Optima: A Model for HIV Epidemic Analysis, Program Prioritization, and Resource Optimization

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Abstract: Optima is a software package for modeling HIV epidemics and interventions that we developed to address practical policy and program problems encountered by funders, governments, health planners, and program implementers. Optima's key feature is its ability to perform resource optimization to meet strategic HIV objectives, including HIV-related financial commitment projections and health economic assessments. Specifically, Optima allows users to choose a set of objectives (such as minimizing new infections, minimizing HIV-related deaths, and/or minimizing long-term financial commitments) and then determine the optimal resource allocation (and thus program coverage levels) for meeting those objectives. These optimizations are based on the following: calibrations to epidemiological data; assumptions about the costs of program implementation and the corresponding coverage levels; and the effects of these programs on clinical, behavioral, and other epidemiological outcomes. Optima is flexible for which population groups (specified by behavioral, epidemiological, and/or geographical factors) and which HIV programs are modeled, the amount of input data used, and the types of outputs generated. Here, we introduce this model and compare it with existing HIV models that have been used previously to inform decisions about HIV program funding and coverage targets. Optima has already been used in more than 20 countries, and there is increasing demand from stakeholders to have a tool that can perform evidence-based HIV epidemic analyses, revise and prioritize national strategies based on available resources, set program coverage targets, amend subnational program implementation plans, and inform the investment strategies of governments and their funding partners.

Key Words: software, modeling, HIV epidemiology, resource optimization, technical efficiency, coverage targets

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INTRODUCTION

Despite decades of research and investment, HIV remains a major contributor to the global burden of disease[1]: each day, more than 7000 people become newly infected with HIV.[2] AIDS remains one of the leading causes of death for adults globally and particularly in sub-Saharan Africa.[3] Furthermore, development assistance for HIV has stabilized and further increases of HIV financing are likely to be from domestic sources.[4,5] In this context of limited resources, it is imperative to allocate available funds as efficiently as possible. Especially as countries transition to domestically funded programs, they can consider different implementation approaches to reduce unit costs.

An allocatively efficient HIV response is one in which the funding for HIV programs (and thus the coverage levels for each program) is allocated in a way that will yield the greatest impact in managing and reducing HIV disease burden over a specified period. Quantifiable improvements in HIV allocative efficiency have long been sought.[6] Although most countries acknowledge the need for allocative efficiency, investing in the right mix of programs for the right populations in the right geographical areas is challenging because of both political interests and the complexity of most HIV epidemics. Consequently, many countries do not prioritize the most efficacious interventions or scale them to appropriate coverage levels.[7] Recently, Anderson et al[8] performed a detailed allocative efficiency analysis of the Kenyan HIV epidemic that examined resource allocations across multiple populations, interventions, and geographical locations. They found that 14% more infections could be averted over the study period (2014–2029) if resources were targeted to the most effective interventions and the regions most in need.

To help national governments and other stakeholders understand their HIV epidemics and allocate limited

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resources most efficiently, we developed Optima (formerly known as Prevtool; eg,[9,10]), a software toolbox that models (1) HIV transmission within and between population groups, (2) disease progression, (3) the effects of HIV prevention and treatment programs, and (4) the economic effects of policy choices. We designed it to be flexible and comprehensive enough to accommodate the regional, national, and epidemiological diversity of HIV epidemics. Optima can be used to (1) estimate epidemiological trends to produce long-term forecasts, including for counterfactual scenarios; (2) calculate program cost-effectiveness, returns on investment, and other economic and HIV-related health outcomes; (3) determine the allocation of resources and associated coverage levels that minimize any of several objectives, including the number of new infections, HIV-related deaths and disease burdens, current and future HIV-related costs, or combinations thereof; and (4) determine the minimal resources required to achieve specific targets regarding those objectives. Innovatively, it performs optimization of resource allocations over different periods using a formal mathematical algorithm.

The Optima model includes sexual, injecting-related, and vertical transmission of HIV and can incorporate an arbitrarily large number of different population groups, including key affected populations and age stratifications. In Figure 1A, we show a typical selection of population groups for a concentrated HIV epidemic. Here, 7 populations are used, including males and females in the general population, sex workers and their clients, males and females who inject drugs, and men who have sex with men (MSM). Populations can also be stratified by age, which is particularly important for generalized epidemics. Optima allows flexible definitions of population groups: for example, all or some MSM may also engage in injecting behavior; alternatively, persons in the general population of different ages may have different sexual behavior and choose partners either younger or older than themselves. The number of HIV programs and their definitions are also not fixed: users can choose HIV programs for specific populations or even to try out the impacts of new HIV programs or new (lower cost) HIV service delivery models. Optima can incorporate different HIV service delivery models, including different unit cost estimates for given program coverage levels; potential impacts of technical (program) efficiency gains can thus be included in the analyses.

We have so far completed allocative efficiency analyses with Optima in more than 20 countries across Africa, Eastern Europe, Latin America and the Caribbean, and Asia. To our knowledge, Optima is the only HIV software package that allows users to optimize funding to meet strategic HIV program impacts without presupposing program coverage levels. This article outlines the methodology underlying Optima and compares Optima to other commonly used HIV models, namely the Goals (Spectrum) Model,[11,12] the AIDS Epidemic Model (AEM),[13] the Estimation and Projection Package (EPP),[14,15] and the Modes of Transmission (MOT) model.[16] To illustrate Optima's use in the real world, we present a case study of how it was applied in Sudan, a low-income country with a low-level HIV epidemic.

METHODS

This section provides a qualitative description of the methods used in Optima; further details are provided in the Supplemental Digital Content (http://links.lww.com/QAI/A662).

