ENDING THE AIDS EPIDEMIC IN CAMBODIA

FINDINGS FROM AN OPTIMA HIV MODELLING ANALYSIS

2020

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Acknowledgements

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Disclaimer: Consultative workshop and scenario analyses were conducted before COVID-19 reached pandemic status. The impact on global health and economy, and uncertainties around COVID-19 in Cambodia were not taken into consideration in this analysis.

Abbreviations

AEM	AIDS Epidemic Model
AGYW	Adolescent girls and young women
AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral
BAU	Business as usual
B-IACM	Boosted integrated active case management
CHAI	Clinton Health Access Initiative
Clients	Clients of entertainment workers
CRS	Catholic Relief Services
FEW	Female entertainment workers
FI	Friends International
FHI	Family Health International
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HACC	Health Action Coordinating Committee
HIV	Human immunodeficiency virus
HSSP	Health Sector Strategic Plan
HTS	HIV testing services
IBBS	Integrated Biological and Behavioural Survey
KHANA	Khmer HIV/AIDS NGO Alliance
KP	Key population (at risk of HIV transmission)
MSM	Men who have sex with men
NAA	National AIDS Authority
NCHADS	National Center for HIV/AIDS, Dermatology and STD
NGO	Non-governmental organization
NSP	National Strategic Plan
PDI+	Peer-driven intervention plus
PEPFAR	President's Emergency Plan For AIDS Relief
PITC	Provider-initiated HIV testing and counselling
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PrEP	Pre-exposure prophylaxis
PWID	People who inject drugs
PWUD	People who use drugs (non-injecting)
RGC	Royal Government of Cambodia
RHAC	Reproductive Health Association of Cambodia
SBCC	Social and behavioural change communication
STI	Sexually transmitted infection
TG	Transgender women
UNAIDS	Joint United Nations Programme on HIV/AIDS
US CDC	United States Centers for Disease Control
VMMC	Voluntary medical male circumcision
WHO	World Health Organization

Executive Summary

Current situation

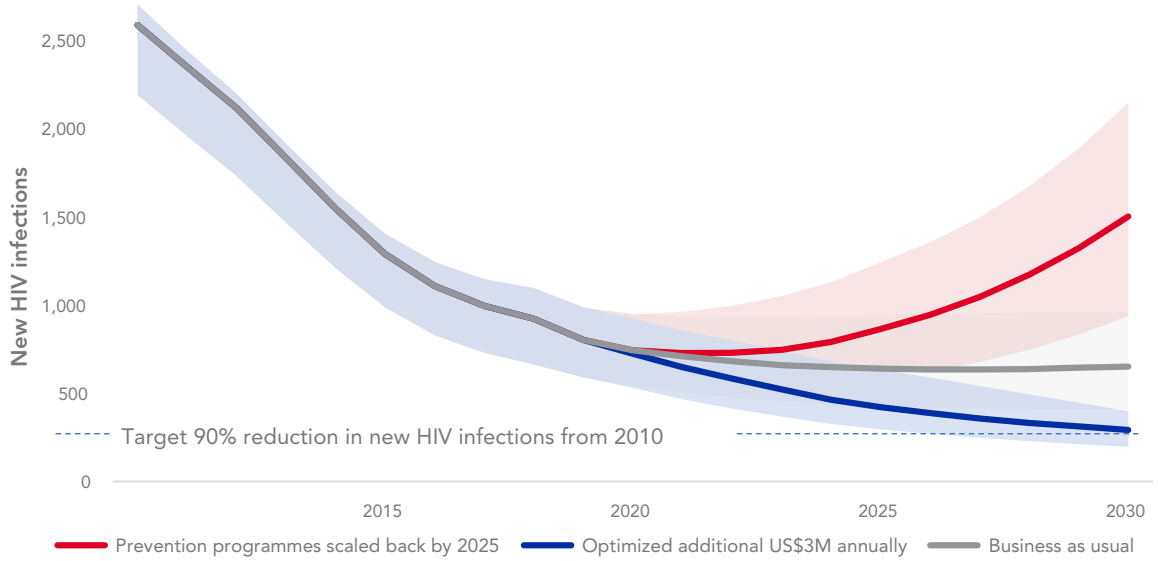
Cambodia has achieved remarkable success in reducing new HIV infections, from an estimated 10,000 in 1998 to 2,500 in 2010, and the **95-95-95 targets for 2025** are within reach (Figure 1). However, based on modelling of business as usual for HIV interventions from 2019, the country is **not on track to reach the 90% reduction in new infections by 2025** from 2010 baseline, and uncertainty in funding for HIV prevention leaves Cambodia at risk of new infections rising.

Optimized response

Maintaining funding for HIV prevention is critical to prevent a rise in new infections in Cambodia. **To reach the 2025 targets, it is estimated that an additional US$3M per year invested in novel HIV prevention programmes** including HIV self-testing and pre-exposure prophylaxis (PrEP), combined with **employing implementation efficiencies** for existing programmes, will be necessary.

Rapid investment to scale **prevention programmes for key populations may avert up to 30% of the projected new HIV infections** from 2021 to 2025 and over 40% from 2020 to 2030 relative to business as usual.

Figure 1: Projected new HIV infections for different resource allocation scenarios



Policy recommendation priorities

Each level of additional resources is with reference to the 2019 annual budget envelope and policy recommendations are cumulative between budget scenarios. The estimated percentage of new HIV infections averted is the percentage of cumulative infections from 2021 until 2025 that are averted relative to the projected number of new HIV infections under the business as usual allocation.

1. **Through cost efficiencies within 2019 budget envelope, averting 3% of new HIV infections**

   Expand novel HIV outreach services for key populations, including self-testing and partner tracing by repurposing cost savings from other programmes toward a target of US$500,000 annually by 2025.

2. **With an additional US$1M annually, averting 10% of new HIV infections**

   Expand coverage of existing physical outreach through HIV prevention programmes for men who have sex with men (MSM) and transgender women (TG) by US$500,000 to US$1M.

   Provide PrEP for MSM and TG up to US$500,000 based on projected uptake.

3. **With an additional US$3M annually, averting 22% of new HIV infections**

   Increase PrEP uptake for MSM with demand creation by increasing the budget by an additional US$500,000 to US$1M each year from 2021 to 2023 based on projected uptake. Maintain this coverage by increasing from US$3M additional to US$5M in additional budget per year from 2025.

   Expand coverage of HIV prevention programmes for female entertainment workers (FEW) by US$250,000 annually.

   Increase the viral load testing budget by US$250,000 annually.

4. **With an additional US$5M annually, averting 28% of new HIV infections**

   Expand coverage of HIV prevention programmes for people who inject drugs (PWID), including needle-syringe programmes.

   Expand eligibility of PrEP to include female entertainment workers (FEW).

Recommended implementation efficiencies include:

Expansion and scale-up of

- Multi-month dispensing (MMD) of antiretroviral therapy (ART),
- Same-day initiation of ART, and
- HIV Recency testing added to diagnostic options.

Explore efficient and additional

- Viral load testing through use of existing GeneXpert machines.

Improve and sustain

- Strategic information using integrated data systems for tracking of key populations and people living with HIV.

Review opportunities for

- System integration of HIV programmes into health budget in the longer term,
- Improvements in joint delivery of PMTCT programme, and
- Reducing cost of antiretrovirals (ARVs) and other consumables.

1 Introduction

1.1 Country context

The AIDS response in Cambodia has been nothing short of remarkable. In the 1990s, Cambodia had one of the fastest growing HIV epidemics in Asia, but Cambodia has successfully turned the epidemic around through phases of Cambodia 1.0, 2.0, and 3.0 responses coupled with strong commitments towards ending the AIDS epidemic as a public health threat. This commendable response and commitment led the country to become one of the first of seven countries globally to achieve the 90-90-90 targets, which were achieved in Cambodia in 2017.

On the prevention front, the country has successfully reduced new infections by 62% between 2010 and 2018. New HIV infections peaked in 1997 at 16,000, but there has been a dramatic decline since. By 2001, new infections had already been halved from the 1997 peak. There has been a continuous decline in new infections over the last two decades, but the pace of decline has noticeably slowed since 2010. Although the epidemic is declining in number, the share of new HIV infections among men who have sex with men (MSM) is growing. In 2019, 40% of new HIV infections were estimated to be through homosexual transmission, a more than four-fold increase from 9% in 2010.

Data from HIV programmes, studies, and case reporting indicated that risk patterns, networks, vulnerabilities, and access to HIV-related services are diverse - not only between female entertainment workers, men who have sex with men, transgender people, and people who inject drugs – but also within subsets of these key populations such as young people from key population groups, key populations with overlapping risk behaviours, and key populations who are not easily reachable through traditional prevention interventions.

Data from innovative testing approaches such as an HIV self-testing pilot study (1) show that these approaches could reach high-risk populations and people living with HIV who were never tested and diagnosed with HIV. Evolving risks, behaviour dynamics, and innovations around biomedical interventions call for understanding of the impact of differentiated and innovative services tailored to the needs of key populations and subsets of key populations.

In terms of AIDS financing, according to the National AIDS Spending Assessment (NASA) 2016-2017 (2), an estimated US$34.5 million was spent in 2017 on the HIV response in Cambodia, 76% of which came from international donors. The Royal Government of Cambodia (RGC) consistently increased its contribution, from US$2.5 million in 2010 to US$8.3 million in 2017. Although domestic spending has gradually been stepped up, the pace of withdrawal of international funding is happening much faster and the potential resource gap to cover basic and essential HIV services is cause for concern should services continue to be delivered with the "business as usual" approach.

In this regard, Cambodia investment needs and investment thinking need to be framed around sustaining the achievements made in reaching the 90-90-90 target, while optimizing prevention efforts to ensure "epidemic control" is maintained, and hard choices may be necessary given resource limitations (3). By the same token, running the last mile with a reduced funding envelope while maintaining achievements calls for an investment scenario analysis around expanding innovative services, such as PrEP and HIV self-testing bolstered by impactful, nuanced, and differentiated approaches and prioritized services for key populations.

1.2 Objectives of the study

The purpose of this study is to provide technical assistance for the development of investment scenario analysis that is tailored to the Cambodia AIDS response. Specifically, this investment scenario analysis was used as an integral component to support Cambodia in the preparation of funding application to the Global Fund for the implementation period from 2021 to 2023.

Investment scenario analysis will be framed around:

- Sustained and improved treatment coverage and retention across all populations and locations,
- Intensified prevention efforts through differentiated combination prevention packages that are adequately diversified to serve nuanced prevention needs among key populations including sub-sets of KP, and
- Bringing new approaches to scale (PrEP, self-testing, index testing) for the right populations and evaluating the impact on the AIDS response.

Primarily, the findings from this analysis will be instrumental for the Global Fund funding application (2021-2023). The recommendations from the study aim to serve as evidence-based advocacy tool to enhance the dialogue of sustainability of the HIV response through optimizing resources, innovations, and differentiated approaches.

2 Methodology

The Optima HIV model, a mathematical tool, was the primary tool used in this analysis to generate key study outcomes. A national level country model for Cambodia was updated to explore the causative relationship between HIV programmes and their impacts on the HIV epidemic in the country.

This section describes (2.1) a summary of why Optima HIV was chosen for this analysis, (2.2) details of the stakeholder consultation process used to inform model inputs, (2.3) the model structure used to follow progression of HIV transmission, including population groups and HIV programmes modelled, and (2.4) a description of the scenarios modelled.

Further details on the Optima HIV model are available in Appendix A, with detailed calibration plots shown in Appendix B, and programme definitions given in Appendix C.

2.1 Model choice

There are three key population-based HIV transmission models: The AIDS Epidemic Model (AEM), the Goals model, and Optima HIV. Each of these models have similar HIV transmission and AIDS disease structures to comprehensively track the HIV epidemic over time, relate behavioural parameters to coverage, can be used to estimate prevalence and incidence, and produce long-term forecasts. The Goals and Optima models can be applied to determine resource needs, and the Optima HIV model has an algorithm for optimizing resource allocation across multiple programmes. Each model requires detailed demographic, epidemiological, behavioural, and programmatic data and estimates, and each model also allows for counterfactual scenario analyses to be run, in terms of both epidemic and programmatic parameters.

Several key differences between models exist. For both AEM and Goals, both the population groups (including people who inject drugs, MSM, and low-, medium-, and high-risk individuals) and types of HIV programmes (including condom promotion programmes, workplace programmes, ART, and HIV testing and counselling) that can be modelled are fixed. In contrast, Optima HIV allows HIV programmes to be defined and customized to target specific subpopulations within specific geographic areas, with different service delivery models, and with user-specified efficacies (noting that efficacies can be adjusted in other models by the modelling groups). Another difference between AEM and Goals compared with Optima HIV is that the former two models do not include a compartment for undiagnosed PLHIV, so HIV testing is instead assigned as a benefit of HIV prevention (i.e., HIV testing directly reduces the incidence of HIV as it is assumed that those testing positive or negative will change their behaviour on average in a population group). Finally, although the AEM model can be used to estimate ART need and produce outputs that allow for costing estimates to be calculated externally, it does not include a full costing module. Neither model has an integrated mathematical optimization algorithm. As part of the optimization analysis, Optima HIV also allows users to incorporate real-world constraints associated with all programmes. For example, no one who starts ART is allowed to stop ART unless by natural attrition, it can be specified that programmes cannot immediately be defunded but funding only be reduced to a certain percentage each year to enable a more realistic transition.

All models produce similar results regarding epidemic trend projections. However, due to the importance of conducting a costed optimization analysis, and since this feature is currently only available in Optima HIV, this model was chosen for the purposes of this study, but calibrated closely

to existing and accepted output from the AIDS Epidemic Model, as incorporated into Spectrum and published by UNAIDS in AIDSinfo (4).

2.2 Stakeholder consultation

To meet stakeholder needs, the flexibility of Optima HIV to model context-specific subpopulations and programmes was leveraged to answer policy questions through scenario and optimization analyses. This study was conducted in consultation with stakeholder groups through a preliminary workshop and individual discussions that were held from January 13 to 17, 2020 as listed in Table 1.

