Chapter __. Using Models to Guide HIV/AIDS Policy:

A Synthesis of Current Models to Determine Resource Allocation Cost-Effectiveness

James G Kahn, Lori Bollinger, John Stover, Elliot Marseille

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Introduction

Resources devoted to the human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) have increased dramatically over the past decade. However, the rate of increase has slowed in recent years and leveled off, even though the commitment required to serve all of those in need and to reverse the epidemic has not been reached. In addition, new recommendations to start people on treatment earlier in the course of the disease mean that more resources will be needed than previously estimated. Although funding has increased, the results achieved have not always kept pace. Ensuring that available resources are allocated to the most cost-effective activities possible is essential to pursuing the “Getting to Zero” goal of the United Nations Joint Programme on HIV/AIDS (UNAIDS)—zero new infections, zero AIDS-related deaths, and zero discrimination. Similar challenges face global efforts to control tuberculosis and malaria: resources fall short of ambitious prevention and treatment targets.

Various effectiveness, cost-effectiveness, and resource allocation models have been developed to evaluate the costs and outcomes of the choices facing HIV/AIDS policy makers at national and international levels. This chapter presents an overview of the use of models for allocating HIV/AIDS resources, including a review of features, uses, and limitations. It does not assess the many models used for analyzing the cost-effectiveness of individual interventions.
Rather, it assesses the set of software-based tools used to describe a range of interventions and combination of interventions in different settings.

**General Overview of the Role of Models**

**What Are Models?**

Three types of models are relevant to determining the cost-effectiveness of interventions. Epidemic and disease models use mathematics to describe the dynamics of disease acquisition or progression within individuals. Cost-effectiveness models combine epidemic and disease models with a quantitative description of an intervention activity, including its cost and effectiveness in reducing morbidity or mortality. Finally, resource allocation models consider multiple interventions simultaneously and in various configurations to inform how effort and funding might be divided among different uses.

This chapter focuses on resource allocation models for several reasons. First, in the field of global health, models provide information that is organized and presented to help decision makers to choose courses of action that result in better population health outcomes. Resource allocation models are designed explicitly for this purpose. Second, they incorporate the two other types of models or practical simplifications of them. For policy makers, it is not essential to understand the individual intervention models, as they often examine narrow technical issues that do not contribute meaningfully to resource allocation decisions. Finally, limiting this chapter to resource allocation is practical. Considering the far more numerous epidemic, disease, and cost-effectiveness models and explaining their incompatibilities would be overwhelming for authors and readers alike. Annex __.A provides a brief review of the models reviewed in this chapter.
Strengths and Weaknesses of Models

Strong models are able to gather and manipulate diverse decision-relevant factors in ways that are impossible otherwise. They highlight and integrate policy-relevant data and dynamics from a complex world, ignoring myriad contextual factors that do not affect the decision under scrutiny. They also portray outcomes that are not measurable empirically, due to technical or time constraints, such as long-term health outcomes and costs. Finally, they offer a more explicit and rational alternative to other approaches to decision making, such as guesses, inertia, political expediency, or ideological biases.

The limitations of models reflect the challenge of analyzing a decision with imperfect information. The best models are parsimonious to be understandable and buildable, yet adequately realistic to be policy relevant. They are technically sophisticated, but easy to use. These competing demands lead to compromises, among which modelers attempt to choose wisely. This is the art of modeling. Despite best efforts, the technical details of models are opaque to all but the most sophisticated users and sometimes even to them. This opacity can be mitigated with clear documentation. Finally, values for the inputs required can be imprecise or biased. For example, efficacy data may derive from programs in different settings or with modified implementation. To understand the importance of these uncertainties, models rely extensively on sensitivity analyses: assessing how results change with different input values. Luckily, the basic findings of models are often robust to input uncertainties.

Comparison of HIV/AIDS Resource Allocation Models

HIV/AIDS resource allocation models include the OneHealth Tool (which contains the Goals model and the Resource Needs Model) by Avenir Health, Optima by the Burnet Institute and the
World Bank, the AIDS Epidemic Model by the East-West Center, Epidemiological Modeling by the Institute for Disease Modeling, and Global Health Decisions by the University of California, San Francisco. Each model is best used as follows:

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- **Goals and Resource Needs Model (RNM)** are widely used and supported by United Nations (UN) agencies and linked with the OneHealth Tool and other disease modeling for broad health sector planning. The process is moderately intensive, although the model has been adapted to specific purposes in an easy-to-use formulation with the “DREAMS” application.
- **Optima** is widely used, supported by the World Bank, and consistent with Goals. It employs an algorithm to optimize resource allocation across interventions and geography for a given objective, subject to budgetary, logistic, ethical, and political constraints. The process for the full model is intensive, but an "Optima Lite" is pending.
- **AIDS Epidemic Model (AEM)** is for studying concentrated epidemics, especially in Asia. The task of calibrating and populating the model is intensive, and exploring the various packages available encourages stakeholders to understand local epidemics and effectiveness of past, present, and potential future responses.
- **Epidemiological Modeling (EMOD)** is used to examine policy issues involving the interplay of demographics, risks, disease progression, and health care. Individual-based modeling captures heterogeneity and permits nuanced portrayal—for example, HIV/AIDS transmission is based on independent risk per sex act within partnerships that evolve over time, and disease progression depends on age. Health system dynamics (cycles of antiretroviral use) reflect factors such as age, gender, geography, and risk.
- *Global Health Decisions* (GHD) is relatively simple to use, with an interface that makes it easy to explore the costs and effects of various combinations of interventions and delivery modalities. It is available for relevant uses by arrangement. GHD and Optima are exploring collaboration to incorporate key GHD features into Optima Lite.