HIV Epidemic Model

Optima is based on a dynamic, population-based HIV model; Figure 1B shows the disease progression implemented in the model. Optima tracks the entire population of people living with HIV (PLHIV) across 5 stages of CD4 count. These CD4 count stages are aligned to the progression of WHO treatment guidelines, namely, acute HIV infection, and CD4 counts of >500, 350–500, 200–350, 50–200, and <50 cells per microliter. Key aspects of the ART service delivery cascade are included: from infection to diagnosis, ART initiation on first-line therapy, treatment failure, subsequent lines of therapy, and HIV/AIDS-related or other death. The primary purpose of HIV testing is to identify those who are HIV positive. With the new UNAIDS global targets of 90% of PLHIV identified by 2020, 90% of them on treatment, and 90% of these virally suppressed,[12] the structure of the disease progression model in Optima is designed to help countries measure and achieve this goal and optimize resource allocations accordingly.

The model uses a linked system of ordinary differential equations to track the movement of PLHIV between HIV health states; the full set of equations is provided in the Supplemental Digital Content (http://links.lww.com/QAI/A662). The overall population is partitioned in 2 ways: by population group and by HIV health state. Individuals are assigned to a given population group based on their dominant risk. However, to capture important cross-modal types of transmission, relevant behavioral parameters can be set to nonzero values (eg, males who inject drugs may engage in commercial sex; some MSM may have female sexual partners).

HIV infections occur through the interaction between different populations by regular, casual, or commercial (including transactional) sexual partnerships, through sharing of injecting equipment, or through mother-to-child transmission. The force-of-infection is the rate at which uninfected individuals become infected, and it depends on the number and type of risk events to which individuals are exposed in a given period (either within their population groups or through interaction with other population groups) and the infection probability of each event. Mathematically, the force-of-infection has the general form:

$$\lambda = 1 - (1 - \beta)^{n},$$

where λ is the force-of-infection, β is the transmission probability of each event, and n is the effective number of at-risk events (ie, n gives the average number of interaction events with HIV-infected people where HIV transmission may occur). The value of the transmission probability β varies across CD4 count compartments (indirectly reflecting the high viral load at early and late stages of infection), differs for different modes of transmission (intravenous drug injection with a contaminated needle–syringe, penile–vaginal or

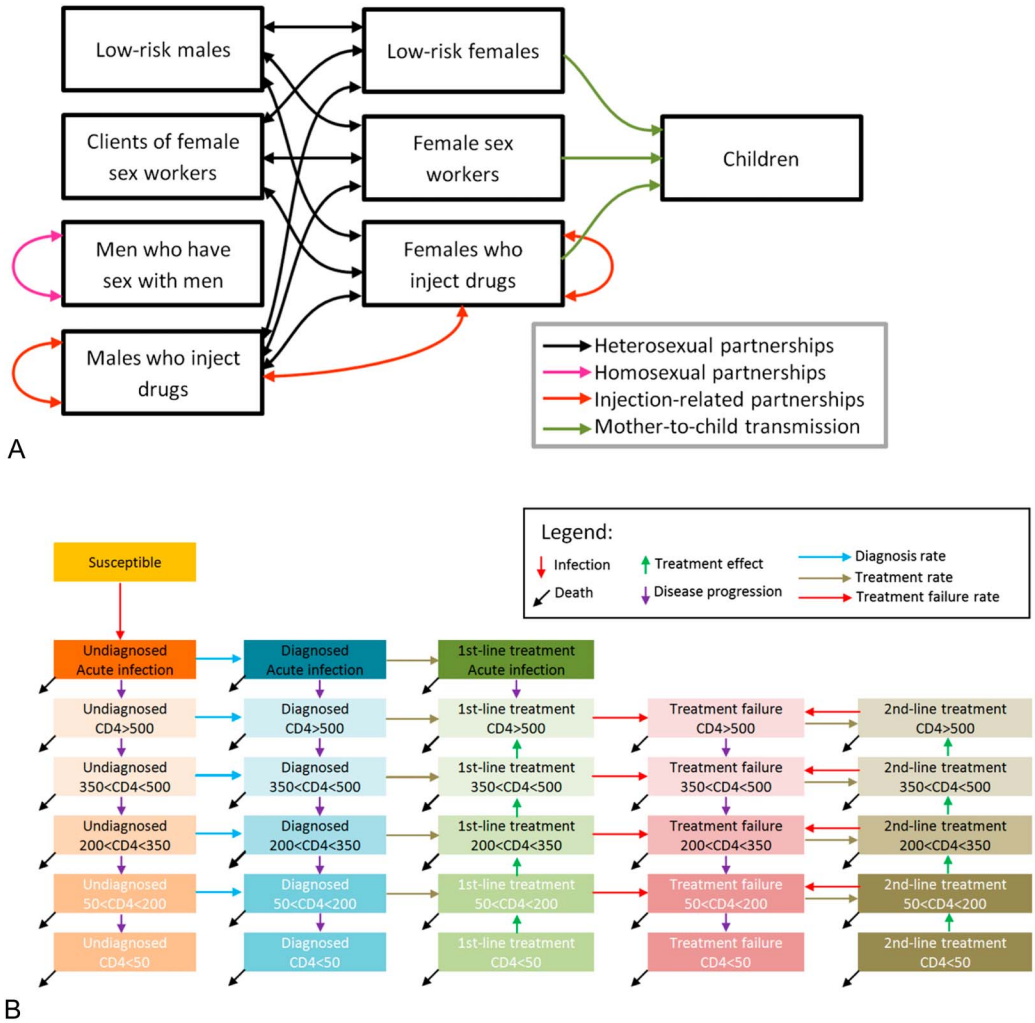


FIGURE 1. A, Example population groups and HIV transmission-related interactions in Optima. B, Schematic diagram of the health state structure of the model. Each compartment represents a single population group with the specified health state while each arrow represents the movement of individuals between health states. All compartments except for "susceptible" represent individuals living with HIV. Death includes all causes of death.

penile–anal intercourse, and mother-to-child), and may be reduced by behavioral interventions (eg, condom use),[17,18] biological interventions (eg, male circumcision), or ART.[19,20] There is one force-of-infection term for each type of interaction [eg, casual sexual relationships between male sex workers and female sex workers (FSW)]; the force-of-infection for a given population will be the sum of all interaction types.

