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Review article

Cost and cost-effectiveness of HIV/AIDS prevention strategies in developing countries: is there an evidence base?

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Many donors and countries are striving to respond to the HIV/AIDS epidemic by implementing prevention programmes. However, the resources available for providing these activities relative to needs are limited. Hence, decision-makers must choose among various types of interventions. Cost information, both measures of cost and cost-effectiveness, serves as a critical input into the processes of setting priorities and allocating resources efficiently. This paper reviews the cost and cost-effectiveness evidence base of HIV/AIDS prevention programmes in low- and middle-income countries (LMICs). None of the studies found have complete cost data for a full range of HIV/AIDS prevention programmes in any one country. However, the range of studies highlight the relative emphasis of different types of HIV/AIDS prevention strategies by region, reflecting the various modes of transmission and hence, to a certain extent, the stage of the epidemic. The costing methods applied and results obtained in this review give rise to questions of reliability, validity and transparency. First, not all of the studies report the methods used to calculate the costs, and/or do not provide all the necessary data inputs such that recalculation of the results is possible. Secondly, methods that are documented vary widely, rendering different studies, even within the same country and programme setting, largely incomparable. Finally, even with consistent and replicable measurement, the results as presented are generally not comparable because of the lack of a common outcome measure. Therefore, the extent to which the available cost and cost-effectiveness evidence base on HIV/AIDS prevention strategies can provide guidance to decision-makers is limited, and there is an urgent need for the generation of this knowledge for planning and decision-making.

Key words: HIV/AIDS, prevention, cost, cost-effectiveness, evidence base

Introduction

Worldwide, only heart disease, strokes and acute lower respiratory infections, typical causes of death in old age, surpass HIV/AIDS as causes of mortality.[1] Estimates suggest that at the end of 2000, there were 36 million people infected with HIV/AIDS and that 18.8 million people had already died due to HIV/AIDS.[2] Infections are concentrated in low- and middle-income countries (LMICs) and particularly in sub-Saharan Africa where 70% of infected people live, the vast majority of whom are unaware of their status. However, infection rates are rising rapidly in Asia and eastern Europe and in some parts of Latin America.[3] Given the impact of the HIV/AIDS epidemic, preventing further HIV infection is critical.

Experience over the last 20 years of the HIV epidemic has shown that there are many modes of HIV prevention. As a result strategies have been developed to control the spread of HIV and include different forms of behavioural change and communication; the promotion of male and female condoms; screening blood; voluntary counselling and testing; harm reduction strategies among drug users; and sexually transmitted disease (STD) prevention and treatment. There are also a number of promising developments, including methods to prevent mother-to-child transmission, microbicides and HIV vaccines.

A recent review on the effectiveness of HIV prevention strategies found that they can be effective in changing risk behaviour and transmission in LMICs, and if the appropriate mix of interventions is applied, this can lead to significant reductions in the prevalence of HIV at the national level.[4] However, while our understanding of some of the features of different prevention strategies is becoming increasingly refined, little information had been compiled on the relative cost and likely impact of each intervention in different settings, either individually or in combination. This is in spite of the fact that resources are scarce, so prioritization is desirable to facilitate decision-making, planning and resource allocation.[5]

Cost-effectiveness analysis provides a systematic and transparent framework for assessing the relative efficiency of

different health interventions. The scale of the HIV/AIDS problem, coupled with limited resources for prevention, makes sound resource allocation critical for LMICs.[6] Several reviews of cost-effectiveness analyses as applied to HIV/AIDS prevention strategies[7–9] have noted the paucity of data, and in particular, the dearth of studies from LMICs. Since these reviews, there has been a relatively significant increase in the number of cost-effectiveness studies published and available in the grey literature. By updating previous reviews and including grey literature, this paper ensures that current and developing debates in the literature are discussed and research results consolidated.

Methods

Several strategies were combined to find literature in the field of cost and cost-effectiveness of HIV/AIDS prevention strategies in LMICs and countries in transition during the period 1984 – February 2001. First, a Medline and HealthStar literature search was performed using the following thesaurus search terms: 'Costs & Cost Analysis' and 'Cost Benefit Analysis' (all subheadings) combined with 'HIV' and 'Acquired Immunodeficiency Syndrome' (all subheadings). Secondly, a free text search (cost*; cost* and effect*; cost* and benefit; cost* and utility; combined with STD; HIV; and AIDS) was conducted on the following databases: Medline, HealthStar, Popline, HEED, ISI Science and Social Sciences, Embase and Cab Health. These two searches were combined and then supplemented by iterative reviews of reference lists attached to papers. In addition, information was sought through correspondence with donor organizations, and centres of HIV/AIDS research and intervention in developing countries, e.g. DFID, UNAIDS and USAID. The following HIV prevention strategies were considered for this review:

- screening blood and promotion of blood safety;
- mass media campaigns;
- projects working with youth;
- social marketing of condoms;
- treatment of STDs;
- projects working with sex workers and their clients;
- harm reduction strategies among injecting drug users (IDUs);
- voluntary counselling and testing;
- prevention of mother-to-child transmission;
- microbicides and female-controlled methods;
- vaccines.

This review has taken an essentially vertical approach in the examination of HIV prevention strategies reflecting the nature of the evidence available. It is likely that undertaking a number of strategies jointly will improve effectiveness[4] and possibly reduce costs, due to economies of scope.[i] However, multi-component interventions *per se* have not been evaluated in the literature.

Where possible, the following three types of data information were documented. First, the impact of each intervention on HIV and STD transmission is presented [including both model-based and randomized controlled trials (RCT) methods to measure impact]. When such data were not available, process and outcome indicators for the intervention were compiled. Secondly, contextual information concerning the forms and scale of intervention, the subgroups reached by the intervention, the existence of complementary interventions and the epidemiological setting has been collated. Thirdly, all costs quoted in the studies were recorded. These were converted to 2000 US dollars, using the US$ annual average official exchange rates in the study year and the US consumer price index.