Table 1: Stakeholder consultations

Stakeholder	Key topics	Study inputs reviewed
National Center for HIV/AIDS, Dermatology and STD (NCHADS)	Outline of consultancy, overview discussions	• All major model inputs including: • Population stratification • Programme modalities
National AIDS Authority (NAA)	Policy and multisectoral response	• Ensuring scenarios and optimizations capture the range of potential future policy decisions
PEPFAR (USAID+ US CDC)	PEPFAR support, sustainability, programme components	• Ensuring risks are represented in scenarios around gaps in future funding • Priorities and realistic constraints on programmes
Clinton Health Access Initiative (CHAI)	Supply chain, ARVs (including paediatric), viral load testing	• Unit costs for ART modalities • Opportunities for stratification of ART modalities • Future costing scenarios to be explored • Unit costs and delivery of PMTCT
USAID	Sustainability and optimization perspectives	• Ensuring risks are represented in scenarios around gaps in future funding • Priorities and realistic constraints on programmes
Community partners and implementing NGOs including KHANA, RHAC, FI, CRS, and HACC	Identifying efficiency gains through community-led response	• Ensuring risks are represented in scenarios around gaps in future funding (what would behavioural impact be if coverage were to be reduced? • Programme saturation levels (could coverage be increased?) • Opportunities for implementation efficiencies?
Family Health International (FHI) 360 Linkages	Innovations and programmatic components	• Programme costing and impacts • PrEP programming • HIV-ST pilot
Health Policy Plus (HP+)	Previous costing work and policy analysis	• Programme costing, reconciling any mismatches and ensuring consistency
UNAIDS	Study overview	• Coordination and overview of all scenarios, optimizations, and inputs

2.3 Model structure and parameters

The Optima HIV model is similar to AEM in terms of overall design principles. Optima HIV can be described in very broad terms as a compartmental HIV epidemic model. A compartmental epidemic model divides the entire population into compartments that (a) characterize their risk of transmitting

a pathogen associated with disease, and/or (b) characterize their chance of experiencing morbidity or mortality. Movement between compartments is determined by the rates of transition. See the Technical Summary of the Optima HIV model for full model details.

The risks of transmitting, acquiring, and dying from HIV depend on a host of different factors that can vary across the population, across partnerships, and over time. In the Optima HIV model, the population is stratified in three different ways to reflect this variation: by demographic and/or risk group, by health/disease state (stratified by CD4 count category), and by stage of care. Optima HIV defines the different demographic/risk groups as populations, the different disease progression stages as health states, and the different care and treatment stages as care states. For example, a person might be a female sex worker (their population), be living with HIV with a CD4 count between 350 and 500 (their health state) and be linked to care but not on treatment (their care state). The different population groups modelled in this analysis are described in Table B1.

HIV programmes can be flexibly defined in the Optima HIV model. HIV programmes modelled in this study are described in Table C1. Programmes are based on the key National AIDS Spending Assessment (NASA) (5) categories and in keeping with the guidelines from the Global Fund Modular Framework Handbook (6). Programmes are divided into four broad categories: prevention, care and treatment, management, administration, and other. Only programmes that have a readily directly quantifiable impact on the epidemic or health outcomes are included in typical Optima HIV analyses. Additional cross-cutting programmes including management, programmes for orphans and vulnerable children, human resources and training, enabling environment, social protection, and Boosted-Integrated Active HIV Case Management (B-IACM) are included as part of the funding landscape in the analysis, but were not included in the optimization or scenario analysis, as the direct impact of these programmes on HIV transmission and treatment is not readily measured, and as such cannot be reliably modelled at this time.

2.4 Scenario analyses

The 2019 annual HIV budget of US$19,696,675 as defined in the Health Sector Strategic Plan (HSSP) 2016 – 2020 (7) was used as the baseline budget for this analysis. This budget only includes programme implementation costs and does not include wider health system costs such as hospital maintenance, capital costs or capital costs outside of programme implementation, meaning that the optimized budget constitutes only a portion of the total US$34,447,888 most recently reported for the 2017 NASA budget for Cambodia (2). Within the nearly US$20 million HIV programmatic budget for HIV, after increasing from US$2.5M in 2010 the absolute amount of public spending has remained relatively stable between US$6M and US$8M from 2011 to 2017, but falling international spending means that it has risen as a percentage from 4% in 2010 to 24% in 2017 (2).

The programme costs within this budget were validated against HIV costing data for specific programmes reported in the 2016 – 2017 NASA report and 2019 HIV programme implementation budgets reported by NCHADS and NGO implementing partners. Full programme details are given in Appendix C.

Stakeholders identified key scenarios in Table 2, covering the risk of reduced resource availability for HIV prevention programmes in the future, the opportunity for increased funding through the Global Fund over the next funding cycle, and what optimized response would be necessary to reach the 2025 targets of 95% diagnosis, 95% treatment coverage, and 95% viral suppression combined with a 90% reduction in new infections from 2010 levels to less than 250 new infections per year.

Table 2: Optimization analyses

Scenario	Description
Prevention programmes scaled back by 2025	This scenario was identified by stakeholders as a 'worst case' if all international support for HIV programmes in Cambodia ceased, with the Royal Government of Cambodia continuing to fund treatment programmes, but where prevention programme funding was phased out by 2025.
Business as usual (BAU)	This scenario represents a continued budget level and allocation of the most recently reported HSSP 2019 budget of US$19.7 million in future years (7).
Outcome optimization for a budget of US$19.7 million on targeted HIV programmes.	These optimizations represent the potential for reduced HIV infections and HIV-related deaths if spending was optimally allocated, both within the 2019 budget envelope, as well as if additional resources were made available. In all scenarios, treatment programmes (ART, PMTCT, OST) were constrained for ethical reasons meaning that budgets could not be reduced to increase budgets for other programmes, but budgets could be increased. The model algorithm aimed to estimate a theoretical optimal distribution of resources and emphasis of different HIV programmatic responses which minimizes both new HIV infections and HIV-related deaths by 2030 given the local epidemic parameters and data, cost of delivering services, subject to the constraints above.
Outcome optimization for an annual budget of US$20.7 million on targeted HIV programmes (an additional $US1 million annually)	
Outcome optimization for an annual budget of US$22.7 million on targeted HIV programmes (an additional $US3 million annually)	
Outcome optimization for an annual budget of US$24.7 million on targeted HIV programmes (an additional $US5 million annually)	
Necessary interventions to meet 95-95-95 targets and a 90% reduction in new HIV infections from 2010 levels (<250) by 2025	This analysis explores the identification of a combination of the most cost-effective interventions and implementation efficiencies that will allow the 2025 targets to be achieved in Cambodia.

3 Results

3.1 Model calibration

Inputs for the model were updated based on sources shared by stakeholders including programmatic data, with historical trends calibrated closely to final 2019 and preliminary 2020 modelled values from AEM and Spectrum (modelling conducted for national HIV estimates) (8-10), as well as with reference to AEM modelling used in the 2017 UNAIDS Case for Investing Cambodia's HIV and AIDS Response. This was done to identify the potential for Cambodia to reach virtual elimination of HIV by 2025 given a rapid and sustained scale-up of funding by the Royal Government of Cambodia (11). See Appendix B for full details of the calibration process and calibration plots.

3.1.1 Uncertainty

Current estimates and future projections for new HIV infections among MSM are highly sensitive to changes in behaviour.

- In the **best case**, new infections for MSM and TG will continue to decrease.
- In the **worst case**, a rising number of new infections among MSM and TG may lead to an increased overall HIV epidemic in Cambodia.

For innovative interventions covering MSM and TG, some uncertainty also:

- Can **HIV prevention programme coverage for MSM and TG** continue to be increased towards improving consistency of condom use and regularity of HIV testing for populations with known risk (i.e., MSM 1, MSW, TG)?
- Can **enhanced HIV key programme outreach programmes** continue to demonstrate high yields among all key populations including MSM 2, if scaled up?
- How quickly could demand be generated for PrEP in known risk key populations?

To ensure that new HIV infections are minimized, and 2025 targets reached, it is important to invest in all programmes for MSM and TG.

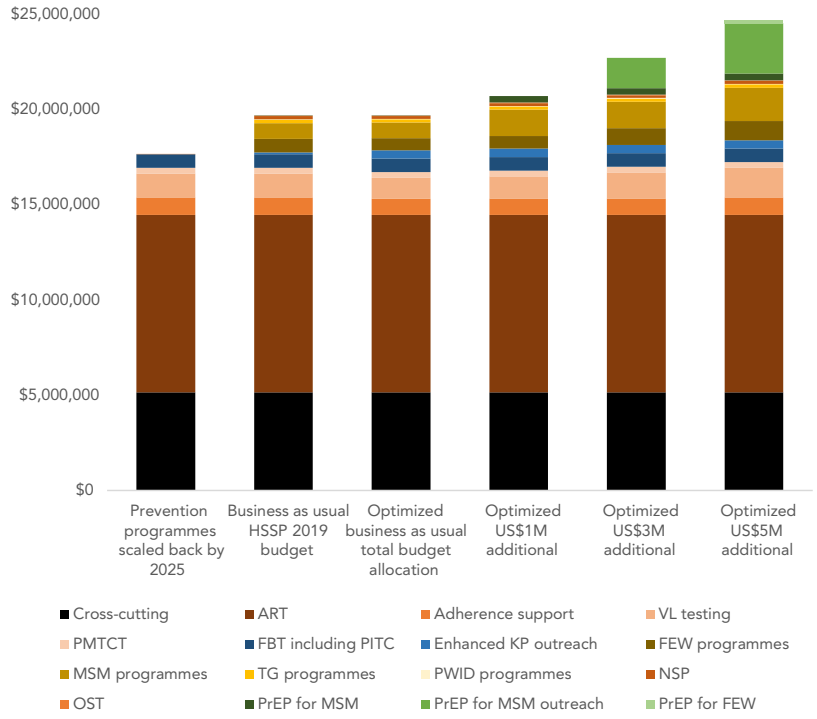
See Appendix C for full details of programme unit costs and modelled impact.

3.2 Optimized budget scenarios

Optimized budget allocations were run with an objective function to minimize the total number of projected HIV infections and HIV-related deaths from 2020 to 2025, using a 1 to 5 weighting ratio for infections to deaths, assuming an immediate change in allocation (Section A.3 gives full details).

Scenario results presented for the scenarios below were rerun based on a realistic timeframe for PrEP uptake determined by NCHADS and other stakeholders as described in Appendix E. For clarity, and as this scenario best demonstrates cost-effective interventions within a budget envelope that may be available to the HIV programme, the US$3M per year additional scenario is compared with the baseline scenario. The prioritization of programmes at different budget levels is shown in Figure 2, summarized in Table 3, and full results are given in Appendix D.

Figure 2: Allocation of annual HIV resources in each scenario by 2025



Under BAU projections with an annual HIV budget of US$19.7M, a cumulative total of 6,700 new HIV infections are projected from 2020 to 2030.

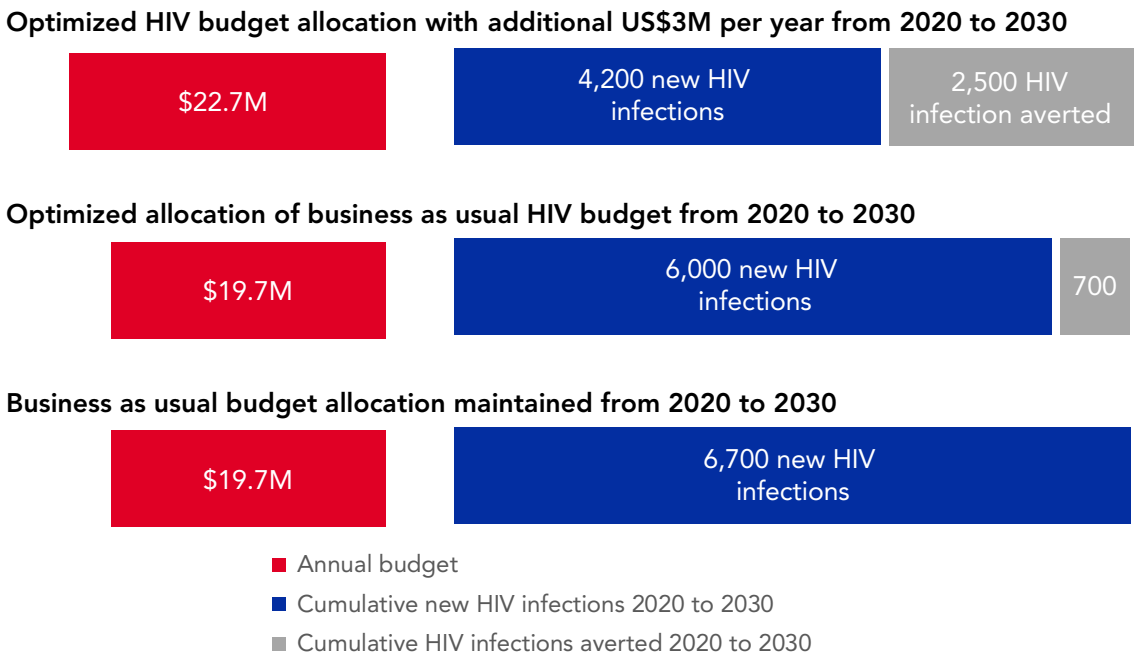
With optimized allocation of the same resources, 6,000 new HIV infections are projected over the same time period, a reduction of 7%, through prioritization of key population outreach and testing programmes including expansion of self-testing and partner tracing, while repurposing spending for existing prevention programmes by up to 10%.

Table 3: Prioritized allocation of HIV resources under optimization allocation, 2020 – 2030

Resource availability	Recommendation	Pathway
2019 estimated budget within HSSP 2015 – 2020	Investigate implementation efficiencies Expand key population outreach (US$500,000) including expansion of self-testing and partner tracing	Efficiencies
Additional US$1M (annual)	Expand and increase continuity of behavioural change through physical outreach prevention programmes for MSM and TG (US$500,000) Provide PrEP for MSM and TG (US$500,000)	• GF PAAR request
Additional US$3M (annual)	Expand PrEP uptake for MSM with demand creation (US$1M from 2022 to 2023 given projected uptake: a further US$2M per year needed to maintain target coverage from 2024) Expand coverage of prevention programmes for FEW (US$250,000) Increased VL testing (US$250,000)	• Potential cost savings • Domestic mobilization
Additional US$5M (annual)	Expand coverage of prevention programmes for PWID including needle-syringe programmes Expand eligibility for PrEP to include FEW	• Private sector engagement

Figure 3 shows that an additional US$3 million per year from 2020 to 2030 is projected to avert an estimated 37% (2,500) of the cumulative new HIV infections over that time. With reallocation of some resources within the 2019 budget envelope to expand outreach to key populations, an estimated 7% (700) of cumulative new HIV infections may be averted.

