



AIDS Policy Modeling for the 21st Century: An Overview of Key Issues

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Abstract. Decisions about HIV prevention and treatment programs are based on factors such as program costs and health benefits, social and ethical issues, and political considerations. AIDS policy models – that is, models that evaluate the monetary and non-monetary consequences of decisions about HIV/AIDS interventions – can play a role in helping policy makers make better decisions. This paper provides an overview of the key issues related to developing useful AIDS policy models. We highlight issues of importance for researchers in the field of AIDS policy modeling as well as for policy makers. These include geographic area, setting, target groups, interventions, affordability and effectiveness of interventions, type and time horizon of policy model, and type of economic analysis. This paper is not intended to be an exhaustive review of the AIDS policy modeling literature, although many papers from the literature are discussed as examples; rather, we aim to convey the composition, achievements, and challenges of AIDS policy modeling.

Keywords: HIV/AIDS, key issues, policy modeling, prevention

1. Introduction

Some 34 million individuals worldwide are infected with human immunodeficiency virus (HIV), the virus that causes AIDS, and 18.8 million people have died from AIDS [103]. AIDS is now the third largest and the most politicized epidemic in the history of mankind, and no end is in sight. It is likely that the HIV epidemic will soon surpass the 20th century influenza epidemic which led to 20 million deaths [38], and the 14th century plague epidemic which led to 25 million deaths in Europe alone [56]. The majority of HIV cases – approximately 95% of the global total – have occurred in developing countries [102].

Experts say that, for developing countries, the most promising means for controlling the epidemic is a vaccine [41,107,218]. However, no vaccine is currently available, nor is one likely to become available in the near future [65]. Thus, efforts to control the epidemic have focused on prevention [105]. Prevention needs around the world differ because of economic constraints, differing modes of transmission, and cultural and political factors [102,105].

New therapies for treating HIV have recently become available. These therapies can prolong the lives of HIV-infected individuals [47,54], can reduce vertical HIV transmission [63], and may reduce the probability of HIV transmission from an infected, treated person [215,216,230].

Available per capita funds for health care differ greatly in different countries, so the appropriate types of HIV/AIDS treatment also differ.

Determining how best to spend limited funds on HIV prevention and treatment programs in different regions of the living world is challenging. Decisions about HIV prevention and acquired immunodeficiency syndrome treatment programs are based on many factors, including program costs and health benefits, available funding, social and ethical issues, and political considerations. AIDS policy models – that is, models that evaluate the monetary and non-monetary consequences of decisions about HIV/AIDS interventions – can play a role in helping policy makers make better decisions.

AIDS policy models can be used to support decisions about investment in HIV interventions. Possible interventions include many types of prevention programs as well as programs for care and treatment of HIV-infected individuals; see figure 1. Policy makers must decide how best to design new interventions, which interventions to initiate or terminate over time, and how to allocate limited resources optimally among competing interventions. By assessing the monetary and non-monetary consequences of existing and potential HIV interventions, AIDS policy models can help support such decisions. For example, AIDS policy models can be used to estimate the relative costs and benefits of different HIV treatment regimens, thus assisting decision mak-

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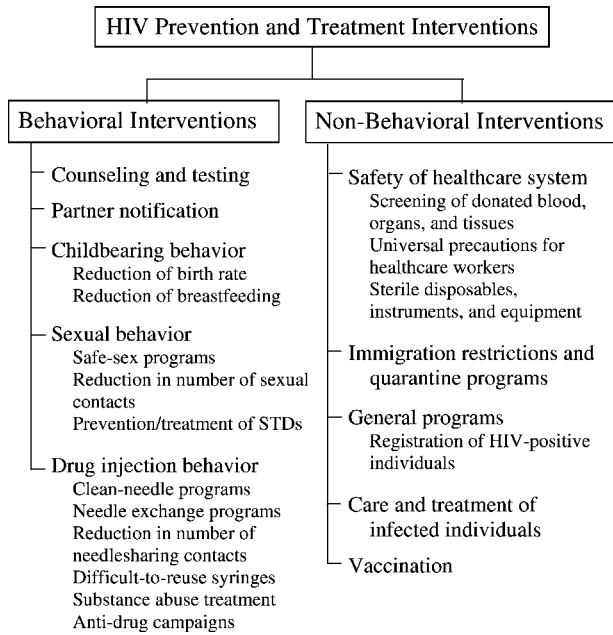


Figure 1. HIV prevention and treatment interventions.

ers in determining the best allocation of limited resources for treating HIV-infected individuals. AIDS policy models can be used to estimate the relative costs and benefits of different HIV treatment and prevention programs, thus assisting decision makers in determining the best allocation of resources between HIV prevention and treatment programs. An AIDS policy model can be used to estimate the relative costs of an HIV prevention program when targeted to different risk groups in the population, thus assisting decision makers in designing a cost-effective prevention program. Sometimes decision makers may choose not to invest in the most cost-effective intervention or set of interventions. In such a case, the information from an AIDS policy model can be used to make explicit the implicit value judgments and assumptions underlying a given policy choice.

AIDS policy models can provide insight into the dynamics of the spread of the epidemic among population groups and can therefore help identify trends, make general forecasts, and even estimate the uncertainty in forecasts. This knowledge is essential for planning future HIV/AIDS resource needs. For example, a model of HIV epidemic dynamics and treatment patterns can be used to determine the number of hospital beds or home health visits that will be needed in the future in a given area.

AIDS policy models can also help guide data collection efforts. Many factors related to HIV prevention and treatment, such as biological, epidemiological, and behavioral factors, are uncertain. Through sensitivity analysis, policy models can identify those uncertain variables that have the greatest effect on program outcomes – and thus identify the variables for which further data are most urgently needed. Where data are uncertain, policy models can also be used to demonstrate when a decision can be justified despite incomplete data. AIDS policy models can also help guide decisions about the types of data that should be collected. For

example, an AIDS policy model can help support decisions about whether to collect HIV versus AIDS surveillance data, or decisions about whether to rely on statistical estimation of HIV incidence or to collect anonymous reporting data or to collect named reporting data.

Decisions about HIV/AIDS interventions are often highly politicized, with many individuals influencing policy decisions, including legislators, public health officials, and advocates for those with HIV/AIDS. The policy making process for HIV/AIDS is often strongly influenced by factors other than program costs and benefits. For example, in many countries, resources devoted to HIV prevention are only a small fraction of the needed funds, not only because of poverty but also because of ignorance of the magnitude of the HIV epidemic and social stigmas against individuals with AIDS. As another example, although routine HIV screening of newborns may be effective in reducing HIV transmission, many have objected to such screening on the grounds that it constitutes a non-consensual HIV test of the mother [206]. Despite the influence of non-quantifiable factors, AIDS policy models can still provide important input to the AIDS policy making process. Although many AIDS policy models have not had a demonstrable effect on policy making, some AIDS policy models have affected policy debates, in areas such as needle exchange programs (e.g., see [99,120,136,156,159]), HIV screening of health care providers (e.g., see [2,164,179]), and HIV screening of the blood supply (e.g., see [202]). For further discussion of the influence of AIDS policy models, see [109,119].

This paper discusses key issues that are relevant to developing useful AIDS policy models – and thus an improved AIDS policy making process and more informed decisions regarding investment in HIV prevention and treatment programs. Previous papers that have reviewed AIDS policy modeling have focused on selected issues such as the types of economic analyses used to evaluate HIV prevention programs [94,177], types of policy models [21,23], and target groups and interventions [86,109,184], often with emphasis only on policy issues most relevant to industrialized nations. This paper aims to provide a more comprehensive overview of the key issues related to developing useful AIDS policy models. We highlight issues of importance for researchers in the field of AIDS policy modeling as well as for policy makers, and we discuss how these issues vary in different regions of the world. This paper is not intended to be an exhaustive review of the AIDS policy modeling literature, although many papers from the current literature are discussed as examples; rather, we aim to convey the composition, achievements, and challenges of AIDS policy modeling.

2. Key issues in AIDS policy modeling

Our framework of key issues in AIDS policy modeling is illustrated in figure 2. These include geographic area, setting, target groups, interventions, affordability and effectiveness of interventions, type and time horizon of policy model, and type of economic analysis.

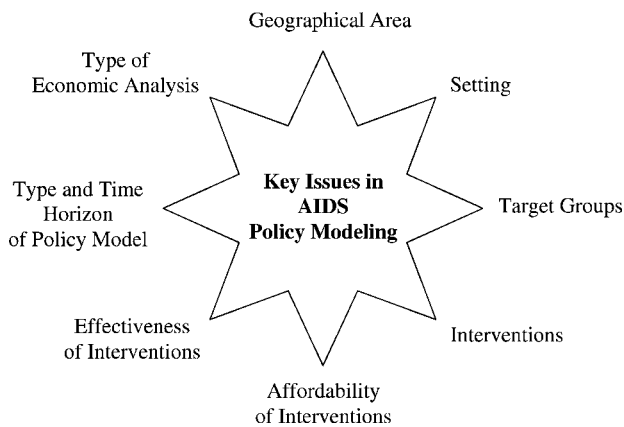


Figure 2. Key issues in AIDS policy modeling.

Many aspects of HIV prevention, care, and treatment require different approaches in different geographical areas, as discussed in section 2.1. Policy makers need different types of AIDS policy models for different settings and target groups, as discussed in section 2.2. In section 2.3 we provide an overview of the most important types of interventions, and we cite a number of policy models that have been developed to assess these interventions. In some cases, effective interventions exist but are not affordable, as discussed in section 2.4. In section 2.5 we examine how the effectiveness of interventions can be measured. In section 2.6 we discuss how AIDS policy models must strike the proper balance between simplicity and tractability versus realism in order to be useful to policy makers. In section 2.7 we discuss the types of economic analysis that can be used to assess the costs and benefits of HIV/AIDS interventions.

2.1. Geographical area

Many aspects of HIV prevention, care, and treatment require different approaches in different geographical areas. For example, in order to develop appropriate communications for HIV prevention programs, it is important to take into account government policy, socioeconomic status, culture, gender relations, and spirituality [105]. As another example, in order to design effective HIV prevention programs, it is important to understand how HIV spreads in different geographical areas: heterosexual transmission is the main mode of infection in sub-Saharan Africa and South and Southeast Asia, whereas injection drug use is a dominant infection mode in regions such as North Africa and the Middle East, East Asia and The Pacific, Latin America, North America, and Western Europe.

Most comprehensive AIDS policy models have been applied to industrialized countries, but over 95% of HIV-infected individuals in the world live in developing countries [102]. The AIDS pandemic has substantially burdened the economies and healthcare systems of developing countries [61,80,92], has led to dramatic falls in life expectancy [19], and has considerably affected the demographic, social, and environmental situation [19,20,78,80]. Agriculture is particularly vulnerable to labor loss from AIDS deaths [80].

Providing care and support to children orphaned from AIDS has also become a critical issue [30,52].

Overviews of AIDS policy models for industrialized countries are given in [21,23,86,109]. Fewer examples of AIDS policy models for developing countries can be found in the literature. For instance, Van der Ploeg et al. [213] used a simulation model for decision support in attempts to control sexually transmitted diseases (STDs), including HIV, in Kenya. Bernstein et al. [15] set up a policy model for Central and East African cities to analyze the main prevention strategies of the United States Agency for International Development and its development partners. Rowley et al. [194,195] analyzed the demographic consequences of reducing heterosexual transmission of HIV in sub-Saharan Africa. Heidenberger and Flessa [85] developed an AIDS policy model to determine the spread of the epidemic in Tanzania and its impact on the resources of a major Tanzanian hospital.

2.2. Setting and target groups

AIDS policy models can be used in a variety of settings. These settings influence the types of interventions that are relevant and the type of policy model that is needed. AIDS policy models can be used by governmental agencies and policy makers. They can be applied by healthcare providers such as general hospitals, ambulatory-care institutions, acute-care hospitals, long-term care institutions, home healthcare institutions, hospices, STD clinics, and physicians' offices, as well as drug treatment centers and street outreach organizations. They can also be used by institutions that do not provide health care, such as companies who wish to determine appropriate HIV/AIDS workplace policies.