Results

During the years 1984–2001, 38 studies were published.[ii] The majority of studies were carried out in sub-Saharan Africa (n = 23), followed by Asia (n = 5) and Eastern Europe (n = 3), and several studies presented results for the developing world as a whole (n = 7). No papers were identified from Latin America. Nine studies provided cost data on blood screening services, three on mass media, three on youth, three on condom social marketing, four on the treatment of symptomatic STDs, four on commercial sex workers (CSWs), three on harm reduction, two on voluntary counselling and testing, ten on the reduction of mother-to-child transmission, two on female-controlled techniques and three on vaccines. The following sections provide a brief description of each type of HIV prevention intervention and the main results of these studies.

Screening blood for HIV infection

An HIV blood screening strategy aims to reduce the estimated 5–10% of HIV infections in developing countries that are transmitted through infected blood transfusions.[10] Screening blood stands out from the other strategies that will be discussed in this review. First, there is general agreement on the degree of the strategy's effectiveness. Consensus that more than 95% of HIV-negative patients transfused with HIV-infected blood will seroconvert enables calculation of the number of cases of HIV infection prevented. Calculations are, however, dependent on the reliability of the blood tests and the chance of transfusing infected blood. Secondly, the responsibility for HIV infection acquired through infected blood products lies almost entirely with health services. Preventive action therefore also lies with them (in contrast to other strategies that stress prevention through individual responsibility and altered behaviour).[11]

Several authors assessed modifications to the existing screening strategies. For example, McFarland et al.[12] compared the cost-effectiveness of three strategies to avert transfusion-associated HIV infection in Zimbabwe: HIV antibody testing; deferral of donors with HIV risk factors (using history of genital ulcer or any STD as a criterion for deferral); and deferral of donors with risk factors followed by antibody testing. The cost per HIV-infected unit of blood averted ranged from $20–121 and $41–246 per HIV infection averted. Laleman et al.[13] assessed the cost-effectiveness of a decentralized approach to HIV screening of blood donors, using an instrument-free rapid test. It was estimated that cases of HIV were prevented at a cost of $210–428 per HIV

infection averted. And Spielberg et al.[14] examined whether a testing hierarchy that utilizes either conventional enzyme-linked immunosorbent assay (ELISA) or Western blot can be reliably used for screening and confirmation of HIV infection in a high-risk population. In a retrospective analysis of 3878 specimens that were screened in Kinshasa, Zaire, the cost per HIV-infected unit averted was $51.55.

Others estimated the cost and cost-effectiveness of existing hospital-based programmes. Foster and Buvé[15] estimated the cost-effectiveness of screening transfusions for HIV for a district hospital in Zambia. In 1991, 1073 transfusions were given and an estimated 150 cases of HIV were prevented by screening at a cost of $40 per case. Jacobs and Mercer[16] estimated the cost-effectiveness of a hospital-based blood banking intervention in Tanzania. They estimated that the cost per safe blood unit produced was $15.25, and the cost per undiscounted year of life saved was $3.30–3.40. Over and Piot[17] also estimated the cost-effectiveness of blood screening in a hospital setting. Using a mathematical model, the authors developed two scenarios, and estimated that the cost per HIV infection and DALY averted would range from $9.50–70 and $0.20–321, respectively.

Two papers assessed the cost and cost-effectiveness of blood screening in Uganda. Watson-Williams and Kataaha[18] estimated the cost of the Ugandan Blood Transfusion System in 1989. Over 5000 units of blood, largely from volunteer donors, were delivered to 19 hospitals. The cost per HIV-infected unit averted was $32.86. Members of the same group[19] undertook further analyses of the Ugandan Blood Transfusion System to estimate the cost-effectiveness of blood screening. The authors estimated that the cost per HIV infection and death averted would range from $96–186 and $168–225, respectively.

The variation among results in Table 1 reflects both the type of delivery structure and nature of testing. The number of HIV infections averted also suggests that the rate of HIV prevalence in both the donor and recipient populations is central to the cost-effectiveness estimates. Given the nature of blood screening, the studies here have generally focused on the primary infections averted, and there has been little consideration of the secondary infections averted, which would improve the cost-effectiveness of the strategy.

Use of the mass media

A mass media strategy entails the development of information, education and communication (IEC) materials and their dissemination to the general population through a variety of media channels.[11] As part of a comprehensive AIDS awareness campaign, the Johannesburg City Health Department, South Africa, used messages placed on the outside of the city buses.[20] Two cross-sectional studies using telephone interviews were done 2.5 and 6 months after the campaign began; 30.2 and 31.5%, respectively, of respondents had seen the message. However, unfortunately, accurate recall of the message was generally poor. The overall cost of the campaign amounted to $25 803, equivalent to $143 per bus per month or $4.80 per day, or a cost per capita of $0.20.

A Médecins sans Frontières (Holland) project implemented a mass media campaign to raise awareness of HIV/AIDS, and promote the practice of safe sex, among young people in Moscow, Russia in 1997.[21] The campaign distributed 800 000 leaflets, broadcast a TV commercial and placed ads in magazines and newspapers, using the equivalent of $9.5 million in free advertising. An impact evaluation was carried out using a random telephone sample of 1228 persons aged 15–25 years

Table 1. Studies on blood screening

	Foster and Buvé[15]	Jacobs and Mercer[16]	Laleman et al.[13]	McFarland et al.[12]	Over and Piot[17]	Spielberg et al.[14]	Watson-Williams and Kataaha[18]	Watson-Williams et al.[19]
Country	Zambia	Tanzania	Zaire	Zimbabwe	Developing countries	Zaire	Uganda	Uganda
Type of service	Rural – hospital	Hospital			Urban – hospital	Urban hospitals (Kinshasa)	National BTS	National BTS
Donor HIV seroprevalence	15.9%	12%	5.4%	19%	<0.1%, >5%, 40%	5.5%	14.6%	5–30%
Cost per HIV-infected unit averted	–	$15.25	–	$57 $20–121 $52–84	–	$51.55	$32.86	–
Cost per HIV-infected transfusion averted	–		$210–428	–	–	–	–	–
Cost per HIV infection averted	$40		–	$116 $41–246 $107–171	$9.5–70	–	–	$96–186
Cost per life saved/death averted	–		–	–	–	–	–	$168–225
Cost per year of life saved	$1.58	$3.30–3.40	–		–	–	–	–
Cost per DALY saved	–		–	–	$0.20–321	–	–	–

old. The survey found that: 80% of the respondents had seen the campaign; 83% thought this type of information was important for a person their age; 84% thought this type of information should continue to be given; and 93% supported the introduction of sex education in schools.