Figure 3: Potential impact of optimization and additional budget



3.3 Progress toward 2025 targets

If HIV programme spending as given in the 2019 HSSP budget were to be maintained from 2020 to 2030 in the business as usual (BAU) scenario, it is projected that 95-95-95 targets are within reach or will be exceeded by 2025, but that the target reduction in new infections will not be possible within the current budget envelope as summarized in Table 4.

Table 4: Projected achievement status of HIV targets by 2025

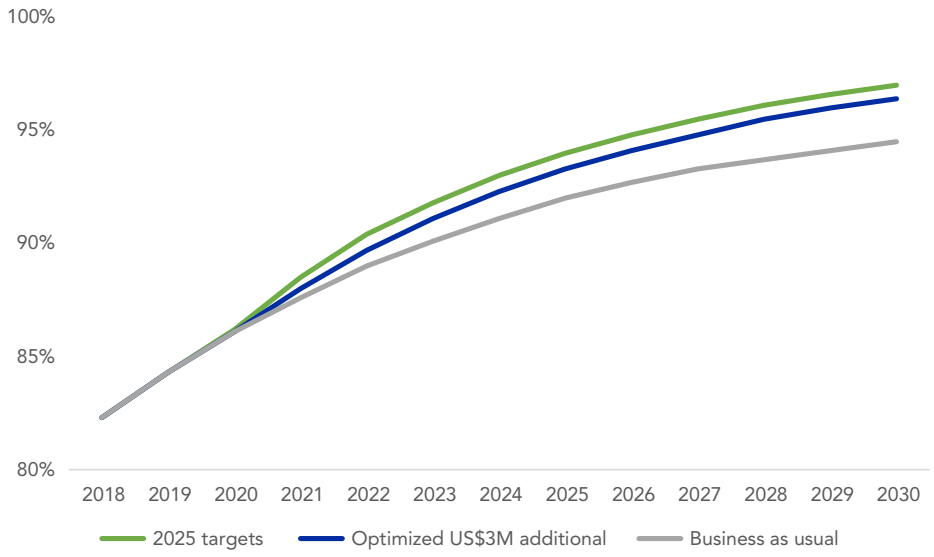
HIV targets by 2025	Projected business as usual status by 2025
95% HIV diagnosis	**Within reach:** 93% projected
95% treatment among those diagnosed	**Exceeded:** 99% achieved
95% viral suppression among those on treatment	**On target:** 96% achieved
<250 new HIV infections, 90% reduction from 2010	**Not on target:** 75% reduction projected Optimally allocated US$3M additional funding may get close (86% reduction) Addition of implementation efficiencies could reach this target.

3.3.1 Within reach: 95% HIV diagnosis

Meeting the target of diagnosing 95% of people living with HIV will be challenging, but it is within reach for Cambodia. If the most recently reported spending is maintained it is projected that diagnosis will be 93% by 2025. However, reaching the remaining population will be increasingly difficult and expensive, as many of those undiagnosed are from key and vulnerable populations with 'unknown risk', as well as their partners who are not being reached at the current scale and modality of prevention interventions.

Additional diagnoses are projected to be possible through a combination of innovative outreach modalities including self-testing (both assisted and unassisted), social media and night-time outreach, peer-driven intervention plus (PDI+), and index testing among key populations. Figure 4 shows that US$3M in additional budget, under an optimized allocation is projected to approach this target, but additional implementation efficiencies may be necessary to reduce undiagnosed infections further.

Figure 4: Projected progress toward 95% HIV diagnosis



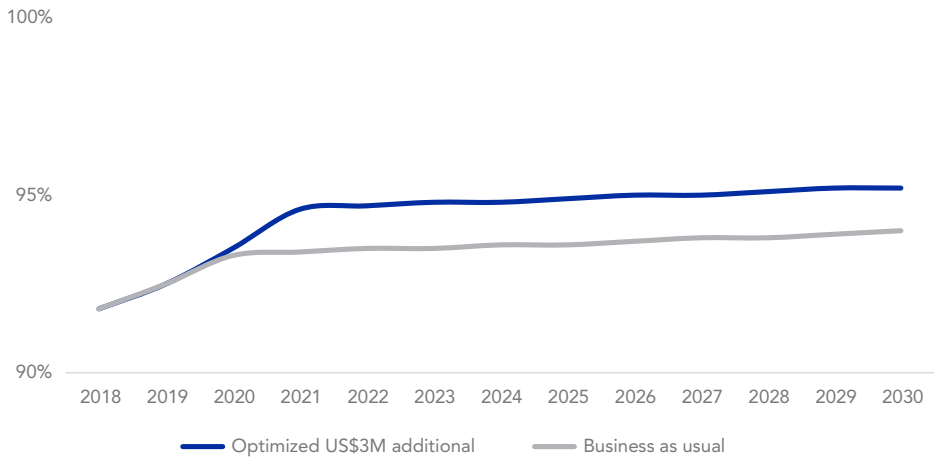
3.3.2 Exceeded: 95% treatment among those diagnosed

Based on programmatic data, Cambodia is already exceeding the 95% target for people living with HIV who are diagnosed and receiving treatment. Further gains in ensuring continuity of care may be possible by reducing rates of loss to follow-up through improved delivery of adherence programmes such as effective enhanced adherence counselling, switching to newer ARV regimens with less toxicity such as Tenofovir, Lamivudine, and Dolutegravir (TLD), and multi-month dispensing

3.3.3 On track: 95% viral suppression among those on treatment

Reported viral suppression is already high at 96% and coverage of viral load testing is improving. In 2018, viral load testing covered 81% of people on ART, and this had expanded to 90% of people on ART by 2019. The risk that those not undergoing viral load testing are also those most at risk of treatment failure, leads to a modelled viral suppression rate of slightly below 95%, but increased coverage of viral load testing in the optimized allocation for the an additional US$3M budget scenario projects that 95% of those on ART will have confirmed viral suppression by target dates (Figure 5).

Figure 5: Projected progress toward 95% viral suppression among people living with HIV on treatment



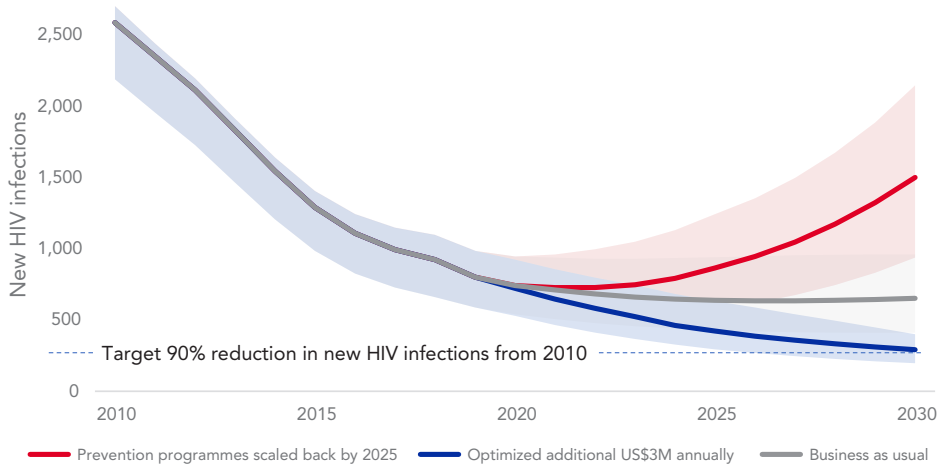
3.3.4 Not on track: Less than 250 new HIV infections per year

Since it is recommended to invest additional resources in new interventions, this may suggest that current prevention programmes are less cost-effective and not important. The scenario whereby prevention programmes are scaled back by 2025 demonstrates, however, that this is not the case.

Cambodia has had great success in reducing the number of new HIV infections, from over 8,000 per year in 2000 to approximately 2,500 in 2010, and Figure 6 demonstrates how this downward trend has continued until 2019. However, the remaining reduction in incidence needed to reach less than 250 new infections per year is also the most difficult, and projections are that under the current interventions, new HIV infections are likely to stabilize at around 700 per year.

In the absence of prevention programmes for key populations, there is the risk that this trend could be reversed, with new infection projected to more than double from 2019 values by 2030 with those new infections primarily in MSM.

Figure 6: Projected progress toward less than 250 new HIV infections per year



With an additional US$3M per year and optimized allocation of resources, the target of less than 250 new infections per year comes close to the uncertainty bound around projections. Drastically

expanded spending would be projected to reach these targets, but as highlighted in Section 3.6 there may be alternative implementation efficiencies that can cross this gap and allow Cambodia to reach all 2025 targets.

3.4 Key population outreach

Through necessity with reduced funding support, NGOs implementing prevention programmes have reduced their unit costs per person reached substantially over recent years, and introduced novel forms of outreach including via social media and peer-driven intervention, which have seen much higher yields from testing (Table 5). This indicates that they have been successful at reaching new, unknown risk populations. However, it was emphasized by NGOs that traditional prevention programmes for key populations, including through physical outreach, were critical to maintain continuity of support for key populations, and allowed trust to be developed and regular testing to occur among those of known risk.

With novel outreach programmes being provided at very small scale on a trial basis alongside traditional prevention programmes, implementing organizations felt that there was significant potential to scale-up their delivery of novel outreach and as a result to increase diagnosis in key populations and their partners.

Table 5: Outreach modality yields reported by NGOs

Modality	Reached (2019)	Yield %	Model assumptions for programme saturation
Physical outreach	52,524 KPs	0.21% (FEW), 0.94% (MSM), 1.76% (TG)	Current coverage levels reach most known-risk key populations over the duration of the year, and support harm reduction as well as provide continuity of care including regular testing. Through physical outreach, it is estimated that 35% of undiagnosed PLHIV among key populations will be tested and know their status annually.
Social media	32 KPs	81.3%	Complementary interventions projected to reach up to 30% of undiagnosed PLHIV annually, based on evidence from other countries, with the availability of unassisted self-testing being a key component of achieving this reach.
PDI+	906 KPs	3.8%	
Assisted self-testing	89 KPs	6.7%	
Unassisted self-testing	Limited application	N/A	

Preliminary programme data KHANA, RHAC January – September 2019 reported by NCHADS
KP: key populations

3.5 Pre-exposure prophylaxis

As PrEP is a newly implemented programme in Cambodia, it is recommended for prioritization in the optimization. Further analysis was conducted to evaluate the impact of implementation of PrEP. See Appendix E for full details of the assumptions around the implementation and targeting of PrEP.

It is also valuable to look at the impact of the HIV prevention programmes both in isolation and together. PrEP, key population testing through novel outreach programmes, and scaling of

current prevention programmes each have an impact on reducing new infections in the same key populations.

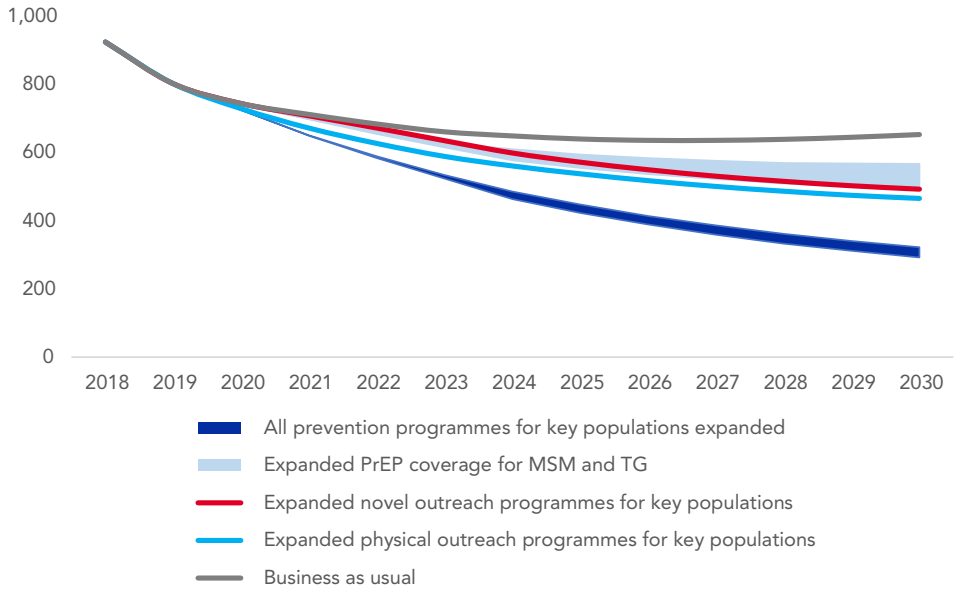
Figure 7 shows the projected impact of each programme on total new HIV infections in isolation, with the shaded area for PrEP representing targeted compared to potentially more rapid uptake. While expanding any one of these is projected to reduce new HIV infections, **it is the combination of these programmes that provides more confidence that new HIV infections will decline in the future.**

PrEP should not come at the cost of other key population programmes and should be prioritized only after maintaining and expanding existing outreach programmes for MSM and TG populations. However, should additional resources become available, target coverage levels of a total of 10,000 MSM and TG by 2023 were set by stakeholders (PrEP workshop, March 2020). With a realistic timeframe for scaling up services, 220 (140-310) annual new infections could be averted in 2025, an estimated 33% reduction from the those projected under the business as usual scenario. Cumulatively, a total of 2,040 (1,250-2,880) infections may be averted from 2020 to 2030 under this condition, a 28% reduction relative to the projected 7,323 cumulative infections from 2020 to 2030 under the business as usual scenario.

While targeted PrEP uptake with demand creation was agreed to by stakeholders there was also an understanding that it may not be possible to reach target coverage levels due to uncertainty around PrEP uptake. In this case, spending should be instead redirected toward other prevention programmes that are prioritized in the optimization.

If the same programme efficacy can be maintained when scaled up, the addition of **PrEP may be what helps Cambodia reach the 2025 targets.** However, if other prevention and outreach programmes are less effective when scaled up either due to underlying changes in risk behaviour or reaching maximum efficiency within the planned delivery modality at a lower level than expected, **PrEP may be vital to maintain control of the HIV epidemic in Cambodia**. Mobilization of additional resources will be necessary to scale up to reach the rapid uptake target for PrEP.