For sexual transmission, the force-of-infection is determined by:

- The HIV prevalence (weighted by viral load) in partner populations;
- The average number of casual, regular, and commercial homosexual and heterosexual acts per person per year;
- The proportion of these acts in which condoms are used;
- The proportion of men who are circumcised;
- The prevalence of sexually transmissible infections (which can increase HIV transmission probability);
- The proportion of acts that are covered by pre-exposure prophylaxis and postexposure prophylaxis;
- The proportion of partners on ART; and
- The efficacies of condoms, male circumcision, postexposure prophylaxis, pre-exposure prophylaxis, and ART at preventing HIV transmission.

For injecting-related transmission, the force-of-infection is determined by:

- The HIV prevalence (weighted by viral load) in populations of people who use a syringe and then share it;
- The number of injections per person per year;
- The proportion of injections that use shared equipment;
- The fraction of people who inject drugs on opioid substitution therapy and its efficacy in reducing injecting behavior.

For mother-to-child transmission, the number of infections is determined by:

- The birth rate among women living with HIV;
- The proportion of women with HIV who breastfeed;
- The probability of perinatal HIV transmission in the absence of intervention; and
- The proportion of women receiving prevention of mother-to-child transmission (PMTCT), including ART.

In addition to the force-of-infection rate, which determines the number of individuals who become infected with HIV per year, there are 7 other ways individuals may change health states. First, individuals may die, either because of an average background death rate for that population (which is greater for older populations or for people who inject drugs) or because of HIV/AIDS (which depends on CD4 count). Second, in the absence of treatment, individuals progress from higher to lower CD4 counts. Third, individuals can move from undiagnosed to diagnosed states based on their HIV testing rate, which depends on CD4 count (eg, people with AIDS symptoms or primary HIV infection may have a higher testing rate) and population type (eg, FSW may test more frequently than females in the general population). Fourth, diagnosed individuals may commence ART, at a rate depending on CD4 count. Fifth, individuals may experience treatment failure because of lack of adherence to therapy or development of drug resistance. Sixth, people may initiate second and subsequent lines of treatment from treatment failure. Finally, while on successful first- or second-line treatment (ie, effective viral suppressive therapy), individuals may progress from lower to higher CD4 counts.

The change in the number of people in each compartment is determined by the sum over the relevant rates described above, multiplied by the population size of the compartments on which they act. For example, the change in the number of undiagnosed HIV-positive FSW with a CD4 count between 200 and 350 cells per microliter is:

$$\frac{dU_{\mathrm{FSW}_{200-350}}}{dt} = U_{\mathrm{FSW}_{350-500}}\tau_{350-500} - U_{\mathrm{FSW}_{200-350}}\left(\mu_{200-350} + \tau_{200-350} + \eta_{\mathrm{FSW}_{350-500}}\right),$$

where $U_{\mathrm{FSW}_{200-350}}$ is the current number of undiagnosed HIV-positive FSW with a CD4 count between 200 and 350 cells per microliter, $U_{\mathrm{FSW}_{350-500}}$ is the same population but with higher CD4 count (350–500 cells/μL), τ is the disease progression rate for the given CD4 count (where $1/\tau$ is the average time to lose 150 CD4 cells/μL), μ is the death rate, and η is the HIV testing rate. (Note: this example does not consider movement between populations, such as FSW returning to the general female population and vice versa—something which is included in Optima.) Each compartment

TABLE 1. Input Parameters of the Model

	Biological Parameters	Behavioral Parameters	Epidemiological/Other Parameters
Population parameters	Background death rate		Population sizes (T, P)
HIV-related parameters	Sexual HIV transmissibilities* (H)		
	STI-related transmissibility increase*	Number of sexual partners* (T, P, S)	
	Condom efficacy*	Number of acts per partner* (S)	HIV prevalence (T, P)
	Circumcision efficacy*	Condom usage probability* (T, P)	STI prevalence (T, P)
	HIV health state progression rates (H)	Circumcision probability* (T)	
	HIV-related death rates (H)		
MTCT parameters	Mother-to-child transmission probability*	Birth rate*	
		PMTCT access rate* (T)	
Injection-related parameters	Injecting HIV transmissibility*	Number of injections* (T)	
	Syringe cleaning efficacy*	Syringe sharing probability* (T)	
	Drug-related death rate	Syringe cleaning probability*	
		Methadone treatment probability (T)	
Treatment parameters	ART efficacy in reducing infectiousness*	HIV testing rates (T, P, H)	Number of people on ART (T)
	ART failure rates		
Economic parameters	Health utilities		Costs of all prevention, care and treatment programs, enablers and management (T, I)
			Cost-outcome curves (T, I)
			Discounting and inflation rates (T)
			Health care costs

*Parameter is used to calculate the force-of-infection.

H, parameter depends on health state; I, parameter depends on intervention type; P, parameter value depends on population group; S, parameter depends on sexual partnership type; STI, sexually transmissible infection; T, parameter value changes over time.

(Fig. 1B, boxes) corresponds to a single differential equation in the model, and each rate (Fig. 1B, arrows) corresponds to a single term in that equation.

Table 1 lists the parameters used in Optima; most of these are for calculating the force-of-infection. We interpret empirical estimates for model parameter values in Bayesian terms as prior distributions. The model must then be calibrated, which is the process of finding posterior distributions of the model parameter values such that the model generates accurate estimates of HIV prevalence, the number of people on treatment, and any other epidemiological data that are available (eg, HIV-related deaths). The calibration can be performed automatically, manually, or a combination of both. This process of model calibration and validation should normally be performed in consultation with governments in the countries in which the model is being applied.