The choice of model for a specific user depends on the user’s needs and the models’ intended uses, strengths, and limitations. As presented in Annex A, some models are uniquely well-suited to specific purposes, such as EMOD for detailed simulation of how individuals’ characteristics affect use of health care, and Avenir Health’s OneHealth Tool for placing HIV programming in the context of the broader health system. When models serve similar purposes, such as Avenir Health’s and Optima’s allocation across HIV interventions, the user may want to consult the contacts for each model to discuss how comprehensively and efficiently that model can address user needs.

Below we discuss each model in more detail.

**Avenir Health Models**

Over the past 40 years, Avenir Health (formerly known as the Futures Institute) has led the development of models across many areas of the health sector. Most of these models are assembled within Spectrum, also widely known by its overlay, the OneHealth Tool. Many also exist as Excel-based models and web-based tools. Here we focus on models useful for resource allocation for HIV in Spectrum: Goals and RNM, in particular.
Spectrum is a system of policy models that support analysis, planning, and advocacy for health programs. The models are used to project future needs and examine the effects of policy choices, including the impact of taking actions now rather than later, evaluating the costs and benefits of a particular policy, examining the interrelatedness of different policy decisions, and evaluating how a change in age and sex distribution can affect a wide range of social indicators.

The central impact model in Spectrum is DemProj, which projects the population for an entire country or region by age and sex, based on assumptions about fertility, mortality, and migration. A full set of demographic indicators can be displayed for up to 100 years into the future, and urban and rural projections can also be prepared. Default data needed to project population are provided from the estimates produced by the Population Division of the United Nations. Models not related to HIV/AIDS include FamPlan, which projects family planning requirements; RAPID (Resources for the Awareness of Population Impacts on Development), which projects the social and economic consequences of high fertility and rapid population growth; TIME (Tuberculosis Impact Model and Estimates), which performs epidemiological and cost-effectiveness analysis of tuberculosis control strategies; LiST (Lives Saved Tool), which estimates the cost and impact of scaling up child and maternal health interventions on mortality; and NCD (Noncommunicable Diseases), which calculates the impact of scaling up interventions on populations affected by noncommunicable diseases.

1. Spectrum was developed with funding from the U.S. Agency for International Development’s Health Policy Project, the Bill and Melinda Gates Foundation, Johns Hopkins University, United States Fund for the United Nations Children’s Fund, UNAIDS, the World Health Organization, Global Health Workforce Alliance, and United Nations Population Fund.
The four models related to HIV/AIDS interact with one another. The AIDS Impact Model (AIM) uses the Epidemic Protection Package module developed by the East-West Center to fit prevalence and incidence trends to surveillance and survey data and then calculates the consequences of these trends for key indicators such as new infections, deaths, need for treatment, and number of orphans. The RNM calculates the costs associated with HIV-related interventions. Goals simulates HIV/AIDS incidence on the basis of behaviors and estimates the epidemiological effects of biomedical interventions and behavioral interventions (using an impact matrix) to calculate infections averted and thus cost-effectiveness ratios. The Lives Saved Tool (LiST) evaluates the cost and impact of child and maternal health interventions, including HIV/AIDS and malaria, using inputs from AIM.

AIM

AIM began as a relatively simple Excel-based tool, developed in 1991 in collaboration with Family Health International under the USAID-funded AIDS Technical Support and AIDS Control and Prevention projects. The program has been revised several times since then in collaboration with the UNAIDS Reference Group on Estimates, Models, and Projections. Since 2009, it has been maintained and updated with support from the Bill & Melinda Gates Foundation and UNAIDS. It has evolved to become a comprehensive model within Spectrum used to estimate the impact of the HIV/AIDS epidemic. Several years ago, EPP was incorporated into Spectrum. Both incidence and prevalence curves are now estimated within AIM, which then projects the consequences of the epidemic, including the number of people living with HIV/AIDS, new infections, and deaths by age and gender, as well as the number of new cases of tuberculosis and the number of orphans. Many of these results are then used in other models in
Spectrum. UNAIDS uses AIM to make the national and regional estimates it releases every two years.

The major inputs and outputs of AIM are as follows. Demographic projections are based on user inputs or projections prepared by the United National Population Division. The projections start with an estimate and projection of adult HIV/AIDS incidence, which is combined with information on the age and sex distribution of incidence and progression to death to estimate the number of new infections in adults, by age and sex. New infections in infants are estimated from prevalence among pregnant women and the rate of mother to child transmission, which is dependent on infant feeding practices and the coverage of prevention with antiretroviral agents. New infections progress over time to lower CD4 cell counts and are subject to HIV/AIDS-related mortality. Persons who receive first-line, second-line, or both antiretroviral therapy live longer than those who do not. People at any stage are subject to other-cause mortality at the same rates as people who are not infected. Adult deaths result in orphans.