Figure 7: Projected new HIV infections by targeted intervention



3.6 Implementation efficiencies

Even with additional spending of up to US$5 million per year it is projected that the 2025 elimination target of less than 250 new infections will not be met. Additional optimizations were conducted at higher budget levels to determine the minimum spending necessary to reach these targets. However, while there are very cost-effective opportunities to reduce new infections through programmes such as PrEP and other expanded prevention programmes for key populations, meeting the target using only defined programme modalities was projected to require prohibitively increased spending to reach people living with HIV outside of the accessible 'known risk' key populations.

Accordingly, stakeholders were consulted on opportunities for implementation efficiencies that could close the gap towards reaching this target, in addition to cost-effective recommendations given in Section 3.2. These recommendations are in keeping with those of the 2019 Joint Programme Review of the Health Sector Response to HIV/AIDS (12).

3.6.1 Multi-month Dispensing of ART

The understanding of direct and measurable impact of multi-month dispensing on both programme cost and treatment outcomes is very limited at the time of the study. With potentially substantial reductions in cost to the health system and people receiving ART through a reduced need to visit clinics that are sometimes distant, giving greater security of supply and better adherence to people receiving treatment who have stable viral suppression. However, this does not necessarily translate into reduced programmatic costs, and there may be logistical challenges around maintaining incentives for clinics to treat patients with IDPoor cards through Cambodia's national poverty identification system. The impact on loss to follow-up is not yet clear, although expansion of multi-month dispensing may provide new evidence to better inform strategy around multi-month dispensing. Most stakeholders considered this to be an 'easy win' in terms of an implementation efficiency.

3.6.2 Same day ART treatment initiation

Similarly, same day treatment initiation for people with a confirmed HIV test was recommended by stakeholders to improve linkages to care and treatment outcomes without additional cost.

3.6.3 Recency testing added to diagnostic routines

The addition of recency testing to diagnostic routines was considered a priority by some development partners and implementing NGOs, who also expressed enthusiasm for these tests. While expensive and thus unlikely to be cost-saving, recency testing provides an additional tool that may help to identify people most at risk of infection and may contribute to moving closer to the 95% diagnosis target.

3.6.4 Viral load testing through use of existing GeneXpert

While it is likely that additional spending on viral load testing would be beneficial to ensure viral load suppression is maintained in people on ART, as shown in the study optimization, it was also identified by implementers that the use of GeneXpert machines to conduct viral load testing could be effective. The cost per GeneXpert cartridge necessary for viral load testing of US$15 is similar to the cost per test consumable with current Abbott machines (US$14). As well, more than 50 GeneXpert machines are located in provinces around Cambodia and would allow for rapid test results for people at high-risk of loss to follow-up, in comparison with Abbott testing only available

in Phnom Penh and Siem Reap, which requires the transport of tests to and from people located outside these cities.

While logistical challenges, including machine maintenance, cartridge procurement, and coordination with the tuberculosis programme, may present challenges to widespread adoption of GeneXpert testing as a cost-saving measure, this modality for viral load testing may be an additional opportunity to further improve linkage to care and rapid identification of treatment failure.

3.6.5 Strategic information and integrated data systems

One of the major challenges for the HIV response in Cambodia is that there are numerous databases which are not well integrated. With many people travelling away from their home to receive testing and treatment who often using fake names, patient tracking is difficult. The Global Fund and other development partners guided by NCHADS have an ongoing project to integrate these systems and databases to better inform the HIV response in Cambodia.

3.6.6 System integration of HIV programmes into health budget

With an increasing proportion of HIV funding coming from the Royal Government of Cambodia, the longer term view from stakeholders and a primary concern of the NAA and NCHADS is how the HIV programme will be integrated into the national health budget in future years as international HIV support is reduced.

It was not possible to model the impact of this integration in this study, and while there were risks to this integration identified in the 2018 Sustainability Roadmap and Transition Readiness Assessment (13, 14), opportunities for efficiencies also exist, with the potential for greater coordination of service delivery for HIV.

3.6.7 Improvements in delivery of PMTCT

It is estimated that more than 95% of pregnant women visit antenatal clinics, but only 85% of pregnant women living with HIV receive antiretroviral treatment in 2018. As such, mother-to-child transmission of HIV (including during breastfeeding) remains high in Cambodia and is estimated at 14% (15). Mother-to-child transmission constituted 12% of new infections in 2018 (8).

This suggests that it may be difficult to achieve higher coverage of the PMTCT programme through the current service delivery approach, so no recommendations are made around increased spending for PMTCT under optimized allocation of the most recently reported budget. However, there may be opportunities to improve delivery of this programme to further reduce MTCT.

3.6.8 Reduced consumable costs

Opportunities may exist to improve supply chain efficiencies due to wastage through overstocking and expiration of consumables in some cases and the need for emergency orders of antiretrovirals due to stockouts in other cases (CHAI programmatic data). While the costs of these are not substantial enough to be included in the optimization analysis, stakeholders identified that there is room for improvement.

Additionally, any savings that could be negotiated in procuring antiretrovirals, the biggest expenditure item, could be immediately reinvested in other programmes to achieve the impact of a higher budget scenario, but with a smaller budget.

4 Conclusions

Key recommendations to improve the HIV response in Cambodia include;

- maintaining coverage of treatment programmes,
- scaling up prevention programmes (prioritizing MSM), and
- working to increase diagnosis through a combination of self-testing, partner tracing, and other innovative modalities.

Reaching 95% targets with current practice is within reach but may require prohibitively expensive testing of hard-to-reach people living with HIV, and as such pursuing implementation efficiencies may be a more cost-effective path. Reaching less than 250 annual new infections by the target year will require both additional spending as well as identifying implementation efficiencies.

Additional recommendations from the Global Fund Request Application (2021-2023) include continuing good practices of HIV prevention interventions and employing the right mix and differentiated prevention modalities to prevent more new HIV infections and to achieve the first 95 by 2025, adoption and scaling of innovations with proven cost-efficiency, and prioritizing HIV self-testing and achieving high yields through this modality by reaching previously unreached key populations (HIV self-testing and other novel outreach are the highest priority).

If the same programme efficacy can be maintained when scaled up, the addition of **PrEP may be what helps Cambodia reach the 2025 targets**. However, if other prevention and outreach programmes are less effective when scaled up either due to underlying changes in risk behaviour or reaching maximum efficiency within the planned delivery modality at a lower level than expected, **PrEP may be vital to maintain control of the HIV epidemic in Cambodia**. Mobilization of additional resources will be necessary to scale up to reach the rapid uptake target for PrEP.

Lastly, it is important to scale up the quality of treatment services including adherence and regimen optimization in Cambodia.

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6 Appendix

Appendix A Technical Summary of the Optima HIV model

The risks of transmitting, acquiring, and dying from HIV depend on a host of different factors that can vary across the population, across partnerships, and over time. In the Optima HIV epidemic model, the population is stratified in three different ways in order to reflect this variation: by demographic and/or risk group, by health/disease state (stratified by CD4 count category), and by stage of care. Optima HIV defines the different demographic/risk groups as populations, the different disease progression stages as health states, and the different care and treatment stages as care states. For example, a given person might be a female entertainment worker (their population) and be living with HIV with a CD4 count of 350–500 (their health state), and currently be linked to care but not on treatment (their care state).

Optima HIV version 2.9.4 updated February 2020, available at hiv.optimamodel.com was used for this analysis.

A.1 Parameterization

Three different types of HIV transmission are modelled: transmission between sexual partners, transmission via sharing injecting equipment, and mother-to-child transmission. The input data associated with populations, sexual partnerships, injecting partnerships, and births are outlined in Table A1.

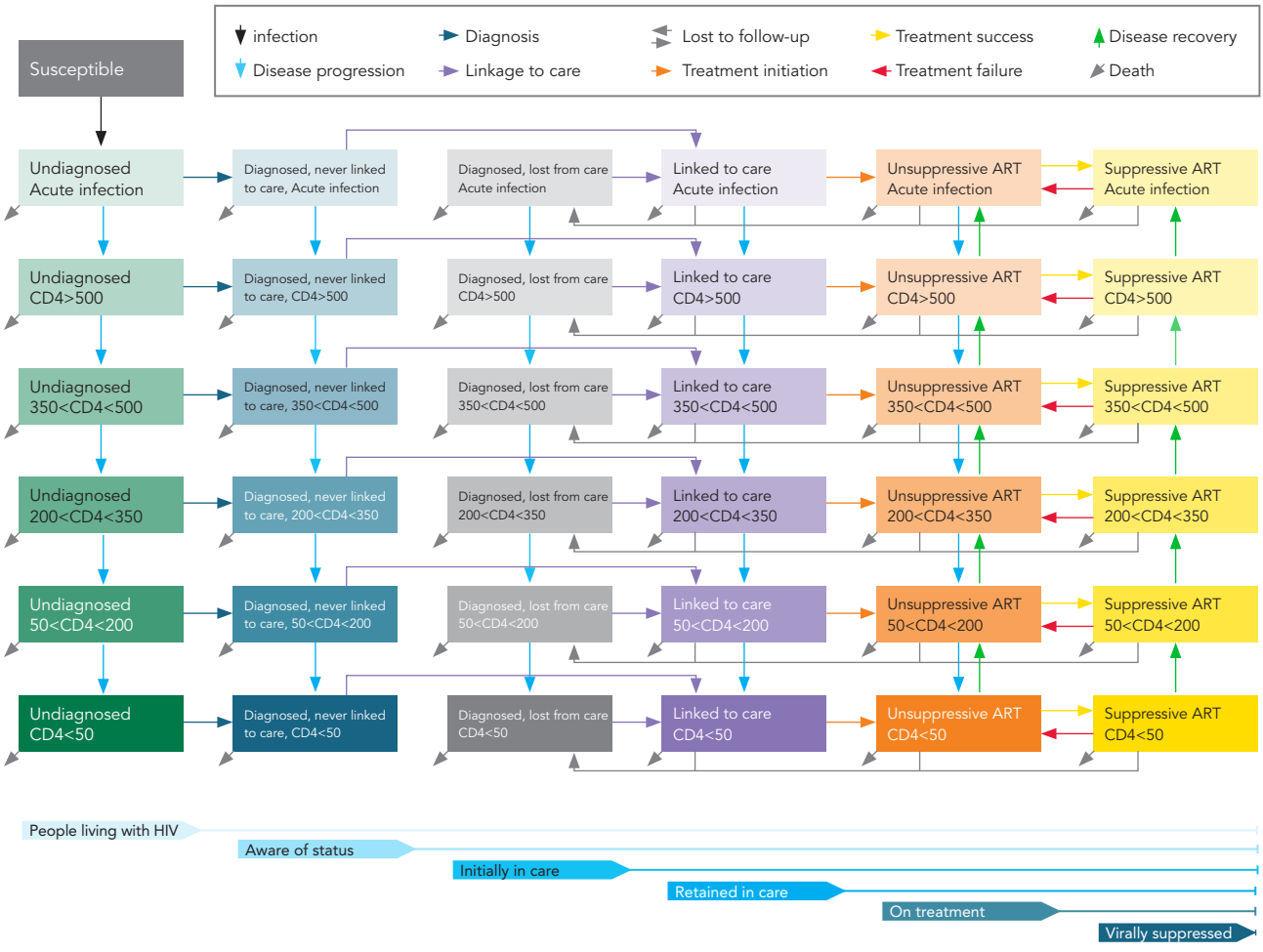
Table A1: Input variables used to characterize population groups in the Optima HIV model

Sexual risk factors
Prevalence of circumcision in population Pi at time t (defined for male populations only)
Prevalence of ulcerative sexually transmitted infections in population Pi at time t
Proportion of population Pi using pre-exposure prophylaxis at time t
Proportion of population Pi covered by PMTCT at time t (defined for female populations only)
The sex of population Pi (can be male, female, transgender, or unspecified)
Factors influencing mortality
Probability of dying of non-HIV-related causes in population Pi between time t and t+dt
Prevalence of tuberculosis in population Pi at time t
Factors influencing testing and treatment uptake
Probability of taking and receiving the results of an HIV test between time t and t+dt for population Pi
Average time taken for population Pi to be linked into care at time t
Proportion of people from population Pi who are lost from care between time t and t+dt
Factors specifying sexual partnerships
Probability at time t that condoms are used in partnerships of type *f* and act a between populations P_i and P_j (where *f is regular, casual, or transactional and a is insertive penile-anal, receptive penile-anal, insertive penile-vaginal, or receptive penile-vaginal*)

Number of interactions that occur between time t and t+dt of type *f* and act a between populations P_i and P_j
Factors specifying injecting partnerships
Number of shared injections that occur between time *t* and *t+dt* between populations P_i and P_j
Factors specifying births
Number of births between time *t* and *t+dt* where population Pi gives birth into population P_j
Proportion of population P_i that breastfeeds population P_j at time t

For female populations, Optima HIV models seven states related to the care and treatment cascade (susceptible, undiagnosed, diagnosed and never linked to care, in care and not receiving ART, receiving ART and not virally suppressed, receiving ART and virally suppressed, and, finally, lost-to-follow-up), and eight for male populations (as above, but with the susceptible compartment divided into those who have been circumcised versus those who have not been circumcised). All infected stages are further disaggregated into six CD4-related health states (acute HIV infection, >500 cells/μL [μL = microliter], 350–500 cells/μL, 200–350 cells/μL, 50–200 cells/μL, <50 cells/μL). Taken together, this gives 38 health and care states (Figure A1), one of which is not included for female populations (circumcised compartments are not shown).

Figure A1: Optima HIV model structure



A.2 Model calibration

The aim of calibration is to match model outputs to available epidemiological data as best as possible given the underlying model structure and assumptions. This is done by running simulations of the model using samples from the joint prior of all the input parameters to produce a posterior distribution for each parameter. These posteriors show how likely different parameter values are given how well the model simulations they produce compare to specific epidemiological data. Using standard Bayesian terminology, this can be reformulated in the following way. Let θ denote the model inputs (i.e., parameters), ρ denote the model outputs (i.e. prevalence), and W denote the empirical prevalence data. The model M maps the input parameters to the output, i.e. $\rho=M(\theta)$. Using empirical measurements of (or expert knowledge on) the parameters θ, it is possible to calculate the prior probability $p(\theta)$, for any choice of θ. Thus, the prior probability $p(\rho)=p(M(\theta))$ can also be estimated. Combining this estimate with the prevalence data yields $p(W|\rho)$, which is the likelihood of the empirical prevalence W given the model output prevalence ρ. The posterior distribution of the output (i.e., the most likely values of the prevalence) is given by $p(\rho \mid W)=p(\rho)p(W|\rho)$, while the posterior distribution of the inputs (i.e., the most likely values of the model parameters) is given by $p(\theta \mid W)=p(\theta)p(W|\rho)$. The likelihood function is based on how closely the outputs of the model given θ matches the observed data W, as well as how much uncertainty there is in W; it can also incorporate any prior knowledge or expert opinion. The basic idea is that when the simulation output resembles the data well, the likelihood is large, and when it does not resemble the data, the likelihood is small.