HIV Resource Optimization and Program Coverage Targets

A novel component of Optima is its ability to calculate allocations of resources that optimally address one or more HIV-related objectives (eg, 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 program coverage levels. The key assumptions of resource optimization are the relationships between (1) the cost of HIV programs for specific target populations, (2) the resulting coverage levels of targeted populations with these HIV programs, and (3) how these coverage levels of HIV programs for targeted populations influence behavioral and clinical outcomes. Such relationships are required to understand how incremental changes in spending (marginal costs) affect HIV epidemics. A traditional approach is to apply unit cost values to inform a linear relationship between money spent and coverage attained. This is a reasonable assumption for programs like an established ART program that no longer incurs start-up or initiation costs, but less appropriate for condom promotion and behavior change communication programs. Most HIV programs typically have initial setup costs, followed by a more effective scale-up with increased funding. However, there are saturation effects for very high coverage levels, since these require increased incremental costs due to demand generation and related activities for the most difficult-to-reach groups.

Optima uses a logistic function fitted to available input data to model cost–coverage curves; Figure 2 shows an example. (Coverage–outcome relationships are assumed to be linear here for illustration purposes.) Logistic functions can incorporate initial start-up costs and allow changes in behavior to saturate at high spending levels, thus better reflecting program reality. The logistic function has the form:

$$L(x) = A + \frac{B - A}{1 + e^{-(x - C)/D}},$$

where $L(x)$ relates spending to coverage, x is the amount of funding for the program, A is the lower asymptote value (adjusted to match the value of L when there is no spending on a program), B is the upper asymptote value (for very high spending), C is the midpoint, and D is the steepness of the transition from A to B. For our fits, we typically choose saturation values of the coverage to match behavioral data in countries with heavily funded HIV responses. Program coverage for zero spending is assumed to be zero; behavioral outcomes for zero coverage are inferred using data from early on in the epidemic or just before significant investment in HIV programs. Practically, we also discuss the zero and high spending cases with local experts who can advise on private sector HIV service delivery outside the governments' expenditure tracking systems.

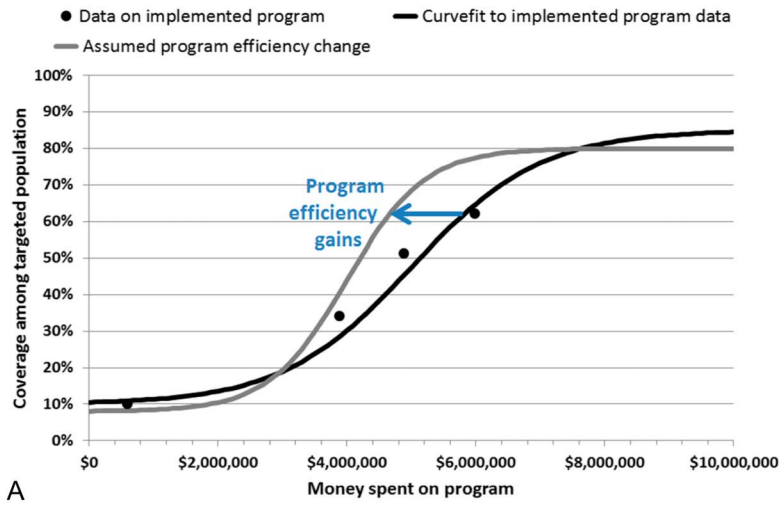
For each HIV program, we derive one set of logistic curves that relate funding to program coverage levels and another set of curves (generally linear relationships) between coverage levels and clinical or behavioral outcomes (ie, the impacts that HIV strategies aim to achieve). In future, Optima will include a default set of these cost-coverage-outcome curves, based on all available international evidence. Outcomes expected from changes in program funding are assumed by interpolating and extrapolating available data using a fitted logistic curve. A limitation of this approach is that all changes in behavior are assumed to be because of changes in program funding.

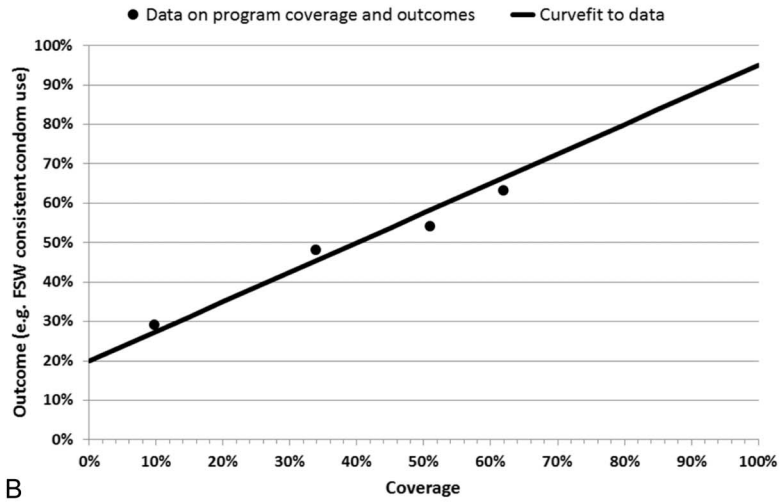
Optima can be used to minimize either (1) a given outcome [eg, number of infections, number of disability-adjusted life years (DALYs), number of HIV-related deaths, or future HIV-related costs] given a fixed total budget over a determined program period, or (2) the amount of funding required to meet a particular epidemiological goal (eg, reducing HIV incidence by 50%). Optima can also determine the amount of money required to simultaneously meet multiple goals (eg, 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. Optima can also be used to help decide in which geographic areas to implement programs for which target populations or how to most effectively reinvest the savings from technical efficiency gains. Constraints may be placed on the optimization; for example, the number of people on ART may not be allowed to decrease, or programs 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 uses a global parameter search algorithm called Bayesian adaptive locally linear stochastic descent (BALLSD).[21] BALLSD is similar to simulated annealing in that it makes stochastic downhill steps in parameter space from an initial starting point. However, unlike simulated annealing, BALLSD chooses future step sizes and directions based on the outcome of previous steps. For certain classes of optimization problems, we have shown that BALLSD can determine optimal solutions with fewer function evaluations than traditional optimization methods, including gradient descent and simulated annealing.[21]

Uncertainty Analyses

Optima uses a Markov chain Monte Carlo (MCMC) algorithm[22–24] for performing automatic calibration and for





