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EDITORIAL

# Measuring the Cost Effectiveness of HIV Prevention Interventions in the US: Pitfalls and Problems

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## 1 Introduction

Each year an estimated 50,000 people are infected with HIV in the US [1], and this number has remained virtually the same for the past decade. Public health officials have struggled to reduce HIV incidence through patient education, counseling, increased condom use, and in some instances through needle exchange programs. Because the number of deaths due to HIV in the US is far below the number of newly diagnosed HIV infections the number of persons living with HIV is growing quickly and now exceeds 1.2 million. For this reason, there is considerable interest in ascertaining the impact of various types of prevention interventions for reducing the spread of HIV in the US.

In this issue of Applied Health Economics and Health Policy, Dr. Huang and colleagues from the Centers for Disease Control and Prevention (CDC) reviewed cost-effectiveness studies of four types of HIV prevention interventions in the US [2]. Each of these types of interventions is highlighted by the CDC in its most recent funding announcement to local and state health departments and 75 % of these funds are earmarked for these types of interventions.

Each of the studies examined in this review estimate the cost per unit of effect for each intervention, and the unit of effect for HIV prevention interventions is usually the number of HIV cases prevented. Yet, this is not always the case. The unit of effect may be the number of newly diagnosed HIV infections, the number of quality-adjusted life-years (QALYs) gained, or simply the number of life-years gained.

The determination of whether a specific HIV prevention intervention is cost effective is a subjective decision that depends on the context of the intervention. For example, interventions that cost US$10,000 per each life-year gained in the US may be considered to be cost effective. Whereas, the same intervention in a nation with more limited resources may not be considered cost effective.

Indeed, a well-publicized study of the impact of routine screening showing that the cost per QALY for routine screening for HIV infection in the US was about US$40,000 is below the range of common thresholds between US$50,000 to US$100,000 that are applied to many studies of prevention interventions in the US [3–5]. However, the US$40,000 cost per QALY is above the threshold level for such programs in lower-income countries.

## 2 Methodology

The article by Huang and colleagues [6, 7] examines cost-effectiveness studies of HIV prevention interventions for the four HIV prevention strategies specified in the most recent CDC announcement that funds HIV prevention interventions through cooperative agreements with state and local health departments. These are: (1) HIV testing, (2) prevention with HIV-positives and their partners, (3) condom distribution and (4) policy initiatives.

In this article, the authors explain how they identified cost-effectiveness studies of the aforementioned HIV prevention interventions using six electronic databases (PubMed, PsycINFO, EMBASE, Cochrane, CINAHL, and EconLit) from the earliest data available in each database through October 2012. In the appendix they present

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information about numerous characteristics (the specific type of intervention, whether the study is model-based or empirical or other, time frame for the intervention, perspective—eg, societal, payer/provider, not stated) of the 50 studies obtained in their search. All in all, the authors do a good job of explaining their methodology (both the electronic databases and the phrases retained in the search terms are suitable) and the appendix provides a useful guide for readers who are interested in understanding what is known about the cost effectiveness of the HIV prevention interventions.

This article is not an exhaustive review because it excludes HIV prevention interventions that are not addressed in the most recent CDC funding announcement for HIV prevention interventions. It also excludes cost-effectiveness studies of HIV prevention interventions that do not derive an estimate of the cost per HIV infection averted or the cost per QALY saved, the cost per life-year saved or the cost per new HIV diagnosis. Furthermore, it excludes studies that examine evidence about the cost effectiveness of HIV prevention interventions generated at sites outside of the US.

## 3 Treatment-Based HIV Prevention

A more comprehensive review that included treatment-based HIV prevention interventions would certainly be valuable because over the past few years several large-scale studies have appeared supporting the usefulness of these interventions and some analysts now believe that successful efforts to reduce the incidence of HIV in the US must include a treatment-based HIV prevention initiative [8–12]. A recent CDC publication states that, "Now that early ART of HIV-infected persons has been shown to be very effective at preventing secondary transmission of HIV among individuals, the current goal is to determine the extent to which ART can be used broadly and effectively to reduce the spread of HIV within a population [13]".