In addition to estimating the epidemic and projecting its impacts, AIM has other features, including the ability to validate the estimates by comparing AIM outputs with other data sources, to perform uncertainty analyses for certain output variables, and to aggregate projections, for example, a series of subnational projection files. The model is continuously updated to reflect the most recent research.

**RNM**

RNM grew out of efforts to estimate the global resources required to combat HIV/AIDS that were developed in 2001 for the first United Nations General Assembly Special Session on HIV/AIDS (Schwartländer and others 2001). Although that first Excel-based model was calculated at the individual country level, it was a global model and not appropriate for country-
level use. After the first few rounds of the Global Resource Needs Estimates (GRNE), in 2007 UNAIDS initiated a consultative process with countries with a high burden of HIV/AIDS to validate their country-specific portion of the GRNE, which required adapting the global model to the country level. By 2009, the consultative process reached 60 countries, and countries began to use the RNM (still in Excel) for their own planning purposes. Because of this, RNM gradually migrated over to Spectrum and now is used to calculate the funding required to expand the national response to HIV/AIDS. It estimates the costs of implementing HIV/AIDS programs, including the costs of care and treatment, prevention, and policy and program support.

RNM projects the costs of various interventions, given assumptions about the size of various population groups, unit costs of interventions, and coverage targets (figure __.1). These projections can then be used to enhance knowledge of HIV/AIDS among policy makers and to build support for effective prevention, treatment, care, and mitigation. The projection results are usually transferred to presentation software, such as PowerPoint, for presentation to leadership audiences.

<<figure __.1 about here>>

Figure __.1 Structure of RNM: DemProj and AIM
<<capitalization = DemProj; initial cap on first word only = Key populations etc.>>

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The RNM estimates the number of people receiving each service by multiplying the number of people needing the service by the coverage rate (percentage of persons needing the service who actually receive it). The resources needed are then estimated by multiplying the number of people receiving the service by the unit cost of providing it. Before RNM can be used, both a demographic and an HIV/AIDS projection must be prepared. The epidemiology section of AIM calculates the number of HIV/AIDS infections, persons needing treatment, and orphans. This information is used in the treatment section to calculate the costs of treatment for preventing mother to child transmission, HIV/AIDS, and associated tuberculosis and opportunistic infections and can be used in the mitigation section to calculate the cost of providing services for orphans. AIM modifies the demographic projection through HIV/AIDS deaths and the impact of HIV/AIDS on fertility.

**Goals**

The Goals model supports efforts to respond to the HIV/AIDS epidemic by showing how the amount and allocation of funding is related to the achievement of national goals, such as the reduction of prevalence and expansion of care and support. It also explores the impact of potential vaccines. The Goals model evolved out of an effort to identify what program managers need in order to plan effectively. Stover and Bollinger (2002) surveyed 14 national program managers and learned that their most challenging issue was using cost-effectiveness information in the country’s key priority-setting exercise, the National Strategic Plan. The model was developed to be used in that process.

The Goals model is intended to support strategic planning at the national level by providing a tool to link program goals and funding. It can help to answer several key questions:

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• How much funding is required to achieve the goals of the strategic plan?
• What goals can be achieved with the available resources?
• What effect do alternate patterns of resource allocation have on the achievement of program goals?

The Goals model does not provide all the answers. It is intended to assist planners in understanding the effects of funding levels and allocation patterns on program impact. The model can help planners to understand how funding levels and patterns can lead to lower incidence and prevalence and improved coverage of treatment, care, and support programs. It does not calculate the “optimum” pattern of allocation or recommend a specific allocation of resources between prevention, care, and mitigation.

The Goals model divides the adult population ages 15–49 years by sex and risk group—not sexually active, low-risk stable couples, medium-risk people engaging in casual sex, sex workers and clients, men who have sex with men, and people who inject drugs (figure __.2). The model calculates new infections by sex and risk group as a function of behaviors and epidemiological factors such as prevalence among partners and stage of infection. The risk of transmission is determined by behaviors (number of partners, number of contacts per partner, and condom use) and biomedical factors (use of antiretroviral agents, male circumcision, prevalence of other sexually transmitted infections). Interventions can change any of these factors and affect the future course of the epidemic.

Figure __.2 Structure of the Goals Model [[AQ: provide a higher resolution]]
The effect of interventions on behaviors is modeled through an impact matrix that summarizes the impact literature to describe changes in behavior by risk group as a result of exposure to behavior change interventions (Bollinger 2008). The Goals model is then linked to the AIM module in Spectrum that calculates the effects on children (ages 0–14) and adults older than 49. The AIM module also includes the effects on pediatric infections of programs to prevent mother to child transmission.

The Goals model has been used to assess the impact of prevention and treatment at the global level (Eaton and others 2013; Schwartländer and others 2011; Stover and others 2006) and at the country level.
OneHealth Tool

The OneHealth Tool is a series of modules overlaid on top of the impact models of Spectrum. It is intended for medium-term strategic health planning (3–10 years) at the national and subnational levels. The OneHealth Tool was developed by a group of UN agencies, the World Bank, and the World Health Organization (WHO) in response to requests made during a 2008 technical consultation in Senegal by countries looking for standardized costing tools. The model builds on the International Health Partnership and Joint Assessment of National Plans framework, and experts in costing from all participating UN agencies contributed to the technical development of the model, including funds and staff time. The project also received funds from the Global Fund to Fight AIDS, Tuberculosis, and Malaria, the Global Health Workforce Alliance, and the Health Metrics Network, as well as from bilateral agencies.