Söderlund et al.[7] identified mass education campaigns from the Dominican Republic and Gabon. The campaigns were operated in the countries' largest cities. Owing to the large size of the campaigns, the small size of the countries and the high proportion of the population resident in the capital cities, the projects were regarded as nation-wide campaigns. The costs of the interventions consisted mostly of media expenditures and ranged from $0.06–0.34 per capita.

There is a clear gap in evidence related to the cost-effectiveness of mass media strategies, in part due to the limited (and generally negative) data on the effectiveness of such interventions in altering behaviour. However, one limitation of evaluating mass media campaigns is that they are also generally implemented in conjunction with other interventions.

Youth interventions

HIV/AIDS education in schools is a specialized type of IEC programme. It is normally undertaken after development of a school curriculum for HIV/AIDS education and is often incorporated into wider sex education activities. The first intervention was undertaken by the World Bank in India.[22] The authors estimated that a highly successful programme, one that achieves 50% reduction in risky behaviour, could avert approximately 3 520 000 HIV infections over 5 years at a cost of $1372 per HIV infection averted and $68.60 per DALY averted. The second, undertaken by Kumaranayake and del Amo,[23] estimated the cost of a school-based programme in Yaounde, Cameroon. The incremental cost of the project was $67 155, of which 40% was due to the development of the educational materials, 30% was due to the actual training, and 30% was for management and administration of the project. A total of 10 000 students were reached through the project, at a cost of $6.72 per capita. The third intervention, based in Hungary, involved a school-based education programme for 11–14-year-olds in Budapest and its environs.[7] It trained 140 teachers and 41 250 pupils per year at a cost of $95.40 per teacher and $1.40 per pupil-year of education, which was defined as a 1-hour lesson per class per month; these costs consisted almost entirely of teachers' salaries.

As with a mass media strategy, resources will initially be invested in the development and production of education materials targeted at school children. However, there is a paucity of data for this strategy, and what exists suggests that the cost of running these programmes is high – unfortunately a lack of information on the impact of the strategy makes it difficult to judge its value for money.

Social marketing of condoms

Condom social marketing (CSM) was initially undertaken as part of contraceptive social marketing. More recently, it has been developed as a strategy for the prevention of HIV/AIDS because of its potential to distribute large numbers of condoms and effective messages.[11] Meerding et al.[24] developed two scenarios to reflect a south-east Asian and urban east African context. They estimated that the cost per HIV infection averted would be $9.60 and $20, and cost per life year saved $0.83 and $1.22, for the Asian and African context, respectively. Over and Piot[17] developed a generic developing country model with 'favourable' (i.e. low cost, core target group and syphilis and HIV target diseases) and 'unfavourable' scenarios (i.e. high cost, non-core target group and chancroid and HIV target diseases). The cost per DALY averted for these two scenarios ranged from $0.14 to $43.22.

A recent analysis by Stallworthy and Meekers of unit costs in selected condom social marketing programmes over the period 1990–96 provides some additional data.[25] The authors found that the cumulative cost per condom sold was $0.09–0.14 in India, Pakistan, Bangladesh and Nigeria, all long-established family-planning-oriented social marketing programmes in very large markets. In the majority of countries, the cumulative cost per condom sold was between $0.19–0.37. The highest costs per condom sold (over $0.44) were observed in special circumstances: pilot programmes, programmes in their first year, countries in civil war, etc. Market size and programme maturity are important determinants of unit costs, and this has been found in social marketing of other contraceptives as well.[26]

Treatment of STDs

STDs are a major health problem in developing countries.[17] As a significant cause of morbidity, there would appear to be a strong case for the provision of STD treatment, and this case is strengthened further when the interaction between STDs and HIV is considered.[27] Unprotected sexual intercourse is a risk factor for both and there are a number of facets to the interaction between the two. HIV infection, through its effect on the immune system, can increase susceptibility to STDs and also inhibit the effectiveness of any STD treatment. In turn, STDs can facilitate transmission of HIV, particularly in infections where there is genital ulceration.[11]

Gilson et al.[28] evaluated a population-based syndromic management strategy to improve treatment services for STDs in the rural Mwanza Region, Tanzania. The authors estimated the cost per STD treated to be $2.51, per DALY averted to be $12.31 and per HIV infection averted to be $259.33. Moses et al.[29] focused on the treatment of STDs among CSWs. The major components of this programme included the diagnosis and treatment of conventional STDs, and the promotion of condom use. The authors estimated that the programme was responsible for preventing between 6000 and 10 000 new cases of HIV infection per year among clients and contacts of clients, at a cost of $10.60–15.80 per case.

Meerding et al.[24] developed two scenarios to reflect a south-east Asian and urban east African context. They estimated that the cost per HIV infection averted would be $9.60 and

$20, and cost per life year saved $0.83 and $1.22, for the Asian and African context, respectively (see Table 2).[iii] The World Bank estimated the cost-effectiveness of an STD intervention in India, which they assumed could match the Mwanza study in reducing HIV incidence by 40%.[28] It was estimated that such an intervention would cost $2.43 per DALY averted and $48.6 per HIV infection averted.

The cost-effectiveness of these studies varied according to the target groups reached. With the exception of Gilson et al.'s paper,[28] all the results were generated by models, which suggests that further applied research is required to validate these findings. In addition, little is known about what the likely costs of scaling-up such interventions might be in reality.

CSW interventions

CSWs are a high-risk group vulnerable to HIV infection because of their number of sexual partners and because they often have other STDs that enhance HIV transmission. They therefore tend to be a high frequency HIV transmitter core group for the rest of the population.[11] In India, the World Bank[22] estimated that an intervention would result in a cost per HIV infection averted and per DALY averted of $56 and $2.81, respectively. In Africa, Kumaranayake et al.[30] evaluated the cost of a CSW peer education project in Cameroon. The financial and economic costs of the project were $55 494 and $177 709, respectively, and unit costs for the activities were as follows: $1479 per trained peer health educator; $125 per education session; and $5.60 per person educated in group sessions. Using a mathematical modelling approach, the cost-effectiveness of the project was estimated to be $55 per HIV infection averted.