From the posterior distribution of the parameters obtained using the algorithm above, posterior predictive distributions of the model can be generated. Furthermore, the empirical posterior distribution can be bootstrapped (i.e., Monte Carlo sampling with replacement) to generate parameter sets for use in further analyses (e.g., scenarios and optimizations).

The main calibration parameters used for Optima HIV are 'initial prevalence' (the percentage of each population with HIV in the first time step of the model, January 1, 2000), and 'force of infection' which represents all factors which are not modelled explicitly but which impact on the likelihood of each population becoming infected relative to other populations.

As priority where available, individual population prevalence estimates are calibrated to prevalence survey data relating to each population, and secondarily to match existing country estimates including new HIV infections and HIV-related deaths to provide consistency with an agreed baseline.

A.3 Optimization analysis

A novel component of Optima HIV is its ability to calculate allocations of resources that optimally address one or more HIV-related objectives (e.g., impact-level targets in a country's HIV national strategic plan). Because Optima also calculates the coverage levels required to achieve these targets, it can be used to inform HIV strategic planning and the determination of programme coverage levels. The key assumptions of resource optimization are the relationships between (1) the cost of HIV programmes for specific target populations, (2) the resulting coverage levels of targeted populations with these HIV programmes, and (3) how these coverage levels of HIV programmes for targeted populations influence behavioural and clinical outcomes. Such relationships are required to understand how incremental changes in spending (marginal costs) affect HIV epidemics. Optima uses a logistic function fitted to available input data to model cost–coverage curves. Logistic functions can incorporate initial start-up costs and allow changes in behaviour to saturate at high spending levels, thus better reflecting programme reality. For best fits, saturation values of the

coverage to match behavioural data in countries with heavily funded HIV responses are typically chosen. Programme coverage for zero spending is assumed to be zero; behavioural outcomes for zero coverage are inferred using data from early in the epidemic or just before significant investment in HIV programmes. Practically, the zero and high spending cases are also discussed with local experts who can advise on private sector HIV service delivery outside the governments' expenditure tracking systems.

For each HIV program, it is necessary to derive one set of logistic curves that relate funding to programme coverage levels and another set of curves (generally linear relationships) between coverage levels and clinical or behavioural outcomes (i.e., the impacts that HIV strategies aim to achieve). Outcomes expected from changes in programme funding are assumed by interpolating and extrapolating available data using a fitted logistic curve. A limitation of this approach is that all changes in behaviour are assumed to be because of changes in programme funding.

Optima HIV can be used to minimize either (1) a given outcome (e.g., number of infections, number of disability-adjusted life years [DALYs], number of HIV-related deaths, or future HIV-related costs) given a fixed total budget over a determined programme period, or (2) the amount of funding required to meet a particular epidemiological goal (e.g., reducing HIV incidence by 50%). Optima HIV can also determine the amount of money required to simultaneously meet multiple goals (e.g., all impact-level targets in an HIV national strategic framework) or the optimal allocation of a fixed amount of resources that will simultaneously get as close as possible to achieving one or multiple target objectives. Constraints may be placed on the optimization; for example, the number of people on ART may not be allowed to decrease, or programmes cannot increase or decrease from a baseline level by more than a defined percentage each year to account for political or other constraints.

To perform the optimization, Optima HIV uses a global parameter search algorithm called adaptive stochastic descent (ASD) (16). ASD is similar to simulated annealing in that it makes stochastic downhill steps in parameter space from an initial starting point. However, unlike simulated annealing, ASD chooses future step sizes and directions based on the outcome of previous steps. For certain classes of optimization problems, ASD has been shown to determine optimal solutions with fewer function evaluations than traditional optimization methods, including gradient descent and simulated annealing.

Appendix B Model calibration

Population definitions are consistent with UNAIDS draft HIV/AIDS Estimates and Projection 2019 (9), however with additional key populations of FWID, MWUD, and FWUD included due to stakeholder concerns on the significance of those population to the HIV epidemic, as well as additional age stratification in both the key populations and general population of low risk males and females.

Key assumptions:

- Data for FWID is limited, with AEM and the UNAIDS draft HIV/AIDS Estimates and Projection 2019 not including FWID as a separate population, but they are included here using behavioural assumptions matching MWID and separate population size estimates based on NGO programmatic data of the age and gender breakdown for those reached with interventions.
- Without available primary data on the size or behaviour of MSM 2, assumptions around behaviour for MSM 2 are similar to MSM 1, although force of infection and prevalence were calibrated at lower levels to match overall epidemic trends. Similarly, it was assumed that prevalence among MSM 2 for those 25 years and older was higher than prevalence for MSM 2 aged 15-24, with a similar ratio for prevalence as these age groups for MSM 1.

Table B1: Population groups modelled in this analysis

Abbreviation	Population group	Definition
Clients	Clients of entertainment workers	Clients of entertainment workers, who have paid money or goods in exchange for sex in the last 12 months.
TG	Transgender women	Biological male at birth, 15-49 years old, self-identified as female or third gender.
MWID	Males who inject drugs	Males and females respectively, 15-49 years old, who injected drug(s) one or more time(s) in the last month. Collectively abbreviated as people who inject drugs (PWID).
FWID	Females who inject drugs	
MWUD	Males who use drugs (non-injecting)	Males and females respectively, 15-49 years old, who used non-injecting drug(s) one or more time(s) in the last month. Collectively abbreviated as people who use drugs (PWUD).
FWUD	Females who use drugs (non-injecting)	
FEW 1	Female entertainment workers 1 (7+ clients per week)	Biological females, 15 to 49 years old, who sell sex in exchange of money or goods, in the last 12 months, and who have 7 or more clients per week.
FEW 2	Female entertainment workers 2 (<7 clients per week)	Biological females, 15 to 49 years old, who sell sex in exchange of money or goods, in the last 12 months, and who have less than 7 clients per week.
MSM 1 15-24	Men who have sex with men 1 (known risk, 15-24)	Biological males, 15 to 24 and 25-49 years old respectively, who have had anal sex with another male in last 12 months including those who find and meet male sex partners though online applications.

Abbreviation	Population group	Definition
MSM 1 25-49	Men who have sex with men 1 (known risk, 25-49)	MSM 1 are those go, work, or visit at hotspot, sauna, spa, beer garden, online and offline, and are also categorized as 'known risk' MSM who can be reached through programmatic interventions.
MSM 2 15-24	Men who have sex with men 2 (unknown risk, 15-24)	Biological males, 15 to 24 and 25-49 years old, respectively, who have had anal sex with another male in last 12 months including those who find and meet male sex partners though online applications.
MSM 2 25-49	Men who have sex with men 2 (unknown risk, 25-49)	MSM 2 are those who are of 'unknown risk', and who cannot readily be reached with location-based physical outreach programmes.
MSW	Male sex workers	Defined as men who have sex with men who are selling sex at hotspot, sauna, spa, online & offline, MSWs are also categorized as 'known risk' for the purpose of being reached with programmatic interventions.
M0-14	Males (0-14)	Age stratified general population 0-14, 15-24, 25-49, and 50 years and older, analogous to low-risk males and low-risk females in AEM.
F0-14	Females (0-14)	
M15-24	Males (15-24)	
F15-24	Females (15-24)	
M25-49	Males (25-49)	
F25-49	Females (25-49)	
M50+	Males (50+)	
F50+	Females (50+)	

Based on a national Optima HIV model of Cambodia developed by the Optima Consortium for Decision Science as part of a global model of HIV (17), the project was updated with data sources for each parameter, supplemented by expert advice from stakeholder consultations.

Table B2: Model parameter data sources

Parameter	Source
Population size	Age and gender stratified population sizes from the United Nations World Population Prospects 2019 (18) Consistent with AEM, key population sizes for higher risk populations are estimated from sources including (10, 19-24):
HIV prevalence by population groups	HIV prevalence data values are used as the primary point of reference during calibration. Values are taken from a combination of primary research including survey data, where available, and expert opinion/assumptions where no data exists. Sources include (4, 10, 12, 20, 25-39):
Other epidemiology • Percentage of people who die from non-HIV-related causes per year • Prevalence of any ulcerative STIs • Tuberculosis prevalence	Key population non-HIV-related mortality and comorbidity estimates consistent with AEM (8). Overall background mortality is taken from (18), with supplementary comorbidity information from (10, 39, 40).
Testing and treatment • Percentage of population tested for HIV in the last 12 months • Probability of a person with CD4<200 being tested per year • Number of people on treatment • Percentage of people covered by ARV-based prophylaxis • Number of women on PMTCT (Option B/B+) • Birth rate (births per woman per year) • Percentage of HIV-positive women who breastfeed	The percentage of the population tested per year represents the likelihood that someone with an undiagnosed HIV infection will be diagnosed over the course of a year. As such inputs may be adjusted as part of calibration to match the proportion of HIV infections estimated to be diagnosed in each year, while maintaining trends in reported testing percentages. Sources include (4, 10, 26, 37, 41-44).
Optional indicators • Number of HIV tests per year • Number of HIV diagnoses per year • Modelled estimate of new HIV infections per year • Modelled estimate of HIV prevalence • Modelled estimate of number of PLHIV • Number of HIV-related deaths • Number of people initiating ART each year • PLHIV aware of their status (%) • Diagnosed PLHIV in care (%) • PLHIV in care on treatment (%) • Pregnant women on PMTCT (%) • People on ART with viral suppression (%)	Data entered in this section of the Optima HIV databook is not used by the model directly to generate output, but rather allows comparison points to be entered from other reliable sources or models in order to ensure consistency, in this case AEM and Spectrum output that has already being accepted nationally through a consultative process (8).

Parameter	Source
Cascade • Average time taken to be linked to care (years) (by population groups) • Average time taken to be linked to care for people with CD4<200 (years) • Percentage of people in care who are lost to follow-up per year (%/year) • Percentage of people with CD4<200 lost to follow up (%/year) • Viral load monitoring (number/year) • Proportion of those with VL failure who are provided with effective adherence support or a successful new regimen (%/year) • Treatment failure rate	Cascade parameters informed by pre- and post-implementation studies including (1, 12, 45)
Sexual behaviour • Average number of acts with regular partners per person per year • Average number of acts with casual partners per person per year • Average number of acts with transactional partners per person per year • %age of people who used a condom at last act with regular partners • Percentage of people who used a condom at last act with casual partners • Percentage of people who used a condom at last act with transactional partners • Percentage of males who have been circumcised	Sources include (10, 29, 44, 46, 47), supplemented by the NCHADS prevention database and regional estimates for sexual behaviour and consistent with AEM and Spectrum (8).
Injecting behaviours • Average number of injections per person per year • Percentage of people who receptively shared a needle/syringe at last injection • Number of people who inject drugs who are on opiate substitution therapy (OST)	Sources for injecting behaviour include (4, 10) with OST coverage supplied through programmatic data.
Partnerships and transitions • Interactions between regular partners • Interactions between casual partners • Interactions between transactional partners • Interactions between people who inject drugs • Birth • Aging • Risk-related population transitions (average number of years before movement)	Informed by population definitions, supplemented by details from (10).

Parameter	Source
Constants • Interaction-related transmissibility (% per act) • Relative disease-related transmissibility • Disease progression (average years to move) • Treatment recovery due to suppressive ART (average years to move) • CD4 change due to non-suppressive ART (%/year) • Death rate (% mortality per year) • Changes in transmissibility (%) • Disutility weights	Source for constant values used for Optima HIV are given in the Optima HIV user guide available through the online tool http://hiv.optimamodel.com

Calibration plots

While the epidemic in Cambodia has remained concentrated in key populations, there has been a shift in incidence from primarily occurring through transactional sex (both clients and female entertainment workers) at the peak of the epidemic in 1998, to rising infection rates among people who inject drugs, and stakeholders expressed concern at rapidly rising risk behaviour and incidence among men who have sex with men and transgender populations, as seen in individual calibration plots for each population below (Figure B2). The model was closely calibrated to the epidemic trends in the most recent AEM estimates, and the proportion of new infections in each population when the populations are categorized to be consistent with AEM is shown in Figure B1.