The OneHealth Tool was developed because most costing tools at the time took a disease-specific approach rather than a health systems approach (figure __.3). In addition to covering public sector health interventions at both national and subnational levels, it incorporates coverage of private sector interventions and includes some selected nonhealth interventions that may have health impacts. It is a unified tool for joint planning, costing, impact analysis, and financial space analysis and can be implemented at either the health system or program level. The OneHealth Tool provides a way to estimate the cost and impact of interventions for HIV/AIDS, tuberculosis, and malaria simultaneously, as well as other diseases, and to examine the resource requirements from the health system.

<<figure __.3 about here>>

<<typesetter: U.S. spelling = center; programs; initial cap on first word only: Health system envelope, etc.>>
Figure 3.3 Structure of the OneHealth Tool
The OneHealth Tool includes the following modules:

- **Human resources.** The human resources module allows the costing of salaries, benefits, and incentives for health service providers and health management and support personnel as well as pre-service training and nonspecific in-service training.

- **Infrastructure.** The infrastructure model provides planning and costing functions for all facilities providing medical interventions, as well as most facilities offering support functions. It also includes planning functions for equipment, furniture, vehicles, and communication.

- **Governance.** The governance module includes costing templates for assessing the costs of governance activities.

- **Logistics.** The logistics module allows for the planning of warehouses and vehicles needed to move commodities or drugs and supplies from central warehouses to the endpoints of a logistics system.

- **Health financing.** The health financing module is used to estimate the costs of implementing health financing programs, such as vouchers, subsidies, or cash transfers.

- **Health information systems.** The health information systems module includes costing templates for assessing the costs of implementing a health information system.
• **Budget mapping.** The budget mapping module can be used to allocate intervention and health system costs across budget categories established by the user, in order to match country or international institution cost categories.

• **Financial space.** The financial space module is used to analyze the financial space within which health plans are expected to be executed.

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**Optima**

Optima is a modeling tool, developed by the Burnet Institute at the University of New South Wales, in collaboration with the World Bank, to help national decision makers, program managers, and funding partners to achieve allocative efficiency and to plan for financial sustainability.

The “Optima approach” involves the following key stages:

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• **Assess the burden of disease** over time, for each population group, and for each disease sequelae or state (through data synthesis and epidemiological modeling)

• **Specify the efficacy and effectiveness of interventions** (including different modes of delivery) that have the potential to reduce incidence, morbidity, and mortality

• **Assess the costs required to deliver services** at different levels of coverage (including through different service modalities and implementation or efficiency options)

• **Define strategic objectives and national priority targets**—as well as the budgetary, logistic, ethical, and political constraints related to achieving these objectives—across the entire population and by disease
• **Use a formal mathematical optimization algorithm** around the constructs from the previous steps to assess the optimal allocation of a given level of resources to reduce disease burden, subject to the defined constraints.

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Optima is a mathematical model of disease transmission and progression that uses an integrated analysis of epidemic, program, and cost data to determine an optimal distribution of investment at different funding levels. Optima is the only quantitative tool currently available that includes a formal mathematical optimization routine; real-world budgetary, logistic and political constraints; and economics of scaling up intervention programs and responses.

Optima is intended to address various policy questions:

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• **How close is achievement of the national strategic plan targets under current funding?**
  
  Over the strategic plan period, how close will the country get to its disease-related targets (a) with the current volume of funding allocated according to current expenditure, and (b) with the current volume of funding allocated optimally?

• **How much funding is required to achieve the national strategic plan targets?** Over the strategic plan period or over a longer time period, according to current program implementation practices and costs, how much total funding is required to meet the targets, and how is this funding optimally allocated between programs?

• **What benefits can be achieved with more efficient implementation?**

• **What impacts have past programs had?** How would the country’s HIV/AIDS trajectory have changed if investment had not occurred in different programs, and what is the estimated cost-effectiveness of the past response?
What is the expected future impact of policy or program implementation scenarios? What is the projected future trajectory of the country’s epidemic with and without investment in specific programs or with and without attaining program-specific targets?

Optima extends allocative efficiency analyses to (a) include geographic prioritization and (b) integrate technical efficiency within allocative efficiency, considering the various modalities of service delivery for different programs. As such, it addresses the following questions: Which service delivery modalities and mechanisms should be implemented in which geographic areas? How should the HIV/AIDS response prioritize investment across population groups and geographic areas, and which service delivery modalities and mechanisms should be implemented and to what extent in each area, in order to get as close as possible to national targets with available resources?

AIDS Epidemic Model

The AEM, developed 25 years ago, is patterned after the HIV/AIDS situation in countries with concentrated epidemics, primarily in Asia. It allows countries to build locally tuned models that accurately represent their epidemiological situation. These models can then be used with a set of analytic tools—the AEM workbooks (baseline, intervention, and impact analysis)—to prepare scenarios that analyze alternative responses to the epidemic, assess the impact of these responses, and estimate the cost of implementation.

These scenarios provide essential inputs to national strategic planning processes, help countries to allocate their resources more efficiently, and help countries to identify weaknesses
that must be addressed to strengthen their responses. Using the AEM is an intensive process that builds stakeholder involvement in and ownership of the planning process.