The existing studies illustrate the enhanced cost-effectiveness of interventions targeted to high-risk groups, although it remains a worry that the effectiveness component was modelled, based largely on untested assumptions in both papers.

Harm reduction strategies among IDUs

Experience suggests that if HIV epidemics associated with IDUs can be prevented or slowed, then the overall HIV epidemic can also be slowed down.[31] The most effective way to prevent HIV transmission among IDUs is the elimination of drug using. However, in reality programmes work towards minimizing or reducing harm.[32] This includes changing drug use, needle practices and sexual behaviours simultaneously. The HIV prevention strategies for IDUs are highly targeted.[11] Söderlund et al.[7] identified a study from Kathmandu, Nepal. This project relied on street-based outreach on foot, and the cost per client contact was $3.21. Two studies on a harm reduction strategy in Svetlogorsk, Belarus have explored the costs and cost-effectiveness of a harm reduction project working with IDUs. Walker et al.[33] found that the cost per person reached was $1.19, and the cost per disposable syringe distributed was $0.39. Using a mathematical model,[34] the cost-effectiveness of the project was estimated to be $71 per HIV infection averted.[35]

Voluntary counselling and testing

A service providing voluntary counselling and testing (VCT) involves pre-test counselling, post-test counselling and the test itself. Counselling should be part of any service that involves testing for HIV. However, the prime concern of this paper is specially organized, self-contained facilities (which may nonetheless be located within general health facilities) that the general population may visit if they wish to find out about their HIV status.[11]

With three exceptions,[22,36,37] the estimates for VCT costs have been derived from several studies focusing on the reduction of mother-to-child transmission of HIV (see section below). The cost of VCT ranged from $4.15–28.93 per person (see Table 3). However, only two studies have attempted to estimate the impact and cost-effectiveness of VCT. The first was performed by the World Bank,[22] and estimated that the cost per HIV infection and DALY averted was $206 and $10.32, respectively, in India. The second, by Sweat et al.,[37] estimated the cost-effectiveness of VCT for a hypothetical cohort of 10 000 people in Kenya and Tanzania. The cost per HIV infection averted was $264 and $367, respectively, and the cost per DALY averted was $12.77 and $17.78. Unfortunately this study's results are based on only a few sites, therefore it is unclear to what extent these findings could be replicated in practice and on a large scale. In addition, this study also used an estimate of HIV transmission that is 10 times that quoted by UNAIDS, which suggests that the authors may have over-estimated the cost-effectiveness of the intervention.

Table 2. Studies on treatment of symptomatic STDs

	Gilson et al.[28]	Moses et al.[29]	Meerding et al.[24]	Meerding et al.[24]	World Bank[22]
Country	Tanzania	Kenya	Urban East Africa	South-east Asia	India
HIV seroprevalence	4%	80%	25%	11%	–
STD prevalence	–	–	–	–	–
Intervention target	Population	CSWs	–	–	–
Cost per DALY saved	$12.31	–	–	–	$2.43
Cost per HIV infection averted	$259.33	$10.60–15.80	$20	$9.60	$48.60
Cost per life year saved	–	–	$1.22	$0.83	–

Table 3. Studies on voluntary counselling and testing

Item	Aisu et al.[36]	Lallemant et al.[47]	Marseille et al.[39]	Söderlund et al.[41]	Sweat et al.[37]	Sweat et al.[37]	Walker[45]	World Bank[22]
Country	Uganda	Developing countries	Sub-Saharan Africa	South Africa	Kenya	Tanzania	Thailand	India
HIV seroprevalence	23%	5%	15%	15%	20%	20%	1.7%	–
Cost per VCT	$21.54	$7.95	$4.15	$7.30	$26.65	$28.93	$4.40	–
Cost per DALY saved	–	–	–	–	$12.77	$17.78	–	$10.32
Cost per HIV infection averted	–	–	–	–	$264	$367	–	$206

Reduction of mother-to-child transmission

Not all women who are infected with HIV will pass it on to their new-borns; it is estimated that the mother-to-child transmission rate is 25–30%. The infant can acquire the infection *in utero*, during labour and delivery, and by breastfeeding. The focus of most of the studies identified has been confined to the evaluation of ARV therapies and formula feeding, with the exception of a paper from India that also evaluated the cost-effectiveness of caesarean section delivery and family planning, and a generic examination of strategies for developing countries that assessed ARV therapies, formula feeding, caesarean section and vitamin A supplementation (see Table 4).

Six studies from sub-Saharan Africa were identified. The potential cost-effectiveness of a short-course of AZT therapy was estimated using a decision model by Mansergh et al.[38] The cost to the health care system was estimated to be $1226 per infant HIV infection averted, and $4122 when productivity losses are included. Similarly, Marseille et al.[39] compared no intervention with three regimens of twice daily zidovudine and lamivudine. The cost per HIV infection and DALY averted ranged between $1173–5334 and $62–285, respectively. Wilkinson, Floyd and Gilks[40] also compared no intervention with three similar scenarios, and found that the cost per infection averted ranged between $2531–5896. Söderlund et al.[41] used a Markov chain model to simulate the cost-effectiveness of four formula feeding strategies, three ARV interventions, and two combined formula feeding and ARV interventions. The authors estimated that the cost per death averted and life-year gained ranged from cost saving to $2441 and cost saving to $134, respectively. In 1999, Marseille et al.[42] compared the cost-effectiveness of five short-course ARV-based strategies. The authors estimated that a universal single-dose regimen of nevirapine would result in a cost of $138 per case averted or $5.25 per DALY averted, versus $298 per case averted or $11.29 per DALY averted for targeted implementation of the same regimen. And most recently, Stringer et al.[43] assessed the cost-effectiveness of alternative strategies of nevirapine administration for early and late groups of pregnant women. The early intervention group targeted strategy resulted in an incremental cost-effectiveness of $83.70 per infection averted, compared with $714.20 for the mass therapy. The late intervention group was estimated to cost $613 per infection averted.