The divergence of geographic areas and settings leads to different risk groups for HIV. The virus can be transmitted through contaminated blood and blood products; from a mother to her offspring during pregnancy, childbirth or breast feeding; through injection with a contaminated needle; or through sexual contacts. Dominant modes of HIV transmission vary in different regions of the world, so key target groups for prevention and treatment also vary. Target groups include homosexuals, bisexuals, heterosexuals, commercial sex workers, injection drug users (IDUs), health care workers, women of childbearing age, and newborns, as well as individuals encountered in a particular setting, such as hospital inpatients or individuals attending an STD clinic. For examples of AIDS policy models focusing on various target groups, see [21,23,86,109]. In the following section we discuss target groups further in the context of HIV interventions.

2.3. Interventions

This section provides an overview of the most important types of HIV/AIDS interventions, and cites a number of policy models that have been developed to assess these interventions. Our aim is to provide the reader with a sense of

the types of available interventions, the range and types of AIDS policy models that have been developed, and areas where further analysis is needed.

A variety of HIV prevention and treatment interventions are available [23,86,93]. We classify the interventions into behavioral and non-behavioral interventions, as illustrated in figure 1. Behavioral interventions aim to change the risky behavior of infected and at-risk individuals, and include general counseling and testing programs, partner notification programs, and programs aimed at slowing HIV transmission from mothers to their offspring, from sexual contacts, and from injection drug use. Non-behavioral interventions include programs to ensure the safety of the healthcare system, immigration restrictions and quarantine programs, general programs such as registration of HIV-positive individuals, care and treatment of individuals with HIV/AIDS, and possible vaccination if a vaccine against HIV becomes available. Interventions that are primarily behavioral may have non-behavioral aspects, and vice versa: for example, programs to ensure the safety of the healthcare system, such as universal precautions against HIV, require some behavior change on the part of healthcare workers.

2.3.1. Behavioral interventions

Many AIDS policy models have examined HIV counseling and testing programs. Such programs offer many benefits [160]. Individuals screened for HIV receive counseling that may encourage them to reduce their high-risk sexual or drug-using behavior, and individuals who are found to be HIV infected can undergo therapy earlier than they would have otherwise. Counseling and testing programs can be targeted to different risk groups in different settings. The literature contains many examples of policy models that evaluate HIV screening programs targeted to various groups such as bisexual and homosexual men [210], IDUs [217], prostitutes [31], women [3, 24–27,98,147,154,162], newborns [226], patients [81,106, 126,132,166], healthcare workers [39,164,179], and immigrants [232]. More general models that evaluate untargeted counseling and testing programs have also been developed [69,97,146,155,184,185].

Recent advances in treatment options for HIV-infected individuals have made partner notification programs more attractive, but such programs often raise ethical issues. Holtgrave and colleagues found that counseling, testing, referral, and partner notification services funded by the Centers for Disease Control and Prevention in the United States resulted in a net economic gain to society [97]. For an overview of studies that evaluate partner notification programs, see [59].

Approximately half of all people who acquire HIV become infected before age 25 [102]. Although antiviral treatment for HIV-infected pregnant women and their offspring has been shown to reduce vertical HIV transmission sharply [29], vertical transmission remains a critical issue in developing countries. In sub-Saharan Africa some 450 000 HIV-infected children are born each year [102]. The child-bearing behavior of HIV-infected mothers can be changed

by reducing the birth rate (e.g., use of contraceptives) or by decreasing the chance of perinatal transmission from an infected mother (e.g., use of safe birth techniques, avoidance of breastfeeding). Some work has been done to investigate policies aimed at reducing vertical transmission in industrialized countries [3,5,24–27,162,226]; less work has been done to analyze policies for reducing vertical transmission in developing countries [139–141,222].

Transmission of HIV via sexual contacts appears to be considerably less efficient and more variable than vertical or bloodborne transmission [214]. Male-to-male sexual contacts have the highest transmission risk, followed by male-to-female sexual contacts, and then female-to-male sexual contacts [167,168,196]. STDs can further increase the risk of HIV transmission. Many HIV prevention programs concentrate on modifying sexual behavior by safe sex techniques, reducing the number of sexual contacts, and combating STDs.

Initially the HIV epidemic in industrialized countries spread rapidly among gay and bisexual men, so many AIDS policy models evaluated interventions targeted to individuals in these risk groups or their partners. For example, Hethcote [90] analyzed several prevention programs for homosexual men in San Francisco, and Kaplan [113] and Kaplan and Abramson [118] analyzed educational programs targeted to gay men. Later, gays and bisexuals, IDUs, and commercial sex workers spread the epidemic to the heterosexual population in industrialized countries. Rauner [186] analyzed the effect of HIV prevention programs targeted to bisexuals, homosexuals, and IDUs in Vienna, Austria. Richter et al. [188] investigated HIV prevention programs targeted to adolescents, including those aimed at reducing sexual transmission of HIV.

Sexual contact is the main mode of HIV transmission in developing countries [102]. Limited work has been done to analyze policies that aim to slow the sexual spread of HIV in developing countries. For example, Moses et al. [151] calculated the costs and effectiveness of an intervention targeted to a high-frequency STD-transmitter core group in Africa. Van der Ploeg et al. [213] investigated efforts to control STDs, including HIV, in Kenya. Bernstein et al. [15] modeled HIV prevention strategies for Central and East African cities, including those aimed at reducing the sexual spread of HIV. Rowley et al. [194,195] analyzed the demographic consequences of reducing heterosexual transmission of HIV in sub-Saharan Africa. Marseille et al. [142] analyzed the cost effectiveness of female condoms to prevent pregnancy, HIV, and STD transmission in southern Africa.

In industrialized countries, injection drug use is a key mode of HIV transmission, both directly through injections with contaminated needles and indirectly through sexual contacts of infected IDUs. HIV risk from drug injections can be reduced by clean-needle programs, needle exchange programs, reductions in needle-sharing contacts, use of difficult-to-reuse syringes, substance abuse treatment, and broad anti-drug campaigns. Researchers have developed AIDS policy models to analyze some of these interventions,

including needle bleaching programs [203], needle exchange programs [87], the use of difficult-to-reuse syringes [32], and methadone maintenance treatment [224,228]. Richter et al. [187] investigated optimal allocation of resources among HIV prevention programs targeted to IDUs and non-IDUs.

2.3.2. *Non-behavioral interventions*

We define non-behavioral interventions as those that do not rely primarily on voluntary behavior change on the part of infected or at-risk individuals. One group of non-behavioral interventions is aimed at ensuring the safety of the healthcare system, through measures such as blood supply screening, universal precautions for healthcare workers, and use of sterile equipment.

Bloodborne transmission of HIV is highly efficient [214]. After the introduction of HIV screening tests in 1985, HIV transmission via blood donations dropped sharply [72], although a residual risk of HIV transmission from window-period donations still exists [134]. In industrialized countries, safeguards for the blood and tissue supply include donor deferral based on a donor's risk factors, confidential exclusion of blood units from donors with self-admitted risk factors, and testing of the blood itself [175]. Major improvements in blood safety have been achieved in industrialized countries, but in developing countries the safety of blood products and injections is still a critical issue [45,62,74,101,112,134,205]. Simonsen et al. [205] reported that at least 50% of injections were unsafe in 14 of 19 countries in developing world regions for which data were available. Researchers have investigated the impact of blood donor screening on the spread of HIV [55,116,117,202] and the impact of transmission via blood products [85]. Other researchers have developed AIDS policy models to consider the effects of preoperative autologous blood donation [16] and to plan the safety of blood products for blood donation centers [55,72,134,202].

Universal precautions for healthcare workers, such as safer surgical techniques [70], trained surgeons and nurses [44], and adoption of devices to prevent needlestick occurrences [8], as well as use of sterile disposables, instruments, and equipment, can play an important role in reducing the spread of HIV. In an analysis of the cost effectiveness of screening surgeons in the United States for HIV, Owens et al. [164] concluded that a better use of healthcare resources would be the adoption of universal precautions in surgical settings.

Some countries have restricted immigration and travel by HIV-infected individuals [57,71,75], and potential quarantine of HIV-infected individuals has been discussed [10, 131]. In the mid-1980's, Cuba quarantined persons with confirmed positive HIV test results in a Havana sanatorium [174]. This policy drew charges of human rights violations, and was discontinued. Currently, most individuals who are newly diagnosed with HIV infection in Cuba are asked to enter a sanatorium for six months to a year to participate in an intensive course that covers mental and physical

hygiene and safe-sex practices [9]. Elsewhere, registration of HIV-infected individuals has been proposed [60]. Limited analysis of such policies has been carried out [231,232].

AIDS policy models can play a role in planning care and treatment for HIV-infected individuals. For example, such models can be used by healthcare providers to help choose affordable therapies and therapy strategies. Some work has been done to analyze the cost effectiveness of zidovudine monotherapy [170]. More recently, multi-drug therapies for treating HIV-infected individuals have become available [51,54,130,176], although little analysis of the cost effectiveness of such therapies has been performed. AIDS policy models have been developed to analyze the cost effectiveness of preventing opportunistic infections in individuals with AIDS [64,172,200]. Choosing effective and affordable HIV therapies is a particularly critical issue in developing countries, where the per capita budgets for health expenditures are a fraction of the available budgets in industrialized countries.

AIDS policy models have also been developed to investigate the effect of therapies on HIV transmission. Examples of AIDS policy models accounting for early therapy with zidovudine monotherapy include [170,184,198]. The effect of more advanced therapies on the spread of the epidemic has been analyzed [53,163,184,185]. Provision of therapy for HIV-infected mothers or their offspring to reduce vertical HIV transmission has become an important issue, particularly in developing countries [3–5,141,144,226]. Several analyses of the cost effectiveness of postexposure prophylaxis following HIV exposure, especially for healthcare workers, have appeared [111,122,180,183]. Recent evidence indicates that multi-drug therapy can lead to increased prevalence of multi-drug-resistance HIV strains in the population [42,223], so some researchers have developed models to investigate the relationship between initiation of therapies for individuals with HIV/AIDS and the emergence of drug-resistant strains [17,219,225,229].

AIDS policy models can also be used by healthcare providers to determine the resources they will need to treat HIV-infected individuals. For example, Heidenberger and Flessa [85] analyzed the resources needed for treating HIV/AIDS cases at a major Tanzanian hospital. Rizakou et al. [190] created a decision support tool for planning resources for agencies that deliver care and treatment to individuals with HIV/AIDS. De Angelis [48] developed a model for allocating resources to home healthcare services for individuals with HIV/AIDS for the City of Rome, Italy. The demand for home healthcare services has increased as advanced therapies prolong the life expectancy of HIV-infected individuals [54].

Clinical trials for HIV vaccines are currently underway, with some progressing to final stages [65]. Although no vaccine is yet available, researchers have developed models to evaluate the potential effect of vaccination programs on spread of the epidemic [53,163,181]. In developing countries, vaccination against HIV may be the only affordable way to halt the epidemic.

2.4. Affordability of interventions

The affordability of HIV interventions is a particularly critical issue in developing countries, and limits the types of prevention and treatment programs that can realistically be implemented. In regions such as sub-Saharan Africa, where less than \$10 per capita per year is spent on health, expensive HIV interventions are an unrealistic option [153].