**Epidemiological Modeling (EMOD)**

The Institute for Disease Modeling developed the EMOD software primarily for use by disease modelers, researchers, epidemiologists, and public health professionals seeking to simulate infectious disease conditions and evaluate the effectiveness of eradication or mitigation approaches. The model is individual (agent)-based and discrete time, using a Monte Carlo simulator to predict populations. The complex architecture provides disease transmission for environmental, sexual, vector-based, and airborne diseases and may be adapted to support additional infectious diseases. The binary software or source files are available for download. Data and training requirements are substantial.

**Global Health Decisions**

The Global Health Decisions model was developed by the University of California, San Francisco, to provide an HIV/AIDS resource allocation model with a sophisticated and flexible user interface prepopulated with epidemiologic and programmatic data. The goals was to permit relatively rapid but nuanced allocation of resources across populations and interventions.

A website allows users to specify a country (among those implemented), verify the default input values (for HIV/AIDS prevalence and use of antiretroviral therapy, for example), alter them as needed, and then run a series of tailored intervention scale-up scenarios. The results of each scenario are incidence, prevalence, deaths, and costs, by risk group, over time. These scenario results are stored and can be named and compared graphically.
The back end is a deterministic compartmental model with five risk groups (general population female and male, sex workers, drug users, and men who have sex with men), implemented in Google Go. Given a set of predictions (for example, from UNAIDS) on treatment and prevalence in future years, the model uses “simulated annealing,” a stepwise statistical sampling approach, to align model predictions with these benchmark projections.

The model provides tiered access to functionality, including the use of country-specific defaults for input values (for example, demographic, epidemiologic, interventions, costs), real-time adjustment of intervention portfolios, and manipulation of input values by more technically informed users. Policy makers have not used Global Health Decisions.

**What Works Reviews**

The Global Health Decisions project initiated an activity called What Works Reviews (WWR) in 2010 to address a perceived gap in the availability of information regarding intervention efficacy for policy discussions and models. One important function of policy modeling is to convey the impact of interventions, translating evidence on how well interventions produce health and economic effects. This means that resource allocation models need to incorporate the latest evidence on intervention effectiveness. Systematic reviews of efficacy are now commonplace, but overwhelming in number and complexity. A distilled review that conveys efficacy and associated strength of evidence can be helpful for informing modeling and educating decision makers about the evidence.

WWR translates empirical evidence on the effects of interventions into a quantitative synthesis that is technically accurate while being concise and accessible to nontechnical audiences. Each estimate of efficacy is accompanied by a strength-of-evidence rating that
reflects the quantity and type of underlying studies. WWR examines both prevention and treatment for each health condition, with a focus on data with the most potential relevance for policy and an emphasis on health outcomes (for example, deaths and disease incidence) rather than process measures (for example, satisfaction with services or adherence).

The WWR includes nearly 50 categories of interventions for HIV/AIDS, including some found to be ineffective.

**Methods**

WWR proceeds in explicit and small steps from existing systematic reviews and important new studies to key findings (see figure __.4).

**Figure __.4 Structure of the WWR Process**

• The first step is to search for systematic reviews and pivotal new studies. Most reviews come from the Cochrane Library, with others identified through PubMed and other sources. The evidence at this level is massive, diverse in form, and technically complex.

• The second step is to select potentially relevant reviews, based on whether the information could affect major decisions on policy or funding, such as whether and at what scale to support a particular intervention. Important but narrower questions, such as drug dosing or comparisons between very similar intervention designs, are usually excluded, as are universally accepted practices. All of these decisions are documented.

• The third step is to extract information from the selected comparisons. This includes the context (for example, country and type of population), research methods (for example, study design and outcome measures), and quantitative findings on efficacy.

• The fourth step is to rate the strength of evidence, based on the quantity and type of studies, as well as the precision of findings, that is, the width of the relative risk confidence interval. The result is a summary table that presents the intervention comparisons, findings (mortality), relative risk reduction, and strength of evidence for each review and study.

• The next step, which is critical, is to combine evidence by intervention type where possible. For example, if different insecticides for environmental control of a disease vector (for example, a mosquito) all work with similar efficacy, the findings are combined into a single row. All summary data are linked to original extractions to allow review of the aggregation decisions.
The last step is to consult with subject area experts to review provisional findings documents. This may result in the addition of new reviews or studies or adjustment of the interpretation of existing evidence.

The key outcome is relative risk reduction. This is a standardized metric, designed to put diverse outcome metrics (means) onto a consistent footing (Mirzazadeh, Malekinejad, and Khan 2015). It equals the percentage reduction in the risk of negative health outcomes and can be used for mortality, morbidity, and indirect health indicators.

Findings are presented in three parts: a key findings table has a row for each type of intervention, with the relative risk reduction and strength of evidence for mortality, morbidity, and other indicators. An overview reviews the health condition, epidemiology, key findings, and future directions. A logic model graphically represents modes of disease acquisition and progression as well as the location of intervention opportunities.