Two studies from Thailand were identified. Prescott[44] modelled 10 possible strategies, eight of which involved ARVs. Two focused on the prevention of mother-to-child transmission of HIV (formula feeding alone and AZT plus formula feeding), while eight targeted infected adults either before or after the onset of AIDS; the AZT regimen studied was the one used by the AIDS Clinical Trials Group (ACTG) 076. The author found that preventing perinatal transmission was 20 times more cost-effective than adult antiretroviral regimens at a cost per QALY gained of $73.4. Similarly, Walker[45] estimated the cost-effectiveness of introducing the ACTG 076 protocol and found that it was more cost-effective than the existing scenario of doing nothing.

Two studies from India evaluated the cost-effectiveness of reducing mother-to-child transmission of HIV. The first, prepared by the World Bank, calculated the cost-effectiveness of AZT and formula feed.[22] It was estimated that providing AZT alone (women continue to breastfeed) is not very cost-effective at low prevalence because most of the effect of AZT is negated by breast-milk transmission. However, AZT and formula feeding was estimated to cost $132 per DALY averted, and $96 per DALY averted if a cost per course of $25 could be obtained. The second study was undertaken to assess the cost-effectiveness of a proposed state-wide comprehensive scheme of mother-to-child prevention to be implemented in government hospitals in Kerala.[46] Interventions evaluated included the Thai AZT regime, nevirapine, caesarean section, abortion, family planning and mixes thereof. The cost-effectiveness of these alternatives ranged from $106 per DALY averted for caesarean section deliveries to $124 for the Thai short-course AZT regimen. The cost-effectiveness of a comprehensive programme including abortions, caesarean sections, the Thai AZT regimen, formula feeding and family planning was $93.

Lallemant et al.[47] examined various interventions to reduce perinatal HIV transmission in developing countries based on preliminary estimates of their effectiveness: the ACTG 076 regimen; a short-course regimen; an ultra short-course regimen; elective caesarean section; and medically supervised bottle feeding alone and combined with the preceding interventions. The authors also examined universal interventions without testing: vaginal disinfection; vitamin A; and oral zidovudine during labour. The authors found that when prevalence is 5% or less, the most cost-effective intervention

Table 4. Studies on strategies to reduce mother-to-child transmission of HIV

	Kumar[46]	Lallemant et al.[47]	Mansergh et al.[38]	Marseille et al.[42]	Marseille et al.[39]	Stringer et al.[43]	Wilkinson et al.[40]	Söderlund et al.[41]	Walker[45]	Prescott[44]	World Bank[22]
Country	– –	Developing countries	Sub-Saharan Africa	Sub-Saharan Africa	Sub-Saharan Africa	Sub-Saharan Africa	South Africa	South Africa	Thailand	Thailand	India
Pregnant women HIV seroprevalence	–	5%	12.5%	30%	15%	15%	26%	15%	1.7%	–	–
Breast-feeding rate	–	–	100%	100%	100%	–	–	95%	0%	–	–
Breast-feeding HIV transmission rate	–	10%	12%	7.4–14.8%	10.4%	–	9%	10–17%	7–22%	–	–
Perinatal HIV transmission rate	–	25%	25%	25.1%	25.5%	–	21%	26%	24%	–	–
Vertical HIV transmission rate	–	35%	37%	32.5–39.9%	35.9%	25.1%	30%	36–43%	31–46%	–	33%
Cost per HIV infection averted	– – – – – – – – –	–	$1226 (societal perspective) $4122 (healthcare perspective)	HIVNET 012 (uni): $138 HIVNET 012 (tar): $298 PETRA-A: $2781 PETRA-B: $1265 Thai: $1109	Arm A: $5334 Arm B: $2784 Arm C: $1173	$83.7–714.2	Scenario A: $5896 Scenario B: $5678 Scenario C: $2531	–	CS	–	$2568
Cost per DALY saved	$93–124 – – – – – – – –	$21–155	–	HIVNET 012 (uni): $5.25 HIVNET 012 (tar): $11.29 PETRA-A: $105.31 PETRA-B: $47.92 Thai: $41.76	Arm A: $285 Arm B: $149 Arm C: $62		–	–	–	–	$96–132
Cost per QALY gained	–	–	–		–		–	–	–	$73.4	
Cost per death averted	–	–	–		–		–	CS-$2441	–	–	
Cost per life year saved	–	–	–		–		$88.4–362.5	CS-$134	–	–	

is the short-course regimen and bottle feeding costing $21 per DALY averted, followed by the ultra short-course regimen and bottle feeding ($22/DALY) and the short-course regimen ($30/DALY). Vaginal disinfection and vitamin A supplementation was found to be inexpensive and moderately cost-effective, while Caesarean section was least cost-effective ($155/DALY). When prevalence is 10%, vaginal disinfection was the most cost-effective and cost saving. However, when prevalence is 20%, it was estimated that the ultra short-course regimen was the most cost-effective strategy and was cost saving.

There is a large variation in the results of these mother-to-child transmission studies, with results highly dependent on the choice of regimen and the prevalence of HIV. The effectiveness of the regimens was sometimes assumed before the results of clinical trials were available and/or often transferred from one setting to another (e.g. the USA to Thailand, and Thailand to Africa) with little consideration of the generalizability of the results. Indeed, given the rapid pace of research in this area, some of these studies are no longer policy relevant, as the regimens are no longer deemed appropriate in that setting, e.g. ACTG 076 in Africa and Asia. In addition, drug prices have dramatically altered since the publication of many of the studies. Another weakness of this collection of studies was that they failed to consider the effect of VCT on horizontal transmission. Finally, some studies presented their results in terms of cost savings and so comparisons were difficult to make.

Microbicides and female-controlled methods

There are a number of producers of female condoms and they are actively being marketed through social marketing programmes in several countries. There is also controversy about the role of existing spermicides in preventing STDs/HIV.[48] Currently there is development of chemical barrier methods such as vaginal microbicides to prevent HIV infections. Both product development, including clinical evaluation, and product acceptability studies are underway.[49,50] Two studies were identified which explored the costs and cost-effectiveness of female condoms in sub-Saharan Africa. Using a mathematical model, Marseille et al.[51] compared the cost-effectiveness of male condom use with a programme of female condom provision to CSWs. Assuming that female condoms were used during 12% of vaginal intercourse episodes, the authors estimated that such a programme would cost $678 per case averted. However, the inclusion of treatment costs averted suggested that such a programme would be cost saving. Homan et al.[52] estimated the cost-effectiveness of promoting female condoms among sex workers in Nairobi, and to 'high' and 'moderate' risk clinic clients. Again, using modelling techniques, the authors estimated that among CSWs, 'high' and 'moderate' risk Ministry of Health (MOH) clinic clients, the cost per HIV infection averted would be $264, $963 and $2223, respectively.