In the early course of the epidemic, when just monotherapy was available, the lifetime cost of treating an HIV-infected person from the time of infection until death was estimated to be approximately \$120,000 [88]. With dual therapy, the lifetime costs for treating individuals with HIV/AIDS decreased by about 20% [68]; compared to monotherapy, drug costs increased and treatment costs decreased. With the introduction of triple therapy, drug costs increased sharply [49], but treatment costs decreased significantly [28,127–129,152]. Triple therapy has increased the life expectancy of individuals with HIV/AIDS and thus the time span during which these individuals can infect others, leading some researchers to observe that triple therapy could lead to a sharp increase in total costs [95]. Rauner [185,186] calculated that the total costs of the HIV epidemic in Vienna, Austria, from 1996 to 2005 would slightly increase compared to monotherapy in the case of long-term effectiveness of triple therapy and sustained success of prevention programs.

Large-scale antiretroviral drug treatment is not affordable in most developing countries [153]. The total cost of providing triple therapy to HIV-infected individuals in 169 countries throughout the world is estimated to be more than \$65.8 billion, or \$11 per capita [92]. This represents 0.2% of the 1995 world Gross National Product (GNP). In East Africa, Central Africa, West Africa, and sub-Saharan Africa, more than 12% of the GNP would be required to provide triple therapy for individuals with HIV/AIDS. As an alternative, the World Health Organization and the United Nations AIDS Program recently recommended that the 23 million Africans infected with HIV be given regular doses of cotrimoxazole, a common and inexpensive antibiotic, to avert the secondary infections associated with AIDS [104].

Zidovudine therapy for HIV-infected pregnant women lowers vertical transmission risk by approximately 70% [29]. Since 1994, the United States Public Health Service has recommended routine voluntary prenatal HIV testing, and zidovudine therapy for HIV-infected pregnant women [133]. This strategy resulted in a 67% decline in perinatal AIDS cases in the United States from 1992 to 1997. Advanced therapies, avoidance of breastfeeding, and safe birth techniques have lowered the vertical HIV transmission risk to 2% in industrialized countries [12,29]. For developing countries, even short-course zidovudine treatment and advice to HIV-infected women to not breastfeed their infants has been found to be cost effective, feasible, and ethical [13,139,222]. As another example, a single-dose of nevirapine administered to mothers and babies just before and soon after birth was estimated to have a major potential impact on reducing

vertical HIV transmission and a reasonable cost compared to other drug treatments [140].

HIV testing costs also burden the budgets of developing countries. Pooled serum testing is a cost-effective alternative for establishing baseline seroprevalence of HIV infection for public health programs, where the cost of testing each individual serum sample is prohibitive [11]. Meda et al. [148] reported that serodiagnosis of HIV in Burkina Faso was possible with reliable, less-expensive strategies that do not require expensive Western blot testing.

2.5. Effectiveness of interventions

The development of a useful AIDS policy model requires knowledge of or assumptions about the effectiveness of the intervention. Appropriate and accurate measures of intervention effectiveness are essential in order to develop policy models that will lead to good decisions. For example, a model that assumes that reductions in risky behavior are linearly related to funds expended on a counseling and testing program may overstate the cost effectiveness of such a program if in fact behavior change is a diminishing function of incremental investment in the program.

For non-behavioral interventions, effectiveness might be measured in terms of reduced infectiousness, increased length of life, or reduced severity of symptoms. For behavioral interventions, effectiveness is likely to be measured in terms of reduced transmission risk. Intervention effectiveness may depend on the amount of money invested in the intervention and the target population, and may change over time (for example, individuals who reduce their risky behavior in response to an HIV risk-reduction program may later relapse partially or completely to their initial risky behavior).

Much research has been done to analyze the effectiveness of non-behavioral HIV interventions. Drug therapies can prolong the lives of HIV-infected individuals, reduce the severity of the disease, and reduce the infectiousness of treated individuals [149]. However, if the drugs are not taken correctly, drug-resistant HIV strains can develop in treated individuals [43] and can potentially spread to a significant portion of the population [225]. Thus, general guidelines have been developed to optimize the effectiveness of therapies for different types of individuals, such as newborns and small children [35], pregnant women [37], adults and adolescents [34], individuals with AIDS [212], and healthcare workers who have been exposed to HIV [36]. Researchers have developed AIDS policy models to determine the appropriate antiviral drug regimen for HIV-infected individuals [17,219,225,229]. Blower et al. [17] investigated different scenarios for the duration of the effectiveness of advanced therapy in a gay community in San Francisco. They concluded that the effectiveness of therapy was particularly dependent on the infectiousness and risk behavior of HIV-infected individuals.

Some AIDS policy models have been set up to analyze the effects of potential HIV vaccines [53,163,181]. Porco and Blower [181] developed a mathematical model to assess

vaccine programs for controlling two subtypes of HIV. Such analysis is especially useful for developing countries where different HIV subtypes are present. Edwards et al. [53] varied both the efficacy and duration of HIV vaccines to analyze potential benefits.

In order to develop a useful policy model for evaluating a behavioral intervention, it is essential to know about the effectiveness of the intervention in changing the risk behavior of those whom the intervention targets. The effectiveness of the intervention may depend on how much money is invested in it. It is possible, for example, that when only a small amount of money is spent on a behavioral intervention, very limited behavior change will occur; when more is spent on the intervention, increasingly greater behavior change will occur; but beyond a certain level of expenditure, no more behavior change will occur. Some researchers have developed production functions to characterize the relationship between the amount of resources invested in an intervention and the level of change in risky behavior [67,187] or to characterize the relationship between the amount of resources invested in an intervention and the number of HIV infections averted [108,114,115,121].

Certain individuals may be more likely than others to change their behavior. For example, a survey of adult sexual behavior in the United States found that highest-risk individuals showed the greatest propensity to change their risky behavior [58]. As another example, a meta-analysis of studies of sexual behavior concluded that HIV counseling and testing was an effective means of inducing HIV-infected individuals to reduce their propensity to transmit the disease, but was ineffective in inducing uninfected individuals to reduce their risk of becoming infected [220].

A behavioral intervention may induce behavior change that lasts only for a limited period [1,33,191,207], or may induce long-term behavior change [124]. A review of behavioral interventions aimed at changing HIV risk behavior found that only about 40% of the reviewed studies produced long-term or short-term behavior change [40]. Some AIDS policy models have dealt with the issue of the long-term effectiveness of behavioral interventions. For example, Owens et al. [162] analyzed the impact of women's relapse to high-risk sexual and needle-sharing behavior on the costs and benefits of a voluntary HIV screening program targeted to women of childbearing age. They concluded that the effect of relapse to high-risk behaviors on screening program costs and benefits could be substantial. Rowley and Anderson [194] found that the faster the spread of the epidemic is, the shorter is the time period over which the impact of limited-term behavioral changes is experienced. These findings support the need for including the possibility of behavioral relapse in models that evaluate behavioral HIV interventions, and for developing behavioral interventions that produce sustained reductions in risk behavior [162].

Interventions may have different effectiveness at different points in the epidemic life cycle or at different points in the course of infection within an individual. For example, Paltiel [173] investigated the cost effectiveness of HIV pre-

vention and treatment interventions at different points during the epidemic life cycle. The analysis suggested that, early in the epidemic, behavioral interventions targeted to infected individuals are the most cost effective; then for some years a combination of interventions targeted to both infected and uninfected individuals is best; and then late in the epidemic life cycle, behavioral interventions targeted to uninfected individuals are the most cost effective. As another example, in an analysis of the cost effectiveness of HIV testing programs for the population of Vienna, Austria, Rauner [184] varied the sensitivity and the specificity of different test types according to the HIV infection stage of tested individuals.

HIV interventions may also influence each other. For example, individuals found by HIV screening to be HIV infected may be given antiviral therapy. As another example, HIV testing and counseling programs are often combined with partner notification programs. These cross-intervention effects may be important to include in certain AIDS policy models.

2.6. Time horizon and type of policy model

The goal of AIDS policy modeling is not to provide an exact valuation of program costs and benefits but, rather, to help in determining the appropriate policy decision. The type of model that is most appropriate for evaluating an HIV intervention depends on factors such as the intervention being evaluated, the time horizon of the intervention's effects, the population group(s) affected by the intervention and the dynamics of the HIV epidemic in those population groups, and the degree of uncertainty that exists regarding the effects of the intervention and dynamics of the epidemic. Like other types of policy models, an AIDS policy model must strike the proper balance between simplicity and tractability versus realism [208].

Sometimes comprehensive, detailed analysis is not necessary to assess the likely worth of an intervention. In that case, a very simple policy model can be developed. Such models can be constructed (and used) quickly, have modest data requirements, and are easy for policy makers to understand [21,23]. For example, Owens and Nease [165] developed a simple decision-analytic model to estimate the occupational risk of HIV infection among health care workers. They found that the HIV transmission risk was comparable to other risks that health care workers have faced knowingly and have accepted in the recent past. However, the loss of quality-adjusted life expectancy associated with a needle-stick exposure was significant. Postma et al. [182] assessed the cost effectiveness of universal, voluntary HIV screening of pregnant women in England. Using a simple staged-progression disease model, they showed that such screening would be cost effective in the London area, and could be cost effective in other areas of England depending on local HIV prevalence and screening costs.

Sometimes models are needed that can capture dynamic epidemic effects, complex dependencies between population groups and interventions, and intervention effects over

a long time horizon [23]. Much effort has gone into developing mathematical and statistical models of the spread of HIV [6,7,100,145,201]. Many of these are complex models aimed at predicting the natural history of the epidemic. Such models can be used, either as is or in a simplified form, as part of an AIDS policy model [123]. For example, Wein et al. [219] developed a dynamic optimization model to determine the best multi-drug therapy for an individual over time. This model considers multiple virus strains, mutations from one strain to another, and different efficacies for each drug against each virus strain, thus allowing analysis of complex drug–virus interactions.

To capture dynamic effects, compartmental epidemic models are often used as part of an AIDS policy model (e.g., [24,27,53,120,184]). These models can be set up to distinguish only broad population groups (e.g., [120]) or to distinguish population subgroups such as core transmitter groups (e.g., [18]). An alternative approach, network-based modeling, examines disease transmission through social networks by considering how individuals form and break social connections within a network [125,150]. A network-based model may be appropriate when HIV transmission is strongly influenced by social networks among individuals targeted by an intervention. For example, studies in a number of cities in the United States have identified large social networks of IDUs [46,66,91,157,158,209]. Network-based models may be more realistic than compartmental epidemic models, but they require significantly more data about individual behavior and the likelihood of HIV transmission from a risky encounter.

In cases when the effects of an intervention, dynamic effects, or other factors are highly uncertain, the development of a stochastic AIDS policy model may be desirable. For example, in their model of multi-drug therapies, Wein et al. [219] included stochastic virus mutation to reflect the highly uncertain nature of HIV propagation within an individual. Blower et al. [17] coupled their model of HIV transmission in the San Francisco gay community with a sophisticated statistical approach that enabled inclusion of a high degree of uncertainty regarding the potential effects of advanced therapy, changes in risky behavior, and rate of emergence of drug resistance. Stochastic models reflect the role of uncertainty in disease spread and intervention effects, and provide confidence intervals on results, but are usually harder to analyze than the corresponding deterministic models [89]. Stochastic models are often solved using approximations [192,193] or evaluated using simulation [219]. An alternative approach, when the development of a stochastic model is not deemed feasible, is the use of sensitivity analysis to determine the effect on policy conclusions of assumptions regarding uncertain parameters. However, additional modeling uncertainties may remain. Manning et al. [138] discuss ways of dealing with uncertainties regarding parameter, modeling, model structure, and model process in policy models.

Dynamic and stochastic models often require a significant amount of data and, because of their complexity, may be

harder to understand and validate than simple models [23]. For a discussion of more sophisticated AIDS policy modeling approaches, see [21,23,86,109,184].

Selecting the appropriate time horizon for an AIDS policy model is important. The time horizon must be sufficiently long to avoid overstating a program's benefits and to avoid understating its downstream costs [178]. For example, Edwards et al. [53] examined the cost and benefits of preventive HIV vaccines using a dynamic HIV transmission model with a 20-year time horizon. A 20-year time horizon was used to account for the period of time during which the vaccine confers protection against infection. Paltiel and Kaplan [171] found that some effects last more than 20 years and contribute significantly to costs and benefits for approximately 100 years. However, the use of too long a time horizon may overestimate the lasting effect of a prevention program and may ignore the possibilities of changes in the epidemic, new treatment options, or behavior changes among the target groups [22].

