Cost effective analysis of strategies to combat HIV/AIDS in developing countries

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The following interventions for the prevention and treatment of human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) in developing countries were examined.

Mass media: this included television and radio episodes and inserts in key newspapers, repeated every two years. Development and administration costs were included. Effectiveness was scaled by the proportion of population reporting weekly exposure to radio, television, or newspapers.

Voluntary counselling and testing (VCT): this was performed in primary care clinics for anyone requesting the services. It included the training of health workers. It was based on a rapid test, and the number of tests over a 5-year period was assumed to be twice the average annual prevalence.

Peer education for female sex workers (FSW): this consisted of the training of selected sex workers by social workers to undertake peer education. It included the provision of condoms.

Peer education and treatment of sexually transmitted infections (STIs) for FSW: in addition to the training of sex workers for peer education, referrals for the testing and possible treatment of STIs were made.

School-based education: this was targeted at youths aged 10 - 18 years. Sessions were provided during regular lessons to all students, to promote the prevention of HIV and other STIs. It included the training of selected teachers at each school.

Treatment of STIs (general population): this was provided in primary care facilities and was available to anyone who requested it. It included visits, drugs, counselling, advice on protection, and condom distribution if requested. Effectiveness was scaled by access and the likelihood of using the services.

Prevention of mother-to-child transmission (pMTCT): information on the benefits and risks of nevirapine for prophylaxis was provided to women seeking antenatal care. Pre-test counselling was offered. A single dose was provided to women who accepted, while a single dose was provided to a child delivered in a health care facility.

Highly-active antiretroviral therapy (HAART): standard HAART involved monthly visits to health care providers, while intensive monitoring involved weekly contact. Either first-line drugs alone or first- plus second-line drugs were given when required.

Type of intervention
Primary prevention and treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised two hypothetical cohorts of adult populations (aged 15 to 49 years) living in two WHO
epidemiological areas (Afr-S and Sear-D).


The Sear-D area refers to Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Maldives, Myanmar and Nepal.

**Setting**
The setting was the community. The economic study was carried out in Afr-S and Sear-D areas.

**Dates to which data relate**
Most of the effectiveness data were derived from studies published between 1989 and 2005. No dates for resource use were explicitly reported. The price year was 2000.

**Source of effectiveness data**
The effectiveness evidence was derived from a synthesis of published studies and authors' opinions.

**Modelling**
An existing model of the transmission and natural course of HIV/AIDS was used to assess the potential impact of preventive interventions. The model included underlying regional demography, acquisition of HIV and other STIs, and progression from HIV infection to AIDS and death. Heterosexual transmission occurred among five interacting risk groups. More specifically, single men, married men, female sex workers, single women and married women. The HIV disease model distinguished five states, while the STI disease model included three states. The states for the HIV disease model were uninfected, primary HIV infection, post-primary/pre-AIDS infection, untreated AIDS and treated AIDS. The states for the STI disease model were uninfected, genital ulcerative disease (GUD) and non-ulcerative disease (non-GUD). In the simulation, the interventions were implemented over the period 2000 - 2009.

**Outcomes assessed in the review**
The outcomes assessed from the literature were behavioural parameters, biological estimates, and the impact of the interventions on behaviour. HAART efficacy was only reported graphically.

**Study designs and other criteria for inclusion in the review**
A review of the literature was undertaken to identify clinical data. Most of the estimates came from epidemiological studies and surveys.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.
Number of primary studies included
Approximately 32 studies provided clinical data.

Methods of combining primary studies
When more than one source was available, a statistical approach was used to combine the primary estimates.

Investigation of differences between primary studies
Not stated.

Results of the review
In the Afr-E region, the sexually active population was 0.76 for males (proportion of all adult males) and 0.92 for females (relative proportion). The proportion married among sexually active males was 0.68. The number of partners per year was 1.09 for married males (excluding FSW partners), 633 for FSWs and 2.2 for single females. The probability that a male visits an FSW was 0.11. The number of visits to an FSW per year was 52 for a single male and 67 for a married male. The acts per partnership were 7 for a single male and 36 for a married female. The risk group transitions (annual probability) were 0.11 for FSW - single female. The FSW maximum proportion of the female population was 0.014.

In the Sear-D region, the sexually active population was 0.8 for males (proportion of all adult males) and 0.97 for females (relative proportion). The proportion married among sexually active males was 0.71. The number of partners per year was 1.05 for married males (excluding FSW partners), 941 for FSWs and 2.3 for single females. The probability a male visits an FSW was 0.14. The number of visits to an FSW per year was 42 for a single male and 48 for a married male. The acts per partnership were 24 for a married female. The risk group transitions (annual probability) were 0.01 for FSW-single female. The FSW maximum proportion of the female population was 0.021.