The existing evaluations of female condoms rely on the use of models to illustrate programme effectiveness, and suggest that targeting women at high risk is cost-effective. Unfortunately no studies were identified that had assessed the cost-effectiveness of microbicides.

Vaccines

Currently, vaccines for HIV are in the clinical trial stage in the USA and Thailand. There is still the issue of whether these clades of the vaccine will be appropriate in other settings, e.g. sub-Saharan Africa. In 1993, Peter Cowley[53] made a preliminary assessment of a hypothetical AIDS vaccine in Abidjan, Ivory Coast. The study was based of the following assumptions: the vaccine will have a two-dose schedule and provide life-long immunity if given under 1 year of age, although its effects will not become fully recognized until the recipient's sexual maturity. The break-even cost per dose was estimated for various combinations of HIV seroprevalence and vaccine efficacy, ranging from $320 for 5% seroprevalence and 60% vaccine efficacy, to $2908 for 30% seroprevalence and 90% efficacy.

Recently, Bishai et al.[54] developed two scenarios for the purchase of an AIDS vaccine costing $10 to produce and offering 60, 75 and 90% reductions in HIV risk for 10 years. Adopting a health care provider perspective, designed to minimize the impact of HIV/AIDS on government health spending, suggested that 766 million courses of vaccine would be purchased, while the adoption of a societal perspective indicated that over 3.7 billion courses of vaccine would be purchased. Researchers in Thailand also evaluated the potential demand for an AIDS vaccine. They identified eight groups as suitable candidates for the vaccine: direct and indirect CSWs, injecting drug users in and out of treatment, transport workers, males with STDs, conscripts and prisoners. It was estimated that the vaccine budget required for these groups of non-infected catch-up was between $1 800 000 and 17 700 000 for a one-dose regimen at $2.60–26.30 per dose, excluding the cost of delivery.[55]

Similar studies should be performed as and when the results of the ongoing clinical trials become available. Pre-sexually active adolescents are likely to be among the first groups targeted, which will mean that the cost of alternative delivery mechanisms to the routine Expanded Programme on Immunization, such as school-based programmes, will have to be assessed.

Discussion

The overall aim of this review was to identify the existing cost and cost-effectiveness evidence-base for HIV/AIDS prevention strategies, and consider its utility to national and international policy-makers. In doing so, three questions should be asked. One, what is the complete set of interventions that comprise HIV/AIDS prevention strategies? Two, what defines sufficient geographic coverage of countries or regions presenting cost data to determine whether a cost estimate is valid for general use? Three, what are the acceptable methods of costing based on available costing studies?[56]

HIV/AIDS prevention activities

This paper has presented the cost and cost-effectiveness data for those interventions for which information were available. However, information on HIV/AIDS prevention activity costs is far from comprehensive. In no instance were cost data identified for a prevention strategy sufficient to conclude that the costs of that intervention are known and generalizable to other settings. If economic, epidemiological and behavioural factors were the same everywhere there would be no need to consider the generalizability of data; we could simply apply the same findings to different settings. Unfortunately differences in these factors exist, both within and between settings (see Figure 1). Hence, there is a need to consider the degree of generalizability of findings from one setting to another.

Individual interventions serve particular needs, and the selection of specific strategies depends on various contextual factors. Because countries find themselves at different stages of the epidemic, individual interventions do not carry equal weight for policy-makers. In particular the cost and cost-effectiveness of certain interventions will vary significantly according to prevalence rates. For example, there is now growing evidence that the impact (and hence cost-effectiveness) is substantially influenced by the level of prevalence, and as the epidemic becomes more widespread in a population, the contribution of STDs to the transmission of HIV infection may become proportionately less.[57] Therefore, it is difficult to draw conclusions about the urgency of filling in missing data, except on a setting-by-setting basis.

Geographic coverage

Many countries/regions do not appear to have any cost data available to promote the more efficient employment of scarce resources, as evidenced by the fact that only 13 countries were explicitly considered in the literature reviewed and that of these, none have comprehensive cost data for a full range of HIV/AIDS prevention programmes, and only four have cost information for more than two prevention activities. Consequently, there is not enough cost information on HIV/AIDS prevention strategies to use the data in assigning national, regional or global priorities. While it may be possible to piece together standardized cost information from various settings to calculate the costs of different HIV/AIDS prevention activities, it would be important to match country settings with comparable programmes, epidemiological and economic conditions. However, more research is required in order to ascertain which key parameters must be the same for generalization of findings from one setting to another to be acceptable.

The relative emphasis on alternative types of HIV/AIDS prevention interventions varies by region, reflecting the various modes of transmission and hence to a certain extent the stage of the epidemic, from transmission among injecting drug users in eastern Europe to mother-to-child transmission in sub-Saharan Africa (Table 5). Therefore, it is important to remember that not all interventions will be appropriate in all settings. This review failed to identify any studies referring to Latin American countries. This is perhaps reflective of the nascent state of the epidemic in this region, and the focus on English-language literature.

Methodological issues

The methods applied to estimate costs in the studies reviewed give rise to questions of reliability, validity and transparency. First, studies failed to systematically report the methods used to compute costs, and/or do not provide all the necessary data inputs such that re-estimation of the results is possible (e.g. by providing menus of disaggregated resource use and cost data). A complete identification of costs was often missing from these studies; detailed information on the measurement of costs, e.g. how staff time and overheads were allocated, was omitted; the valuation of costs was at times opaque, as evidenced by the absence of a base year relevant to the value of the chosen currency or the appropriate exchange rate and

