PrEP: pre-exposure prophylaxis; PEP: post-exposure prophylaxis.

TABLES

Table 1: Characteristics of clients in the online PrEP/PEP Kenya pilot

	PrEP (n=208)	PEP (N=1549)
Demographics		
Age: Median [IQR]	28 [25,34]	27 [24,33]
Age ≥ 25 years	154 (74%)	1119 (72%)
Sex: *Male*	155 (75%)	966 (62%)
Married	24 (12%)	196 (13%)
Behaviours associated with risk of HIV acquisition		
In the past 6 months		
Multiple concurrent sexual partners	136 (65%)	716 (46%)
Partner(s) of unknown HIV status	153 (74%)	1384 (89%)
Partner(s) living with HIV	24 (12%)	42 (3%)
Transactional sex	6 (3%)	41 (3%)

Table 2: Model parameters, assumptions, and cost inputs [¥]

Model assumptions	Value	Source
Oral PrEP effectiveness	75%	Baeten 2012 [25]
PEP effectiveness	95%	Zhang 2024[1]
Online Pharmacy PrEP scaleup period	2026 – 2029	Assumption
Online Pharmacy PrEP/PEP implementation period	2026 – 2035	Assumption

Analytic time horizon	2026 – 2060	Assumption
Costs (MOH perspective)		
PrEP drugs (30-day supply)	$4.92	Chen 2025[19], Includes 15% supply chain costs07/05/2026 12:19:00
PEP drugs (28-day supply)	$6.94	Chen 2025[19]. Includes 15% supply chain costs
monthly oral MK 8527 (per pill)	$2.88	Assumed at $2.50 per pill + 15% supply chain costs
Background facility-based oral PrEP (monthly)	$10.88	Wanga 2021[26]
Annual health care costs (among PLHIV not on ART)		
CD4 < 200	$110.30	Eaton 2014 [27]
CD4 200 - 349	$30.38	Eaton 2014 [27]
CD4 > 350	$8.59	Eaton 2014 [27]
End of life care	$105.68	Eaton 2024 [27]
ART provision (annual)	$196.85	Larson 2018 [28], Long 2010 [29], The Global Fund [30], and Haas 2015 [31]
Facility-based HIV-positive test	$3.68	Meisner 2021[32] 5/7/2026 12:19:00 PM
Facility-based HIV-negative test	$2.64	Meisner 2021[32]
Costs (online pharmacy perspective)		
HIVST	$4.05	Chen 2025[19]
Costs (client perspective)		
HIVST delivery fee	$1	Chen 2025[19]
PrEP/PEP drug delivery fee	$1	Chen 2025[19]

¥PrEP: pre-exposure prophylaxis, ART: antiretroviral therapy. Costs are adjusted for inflation and GDP per capita ratio where applicable (Supplementary Text, Section 1.2). ART costs are of

delivery costs and assume 3% of patients receive 2nd-line ART. Additional details on costing methods are available in the Supplementary Text.

Table 3: Heath and economic impact of PrEP/PEP delivery via online pharmacies in Kenya

	Main scenario	Only online PEP available (no online PrEP)	Higher PrEP effectiveness (95%)	Lower PEP effectiveness (75%)	PEPFAR reduction: Lower HIV testing	PEPFAR reduction: lower HIV testing and ART	Main scenario with full payer perspective (theoretical)
PEP coverage (%)	0.7% (0.7% - 0.8%)	0.7% (0.7% - 0.8%)	0.7% (0.7% - 0.8%)	0.7% (0.7% - 0.8%)	0.7% (0.7% - 0.8%)	0.7% (0.6% - 0.7%)	0.7% (0.7% - 0.8%)
PrEP coverage (%)	0.3% (0.2% - 0.3%)	---	0.3% (0.2% - 0.3%)	0.3% (0.2% - 0.3%)	0.3% (0.2% - 0.3%)	0.2% (0.2% - 0.3%)	0.3% (0.2% - 0.3%)
PEP doses (millions)	4.40	4.52	4.41	4.40	4.39	4.28	4.40
PrEP doses (millions)	1.62	0.25	1.62	1.61	1.62	1.54	1.62
HIV infections averted (%)	13.9% (10.1% - 17.1%)	11.6% (8.6% - 15.2%)	14.2% (11.0% - 17.9%)	12.5% (9.0% - 16.2%)	13.7% (10.3% - 17.3%)	11.8% (9.0%, 14.0%)	13.9% (10.1% - 17.1%)
HIV deaths averted (%)	4.3% (2.0% - 6.9%)	3.8% (1.5% - 6.0%)	4.4% (1.7% - 6.3%)	4.2% (1.3% - 6.2%)	4.3% (2.3% - 7.1%)	4.6% (3.3% - 5.8%)	4.3% (2.0% - 6.9%)
DALYs averted	36,304	22,686	35,798	32,178	41,246	194,502	36,304

Incremental cost-effectiveness ratio (ICER)	$212 ($15 - $1409)	$210 ($41 - $3,798)	$178 ($22 – $1831)	$260 ($31 - $3,865)	$198 ($20 - $1671)	Cost saving	$771 ($250 - $4798)
5-year budget impact	$14.6M	$12.1M	$14.2M	$14.3M	$14.2M	14.0M	$23.2M

Health impacts are compared to the baseline scenario of daily oral pre-exposure prophylaxis only. HIV infections averted are reported for people aged 15–65 years over 10 years of PEP/PrEP implementation; deaths averted are calculated over the 35-year time horizon. PEP/PrEP coverage is reported for people aged 15–49 years over 10 years of implementation. Values in parentheses show 95% uncertainty intervals representing the 2·5th and 97·5th percentiles across 100 parameter sets. DALYs: disability-adjusted life-years.

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Supplemental Appendix accompanying the manuscript: "Health and economic impact of providing pre- and post-exposure prophylaxis via online pharmacy in Kenya"

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Section 1 | Interventions and Analysis Design

1.1 Intervention design

Summary of populations targeted and implementation scenarios

Table S1a. Target populations

Target population	Description
People with multiple concurrent partners	Individuals with 2 concurrent partners simultaneously.
People with more than 1 partner in the last 3 months	Individuals with 2 or more partners in the past 3 months.
Men and women in serodiscordant relationships and with multiple concurrent partners	Serodiscordant couples; persons aware their partner has HIV and is not on ART* and who have 2 concurrent partners.
Men and women in serodiscordant relationships and with more than 1 partner in the last 3 months	Serodiscordant couples; individuals who are aware their partner has HIV and is not on ART*. Additionally, these people have 2 or more partners in the last 3 months.

*We assume 50% of individuals with diagnosed HIV in a partnership disclose their status to their partners.

Table S1b: Probability of up-taking PrEP or PEP among eligible subgroups

	PrEP	PEP
AGYW with multiple concurrent partners	0.38%	0.60%
AGYW with >1 partners in the last 3 months	0.70%	1.06%
ABYM with multiple concurrent partners	0.90%	2.40%
ABYM with >1 partners in the last 3 months	1.28%	2.24%
Women with multiple concurrent partners	1.67%	3.79%
Women with multiple concurrent partners and in serodiscordant relationships	3.25%	-
Women with >1 partners in the last 3 months	2.90%	5.19%
Women with >1 partners in the last 3 months and in serodiscordant relationships	5.50%	-
Men with multiple concurrent partners	1.15%	3.50%
Men with multiple concurrent partners and in serodiscordant relationships	1.75%	-
Men with >1 partners in the last 3 months	1.50%	2.89%
Men with >1 partners in the last 3 months and in serodiscordant relationships	2.80%	-

Table S1c. PrEP uptake in the model compared to pilot study

Population	Pilot uptake	Model uptake
ABYM with multiple concurrent partners	10%	10%
ABYM with multiple partners in the last 3 months	8%	8%

AGYW with multiple concurrent partners	7%	6%
AGYW with multiple partners in the last 3 months	6%	6%
Men with multiple concurrent partners	28%	27%
Men with multiple concurrent partners and in serodiscordant relationships	3%	3%
Men with multiple partners in the last 3 months	13%	12%
Men with multiple partners in the last 3 months and in serodiscordant relationships	2%	4%
Women with multiple concurrent partners	10%	11%
Women with multiple concurrent partners and in serodiscordant relationships	2%	2%
Women with multiple partners in the last 3 months	10%	9%
Women with multiple partners in the last 3 months and in serodiscordant relationships	1%	2%

Table S1d. PEP uptake in the model compared to pilot study

Population	**Pilot uptake**	**Model uptake**
AGYW with multiple concurrent partners	4%	4%
AGYW with multiple partners in the last 3 months	7%	8%
ABYM with multiple concurrent partners	8%	8%
ABYM with multiple partners in the last 3 months	9%	9%
Women with multiple concurrent partners	10%	10%
Women with multiple partners in the last 3 months	15%	14%
Men with multiple concurrent partners	24%	25%
Men with multiple partners in the last 3 months	22%	21%
Relative uptake of PEP vs PrEP		

All populations	6.8x	6.4x

Definitions

Initiation: Start of a PrEP or PEP course by an eligible individual following screening and eligibility assessment.

PrEP or PEP use: Periods during which an individual is receiving PrEP or PEP , for PrEP this represents both initiation and continuation.

Coverage: total number of person-months on PrEP or PEP, divided by total population person-months during the analysis period.

Background HIV testing

Background HIV testing was assumed to be a provider-administered Ab rapid diagnostic test (RDT). Test sensitivity increased from 0.0% in the first 19 days of infection to 99.9% after 120 days of infection. These values were derived from a review of empiric data in the literature, including data from *Taylor et al* on the cumulative probability of a negative test result for a third- & fourth-generation HIV test at various time points in an HIV-positive individual[1]. We first calculated the inverse of cumulative probability to obtain the cumulative probability of a positive test result. To adjust for RDTs (as these were excluded from Taylor et al. 2015), we shifted the inverse cumulative probability 10 days forward. Finally, we made an adjustment to Ab RDT at day 45 by using mean of day 30 and 60 (0.865 vs. 0.950). See Cox, Wu et al 2024 for additional information on test sensitivity parameterization in this model[2].

Table S2. Assumed RDT sensitivity

Day from exposure:	0-18.9	19-21.9	22-29.9	30-44.9	45-59.9	60-89.9	90-119.9	120+
Ab RDT sensitivity:	00.0%	20.0%	37.0%	78.0%	86.5%	95.0%	97.0%	99.9%