Mass media reduced condom non-use by 17% among singles and 14% among married.

VCT reduced condom non-use by 44% among FSWs, 24% among singles and 12% among married.

Peer counselling by FSWs reduced condom non-use by 44%, the number of partners by 11%, and the probability of men visiting FSWs by 11%.

Peer counselling and STI treatment by FSWs reduced condom non-use by 44%, non-treatment of STIs by 63%, the number of partners by 11%, and the probability of men visiting FSWs by 11%.

School-based programmes reduced condom non-use by 17% among singles, non-treatment of STIs by 18% among singles, the number of partners by 33%, and increased the age of sexual debut by 0.1.

The STI treatment reduced condom non-use by 2% among singles, and non-treatment of STIs by 63% among FSWs and 31% among singles.

The pMTCT reduced condom non-use by 24% among singles and 12% among married.

Biological parameters were also reported.

For the Afr-E and Sear-D regions, respectively:
the HIV transmission probabilities (per act) were 2.8 and 1.4 for male-female, and 0.0010 and 0.0012 for female-male;
the primary infection co-factors (primary HIV infection was assumed to last 0.2 years) were 17 and 13.3;
the GUD co-factors were 9.5 and 9.8 for male-female, and 11.1 for female-male;
the non-GUD co-factors were 4.4 and 3.8 for male-female, and 3.5 and 3.7 for female-male;

the GUD co-factor transmission probabilities (per act) were 0.20 and 0.28 for male-female, and 0.20 and 0.10 for female-male;

the non-GUD co-factor transmission probabilities (per act) were 0.16 and 0.20 for male-female, and 0.14 and 0.17 for female-male.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the model.

Estimates of effectiveness and key assumptions
In the Afr-E region, it was assumed that the number of partners per year was 1 for married females. In addition, the risk group transitions (annual probability) were 0.15 for single male-married male and 0.03 for single female-married female.

In the Sear-D region, it was assumed that the number of partners per year was 1 for married females and the acts per partnership were 9 for a single male. In addition, the risk group transitions (annual probability) were 0.16 for single male-married male and 0.16 for single female-married female.

Measure of benefits used in the economic analysis
The main summary benefit measure in the cost-utility analysis was the expected number of disability-adjusted life-years (DALYs). The number of yearly infections averted was also reported, as used in the cost-effectiveness analysis. DALYs were calculated as the sum of years lived with disability, using disability weights for HIV and AIDS from the Global Burden of Disease Study, and also as years of life lost due to premature mortality, applying standard life expectancies to the number of deaths in each age group and including a 3% discount rate and non-uniform age weights.

Direct costs
The perspective adopted in the study was unclear, although it appears to have been that of the national funding authority. The health services included in the cost analysis were:

for mass media, information leaflets, TV emissions, and radio emissions;

for VCT, rapid test, outpatient visits, and the training of health workers;

for educating FSWs, condoms, posters, information leaflets, and the training of social workers;

for school-based education, the training of teachers;

for the treatment of STIs, syphilis or chancroid HSV2, gonorrhoea or chlamydia, trichomoniasis, outpatient visits, and the training of health workers;

for pMTCT, nevirapine for the infant, nevirapine for the mother, outpatient visits, and the training of health workers;

for HAART, drugs, the training of health workers, treatment of opportunistic infections, outpatient visits, and diagnostic tests.

The unit costs were presented separately from the quantities of resources used. The unit costs came from WHO sources. The quantities were determined by demographic and epidemiological outputs from the model, combined with assumptions about coverage levels and uptake of the interventions. It was unclear whether discounting was applied, although it might have been relevant given the long timeframe of the analysis. The price year was 2000.
**Statistical analysis of costs**
The costs appear to have been treated deterministically.

**Indirect Costs**
The indirect costs were not considered in the economic evaluation.

**Currency**
International US dollars (Int$).

**Sensitivity analysis**
A sensitivity analysis was carried out to assess the robustness of the model results. Assumptions about the input costs and behavioural impacts of the interventions were varied. The model was also run using different epidemiological projections. Alternative values were derived from the literature or set by the authors.