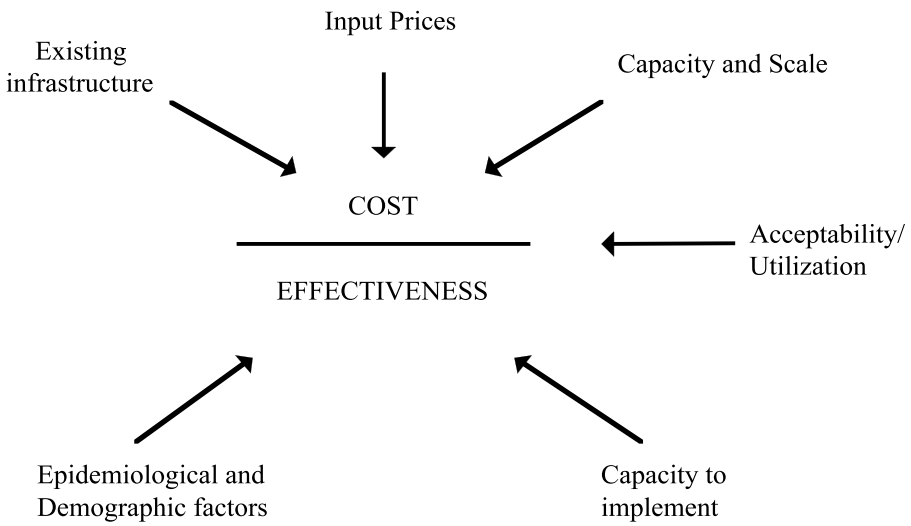

Figure 1. Key factors affecting cost-effectiveness ratios

Table 5. List of studies reviewed by country/region, author, year and strategies examined

Country	Author (reference)	Year	Strategies examined
General			
Developing countries	Bishai et al.[54]	2000	Vaccine
Developing countries	Lallemant et al.[47]	1998	Reduction of mother-to-child transmission
Developing countries	Meerding et al.[24]	1999	Social marketing of condoms Treatment of STDs
Developing countries	Over and Piot[17]	1993	Blood screening Social marketing of condoms
Developing countries	Söderlund et al.[41]	1999	Blood screening Mass media Youth interventions Injecting drug users
Developing countries	Stallworthy and Meekers[25]	1998	Social marketing of condoms
Developing countries	Watson-Williams et al.[19]	1992	Blood screening
Sub-Saharan Africa			
Cameroon	Kumaranayake et al.[30]	1998	Commercial sex workers
Cameroon	Kumaranayake and del Amo[23]	1997	Youth interventions
Ivory Coast	Cowley[53]	1993	Vaccine
Kenya	Homan et al.[52]	1999	Female condoms
Kenya	Moses et al.[29]	1991	Treatment of STDs Commercial sex workers
Kenya Tanzania	Sweat et al.[37]	2000	Voluntary counselling and testing
South Africa	Evian et al.[20]	1991	Mass media
South Africa	Marseille et al.[51]	2001	Commercial sex workers Female condom
South Africa	Söderlund et al.[41]	1999	Reduction of mother-to-child transmission
South Africa	Wilkinson et al.[40]	1998	Reduction of mother-to-child transmission
Tanzania	Gilson et al.[28]	1997	Treatment of STDs
Tanzania	Jacobs and Mercer[16]	1999	Blood screening
Uganda	Aisu et al.[36]	1995	Voluntary counselling and testing
Uganda	Watson-Williams and Kataaha[18]	1990	Blood screening
Zaire	Laleman et al.[13]	1992	Blood screening
Zaire	Spielberg et al.[14]	1990	Blood screening
Zambia	Foster and Buvé[15]	1995	Blood screening
Zimbabwe	McFarland et al.[12]	1995	Blood screening
Sub-Saharan Africa	Mansergh et al.[38]	1996	Reduction of mother-to-child transmission
Sub-Saharan Africa	Marseille et al.[39]	1998	Reduction of mother-to-child transmission
Sub-Saharan Africa	Marseille et al.[42]	1999	Reduction of mother-to-child transmission
Sub-Saharan Africa	Stringer et al.[43]	2000	Reduction of mother-to-child transmission
Asia			
India	Kumar[46]	2000	Reduction of mother-to-child transmission
India	World Bank[22]	1999	Youth interventions Treatment of STDs Commercial sex workers Voluntary counselling and testing Reduction of mother-to-child transmission
Thailand	Prescott[44]	1997	Reduction of mother-to-child transmission
Thailand	Tangcharoensathien et al.[55]	2000	Vaccine
Thailand	Walker[45]	1997	Reduction of mother-to-child transmission
Eastern Europe			
Belarus	Kumaranayake et al.[35]	2000	Injecting drug users
Belarus	Walker et al.[33]	2001	Injecting drug users
Russia	UNAIDS[21]	1999	Mass media

details concerning adjustments made for differential timing of costs; and finally a comprehensive description of the competing alternatives was rarely provided, e.g. the client or population base for which costs were estimated, age of the project, scale of the project, etc. These types of omissions make it difficult for researchers and programme managers to assess the reliability of the cost data, thereby limiting their use in perhaps their own, but certainly other, programme settings. Many of these issues may be reflective of the restrictions on space enforced by the editors of journals, although some journals are now requesting that authors deposit their spreadsheets on the journal's webpage in a bid to improve the transparency of methods. However, given that many of the reviewed studies were project reports, the omission of this

information is perhaps less acceptable. The lack of methodological rigour is also perhaps a reflection of the preliminary nature of some of the findings (of the 38 studies reviewed here, there were five project reports, five conference proceedings, two book chapters, two abstracts and one web-page article – the remaining 23 were peer-reviewed articles).