PEP provision

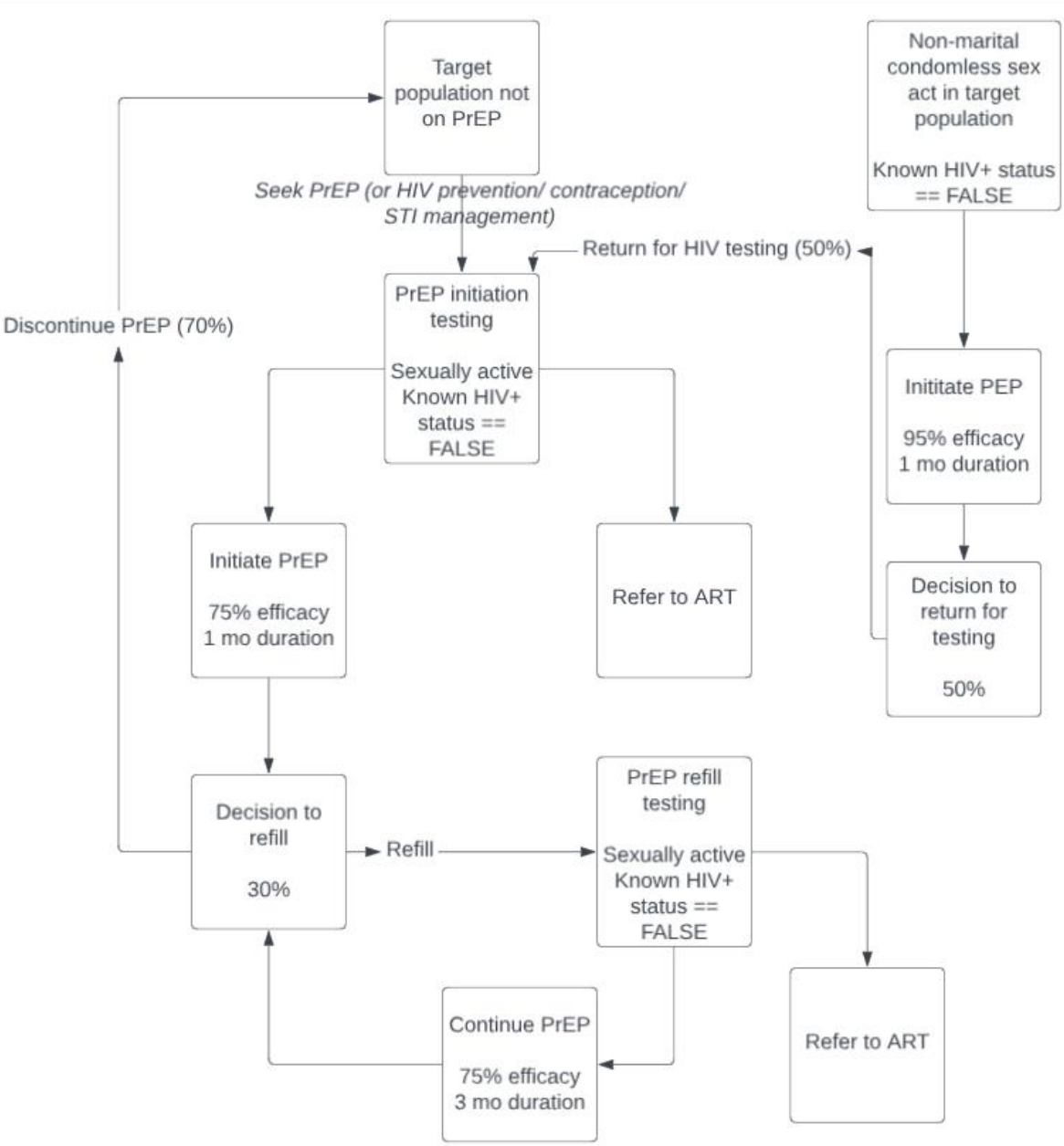
PEP was modeled as a 1-month regimen with 95% efficacy, initiated by a proportion of those in the target population with a recent non-marital condomless sex act and not known to be HIV-positive. Clients initiated PEP after the exposure (26 hours median time from exposure to PEP initiation reported in the pilot study)[3]. After completing the 1-month PEP course, individuals had a 50% probability of returning for follow-up HIV testing. Those who tested positive were referred to ART, those who tested HIV-negative could transition to PrEP at the rates observed in the pilot if they met eligibility criteria.

In EMOD-HIV, PEP is implemented using the ControlledVaccine intervention class. When a PEP-eligible coital act occurs within a monthly time step, it can trigger PEP distribution, based on the modelled person's probability of seeking PEP which we set to be dependent on individual's demographics and sexual behavior. PEP distribution reduces the individual's likelihood of acquiring HIV within the time step. It acts as an acquisition-blocking intervention that prevents the person from getting infected during the timestep when PEP is distributed rather than curing an infection after it occurs.

PrEP provision

Individuals without known HIV and who tested HIV-negative initiated PrEP (30 day supply with 75% efficacy). After 30 days, individuals had a 30% probability returning for a PrEP refill; those testing HIV-negative and had at least one sexual partner received PrEP (3-monthly supply). Individuals who tested HIV-positive via the PrEP cascade were assumed to link to ART.

Figure S1. Schematic depicting model implementation of e-PEP and PrEP delivery



1.2 Cost approach and calculations

Service delivery model: We assume a public/private partnership cost-sharing model for ePharmacy-based PrEP and PEP delivery with pharmacy costs partially offset by client fees. We assumed the Ministry of Health (MoH) incurred costs for PrEP and PEP drugs, ART, HIV-related

hospitalizations, and HIV-related deaths. All over service delivery costs including pharmacy staff salaries and benefits, demand generation, clinical consultations, microplanning and training, user support, vehicles, equipment, fuel, and utilities were incurred by the ePharmacy. Detailed breakdown of these costs from a microcosting of the pilot study have been reported (Chen et al., 2025)[4]. Clients are assumed to pay for HIV self-test kits ($4.05 per kit) and a $1 delivery fee for HIVST or drug delivery. In a willingness-to-pay study (Montano et al., 2025), current and potential ePharmacy clients reported willingness to pay an additional $7 for a bundled HIV prevention package (excluding delivery and HIV testing costs)[5].

Perspective for economic evaluation: Cost-effectiveness was evaluated from the Ministry of Health perspective. Costs borne by the epharmacy and clients were excluded from the economic evaluation.

Cost sources and adjustments: Cost estimates were derived from the published literature. Estimates for some components (e.g., RDT costs) varied widely among published studies, and in these cases, we prioritized studies based on geographic relevance, recency, sample size, and methodology. For all studies conducted prior to 2017, we adjusted for inflation to 2021 US$ using World Bank inflation estimates[6]. For all studies which collected data in a country besides Kenya, we adjusted the estimates by taking a ratio of the GDP per capita of the two countries to approximate the differences in purchasing power parity between the two settings, since PPP or health-specific CPIs were not reliably available in these settings[6,7]. We discounted costs and health outcomes by 3% annually.[8]

Table S2. Cost parameter calculations [¥]

Cost Parameter	Estimate (US$)	Year [†]	Data source	Calculation details, notes
Annual health care costs (among those not on ART)				
HIV-positive CD4 < 200	110.30	2021	Eaton[9]	Adjusted for inflation and GDP/capita ratio using this approach: Step 1: Adjust South Africa value in 2012 US$ for inflation to be in 2021 US$ ($374.08 = $167*2.24) ● Cost of health care use, CD4 count <200 cells per µL, not in HIV care (per person-year) in South Africa= $167 ● US$ Inflation Rate between time of costing (2012) and 2021: 2.24 =4.7/2.1 Step 2: Adjust South Africa 2021 US$ value by multiplying by the Kenya GDP/cap ratio ($374.08*0.295) ● South Africa 2021 GDP per capita in US$ = 7,055; Kenya US$ = 2,082 ● Kenya GDP/ ZA GDP ratio adjustment: (2,082/7,055)= 0.295
HIV-positive CD4 200 - 349	30.38	2021	Eaton[9]	Adjusted for inflation and GDP/capita ratio (see steps above)
HIV-positive CD4 > 350	8.59	2021	Eaton[9]	Adjusted for inflation and GDP/capita ratio (see steps above)
End of life care	105.68	2021	Eaton[9]	Adjusted for inflation and GDP/capita ratio (see steps above)

Annual ART provision costs	140.89	2021 / 2016	Phillips[10] , Larson[11] , Global Fund[12]	Includes 20% mark up on ART drug costs to account for supply chain (2021 US$). ART delivery costs are from an in-country micro-costing study and include lab tests and staff encounters (2016 US$). Step 1: Calculate annual ART cost accounting for 20% supply chain cost mark-up ($57.89= $48.24*1.2) ● Monthly ART cost (per pack, 30 for Dolutegravir/Lamivudine/Tenofovir 50/300/300mg tablet)= $4.02 ● Annual ART cost= $48.24= $4.02*12 ● 20% supply chain cost mark-up= *1.2 Step 2: Calculate total cost of ART delivery ($83=45+38) and add to Step 1 ● $45 lab costs ● $38 staff encounters
Cost of 30 days of PrEP medication	4.92	2025	Chen[4]	-
Cost of 30 days of PEP medication	6.94	2025	Chen[4]	-
Facility-based HIV-positive test	3.68	2017	Meisner[13]	Data from micro-costing study. Inputs include screening test kit, other supply costs, and personnel costs.
Facility-based HIV-negative test	2.64	2017	Meisner[13]	Data from micro-costing study. Inputs include screening test kit, other supply costs, and personnel costs.

Referral if the HIV test for PrEP initiation is positive	$0.31	2016 / 2022	Meisner[13], Mangale[14]	-

[¥]PrEP: pre-exposure prophylaxis, PEP: post-exposure prophylaxis ART: antiretroviral therapy. All HIV test, ART provision costs include personnel, overhead, and supplies.

[†]Inflation adjustment using data from the World Bank (% inflation, consumer prices), applied only if reference provides cost estimates for years prior to 2016.

1.3 Client volume data before and after pilot completion

Based on project volume data obtained from MYDAWA on September 18, 2025, client volumes were stable after the pilot ended and MYDAWA continued services and implemented additional client fees[15].

Figure S2.1 Monthly number of clients accessing MYDAWA's online PrEP and PEP services

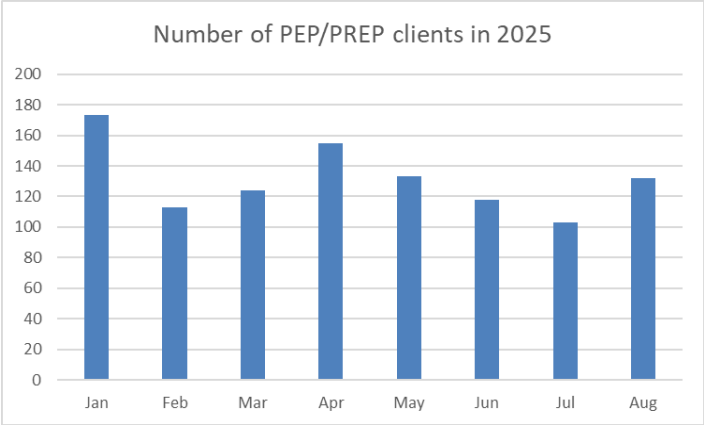


Figure S2.2 Number of MYDAWA online PrEP vs PEP clients

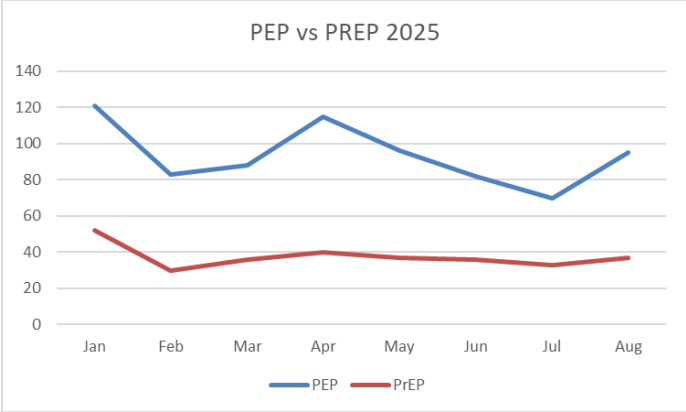
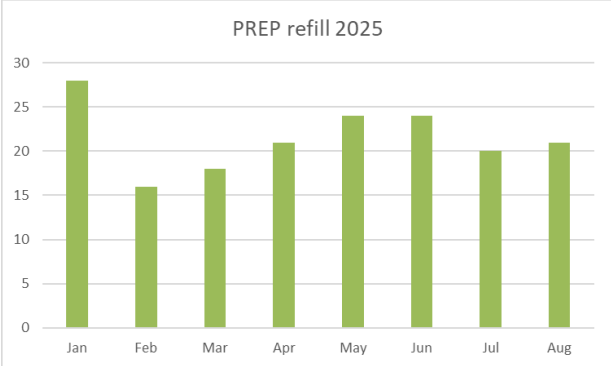


Figure S2.3 Number of online PrEP refills via MYDAWA



Section 2 | Model Calibration and Key Parameters

2.1 Model calibration to HIV parameters

Model calibration

Table S3a. HIV prevalence in counties of the former Nyanza province, by age and sex¥

Age group	2003		2007		2008		2012		2018	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
15 - 19	0.0015	0.0459	0.0121	0.0773	0.0184	0.1078	0.0151	0.0486	0.0025	0.0294
20 - 24	0.0562	0.2997	0.0257	0.2056	0.0578	0.1201	0.0289	0.1411	0.0216	0.0910
25 - 29	0.2429	0.2301	0.1956	0.2454	0.2450	0.2228	0.2107	0.2454	0.0705	0.2334
30 - 34	0.1840	0.1632	0.2578	0.2576	0.1530	0.2593	0.2392	0.2047	0.0911	0.2696
35- 39	0.2064	0.1838	0.2384	0.2227	0.2275	0.2259	0.1955	0.2811	0.1675	0.2705

40 - 44	0.2533	0.3500	0.2024	0.1799	0.2501	0.0927	0.3132	0.1694	0.2075	0.2765
45 - 49	0.1624	0.1651	0.2103	0.1291	0.1331	0.1716	0.1623	0.2287	0.2796	0.1991
15 - 49	0.1160	0.1830	0.1140	0.1760	0.1140	0.1600	0.1340	0.1760	0.0826	0.1667

[¥]**Sources:** Kenya Demographic and Health Surveys, 2003 & 2008; Kenya AIDS Indicator Surveys, 2007 & 2012; Kenya Population-based HIV Impact Assessment 2018. The counties of the former Nyanza province are Homa Bay, Kisii, Kisumu, Migori, Nyamira, and Siaya.