**Estimated benefits used in the economic analysis**
In the Afr-E region, the yearly DALYs averted (in millions) were:

- 4.5 with mass media,
- 9.2 to 16.7 (depending on coverage rate) with peer education for sex workers,
- 11.6 to 20.2 (depending on coverage rate) with peer education and treatment of STIs for sex workers,
- 0.1 to 0.2 (depending on coverage rate) with school-based education,
- 5.0 with VCT,
- 4.7 with pMTCT,
- 2.3 to 7.1 (depending on treatment intensity) with the treatment of STIs, and
- 2.4 to 3.5 with HAART (depending on the type of monitoring and use of first- and second-line drugs).

The corresponding values in the Sear-D region were:

- 1.8 with mass media,
- 24.6 to 40.9 (depending on coverage rate) with peer education for sex workers,
- 29.9 to 46.6 (depending on coverage rate) with peer education and treatment of STIs for sex workers,
- 0.2 to 0.4 (depending on coverage rate) with school-based education,
- 5.2 with VCT,
- 0.9 with pMTCT,
- 5.6 to 17.7 (depending on treatment intensity) with the treatment of STIs, and
- 1.0 to 1.4 with HAART (depending on the type of monitoring and use of first- and second-line drugs).

In the Afr-E region, the yearly infections averted (in millions) were:
0.27 with mass media,
0.57 to 1.04 (depending on coverage rate) with peer education for sex workers,
0.72 to 1.26 (depending on coverage rate) with peer education and treatment of STIs for sex workers,
0.01 with school-based education,
0.31 with VCT,
0.19 with pMTCT,
0.14 to 0.45 (depending on treatment intensity) with the treatment of STIs, and
0.05 to 0.04 with HAART.

The corresponding values in the Sear-D region were:

0.11 with mass media,
1.49 to 2.49 (depending on coverage rate) with peer education for sex workers,
1.82 to 2.85 (depending on coverage rate) with peer education and treatment of STIs for sex workers,
0.01 to 0.02 with school-based education,
0.32 with VCT,
0.04 with pMTCT,
0.34 to 1.08 (depending on treatment intensity) with the treatment of STIs, and 0.03 with HAART.

**Cost results**

In the Afr-E region, the yearly costs (in millions) were:

Int$16 with mass media,
Int$40 to Int$70 (depending on coverage rate) with peer education for sex workers,
Int$42 to Int$74 (depending on coverage rate) with peer education and treatment of STIs for sex workers,
Int$58 to Int$77 (depending on coverage rate) with school-based education,
Int$406 with VCT,
Int$161 with pMTCT,
Int$43 to Int$229 (depending on treatment intensity) with the treatment of STIs, and
Int$1,350 to Int$6,945 with HAART.

The corresponding values in the Sear-D region were:

Int$33 with mass media,
Int$78 to Int$133 (depending on coverage rate) with peer education for sex workers,
Int$83 to Int$141, (depending on coverage rate) with peer education and treatment of STIs for sex workers,
Int$174 to Int$176 (depending on coverage rate) with school-based education,
Int$207 with VCT,
Int$268 with pMTCT,
Int$177 to Int$356 (depending on treatment intensity) with the treatment of STIs, and
Int$550 to Int$1774 with HAART.

**Synthesis of costs and benefits**

Average cost-effectiveness and cost-utility ratios were calculated to combine the costs and benefits of the alternative prevention or treatment strategies.

In the Afr-E region, the average cost per infection averted (averted in comparison with no intervention) was:

Int$58 with mass media,
Int$70 to Int$68 (depending on coverage rate) with peer education for sex workers,
Int$58 to Int$59 (depending on coverage rate) with peer education and treatment of STIs for sex workers,
Int$9,448 to Int$6,704 (depending on coverage rate) with school-based education,
Int$1,315 with VCT,
Int$847 with pMTCT,
Int$304 to Int$514 (depending on treatment intensity) with the treatment of STIs, and Int$28,038 to Int$185,396 with HAART.

The corresponding values in the Sear-D region were:

Int$309 with mass media,
Int$52 to Int$53 (depending on coverage rate) with peer education for sex workers,
Int$45 to Int$50 (depending on coverage rate) with peer education and treatment of STIs for sex workers,
Int$13,326 to Int$7,288 (depending on coverage rate) with school-based education,
Int$642 with VCT,
Int$7,191 with pMTCT,
Int$522 to Int$330 (depending on treatment intensity) with the treatment of STIs, and
Int$18,884 to Int$55,188 with HAART.

In the Afr-E region, the average cost per DALY averted (in comparison with no intervention) was:

Int$3 with mass media,
Int$4 with peer education for sex workers and with peer education and treatment of STIs for sex workers,
Int$530 to Int$376 (depending on coverage rate) with school-based education,
Int$82 with VCT,
Int$34 with pMTCT,
Int$19 to Int$32 (depending on treatment intensity) with the treatment of STIs, and
Int$556 to Int$1,977 with HAART.