Secondly, even among those studies that document their methods, these vary widely, making different studies, even within the same country and programme setting, largely incomparable. In addition, the treatment of shared (resources which are used jointly by one or more programmes) and capital (defined as goods that last for more than 1 year) costs varies among studies. Furthermore, either due to poor practice or intent, the studies do not include a constant or exhaustive list of inputs, which may lead to underestimating the cost of an intervention, and hence an overestimation of cost-effectiveness. While some researchers are thorough in their inclusion of capital, administrative, overhead, depreciation and opportunity costs, others only performed an incremental analysis focusing on the recurrent costs that represent the cost difference to the institution, adding further to the lack of comparability between studies. Unfortunately, it is difficult to know the impact the variable methods had on estimates of cost and cost-effectiveness, and the only attempt to standardize the findings was to present all results in year 2000 prices. However, it should be noted that similar weaknesses have been documented for studies with an industrialized country focus.[8] Also, previous studies among different disease groups have illustrated inconsistencies in costing methodologies among researchers.[58–66]

However, the widely varying purposes that underlie costing exercises can explain in part the variability in methodologies used and inputs costed. For example, decision-makers may require cost information to: analyze ongoing costs of an established project to identify potential cost savings and to improve the efficiency of the service; assess the sustainability of an HIV/AIDS prevention programme and be seeking an accurate estimate of the budget necessary to maintain it; provide information on the total costs of the strategy with a view to replication; and to examine the relative cost-effectiveness of alternative ways of delivering a prevention strategy or relative to each other (e.g. compare schools education relative to peer education of CSW strategies).[67]

Finally, even with consistent identification, measurement and valuation of costs, the results as presented are generally not comparable because of the lack of a common outcome measure. This is in contrast to the family planning literature, where the couple-year of protection (CYP), despite its weakness as a measure of effectiveness, has facilitated the comparison of different contraceptive methods delivered through various mechanisms in many different settings and countries.[68–70] Only 11 of the 36 studies with cost data present cost-effectiveness results based on a final outcome indicator: deaths, HIV infections and DALYs averted, lives saved and QALYs gained. But a comparison of how DALYs were calculated illustrated that methods for estimating DALYs vary such that a DALY is not always a DALY. However, measuring the effectiveness of interventions that aim to reduce HIV transmission poses several challenges. The primary impact measure should be the number of HIV infections prevented. However, this is difficult to measure, as averting one case will also result in a chain of further infections being averted. Thus if one only considers the benefits to groups in direct contact with the intervention, the impact is likely to be underestimated. The direct measure, or 'gold-standard', for quantifying impact is an RCT. Yet an RCT is expensive and difficult to implement and so far has only been conducted in a limited number of settings. In particular, there have been only a couple of RCTs conducted in LMICs to assess interventions to prevent HIV infection.[37,55] Therefore, estimates of the potential impact of different interventions are difficult to make. Unsurprisingly the dynamic impact of averting secondary cases of HIV infection was not routinely captured in the studies reviewed here. Much of this is due to the small-scale nature of the interventions assessed, the study design (in particular a lack of RCTs), age of the projects or the short analytic horizon adopted. Therefore there has been a move towards model-based techniques, using computer models to simulate transmission dynamics of HIV infection to assess the impact of interventions.[71] While this has enabled the generation of impact measures, results should once again be interpreted with caution due to the fact that different models have different structures and assumptions, and are therefore not always comparable.

Conclusions

The current HIV/AIDS epidemic has forced governments and donors to respond by implementing prevention programmes. However, resources are scarce, ensuring that policy-makers must choose the optimal mix of strategies. Cost information can serve as a critical input into the processes of setting priorities and the efficient allocation of resources. Unfortunately, the collection of cost information is expensive, in terms of both physical and financial resources, and collecting it in a manner that will be useful beyond a local setting is challenging. Ideally, planners would have access to cost-effectiveness information comparable across the range of strategies, and for which the methods are clearly specified such that adjustments could be made for different economic, epidemiological and programme settings. Perhaps a global standard costing methodology should be sought? However, the use of such a global standard is not necessarily feasible,[56] even though comparisons between interventions are desired to improve allocative efficiency. This is because the purpose of cost and cost-effectiveness analyses differs according to local information needs and circumstances, and thus may not be designed to collect the same information.[67] In addition, there is no universally accepted outcome measure for comparing cost-effectiveness across health interventions. The advantages and disadvantages of DALYs continue to be debated by researchers,[72,73] as do other measures and valuations of health outcomes, such as QALYs and willingness-to-pay, all of which have their own practical limitations and questions of validity.[74] Nevertheless, WHO will shortly be releasing their recommendations for 'generalised cost-effectiveness analysis'[75] and it remains to be seen what impact their approach will have on the quality and comparability of future cost-effectiveness analyses.

Despite the methodological limitations of many of the studies reviewed, the results of the papers suggest that HIV/AIDS intervention strategies represent a cost-effective use of limited resources. The 1993 World Development Report[76] suggested that any intervention achieving averting a DALY at a cost of $50 or less ($62 in year 2000 prices) was highly cost-effective in the context of the developing world. Among the strategies reviewed here for which a DALY was estimated (blood screening, social marketing of condoms, the treatment of STDs, commercial sex worker interventions, voluntary counselling and testing, programmes to reduce mother-to-child-transmission), all had costs per DALY averted of less than $50. In addition, the cost-effectiveness of a youth intervention in India was estimated to be $69 per DALY averted, which still represents a relatively cost-effective use of resources. Among those that did not present the impact in terms of DALYs, harm reduction and female-controlled strategies averted an HIV infection at costs of $71 and $678, respectively, which are of a similar magnitude to those that estimated the impact in DALYs and HIV infections averted. It is not possible to comment of the relative cost-effectiveness of mass media and vaccines as only unit costs were estimated. Nevertheless, it is crucial to bear in mind the context-specificity of these findings, such that similar results may not be replicated in different settings.

To conclude, the estimates reported in this review show the extent of the cost and cost-effectiveness evidence base available in international sources; unfortunately, it is limited in scope and sometimes questionable in quality. It is possible that further cost information exists that would expand understanding in specific localities, be they programmes or countries. Therefore, efforts should be made to unearth and collate all available data. A collection of the existing cost information, specific to local epidemiological and economic conditions and health system capabilities and constraints, would inform national and regional policy-makers interested in making best use of constrained resources. In turn, donors' responsibilities are clearer when local decision-makers understand the inevitable resource allocation choices to be made. There is an urgent need for the generation of this evidence base for planning and decision-making.

Endnotes

[i] Economies of scope occur when it is possible to deliver several forms of prevention strategy jointly more cheaply than if they were implemented separately.

[ii] Some papers performed analyses of several interventions. Therefore, the presentation of results may suggest that there are more than 38 papers, which is not the case.

[iii] The results of the Meerding et al.[24] study are reported under the 'Social marketing of condoms' and 'Treatment of STDs' headings, because the authors gave equal importance to both strategies in their two scenarios and it was impossible to disaggregate the cost-effectiveness of each strategy in isolation. This should be borne in mind when making comparisons with the other studies under these headings.

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