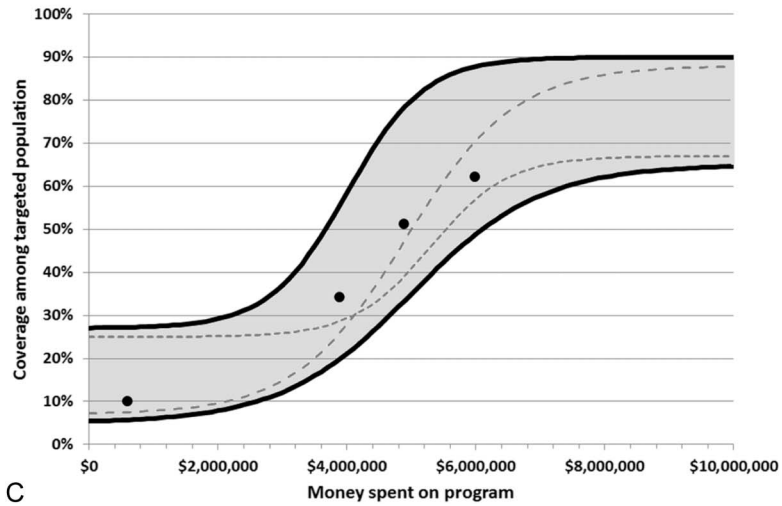


FIGURE 2. A, Example cost–coverage curve, showing the relationship between spending on a program and the associated coverage attained among the target population, including technical efficiency gains. B, Example coverage–outcome curve, showing the relationship between coverage of a minimum service package to a targeted population (eg, outreach and condom distribution with minimum service package to FSW) and the resultant outcome (eg, percentage of FSW consistently using condoms with their commercial partners). C, Example of uncertainty incorporated in the cost–coverage curves used in Optima.

computing uncertainties in the model fit to epidemiological data. With this algorithm, the model is run many (typically 1000–10,000) times to generate a range of epidemic projections; their differences represent uncertainty in the expected epidemiological trajectories.

The most important assumptions in the optimization analysis are associated with the cost–coverage and coverage–outcome curves. To incorporate uncertainty in these curves, users define upper and lower limits for both coverage and behavior for no spending and for very high spending. All available historical spending data and achieved outcomes of spending, data from comparable settings, experience, and extensive discussion with stakeholders in the country of application can be used to inform these ranges. All logistic curves within these ranges are then allowable (Fig. 2C) and are incorporated into uncertainty analyses of Optima. These cost–coverage and coverage–outcome curves are thus reconciled with the epidemiological, behavioral, and biological data in a Bayesian optimal way, thereby allowing the calculation of unified uncertainty estimates.

Time-Varying Optimization and Periods

Optima can also optimize program funding over time. The funding to each program is able to vary either (1) by a predetermined year-by-year total budget or (2) such that the total pool of funding is distributed across time in an optimal manner for the best overall outcome at the end of the analysis period. The optimal allocation of resources to each program may change over time in either situation. Time-varying program allocation is governed by the equation:

$$A(t) = be^{st^2},$$

where A is the allocation of program funding as a function of time t, b determines the overall budget for a given program, and s is a shape parameter such that program funding is constant if $s = 0$, increases over time if $s > 0$, and decreases if $s < 0$. The time points t are normalized such that the analysis period is mapped onto the closed interval [0, 1].

Periods are an important consideration in any resource allocation analysis. Some programs maybe effective over the long term but fail to receive funding if optimizations only consider the short term, because of the time required to reach sufficient coverage and for effectiveness to become apparent (eg, circumcision of male youth before sexual debut). Consequently, Optima allows 2 time frames to be specified: the period over which the *funding* is to be optimized and the period over which the *impacts* of said funding are to be optimized. For example, Optima can be used to calculate the optimal budget allocation for a 4-year national strategic plan in minimizing infections over the next 30 years. Of course, the 2 periods may align: for example, Optima can optimize funding over the next 10 years with respect to minimizing DALYs over the same period.[1] This flexibility in periods allows users to explore short- and long-term impacts of different investment strategies.

Technical Efficiency Gains

Technical (program) efficiency focuses on minimizing unit costs of overall service delivery, subject to community-level factors, the policy environment, and considerations regarding implementation quality. Equally important are administrative rules and regulations, which can hinder timely provision of resources from central to community levels. Understanding how management, financial analysis, and institutional efficiencies affect delivery costs can result in changes to service delivery models. These differences ultimately change the overall cost required to reach a target population with services of a given quality. Accordingly, program efficiency data and/or assumptions can be incorporated within Optima epidemic projections or allocative efficiency analyses by modifying the cost–coverage logistic curves; the initial start-up costs and/or slope of the curves can be adjusted to account for different program efficiency options (Fig. 2). Optima can therefore show how to best allocate the savings incurred from less expensive service delivery to further maximize the achievement of HIV program impact targets.

Future Financial Commitments

Optima calculates the costs incurred per HIV infection, including costs for first-line and subsequent lines of treatment, PMTCT, treatment of opportunistic infections, and care and treatment related to other HIV-related morbidities. It can also estimate the future financial liability to governments for the care and treatment of people currently living with HIV, and from people who are projected to become infected in the future.

From a public debt perspective, expressing this total cost as a percentage of annual GDP, over time, shows a government the total long-term financial implications of its HIV strategy and commitments. This is essential when (1) projecting long-term financial costs of HIV, (2) considering the financial sustainability and fiscal space available for HIV programs, and (3) determining whether resources may become available for non–HIV-related programs. HIV program financial sustainability is achieved when a country can reliably mobilize domestic and external resources to achieve the current and future coverage of HIV services necessary to achieve that country's HIV strategy goals. In the context of a rapidly changing AIDS funding landscape, it is important for governments to understand the long-term financial burdens of their HIV epidemics and consider how their HIV programs could be financed and sustained if donor funding were scaled down or became unavailable.