2.7. Type of economic analysis

Program managers and policy makers need to understand the costs and benefits of various interventions when planning and evaluating HIV prevention and treatment programs [96]. Economic analysis can be used to assess many of the likely costs and benefits of such programs.

Economic evaluations of HIV interventions usually employ cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), or cost-utility analysis (CUA) [177]. These approaches compare the total costs of an intervention with its resulting outcomes. CBA assigns monetary values to outcomes such as a human life saved. Because making such valuations is difficult, CBA is controversial. However, CBA allows policy makers to compare projects in different government sectors such as public health (e.g., HIV prevention programs) and public education (e.g., school renovation projects) [84]. CEA and the CUA do not assign a monetary value to outcomes. CEA considers only the quantity of life (e.g., life years lived), while CUA also considers the impact of interventions on the quality of life [177]. CUA uses quality-adjusted life years as a main outcome measure.

The Panel on Cost Effectiveness in Health and Medicine recommends that CUA be used as the standard tool for economic analysis of health-related interventions, that the analysis take a societal perspective, and that costs and benefits be discounted at the same rate [77]. Phillips and Holtgrave [178] argue that if an economic analysis is from the societal perspective, external costs and benefits of the interventions can be significant. For example, analyses of methadone maintenance programs have shown that such programs not only benefit the methadone clients themselves, but also benefit society at large through reduced HIV transmission and through reduced burdens on the criminal justice and welfare systems [14,73,82,83,137,199,224,228]. Programs aimed at slowing the spread of HIV may also slow the spread of other STDs [50]. For a comprehensive discussion of CEA

and recommendations for its application in health and medicine see [77,197,204,221]. Recommendations for economic analysis particularly relevant to HIV prevention can be found in [177].

Outcomes can be classified as monetary or non-monetary [86,184]. Monetary outcomes are the direct and indirect monetary costs and benefits of the intervention [86,184]. Direct monetary costs include those directly associated with an intervention, such as the cost of the intervention itself and resulting changes in health care costs for the affected population. Indirect costs are those associated with lost or impaired ability to work or to engage in leisure activities due to morbidity and lost economic productivity due to mortality [135].

Non-monetary outcomes can be classified as biological, behavioral, or psychological [143]. Biological outcome measures include HIV and AIDS incidence and prevalence, the number of cumulative HIV and AIDS cases in a given period, the number of AIDS deaths, and the number of averted HIV infections [86,184]. Other commonly employed biological outcome measures are gains in the number of lives, life-years (LYs), disability-adjusted life-years (DALYs), and quality-adjusted life-years (QALYs) [79]. DALYs gained from the interventions are the sum of the years of life saved weighted to reflect both quality of life and the socioeconomic value of each life year [141]. Healthy-years equivalents (HYES) have been suggested as an alternative to QALYs [76]. The HYE approach uses utility functions to account for an individual's time preference for health [189].

Martin and Coyle [143] distinguish two types of behavioral outcomes: primary and complementary prevention behaviors. Primary prevention behaviors include risk behaviors among those whom an intervention targets. Complementary prevention behaviors are those indirectly related to the intervention. They include, for example, the number of people enrolled in drug treatment programs, the number of visits to family planning services, and the number of people who undergo HIV testing and counseling.

Psychological outcomes include awareness of HIV and AIDS, knowledge of HIV transmission modes, and stigmatization of persons with HIV infection and AIDS. Such outcomes can play a key role in whether the target population of a prevention program reduces risky behaviors [143].

General frameworks exist for choosing cost-effective health-care interventions. Interventions commonly accepted as cost effective in industrialized countries usually cost between \$10,000 and \$150,000 per life-year saved [160], whereas in developing countries the cost-effectiveness threshold is much lower. The choice of a cost-effectiveness threshold depends on the policy makers, the purpose of the analysis, the valuation of health, money, and risk by policy makers, and the availability of resources [161]. For recent reviews of economic evaluations of HIV interventions, see [211].

Recently, the issue of optimal allocation of resources among HIV prevention programs has been discussed [21,22, 108,115,121]. Friedrich and Brandeau [67] suggested rules

of thumb for decision makers to determine the optimal level of investment in a single HIV prevention program targeted to a single population. Other researchers have considered the problem of allocating HIV prevention resources across populations and prevention programs [108,115,121,187,227]. The optimal allocation depends on factors such as the relative size of the target groups, the initial infection prevalence and incidence in each target group, and the production functions that relate expenditures on prevention with changes in risky behavior or HIV infections averted. The model of Zaric and Brandeau [227] allows for the possibility that HIV interventions may interact with one another: for example, a television advertising campaign aimed at one target group may also lead to behavior change in other population groups. These approaches are more comprehensive than simply choosing prevention programs according to a cost-effectiveness threshold that might not lead to a good allocation of scarce resources.

3. Conclusions and directions for further research

The AIDS pandemic continues to grow, with no end in sight. Resources for preventing the spread of HIV and for treating infected individuals are limited, particularly in developing countries. Thus, it is important to make the best use of available HIV prevention and treatment resources in different geographic areas and settings. Although decisions about HIV/AIDS interventions are based on many factors, not just considerations of intervention cost and effectiveness, AIDS policy models can play an important role in the development of sound HIV/AIDS policies. This paper has discussed the types of decisions that AIDS policy models can impact. We have discussed key issues that are relevant to developing useful AIDS policy models, and we have provided an overview of the most important types of HIV/AIDS interventions, with reference to a number of policy models that have been developed to assess these interventions.

Many challenges in AIDS policy making – and thus AIDS policy modeling – remain. The importance of various HIV interventions and target groups have changed over time and will likely to continue to change in the future. At the beginning of the epidemic, decision makers focused on HIV prevention programs and HIV testing policies. Key risk groups included gay men and then later commercial sex workers and IDUs. In recent years, the HIV epidemic has increasingly spread to heterosexuals. In developing countries, the overwhelming majority of HIV cases occur among heterosexuals or their offspring. Thus, prevention programs aimed at these groups, including women of childbearing age and their children, have increasingly gained relevancy for policy makers. However, interventions targeted to gay men and IDUs continue to be important, particularly in regions of the world outside of Africa, because a number of studies have documented relapse to risky behavior after an HIV intervention, and because many heterosexuals are infected by sexual contacts with IDUs.

As better therapies have become available, decisions regarding treatment options for individuals with HIV and AIDS have become important. Advanced therapies have been shown to prolong the lives of HIV-infected individuals, but are costly and may lead to the development and transmission of drug-resistant strains of HIV. In developing countries, large-scale antiretroviral therapy is not affordable. In such countries, short regimens of antiretroviral drugs (for example, to HIV-infected pregnant women) or the administration of inexpensive antibiotics to HIV-infected individuals may be the only affordable treatment options. The development of a potential HIV vaccine, which currently appears to be the most promising way to control the HIV epidemic in developing countries, will lead to important policy decisions such as the fraction of health care budgets to spend on vaccination programs, and the selection and timing of population groups to vaccinate.

Policy modeling does not serve its purpose unless the results of such analyses are taken into consideration by decision makers. Thus, AIDS policy modelers must work to understand how modeling approaches, analyses, and presentation of findings relate to model use by those faced with important decisions [110], and must develop approaches by which the results of policy models can be incorporated into the policy making process [169].

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References

- [1] S.M. Adib, J.G. Joseph, D.G. Ostrow, M. Tal and S.A. Schwartz, Relapse in sexual behavior among homosexual men: a 2-year follow-up from the Chicago MACS/CCS, *AIDS* 5(6) (1991) 757–760.
- [2] AIDS/TB Committee of the Society for Healthcare Epidemiology of America, Management of healthcare workers infected with hepatitis B virus, hepatitis C virus, human immunodeficiency virus, or other bloodborne pathogens, *Infection Control and Hospital Epidemiology* 18(5) (1997) 349–363.
- [3] J.G. Anderson and M.M. Anderson, HIV screening and treatment of pregnant women and their newborns: a simulation-based analysis, *Simulation* 71(4) (1998) 276–284.
- [4] J.G. Anderson and M.M. Anderson, Predicting the economic impact of treatment of HIV – positive pregnant women and their newborns, in: *Proceedings of the 1998 Medical Sciences Simulation Conference*, eds. J. Anderson and M. Katzper (Society for Computer Simulation International, San Diego, CA, 1998).
- [5] J.G. Anderson, M.M. Anderson, L.L. Casebeer and R.E. Kristofco, Physician management of the care of the HIV-infected pregnant women: a simulation, in: *Proceedings of the International Conference on Health Sciences Simulation*, 2000 Western MultiConference, San Diego, California, eds. J.G. Anderson and M. Katzper (Society for Computer Simulation International, San Diego, CA, 2000).
- [6] R.M. Anderson, The role of mathematical models in the study of HIV transmission and the epidemiology of AIDS, *Journal of AIDS* 1(3) (1988) 241–256.
- [7] R.M. Anderson, Mathematical and statistical studies of the epidemiology of HIV, *AIDS* 3(6) (1989) 333–346.
- [8] Anonymous, Reducing needlesticks and blood exposure: tracking, training, technology, *Hospital Security and Safety Management* 19(11) (1999) 5–10.
- [9] M. Barry, Effect of the U.S. embargo and economic decline on health in Cuba, *Annals of Internal Medicine* 132(2) (2000) 151–154.
- [10] R. Bayer and A. Fairchild-Carrino, AIDS and the limits of control: public health orders, quarantine, and recalcitrant behavior, *American Journal of Public Health* 83(10) (1993) 1471–1476.
- [11] F. Behets, S. Bertozzi, M. Kasali, M. Kashamuka, L. Atikala, C. Brown, R.W. Ryder and T.C. Quinn, Successful use of pooled sera to determine HIV-1 seroprevalence in Zaire with development of cost-efficiency models, *AIDS* 4(8) (1990) 737–741.
- [12] M. Beichert, B. Buchholz, M. Weigel, M. Martini, R. Breitkreutz and F. Melchert, Prenatal care of a HIV-1-positive pregnancy and birth, *Zentralblatt fuer Gynaekologie* 121(11) (1999) 549–552.
- [13] M. Berer, Reducing perinatal HIV transmission in developing countries through antenatal and delivery care, and breastfeeding: supporting infant survival by supporting women's survival, *Bulletin of the World Health Organization* 77(11) (1999) 871–877.
- [14] H. Berger and M.J. Smith, Economics of methadone maintenance, *New England Journal of Medicine* 290(13) (1974) 751.
- [15] R.S. Bernstein, D.C. Sokal, S.T. Seitz, B. Auvert, J. Stover and W. Naamara, Simulating the control of a heterosexual HIV epidemic in a severely affected east African city, *Interfaces* 28(3) (1998) 101–126.
- [16] J.D. Birkmeyer, J.P. AuBuchon, B. Littenberg, G.T. O'Connor, R.F. Nease, Jr., W.C. Nugent and L.T. Goodnough, Cost-effectiveness of preoperative autologous donation in coronary artery bypass grafting, *Annals of Thoracic Surgery* 57(1) (1994) 161–168.
- [17] S.M. Blower, H.B. Gershengorn and R.M. Grant, A tale of two futures: HIV and antiretroviral therapy in San Francisco, *Science* 287(5453) (2000) 650–654.
- [18] S.M. Blower, D. Hartel, H. Dowlatabadi, R.M. Anderson and R.M. May, Drugs, sex and HIV – a mathematical model for New York City, *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences* 331(1260) (1991) 171–187.
- [19] J.T. Boerma, A.J. Nunn and J.A. Whitworth, Mortality impact of the AIDS epidemic: evidence from community studies in less developed countries, *AIDS* 12(Supplement 1) (1998) S3–S14.
- [20] E. Bos and R.A. Bulatao, The demographic-impact of AIDS in sub-Saharan Africa – short- and long-term projections, *International Journal of Forecasting* 8(3) (1992) 367–384.
- [21] M.L. Brandeau, AIDS policy modeling: a social role for operations research, *Ricerca Operativa* 27(81–82) (1998) 5–33.
- [22] M.L. Brandeau, Difficult choices, urgent needs: optimal investment in HIV prevention programs, in: *Quantitative Evaluation of HIV Prevention Programs*, eds. E.H. Kaplan and R. Brookmeyer (Yale University Press, New Haven, CT), in press.
- [23] M.L. Brandeau, H.L. Lee, D.K. Owens, C.H. Sox and R.M. Wachter, Policy analysis of human immunodeficiency virus screening and intervention: a review of modeling approaches, *AIDS and Public Policy Journal* 5(2) (1990) 119–131.
- [24] M.L. Brandeau, H.L. Lee, D.K. Owens, C.H. Sox and R.M. Wachter, A policy model of human-immunodeficiency-virus screening and intervention, *Interfaces* 21(3) (1991) 5–25.
- [25] M.L. Brandeau and D.K. Owens, When women return to risk: costs and benefits of HIV screening in the presence of relapse, in: *Modeling the AIDS Epidemic: Planning, Policy and Prediction*, eds. E. Kaplan and M.L. Brandeau (Raven Press, New York, NY, 1994).