Table S3b. HIV prevalence among men and women ages 15-49, by county and gender[¥]

County	2003		2007		2008		2012		2018	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Homa Bay	0.1097	0.2458	0.2514	0.3259	0.1737	0.2524	0.2217	0.2787	0.1279	0.2532
Kisii	0.0114	0.0853	0.0445	0.0693	0.0330	0.0573	0.0346	0.0368	0.0458	0.0684
Kisumu	0.1663	0.1914	0.1139	0.1847	0.1109	0.1810	0.1940	0.2022	0.0960	0.2096
Migori	0.1804	0.1860	0.1685	0.2181	0.1923	0.2228	0.1435	0.1925	0.0706	0.1758
Nyamira	0.0029	0.0742	-	-	0.0234	0.0544	0.0419	0.1045	0.0247	0.0432
Siaya	0.1824	0.2424	0.1445	0.2130	0.1526	0.1921	0.2596	0.2990	0.0961	0.1905

[¥]**Sources:** Kenya Demographic and Health Surveys, 2003 & 2008; Kenya AIDS Indicator Surveys, 2007 & 2012; Kenya Population-based HIV Impact Assessment 2018.

Table S4. Number of people on ART by county, sex, and age group¥

Gender	County	Age group	Year													
			2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Men	Homa Bay	0 - 14	-	-	-	-	-	-	-	-	-	-	2,945	3,583	4,109	4,192
		15 - 99	1,067	2,313	5,148	7,194	10,002	14,436	17,178	15,954	17,522	18,279	19,157	22,834	26,441	29,220
	Kisii	0 - 14	-	-	-	-	-	-	-	-	-	-	828	993	1,109	1,083
		15 - 99	-	-	-	-	-	-	-	2,972	-	-	4,614	5,451	6,604	7,169
	Kisumu	0 - 14	-	-	-	-	-	-	-	-	-	-	3,101	3,245	3,525	3,607
		15 - 99	945	2,047	4,557	6,368	8,853	12,779	15,206	14,122	15,511	16,180	21,216	24,550	28,082	31,021
	Migori	0 - 14											2,309	2,295	2,678	2,673
		15 - 99	711	1,541	3,430	4,793	6,664	9,619	11,446	10,630	11,675	12,179	13,929	15,165	17,438	18,455
	Nyamira	0 - 14	-	-	-	-	-	-	-	-	-	-	484	552	578	611
		15 - 99	-	-	-	-	-	-	-	1,362	-	-	2,120	2,585	3,142	3,474
	Siaya	0 - 14	-	-	-	-	-	-	-	-	-	-	2,645	2,950	3,017	3,197
		15 - 99	860	1,864	4,148	5,797	8,060	11,633	13,843	12,856	14,120	14,730	16,163	18,611	21,477	23,762

Women	Homa Bay	0 - 14	-	-	-	-	-	-	-	-	-	-	3,431	3,835	4,426	4,535
		15 - 99	1,359	2,944	6,551	9,155	12,522	17,202	21,798	31,454	35,182	38,819	40,118	49,956	57,286	61,811
	Kisii	0 - 14	-	-	-	-	-	-	-	-	-	-	906	1,079	1,200	1,146
		15 - 99	-	-	-	-	-	-	-	7,902	-	-	11,691	14,350	17,274	19,044
	Kisumu	0 - 14	-	-	-	-	-	-	-	-	-	-	3,241	3,393	3,810	3,831
		15 - 99	1,203	2,606	5,799	8,104	11,084	15,227	19,296	27,843	31,143	34,362	41,230	48,424	56,384	60,789
	Migori	0 - 14	-	-	-	-	-	-	-	-	-	-	2,526	2,448	2,868	2,884
		15 - 99	905	1,961	4,365	6,100	8,343	11,461	14,524	20,958	23,442	25,865	27,896	31,964	38,637	40,891
	Nyamira	0 - 14	-	-	-	-	-	-	-	-	-	-	506	567	601	622
		15 - 99	-	-	-	-	-	-	-	3,766	-	-	5,964	7,210	8,258	8,654
	Siaya	0 - 14	-	-	-	-	-	-	-	-	-	-	2,778	3,136	3,299	3,569
		15 - 99	1,095	2,372	5,279	7,377	10,090	13,862	17,566	25,347	28,351	31,281	33,911	39,853	44,892	48,808
Both	All	15-99	8,954	19,404	43,185	60,350	83,142	116,787	143,877	175,003	194,552	210,769	246,293	301,029	333,333	389,159

¥Source: Kenya Ministry of Health

Table S5. Circumcision status quo by county, age group, and year [¥]

	Homa Bay			Kisii			Kisumu			Migori			Nyamira			Siaya		
Year	10-14	15-24	25-49	10-14	15-24	25-49	10-14	15-24	25-49	10-14	15-24	25-49	10-14	15-24	25-49	10-14	15-24	25-49
Pre-2008	0.249	0.249	0.249	0.948	0.948	0.948	0.322	0.322	0.322	0.410	0.410	0.410	0.965	0.965	0.965	0.252	0.252	0.252
2008	0.118	0.235	0.275	0.948	0.948	0.948	0.152	0.303	0.333	0.194	0.385	0.451	0.965	0.965	0.965	0.119	0.243	0.270
2009	0.122	0.240	0.283	0.948	0.948	0.948	0.178	0.315	0.339	0.199	0.388	0.463	0.965	0.965	0.965	0.127	0.250	0.277
2010	0.166	0.285	0.299	0.948	0.948	0.948	0.324	0.389	0.362	0.214	0.395	0.478	0.965	0.965	0.965	0.222	0.310	0.293
2011	0.226	0.355	0.313	0.948	0.948	0.948	0.450	0.479	0.385	0.280	0.423	0.486	0.965	0.965	0.965	0.293	0.375	0.304
2012	0.337	0.486	0.339	0.948	0.948	0.948	0.516	0.559	0.409	0.516	0.530	0.509	0.965	0.965	0.965	0.417	0.483	0.324
2013	0.368	0.565	0.361	0.948	0.948	0.948	0.564	0.634	0.436	0.587	0.614	0.528	0.965	0.965	0.965	0.435	0.549	0.340
2014	0.471	0.710	0.399	0.948	0.948	0.948	0.620	0.712	0.467	0.717	0.726	0.554	0.965	0.965	0.965	0.537	0.659	0.368
2015	0.506	0.811	0.438	0.948	0.948	0.948	0.672	0.790	0.502	0.742	0.813	0.580	0.965	0.965	0.965	0.562	0.739	0.395

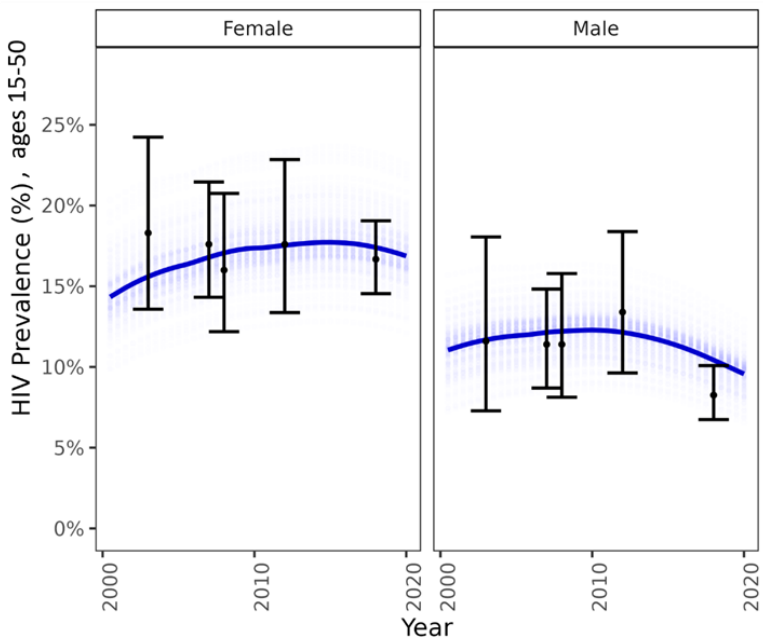
2016	0.476	0.894	0.488	0.948	0.948	0.948	0.756	0.844	0.538	0.697	0.891	0.613	0.965	0.965	0.965	0.628	0.841	0.425
2017	0.489	0.937	0.537	0.948	0.948	0.948	0.863	0.889	0.572	0.680	0.949	0.648	0.965	0.965	0.965	0.759	0.917	0.457
2018	0.589	0.925	0.637	0.948	0.948	0.948	0.944	0.925	0.651	0.775	0.976	0.744	0.965	0.965	0.965	0.844	0.959	0.562
2019	0.741	0.904	0.678	NA	NA	NA	0.784	0.943	0.677	0.785	NA	0.775	NA	NA	NA	0.790	0.976	0.596
2020	0.802	0.901	0.717	NA	NA	NA	0.787	0.925	0.703	0.800	NA	0.808	NA	NA	NA	0.800	NA	0.633
2021	0.802	0.909	0.749	NA	NA	NA	0.836	0.913	0.727	NA	NA	0.836	NA	NA	NA	NA	NA	0.668
2022	NA	0.917	0.779	NA	NA	NA	0.804	0.947	0.750	NA	NA	0.865	NA	NA	NA	NA	NA	0.704
2023	NA	0.926	0.807	NA	NA	NA	0.804	NA	0.773	NA	NA	0.892	NA	NA	NA	NA	NA	0.738
2024	NA	0.935	0.833	NA	NA	NA	0.804	NA	0.795	NA	NA	0.918	NA	NA	NA	NA	NA	0.772
2025	NA	0.944	0.858	NA	NA	NA	0.804	NA	0.815	NA	NA	0.942	NA	NA	NA	NA	NA	0.803
2026	NA	0.949	0.879	NA	NA	NA	0.801	NA	0.832	NA	NA	0.961	NA	NA	NA	NA	NA	0.832