RESULTS

Here, we present a case study summarizing the findings of an allocative efficiency analysis of Sudan's national HIV epidemic and response. The analysis was conducted in support of the government's preparation of a concept note for submission to the Global Fund, the largest funding body in the nation's HIV response. Two key policy questions were formulated in consultation with the Sudanese National AIDS Program:

- Finding the optimal allocation of HIV funds to minimize either cumulative HIV incidence by 2020 or cumulative HIV-related DALYs by 2020; and
- Determining the HIV funding required to achieve impact targets that were either moderate (25% reduction in HIV incidence and deaths by 2020 compared to 2010 levels) or ambitious (50% reduction in HIV incidence and deaths by 2020 compared to 2010 levels).

Data to inform the modeling were gathered from a comprehensive literature review and validated in consultation with key in-country and donor stakeholders. Ten populations were defined for inclusion in the model: FSW; their clients (SWC); MSM; children; and youth (aged 15–24 years), adults (aged 25–49 years), and older people (aged older than 50 years), each disaggregated by sex. Seven core HIV programs were identified for optimization: programs for FSW, programs for MSM, programs for SWC, general population condom programs, HIV testing and counseling for the general population, ART, and PMTCT. Expenditure from the National AIDS Spending Assessment for 2013 was used as a baseline; total spending was 12.2 million USD, with spending on these 7 programs of 6.4 million USD.

The results addressing the first key policy question established that by optimally reallocating the same 6.4 million USD in programmatic spending as in 2013, Sudan could avert an additional 19,000 HIV infections (or 36% of cumulative new HIV infections) between 2014 and 2020. The simulations showed that to minimize incidence or DALYs, scaling up the ART program is highest priority, followed by targeted primary prevention programs for FSW, their clients, and MSM, with some adjustments to the allocation given to each of these programs depending on the choice of strategic objective (Fig. 3). Should more programmatic funding become available—for example, by mobilizing additional funds or reducing management costs—HIV incidence (or DALYs) could be reduced further (Fig. 4).

In answer to the second key policy question, the modeling results showed that the minimum annual programmatic spending required to achieve the moderate impact targets outlined in the National Strategic Plan was 8.1 million USD. Achieving the more ambitious targets of a 50% reduction in HIV incidence and AIDS-related deaths by 2020 would require an estimated 34 million USD annually for programs—over 5 times the spend of USD 6.4 million in 2013. The cost of reaching HIV incidence reduction targets is estimated to be lower than cost of reaching HIV mortality targets, which require extensive coverage of HIV testing programs in the general population.

A key finding of all the analyses conducted was that targeting programmatic resources almost exclusively to ART and prevention programs for FSW, SWC, and MSM has downstream effects on all population groups and leads to HIV incidence reductions in all populations over the medium term and at lower cost than targeting the general population directly. This is as expected in a low-level HIV epidemic, where transmission in the general population is largely fueled by new infections occurring in the key populations.

The allocative efficiency study carried out in Sudan broadly highlighted some of Optima's ability to provide policy-relevant information for high-level decision making and planning. Based on these results, the Sudanese government shifted their program priorities and budgets in their request for funding from the Global Fund.

DISCUSSION

Optima has been designed to answer the key questions that arise as national governments and other HIV stakeholders

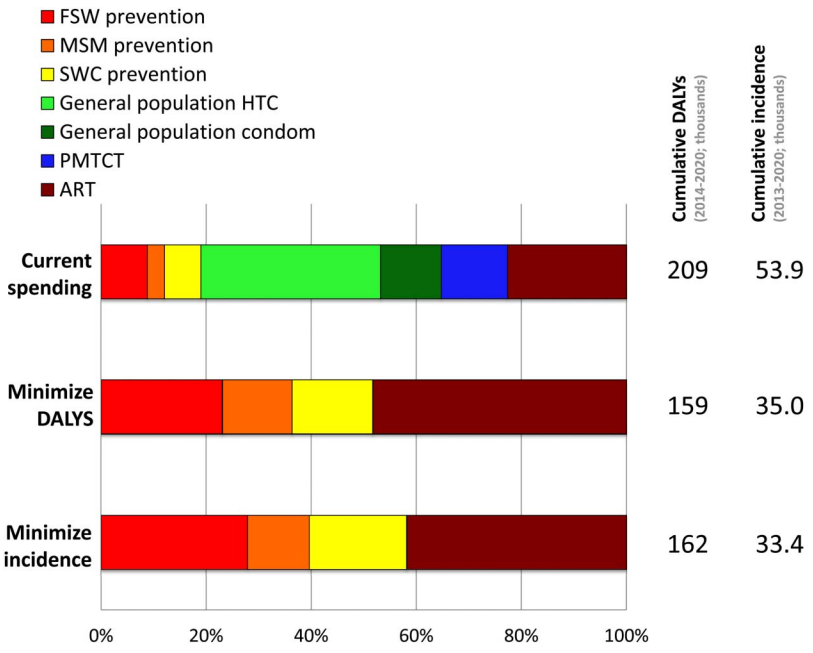


FIGURE 3. Current (2013) versus optimal allocations of HIV resources in Sudan for 2 different optimization objectives.

TABLE 2. Comparison of HIV Epidemic Model Characteristics

Model	Approach	Populations	Purpose	Inputs	Outputs
EPP	Fits 4 parameters to a simple model; written in Java	MSM, PWID, FSW, male SW, SWC, and low-risk groups (separated into urban and rural)	Estimate and project adult HIV prevalence and incidence	Size of subpopulations; HIV prevalence among subpopulations; treatment data	Current number of HIV infections; HIV infection trends (5-yr projections)
AEM	Semiempirical process model; written in Java	PWID, direct FSW, indirect FSW, MSW, SWC, and MSM	Provide a policy and planning tool for national governments	Size of subpopulations; HIV and STI prevalence; risk behavior data; average duration in each population	Trends of HIV infections; impacts on AIDS cases, ART needs, deaths, etc. (long-term projections)
MOT	Risk equations; written in Excel	PWID, FSW, MSM, and low-risk groups (separated into males and females)	Calculate expected number of infections over coming year	HIV prevalence; number of individuals with particular exposure; rates of exposure	Incidence (HIV acquisition) per risk group
Goals/ Spectrum	Compartmental rate-based model; written in Delphi	MSM and high-, medium-, and low-risk groups	Estimate costs and impact of different interventions	Sexual behavior by risk group; demographic data; base year human capacity	Costs; HIV prevalence and incidence (5-yr projections)
Optima	Compartmental rate-based model; versions available for MATLAB and Python	Flexible; unlimited but usually approximately 8–20 groups, including key affected and general populations and different age groups	Analyze and project HIV epidemics; determine optimal resource allocations	Size of population groups; HIV and STI prevalence; risk behavior data (eg, condom use); biological constants (eg, background death rates)	HIV prevalence and incidence trends; health care costs; deaths; optimal resource allocations