- [26] M.L. Brandeau, D.K. Owens, C.H. Sox and R.M. Wachter, Screening women of childbearing age for human immunodeficiency virus. A cost-benefit analysis, *Archives of Internal Medicine* 152(11) (1992) 2229–2237.
- [27] M.L. Brandeau, D.K. Owens, C.H. Sox and R.M. Wachter, Screening women of childbearing age for human immunodeficiency virus – a model-based policy analysis, *Management Science* 39(1) (1993) 72–92.
- [28] R.P. Brettell, A. Wilson, S. Povey, S. Morris, R. Morgan, C.L. Leen, S. Hutchinson, S. Lewis and S. Gore, Combination therapy for HIV: the effect on inpatient activity, morbidity and mortality of a cohort of patients, *International Journal of STD and AIDS* 9(2) (1998) 80–87.
- [29] Y.J. Bryson, Perinatal HIV-1 transmission: recent advances and therapeutic interventions, *AIDS* 10(Supplement 3) (1996) S33–S42.
- [30] T. Cameron, Proposed initiatives for healthy children orphaned by AIDS, *Journal of Health and Social Policy* 11(4) (2000) 15–39.
- [31] C.A. Campbell, Prostitution, AIDS, and preventive health behavior, *Social Science and Medicine* 32(12) (1991) 1367–1378.
- [32] J.P. Caulkins, E.H. Kaplan, P. Lurie, T. O'Connor and S.H. Ahn, Can difficult-to-reuse syringes reduce the spread of HIV among injection drug users?, *Interfaces* 28(3) (1998) 23–33.
- [33] Centers for Disease Control and Prevention, Patterns of sexual behavior change among homosexual/bisexual men – selected U.S. sites, 1987–1990, *Morbidity and Mortality Weekly Report* 40(46) (1991) 792–794.
- [34] Centers for Disease Control and Prevention, Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents, *Morbidity and Mortality Weekly Report* 47(RR-5) (1998) 42–82.
- [35] Centers for Disease Control and Prevention, Guidelines for the use of antiretroviral agents in pediatric HIV infection, *Morbidity and Mortality Weekly Report* 47(RR-4) (1998) 1–44.
- [36] Centers for Disease Control and Prevention, Public health service guidelines for the management of health-care worker exposures to HIV and recommendations for postexposure prophylaxis, *Morbidity and Mortality Weekly Report* 47(RR-7) (1998) 1–34.
- [37] Centers for Disease Control and Prevention, Public health service task force recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1 transmission in the United States, *Morbidity and Mortality Weekly Report* 47(RR-2) (1998) 1–30.
- [38] Centers for Disease Control and Prevention, Achievements in Public Health, 1900–1999: control of infectious diseases, *Morbidity and Mortality Weekly Report* 48(29) (1999) 621–629.
- [39] W.E. Chavey, S.B. Cantor, R.D. Clover, J.A. Reinartz and S.J. Spann, Cost-effectiveness analysis of screening health care workers for HIV, *Journal of Family Practice* 38(3) (1994) 249–257.
- [40] K.H. Choi and T.J. Coates, Prevention of HIV infection, *AIDS* 8(10) (1994) 1371–1389.
- [41] J. Cohen, HIV transmission. AIDS researchers look to Africa for new insights, *Science* 287(5455) (2000) 942–943.
- [42] O.J. Cohen and A.S. Fauci, Transmission of drug-resistant strains of HIV-1: unfortunate, but inevitable, *Lancet* 354(9180) (1999) 697–698.
- [43] J.H. Condra, W.A. Schleif, O.M. Blahy et al., In-vivo emergence of HIV-1 variants resistant to multiple protease inhibitors, *Nature* 374 (1995) 569–571.
- [44] S. Conquy, E. Chartier, M. Zerbib, N. Thiounn, T. Flam and B. Debre, Risk of accidental contamination by the human immunodeficiency virus (HIV): review and management, *Progres en Urologie* 9(2) (1999) 330–341.
- [45] B. Crossette, Most nations fail to supply safe blood, W.H.O. finds, *New York Times*, April 7 (2000) A6.
- [46] W.W. Darrow, J.J. Potterat, R.B. Rothenberg, D.E. Woodhouse, S.Q. Muth and A.S. Klovdahl, Using knowledge of social networks to prevent human immunodeficiency virus infections: the Colorado Springs study, *Sociological Focus* 32(2) (1999) 143–158.
- [47] D. Davies, C. Carne and C. Camilleri-Ferrante, Combined antiviral treatment in HIV infection. Is it value for money?, *Public Health* 113(6) (1999) 315–317.
- [48] V. De Angelis, Planning home assistance for AIDS patients in the city of Rome, Italy, *Interfaces* 28(3) (1998) 75–83.
- [49] S.G. Deeks, M. Smith, M. Holodniy and J.O. Kahn, HIV-1 protease inhibitors. A review for clinicians, *Journal of the American Medical Association* 277(2) (1997) 145–153.
- [50] D.C. Des Jarlais and N. Padian, Strategies for universalistic and targeted HIV prevention, *Journal of AIDS and Human Retrovirology* 16(2) (1997) 127–136.
- [51] R. Detels, A. Munoz, G. McFarlane, L.A. Kingsley, J.B. Margolick, J. Giorgi, L.K. Schragr and J.P. Phair, Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration, *Journal of the American Medical Association* 280(17) (1998) 1497–1503.
- [52] R.S. Drew, C. Makufa and G. Foster, Strategies for providing care and support to children orphaned by AIDS, *AIDS Care* 10(Supplement 1) (1998) S9–S15.
- [53] D.M. Edwards, R.D. Shachter and D.K. Owens, A dynamic HIV-transmission model for evaluating the costs and benefits of vaccine programs, *Interfaces* 28(3) (1998) 144–166.
- [54] M. Egger, B. Hirschel, P. Francioli, P. Sudre, M. Wirz, M. Flepp, M. Rickenbach, R. Malinverni, P. Vernazza and M. Battegay, Impact of new antiretroviral combination therapies in HIV infected patients in Switzerland: prospective multicentre study, *British Medical Journal* 315(7117) (1997) 1194–1199.
- [55] R.S. Eisenstaedt and T.E. Getzen, Screening blood donors for human immunodeficiency virus antibody: cost-benefit analysis, *American Journal of Public Health* 78(4) (1988) 450–454.
- [56] *Encyclopedia Britannica Online* (Britannica Advanced Publishing Inc., Chicago, IL, 1994).
- [57] A.L. Fairchild and E.A. Tynan, Policies of containment: immigration in the era of AIDS, *American Journal of Public Health* 84(12) (1994) 2011–2022.
- [58] J.A. Feinleib and R.T. Michael, Reported changes in sexual behavior in response to AIDS in the United States, *Preventive Medicine* 27(3) (1998) 400–411.
- [59] K.A. Fenton and T.A. Peterman, HIV partner notification: taking a new look, *AIDS* 11(13) (1997) 1535–1546.
- [60] S. Fluss, National AIDS legislation: an overview of some global developments, in: *International Law and AIDS, International Response, Current Issues, and Future Directions*, eds. L. Gostin and L. Porter (American Bar Association, USA, 1992).
- [61] S.S. Forsythe, The affordability of antiretroviral therapy in developing countries: what policymakers need to know, *AIDS* 12(Supplement 2) (1998) S11–S18.
- [62] S. Foster and A. Buve, Benefits of HIV screening of blood transfusions in Zambia, *Lancet* 346(8969) (1995) 225–227.
- [63] M.G. Fowler, R.J. Simonds and A. Roongpisuthipong, Update on perinatal HIV transmission, *Pediatric Clinics of North America* 47(1) (2000) 21–38.
- [64] K.A. Freedberg, J.A. Scharfstein, G.R. Seage, 3rd, E. Losina, M.C. Weinstein, D.E. Craven and A.D. Paltiel, The cost-effectiveness of preventing AIDS-related opportunistic infections, *Journal of the American Medical Association* 279(2) (1998) 130–136.
- [65] S.E. Frey, HIV vaccines, *Infectious Disease Clinics of North America* 13(1) (1999) 95–112.
- [66] S.R. Friedman, A. Neaigus, B. Jose, R. Curtis, M. Goldstein, G. Ildelfonso, R.B. Rothenberg and D.C. Des Jarlais, Sociometric risk networks and risk for HIV infection, *American Journal of Public Health* 87(8) (1997) 1289–1296.
- [67] C.M. Friedrich and M.L. Brandeau, Using simulation to find optimal funding levels for HIV prevention programs with different costs and effectiveness, in: *Proceedings of the 1998 Medical Sciences Simulation Conference*, eds. J.G. Anderson and M. Katzper (Society for Computer Simulation International, San Diego, CA, 1998).
- [68] C.B. Gable, J.C. Tierce, D. Simison, D. Ward and K. Motte, Costs of HIV+/AIDS at CD4+ counts disease stages based on treatment