Specifically, evidence from several multinational randomized clinical trials has shown that antiretroviral therapy (ART) reduces the rate of HIV transmission by both lessening the infectivity of persons with HIV and by diminishing the susceptibility of persons without HIV who participate in risky behaviors such as having sex with a person with HIV disease or sharing needles with individuals with HIV disease. Indeed, optimism has grown over the past few years regarding the potential of treatment-based prevention strategies to reduce the number of new HIV infections in the US.

Nevertheless, at this time, the dissemination of evidence supporting the effectiveness of treatment-based HIV prevention interventions and the increase in the number of patients receiving ART have not led to noticeable reductions in the number of persons being diagnosed with HIV in the US. Indeed, it remains unclear whether or not the uptake of ART by infected and high-risk uninfected persons will ever result in the anticipated reductions in new HIV infections. Even so, the thinking among health-care experts has changed and many policy makers now believe that there should be greater emphasis on initiating HIV treatment as a means by which to prevent the transmission of HIV infection. Also, there are some who believe that simply stepping up the treatment of people with HIV will eventually reduce the spread [14].

## 4 HIV Cases Averted and QALYs Gained

Since this review article examines the cost effectiveness of four HIV prevention interventions designed to reduce the transmission of HIV it is reasonable to expect that each of the studies cited in this review would estimate the cost savings from averting an HIV infection. Surprisingly, this is not the case (see [2], Table 1). In particular, of the 33 studies of the cost effectiveness of HIV testing scrutinized in this review that provided estimates of the cost per QALY gained through these programs, only six reported an estimate of the average cost per HIV infection averted. This is important because there is a great deal of uncertainty about the best method of translating a reduction in the number of HIV cases into an estimate of the number of QALYs gained.

The authors state that, (page 9) "We did not attempt to assess the quality of the methods used to estimate costs or effectiveness. The diversity in methodology, assumptions, and models used to estimate the cost-effectiveness outcomes across studies and interventions makes it difficult to evaluate quality". This statement is accurate but there are methods of grouping these studies and there are methods to evaluate the rationality of the postulations motivating each of these studies. Moreover, it is important to assess the merit of particular cost-effectiveness studies of HIV prevention interventions otherwise it is difficult to make any recommendations regarding the desirability of different methods of preventing the transmission of HIV.

In particular, it would have been useful if the authors had evaluated the reasonableness of the methodologies used to estimate the number of QALYs saved by averting a single case of HIV. This is especially important for studies that were conducted a number of years ago, because estimates of the number of years gained by averting a single case of HIV have fallen as the expected lifespan of persons newly infected with HIV approaches that of persons who remain uninfected. Thus, studies conducted several years ago are likely to overstate the effectiveness of HIV

interventions because they used inflated and now out-of-date estimates for the number of years gained as a result of preventing an HIV infection.

In fact, it is now realistic to assume that averting an HIV infection has little or no effect on the expected lifespan. A recent article by researchers with the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) analyzed health-related information from 22,937 trial participants who had initiated ART between January 1, 2000 and December 31, 2007. They concluded that, "based on current patterns of ART use among participants observed from 2000 to 2007 in the NA-ACCORD, a 20-year-old individual on ART today in the US or Canada would expect to live into their early 70s, a life expectancy that approaches that of a 20-year-old person in the general population [15]".

## 5 Secondary Benefits

One subject, which is not mentioned in most cost-effectiveness studies of HIV prevention interventions, is the inclusion of secondary benefits related to the reduction in the number of HIV positive individuals in a community. Any decrease in the prevalence of HIV reduces the probability of any given individual of becoming infected and this benefit continues many years into the future. This benefit is rarely included in cost-effectiveness studies of HIV prevention interventions because, in order to quantify the value of this secondary benefit, it is necessary to postulate many behavioral characteristics of at-risk individuals and this type of personal information is generally unavailable. Nevertheless, the exclusion of this benefit may result in sizeable underestimates of the merit of prevention interventions.