PWID, people who inject drugs; STI, sexually transmitted infection; SW, sex workers; SWC, sex worker clients.

decide how to fund their HIV responses and make choices regarding allocations and target program coverage levels. Specifically, it allows them to:

- Understand what population groups and behaviors are chiefly responsible for new HIV infections in the relevant settings, and how these change over time;
- Project current trends and understand what the likely trajectory of their HIV epidemics are if current conditions continue;
- Explore the epidemiological, health, and economic benefits that past investments in packages of HIV programs have likely had, which maybe used as either an evaluation or an advocacy tool;
- Predict the outcomes of different possible future funding scenarios, such as scenarios that prioritize treatment over prevention or vice versa, or certain subpopulations or geographical regions over others;
- Formally and quantitatively determine the funding allocation given the currently available budget that minimizes specific epidemiological or economic indicators (eg, new HIV infections, DALYs, HIV-related deaths, or long-term HIV-related health care costs);
- Estimate the minimum resources and coverage targets required to meet specific epidemiological, economic, and program impact targets, including multiple targets (eg, 90% reductions in both incidence and DALYs by 2030);
- Estimate the impacts and marginal effects of new programs being introduced (provided that basic information about the program's efficacy at the individual level is known);
- Estimate where to best allocate savings from technical efficiency gains;
- Understand how optimal responses may change over time by front-loading some programs and then reducing them while scaling up others;
- Explore geospatial optimized allocations and priority program coverage;
- Conduct analyses over different periods to explore the short- and long-term impacts of certain investment strategies over a specific period (such as over a national strategy); and
- Calculate the long-term financial commitment caused by one new HIV infection, as well as annual and total future costs for care and treatment of PLHIV.

A number of alternative software packages for modeling HIV epidemics and HIV program impacts and costs already exist. Several of the models that have historically been used widely in advising governments on the resource needs, expected impacts, and progression of HIV epidemics are compared in Table 2, including the AEM, the EPP, the Goals Model, and the MOT model. Of these, only AEM and Goals are full process models that track epidemics over time, relate behavioral parameters to coverage, prevalence and incidence, and produce long-term forecasts. Although AEM and Optima share a similar fundamental structure, AEM supports only a limited number of population groups; for example, transgender populations are important contributors to several national HIV epidemics (eg, Indonesia), but there has historically been no scope for including this population group in AEM. AEM currently only has a basic costing component, which does not allow complete cost-effectiveness analyses nor resource estimation or allocation studies to be conducted. AEM has

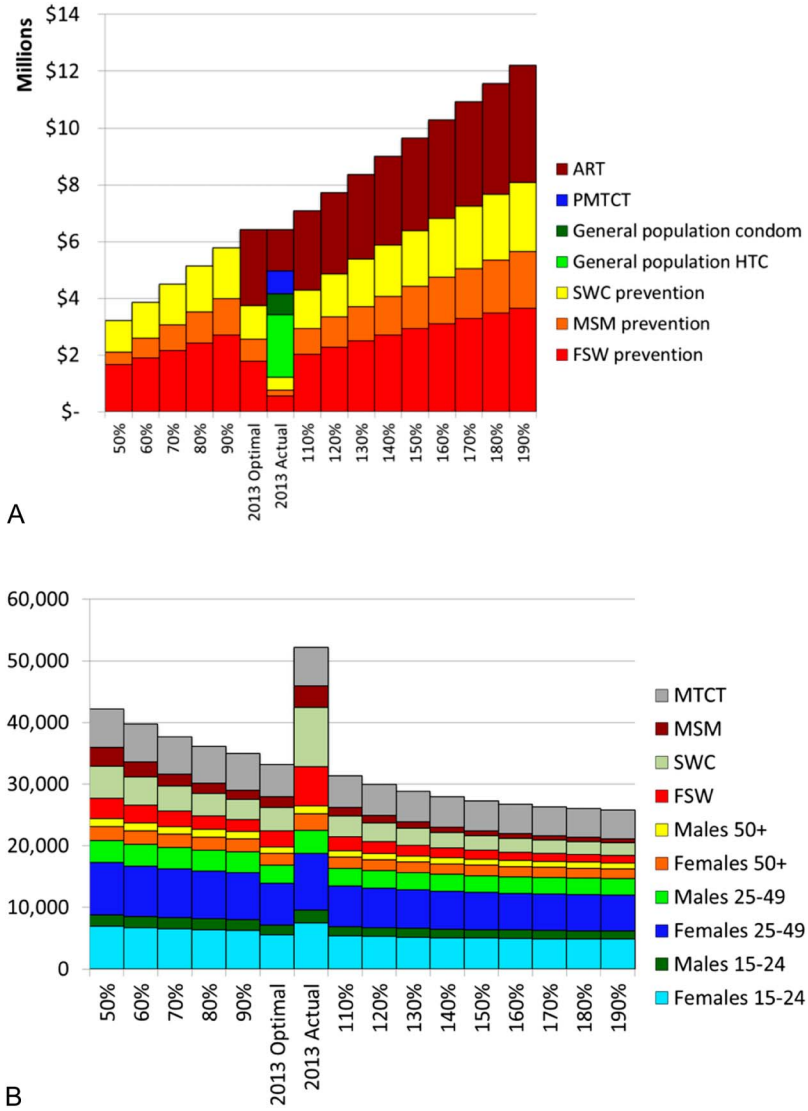


FIGURE 4. A, Resource allocations optimized to minimize HIV incidence by 2020 at different budget levels for Sudan. Prevention packages for key populations include outreach, condoms, and HTC but do not include ART (which is shown separately). B, The model-estimated number of cumulative infections resulting from the allocations shown in Figure 4A.