Figure B1: Modelled new HIV infections by key population

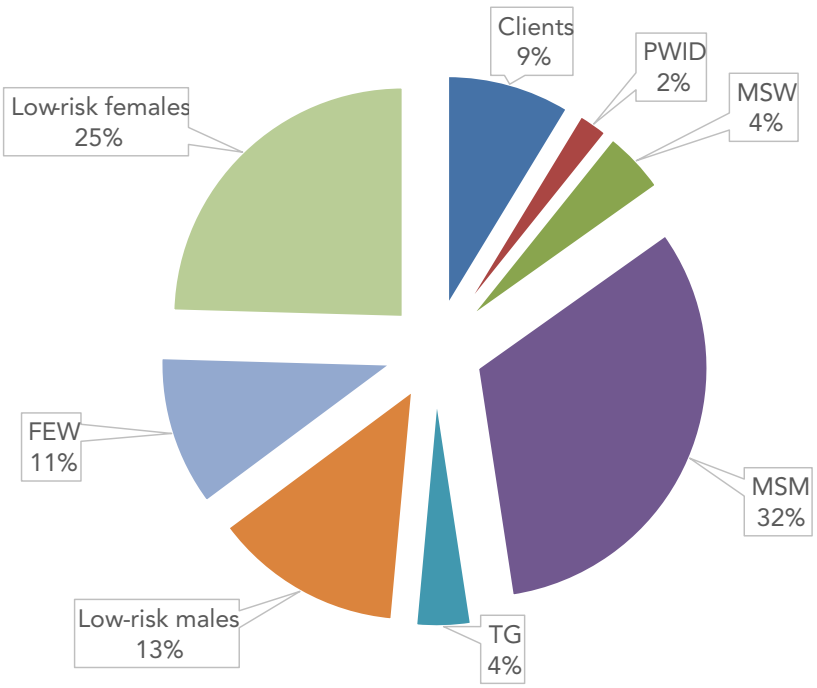
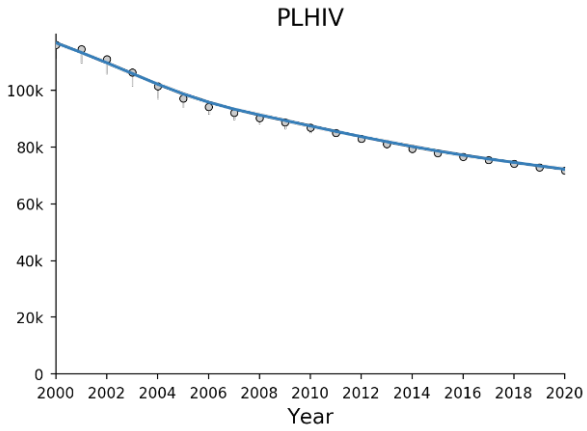
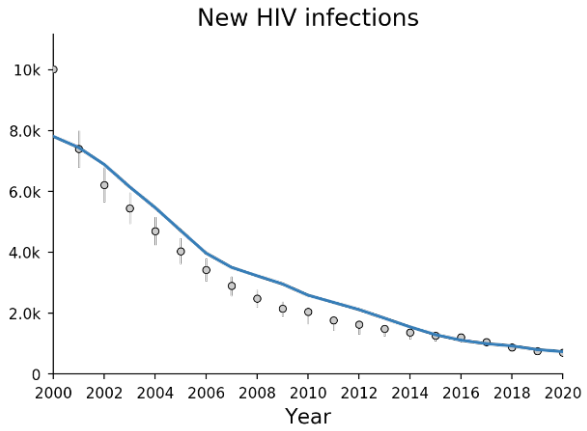
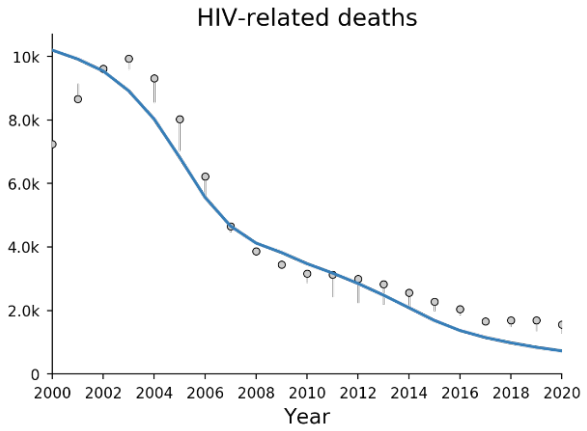
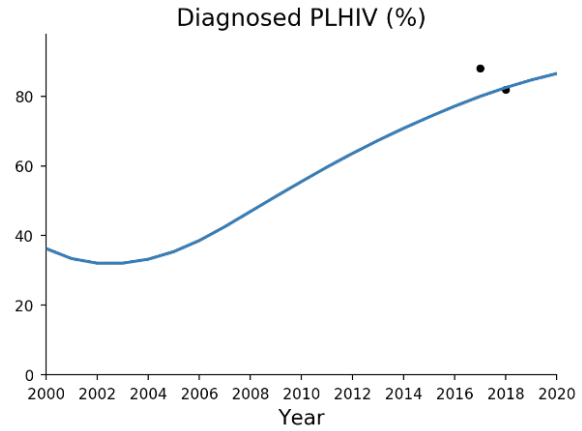


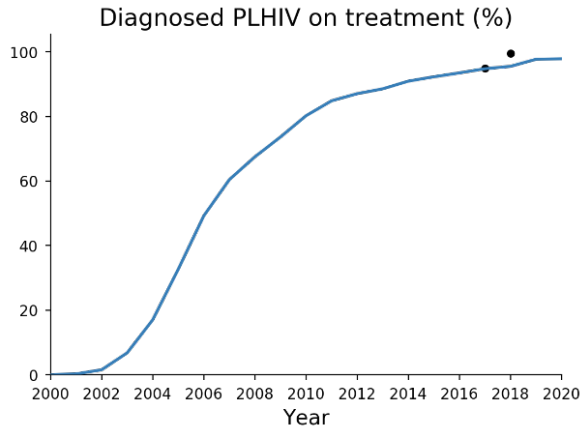
Figure B2: Calibration plots (following pages)