## 6 Combination Interventions

Another issue of growing importance in cost-effectiveness studies of HIV prevention interventions is how to isolate the impact of a specific HIV prevention intervention in situations where the intervention under study is not the only prevention intervention. Earlier studies have assessed specific HIV interventions, but only a few studies have attempted to estimate the impact of a combination of interventions [16, 17]. Yet, many public health officials now believe that a flexible approach that entails a combination of HIV prevention interventions represents the best way to curb the transmission of HIV, and studies that evaluate the impact of a combination of HIV prevention interventions require the development of models that are capable of estimating the combined effect of multiple interventions. Unfortunately, models that are capable of estimating the impact of a combination of interventions are unlikely to be simple, separable additive models because the interventions may overlap in the mechanisms by which they are transmitted as well as in the population that they are attempting to alter.

For example, HIV screening programs increase the number of persons identified with HIV, and programs that expand access to ART increase the number of infected persons on drug therapies that help control their infection and reduce the probability that they will infect partners who are uninfected. These programs may have synergistic effects because individuals with HIV must be identified before they are placed on an appropriate antiretroviral drug regimen and the impact of both programs may reduce the likelihood of secondary transmission among partners of program recipients. Thus, the total effect of these two interventions may be greater than the sum of their individual effects.

The absence of randomized clinical trials that address several interventions simultaneously makes it even more challenging to accurately predict how people will react to multiple interventions of the same or different type. Indeed, it is difficult to predict how people will react to the provision of a specific prevention intervention, much less how people will react to the provision of two or three prevention interventions. This is especially true for HIV prevention interventions that are designed to influence the behavior of people regarding the manner in which they deal with their sexual partners. In most studies it is not possible to acquire information about the response that people assert they will follow, much less gather information about how they actually do respond to attempts to alter their habits, attitudes, and behavior.

## 7 Discounting

Another important issue of continued interest in the cost effectiveness of studies of HIV prevention interventions is the discounting of future health benefits. Although most studies discount health benefits at the same rate as costs, this is only appropriate if the value of health does not increase over time. If the value of health increases over time then the rate at which health benefits is discounted should be less than the rate at which costs are be discounted. Gravelle and Smith [18] state that, "If health effects are measured in quantities (eg, QALYs) as in cost-effectiveness analysis (CEA) and the value of health effects is increasing over time, discounting the volume of health effects at a lower rate than costs is a valid method of taking account of the increase in the future value of health effects".

Data supporting the belief that people discount their future health at about the same rate that they discount the value of future consumption are lacking and this has helped fuel the methodological debate over the appropriateness of discounting health benefits in cost-effectiveness studies. Notwithstanding the dearth of empirical evidence, almost all cost-effectiveness studies of health interventions in the US discount future health benefits and costs at the rate of 3 % as recommended in a widely cited 1996 publication [12]. In the UK, the National Institute for Health and Care Excellence (NICE) provides assistance to the National Health Service and NICE recommends that cost-effectiveness studies of health technologies discount both costs and health benefits at the same rate of 3.5 % and the World Bank urges analysts to discount the number of QALYs gained in cost-effectiveness studies be discounted at 3 % per year.

There are many reasons why individuals may discount the value of future health benefits and there are numerous explanations for why individuals may discount the value of future consumption. It is generally agreed that positive time preferences for utility reduces the benefit of future income but there is less agreement regarding the importance of time preference when evaluating the benefits of future health benefits. It is clear, however, that inferring a positive rate of time preference for future consumption does not imply a positive rate of time preference for health effects. Moreover, if future health effects influence future income levels then it makes sense to discount future health benefits at a lower rate than future costs. In any case, reviews of cost-effectiveness studies of HIV prevention interventions should acknowledge the unresolved methodological issues related to the discounting of future streams of health benefits and they should explore how these issues affect the usefulness of existing studies for public health officials and policy makers.

## 8 Final Remarks

To summarize, the primary finding of this article is that, "more cost-effectiveness research is needed to fill the knowledge gaps of interventions related to prevention for HIV-positives, condom distribution, and policy initiatives, in order to help guide the most efficient use of resources". This conclusion is evident from the paucity of studies the authors were able to identify that examine the cost effectiveness of the three aforementioned HIV prevention interventions that are included in the most recent CDC funding announcement addressed in this review. The fourth HIV prevention intervention included in the most recent CDC funding announcement for state and local health departments is HIV testing and the authors found that 33 of the 50 cost-effectiveness studies of the four HIV prevention intervention types identified in their review involved HIV testing.

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