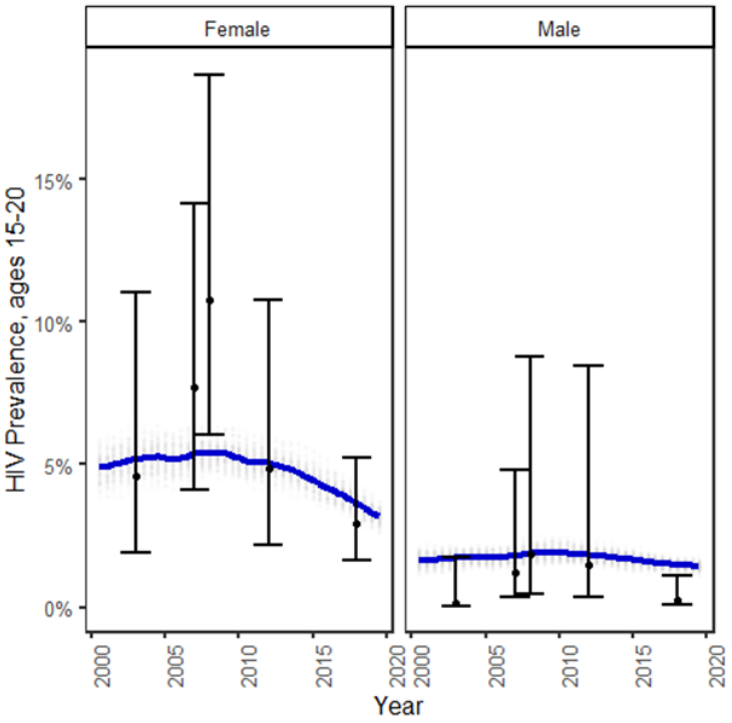
2027	NA	0.953	0.898	NA	NA	NA	0.801	NA	0.848	NA	NA	0.976	NA	NA	NA	NA	NA	0.976
2028	NA	0.955	0.915	NA	NA	NA	0.801	NA	0.862	NA	NA	NA	NA	NA	NA	NA	NA	NA
2029	NA	NA	0.931	NA	NA	NA	0.801	NA	0.874	NA	NA	NA	NA	NA	NA	NA	NA	NA
2030	NA	NA	0.945	NA	NA	NA	0.801	NA	0.885	NA	NA	NA	NA	NA	NA	NA	NA	NA
2031	NA	NA	0.955	NA	NA	NA	0.802	NA	0.897	NA	NA	NA	NA	NA	NA	NA	NA	NA
2032	NA	NA	NA	NA	NA	NA	NA	NA	0.907	NA	NA	NA	NA	NA	NA	NA	NA	NA
2033	NA	NA	NA	NA	NA	NA	NA	NA	0.917	NA	NA	NA	NA	NA	NA	NA	NA	NA
2034	NA	NA	NA	NA	NA	NA	NA	NA	0.924	NA	NA	NA	NA	NA	NA	NA	NA	NA
2035	NA	NA	NA	NA	NA	NA	NA	NA	0.931	NA	NA	NA	NA	NA	NA	NA	NA	NA

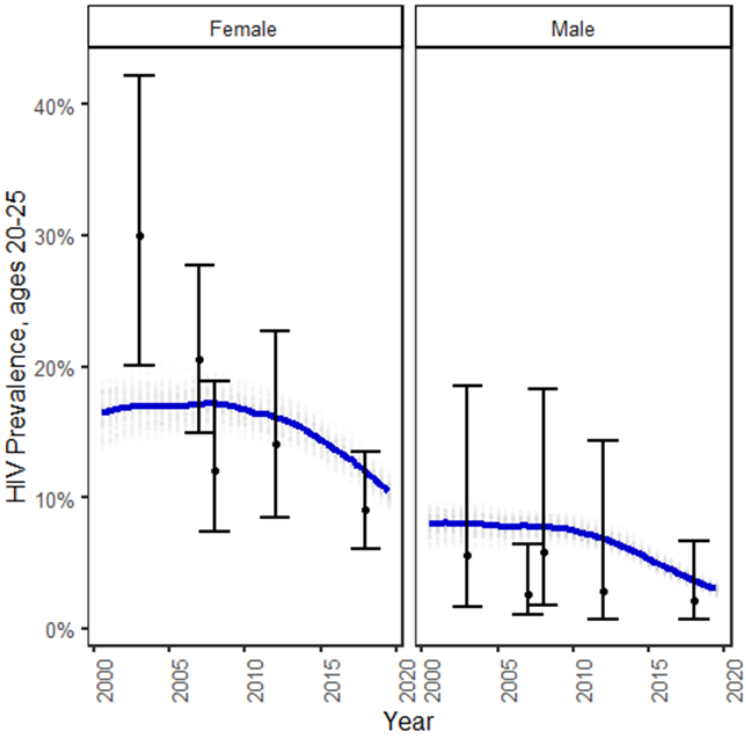
[¥]**Source:** Circumcision prevalence prior to 2008 is obtained from the Kenya Demographic and Health Survey, 2003. Prevalence of circumcision from 2008 onward combines prevalence of traditional male circumcision and voluntary medical male circumcision estimates obtained from the Decision-Makers' Program Planning Toolkit 2.

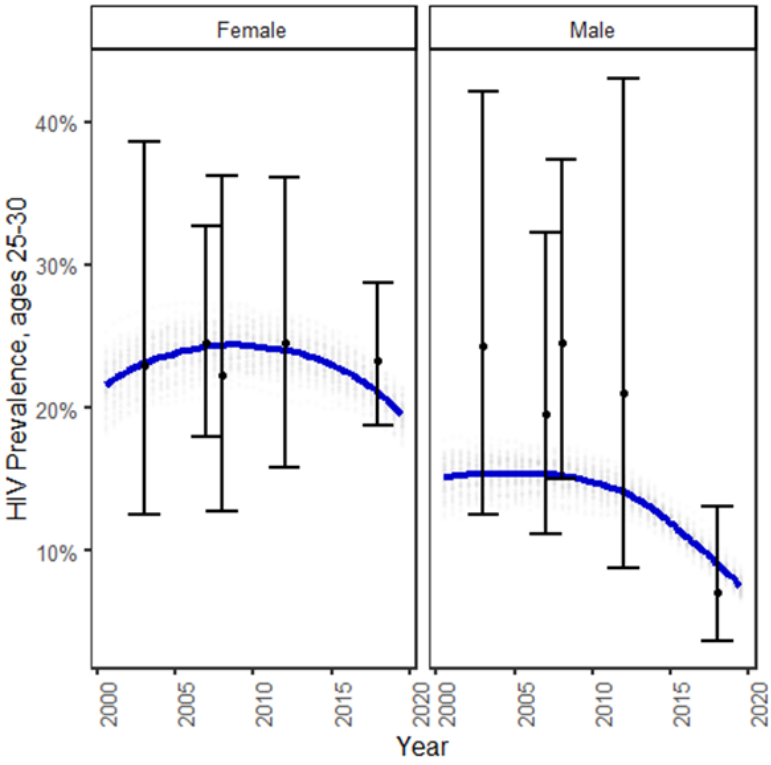
Figure S3. Model fit to age-specific and overall prevalence from population-based surveys by sex

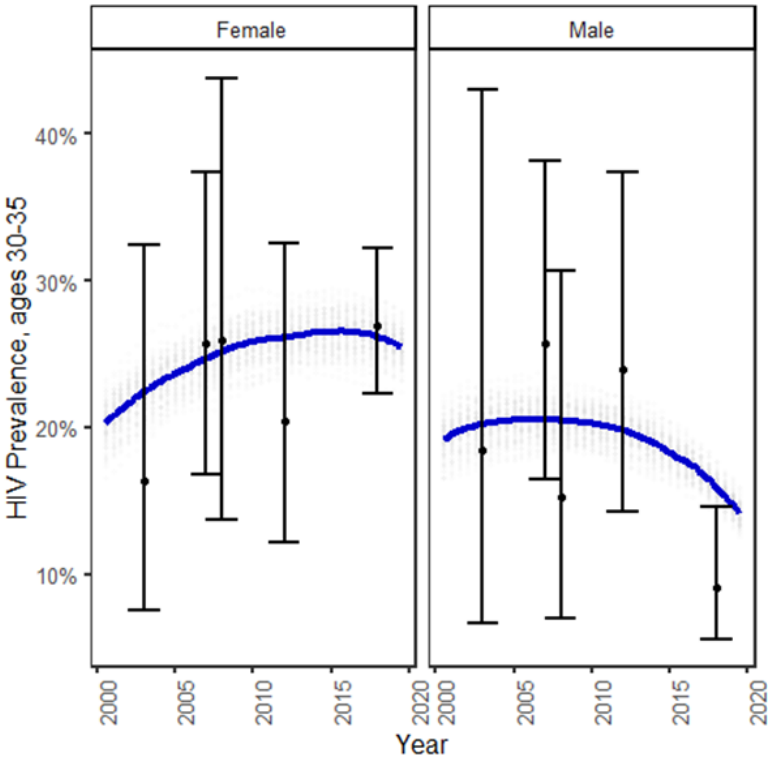
* Blue curves refer to the LOESS line fitting to the 100 simulations; the error bars refer to the empirical estimates and 95% confidence intervals for HIV prevalence obtained from Kenya Demographic and Health Surveys and Kenya AIDS Indicator Surveys.

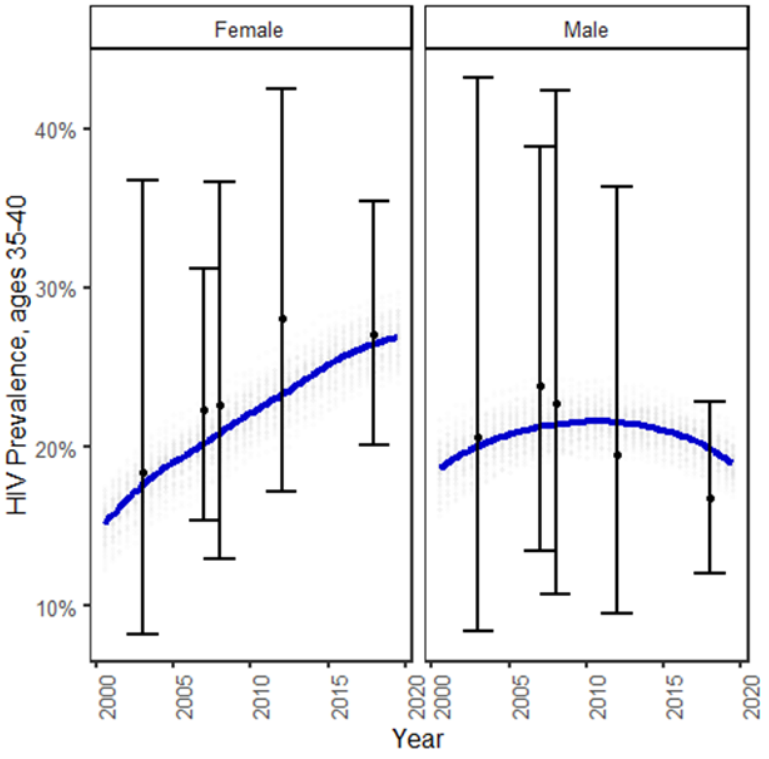

Female
Male
HIV Prevalence (%), ages 15-50
25%
20%
15%
10%
5%
0%
2000
2010
2020
Year

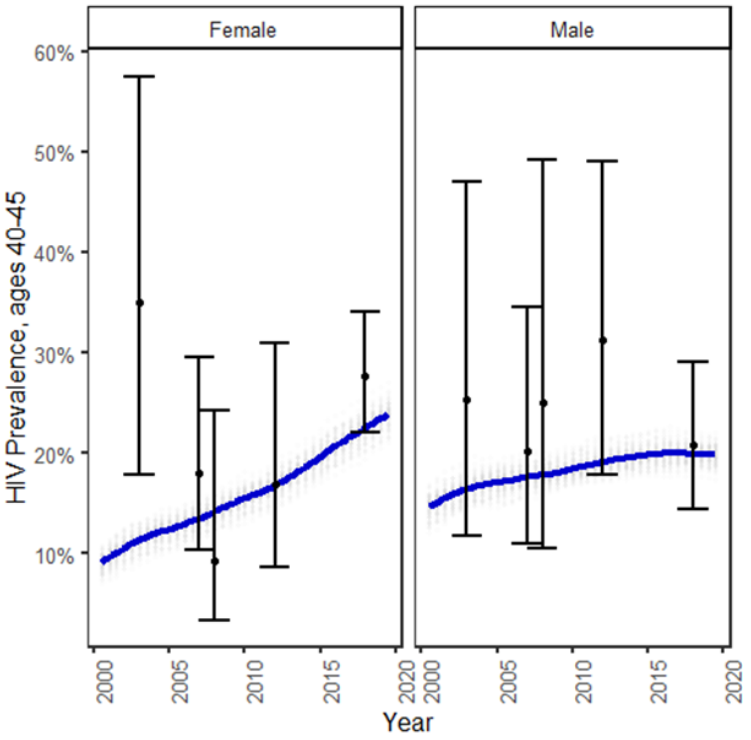

Female
Male
HIV Prevalence, ages 15-20
15%
10%
5%
0%
2000
2005
2010
2015
2020
Year