- protocols, *Journal of AIDS and Human Retrovirology* 12(4) (1996) 413–420.
- [69] M.H. Gail, D. Preston and S. Piantadosi, Disease prevention models of voluntary confidential screening for human immunodeficiency virus (HIV), *Statistics in Medicine* 8(1) (1989) 59–81.
- [70] H.K. Geiss, Recommendations for surgical therapy planning and interventions in patients with AIDS, *Chirurg* 69(5) (1998) 503–510.
- [71] G.A. Gellert, International migration and control of communicable diseases, *Social Science and Medicine* 37(12) (1993) 1489–1499.
- [72] G.M. Gelles, Costs and benefits of HIV-1 antibody testing of donated blood, *Journal of Policy Analysis and Management* 12(3) (1993) 512–531.
- [73] D.R. Gerstein, R.A. Johnson, H. Harwood, D. Fountain, N. Suter and K. Malloy, Evaluating recovery services: The California Drug and Alcohol Treatment Assessment (CALDATA), California Department of Alcohol and Drug Programs, Sacramento, CA (1994).
- [74] W.N. Gibbs and P. Corcoran, Blood safety in developing countries, *Vox Sanguinis* 67(4) (1994) 377–381.
- [75] N. Gilmore, A.J. Orkin, M. Duckett and S.A. Grover, International travel and AIDS, *AIDS* 3(Supplement 1) (1989) S225–S230.
- [76] M.R. Gold, D.L. Patrick, G.W. Torrance, D.G. Fryback, D.C. Hadorn, M.S. Kamlet, N. Daniels and M.C. Weinstein, Identifying and valuing outcomes, in: *Cost-Effectiveness in Health and Medicine*, eds. M.R. Gold, J.E. Siegel, L.B. Russell and M.C. Weinstein (Oxford University Press, New York, NY, 1996).
- [77] M.R. Gold, J.E. Siegel, L.B. Russell and M.C. Weinstein, *Cost-Effectiveness in Health and Medicine* (Oxford University Press, New York, NY, 1996).
- [78] K. Goldin, Long-run impacts of AIDS, *Contemporary Policy Issues* 10(1) (1992) 21–30.
- [79] J.D. Graham, P.S. Corso, J.M. Morris, M. Segui-Gomez and M.C. Weinstein, Evaluating the cost-effectiveness of clinical and public health measures, *Annual Review of Public Health* 19(1998) 125–152.
- [80] K. Hanson, AIDS: What does economics have to offer?, *Health Policy and Planning* 7(4) (1992) 315–328.
- [81] R.L. Harris, E.V. Boisubain, P.D. Salyer and D.F. Semands, Evaluation of a hospital admission HIV antibody voluntary screening program, *Infection Control and Hospital Epidemiology* 11(12) (1990) 628–634.
- [82] H.J. Harwood, R.L. Hubbard, J.J. Collins and J.V. Rachal, The costs of crime and the benefits of drug abuse treatment: a cost-benefit analysis using TOPS data, *NIDA Research Monograph* 86 (1988) 209–235.
- [83] J.J. Harwood, R.L. Hubbard, J.J. Collins and J.V. Rachal, A cost benefit analyses of drug abuse treatment, *Research in Law and Policy Studies* 3 (1995) 191–214.
- [84] K. Heidenberger, Strategic investment in preventive health care: quantitative modelling for programme selection and resource allocation, *OR-Spektrum* 18(1) (1998) 1–14.
- [85] K. Heidenberger and S. Flessa, A system dynamics model for AIDS policy support in Tanzania, *European Journal of Operational Research* 70(2) (1993) 167–176.
- [86] K. Heidenberger and M. Roth, Taxonomies in the strategic management of health technologies: the case of multiperiod compartmental HIV/AIDS policy models, *International Journal of Technology Management* 15(3/4/5) (1998) 336–358.
- [87] R. Heimer, E.H. Kaplan, K. Khoshnood, B. Jariwala and E.C. Cadman, Needle exchange decreases the prevalence of HIV-1 proviral DNA in returned syringes in New Haven, Connecticut, *American Journal of Medicine* 95(2) (1993) 214–220.
- [88] F.J. Hellinger, The lifetime cost of treating a person with HIV, *Journal of the American Medical Association* 270(4) (1993) 474–478.
- [89] H.W. Hethcote and J.W. Van Ark, *Modeling HIV transmission and AIDS in the United States* (Springer, Berlin, 1992).
- [90] H.W. Hethcote, Modeling AIDS prevention programs in a population of homosexual men, in: *Modeling the AIDS Epidemic: Planning, Policy and Prediction*, eds. E. Kaplan and M.L. Brandeau (Raven Press, New York, NY, 1994).
- [91] J.P. Hoffmann, S.S. Su and A. Pach, Changes in network characteristics and HIV risk behavior among injection drug users, *Drug and Alcohol Dependence* 46(1–2) (1997) 41–51.
- [92] R.S. Hogg, A.E. Weber, K.J. Craib, A.H. Anis, M.V. O’Shaughnessy, M.T. Schechter and J.S. Montaner, One world, one hope: the cost of providing antiretroviral therapy to all nations, *AIDS* 12(16) (1998) 2203–2209.
- [93] D.R. Holtgrave, The cost-effectiveness of the components of a comprehensive HIV prevention program, A road map of the literature, in: *Handbook of HIV Prevention Policy Analysis*, ed. D.R. Holtgrave (Plenum, New York, NY, 1998).
- [94] D.R. Holtgrave, *Handbook of HIV Prevention Policy Analysis* (Plenum, New York, NY, 1998).
- [95] D.R. Holtgrave and S.D. Pinkerton, Updates of cost of illness and quality of life estimates for use in economic evaluations of HIV prevention programs, *Journal of AIDS and Human Retrovirology* 16(1) (1997) 54–62.
- [96] D.R. Holtgrave, N.L. Qualls and J.D. Graham, Economic evaluation of HIV prevention programs, *Annual Review of Public Health* 17(1996) 467–488.
- [97] D.R. Holtgrave, R.O. Valdiserri, A.R. Gerber and A.R. Hinman, Human immunodeficiency virus counseling, testing, referral, and partner notification services. A cost-benefit analysis, *Archives of Internal Medicine* 153(10) (1993) 1225–1230.
- [98] A. Houshyar, Screening pregnant women for HIV antibody: cost-benefit analysis, *AIDS and Public Policy Journal* 6(2) (1991) 98–103.
- [99] Intergovernmental Health Policy Project, State legislatures revisit the needle exchange and prescription-for-needles controversy, *Intergovernmental AIDS Reports* 5(2) (1992) 1–5.
- [100] V. Isham, Mathematical-modeling of the transmission dynamics of HIV infection and AIDS – a review, *Journal of the Royal Statistical Society Series A, Statistics in Society* 151 (1988) 5–30.
- [101] Joint United Nations Programme on HIV/AIDS, Blood Safety and AIDS, UNAIDS point of view, World Health Organization, Geneva, Switzerland (1997).
- [102] Joint United Nations Programme on HIV/AIDS, AIDS epidemic update: December 1999, World Health Organization, Geneva, Switzerland (1999).
- [103] Joint United Nations Programme on HIV/AIDS, AIDS epidemic update: December 1999, World Health Organization, Geneva, Switzerland (2000).
- [104] Joint United Nations Programme on HIV/AIDS, Use of cotrimoxazole prophylaxis in adults and children living with HIV/AIDS in Africa, Recommendations and operational issues, World Health Organization, Geneva, Switzerland (2000).
- [105] Joint United Nations Programme on HIV/AIDS and Pennsylvania State University, Communications framework for HIV/AIDS, World Health Organization, Geneva, Switzerland (1999).
- [106] A.C. Justice and J.T. King, Jr., The case for a full cost-benefit analysis of preoperative HIV screening, *Journal of Clinical Epidemiology* 46(11) (1993) 1229–1231.
- [107] J. Kahn, Building and testing an effective HIV vaccine, *Western Journal of Medicine* 171(5–6) (1999) 363–365.
- [108] J.G. Kahn, The cost-effectiveness of HIV prevention targeting: how much more bang for the buck?, *American Journal of Public Health* 86(12) (1996) 1709–1712.
- [109] J.G. Kahn, M.L. Brandeau and J. Dunn-Mortimer, OR modeling and AIDS policy: from theory to practice, *Interfaces* 28(3) (1998) 3–22.
- [110] J.G. Kahn, J. Dunn-Mortimer and P. Franks, The use of quantitative data and modeling in HIV policy formulation, Institute for Health Policy Studies, University of California, San Francisco (1999).
- [111] J.G. Kahn, S.D. Pinkerton and A.D. Paltiel, Postexposure prophylaxis following HIV exposure, *Journal of the American Medical Association* 281(14) (1999) 1269–1270.

- [112] A. Kane, J. Lloyd, M. Zaffran, L. Simonsen and M. Kane, Transmission of hepatitis B, hepatitis C and human immunodeficiency viruses through unsafe injections in the developing world: model-based regional estimates, *Bulletin of the World Health Organization* 77(10) (1999) 801–807.
- [113] E.H. Kaplan, What are the risks of risky sex – modeling the AIDS epidemic, *Operations Research* 37(2) (1989) 198–209.
- [114] E.H. Kaplan, Economic analysis of needle exchange, *AIDS* 9(10) (1995) 1113–1119.
- [115] E.H. Kaplan, Economic evaluation and HIV prevention community planning: a policy analyst's perspective, in: *Handbook of HIV Prevention Policy Analysis*, ed. D.R. Holtgrave (Plenum, New York, NY, 1998).
- [116] E.H. Kaplan, Israel's ban on use of Ethiopians' blood: how many infectious donations were prevented?, *Lancet* 351(9109) (1998) 1127–1128.
- [117] E.H. Kaplan, Implicit valuation of a blood-exclusion decision, *Medical Decision Making* 19(2) (1999) 207–213.
- [118] E.H. Kaplan and P.R. Abramson, So what if the program ain't perfect – a mathematical model of AIDS education, *Evaluation Review* 13(2) (1989) 107–122.
- [119] E.H. Kaplan and M.L. Brandeau, AIDS policy modeling by example, *AIDS* 8(Supplement 1) (1994) S333–S340.
- [120] E.H. Kaplan and E. O'Keefe, Let the needles do the talking! Evaluating the New Haven needle exchange, *Interfaces* 23(1) (1993) 7–26.
- [121] E.H. Kaplan and H. Pollack, Allocating HIV prevention resources, *Socio-Economic Planning Sciences* 32(4) (1998) 257–263.
- [122] M. Katz and J. Gerberding, Postexposure treatment of HIV, *New England Journal of Medicine* 337(7) (1997) 501.
- [123] D.A. Kaul, Modelling AIDS reduction strategies, *International Journal of Epidemiology* 24(1) (1995) 188–197.
- [124] J.A. Kelly, Behavior changes disease prevention: MCW research shows effectiveness of HIV/AIDS risk reduction interventions, *Wisconsin Medical Journal* 99(1) (2000) 41–43, 47.
- [125] M. Kretzschmar and L.G. Wiessing, Modeling the spread of HIV in social networks of injecting drug users, *AIDS* 12(7) (1998) 801–811.
- [126] S.J. La Croix and G. Russo, A cost-benefit analysis of voluntary routine HIV-antibody testing for hospital patients, *Social Science and Medicine* 42(9) (1996) 1259–1272.
- [127] L. Lacey and M.J. Gill, Lamivudine reduces healthcare resource use when added to zidovudine-containing regimens in patients with HIV infection, *Pharmacoeconomics* 15(Supplement 1) (1999) S13–S22.
- [128] L. Lacey, J. Mauskopf, R. Lindrooth, S. Pham, M. Saag and W. Sawyer, A prospective cost-consequence analysis of adding lamivudine to zidovudine-containing antiretroviral treatment regimens for HIV infection in the US, *Pharmacoeconomics* 15(Supplement 1) (1999) S23–S37.
- [129] L. Lacey, M. Youle, P. Trueman, S. Staszewski, M. Schrappe and M. Behrens, A prospective evaluation of the cost effectiveness of adding lamivudine to zidovudine-containing antiretroviral treatment regimens in HIV infection – European perspective, *Pharmacoeconomics* 15(Supplement 1) (1999) S39–S53.
- [130] J.M. Lange, Changing therapy in HIV, *AIDS* 10(Supplement 1) (1996) S27–S30.
- [131] G.T. Lansdell, AIDS, the law and civil liberties, *Medical Journal of Australia* 154(1) (1991) 61–67.
- [132] C. Le Gales and J.P. Moatti, Cost-effectiveness of HIV screening of pregnant women in hospitals of the Paris area. The Paris-Tours study group of antenatal transmission of HIV, Group "9 maternites", *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 37(1) (1990) 25–33.
- [133] M.L. Lindegren, R.H. Byers, Jr., P. Thomas, S.F. Davis, B. Caldwell, M. Rogers, M. Gwinn, J.W. Ward and P.L. Fleming, Trends in perinatal transmission of HIV/AIDS in the United States, *Journal of the American Medical Association* 282(6) (1999) 531–538.
- [134] E. Litvak, J.E. Siegel, S.G. Pauker, M. Lallemand, H.V. Fineberg and M.C. Weinstein, Whose blood is safer? The effect of the stage of the epidemic on screening for HIV, *Medical Decision Making* 17(4) (1997) 455–463.
- [135] B.R. Luce, W.G. Manning, J.E. Siegel and J. Lipscomb, Estimating costs in cost-effectiveness analysis, in: *Cost-Effectiveness in Health and Medicine*, eds. M.R. Gold, J.E. Siegel, L.B. Russell and M.C. Weinstein (Oxford University Press, New York, NY, 1996).
- [136] P.G. Lurie and A.L. Reingold, The public health impact of needle exchange programs in the United States and abroad, *Institute for Health Policy Studies, University of California, San Francisco* (1993).
- [137] S.T. Maidlow and H. Berman, The economics of heroin treatment, *American Journal of Public Health* 62(10) (1972) 1397–1406.
- [138] W.G. Manning, D.G. Fryback and M.C. Weinstein, Reflecting uncertainty in cost-effectiveness analysis, in: *Cost-Effectiveness in Health and Medicine*, eds. M.R. Gold, J.E. Siegel, L.B. Russell and M.C. Weinstein (Oxford University Press, New York, NY, 1996).
- [139] G. Mansergh, A.C. Haddix, R.W. Steketee, P.I. Nieburg, D.J. Hu, R.J. Simonds and M. Rogers, Cost-effectiveness of short-course zidovudine to prevent perinatal HIV type 1 infection in a sub-Saharan African developing country setting, *Journal of the American Medical Association* 276(2) (1996) 139–145.
- [140] E. Marseille, J.G. Kahn, F. Mmiro, L. Guay, P. Musoke, M.G. Fowler and J.B. Jackson, Cost effectiveness of single-dose nevirapine regimen for mothers and babies to decrease vertical HIV-1 transmission in sub-Saharan Africa, *Lancet* 354(9181) (1999) 803–809.
- [141] E. Marseille, J.G. Kahn and J. Saba, Cost-effectiveness of antiviral drug therapy to reduce mother-to-child HIV transmission in sub-Saharan Africa, *AIDS* 12(8) (1998) 939–948.
- [142] E. Marseille, J.G. Kahn and J. Saba, The cost-effectiveness of female condoms to prevent pregnancy, HIV, and STD transmission in Southern Africa, *Institute for Health Policy Studies, University of California, San Francisco* (2000).
- [143] J. Martin and S. Coyle, Measurement of outcomes, in: *Evaluating AIDS Prevention Programs*, eds. S. Coyle, R. Boruch and C. Turner (National Academy Press, Washington, DC, 1991).
- [144] J.A. Mauskopf, J.E. Paul, D.S. Wichman, A.D. White and H.H. Tilson, Economic impact of treatment of HIV-positive pregnant women and their newborns with zidovudine. Implications for HIV screening, *Journal of the American Medical Association* 276(2) (1996) 132–138.
- [145] R.M. May and R.M. Anderson, The transmission dynamics of Human Immunodeficiency Virus (HIV), *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences* 321(1207) (1988) 565–607.
- [146] B.D. McCarthy, J.B. Wong, A. Munoz and F.A. Sonnenberg, Who should be screened for HIV infection? A cost-effectiveness analysis, *Archives of Internal Medicine* 153(9) (1993) 1107–1116.
- [147] N.L. McKay and K.M. Phillips, An economic evaluation of mandatory premarital testing for HIV, *Inquiry* 28(3) (1991) 236–248.
- [148] N. Meda, L. Gautier-Charpentier, R.B. Soudre, H. Dahourou, R. Ouedraogo-Traore, A. Ouangre, A. Bambara, A. Kpozehouen, H. Sanou, D. Valea, F. Ky, M. Cartoux, F. Barin and P. Van de Perre, Serological diagnosis of human immunodeficiency virus in Burkina Faso: reliable, practical strategies using less expensive commercial test kits, *Bulletin of the World Health Organization* 77(9) (1999) 731–739.
- [149] J. Misson, W. Clark and M.J. Kendall, Therapeutic advances: protease inhibitors for the treatment of HIV-1 infection, *Journal of Clinical Pharmacy and Therapeutics* 22(2) (1997) 109–117.
- [150] M. Morris and M. Kretzschmar, Concurrent partnerships and the spread of HIV, *AIDS* 11(5) (1997) 641–648.
- [151] S. Moses, F.A. Plummer, E.N. Ngugi, N.J. Nagelkerke, A.O. Anzala and J.O. Ndinya-Achola, Controlling HIV in Africa: effectiveness and cost of an intervention in a high-frequency STD transmitter core group, *AIDS* 5(4) (1991) 407–411.
- [152] Y. Mouton, S. Alfandari, M. Valette, F. Cartier, P. Dellamonica, G. Humbert, J.M. Lang, P. Massip, D. Mechali, P. Leclercq, J. Modai and H. Portier, Federation National des Centres de Lutte contre le SIDA, Impact of protease inhibitors on AIDS-defining events and