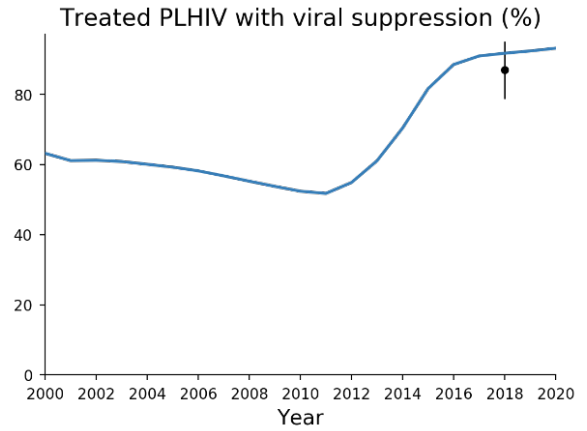


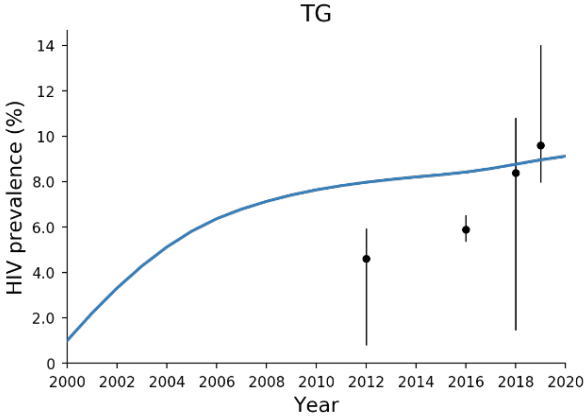


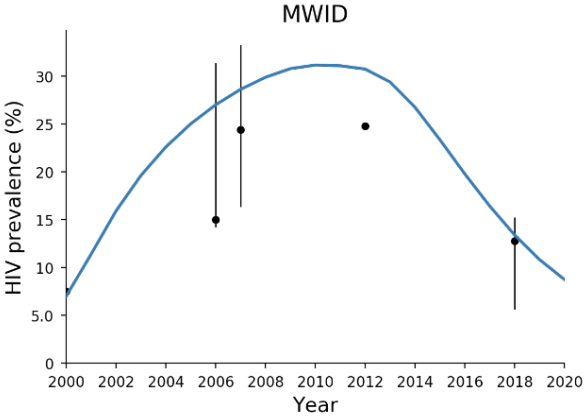


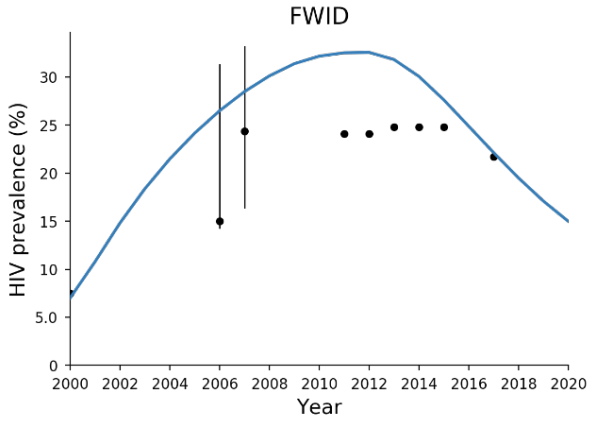


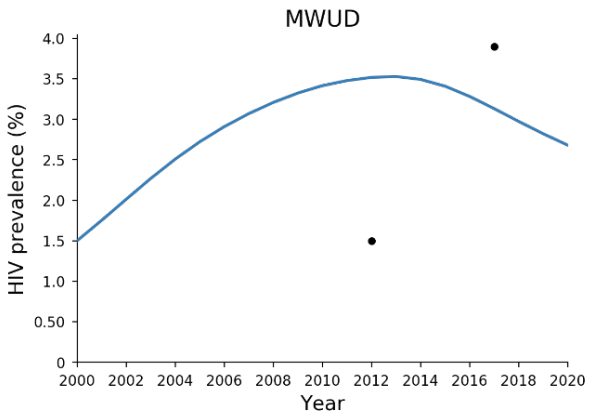


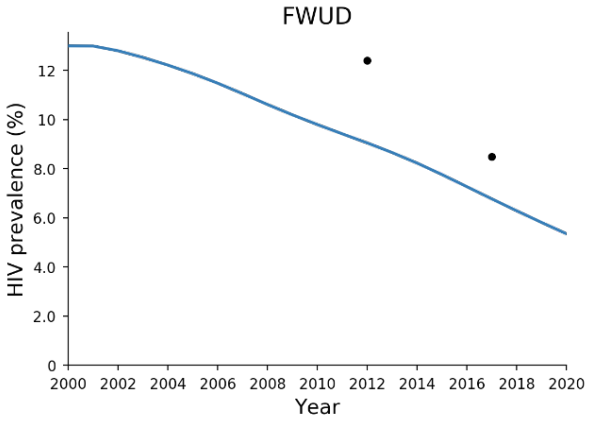


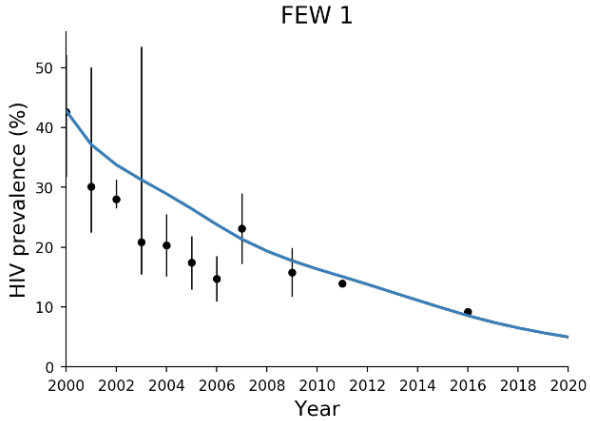


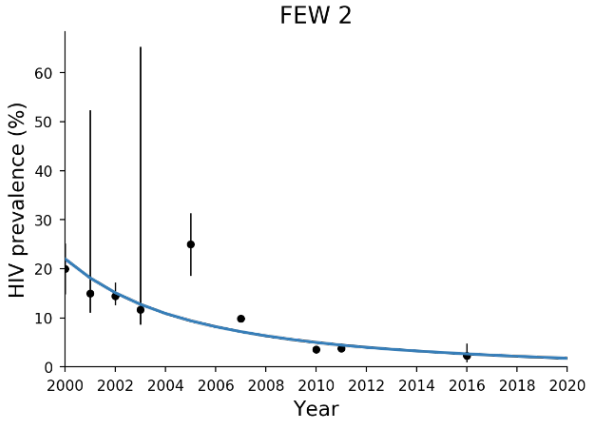


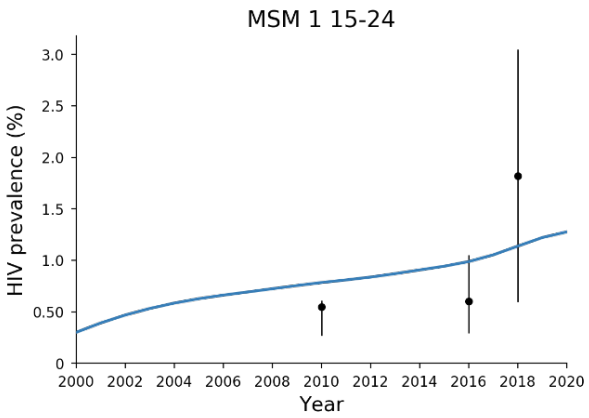

FWID
HIV prevalence (%)
Year

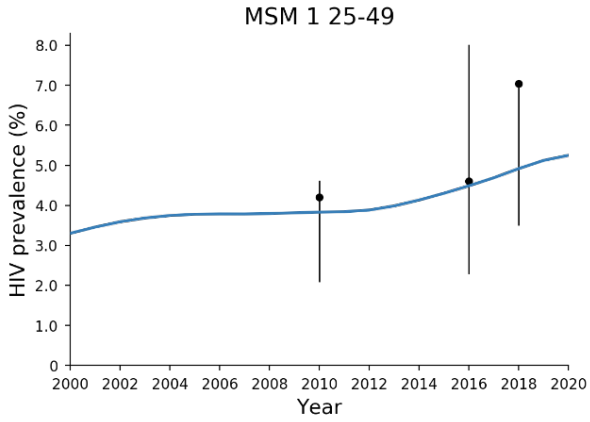

MWUD
HIV prevalence (%)
Year

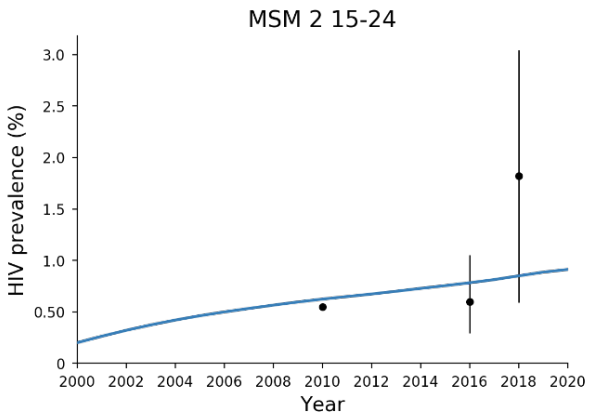

FWUD
HIV prevalence (%)
Year

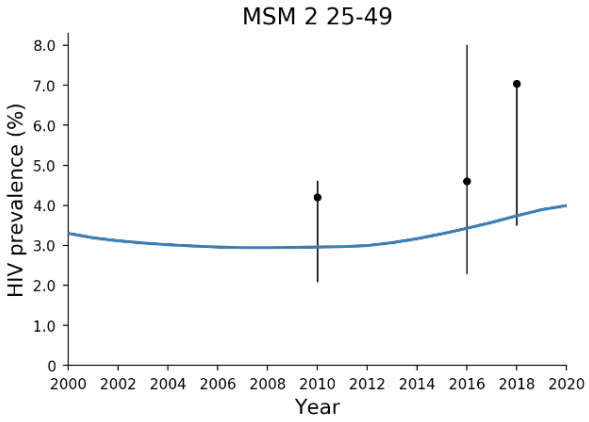

FEW 1
HIV prevalence (%)
Year

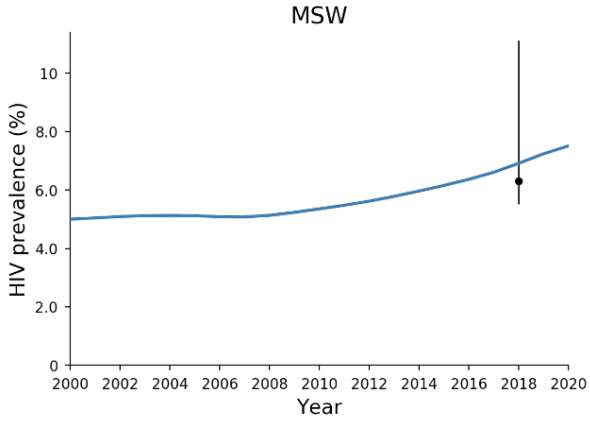

FEW 2
HIV prevalence (%)
Year

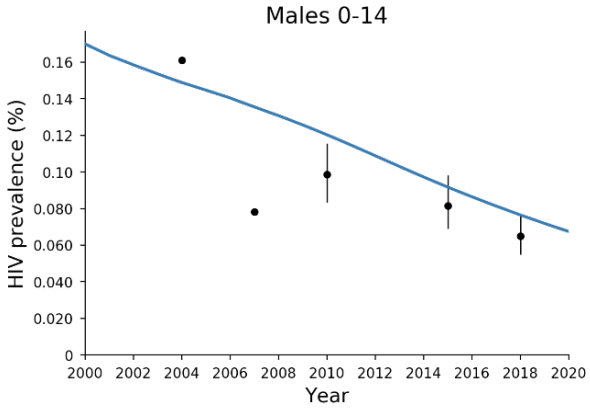

MSM 1 15-24
HIV prevalence (%)
Year

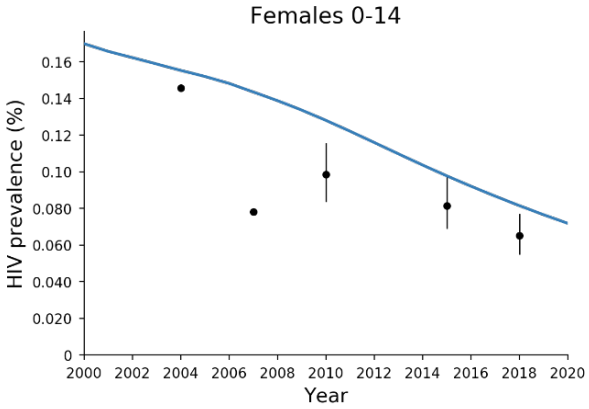

MSM 1 25-49
HIV prevalence (%)
Year

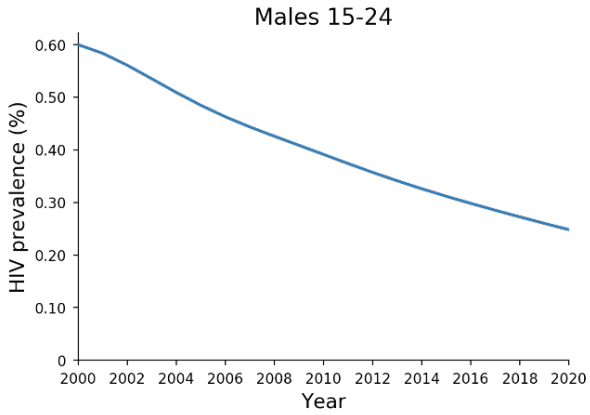

MSM 2 15-24
HIV prevalence (%)
Year

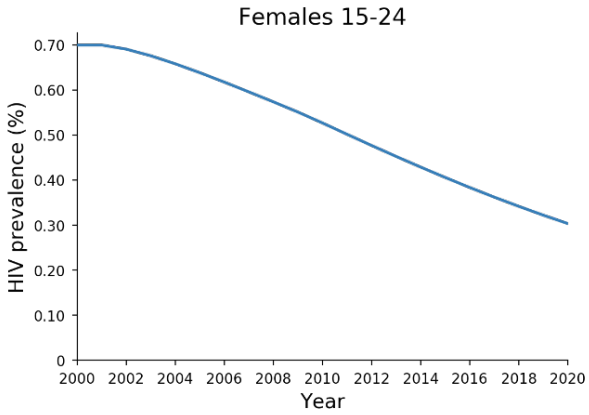

MSM 2 25-49
HIV prevalence (%)
Year

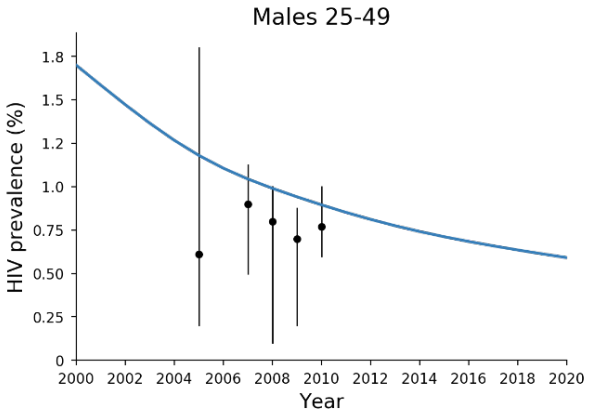

MSW
HIV prevalence (%)
Year

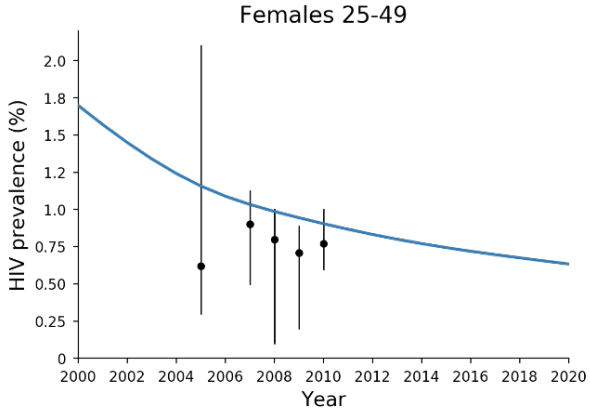

Males 0-14
HIV prevalence (%)
Year

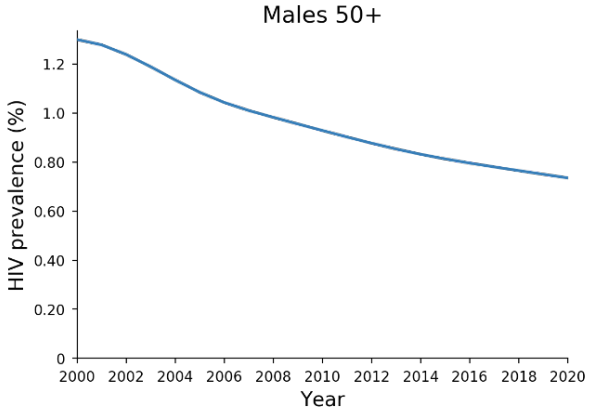

Females 0-14
HIV prevalence (%)
Year

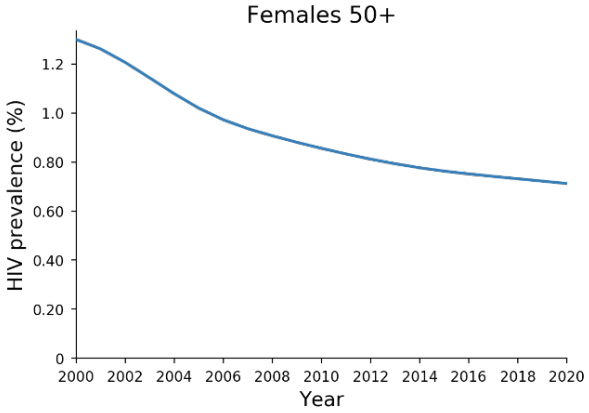

Males 15-24
HIV prevalence (%)
Year


Females 15-24
HIV prevalence (%)
Year


Males 25-49
HIV prevalence (%)
Year


Females 25-49
HIV prevalence (%)
Year


Males 50+
HIV prevalence (%)
Year


Females 50+
HIV prevalence (%)
Year

Appendix C Programme definitions

Individual programme budgets reconciled between HSSP budget total, NASA definitions, and spending data from implementing partners.

Table C1: HIV programmes included in the model; budget and unit costs US dollars

Category	Programme	Budget 2019	Unit cost 2019	Coverage 2019	Target population(s) and saturation	Impact per person covered
Treatment	Antiretroviral therapy (ART)	$9,301,548	$151.98	61,193	100% of diagnosed PLHIV	ARVs for one year.
	ART adherence support programmes	$935,376	$15.28	61,193	100% of PLHIV on treatment	Reduced loss to follow-up rate by approximately 30%, varying by population. Reduced time to be linked to care by 20%. Baseline loss to follow-up rate is up to 12-13% in key populations, and as low as 2-3% in general populations.
	Treatment monitoring - viral load (VL) testing	$1,239,366	$18.56	66,777 (tests)	PLHIV on treatment (the number of tests is applied to people on ART)	Average frequency of testing increases, with an assumption that all people on ARVs have an equal likelihood of receiving a viral load test, reducing the time to identify treatment failure and initiate second line treatment if necessary.
	Prevention of mother-to-child transmission (PMTCT)	$300,000	$509.34	586	100% of diagnosed pregnant women with HIV	PMTCT covering one pregnancy per year (including post-childbirth), not including ARVs. Includes HIV testing for infants.
Diagnostic outreach	Facility-based testing services (FBT), including provider-initiated testing and counselling (PITC)	$716,900	$10.48	68,402	Demand based, available to entire population, baseline coverage and calibration suggests approximately 15% annual probability of diagnosis through FBT and PITC for undiagnosed PLHIV without scope for increase through this modality.	One test per year including consultation costs.

Category	Programme	Budget 2019	Unit cost 2019	Coverage 2019	Target population(s) and saturation	Impact per person covered
	Enhanced key population tracing and outreach (social media, assisted self-testing, PDI+, and index testing)	$98,052	$34.64	2,831	Up to 30% of known and unknown risk MSM including MSW, TG, and FEW	One test per year including outreach costs. For each key population reached, 50% chance to also test partner including clients, PWUD, and unknown risk MSM.
HIV prevention in key populations	Prevention programmes for female entertainment workers (including physical outreach testing)	$702,731	$23.15	30,353	Up to 90% of FEW 1 and FEW 2	60% annual probability of testing for undiagnosed PLHIV in FEW 1. 40% annual probability of testing for undiagnosed PLHIV in FEW 2. Approximately 50% reduction in STI prevalence for both FEW 1 and FEW 2. Increased condom usage for casual acts from 40%-80% to 70-95% between people reached by the programme. Increased condom usage for transactional acts from 50%-80% to 80-95% between people reached by the programme.
	Prevention programmes for men who have sex with men (including physical outreach testing)	$832,292	$43.55	19,110	100% of known risk MSM including MSM 1 and MSW (no coverage of unknown risk MSM)	70% annual probability of testing for undiagnosed known risk MSM. Increased condom usage for casual acts from 50%-80% to 70-95% between known risk MSM and their partners.
	Prevention programmes for transgender people (including physical outreach testing)	$177,477	$43.55	4,075	90% of TG	146% annual probability of testing for undiagnosed TG (1 test per 8 months). Increased condom usage for casual acts from 40%-80% to 70-95% between people reached by the programme. Increased condom usage for transactional acts from 60%-90% to 80-90% between people reached by the programme.

Category	Programme	Budget 2019	Unit cost 2019	Coverage 2019	Target population(s) and saturation	Impact per person covered
	Prevention programmes for people who inject drugs and their partners (including physical outreach testing)	$34,320	$43.55	788 PWID (18%)	75% of PWID	94% annual probability of testing for undiagnosed PWID. Increased condom usage for casual acts from 30%-70% to 60-90% between people reached by the programme.
	Needle and syringe programmes (NSP)	$155,197	$114.16	1,359 PWID (31%)	65% of PWID	Reduced needle sharing from baseline of 12% to 0% for those covered.
	Opiate substitution therapy (OST)	$29,924	$440.06	68 PWID (2%)	10% of PWID	OST for one person for one year.
	Pre-exposure prophylaxis (PrEP)	$9,717	$123.00	79 (provisional 2019 data from Chhouk Sar clinic after July 2019 initiation of the PrEP programme)	4% of known risk MSM and TG, approximately 1,800 MSM	PrEP for one person for one year, covering up to 10% of acts in known risk MSM and TG due to self-selection of highest-risk population.
	Pre-exposure prophylaxis (PrEP) with demand creation	$0	$179	Not available	20% of known risk MSM and TG, approximately 9,000 additional MSM	PrEP for one person for one year, covering up to 50% of acts in known risk MSM and TG due to targeted outreach and self-selection of highest-risk population.
	Pre-exposure prophylaxis (PrEP) for FEW	$0	$179	Not available	30% of FEW 1	PrEP for one person for one year, without targeted coverage within FEW.
Non-targeted HIV programmes	Cross-cutting (management, OVC, HR and training, enabling environment, social protection, B-IACAM)	$5,164,775				

1. *Saturation: maximum possible coverage of the defined modality. Coverage increases non-linearly approaching the saturation value as spending increases, to reflect increased delivery costs.*
2. *Baseline HIV testing values: 5% annual probability of testing for key populations and 1-3% annual probability of testing for general populations in the absence of any interventions including FBT and PITC, 36% annual probability of testing for all populations with AIDS in the absence of interventions.*

Appendix D Optimization results

The below tables show the detailed budget scenarios based on the business as usual (BAU) scenario matching the 2019 HSSP programmatic budget (7), the prevention programmes scaled back by 2025 scenario which represents a steady shift from BAU in 2019 to no spending on prevention programmes by 2025, and optimized allocations if US$1 million, US$3 million, or US$5 million additional budget was respectively made available above the business as usual allocation.