Female
Male
HIV Prevalence, ages 20-25
40%
30%
20%
10%
0%
2000
2005
2010
2015
2020
Year


Female
Male
HIV Prevalence, ages 25-30
40%
30%
20%
10%
2000
2005
2010
2015
2020
Year


Female
Male
HIV Prevalence, ages 30-35
40%
30%
20%
10%
2000
2005
2010
2015
2020
Year


Female
Male
HIV Prevalence, ages 35-40
40%
30%
20%
10%
2000
2005
2010
2015
2020
Year


Female
Male
60%
50%
40%
30%
20%
10%
HIV Prevalence, ages 40-45
2000
2005
2010
2015
2020
Year

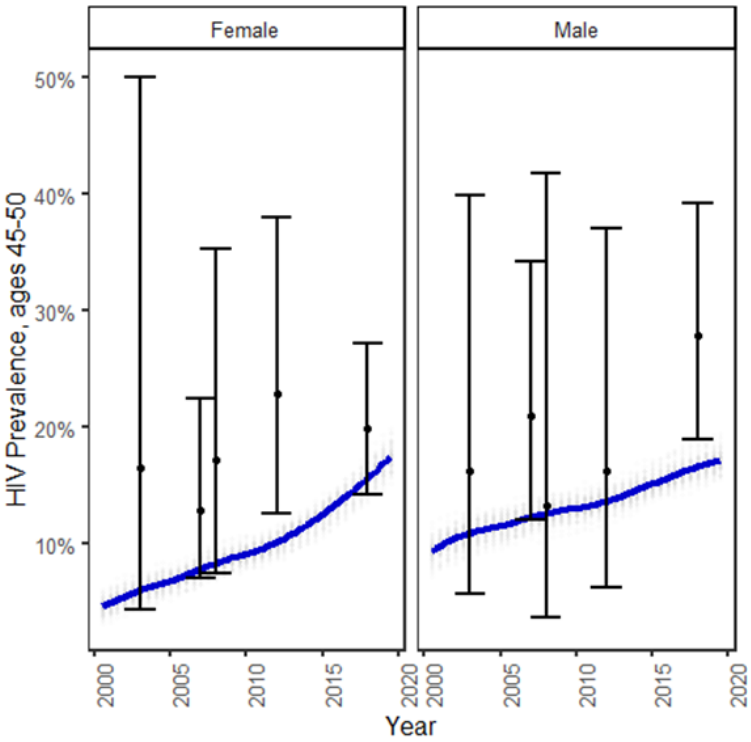

Female
Male
50%
40%
30%
20%
10%
HIV Prevalence, ages 45-50
2000
2005
2010
2015
2020
Year

Table S6. Key model parameters.

Select model parameters used to fit the EMOD-HIV transmission model to survey data on prevalence and ART coverage from Kenya. Median and interquartile ranges (IQRs) reported for all dynamic parameters used in the calibration process from 100 best-fitting parameter sets. †

Parameter	Parameter Description	Fitted median	(IQR)
ARTLinkMax	Maximum probability of linkage to ART	0.999	(0.978, 1.000)
ARTLinkMid	Year of ART linkage (given eligibility), that is, time of the inflection point in the sigmoid trend.	2003.008	(2002.920, 2003.837)
AcuteDurationMonths	The time since infection, in months, over which the Acute_Stage_Infectivity_Multiplier is applied to coital acts occurring in that time period.	1.000	(1.000, 1.331)
CircumcisionReducedAcquire	The reduction of susceptibility to STI by voluntary male medical circumcision (VMMC).	0.600	(0.598, 0.600)
Homa_BayInfrmlCondomsMax	Maximum rate of condom use in informal relationships in Homa Bay	0.231	(0.230, 0.233)
Homa_BayLOWRisk	Proportion of the population that is low-risk in Homa Bay	0.557	(0.549, 0.559)
Homa_BayTrnsCondomsMax	Maximum rate of condom use in transitory relationships in Homa Bay	0.244	(0.232, 0.245)
InfmrlFormRate	Informal relationship formation rate	0.000	(0.000, 0.000)
InfrmlCondomMid	Year midpoint of logistic scale-up of condom use in informal relationships	1993.007	(1991.629, 1998.680)

Parameter	Parameter Description	Fitted median	(IQR)
InfrmlCondomRate	Rate of logistic scale-up of condom use in informal relationships	2.661	(1.953, 2.909)
InfrmlCondomsMax	Maximum rate of condom use in informal relationships	0.216	(0.215, 0.217)
InfrmlDurHet	Heterogeneity in duration of informal relationships	0.750	(0.750, 0.750)
KisiiInfrmlCondomsMax	Maximum rate of condom use in informal relationships in Kisii	0.231	(0.226, 0.232)
KisiiLOWRisk	Proportion of the population that is low-risk in Kisii	0.938	(0.935, 0.939)
KisiiTrnsCondomsMax	Maximum rate of condom use in transitory relationships in Kisii	0.375	(0.369, 0.376)
KisumuInfrmlCondomsMax	Maximum rate of condom use in informal relationships in Kisumu	0.182	(0.181, 0.183)
KisumuLOWRisk	Proportion of the population that is low-risk in Kisumu	0.764	(0.762, 0.765)
KisumuTrnsCondomsMax	Maximum rate of condom use in transitory relationships in Kisumu	0.338	(0.337, 0.347)
LogBaseInfectivity	The probability of transmission when none of the transmission multipliers apply to a particular coital act.	0.002	(0.002, 0.002)
MaleToFemaleOld	Male-to-female relative risk of infection among older individuals	2.012	(1.506, 2.132)

Parameter	Parameter Description	Fitted median	(IQR)
MaleToFemaleYoung	Male-to-female relative risk of infection among young individuals	1.116	(1.000, 1.242)
MaxInfrmlFLOW	Maximum number of informal relationships among low-risk females	1.311	(1.255, 1.315)
MaxInfrmlFMED	Maximum number of informal relationships among medium-risk females	2.050	(2.002, 2.351)
MaxInfrmlMLOW	Maximum number of informal relationships among low-risk males	1.165	(1.159, 1.203)
MaxInfrmlMMED	Maximum number of informal relationships among medium-risk males	2.530	(2.442, 2.735)
MaxMrtlFMED	Maximum number of marital relationship among medium-risk females	1.139	(1.136, 1.159)
MaxMrtlMMED	Maximum number of marital relationship among medium-risk males	1.302	(1.268, 1.316)
MaxTrnsFLOW	Maximum number of transitory relationships among low-risk females	1.599	(1.580, 1.625)
MaxTrnsFMED	Maximum number of transitory relationships among medium-risk females	2.943	(2.891, 3.000)
MaxTrnsMLOW	Maximum number of transitory relationships among low-risk males	1.599	(1.588, 1.677)
MaxTrnsMMED	Maximum number of transitory relationships among medium-risk males	2.557	(2.475, 2.879)

Parameter	Parameter Description	Fitted median	(IQR)
MigoriInfrmlCondomsMax	Maximum rate of condom use in informal relationships in Migori	0.186	(0.185, 0.189)
MigoriLOWRisk	Proportion of the population that is low-risk in Migori	0.795	(0.793, 0.797)
MigoriTrnsCondomsMax	Maximum rate of condom use in transitory relationships in Migori	0.249	(0.248, 0.257)
MrtlCondomMax	Maximum rate of condom use in marital relationships	0.192	(0.191, 0.193)
MrtlCondomMid	Year midpoint of logistic scale-up of condom use in marital relationships	2003.131	(1999.017, 2005.000)
MrtlCondomRate	Rate of logistic scale-up of condom use in marital relationships	2.971	(2.595, 3.000)
MrtlFormRate	Marital relationship formation rate	0.000	(0.000, 0.000)
NyamiraInfrmlCondomsMax	Maximum rate of condom use in informal relationships in Nyamira	0.096	(0.093, 0.097)
NyamiraLOWRisk	Proportion of the population that is low-risk in Nyamira	0.902	(0.900, 0.910)
NyamiraTrnsCondomsMax	Maximum rate of condom use in transitory relationships in Nyamira	0.309	(0.304, 0.313)
PrExInfrmlFemLOW	Probability of potential for extra-relational informal relationship among low-risk females	0.366	(0.364, 0.371)

Parameter	Parameter Description	Fitted median	(IQR)
PrExInfrmlFemMED	Probability of potential for extra-relational informal relationship among medium-risk females	0.401	(0.401, 0.407)
PrExInfrmlMaleLOW	Probability of potential for extra-relational informal relationship among low-risk males	0.244	(0.222, 0.249)
PrExInfrmlMaleMED	Probability of potential for extra-relational informal relationship among medium-risk males	0.382	(0.379, 0.389)
PrExTrnsFemLOW	Probability of potential for extra-relational transitory relationship among low-risk females	0.033	(0.033, 0.033)
PrExTrnsFemMED	Probability of potential for extra-relational transitory relationship among medium-risk females	0.460	(0.450, 0.468)
PrExTrnsMaleLOW	Probability of potential for extra-relational transitory relationship among low-risk males	0.330	(0.328, 0.332)
PrExTrnsMaleMED	Probability of potential for extra-relational transitory relationship among medium-risk males	0.593	(0.589, 0.611)
PreARTLinkMax	Maximum probability of linkage to pre-ART care	0.715	(0.708, 0.737)
PreARTLinkMid	Year midpoint of logistic scale-up of pre-ART linkage	1996.709	(1995.685, 1998.896)
PreARTLinkMin	Minimum probability of linkage to pre-ART care	0.435	(0.416, 0.442)
RiskAssortivity	Risk assortivity	0.663	(0.648, 0.673)
SeedYrHigh	Seed year	1986.562	(1982.000, 1988.000)

Parameter	Parameter Description	Fitted median	(IQR)
SexualDebutAgeFemaleWeibullHeterogeneity	Heterogeneity parameter of Weibull distribution of female age of sexual debut	0.086	(0.083, 0.086)
SexualDebutAgeFemaleWeibullScale	Scale parameter of Weibull distribution of female age of sexual debut	16.013	(15.540, 16.038)
SexualDebutAgeMaleWeibullHeterogeneity	Heterogeneity parameter of Weibull distribution of male age of sexual debut	0.040	(0.040, 0.040)
SexualDebutAgeMaleWeibullScale	Scale parameter of Weibull distribution of male age of sexual debut	15.708	(15.155, 16.090)
SiayaInfrmlCondomsMax	Maximum rate of condom use in informal relationships in Siaya	0.160	(0.148, 0.161)
SiayaLOWRisk	Proportion of the population that is low-risk in Siaya	0.729	(0.722, 0.731)
SiayaTrnsCondomsMax	Maximum rate of condom use in transitory relationships in Siaya	0.300	(0.293, 0.304)
TrnsCondomMax	Maximum rate of condom use in transitory relationships	0.243	(0.242, 0.253)
TrnsCondomMid	Year midpoint of logistic scale-up of condom use in transitory relationships	1997.960	(1996.962, 1999.273)
TrnsCondomRate	Rate of logistic scale-up of condom use in transitory relationships	0.999	(0.978, 1.000)
TrnsFormRate	Transitory relationship formation rate	2003.008	(2002.920, 2003.837)

† We utilized previously published version of EMOD-HIV and recalibrated with most recent data. The only modifications to the default parameterization outside of PrEP implementation and HIV test sensitivity (described in the main manuscript text) are detailed in Table S9 above. A full description of all parameters and references available is at: https://docs.idmod.org/projects/emod-hiv/en/latest/parameter-overview.html and elsewhere.