- hospitalizations in 10 French AIDS reference centres, *AIDS* 11(12) (1997) F101–F105.
- [153] O. Mueller, T. Corrah, E. Katabira, F. Plummer and D. Mabey, Antiretroviral therapy in sub-Saharan Africa, *Lancet* 351(9095) (1998) 68.
- [154] E.R. Myers, J.W. Thompson and K. Simpson, Cost-effectiveness of mandatory compared with voluntary screening for human immunodeficiency virus in pregnancy, *Obstetrics and Gynecology* 91(2) (1998) 174–181.
- [155] S. Nahmias and C.D. Feinstein, Screening strategies to inhibit the spread of AIDS, *Socio-Economic Planning Sciences* 24(4) (1990) 249–260.
- [156] M. Navarro, Studies (and politics) guided switch on needles, *New York Times*, November 12 (1991) 1.
- [157] A. Neaigus, S.R. Friedman, R. Curtis, D.C. Des Jarlais, R.T. Furst, B. Jose, P. Mota, B. Stepherson, M. Sufian, T. Ward et al., The relevance of drug injectors' social and risk networks for understanding and preventing HIV infection, *Social Science and Medicine* 38(1) (1994) 67–78.
- [158] A. Neaigus, S.R. Friedman, B. Jose, M.F. Goldstein, R. Curtis, G. Ildefonso and D.C. Des Jarlais, High-risk personal networks and syringe sharing as risk factors for HIV infection among new drug injectors, *Journal of AIDS and Human Retrovirology* 11(5) (1996) 499–509.
- [159] J. Normand, D. Vlahov and L. Moses, *Preventing HIV Transmission: The Role of Sterile Needles and Bleach* (National Academy Press, Washington, DC, 1995).
- [160] D.K. Owens, Economic evaluation of HIV screening, in: *Handbook of HIV Prevention Policy Analysis*, ed. D.R. Holtgrave (Plenum, New York, NY, 1998).
- [161] D.K. Owens, Interpretation of cost-effectiveness analyses, *Journal of General Internal Medicine* 13 (1998) 716–717.
- [162] D.K. Owens, M.L. Brandeau and C.H. Sox, Effect of relapse to high-risk behavior on the costs and benefits of a program to screen women for human immunodeficiency virus, *Interfaces* 28(3) (1998) 52–74.
- [163] D.K. Owens, D.M. Edwards and R.D. Shachter, Population effects of preventive and therapeutic HIV vaccines in early- and late-stage epidemics, *AIDS* 12(9) (1998) 1057–1066.
- [164] D.K. Owens, R.A. Harris, P.M. Scott and R.F. Nease, Jr., Screening surgeons for HIV infection. A cost-effectiveness analysis, *Annals of Internal Medicine* 122(9) (1995) 641–652.
- [165] D.K. Owens and R.F. Nease, Jr., Occupational exposure to human immunodeficiency virus and hepatitis B virus: a comparative analysis of risk, *American Journal of Medicine* 92(5) (1992) 503–512.
- [166] D.K. Owens, R.F. Nease, Jr. and R.A. Harris, Cost-effectiveness of HIV screening in acute care settings, *Archives of Internal Medicine* 156(4) (1996) 394–404.
- [167] N. Padian, L. Marquis, D.P. Francis, R.E. Anderson, G.W. Rutherford, P.M. O'Malley and W. Winkelstein, Jr., Male-to-female transmission of human immunodeficiency virus, *Journal of the American Medical Association* 258(6) (1987) 788–790.
- [168] N.S. Padian, S.C. Shiboski and N.P. Jewell, Female-to-male transmission of human immunodeficiency virus, *Journal of the American Medical Association* 266(12) (1991) 1664–1667.
- [169] A.D. Paltiel, Five minutes with the governor, *Medical Decision Making* 20(2) (2000) 239–242.
- [170] A.D. Paltiel and E.H. Kaplan, Modeling zidovudine therapy: a cost-effectiveness analysis, *Journal of AIDS* 4(8) (1991) 795–804.
- [171] A.D. Paltiel and E.H. Kaplan, The epidemiologic and economic consequences of AIDS clinical-trials, *Journal of AIDS and Human Retrovirology* 6(2) (1993) 179–190.
- [172] A.D. Paltiel, J.A. Scharfstein, G.R. Seage, 3rd, E. Losina, S.J. Goldie, M.C. Weinstein, D.E. Craven and K.A. Freedberg, A Monte Carlo simulation of advanced HIV disease: application to prevention of CMV infection, *Medical Decision Making* 18(Supplement 2) (1998) S93–S105.
- [173] D.A. Paltiel, Timing is of the essence: matching AIDS policy to the epidemic life cycle, in: *Modeling the AIDS Epidemic: Planning, Policy and Prediction*, eds. E. Kaplan and M.L. Brandeau (Raven Press, New York, NY, 1994).
- [174] E.J. Perez-Stable, Cuba's response to the HIV epidemic, *American Journal of Public Health* 81(5) (1991) 563–567.
- [175] J.C. Petricciani and J.S. Epstein, The effects of the AIDS epidemic on the safety of the nation's blood supply, *Public Health Reports* 103(3) (1988) 236–241.
- [176] P. Pezzotti, P.A. Napoli, S. Acciai, S. Boros, R. Urciuoli, V. Lazzeri and G. Rezza, Increasing survival time after AIDS in Italy: the role of new combination antiretroviral therapies. Tuscany AIDS Study Group, *AIDS* 13(2) (1999) 249–255.
- [177] K.A. Phillips, A. Haddix and D.R. Holtgrave, An overview of economic evaluation methodologies and selected issues in methods standardization, in: *Handbook of HIV Prevention Policy Analysis*, ed. D.R. Holtgrave (Plenum, New York, NY, 1998).
- [178] K.A. Phillips and D.R. Holtgrave, Using cost-effectiveness/cost-benefit analysis to allocate health resources: a level playing field for prevention?, *American Journal of Preventive Medicine* 13(1) (1997) 18–25.
- [179] K.A. Phillips, R.A. Lowe, J.G. Kahn, P. Lurie, A.L. Avins and D. Ciccarone, The cost-effectiveness of HIV testing of physicians and dentists in the United States, *Journal of the American Medical Association* 271(11) (1994) 851–858.
- [180] S.D. Pinkerton, D.R. Holtgrave and F.R. Bloom, Cost-effectiveness of post-exposure prophylaxis following sexual exposure to HIV, *AIDS* 12(9) (1998) 1067–1078.
- [181] T.C. Porco and S.M. Blower, Designing HIV vaccination policies: subtypes and cross-immunity, *Interfaces* 28(3) (1998) 167–190.
- [182] M.J. Postma, E.J. Beck, S. Mandalia, L. Sherr, M.D. Walters, H. Houweling and J.C. Jager, Universal HIV screening of pregnant women in England: cost effectiveness analysis, *British Medical Journal* 318(7199) (1999) 1656–1660.
- [183] S.D. Ramsey and M.D. Nettleman, Cost-effectiveness of prophylactic AZT following needlestick injury in health care workers, *Medical Decision Making* 12(2) (1992) 142–148.
- [184] M.S. Rauner, *Strategisches Management von Praeventivprogrammen. Ein umfassendes Entscheidungsunterstützungssystem fuer die AIDS-Epidemie* (Peter Lang, Frankfurt am Main, 1999).
- [185] M.S. Rauner, Managing the AIDS epidemic in Vienna, Austria: prevention strategies for the 21st century, in: *Information, Management and Planning of Health Services, Proceedings of the 25th Meeting of the European Working Group on Operational Research Applied to Health Services*, Valmiera, Latvia, 18–23 July 1999, ed. E. Mikitis (Health Statistics and Medical Technology Agency, Riga, Latvia, 2000).
- [186] M.S. Rauner, Using simulation to analyze the effects of prevention programs on the HIV epidemic in Vienna, Austria, in: *Proceedings of the International Conference on Health Services Simulation*, 2000 Western MultiConference, San Diego, CA), eds. J.G. Anderson and M. Katzper (Society for Computer Simulation International, San Diego, CA, 2000).
- [187] A. Richter, M.L. Brandeau and D.K. Owens, An analysis of optimal resource allocation for prevention of infection with human immunodeficiency virus (HIV) in injection drug users and non-users, *Medical Decision Making* 19(2) (1999) 167–179.
- [188] A. Richter, M.L. Brandeau and D.W. Owens, Policy analysis of preventive HIV interventions targeted to adolescents: an application of Stella, in: *Simulation in the Medical Sciences Conference: Proceedings of the 1996 Western MultiConference*, eds. J.G. Anderson and M. Katzper (Society for Computer Simulation International, San Diego, CA, 1996).
- [189] W. Ried, QALYs versus HYEes-what's right and what's wrong. A review of the controversy, *Journal of Health Economics* 17(5) (1998) 607–625.
- [190] E. Rizakou, J. Rosenhead and K. Reddington, AIDS plan: a decision support model for planning the provision of HIV/AIDS-related services, *Interfaces* 21(3) (1991) 117–129.