The corresponding values in the Sear-D region were:
Int$18 with mass media,
Int$3 with peer education for sex workers,
Int$3 with peer education and treatment of STIs for sex workers,
Int$790 to Int$432 (depending on coverage rate) with school-based education,
Int$40 with VCT,
Int$310 with pMTCT,
Int$32 to Int$20 (depending on treatment intensity) with the treatment of STIs, and
Int$542 to Int$1,280 with HAART.

When combination strategies were considered, DALYs would be maximised in the Afr-E region by adding the pMTCT of HIV and the treatment of STIs in the community next, followed by VCT, antiretroviral therapy and school-based education. These interventions would be regarded as highly cost-effective on the basis of standard benchmarks.

In Sear-D, if only the maximisation of population health was considered, the treatment of STIs in the community, VCT, antiretroviral therapy (with first-line drugs) and the pMTCT should be added before adding school-based education, which would be categorised as "cost-effective" but not "highly cost-effective", or second-line antiretrovirals, which fall just beyond the threshold defining "cost-effective" interventions.

The sensitivity analysis confirmed the robustness of the base-case results. The ranges in interventions remained stable to variations in the model inputs.

Authors' conclusions
The authors concluded that "best buys" in human immunodeficiency virus (HIV) prevention included mass media campaigns, interventions focused on female sex workers (FSWs), and the treatment of other sexually transmitted infections (STIs). Highly active antiretroviral therapy (HAART) was also cost-effective in developing areas. Overall, the analysis suggested "the financial constraints to implementing such a comprehensive approach to combating HIV/AIDS should not be regarded as the principal obstacle". Rather, programmes should focus on potential constraints, such as managerial needs, political commitment, infrastructure and human resource requirements.

CRD COMMENTARY - Selection of comparators
The selection of the comparators was appropriate as a wide range of interventions was considered. However, the authors stated that some interventions that were not included in this analysis could have been effective strategies. Further, the interventions that were included were formulated in a small number of ways among the many possibilities. You should decide whether they are valid comparators in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness evidence came from a synthesis of published studies that were identified from a review of the literature. Limited information on the conduct and method of the review was provided. Most of the estimates were derived from surveys and epidemiological studies. However, the details and other characteristics of the primary studies were not described. Thus, it was difficult to assess the validity of the primary data. Some assumptions were also made. The issue of uncertainty in some key clinical data was extensively investigated in the sensitivity analysis.

Validity of estimate of measure of benefit
DALYs are a typical measure used to assess the benefits of interventions implemented in developed countries. The approach used to calculate DALYs was described in a technical appendix. Discounting was applied because of the long timeframe of the analysis. DALYs are comparable with the benefits of other health care interventions. Disease-specific benefits (i.e. cases averted) were also reported.

Validity of estimate of costs
The perspective adopted in the study was not explicitly stated. A detailed breakdown of cost items was provided, and the unit costs were presented separately from the quantities of resources used. These enhance the possibility of replicating the study in other settings. The source of the data was reported for all items. The costs were treated deterministically, but extensive sensitivity analyses were carried out. The price year was provided, which will facilitate reflation exercises in other time periods.

Other issues
The authors stated that their findings were consistent with those from clinical trials of that concluded that the treatment of STIs reduced HIV transmission. The issue of the generalisability of the study results to other settings was not explicitly addressed, although extensive sensitivity analyses were performed. The authors stated that a better understanding of sexual behaviours in different settings could strengthen the empirical link between behavioural and epidemiological models.

Implications of the study
The study results support a policy of treating STIs to reduce the clinical and economic burden of HIV and AIDS in developing countries. HAART offers good value for money, especially if drug prices keep on falling. The authors stated that more precise and reliable estimates of effectiveness are required to assess the benefits of large-scale prevention programmes.

Source of funding
Supported by the World Health Organization and the National Institute on Aging.

Bibliographic details

PubMedID
16282380

DOI
10.1136/bmj.38643.368692.68

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Africa; Asia, Southeastern; Cost-Benefit Analysis; Developing Countries; HIV Infections /economics /prevention & control; Health Education /economics; Health Personnel /economics /education; Health Promotion /economics; Healthy People Programs; Humans; Prostitution; School Health Services /economics

AccessionNumber
22005008484

Date bibliographic record published
31/03/2006

Date abstract record published
31/03/2006