Table S7. Disability weights for estimating disability-adjusted life-years averted

Health State	**DALY Weight**	**Reference**
HIV-negative	0	Vos *et al*[16]
HIV and not on ART	0.274	
HIV and on ART	0.078	

Instead of calculating total DALYs associated with each scenario using life tables (i.e. conditional life expectancy by age), we calculated DALYs averted the intervention scenario compared to the baseline scenario as the difference in life years and years lived with disability in the intervention compared to the baseline scenario. Years of life lost (YLL) are captured through as the difference in years of life lived between scenarios, while difference in years lived with disability (YLD) are calculated by applying disability weights to time spent in each health state and subtracting the total YLD in the baseline vs intervention scenario over the analytic time horizon.

2.2 Model calibration to population parameters

Population scaling factor

We applied scaling factors of approximately 60 to each run to increase the size of our modeled population and outcomes to reflect the actual population size in western Kenya. To determine the scaling factor for each simulation, we divided the size of the Kenya 2019 census population by the size of the population in 2019 and multiplied this ratio by the modeled population and outcomes. The size of the scaling factor varied slightly depending on model run due to stochastic variability in modeled population size.

Table S8. Population size by gender, county, and age group in 2009¥

Age Group	Men						Women					
	Homa Bay	Kisii	Kisumu	Migori	Nyamira	Siaya	Homa Bay	Kisii	Kisumu	Migori	Nyamira	Siaya
0 - < 1	18,335	18,236	17,457	19,265	10,313	15,093	18,354	17,993	16,926	19,309	10,263	14,860
1 - 4	69,799	69,529	63,054	69,921	41,165	56,269	69,250	69,023	63,172	69,519	40,396	55,901
5 - 9	75,926	76,757	67,083	73,872	46,450	60,966	75,973	75,778	67,779	74,333	46,867	60,710
10 - 14	68,689	68,473	62,706	64,300	42,590	58,296	67,159	68,072	63,359	63,249	42,198	56,248
15 - 19	57,430	59,228	55,597	53,075	36,604	49,220	54,119	60,776	56,741	52,238	36,786	47,825
20 - 24	39,573	41,898	47,281	38,690	24,409	32,725	50,309	58,225	57,649	48,004	34,184	41,443
25 - 29	30,437	32,792	40,964	30,727	19,515	25,961	36,016	42,878	40,614	34,670	27,273	30,135

30 - 34	23,259	26,678	30,412	23,344	16,605	20,359	26,342	30,031	27,515	25,630	19,487	22,328
34 - 39	16,013	21,766	21,251	17,024	14,039	14,793	20,010	26,051	20,611	19,313	17,106	17,932
40 - 44	11,914	15,718	15,145	12,170	10,470	11,118	16,513	18,360	16,894	14,773	11,377	16,082
45 - 49	11,124	16,797	13,361	10,549	11,318	10,390	15,248	19,181	15,298	12,888	11,886	15,486
50 - 54	9,705	12,789	11,251	8,565	8,379	9,079	12,942	14,136	12,504	10,314	8,703	14,541
55 - 59	8,159	9,527	8,718	6,399	5,999	8,414	9,833	9,528	9,175	7,692	5,819	12,265
60 - 64	6,989	7,395	7,054	5,250	5,026	7,712	8,587	7,654	7,597	6,000	5,107	11,081
65 - 69	4,325	4,637	4,163	3,382	3,094	5,107	5,957	5,320	5,402	4,508	3,322	7,732
70 - 74	4,029	3,945	3,777	2,907	2,753	5,175	5,355	5,017	4,757	3,524	3,153	7,173
75 - 79	2,835	2,743	2,392	2,033	1,778	3,549	3,891	3,338	3,356	2,968	1,919	5,464
80 - 99	3,726	3,701	2,821	2,624	2,393	4,159	5,316	5,891	4,615	3,636	3,475	6,155

¥Source: Kenya National Bureau of Statistics, 2009 Census

Table S9a. Age-specific population fertility rates in Kenya 1950-2049[¥]

	Age-specific fertility rates (births per 1,000 women)						
Year	15-19	20-24	25-29	30-34	35-39	40-44	45-49
1950-1955	169.1	351.6	338.1	284.3	203.5	110.7	38.9
1955-1960	175.9	365.9	351.9	295.8	211.8	115.2	40.5
1960-1965	182.3	379.1	364.5	306.5	219.4	119.4	41.9
1965-1970	183.3	381.2	366.6	308.2	220.6	120	42.2
1970-1975	180.6	375.5	361.1	303.6	217.3	118.3	41.5
1975-1980	172.7	359.1	345.3	290.3	207.8	113.1	39.7
1980-1985	163.1	339.2	326.2	274.2	196.3	106.8	37.5
1985-1990	147.8	307.3	295.5	248.4	177.8	96.8	34.0
1990-1995	115.3	268.9	252.0	206.8	161.6	73.4	52.0
1995-2000	111.5	260.7	253.3	196.2	143.3	62.4	42.7
2000-2005	104.2	243.6	236.7	183.4	133.9	58.3	39.9
2005-2010	97.1	227.1	221.4	170.6	123.7	53.6	36.5
2010-2015	86.2	201.9	202.3	149.2	102.1	42.4	27.9
2015-2020	75.1	176.5	179.8	129.6	85.8	34.8	22.4
2020-2024	69.9	165.1	171.8	120.2	76.2	29.9	18.6
2025-2029	65.0	154.7	164.8	112.6	68.5	26.0	15.5
2030-2034	60.6	145.7	159.1	106.7	62.5	22.9	13.1
2035-2039	56.2	137.2	153.6	101.8	57.6	20.4	11.0
2040-2044	52.2	129.7	149.3	98.2	53.8	18.5	9.4

[¥]**Source**: 2019 World Population Prospects

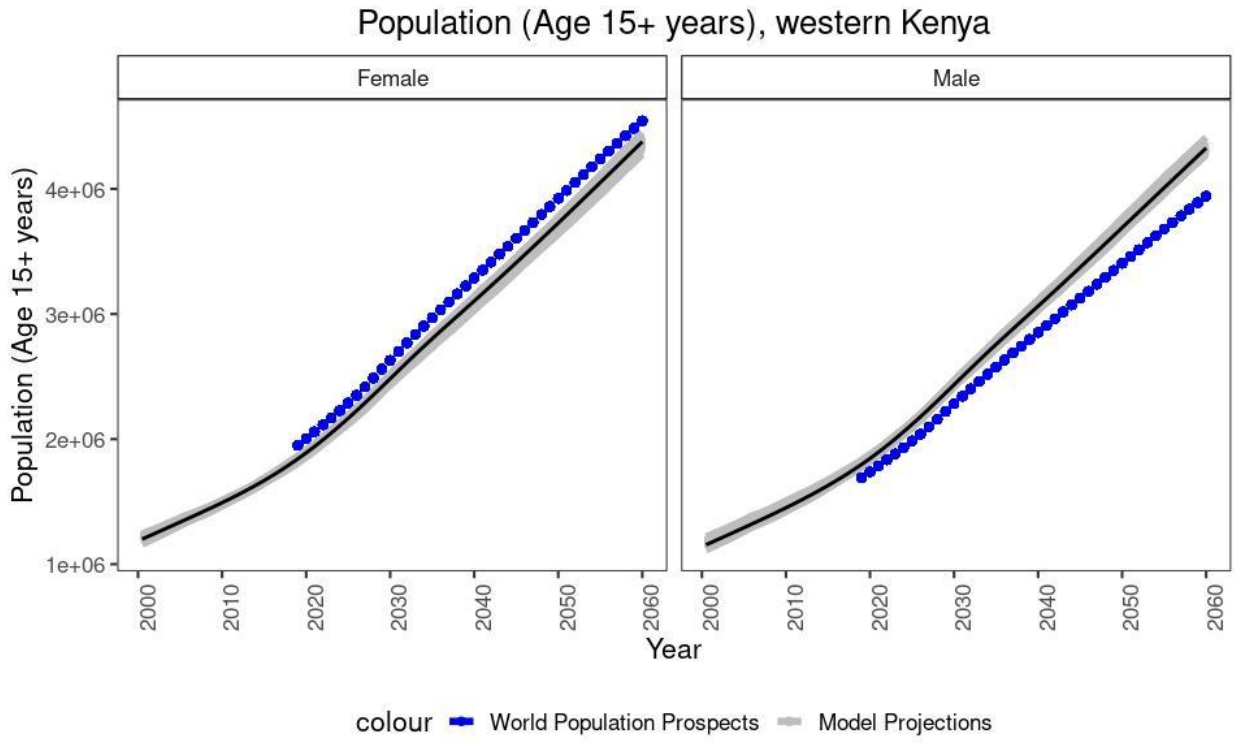
Table S9b. Age-specific mortality rates among in Kenya 1950-2049 by gender ¥

		Age-specific mortality rates (%)						
Sex	Year	15-19	20-24	25-29	30-34	35-39	40-44	45-49
Women	1997.5	0.136	0.191	0.244	0.294	0.361	0.453	0.542
	2002.5	0.116	0.167	0.215	0.259	0.321	0.408	0.493
	2007.5	0.100	0.145	0.188	0.229	0.286	0.367	0.449
	2012.5	0.085	0.127	0.166	0.202	0.254	0.331	0.408
	2017.5	0.073	0.110	0.145	0.178	0.226	0.298	0.371
	2022.5	0.063	0.096	0.128	0.158	0.201	0.268	0.338
	2027.5	0.054	0.084	0.112	0.139	0.179	0.241	0.307
	2032.5	0.046	0.073	0.099	0.123	0.160	0.217	0.280
	2037.5	0.039	0.064	0.087	0.108	0.142	0.196	0.254
	2042.5	0.034	0.055	0.076	0.096	0.126	0.176	0.231
Men	1997.5	0.165	0.253	0.288	0.345	0.433	0.551	0.713
	2002.5	0.142	0.219	0.251	0.304	0.385	0.494	0.648
	2007.5	0.121	0.189	0.219	0.267	0.343	0.443	0.589
	2012.5	0.104	0.163	0.191	0.235	0.305	0.398	0.535
	2017.5	0.089	0.141	0.166	0.207	0.271	0.357	0.486
	2022.5	0.076	0.122	0.145	0.182	0.241	0.320	0.441
	2027.5	0.065	0.106	0.126	0.160	0.215	0.287	0.401

	2032.5	0.056	0.091	0.110	0.141	0.191	0.258	0.364
	2037.5	0.048	0.079	0.096	0.124	0.170	0.231	0.331
	2042.5	0.041	0.068	0.083	0.109	0.151	0.208	0.300

¥**Source**: 2019 World Population Prospects

Figure S4. Model predicted population growth by sex



Section 3 | Additional Results

3.1 Sensitivity analyses

Higher MOH costs: We applied a 15% markup to the MOH-perspective costs to account for regulatory oversight, quality assurance, pharmacovigilance, data reporting integration, and referral pathway strengthening which increased the ICER to $339 per DALY averted (vs $212 per DALY averted in the main analysis).