- [191] R.A. Roffman, R.S. Stephen, L. Curtin, J.R. Gordon, J.N. Craver, M. Stern, B. Beadnell and L. Downey, Relapse prevention as an interventive model for HIV risk reduction in gay and bisexual men, *AIDS Education and Prevention* 10(1) (1998) 1–18.
- [192] C. Rossi, Estimating the prevalence of injecting drug users on the basis of Markov models of the HIV/AIDS epidemic: applications to Italian data, *Health Care Management Science* 2(3) (1999) 173–179.
- [193] C. Rossi and G. Schinaia, The mover-stayer model for the HIV/AIDS epidemic in action, *Interfaces* 28(3) (1998) 127–143.
- [194] J.T. Rowley and R.M. Anderson, Modeling the impact and cost-effectiveness of HIV prevention efforts, *AIDS* 8(4) (1994) 539–548.
- [195] J.T. Rowley, R.M. Anderson and T.W. Ng, Reducing the spread of HIV infection in sub-Saharan Africa: some demographic and economic implications, *AIDS* 4(1) (1990) 47–56.
- [196] R.A. Royce, A. Seña, W. Cates and M.S. Cohen, Sexual transmission of HIV, *New England Journal of Medicine* 336(15) (1997) 1072–1078.
- [197] L.B. Russell, M.R. Gold, J.E. Siegel, N. Daniels and M.C. Weinstein, The role of cost-effectiveness analysis in health and medicine. Panel on Cost-Effectiveness in Health and Medicine, *Journal of the American Medical Association* 276(14) (1996) 1172–1177.
- [198] A.M. Salzberg and D. Macrae, Policies for curbing the HIV epidemic in the United-States: implications of a simulation model, *Socio-Economic Planning Sciences* 27(3) (1993) 153–169.
- [199] J.C. Scanlon, Proceedings: Cost savings/benefit analysis of drug abuse treatment, *American Journal of Drug and Alcohol Abuse* 3(1) (1976) 95–101.
- [200] J.A. Scharfstein, A.D. Paltiel and K.A. Freedberg, The cost-effectiveness of fluconazole prophylaxis against primary systemic fungal infections in AIDS patients, *Medical Decision Making* 17(4) (1997) 373–381.
- [201] S.J. Schwager, C. Castillo-Chavez and H.W. Hethcote, Statistical and mathematical approaches in HIV/AIDS modeling: a review, in: *Mathematical and Statistical Approaches to AIDS Epidemiology*, ed. C. Castillo-Chavez (Springer, Berlin, 1989).
- [202] J.S. Schwartz, B.P. Kinosian, W.P. Pierskalla and H. Lee, Strategies for screening blood for human immunodeficiency virus antibody. Use of a decision support system, *Journal of the American Medical Association* 264(13) (1990) 1704–1710.
- [203] J.E. Siegel, M.C. Weinstein and H.V. Fineberg, Bleach programs for preventing AIDS among IV drug users: modeling the impact of HIV prevalence, *American Journal of Public Health* 81(10) (1991) 1273–1279.
- [204] J.E. Siegel, M.C. Weinstein, L.B. Russell and M.R. Gold, Recommendations for reporting cost-effectiveness analyses. Panel on Cost-Effectiveness in Health and Medicine, *Journal of the American Medical Association* 276(16) (1996) 1339–1341.
- [205] L. Simonsen, A. Kane, J. Lloyd, M. Zaffran and M. Kane, Unsafe injections in the developing world and transmission of blood-borne pathogens: a review, *Bulletin of the World Health Organization* 77(10) (1999) 789–800.
- [206] D. Sontag, HIV testing for newborns debated anew, *The New York Times* (10 February 1997) A1, B8.
- [207] R. Stall, M. Ekstrand, L. Pollack, L. McKusick and T.J. Coates, Relapse from safer sex: the next challenge for AIDS prevention efforts, *Journal of AIDS* 3(12) (1990) 1181–1187.
- [208] E. Stokey and R. Zeckhauser, *A Primer for Policy Analysis* (Norton, New York, NY, 1978).
- [209] T. Suh, W. Mandell, C. Latkin and J. Kim, Social network characteristics and injecting HIV-risk behaviors among street injection drug users, *Drug and Alcohol Dependence* 47(2) (1997) 137–143.
- [210] G. Tao and G. Remafedi, Economic evaluation of an HIV prevention intervention for gay and bisexual male adolescents, *Journal of AIDS and Human Retrovirology* 17(1) (1998) 83–90.
- [211] T.O. Tengs, M.E. Adams, J.S. Pliskin, D.G. Safran, J.E. Siegel, M.C. Weinstein and J.D. Graham, Five-hundred life-saving interventions and their cost-effectiveness, *Risk Analysis* 15(3) (1995) 369–390.
- [212] United States Public Health Service and Infectious Diseases Society of America, 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus, *Morbidity and Mortality Weekly Report* 48(RR-10) (1999) 1–59, 61–56.
- [213] C.P.B. Van der Ploeg, C. Van Vliet, S.J. De Vlas, J.O. Ndinya-Achola, L. Fransen, G.J. Van Oortmarsen and J.D.F. Habbema, STDSIM: a microsimulation model for decision support in STD control, *Interfaces* 28(3) (1998) 84–100.
- [214] P.L. Vernazza, J.J. Eron, S.A. Fiscus and M.S. Cohen, Sexual transmission of HIV: infectiousness and prevention, *AIDS* 13(2) (1999) 155–166.
- [215] P.L. Vernazza, B.L. Gilliam, J. Dyer, S.A. Fiscus, J.J. Eron, A.C. Frank and M.S. Cohen, Quantification of HIV in semen: correlation with antiviral treatment and immune status, *AIDS* 11(8) (1997) 987–993.
- [216] P.L. Vernazza, L. Troiani, M.J. Flepp, R.W. Cone, J. Schock, F. Roth, K. Boggian, M.S. Cohen, S.A. Fiscus and J.J. Eron, Potent antiretroviral treatment of HIV-infection results in suppression of the seminal shedding of HIV. The Swiss HIV Cohort Study, *AIDS* 14(2) (2000) 117–121.
- [217] P. Villari, G. Fattore, J.E. Siegel, A.D. Paltiel and M.C. Weinstein, Economic evaluation of HIV testing among intravenous drug users. An analytic framework and its application to Italy, *International Journal of Technology Assessment in Health Care* 12(2) (1996) 336–357.
- [218] R. Voelker, Poor nations ravaged by AIDS need the right resources now, *Journal of the American Medical Association* 282(21) (1999) 1992–1994.
- [219] L.M. Wein, S.A. Zenios and M.A. Nowak, Dynamic multidrug therapies for HIV: a control theoretic approach, *Journal of Theoretical Biology* 185(1) (1997) 15–29.
- [220] L.S. Weinhardt, M.P. Carey, B.T. Johnson and N.L. Bickham, Effects of HIV counseling and testing on sexual risk behavior: a meta-analytic review of published research, 1985–1997, *American Journal of Public Health* 89(9) (1999) 1397–1405.
- [221] M.C. Weinstein, J.E. Siegel, M.R. Gold, M.S. Kamlet and L.B. Russell, Recommendations of the Panel on Cost-effectiveness in Health and Medicine, *Journal of the American Medical Association* 276(15) (1996) 1253–1258.
- [222] D. Wilkinson, K. Floyd and C.F. Gilks, Antiretroviral drugs as a public health intervention for pregnant HIV-infected women in rural South Africa: an issue of cost-effectiveness and capacity, *AIDS* 12(13) (1998) 1675–1682.
- [223] S. Yerly, L. Kaiser, E. Race, J.P. Bru, F. Clavel and L. Perrin, Transmission of antiretroviral-drug-resistant HIV-1 variants, *Lancet* 354(9180) (1999) 729–733.
- [224] G.S. Zaric, P.G. Barnett and M.L. Brandeau, HIV transmission and the cost effectiveness of methadone maintenance, *American Journal of Public Health* 90(7) (2000) 1100–1111.
- [225] G.S. Zaric, A.M. Bayoumi, M.L. Brandeau and D.K. Owens, The effects of protease inhibitors on the spread of HIV and the development of drug-resistant HIV strains: a simulation study, *Simulation* 71(4) (1998) 262–275.
- [226] G.S. Zaric, A.M. Bayoumi, M.L. Brandeau and D.K. Owens, The cost effectiveness of voluntary prenatal and routine newborn HIV screening in the United States, *Journal of AIDS and Human Retrovirology* 25(5) (2000) 403–416.
- [227] G.S. Zaric and M.L. Brandeau, Resource allocation for epidemic control over short time horizons, *Mathematical Biosciences* 171(1) (2000) 33–38.
- [228] G.S. Zaric, M.L. Brandeau and P.G. Barnett, Methadone maintenance and HIV prevention: a cost-effectiveness analysis, *Management Science* 46(8) (2000) 1013–1031.
- [229] G.S. Zaric, M.L. Brandeau, A.M. Bayoumi and D.K. Owens, Simulating the effects of protease inhibitors on the HIV epidemic: treatment compliance, and drug resistance, in: *Proceedings of the 1998 Medical Sciences Simulation Conference*, eds. J.G. Anderson and M.

- Katzper (Society for Computer Simulation International, San Diego, CA, 1998).
- [230] L. Zhang, B. Ramratnam, K. Tenner-Racz, Y. He, M. Vesanen, S. Lewin, A. Talal, P. Racz, A.S. Perelson, B.T. Korber, M. Markowitz and D.D. Ho, Quantifying residual HIV-1 replication in patients receiving combination antiretroviral therapy, *New England Journal of Medicine* 340(21) (1999) 1605–1613.
- [231] H. Zowall, L. Coupal, R.D. Fraser, N. Gilmore, A. Deutsch and S.A. Grover, Economic impact of HIV infection and coronary heart disease in immigrants to Canada, *Canadian Medical Association Journal* 147(8) (1992) 1163–1172.
- [232] H. Zowall, R.D. Fraser, N. Gilmore, A. Deutsch and S. Grover, HIV antibody screening among immigrants: a cost-benefit analysis, *Canadian Medical Association Journal* 143(2) (1990) 101–107.