Table D1: Optimized spending allocation with varying resource availability, rounded to nearest thousand, average US dollar budget 2021 to 2023 given planned time to reach scale on programmes

Budget	Prevention programmes scaled back by 2025	Business as usual	Optimized business as usual budget	Optimized US$1M additional	Optimized US$3M additional	Optimized US$5M additional
Cross-cutting (management, OVC, HR and training, enabling environment, social protection, B-IACAM)	$5,152,000	$5,152,000	$5,152,000	$5,152,000	$5,152,000	$5,152,000
Antiretroviral therapy (ART)	$9,302,000	$9,302,000	$9,302,000	$9,302,000	$9,302,000	$9,302,000
ART adherence support programmes	$935,000	$935,000	$842,000	$875,000	$875,000	$925,000
Treatment monitoring - viral load (VL) testing	$1,239,000	$1,239,000	$1,116,000	$1,159,000	$1,353,000	$1,551,000
Prevention of mother-to-child transmission (PMTCT)	$300,000	$300,000	$300,000	$300,000	$300,000	$300,000
Facility-based testing services (FBT), including provider-initiated testing and counselling (PITC)	$717,000	$717,000	$717,000	$717,000	$717,000	$717,000

Budget	Prevention programmes scaled back by 2025	Business as usual	Optimized business as usual budget	Optimized US$1M additional	Optimized US$3M additional	Optimized US$5M additional
Enhanced key population tracing and outreach (social media, assisted self-testing, PDI+, and index testing)	$50,000 ($0 by 2025)	$98,000	$420,000 (scaling up from BAU to $475,000 by 2023)	$436,000 (scaling up from BAU to $475,000 by 2023)	$436,000 (scaling up from BAU to $475,000 by 2023)	$436,000 (scaling up from BAU to $475,000 by 2023)
Prevention programmes for female entertainment workers (including physical outreach testing)	$350,000 ($0 by 2025)	$703,000	$633,000	$657,000	$880,000	$1,008,000
Prevention programmes for men who have sex with men (including physical outreach testing)	$416,000 ($0 by 2025)	$832,000	$833,000	$1,385,000	$1,385,000	$1,746,000
Prevention programmes for transgender people (including physical outreach testing)	$90,000 ($0 by 2025)	$177,000	$160,000	$166,000	$166,000	$176,000
Prevention programmes for people who inject drugs and their partners (including physical outreach testing)	$17,000 ($0 by 2025)	$34,000	$31,000	$32,000	$32,000	$34,000
Needle and syringe programmes (NSP)	$80,000 ($0 by 2025)	$155,000	$140,000	$145,000	$145,000	$153,000
Opiate substitution therapy (OST)	$30,000	$30,000	$30,000	$30,000	$30,000	$30,000
Pre-exposure prophylaxis (PrEP)	$12,000 ($0 by 2025)	$24,000	$22,000	$342,000 (scaling up from BAU to $410,000 in 2023 and $464,000 in 2025)	$342,000 (scaling up from BAU to $410,000 in 2023 and $464,000 in 2025)	$342,000 (scaling up from BAU to $410,000 in 2023 and $464,000 in 2025)

Budget	Prevention programmes scaled back by 2025	Business as usual	Optimized business as usual budget	Optimized US$1M additional	Optimized US$3M additional	Optimized US$5M additional
Pre-exposure prophylaxis (PrEP) with demand creation	$0	$0	$0	$0	$1,583,000 (scaling up from BAU to $2.3 million in 2023 and $2.5 million in 2025)	$2,644,000 (scaling up from BAU to $3.9 million in 2023 and $5.1 million in 2025)
Pre-exposure prophylaxis (PrEP) for FEW	$0	$0	$0	$0	$0	$182,000 (scaling up from BAU in 2019 to $230,000 in 2023 and $270,000 in 2025)
Total	**$17,675,000**	**$19,698,000**	**$19,698,000**	**$20,698,000**	**$22,698,000**	**$24,698,000**

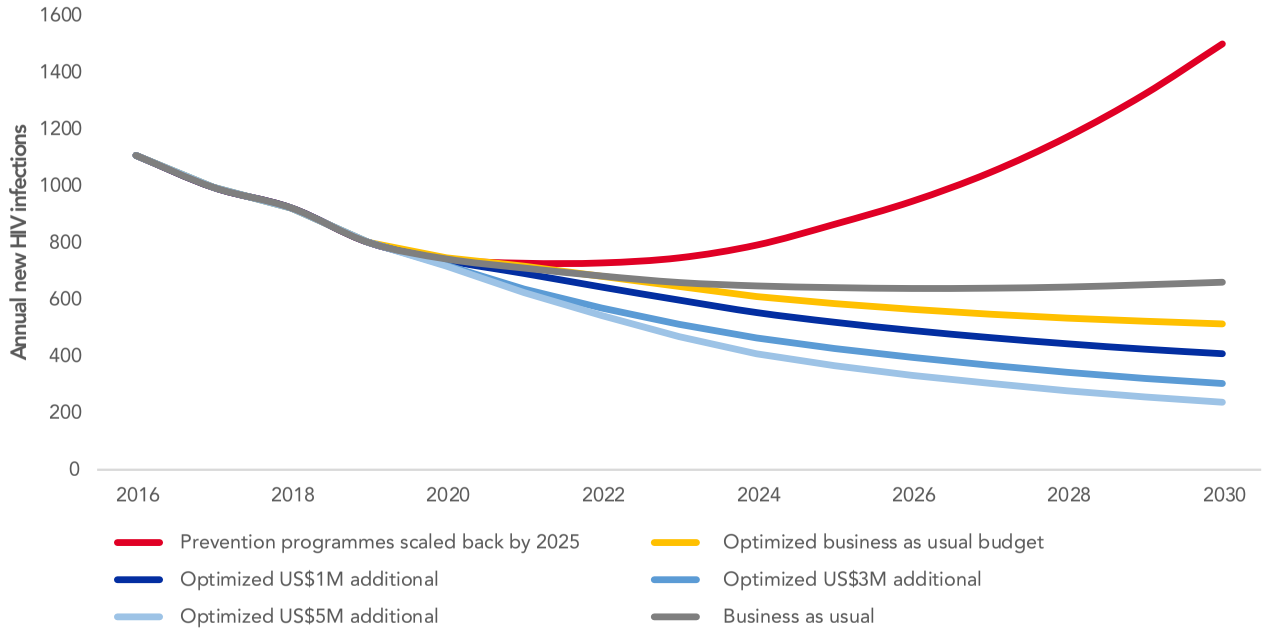
Table D2: Annual new HIV infections projected under each scenario, given as best (low-high)

Scenario	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Prevention programmes scaled back by 2025	801 (589-986)	742 (542-947)	728 (519-961)	729 (510-996)	747 (515-1,051)	792 (537-1,131)	865 (576-1,243)	946 (619-1,357)	1,047 (675-1,498)	1,173 (746-1,674)	1,324 (833-1,888)	1,501 (937-2,147)
Business as usual	801 (589-986)	743 (542-948)	711 (506-937)	683 (478-930)	660 (457-931)	648 (442-936)	642 (432-945)	639 (424-953)	640 (419-961)	644 (416-968)	652 (416-971)	661 (417-974)
Optimized business as usual budget	801 (589-986)	747 (545-953)	718 (510-945)	682 (474-931)	646 (443-918)	611 (416-906)	586 (393-893)	565 (374-878)	548 (358-862)	534 (344-843)	523 (333-820)	514 (323-791)
Optimized US$1M additional	801 (589-986)	738 (539-940)	692 (493-906)	644 (450-875)	598 (413-844)	554 (380-814)	520 (353-783)	491 (329-750)	466 (308-716)	444 (291-679)	425 (275-639)	409 (262-596)
Optimized US$3M additional	801 (589-986)	721 (528-919)	637 (459-838)	570 (406-777)	513 (363-724)	464 (328-677)	428 (299-636)	396 (275-593)	368 (253-549)	343 (235-504)	322 (219-457)	304 (205-413)
Optimized US$5M additional	801 (589-986)	718 (526-916)	624 (450-820)	543 (387-735)	470 (334-655)	408 (292-584)	367 (261-531)	333 (236-481)	304 (214-433)	279 (195-385)	257 (179-339)	238 (166-299)

Table D3: Annual HIV-related deaths projected under each scenario, given as best (low-high)

Scenario	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Prevention programmes scaled back by 2025	841 (686-896)	726 (589-781)	631 (507-685)	551 (438-605)	485 (382-539)	432 (337-486)	390 (302-445)	359 (274-414)	336 (253-393)	320 (239-382)	312 (229-380)	311 (224-387)
Business as usual	841 (686-896)	726 (589-781)	631 (507-685)	550 (437-604)	482 (380-536)	425 (332-479)	378 (292-431)	338 (259-391)	305 (232-358)	278 (209-330)	255 (190-306)	236 (175-286)
Optimized business as usual budget	841 (686-896)	727 (589-781)	634 (508-687)	552 (438-605)	482 (379-535)	423 (329-476)	373 (288-425)	331 (253-382)	295 (224-346)	265 (200-314)	240 (180-287)	219 (163-264)
Optimized US$1M additional	841 (686-896)	727 (589-781)	633 (508-687)	552 (437-604)	481 (378-534)	421 (328-473)	371 (286-422)	328 (251-377)	291 (222-339)	260 (197-306)	234 (176-277)	212 (159-251)
Optimized US$3M additional	841 (686-896)	726 (588-780)	626 (504-681)	543 (433-598)	472 (374-527)	412 (324-466)	361 (282-413)	318 (247-367)	281 (217-327)	249 (191-292)	223 (170-261)	200 (152-234)
Optimized US$5M additional	841 (686-896)	725 (588-780)	626 (504-681)	542 (433-597)	471 (373-526)	411 (323-464)	359 (281-410)	315 (245-363)	278 (215-322)	246 (189-285)	219 (168-253)	195 (149-226)

Figure D1: Projected new HIV infections by scenario



Appendix E Pre-exposure prophylaxis assumptions

With a focus on pre-exposure prophylaxis (PrEP) as a new intervention being brought to scale in Cambodia in future years, assumptions around this programme are given in more detail below.

Cost and efficacy of PrEP among female entertainment workers (FEW) were assumed to be the same as for MSM, but with reduced ability to target the highest risk FEW.

Table E1: Pre-exposure prophylaxis assumptions

Indicator	Value (2019)	Reference/assumption
MSM population size	MSM 1 15-24: 16,157 MSM 1 25-49: 24,743 MSM 2 15-24: 17,579 MSM 2 25-49: 26,921 MSW: 3,600 TG women: 6,371 Total: 95,371	AEM populations: MSM 1, MSM 2, MSW, TG Assumption that proportion of males 15-24 that are MSM is the same as the proportion of males 25-49 that are MSM
Eligible MSM population	MSM 1, MSW, and TG eligible for PrEP (50,871 people)	These are 'known risk' population that can be reached with programmes
MSM infections as proportion of new infections	40% of new infections estimated to be in MSM/TG Within MSM/TG, 49% in MSM 1 31% in MSM 2 11% in MSW 9% in TG Total of 28% of all new infections among eligible MSM/TG	40% matches AEM 2019 (8) Optima model calibration for breakdown. Proportion of new infections in MSM/TG projected to rise to 63% by 2030 under current conditions given recent behavioural data.

Indicator	Value (2019)	Reference/assumption
'High-risk' MSM	Among MSM/TG, 30% of MSM/TG account for 75% of higher risk acts This implies that 70% of MSM/TG are lower risk, including 50% who have regular partners and 20% who may have less frequent contact with high risk partners.	Historical assumptions around the number acts per week are in the region of 1.28 – 1.5 acts per week, half of which are with regular partners and half with casual partners (8). Most recent behavioural data (NCHADS prevention database 2020) suggests the number of acts may have climbed to over 4 per week average especially among MSM aged 15-24, and over 2 in MSM aged 25-49, with 30% reporting recent casual partners. This increase is likely related to high-risk behaviours such as chemsex and would be concentrated within those who previously had casual partners rather than regular partners, who would be assumed to have a similar number of acts. High uncertainty remains around this assumption, but it is a reasonable estimate based on experience with other countries, anecdotal evidence, and behavioural surveys.
'Saturation' coverage	4% (2,035) who might be reached over time without significant scaleup of demand creation from current delivery 20% (10,174) additional who might be reached with significantly scaled up demand creation through service providers and social media.	Assumption based on experience with other countries
Unit cost	$123 without demand creation $179 with demand creation	FHI 360 calculations for component costs of PrEP, including training, testing, and prophylactic drugs, but not including monitoring and evaluation or other external costs are approximately $123. These costs assume that the programme reaches a larger scale than early pilots, reducing the cost-per-person attributed to training. Higher costs of demand creation are also based on the higher estimate of the FHI 360 calculations of US$175 per person per year, with an addition component of a planned US$200,000 in outreach divided among the target population. An addition of approximately US$50 is in keeping with demand creation costs for PrEP in Thailand (48) or the combination of adherence and demand creation costs in Kenya and Uganda (49).

Indicator	Value (2019)	Reference/assumption
'Target' coverage with US$3M additional	From within the highest risk 30% of MSM, and within a total increase of US$3M per year until 2025, target PrEP coverage is 1,259 without demand creation through existing clinics, and an additional 4,120 reached through demand creation. These numbers translate to covering 26% of high-risk interactions in MSM/TG through covering 10.5% of MSM/TG, at a cost of approximately US$1 million per year. Within a total increase of US$5M per year, these target numbers would rise to 1,521 and 6,283, respectively.	Based on mathematical optimization and saturation curves – e.g. more might be covered without demand creation, but the cost for that would rise as well through having to make drugs available at more clinics where there may be minimal demand. A key point of agreement between stakeholders when discussing the implementation of PrEP was that asking for PrEP should be a primary factor in eligibility for anyone who understands what they are asking for, given that accurately stating sexual and other risk behaviour can be very challenging. One risk that could increase the cost of this programme is that in order to cover the target proportion of higher risk individuals, PrEP may additionally need to be supplied on-demand to those at lower risk, so the coverage costs would need to rise in order to achieve the target impact.
PrEP efficacy	73% [65% - 80%] efficacy in preventing new infections	See Optima HIV user guide for detailed sources. At http://hiv.optimamodel.com
Time to implement PrEP	With demand creation, targets of: 141 as of March 2020 increased to 1,000 by end of 2020, then 3,000 additional per year by 2023, up to 10,000 total MSM and TG by the end of 2023.	PrEP workshop, March 2020
Reduction in new infections	Covering 26% of high-risk interactions in populations accounting for 40% of new infections, covered multiplied by a 73% reduction in transmission would suggest an 8% reduction in infections (rising to 12% by 2030), but as modelled, the flow on effect in reducing transmission between MSM/TG is more significant as averted infections amongst those on PrEP become averted infections amongst those they later interact with, leading to an approximately 20% total projected reduction in new infections from 2020 to 2030.	Optima HIV model projections under alternative scenarios.