PEPFAR interruption scenario: 20% reduction in testing and ART linkage. We assessed an additional PEPFAR interruption scenario in which the Kenya MOH covers 50% of the funding gaps in HIV testing and treatment, resulting in a 20% reduction in services instead of 41%

Table S10: Sensitivity analyses: higher MOH costs and PEPFAR interruptions

	Higher MOH costs scenario	**PEPFAR interruption scenario (20% reduction in testing and ART linkage)**
PEP coverage (%)	0.7% (0.7% - 0.8%)	0.7% (0.6% - 0.7%)
PrEP coverage (%)	0.3% (0.2% - 0.3%)	0.2% (0.2% - 0.3%)
HIV infections averted (%)	13.9% (10.1% -17.1%)	12.8% (10.1% - 15.7%)
HIV deaths averted (%)	4.3% (2.0% - 6.9%)	4.0% (2.6% - 5.3%)
DALYs averted	36,304 (-39,887 – 108,288)	99,589 (23,760 – 159,595)
Incremental cost-effectiveness ratio (ICER)	$339 ($61 - $2,223)	Cost-saving

Broader PEP and PrEP targeting: We conducted structural sensitivity analyses varying uptake and targeting assumptions. In these scenarios, we remove all targeting assumptions and assume all individuals with a non-marital partner are eligible for PrEP and PEP and initiate at equal rates. We maintain the sex ratio observed in our pilot study

Table S11a. Uptake for individuals aged 15-49 with any condomless sex act with a non-marital partner

	PrEP	PEP
Low coverage	1%	2%
Medium coverage	1%	3%
High coverage	1%	4%
Highest coverage	1%	5%

Table S11b. Health and economic impact of broad PEP and PrEP targeting

		Broad targeting			
	Main scenario	Low coverage	Medium coverage	High coverage	Highest coverage
PEP coverage (%)	0.7% (0.7% - 0.8%)	0.6% (0.6% - 0.6%)	0.9% (0.8 % - 0.9%)	1.1% (1.1% - 1.2%)	1.4% (1.3% - 1.5%)
PrEP coverage (%)	0.3% (0.2% - 0.3%)	0.3% (0.3% - 0.3%)	0.3% (0.3% - 0.3%)	0.3% (0.3% - 0.4%)	0.4% (0.3% - 0.4%)
HIV infections averted (%)	13.9% (10.1% - 17.1%)	8.8% (4.2% - 12.5%)	11.1% (7.9% - 14.5%)	13.6% (9.7% - 17%)	15.3% (12.0% - 18.4%)

HIV deaths averted (%)	4.3% (2.0% - 6.9%)	3.1% (0.7% - 5.3%)	3.6% (1.4% - 5.7%)	4.5% (2.3% - 6.7%)	5.1% (2.5% - 7.7%)
ICER	$212 ($15 - $1409)	$440 ($165 - $6703)	$580 ($223 - $5548)	$647 ($262 - $11601)	$812 ($316 - $6414)

3.2 Replacing daily oral PrEP and PEP with a long acting monthly oral pill

To understand the impact of anticipated novel long acting PrEP/PEP products, we evaluated a scenario where we replaced daily oral PrEP/PEP with MK-8527, a monthly oral pill currently in clinical trials. We set the effectiveness of both PEP and PrEP using MK-8527 at 95%, and assumed the cost of the monthly pill to be $2.88, inclusive of a 15% mark up for supply chain.

The scenario averted 14.1% (10.1% - 17.7%) HIV infections over 10 years and averted 4.6% (1.7% - 7.3%) deaths and 36,257 DALYs over 35 years. Additional details can be found in Section 3.3.

Table S12. Incremental cost-effectiveness ratio using MK-8527 at varying costs

Cost of MK-8527	$2.88	$5.76	$11.52
Incremental cost-effectiveness ratio	Cost-saving	$269/DALY averted	$1231/DALY averted

3.3 Additional Results

Table S13a. HIV infections averted among ages 15-49 in each scenario (2026 - 2036)

Year	Pilot study	PEP only	High efficacy PEP And PrEP	Low efficacy PEP and PrEP	PrEP/PEP provision using MK-8527	Interrupted testing (PEPFAR cuts)	Interrupted testing and ART (PEPFAR cuts)
2026	462	425	435	403	501	401	807
2027	659	589	630	591	713	753	1276
2028	922	832	885	754	910	856	1650
2029	960	741	991	799	916	921	1852
2030	915	741	911	830	862	902	1953
2031	927	769	1001	850	941	897	1977
2032	878	679	845	765	886	969	2201
2033	938	785	974	808	889	903	2320

2034	853	705	878	778	902	903	2335
2035	821	682	821	712	841	768	2353
2036	764	624	752	718	815	778	2366
TOTAL	**9099**	**7573**	**9122**	**8008**	**9177**	**9051**	**21089**

Table S13b. HIV deaths averted among ages 15-49 in each scenario (2026 - 2061)

Year	Pilot study	PEP only	High efficacy PEP And PrEP	Low efficacy PEP and PrEP	PrEP/PEP provision using MK-8527	Interrupted testing (PEPFAR cuts)	Interrupted testing and ART (PEPFAR cuts)
2026	-96	-51	-92	-68	-93	-72	-89
2027	-69	-63	-52	-92	-110	-78	-86
2028	-18	-38	-51	-44	-24	-45	18
2029	-27	-6	-8	-18	-7	31	12
2030	74	82	78	87	73	59	111
2031	148	125	131	125	146	138	274
2032	128	98	134	122	152	108	315
2033	167	128	153	178	153	160	209
2034	155	125	171	167	167	158	322
2035	156	128	129	155	189	151	368

2036	157	160	148	159	166	170	475
2037	171	120	149	151	149	133	550
2038	130	113	120	118	142	103	587
2039	123	116	144	113	116	128	616
2040	101	77	109	93	81	91	559
2041	115	81	107	89	85	82	703
2042	73	99	85	108	101	98	695
2043	112	82	88	76	98	74	649
2044	21	26	27	12	39	71	726
2045	67	69	107	87	82	68	618
2046	49	53	47	63	54	58	726
2047	46	45	65	69	54	64	674
2048	32	23	56	65	49	76	607
2049	30	32	16	47	30	54	688
2050	40	31	33	15	28	6	636
2051	47	29	46	44	54	32	635
2052	37	36	42	39	37	6	647
2053	21	24	29	10	19	48	614
2054	36	23	41	15	30	33	534
2055	26	16	29	18	27	26	488
2056	36	20	25	28	50	27	532

2057	17	12	18	19	19	40	468
2058	35	29	29	36	31	17	459
2059	23	21	25	19	19	44	444
2060	23	12	26	15	29	22	399
2061	30	20	39	22	29	24	357
TOTAL	**2215**	**1896**	**2243**	**2141**	**2264**	**2207**	**16541**

Table S13c. Distribution of PEP initiations per person year across by age, sex, and partnership type.

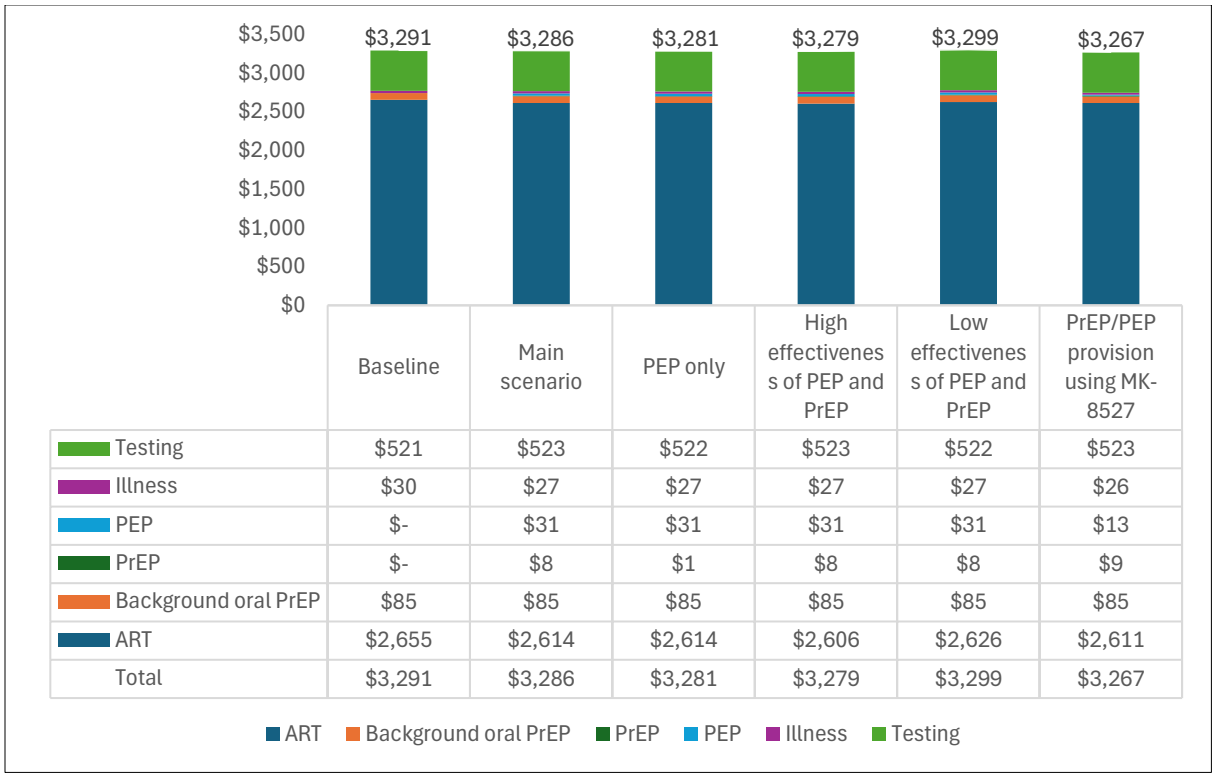
	Number of time PEP was initiated among PEP users (%)			
	1	**2**	**3**	**4+**
ABYM with multiple concurrent partners	76.8%	19.5%	3.3%	0.4%
ABYM 15-24 with multiple partners in the past 3 months	79.0%	17.7%	3.0%	0.3%
AGYW 15-24 with multiple concurrent partners	81.0%	16.4%	2.3%	0.3%
AGYW 15-24 with multiple partners in the past 3 months	81.7%	15.8%	2.2%	0.3%
Men 25-49 with multiple concurrent partners	69.4%	23.8%	5.9%	0.9%
Men 25-49 with multiple partners in the past 3 months	71.1%	22.5%	5.5%	0.9%
Women 25-49 with multiple concurrent partners	50.6%	26.7%	16.7%	6.0%
Women 25-49 with multiple partners in the past 3 months	54.3%	25.0%	15.3%	5.4%

Table S13d. HIV infections averted by age and sex (2026-2036)

	Mean	CI low	CI high	Mean %	CI low	CI high

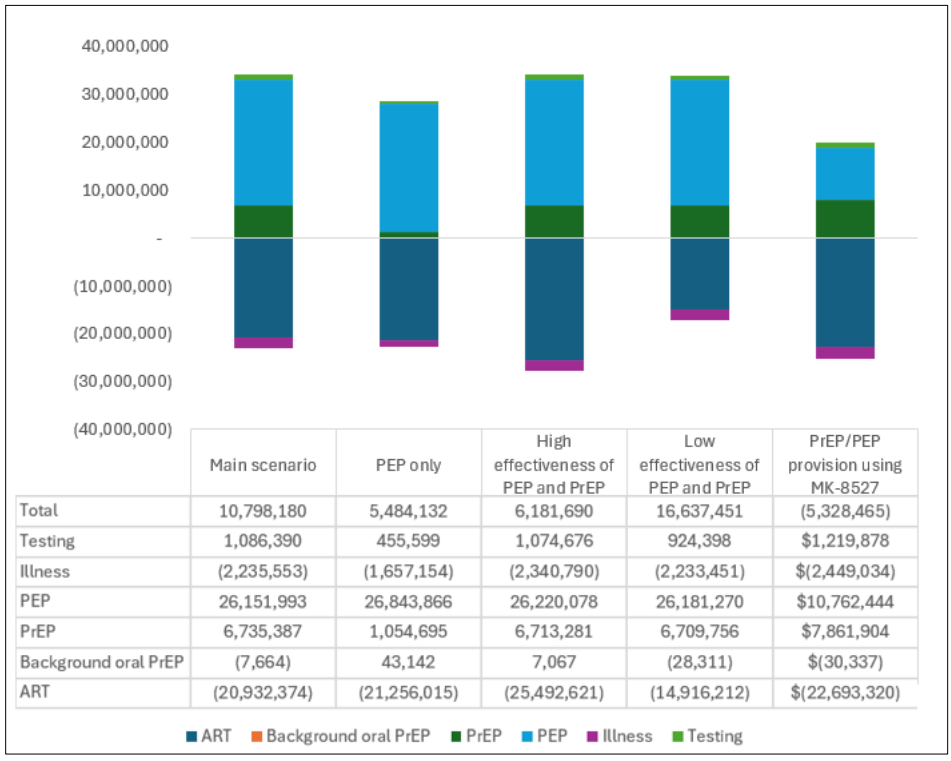
ABYM 15-24	766	202	1356	19%	6%	31%
Male 25-49	2859	1926	3760	17%	12%	21%
Male 50+	38	-232	389	2%	-13%	19%
AGYW 15-24	2195	1231	3530	13%	8%	19%
Female 25-49	3814	2610	5047	13%	9%	17%
Female 50+	34	-198	242	2%	-15%	15%