Strength of Evidence

The WWR rates strength of evidence on a scale of 0–6 (visually represented by bars as in mobile phone reception). The score is based on the extent and type of studies (for example, random control trials or RCTs), quality of available systematic reviews, and precision (that is, narrowness of uncertainty bounds). The following is the typical evidence associated with each score:

6 = three or more RCTs, well reviewed, good precision (very strong)
5 = three or more RCTs, minor problems with review or precision (strong)
4 = two RCTs, good review and precision (moderate strength)
3 = one RCT or multiple non-RCTs, good review and precision (moderate strength)
2 = one RCT or multiple non-RCTs, problems with review or precision (weak)
1 = one or more non-RCTs, serious problems with review or precision (very weak)
0 = no evidence, due to lack of studies or extreme imprecision.

<<end list>>

Application to HIV/AIDS

The HIV/AIDS component of WWR was updated with new literature searches and extractions between December 2015 and January 2016. Figure __.5 presents the logic model for the broad context of HIV/AIDS intervention. Key findings for all intervention types are presented in annex __.B. To illustrate results, this section summarizes the findings for biological prevention strategies.

Figure __. 5 Logic Model for the HIV/AIDS Component of WWR
<<spell eg = for example
Spell HCT = HIV/AIDS counseling and testing; & = and; / = or; no italic on in utero; replace slash as follows: in utero, perinatal, breastfeeding>>
Circumcision of adult males is 70 percent effective in reducing transmission from females to males, based on three RCTs, other studies, and long follow-up (very strong evidence). Evidence for MSMs and transgender individuals suggest little if any protection (strong evidence). Treatment of sexually transmitted infections has been examined in eight studies, with a 12 percent non-statistically significant reduction in incidence and a wide confidence interval, including a negative effect (−49–48 percent), with lower incidence of sexually transmitted infections and risk behaviors (16–23 percent, moderate strength evidence). Nonoxynol-9 and microbicides failed to reduce HIV/AIDS incidence. Data on microbicides containing an
antiretroviral drug suggest a 37 percent reduction in HIV/AIDS incidence (weak evidence). Vaccines did not work, and neither did the latex diaphragm. Pre-exposure prophylaxis with the antiretroviral combination tenofovir plus emtricitabine reduced HIV/AIDS transmission in several RCTs by 47 percent (very strong evidence). Two trials found no effect, due to low sample size and adherence. Use of antiretrovirals reduced incidence by 96 percent in serodiscordant couples in a large RCT in Africa, with similar results from several earlier non-RCTs (strong evidence). The female condom reduced the nonuse of condoms.

Field Experience with Models Influencing Policy Decisions

Of the many models described here, several have been influential in policy making. However, models not only can be influential in changing policy and the policy-making process, but the interaction of that process can change the models and affect their evolution over time.

One model that both changed policy and itself was changed through the policy-making process is the Decision-Makers’ Program Planning Tool (DMPPT), developed by the USAID Health Policy Initiative in collaboration with UNAIDS, to inform decision makers about the potential cost and impact of options for scaling up voluntary medical male circumcision (VMCC). When the RCT results for the effect of VMMC on HIV/AIDS transmission were first announced, no publicly available, flexible, and supported models were available to estimate the costs and impact of providing VMMC services. In 2007, a large consultative meeting was held by UNAIDS and the WHO, at which consensus was reached to prioritize VMMC in countries with high prevalence of HIV/AIDS and low prevalence of male circumcision (UNAIDS, WHO, and SACEMA Expert Group 2009).
After the model was developed, model applications were performed for 14 Sub-Saharan African countries, using readily available data. Based on these results, a series of briefs were written, one for each country and a summary brief for the region as a whole (Njeuhmeli and others 2011). The U.S. President’s Emergency Plan for AIDS Relief used the briefs heavily to persuade countries either to investigate further the potential cost and impact of VMMC in their country, based on primary source data, or simply to adopt a VMMC policy based on the initial results. The briefs were extremely useful in showing the magnitude of those results so clearly.

The original model targeted males ages 15–49 years. Since then, evidence on VMMCs began to show that males under age 25 years were most likely to use VMMC services. Because of this finding, a new version of the model, DMPPT 2.0, was developed to estimate the impact of targeting VMMC services by five-year age groups (Stover and Kripke 2014). Several applications of the new DMPPT are under way; new applications of the costing tool are sometimes included, in order to update previous cost estimates based on older technology.

Another example of how a model can affect policy is the development and use of the Global Resource Needs Estimates. As described, the first estimates were developed at the request of UNAIDS to have a global price tag for the estimated funding required for a comprehensive response to the HIV/AIDS epidemic. Those results were highly influential in setting the agenda for HIV/AIDS, including the establishment of the Global Fund to Fight AIDS, Tuberculosis, and Malaria.

As both the epidemic and the GRNE evolved over time, each iteration added various interventions in response to perceived needs. For example, since the original estimates, interventions such as post-exposure prophylaxis, safe injection, community mobilization, and prevention for people living with HIV/AIDS were added. Health system considerations began to
be included, including health systems strengthening, training, incentives, and infrastructure. A separate effort to estimate the resources needed to support orphans and vulnerable children was spawned and then fed into the existing estimates (Stover and others 2007).

By 2010, the GRNE had expanded to contain many interventions and the total price tag had grown commensurately, while the recent growth in financial resources had begun to flatten out. In response to these policy issues, the next round of estimates underwent an extensive consultative process to devise a more targeted and strategic approach, identifying interventions that would have relatively higher impact, known as the Investment Framework (Schwartländer and others 2011). Since then, many countries and donors have adopted this approach and developed investment cases to illustrate the validity of the choice of strategy. Throughout this process, models have informed policy making, and the models have evolved and adapted to changes in the policy environment.