been used in a number of epidemic settings, particularly in Asia.[13,25]

EPP and Goals are both components of the Spectrum software package.[11] In contrast to AEM and Optima, EPP does not model the actual epidemic dynamics; instead, it is a phenomenological model that calibrates to past epidemic trends and projects them into the future. It has been used extensively to predict trends in African epidemics and is used for HIV estimates in many countries around the world, including by UNAIDS.[2,11,14,15]

The Goals model is closer to Optima in its structure, data requirements, and purpose: both models require detailed demographic, epidemiological, behavioral, and clinical data, and both have been used as part of HIV strategic planning. The Goals model has been used by countries and UNAIDS in resource needs estimates and epidemic projections. Like Optima, the key inputs of the Goals model are used to determine the force-of-infection for each population. However, in the Goals model, both the population groups (including people who inject drugs, MSM, and low-, medium-, and high-risk individuals) and the types of HIV programs that can be modeled (including condom promotion programs, workplace programs, male circumcision, ART, HIV testing and counseling, and PMTCT) are fixed. In contrast, Optima allows HIV programs to be defined to target specific subpopulations within specific geographic areas, with different service delivery models, and with user-specified efficacies. Another difference between the Goals model and Optima is that the Goals model does not include undiagnosed PLHIV, so HIV testing is instead assigned an HIV prevention benefit (ie, HIV testing directly reduces HIV incidence because of behavioral changes by those who either test positive or negative).

MOT contains a detailed process model of HIV acquisition, requiring similar data inputs as are used in Optima to calculate the force-of-infection.[16] However, unlike Optima, AEM, and Goals, MOT's sole output is a prediction of the acquisition of new infections in each population group

in the current year—which is one of the standard outputs produced by AEM, the Goals model, and Optima. Recently, concerns have been raised regarding the validity of the epidemic drivers identified by MOT.[26]

Thus, although each of these previously used packages has a potentially useful role in informing policymakers of certain aspects of an HIV epidemic, none of them allow a unified approach across (1) different types of epidemics (eg, concentrated vs. generalized), (2) different types of analysis (eg, cost-effectiveness of past investments and projections of future epidemic trends at different funding levels and for different HIV program impact objectives), (3) different population groups (eg, people who inject drugs, transgender individuals, migrant workers, and persons of different age groups), and (4) different HIV program impact targets at different funding levels.

Optima analyses translate inherent uncertainty in data and assumptions into uncertainty in outputs. The analyses also allow users to incorporate real-world constraints associated with all programs in the optimization analyses (eg, no one who starts ART is to stop ART; programs cannot be immediately defunded but may only have reduced funding up to a certain percentage each year to enable a realistic transition). Graphical, tabular, and other numeric outputs provide stakeholders with clear qualitative and quantitative conclusions to assist in HIV policy and programming decision making.

The main limitation of Optima is its requirement for data. Optima's strength is that it can use a far larger quantity of data than most other HIV models; however, this advantage wanes in the absence of good data availability. In general, the model used for a given analysis should be commensurate with the amount of data available: if ample data are available, a complex model such as Optima is likely to provide informative results; conversely, if data are strictly limited, then a simple model with few parameters (such as EPP) may give more robust and meaningful results on epidemic trajectories. However, the flexible nature of Optima means that by reducing the number of population groups and the number of modes of transmission, its data requirements can be reduced to be in line with those of other simpler models. Similarly, the large number of parameters supported by Optima risks overparameterization and overfitting. To circumvent this, most parameters in the model are set to values determined by the best available data; only a relatively small number of parameters (relating to the initial HIV prevalence, force-of-infection, and testing and treatment rates) are varied during calibration.

A second limitation of Optima is its reliance on assumed cost–coverage and coverage–outcome curves to determine the optimal allocations. Actual data from the field, along with input from country experts, can be used to inform the parameters of these curves and their uncertainty. Typically, the data available to constrain these are limited, and thus, assumptions must be made to fill these data gaps, particularly regarding expected behaviors for the extremes of zero and saturation funding. Because the optimal allocation is determined by the slopes of the cost–coverage–outcome relationships, the results are especially sensitive to uncertainty in these curves.

Third, because Optima is a population- and rate-based model, it relies on average quantities rather than full distributions. Thus, although it is possible to introduce heterogeneity in populations (eg, population groups can be further subdivided into low- and high-risk subgroups), continuous distributions of risk behaviors are not modeled. In addition, rate-based models have inherent limitations in modeling certain kinds of processes. For example, while a death rate maybe chosen that results in the correct mean life expectancy, a rate-based process will produces an exponential distribution of life expectancies, which is only a rough approximation of the true distribution, which is more Gaussian.

To allow policymakers to access Optima's functionality without requiring detailed knowledge of computer programming or mathematical modeling, we have developed a Python-based version of the software, along with a user-friendly JavaScript-based graphical interface (available at www.optimamodel.com). This version uses Amazon Web Services' Elastic Compute Cloud[27,28] to implement parallelization, allowing the computationally intensive tasks of calibration, uncertainty analysis, and optimization to be performed with minimal delay to the user. Users are able to select and modify population groups and HIV programs to suit their needs, as well as define objectives and constraints relevant to their particular setting.

Optima has already been used in numerous countries to inform the development of HIV investment cases and concept notes (as are now required to apply for Global Fund grants), contribute to the development of National Strategic Plans and Operational Plans to help allocate domestic and international funds, and act an advocacy tool to demonstrate the benefits of past HIV investments and justify future resource allocations to HIV. In conclusion, we hope that Optima proves to be a useful tool to help policymakers understand their countries' HIV epidemics and to allocate resources efficiently for maximal impact.

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