Figure S5. Total 35 year undiscounted costs (in $M) by category for each modeled scenario



	Baseline	Main scenario	PEP only	High effectiveness of PEP and PrEP	Low effectiveness of PEP and PrEP	PrEP/PEP provision using MK-8527
Testing	$521	$523	$522	$523	$522	$523
Illness	$30	$27	$27	$27	$27	$26
PEP	$-	$31	$31	$31	$31	$13
PrEP	$-	$8	$1	$8	$8	$9
Background oral PrEP	$85	$85	$85	$85	$85	$85
ART	$2,655	$2,614	$2,614	$2,606	$2,626	$2,611
Total	$3,291	$3,286	$3,281	$3,279	$3,299	$3,267

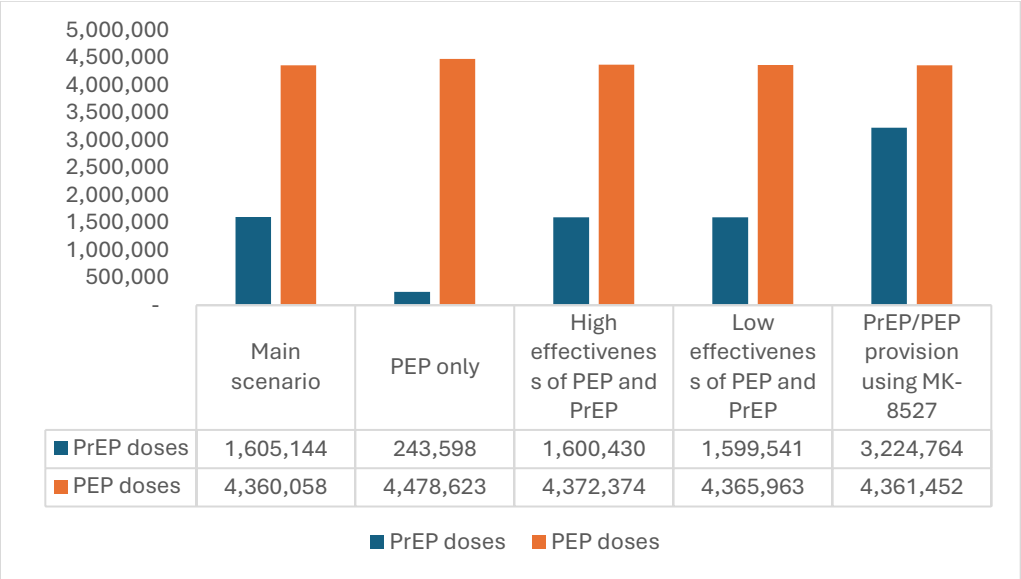
Figure S6. Cost difference by component relative to baseline over 35 years



	Main scenario	PEP only	High effectiveness of PEP and PrEP	Low effectiveness of PEP and PrEP	PrEP/PEP provision using MK-8527
Total	10,798,180	5,484,132	6,181,690	16,637,451	(5,328,465)
Testing	1,086,390	455,599	1,074,676	924,398	$1,219,878
Illness	(2,235,553)	(1,657,154)	(2,340,790)	(2,233,451)	$(2,449,034)
PEP	26,151,993	26,843,866	26,220,078	26,181,270	$10,762,444
PrEP	6,735,387	1,054,695	6,713,281	6,709,756	$7,861,904
Background oral PrEP	(7,664)	43,142	7,067	(28,311)	$(30,337)
ART	(20,932,374)	(21,256,015)	(25,492,621)	(14,916,212)	$(22,693,320)

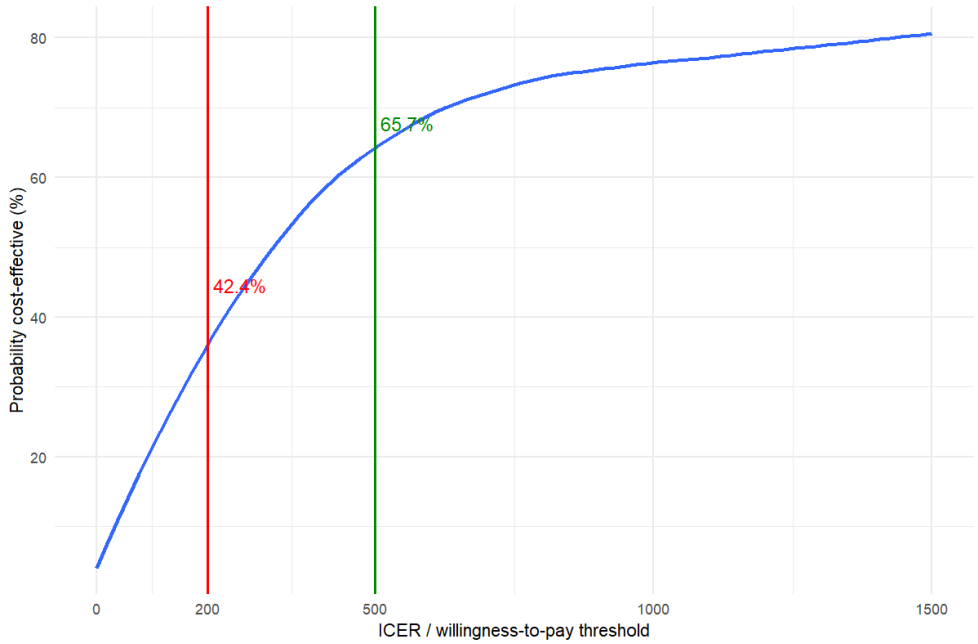
Figure S6 presents the cost difference from the baseline scenario for each online PrEP/PEP scenario compared to the baseline counterfactual. Cost savings in ART and HIV-related illnesses are observed across scenarios while costs for PrEP, PEP, and HIV testing increase relative to baseline.

Figure S7. Total PrEP and PEP doses by scenario (2026-2036)



	Main scenario	PEP only	High effectiveness of PEP and PrEP	Low effectiveness of PEP and PrEP	PrEP/PEP provision using MK-8527
PrEP doses	1,605,144	243,598	1,600,430	1,599,541	3,224,764
PEP doses	4,360,058	4,478,623	4,372,374	4,365,963	4,361,452

Figure S8. Cost-effectiveness acceptability curve



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CHAPTER 5 – CONCLUSION

This dissertation examined the health and economic impact of decentralized care models in sub-Saharan Africa. Results showed integrated HIV–hypertension care, and HIV prevention can deliver health gains efficiently and in a cost-effective manner within constrained health systems.

All three aims addressed a common question: how can limited health system resources be deployed most effectively to expand access to care while maintaining value for money? By embedding economic evaluation within real-world implementation contexts, this dissertation provides evidence that decentralized care models can be cost-effective, but that their success depends on delivery strategies, system readiness, and alignment with patient behavior.

Together, the findings illustrate that economic evaluation is not merely a retrospective accounting exercise, but a critical implementation science tool for understanding what works, why it works, and under what conditions it can be scaled.

In **Aim 1**, we found that decentralizing molecular TB diagnostics to near point-of-care settings has the potential to improve access to timely testing and treatment initiation, but that these benefits must be evaluated alongside their economic implications.

We observed that under conditions of high TB prevalence, and high testing demand, decentralized molecular testing for TB using Truenat MTB assays can link more participants to TB treatment within seven days, at a cost per 7-day treatment initiation that is similar to, or lower than, traditional hub-and-spoke testing. Cost-effectiveness could be enhanced further by placing instruments in locations with high TB prevalence and high testing volume – including using the same equipment for diagnosis of multiple diseases. While decentralized testing for TB is likely to be effective and cost-effective, it will require more resources to implement; thus, implementation of this strategy must be accompanied by a careful assessment of existing service volumes, testing infrastructure across disease areas, equity, epidemiology of TB, and budget availability.

In **Aim 2**, we found that distinguishing between the cost-effectiveness of an evidence-based intervention and the cost-effectiveness of the strategy used to implement it is essential.

By modeling both the hypertension intervention and the SAIA implementation strategy separately, Aim 2 showed that implementation strategies can unlock substantial health gains at relatively low incremental cost, but only when a minimum level of health system readiness is present. Investments in blood pressure equipment, medications, and trained staff are prerequisites; implementation strategies amplify impact rather than substitute for core system inputs. This aim contributes an important conceptual lesson for implementation science: implementation strategies are not universally effective or cost-effective in isolation. Their value is context-dependent and contingent on foundational system capacity.

In **Aim 3**, we found that differentiated delivery models leveraging private-sector and digital platforms to provide HIV prevention can reduce HIV incidence at relatively low population coverage if uptake aligns with periods of HIV risk. Delivering PrEP and PEP through online pharmacies reached individuals who may not engage with traditional clinic-based services and demonstrated cost-effectiveness from a public-sector payer perspective when implemented through a public–private partnership, with uptake parameterized by participant demographics and sexual behavior to reflect real-world patterns of HIV risk.

Online PrEP/PEP provision has the potential to efficiently increase coverage of biomedical prevention in Kenya and similar settings. PEP is an underused prevention tool at high demand that can complement PrEP scale up. Policymakers could consider integrating PEP and PrEP in differentiated delivery models and consider public/private partnerships to maximize reach of HIV prevention in the context of constrained budgets and donor transition.

Across all three aims, several cross-cutting themes emerged.

First, decentralization is not a single intervention, but a spectrum of delivery choices involving diagnostics, workforce, decision-making authority, and service platforms. Each choice carries distinct cost and effectiveness implications that must be evaluated empirically.

Second, economic evaluation makes trade-offs explicit. Rather than asking whether an intervention works, economic evaluation asks whether it delivers sufficient value relative to

alternative uses of limited resources. In the context of implementation, these trade-offs are not only financial, but they involve choices about delivery strategy, system readiness, and who gets reached. In this dissertation, such trade-offs surface across all three aims: between centralized and decentralized diagnostic placement depending on testing volume and geography; between investing in a clinical intervention versus the implementation strategy used to deliver it; and between different delivery models that may efficiently serve some populations but require complementary approaches to maximize reach.

Third, context matters. Implementation strategies that are highly effective in one setting may yield limited returns in another without foundational investments.

This dissertation **contributes methodologically** by demonstrating how diverse economic evaluation approaches: trial-based costing, decision-analytic modeling, and agent-based transmission modeling can be applied.

This dissertation has several limitations. First, while all three aims relied on high-quality data, generalizability may be limited by context-specific costs, behaviors, and health system structures. At the same time, each aim was designed with generalizability in mind: Aim 1 was conducted across two distinct country settings with differing cost structures; Aim 2 developed a model deliberately simple enough to be adapted to other LMIC settings and health conditions; and Aim 3 used a parameter sweep across 100 input sets, and simulated multiple scenarios, to capture uncertainty. Future work should adapt these analyses to additional countries and settings. Second, indirect societal costs such as patient time, productivity losses, and household economic impacts were captured only partially. Incorporating broader perspectives could strengthen future evaluations.

In conclusion, this dissertation demonstrates that decentralized care models can efficiently deliver health gains in sub-Saharan Africa when implemented. However, decentralization is not inherently efficient; its value depends on delivery strategies, system readiness, and alignment with patient needs.

This work provides tools and evidence to help policymakers move beyond questions of feasibility toward informed decisions about scale, sustainability, and value. As health systems

face increasing resource constraints, such evidence will be essential for designing interventions that are not only effective, but implementable and sustainable.