**Role for Multiple Models versus Convergence**

With the availability of multiple cost-effectiveness models, often addressing similar policy territory, the question arises, What are the relative merits of multiple models versus convergence on a single model? The following presents some of the pros and cons of each approach.

- **Complementary substantive areas of focus.** Different models may vary in areas of focus. For example, one model may consider the general features of antiretroviral therapy, whereas another may highlight differences among regimens or monitoring strategies. Thus policy makers may decide an allocation for antiretroviral therapy overall based on one model and allocations for specific activities within an antiretroviral program based on
another. The downside is the lack of an integrated assessment and the need to use an extra model. Of note, misalignment of two models may create confusion. If one model considers options A, B, and C, but another model considers B, C, and D, users may become frustrated.

- *Differing level of technical engagement by users.* Some users prefer simpler (but less flexible) engagement with a model, whereas others prefer more complex (and flexible) engagement. Policy makers may fall in the former camp, and epidemiologists and other academics may fall in the latter. Although some models offer choice in level of engagement, obviating this distinction, they may excel in the simpler or more detailed engagement.

- *Competition.* Having multiple models may provide the impetus to improve model design in order to build a user base through quality improvement.

- *Confirmation and confidence building.* When different models yield substantially similar results, confidence in the validity of the findings is stronger (Hankins, Forsythe, and Njeuhmeli 2011). When results diverge, the attempt to resolve differences can illuminate variations in assumptions or data values that would not otherwise have come under scrutiny.

- *Efficiency.* Perhaps the strongest argument for convergence is efficiency: interested parties can focus efforts on one model, building consensus on methods and inputs. A rigorous review process is essential to provide the quality control that would otherwise arise from competition and comparison.

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In 2015, there is one dominant modeling system and a plethora of less widely used models. Avenir Health’s models are widely used in policy-making discussions. Other models are used in more limited settings (in specific countries) and published in academic journals. They have served many of the quality control functions that might otherwise arise from more balanced competition.

Frontiers of Modeling: Where Is Added Value Possible?

Unit Cost Repository

All cost-effectiveness models for HIV/AIDS, tuberculosis, and other diseases suffer from a significant gap in required input data: the unit cost of delivering interventions. Although there are costing studies for many interventions, they suffer from several serious limitations: many interventions or important variations in intervention delivery have not been formally costed; many geographic settings are poorly represented in costing studies overall or for specific interventions; and costing methods are inconsistent across studies. The Global Health Cost Consortium, funded by the Bill & Melinda Gates Foundation, is developing a strategy to standardize existing cost data to improve comparability, extrapolate to new geographic settings, strategically fill gaps in existing data, and improve the efficiency and quality of collecting and analyzing cost data. These data will improve the reach of and confidence in cost-effectiveness models.

Model Comparisons

The multiple HIV/AIDS resource allocation models offer important choices for potential users, with preferences based on the policy questions being examined and the availability of detailed
local data. Comparing the models is highly desirable to ensure that estimates are comparable and valid. This has been done for general predictions, male circumcision (Hankins, Forsythe, and Njeuhmeli 2011), and antiretroviral therapy as prevention (Eaton, Menzies, and others 2013) but not for detailed resource allocation issues. A structured comparison is needed.

**External Validity**

It has long been recognized that efficacy data collected from research projects, often in atypically well-resourced situations, may not translate directly to operating programs; the research findings have low external validity. However, enumeration of the challenges has far exceeded the efforts to improve the translation. The Global Health Decisions project has made initial steps to bridge the gap between research and practice settings. Six external indicators were associated with the effect of HIV/AIDS testing on condom use: number of implementation sites, financial incentives, mobile mode of delivering testing and counseling, female sex workers as the target, requirement that clients return to receive test results, and indeterminate or positive HIV/AIDS test results. These results are limited and preliminary, and the analysis needs to be repeated for other interventions.

**Implementation Approaches**

The bulk of massive recent spending on HIV services has been vertical: programs focused entirely on HIV prevention, treatment, or care, with no resources for other diseases and largely separate operational structures. Yet various factors highlight the need to consider horizontal implementation: the control of HIV disease, meaning that infected individuals live long enough to experience other illnesses; the ability to identify HIV-infected individuals in other service settings, such as reproductive health; and renewed interest in health system strengthening, such as highlighted in the Lancet Global Health 2035 Commission on Investing in Health. Current
resource allocation models permit limited examination of implementation approaches, but not comprehensively (the OneHealth Tool comes closest, with explicit consideration of system costs); future modeling would do well to build in more specific options. Other implementation issues, such as facility- versus community-based service delivery, with or without demand generation, and geographically targeted to high risk or high need areas, would be valuable.

**Interactions**

HIV interacts with other diseases in several ways. It co-occurs in certain populations, such as with Hepatitis C among persons who inject drugs (PWIDs). The pathophysiology interact, e.g., Hepatitis C progression is sped by HIV, and CD4 decline accelerates with episodes of malaria. Therapy for HIV affects the risk of other diseases, such as TB. Capturing these interactions and their potential implications for intervention opportunities and health impact will more accurately portray the relative merits of alternative investment strategies.

**Behavioral Economics**

Increasingly, behavioral economics—the use of cognitive psychology to influence economically relevant behaviors such as taking risks and seeking care—is gaining traction in health. Cost-effectiveness models can start to incorporate behavioral economics strategies known to be effective. The evidence relevant for infectious and maternal-child disease is in the process of being reviewed. In addition, cost-effectiveness analysis can potentially benefit from the insights of behavioral economics. For example, behavioral economics and its underlying “prospect theory” note that individuals are more averse to loss than attracted to equivalent gains; perhaps users of a model will be more influenced if the presentation is framed as missed opportunities to avert infections rather than as new opportunities to avert infections.
New Cost-Effectiveness Analysis Outcomes

Cost-effectiveness analysis traditionally compares average incremental health impact and cost. It does not consider the effects of high expenditures on financial solvency, nor does it address equity. Extended cost-effectiveness analysis assesses three important considerations for policymakers: (a) household out-of-pocket private expenditures, (b) financial risk protection (number of cases of poverty averted), and (c) distributional consequences (per socioeconomic status or geographic setting) (Verguet, Laxminarayan, and Jamison 2014). An example is provided in the chapter on health gains and financial risk protection in volume 2 of this series (Verguet and others 2016).

Controversies in Modeling

The use of models to inform health policy in general and cost-effectiveness models, in particular, has stimulated debate and controversy.

One of the objections is that cost-effectiveness modeling tacitly reflects ethical judgments about which thoughtful people can disagree. For example, in any comparison of outcomes that uses life years, such as quality-adjusted life years or disability-adjusted life years, a life-saving intervention will, all else equal, favor younger rather than older people. Most people accept the utilitarian principle on which this rests—as a society we prefer to save more life years than fewer; others perceive it as a systematic bias against older people. Similarly, and perhaps more controversial, cost-effectiveness analysis puts no greater value on identified lives such as particular people who are eligible for treatment, than on anonymous, statistical lives that might be saved through, for example, prevention activities. Trading-off identified and statistical lives challenges, even offends, the ethical intuitions of some people.
Another area of controversy concerns a central question in cost-effectiveness modeling: the determination that an evaluated option is or is not cost-effective. One way to answer this question is by determining that the incremental cost-effectiveness ratio is above or below a threshold cost-effectiveness. The most widely adopted threshold was initially promoted by the Commission on Macroeconomics and Health and adopted by the WHO and by WHO-CHOICE. This threshold links per capita gross domestic product with returns on investments in health to define the characteristics of a cost-effective and a very cost-effective intervention (Hutubessy, Chisholm, and Edejer 2003; WHO 2002; WHO-CHOICE 2014).

Many published cost-effectiveness analyses of health interventions in low-resource countries explicitly refer to these WHO criteria as the standard for determining cost-effectiveness. This approach is extremely easy to apply and reflects the fact that willingness to pay for health care depends in part on national income. However, critics argue that these criteria have at least four major limitations. They have little theoretical justification. They skirt the difficult but necessary ranking of the relative values of locally applicable interventions. They omit any consideration of affordability. Finally, the thresholds set such a low bar for cost-effectiveness that very few interventions with evidence of efficacy can be ruled out. An alternative, if more labor-intensive approach, would compare the cost-effectiveness of an intervention being analyzed with the cost-effectiveness of as many locally relevant interventions as possible (Marseille and others 2015).

Other controversies are rooted in methodological concerns. For example, health-state “utility” is difficult to measure, and results vary for the same disease or condition according to which of a number of accepted methods is used to determine it.
In addition, the related concept, disability weight, does not vary by setting for any chosen disease or condition. For example, the disability weights for mobility, visual, or hearing impairment are the same regardless of the economic status of the country or region in which the analyses are being applied. Yet the practical effect on peoples’ lives of the same disability is likely to be greater in poorer countries where, for example, roads are more difficult to navigate and fewer aids are available to assist persons with disabilities.

Other concerns pertain to the fact that the data used in models are rarely perfectly suited to the setting or population being studied. Some critics believe that, in view of these and other limitations, undue reliance is placed on the results of models, they are treated as more reliable than they actually are, and they are used to address consequential policy questions for which they are unsuitably designed or parameterized.

Conclusions

The foregoing tour of HIV resource allocation models demonstrates a robust set of options. Existing models permit examining the most critical questions – what will be the cost and health outcomes of investing in substantially different combinations of prevention and treatment interventions, and how will those outcomes vary according to local factors such as epidemiology, existing interventions, and costs? The models require some initial set-up, though less so with the newer streamlined versions. More nuanced questions (such as the experience of individuals with particular traits) can be examined, albeit with substantially more investment of effort.

A long-term challenge for models is keeping up with an ever-evolving set of prevention and intervention tools, and with micro-targeting of interventions to disease hot-spots. The models are constantly improving, and we believe will continue to provide up-to-date assistance to HIV
policy-makers, program designers, and other users. Further, the technology is adaptable to health areas outside HIV, with some modeling techniques already applied to other diseases and others anticipated.

Note

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References


Stover, J., and K. Kripke. 2014. “Estimating the Effects of Targeting Voluntary Medical Male Circumcision (VMMC) Programs to Different Age Groups: The Decision Makers


